ACKNOWLEDGMENT.

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A STUDY OF THE RACEMISATION RATES OF 2,2' -DISUBSTITUTED BIPHENYL DERIVATIVES

A Thesis submitted to the University of London

for the Degree of Doctor of Philosophy

by CHEUNG KING LING

September 1962

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ABSTRACT.

Experimental data have been accumulated which appears to reveal a relationship between optical stability and electron density in the region of the 1,1'-bond of sterically hindered biphenyls: an attempt has been made to isolate this factor by working with a series of 2,2'-di-iodobiphenyls in which 4,4'-substituents of varying electron donating power are introduced.

2,2'-di-iodobiphenyl and four of its 4,4'-derivatives (dicarboxy, dicarbomethoxy, diacetamido and diamino) have been obtained in their optically active states; for the first time, except for the 4,4'-dicarboxylic acid. Their rate coefficients of racemisation have been determined at several temperatures. The solvent used in all the five cases was N,N'-dimethylformamide, but in addition, racemisation has been followed in absolute ethanol and in 0.1N aqueous sodium hydroxide for 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid, and in 0.5N aqueous alcoholic hydrochloric acid for 2,2'-di-iodobenzidine. From the experimental results, the Arrhenius parameters E and $\log_{10}A$, and the transition state theory functions $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta F^{\ddagger}$ were evaluated.

In the discussion, a suggested geometry of the ground state, and of the transition state during racemisation, of 2,2'-di-iodobiphenyl are described and whenever possible, are correlated with the experimental values of the entropy and energy of activation, which determine the optical stability. The experimentally determined activation energies for the series of 2,2'-di-iodobiphenyl derivatives have been compared with theoretically calculated values, and discussed with respect to the geometry of the ground and transition states.

The experimental results show a decrease in energy of activation with increasing electron donating power of the 4,4'-substituents. This observation is discussed in terms of resonance involving the 1,1'-bond, and in terms of out-of-plane bond distortion of the 1 and 1'-carbon atoms.

The preparations of this series of 2,2'-di-iodo-biphenyl derivatives are described in the experimental sections, which also include descriptions of the syntheses of three 4,4'-derivatives of 2,2'-di-bromobiphenyl, and of the attempts to obtain these in the optically active state.

C O N T E N T S.

		Page.
PART I.	OPTICAL WORK.	
Introduction:	Historical	7
	Scope of present work	32
A brief survey of previous work on 2,2'-disubstituted biphenyl derivatives.		35
Summary of present results of optical work on some 2,2'-dibromo and 2,2'-di-iodo biphenyl derivatives.		38
Discussion:	2,2'-di-iodobiphenyl and its 4,4'-derivatives.	41
	The ground state of the molecule	42
	The transition state for racemisation	48
	The entropy of activation	50
	the energy of activation	52
Optical experimental:		74
2,2'-dibromobenzidine: attempted optical activation.		79
N,N'-tetramethyl-2,2'-dibromobenzidine attempted optical activation.		81
2,2'-dibromo-4'-[N,N'-dimethylamino]-biphenyl-4-yl-trimethyl ammonium iodide: attempted optical activation		82
Optically activated 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid		83
Optically activated Dimethyl 2,2'-di-iodo-biphenyl-4,4'-dicarboxylate		98
Optically activated 2,2'-di-iodobenzidine		104
" " 2,2'-di-iodo-4,4'-diacetamidobiphenyl		116
Optically activated 2,2'-di-iodobiphenyl		123.

Contents (contd.)

		Page
PART II.	SYNTHETIC WORK - Experimental.	130
	2,2'-dibromobenzidine	130
	N,N'-tetramethyl-2,2'-dibromobenzidine	133
	2,2'-dibromo-4'[N,N'-dimethylamino]-biphenyl-4-yl-trimethyl ammonium iodide	135
	2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid -	136
	(a) synthesis	136
	(b) synthesis and iodination of diethyl biphenyl-4,4'-dicarboxylate	147
	2,2'-di-iodobenzidine -	151
	(a) preparation by Curtius Rearrangement	151
	(b) Preparation by benzidine rearrangement.	154.

A STUDY OF THE RACEMISATION RATES OF 2,2'-DISUBSTITUTED BIPHENYL DERIVATIVES.

I N T R O D U C T I O N.

Restricted rotation and Asymmetry. Investigations designed to establish the configuration of biphenyl and its derivatives, and the structure of the latter, led to the discovery in 1926, of an entirely new field of stereochemistry, that of molecules owing their molecular dissymmetry to restricted internal rotation about a single bond.

The two benzene nuclei in biphenyl and its derivatives were considered to be coaxial and coplanar, until 1907, when Kaufler suggested that they were non-coplanar and were inclined towards each other. (Ann., 1907, 351, 151; Ber., 1907, 40, 3250). Kaufler based his view on certain condensation products of benzidine, which he considered to be structurally analogous to cyclic compounds obtained from O-diamines:-

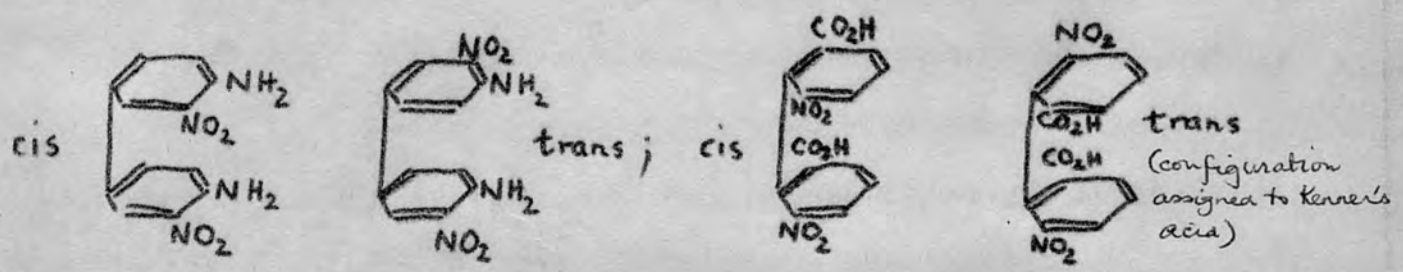
e.g.

Fig. 1.

His view was apparently confirmed by later experiments on the condensation of benzidine with benzil and glyoxal. (Cain and Micklethwait, J., 1914, 105, 1437).

The Kaufler formula for biphenyl implies that there is no rotation about the interannular bond, and cis-trans-isomerism should be possible. Thus, two isomeric dinitrobenzidines were treated as such a pair of geometrical isomers. (Cain and Micklethwait, ibid.) (Fig. 2a)

Similarly, this kind of isomerism was used by Kenner (Christie and Kenner, J., 1922, 121, 614), as an explanation for the reported existence (Schultz, Ann., 1880, 203, 95; Schmidt and Kämpf, Ber., 1903, 36, 3745) of a 6,6'-dinitrodiphenic acid, different from the one which he had synthesised. (Kenner and Stubbings, J., 1921, 119, 593).



It was pointed out that the trans-, but not the cis-isomer in each pair of these compounds possesses molecular dissymmetry, and should therefore be resolvable. (King, J., 1914, 30, 250; Christie and Kenner, loc. cit.) Kenner also

showed the possibility of geometrical isomerism in two postulated coaxial configurations of biphenyl, one planar and the other with the planes of the benzene rings maintained at an angle greater than 0° and less than 90°. (If the angles were 90°, there would be one resolvable and no cis-trans isomerism.)

Optical isomerism is impossible in the planar configuration, but in the other configuration, both cis- and trans-isomers should be resolvable. These considerations led Kenner to attempt the resolution of his 6,6'-dinitrodiphenic acid (considered to be trans) and also the resolution of 4,6,4',6'-tetranitrodiphenic acid and 4,4'-dinitrodiphenic acid in 1922. (Christie and Kenner, loc.cit.) The successful resolution of the first two acids ruled out the planar configuration, whereas lack of success in resolving the last acid was inconsistent with the other postulated coaxial configuration of biphenyl. These resolution experiments were therefore regarded as evidence in favour of the Kaufler formula.

By 1926, however, it was realised, on the ground of various pieces of chemical evidence, that there was no justification for retaining the Kaufler formula: the supposed cyclic condensation products of benzidine were shown to be non-existent (Turner, J., 1915, 107; Ferris and Turner, J., 1920, 117, 1140; Le Fevre and Turner, J., 1926, 2476); the dinitrobenzidines were shown to be structural and

not geometrical isomers (Brady and McHugh, J., 1923, 123, 2047; Le Fevre and Turner, J., 1926, 1759); and moreover, the 6,6'-dinitrodiphenic acid recorded in literature was shown to be the structurally isomeric 4,6'-dinitrodiphenic acid (Christie, Holderness and Kenner, J., 1926, 671). This conclusion was later confirmed by dielectric measurements on biphenyl derivatives. (Bretscher, Helv.Phys.Acta., 1929, 2, 257-70). The problem which remained to be solved was the molecular dissymmetry of 6,6'-dinitrodiphenic acid and other similar compounds which had been resolved. (Christie, James and Kenner, J., 1923, 1948; Christie and Kenner, J., 1923, 784). This problem was tackled in 1926 by Turner and Le Fevre (Chem. and Ind., 45, 831, 883), Bell and Kenyon (ibid, 864) and W. H. Mills (ibid, 884, 905), the three publications appearing almost simultaneously.

All three papers postulated for the optically active biphenyl derivatives, a coaxial arrangement for the two benzene nuclei, in which groups in the ortho positions would restrict or inhibit free rotation about the coaxis, preventing the molecule from becoming planar and thus causing molecular dissymmetry. The way in which these groups prevent coplanarity was considered in terms of size and electrical effects by Bell and Kenyon, and in terms of volume effects by Mills. Turner and Le Fevre account also for the recorded ready racemisation of Kenner's acids which had not been explained by

the other authors. Using Thiele's concept of "residual affinity", they considered the attraction between the "residual affinity" of the 2, and 2'-C-atoms, together with the "residual valency" across the 1,1'-bond as operative in attaining coplanarity, thus more or less balancing the effect of the O- substituents to twist the molecule from a planar configuration. Though later work showed that Kenner's acids were, in fact, optically stable, and the general "obstacle theory" of Bell, Kenyon and Mills proved sufficient, it is nevertheless interesting to note that the residual affinity picture of biphenyl

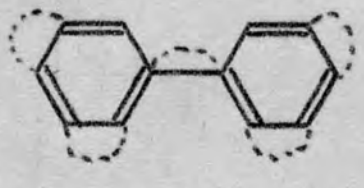


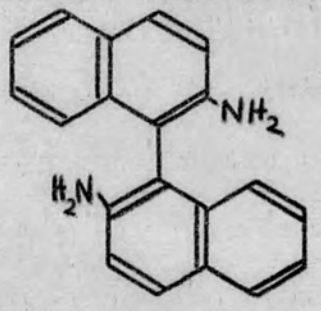
Fig. 3

can be translated into the modern counterpart involving resonance, and this is not without significance as the subject of restricted rotation about a single bond develops.

The resolution of 6,6'-dinitrodiphenic acid by Kenner in 1922 thus became the first demonstration of molecular dissymmetry arising from restricted rotation about a single bond. The general theory of restricted rotation with special emphasis on the idea of "obstacle groups" was soon tested by much experimental work, mainly by Turner and co-workers in England, and by Adams and his school in the States. Investigations in O,O'-substituted biphenyls soon broadened to include

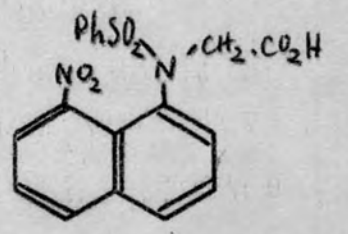
other types of molecules: 1,1'-binaphthyls were recognised as analogous to 0,0'-substituted biphenyls with 8,8'-H-atoms and 2,2'-substituents acting as obstacle groups, and many other compounds with restricted rotation in different types of structure were resolved. Some examples are given below:

(I)



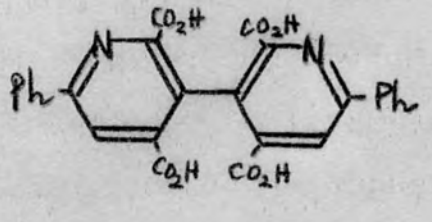
(Mascarelli, Gazz.Chim.ital., 1928, 58, 627)

(IV)



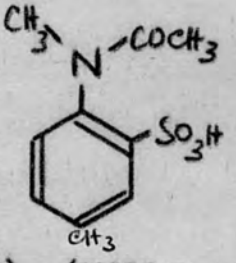
(Mills & Elliott, J., 1928, 1291.)

(II)



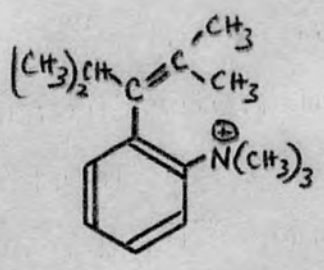
(Woodruff and Adams, J.A.C.S., 1932, 54, 1977)

(V)



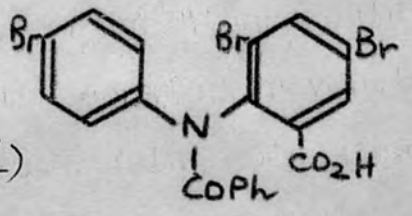
(Mills and Kelham, J., 1937, 274.)

III



(Mills, J., 1939, 460)

(VI)



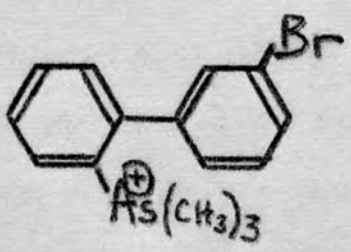
(Jamison and Turner, J., 1938 1646)

The resolution of these compounds showed the general application of the theory of restricted rotation and thus proved its validity.

The Obstacle Theory. The idea of "obstacle groups" was tested in 1927, when Meisenheimer and Höring (Ber., 60, 1425) resolved 2,2'-diamino-6,6'-dimethyl biphenyl, the molecular dissymmetry of which was predicted on the basis of molecular dimensions, deduced from X-ray measurements of solids. Similar tests were soon applied to other O,O'-substituted biphenyls: Lesslie and Turner (J., 1932, 2021) used the concept of atomic radii, while Adams' school defined the "interference value" from bond lengths, as a rough measure of optical stability (J.A.C.S., 1930, 52, 1200). Both groups of workers predicted the resolvability of 2,2'-disubstituted biphenyl in which the O-substituent was a sufficiently large group of the structure AX_3, or alternatively, a single atom of the size of bromine or iodine (Lesslie and Turner, ibid; Stanley and Adams, J.A.C.S., 1930, 52, 4471). Turner and co-workers were able to resolve compounds of the first kind where $-AX_3$ = SO_3Ph, SO_3H and $-\overset{+}{N}(CH_3)_3$ (Lesslie and Turner, J., 1932, 2021; 2394, Shaw and Turner, Nature, 130, 315; J., 1933, 135), while Searle and Adams were able to obtain 2,2'-dibromo-

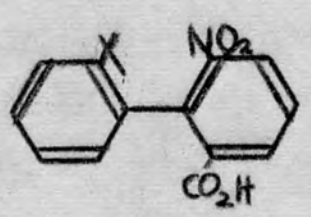
and 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid in the optically active condition (J.A.C.S., 1933, 55, 1649; 1934, 56, 2112). Predications were also made for biphenyls with only one obstacle group, but only one compound of this kind was resolved (Lesslie and Turner, J., 1933, 1588).

(VII)



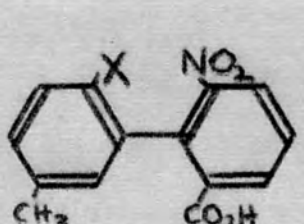
Adams' school also studied the correlation of "interference values" with the actual effectiveness of a blocking group, X, in terms of the racemisation rates of a series of 2-nitrobiphenyl-6-carboxylic acids:

(VIII)



X = OCH_3, CH_3, CO_2H, NO_2

(IX)



X = F, Cl, Br

(Hale and Adams, unpublished results quoted by Yuan and Adams, Chem.Rev., 1933, 12, 261; Stoughton and Adams, J.A.C.S., 1932, 54, 4426).

These experiments gave the effectiveness of X in preventing racemisation in the order Br > CH_3 > Cl > NO_2 > CO_2H > OCH_3 F, in fairly good agreement with the order of the interference values.

Quantitative assessment of optical stability and insufficiency of "obstacle theory". The rate of racemisation of an 0,0'-substituted biphenyl was first observed by Kuhn and Albrecht, who found that the racemisation of 4,6'-dinitro diphenic acid, and of 4,6,4'-trinitro diphenic acid in sodium carbonate solution obeyed first order kinetics (Ann., 1927, 455, 272; 458, 221). Since then, the first order rate constant k, and the resulting half life period, $t_{\frac{1}{2}}$, for racemisation in a given solvent at a given temperature, have been used as a quantitative measure of optical stability. Besides its application to the determination of the relative blocking effect of o-substituents, racemisation rate studies have been applied to determine semi-quantitatively the effect of altering the relative positions of obstacle groups, and the effect of substituents in positions other than the "blocking" ones, on optical stability. Kuhn and Albrecht also used the Arrhenius relationship to determine the activation energy of racemisation for 4,6'-dinitro- and 4,6,4'-trinitrodiphenic acid from rate constants at two different temperatures.

$$k = Ae^{\frac{-E}{RT}}$$

$$\log_{10} k = \log_{10} A - \frac{E}{2.303RT}$$

E = activation energy

R = gas constant

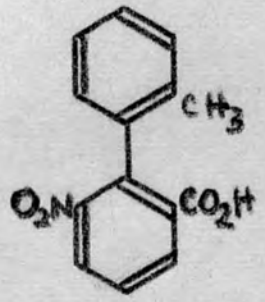
A = Arrhenius constant or frequency factor

T = Absolute Temperature

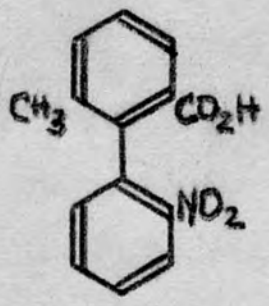
(E and $\log_{10} A$ will hence be called the Arrhenius parameters) However, experimental determinations of Arrhenius parameters were not forthcoming during the first twenty years of the development of the subject of restricted rotation. Kornblum and Adams (J.A.C.S., 1941, 63, 188) commented on the large errors involved in such determinations and concluded that the use of the half-life period as a measure of optical stability was to be preferred. Such determinations were later stimulated by theoretical calculations on activation energies of racemisation for sterically hindered biphenyl derivatives, and by the application of the Absolute Reaction Rate Theory to this type of racemisation process.

Studies in altering the relative positions of obstacle groups in two series of three isomeric compounds (X-XII; XIII-XV) show that although the "obstacle theory" holds in general, the size effect cannot be the only factor governing the ease of racemisation (Adams and Finger, J.A.C.S., 1939, 61, 2828; Adams and Hale, ibid, 2825).

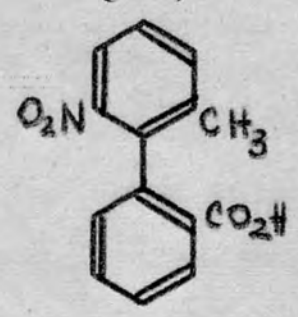
(X)

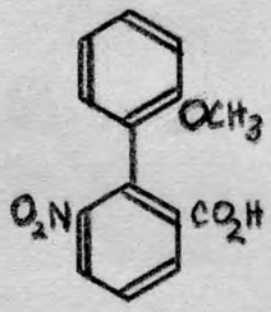


(XI)

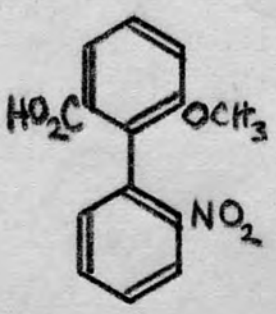


(XII)

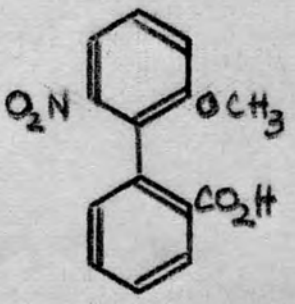




(XIII)



(XIV)



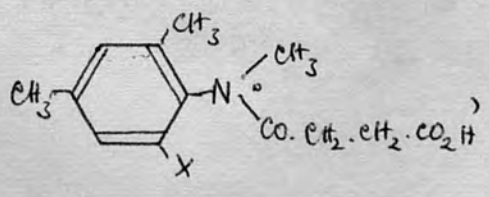
(XV)

According to size, the optical stability should be in the order (XI) > (XI) ≃ (XII) and (XIV) > (XIII) ≃ (XV)

The experimental results, however, give the order (XII) ⟩ (XI) ⟫ (X) and (XIV) ⟩ (XV) ⟫ (XIII). These results have not been satisfactorily explained.

In the study of restricted rotation about a C-N bond, however, experimental deviations from the concept of size effects have been attributed to conjugation of the lone pair electrons on the nitrogen atom with the phenyl ring. The relative optical stabilities of compounds of the type

(XVI)



, X = I, Br, Cl, OCH_3, NO_2.

where X=I, Br, Cl, OMe, NO_2 was found to be in the order I > Br > Cl > OMe > NO_2 (Adams and Sundholm, J.A.C.S., 1948, 70, 2667; Adams and Gordon, ibid, 1950, 70, 2454). The anomalous optical instability of the nitro compound was explained in terms of the dipolar nature of the nitro group, which would induce an electromeric change with the development of coplanarity:

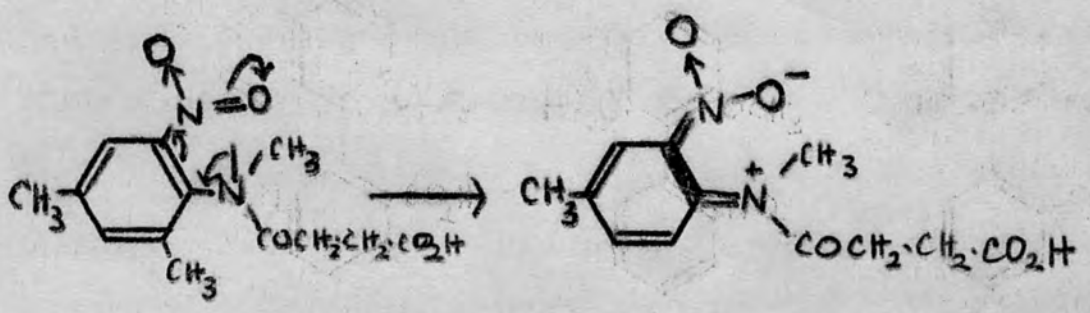
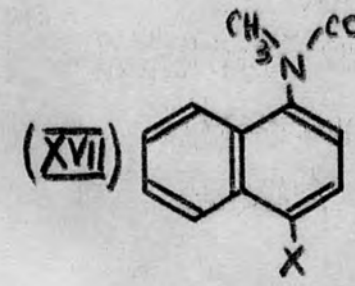


Fig 4.

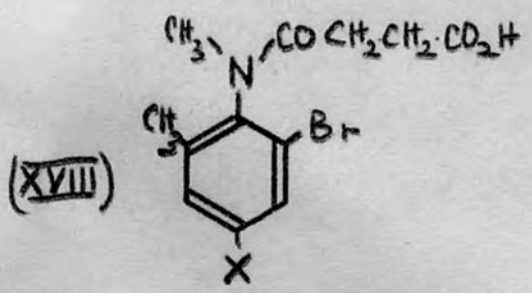
The same explanation has been applied to the effect of 4-substituents on the optical stability of similar compounds (Adams and Albert, J.A.C.S., 1942, 64, 1475; Adams and Gordon, loc.cit.)



(XVII)

X = H, $t_{\frac{1}{2}}$ = 5·7 hrs in boiling butanol

X = Cl, $t_{\frac{1}{2}}$ = 4·1 hrs " " "



(XVIII)

X = CH_3, $t_{\frac{1}{2}}$ = 3·1 hrs in boiling butanol

X = Br, $t_{\frac{1}{2}}$ = 1·1 hrs " " " .

The Cl and Br atoms, by virtue of their negative inductive effect, would promote, while the methyl group, by virtue of its positive inductive effect would discourage electromeric changes involving the lone pair electrons of the nitrogen atom in these compounds.

In the biphenyl series, studies in the effect of substituents other than those in blocking positions, were made by Adams and his students, and their work on the 2-nitro-6-carboxy-2'-methoxy-biphenyl derivatives may be summarised in the following table:

(XIX)

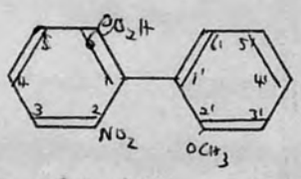


Table 1.

Solvent	Temp. °C.	Substituent	$t_{\frac{1}{2}}$ in minutes NO_2	Br	Cl	CH_3	OCH_3	H
ethanol	25°	in position 3'	1905	827	711	331	98	
ethanol	26-28°	" " 5'	35	32	31	12	11	10.2
acetone	24-26.5°	" " 4'	115	25	12	2.5	3.6	
ethanol	28°	" " 4	4	9	11	5	-	

(Yuan and Adams, J.A.C.S., 1932, 54, 4434; Chien and Adams, ibid, 1934, 56, 1787; Hanford and Adams, ibid, 1935, 57, 1592; Adams and Snyder, ibid., 1938, 60, 1411).

The effect of all 3'-substituents in reducing the rate of racemisation was explained in terms of the "buttressing effect"; the repulsion of the 2'-obstacle towards the other ring by the adjacent 3'-substituent,

opposing in-plane distortion of bond angle required for racemisation. The increase in energy barrier due to the "buttressing effect" has been demonstrated both by experiment and calculation, in the case of 2,3,2',3'-tetraiodobiphenyl-5,5'-dicarboxylic acid (Reiger and Westheimer, J.A.C.S., 1950, 50, 72, 19). The effect of substituents in the 5',4' and 4-positions on the optical stability of (XIX) has not, however, been satisfactorily explained.

Calculation of energy of activation for racemisation. The first theoretical calculation of the activation energy of racemisation for a sterically hindered biphenyl derivative was made by Mayer and Westheimer in 1946. They estimated an activation energy of 18kcals for 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid, by minimising the energy of a planar transition state with respect to bond deformations and Van der Waals' interactions (Mayer and Westheimer, J.Chem.Phys., 1947, 15, 252). Since then their method has been applied, with slight modifications to several other o,o'-halogenated biphenyls, and also to some bridged biphenyls (Reiger and Westheimer, loc.cit.; Howlett, J., 1960, 1055; Hall and Turner, J., 1955, 1242-appendix; Mislow, Hyden and Schoefer, J.A.C.S., 1962, 84, 1451). Such theoretical calculations naturally stimulate experimental work on the determination of activation energies of sterically hindered biphenyl derivatives.

Entropy of activation and optical stability. In 1951, Cagle and Eyring, (J.A.C.S., 1951, 73, 5628) collected the racemisation rate data which were then available, and applied the Absolute Reaction Rate Theory to the racemisation of ten o,o'-substituted biphenyls and related compounds.

$$k = \kappa \frac{kT}{h} e^{\frac{-\Delta H^{\ddagger}}{RT}} e^{\frac{\Delta S^{\ddagger}}{R}} ;$$ k = Boltzman Constant; h = Planck's constant

κ = transmission coefficient

$\Delta S^{\ddagger}$ = entropy of activation

$\Delta H^{\ddagger}$ = enthalpy of activation

$$\log_{10} \frac{k}{T} = 10.319 - \frac{1}{T}\left(\frac{\Delta H^{\ddagger}}{4.576}\right) + \frac{\Delta S^{\ddagger}}{4.576}$$

They evaluated the entropy and enthalpy of activation from the above equation and the free energy of activation $\Delta F^{\ddagger}$ from the relationship

$$\Delta F^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$$

($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ and $\Delta F^{\ddagger}$ will hence be called the transition state theory functions).

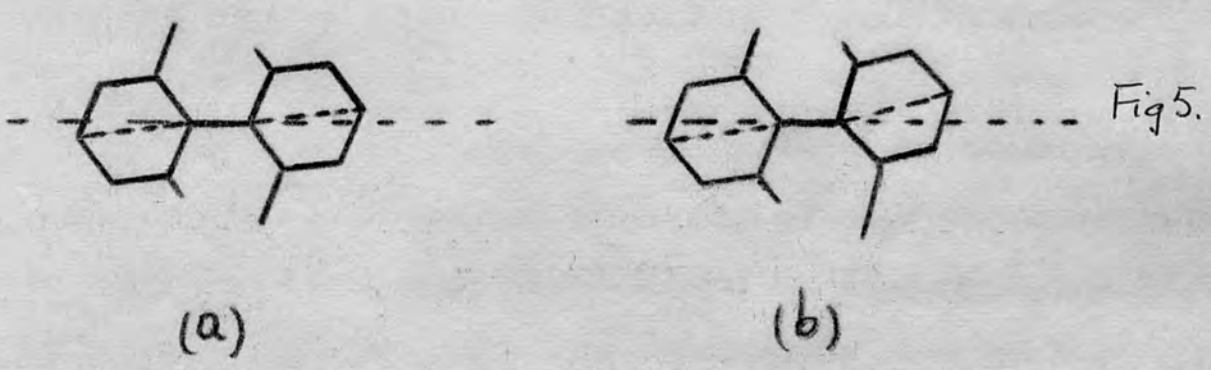
Their purpose was to relate reaction rate with structure, and in particular to find out more about the nature of the activated complex in the process of racemisation. Their values for the transition state theory functions of these compounds revealed the importance of the contribution of the entropy factor $\Delta S^{\ddagger}$ to the racemisation of sterically hindered biphenyl derivatives, and pointed to the possibility of correlating structure with $\Delta S^{\ddagger}$ values. Though their work

was limited both by the small number of experimental data available, as well as by the large errors involved in these data, their approach aroused great interest and called for more accurate measurements of racemisation rates as a means of obtaining more reliable values for the transition state functions. In 1960, Hall and Harris (J., 1960, 490-494) were able to compile a table of Arrhenius parameters and transition state theory functions for 34 compounds which owe their optical activity to restricted rotation, and many more compounds can now be added to the list.

The original theories of restricted rotation in biphenyls, and the methods used in the investigation of compounds which possess optical activity of this type have been briefly outlined. As a result of these investigations several theories have been put forward to explain the course of racemisation, and to describe the transition state in the racemisation of these compounds.

Suggested distortion within a planar transition state. It is generally accepted that the sterically hindered biphenyl racemises by rotating about the interannular bond, through a planar transition state. In 2,6,2',6'-tetrasubstituted biphenyls in which all o-substituents are the same, the two benzene rings in the transition state are assumed to be coaxial; in symmetrical 2,2'-disubstituted biphenyls and compounds with the same structure, they are thought to be

slightly inclined at equal angles to, and on the opposite sides of the interannular bond (Fig 5a) ("Steric Effects in Organic Chemistry", New York, Wiley, 1956, p.549-550); in biphenyls with structures similar to those with 1 or 3 obstacle groups, however, there is more deviation from collinearity and the angles between the benzene rings and the interannular bond will not be equal. (Fig 5b) (Stanley and Adams, J.A.C.S., 1930, 52, 1200-5).



(a) (b) Fig 5.

The main forces at work during racemisation are considered to be steric rather than electronic. However, the effect of resonance involving the interannular bond on optical stability has also been considered.

It has already been seen that the Le Fevre-Turner theory when translated into modern language states that conjugation across the interannular bond in sterically hindered biphenyls is a major factor causing racemisation. In later times resonance involving the interannular bond has been considered as an appreciable, but minor factor in promoting

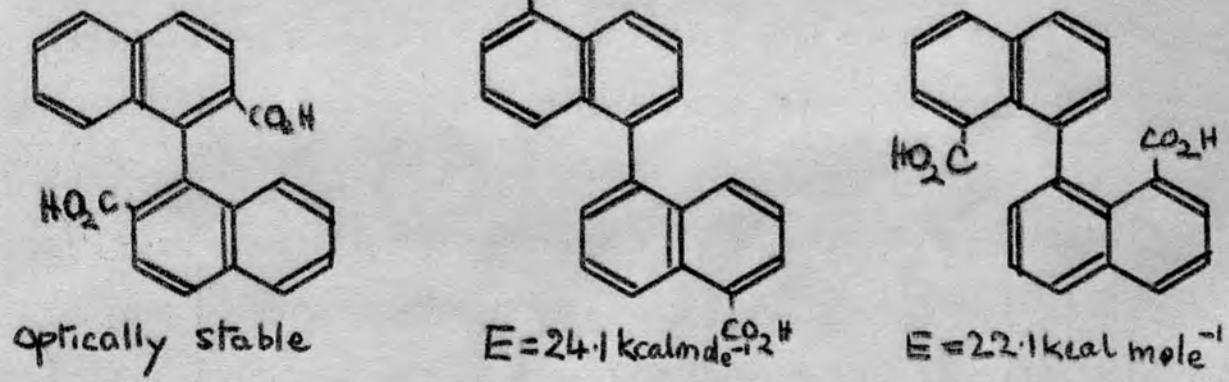
racemisation. Howlett, in calculating the activation energies of o,o-halogenated biphenyls, attributed a value of 7 kcals. to resonance energy (involving the 1,1'-bond) in the transition state (J., 1962, 1055); Mislow, Hyden and Schoefer (loc.cit.) in calculating the activation energies of some bridged biphenyls used a value of 4 kcals., a value calculated for planar biphenyl itself and Westheimer recognised some resonance stabilisation in the planar transition state, though he neglected this as insignificantly small in his calculations. ("Steric Effects in Organic Chemistry", Wiley, 1956, p.550).

The opposing idea that interannular resonance would increase the optical stability of an o,o'-disubstituted biphenyl has been put forward by Calvin (J.Org.Chem., 1939, 4, 256). He suggested that resonance would shorten the interannular bond and therefore increase the interference between obstacle groups. Specifically, he attributed the detected optical activity of 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid to resonance between the carboxyl groups, and the non-resolvability of 2,2'-dibromobenzidine to the inability of the amino groups to receive electrons; he consequently suggested that 2,2'-dibromo-4-amino-4'-nitrobiphenyl should be more stable than the corresponding dicarboxylic acid. Westheimer pointed out that Calvin's argument was faulty: "Resonance always decreases the energy of a molecule, never increases it. The interannular bond

in a planar biphenyl can be shortened by resonance if, and only if resonance lowers the energy of the planar conformation. If the planar conformation (which is the transition state for racemisation) has less energy the reaction would proceed more rapidly. Conversely, if resonance cannot lower the energy of the planar conformation of the biphenyl, it cannot shorten the interannular bond either." ("Steric Effects in Organic Chemistry", p.550-1).

Experimental work in compounds with restricted rotation about a C-N bond has already shown that Calvin's argument does not hold: increased conjugation across the C-N bond decreases the optical stability, and vice versa, (compounds XVI, XVII, XVIII). In a biphenyl, where there is no "lone pair" electron at the 1 or 1'-carbon atom available for conjugation across the interannular bond, this effect may be less marked.

* (XX) (XXI) (XXII)



Out-of-plane distortion due to molecular overcrowding in an essentially coplanar transition state. Recently the mental picture of a planar transition state has been

* diagram should be on p. 25.

modified in the case of 1,1'-binaphthyl-8,8'-dicarboxylic acid (XXII), to allow for molecular overcrowding in this molecule. The anomalously low optical stability of this compound, in comparison with the corresponding (XX) 2,2'- and 5,5'-dicarboxylic acids (XXI) is explained in terms of in-plane and out-of-plane distortions in both the ground and transition states. The energy barrier to racemisation is reduced, not only by ground state strain, but also by the existence of a mesoid transition path, which is made possible by out of plane distortions (Harris and Mellor, Chem.and Ind., 1961, 557; Cheung and Harris, Chem.and Ind., 1962, 1378)

The 8-carboxyl carbon atom and the 1-carbon atom in 1,1'-binaphthyl-8,8'-dicarboxylic acid, are displaced out of the main plane of the naphthalene unit, as the distance between them, on a model with normal bond lengths and bond angles, would be 2.4Å, a value less than the least distance of approach, 3.0Å, between two non-bonded C-atoms.

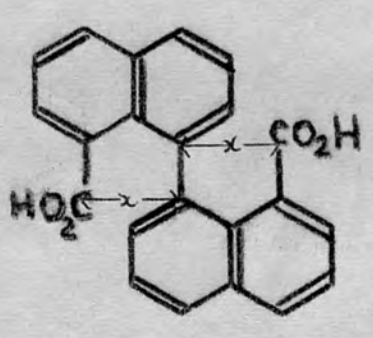


Fig. 6.

$x = 2.4\text{Å} < 3.0\text{Å}$

Such out-of-plane displacement enables the carboxyl groups to pass the relevant (2 and 2') hydrogen atoms with greater ease, and lowers the energy barrier to racemisation by an amount, Es.g., equal to the strain energy in the ground state.

The out-of-plane distortion gives rise to asymmetry in the individual substituted naphthalene units:

Fig 7

These give rise to three possible conformations (+)(+). (-)(+), (-)(-), for each configuration, R or S, in 1,1'-binaphthyl -8,8'-dicarboxylic acid. Conformational inversions (+)$\rightleftharpoons$(-) are considered to be fast in comparison with configurational inversions, and the existence of these conformers does not affect the observable kinetics, nor the Arrhenius plot for racemisation. However, examination of models of these conformers shows that the three possible transition paths are associated with two different energy barriers. The (+)(+) and (-)(-) conformers (racemoid) pass through a

transition state in which both barriers of maximum interference are encountered simultaneously. These transition paths are thus equivalent with respect to energy barrier. For the (+)(-) conformer (mesoid), however, one pair of obstacles (8-CO_2H and 2'-H) are at maximum interference while the other pair of obstacles are still quite a distance apart. The molecule then passes through an intermediate state in which the interference of both pairs of obstacles is the same, but not maximum, before the second barrier of maximum interference is encountered. The mesoid transition path will thus be associated with a lower energy barrier than the racemoid transition paths. As conformational inversions are fast in comparison with configurational inversions, the latter will take place through the mesoid transition path, resulting in a further lowering of the energy barrier to racemisation.

$$R(+)(+) \rightleftharpoons R(-)(+) \rightleftharpoons R(-)(-)$$
$$S(+)(+) \rightleftharpoons S(-)(+) \rightleftharpoons S(-)(-)$$

Though there is appreciable out-of-plane distortion in the transition state of 1,1'-binaphthyl-8,8'-dicarboxylic acid, the two naphthalene nuclei will be nearer to coplanarity in the transition state than in the ground state. If interannular resonance can occur in the transition state, the energy barrier to racemisation for this compound and

similar compounds will be further lowered by an amount E_r, equal to the gain in resonance energy in the transition state. The energy of activation, E, for such a compound may be represented by the equation:-

$$E = Es.m - Es.g - Er \quad \ldots\ldots\ldots\ldots\ldots \quad (1)$$

(Es.m = strain energy of the mesoid transition state).

Suggested non-planar transition state involving a tetrahedral carbon atom. Adams' work on the effect of altering the relative positions of obstacle groups could not be explained in terms of the simple obstacle theory. Baddeley (Nature, 1946, 157, 694) pointed out that in these two sets of compounds, the electron densities in the upper rings (referring to compounds X-XV, as drawn on p. 16) are in the same order as their rates of racemisation. He suggested that electron availability in the ring would enable the 1 or 1' carbon atom to acquire a negative charge, becoming tetrahedral, and thus lowering the energy required for rotation about the interannular bond.

Fig. 8.

Crawford and Smyth (J., 1954, 3464) discussing Adams' work on the effect of 4' and 5' substituents on the optical stability of 2-nitro-6-carboxy-2'-methoxybiphenyl

derivatives, noted that the rates of racemisation paralleled the effectiveness of the substituents in activating the aromatic ring to electrophilic substitution. They suggested that the racemisation was brought about by the electrophilic attack of a protium cation from the solvent, resulting in a transition state in which the 1 or 1'-carbon atom became tetrahedral, and so facilitating rotation about the 1,1'-bond.

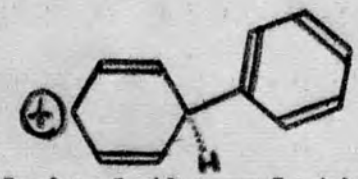
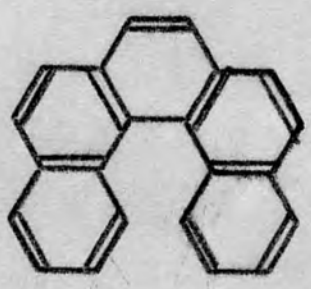
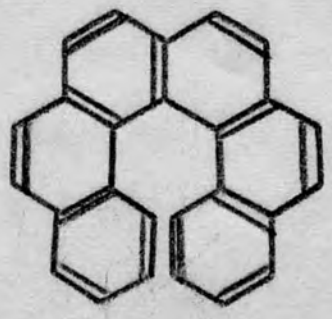


Fig. 9.

They also explained the relative stability of binaphthyl derivatives, diquinolyls and di-isoquinolyls in this way. These two proposals of a transition state involving a tetrahedral C-atom have not received general acceptance (Harris, Progress in Stereochemistry, 2, p.192), partly because specifically designed experiments to test the theory, which are not explainable in some other way, have not yet been carried out. Some objections can be raised against the need for such an explanation on the ground of physical and chemical evidence.

The preparation of overcrowded molecules in recent years (Newman, "Steric Effects in Organic Chemistry", Ch.10 p.476) shows that polynuclear aromatic molecules with a considerable amount of strain energy can exist. Deformation in bond lengths and bond angles throughout the molecule has made

possible the preparation of such compounds which would otherwise be non-existent. Coulson and Sennent (J., 1955, 1819) have estimated a total strain energy of roughly 28 kcals. for 3,4-5,6-dibenzophenanthrene (XXIII), and molecules with even greater strain energies have been prepared (e.g. XXIV) and are stable.

(XXIII)   (XXIV)

This means that it is not necessary to relieve strain energies of 20-30 kcals. in overcrowded aromatic molecules by localisation of electrons to give sp^3-carbon atoms at the overcrowded regions. As E_{racem} values for readily racemisable o,o'-substituted biphenyls lie between 20 and 30 kcals., it seems unnecessary to postulate a tetrahddral C-atom in the transition state of racemisation of these compounds.

The attack of an electrophilic reagent at the 1 or 1'-C-atom would give rise to an sp^3-C-atom in the transition state. However, it seems unlikely that such an attack should come from the solvent in the very crowded region. Moreover, such a mechanism would require second order kinetics, the formation of the transition state being

dependent on the proton attack. Deviation from first order kinetics should be observed for racemisations carried out in solvents which can produce only a limited amount, if any, of protium cations. No such deviations have been reported. The theory could be further tested experimentally by deliberately introducing protium cations into the racemising system: the rate of racemisation should be faster in the presence of protium cations.

Both Baddeley and Crawford and Smyth based their theories on the observation that increase in electron availability in one of the benzene nuclei of certain o,o'-substituted biphenyl derivatives increases the rate of racemisation. In both theories, electron availability in the benzene ring means electron availability at the 1 (or 1') carbon atom. The experimental data on which they made their observations were not designed to study the effect of electron density at the 1 or 1' C-atom on optical stability. A glance at compounds X to XV and XIX will show that the structures of the obstacle groups are fairly complicated, and besides affecting the electron density at the 1 or 1'-C-atom, they may well influence other factors (such as, for example, the angle between the plane of the -COOH group and the phenyl nucleus) which may cause a change in optical stability. Table I shows that the half life periods given are obtained from racemisations, not at one fixed temperature,

but over a range of 2-3°. These values are therefore not strictly comparable. Moreover, optical stability, as measured by the half life period at a given temperature, depends on both energy and entropy of activation, and these experimental data will be insufficient to show whether electron density at the 1 or 1'-C-atom affects the energy or entropy of activation, or both.

Scope of present work.

Experimental data have been sought to investigate the possibility that optical stability decreases with increasing electron density in the region of the 1,1'-bond; an attempt has been made to isolate this factor, in a series of 2,2'-disubstituted biphenyls by introducing 4,4'-substituents of varying electron-donating power.

4,4'-Derivatives of 2,2'-dibromo- and 2,2'-diiodo-biphenyl have been chosen for studying the effect of electron density in the region of the 1 and 1'-C-atoms on optical stability. 4,4'-Derivatives are chosen because substituents in the 4, and 4'-positions will directly affect the electron densities at the 1 and 1'-C-atoms but, being meta to the obstacle groups, will not appreciably affect the latter, either by the buttressing effect, or by eletronic effects. 2,2'-Dibromo- and 2,2'-diiodobiphenyl derivatives are chosen

because they are readily racemisable, and are the simplest optically active biphenyls known: the obstacle groups are single atoms, which possess only small negative inductive effects. In these compounds, it is reasonable to assume that the obstacle groups do not appreciably affect the electron density at the 1 and 1'-C-atoms in comparison with the 4,4'-groups, and that their effect on the optical stability is the same in all and is mainly due to their size.

From the practical point of view it has proved to be much more difficult to work with optical activity in the bromo-series, because the compounds have such low optical stability. Most of the work refers therefore to the iodo-series.

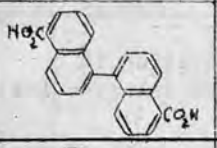
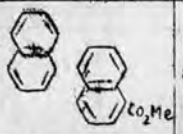
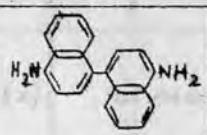
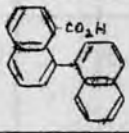
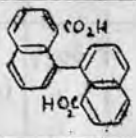
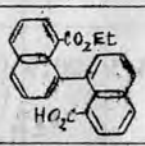
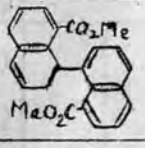
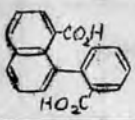
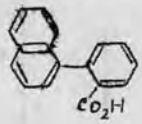
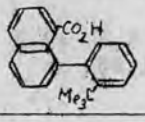
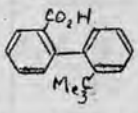
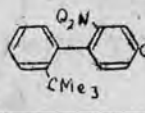
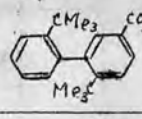
In connection with 2,2'-dihalogeno-biphenyls, it has been pointed out that owing to their similarity in structure, their entropies of activation should be approximately equal, though there may be room for some variation with addition of different substituents in different positions of the ring (Reiger and Westheimer, loc.cit.; Harris and Mitchell, J., 1960, 1905). The energies of activation for these compounds have also been recently recalculated (Howlett, loc.cit.) Determination of the Arrhenius parameters and transition state theory functions for the

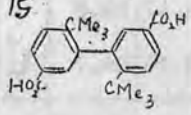
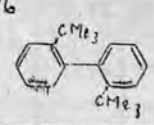
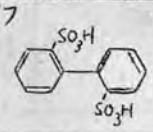
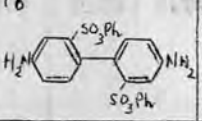
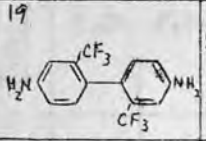
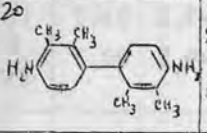
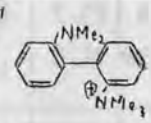
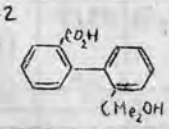
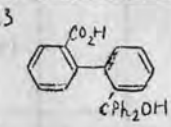
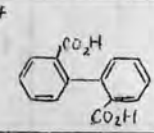
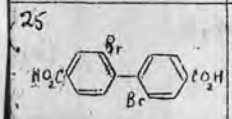
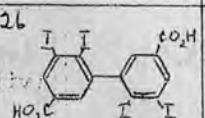
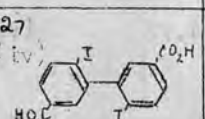
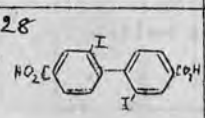
racemisation of these compounds should therefore be of great interest and, on account of their simplicity in structure, would probably be more revealing than similar determinations for other compounds.

A Survey of optically active 2,2'-disubstituted biphenyl derivatives.

In September 1959, a survey of the literature revealed activation energy determinations for only three 2,2'-disubstituted biphenyls (Reiger and Westheimer, J.A.C.S., 1950, 72, 19; Graham and Leffler, J.Chem.Phys., 1959, 63, 1274). Since then it has been of great interest to follow such racemisation rate studies for another fourteen 2,2'-disubstituted biphenyl derivatives, including a series of eight 1,1'-binaphthyls. A brief survey of the work done on the optically active 2,2'-disubstituted biphenyl derivatives has therefore been made, with special emphasis on values for energy and entropy of activation. This survey is summarised in Table II.

Table II

	2,2'-di-substituted Biphenyl	Methods by which optical activity was detected: resolution or optical activation.	PACEMISATION DATA Solvent	$t_{\frac{1}{2}}$ mins.	E kcal. mole^{-1}	logA	$\Delta H^{\ddagger}$ kcal. mole^{-1}	$\Delta S^{\ddagger}$ e.u.	$\Delta F^{\ddagger}$ kcal. mole^{-1}	Ref
1		Second order asymmetric transformation with brucine from aq. ethyl cellosolve.	N,N'-DMF	271.5	24.1	12.3	23.5	-4.47	24.9	(i) & (ii
			$\frac{N}{10}$NaOH	94.2 at 50°	24.9	12.9	24.2	-1.54	24.7	
2.		(+) form obtained by the action of diazomethane on (+)-(1).	N,N'-DMF	111.9 at 50°	23.8	12.2	23.1	-5.09	24.8	(i)
3.		De-amination of (+)-(4) at low temperatures, using hypophosphorous acid.	N,N'-DMF	14.5 at 50°	22.5	12.12		-5.17		(i)
4.		Second ord.asym.trans. with 2 mols. of (+)- -bromo-camphor- -sulphonate, from 60% aq. ethanol.	Acetone	24.6 at 38°	21.4		20.8	-7.1	22.9	(ii
5.		Resolved through brucine salt, from ethyl acetate.	N,N'-DMF	5.5 at 50°	22.4	12.0	21.8	-5.5	23.5	(i) & (iv
6.		Resolved through brucine salt, from methanol.	N,N'-DMF	55	22.1	11.3	21.4	-9.1	24.5	(i) & (iv
			M/10NaOH	2.3 at50°	26.01	15.2	25.4	+9.2	22.7	
7.		Second ord,asym.trans. with brucine,from aqueous ethyl cellosolve.	N,N'-DMF	17.2	21.6	11.4	20.9	-8.4	23.7	(i) & (iv
			$\frac{N}{10}$NaOH	31.1 at50°	25.7	14.0	25.0	+3.18	24.4	
8.		Both (+) & (-) antipodes obtained by the action of CH_2N_2 on active forms of(6).	N,N'-DMF	22.7 at 50°	22.0	11.6	21.4	-7.54	23.9	(i)
9.		Second ord.asym.tran. with brucine, from benzene. First ord.asym.trans. with brucine in chloroform.	B.P. $CHCl_3$	60 at 20°						(v)
10.		2nd. ord.asym.trans. with brucine & cinchonidine in acetone. 1st. ord.asym. trans. with brucine, quinidine & cinchonidine in $CHCl_3$.	B.P. $CHCl_3$	2 at 20°						(v)
11.		Resolved through strychine salt, in ethanol.	EtPh	183 at 121°	*29	*11.9		*-6.8		(vi)
12.		2nd. ord. asym. trans. with brucine & strychnine, from ethanol and methanol.	EtOH	35 at 57°	24	*12.2		*-5.6		(vii
13.		2nd. ord.asym.trans. with strychnine, from ethanol.	CH_3Ph	110 at 55.8°	25.4	*12.9		*-1.92		(vi)
14.		Resolved through strychnine salt: fractional crystallisation from ethanol.	Activity remained unchanged after melting at 193°.							

2,2'-di-substituted Biphenyl	Methods by which optical activity was detected: resolution or optical activation.	RACEMISATION DATA							Ref.
		Solvent	$t_{\frac{1}{2}}$ mins.	E kcal. mole^{-1}	logA	$\Delta H^{\ddagger}$ kcal. mole^{-1}	$\Delta S^{\ddagger}$ e.u.	$\Delta F^{\ddagger}$ kcal. mole^{-1}	
15 	Resolved through brucine salt: fractional crystallisation from ethanol	Activity remained unchanged after boiling in aqueous sodium hydroxide or pyridine solution for three hours.							(vi)
16 	Both (+) &(-) forms obtained from active forms of (15) through the Schmidt reaction	Optically stable.							(vi)
17 	Resolved through mono-brucine salt by successive addition of .25mole of strychnine,HCl to the Na salt.	aqueous solution of ammonium salt racemised rapidly at 100°.							(viii) & (ix)
18 	2nd. ord.asym.trans. with (+)camphoric acid from abs. ethanol and methanol.	Pyridine solution completely racemised in ten minutes at 100°.							(x)
19 	2nd. ord.asym.trans. with (+)-tartaric acid, at 50° from ethanol.	EtOH	58.4 at 39°	19.5	9.92		-15.3		(xi)
20 	2nd.ord.asym.trans. with (+)- -bromocamphor- -sulphonic acid, from 95% ethanol.	EtOAc	54.5 at 30°	17.7		17.0	-19	22.7	(iii)
21 	Resolved through (+)camphor-10-sulphonate by crystallisation from a mixture of alcohol, benzene,& light pet.	Water	125 at 99.5°	27.6	12.2	26.9	- 5.3	28.9	(xii) (xiii) & (xiv)
22 	2nd. ord.asym.trans. with brucine, from ethanol & $CHCl_3$ 1st. ord.asym.trans. in " .		26.6hr. at 25.15°						(xv) & (xvi)
23 	Resolution through brucine salt: fractional crystallisation from ethanol.	Gradually racemised at room temperature.							(xvii)
24 	Fast mutarotation with nor-(+)- -ephedrine at -30° in chloroform.								(xviii)
25 	2nd. ord.asym.trans. with brucine from ethyl acetate.	EtOH	13.4 at 1°	19.0 ±0.5	12.1 ±0.4	18.5 ±0.5	- 4.9 ±1.85	19.9 at 5.6°	(xix) (xx) (xxi)
26 	Resolution difficult: through mono- and di-brucine salts, from ethanol.	NaOH aq.		28.05	11.7	27.3	- 7.6	30.2	(xiv) & (xxii)
27 	2nd. ord.asym.trans. with 1 mole of brucine from ethanol.	aq.alc. 1% $NaHCO_3$		21.6	11.5	21.0	- 7.7	23.4	(xiv) & (xxii)
28 	2nd. ord. asym.trans. with brucine, from ethanol.	EtOAc	125,4 at 25°						(xxiii)

References for Table II.

(i) A.S.Mellor. Ph.D. thesis submitted to University of London in March 1961. Over 7 rate measurements were carried out, covering a temperature range of about 30° for each set of results.

(ii) Bell, Morgan, and Smyth, Chem. & Ind., 1951, 634.

(iii) Theilacker and Hopp, Ber., 1959, 2299. 7 rate measurements from 10.5° to 38° for compound (4); and 5 rates from 9.3° to 30° for compound (20).

(iv) Meisenheimer and Besswenger, Ber., 1932, 65, 32.

(v) Hall, Ridgwell and Turner, J., 1954, 2498.

(vi) U.J.H.Mayer, Ph.D. Thesis submitted to University of London in July 1961. 4 rate measurements from 121° to 136° for compound (11), and 6 rates from 51° to 75° for compound (13).

(vii) Lesslie and Mayer, J., 1961, 611. 3 rate measurements at 57° 67° and 79°.

(viii) Stanley and Adams, J.A.C.S., 1930, 52, 4471.

(ix) Lesslie and Turner, J., 1932, 2394.

(x) Lesslie and Turner, J., 1932, 2021.

(xi) Hall and Harris, J., 1959, 396; and private communication (unpublished).

(xii) Shaw and Turner, Nature, 130, 315; J., 1933, 135.

(xiii) Graham and Leiffler, J.Phys.Chem., 1959, 63, 1274.

(xiv) Hall and Harris, J., 1960, 490.

(xv) Corbellini and Angeletti, Atti.acad.Lincei, 1932, 15, 968-73.

(xvi) Jamison and Turner, J., 1942, 437.

(xvii) Corbellini and Pizzi, Atti.accad.Lincei, 1932, 15, 287.

(xviii) Lesslie, Turner and Winton, J., 1941, 257.

(xix) Searle and Adams, J.A.C.S., 1934, 56, 2112.

(xx) M.M.Harris, Proc.Chem.Soc., 1959, 367.

(xxi) Harris and Mitchell, J., 1960, 1905. 6 rate measurements from -20.7° to +5.6°.

(xxii) Reiger and Westheimer, J.A.C.S., 1950, 72, 19. 2 rate measurements at 80.16° and 99.72° for compound (26), and 3 rates from 19.90° to 38.22° for compound (27).

(xxiii) Searle and Adams, J.A.C.S., 1933, 55, 1649.

* Calculated [from experimental results — (vi) + (vii) —] by the present author.

These 2,2'-disubstituted biphenyls cover a wide range of optical stability. The 2,2'-ditertiarybutylbiphenyl derivatives are optically stable to ordinary methods of racemisation, while 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid represents, among compounds which owe their optical activity to restricted rotation, the most labile compound that has been obtained optically active. These compounds may be roughly classified as follows:

(I) 1,1'-binaphthyl derivatives in which the 2,2', 8 and 8' positions are not substituted - Compounds (1) to (4). It is interesting to note that the racemisation data for these compounds can be used to supplement the present study on the effect of electron availability in the region of the 1,1'-bond on optical stability.

(II) 1,1'-binaphthyl derivatives in which the 8 and/or 8'-positions are substituted. Compounds (5) to (8). The optical stability of these compounds is anomalously low. The cause of this low optical stability lies in a strained ground state, as has already been described in the introduction. These compounds are of particular interest with respect to the present work, which leads to the conclusion that 2,2'-di-iodobiphenyl is stereochemically similar.

(III). Biphenyls which contain obstacle groups of the structural type AX_3 - Compounds (11) to (23):

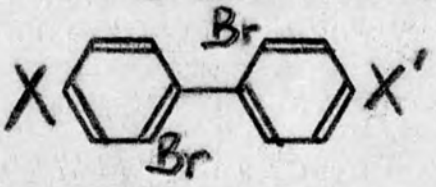
(a) those in which both 2 and 2' positions are occupied by AX_3 - compounds (14) - (20). The available racemisation data seem to point to large negative entropy factors for these compounds.

(b) those in which only one of the 2 and 2'- positions is occupied by AX_3, while the other is occupied by a second, usually smaller group - compounds (11) - (13); (21) - (23). The available racemisation data point to relatively small negative entropy factors for these compounds.

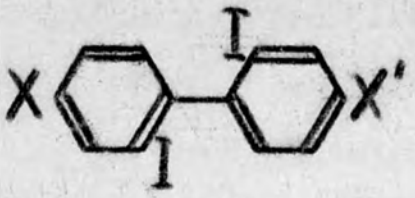
(IV). Biphenyls in which the obstacle groups are single atoms - Compounds (25) - (28). Several compounds belonging to this group are studied in connection with the present work.

SUMMARY OF OPTICAL WORK.

The following 4,4'-derivatives of 2,2'-dibromo- and 2,2'-di-iodobiphenyl have been prepared:-

(A) 

1. $X = X' = NH_2$
2. $N(CH_3)_2$
3. $X = N(CH_3)_2$, $X' = \overset{\oplus}{N}(CH_3)_3 I^{\ominus}$

(B) 

1. $X = X' = CO_2CH_3$
2. CO_2H
3. H
4. $NHCOCH_3$
5. NH_2

All attempts to detect optical activity in the three 4,4'-derivatives of 2,2'-dibromobiphenyl failed, in contrast with similar experiments carried out for 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid. The 4,4'-dicarboxylic acid was first obtained optically active by Searle and Adams (J.A.C.S., 1934, 56, 2112), and its Arrhenius parameters and transition state functions for racemisation were determined by Harris (Proc.Chem.Soc., 1959, 367; Harris and Mitchell, J., 1960, 1905) from rate measurements in absolute ethanol at low temperatures, -20.7° to $+5.6^{\circ}$.

However, all the di-iodo compounds, including 2,2'-di-iodobiphenyl itself, have been obtained optically active. The 4,4'-dicarboxylic acid was first prepared and obtained optically active by Searle and Adams (J.A.C.S., 1933, 55, 1649) who determined its rate of racemisation at only one temperature, though in different solvents. Racemisation rate measurements for this, and all the other 2,2'-di-iodobiphenyl derivatives have now been carried out in N,N'-dimethylformamide, at several temperatures, covering suitable ranges of temperature. Measurements were also carried out in absolute ethanol (for comparison with 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid) and in N/10 sodium hydroxide solution for the 4,4'-dicarboxylic acid, and in $\frac{N}{2}$ aqueous alcoholic hydrochloric acid for the 4,4'-diamino compound. First order kinetics were observed for all rate measurements. The Arrhenius parameters and transition state functions for racemisation have been evaluated and the results are shown in Table III.

4,4'-substituent	Solvent	$t_{\frac{1}{2}}$ at 25° mins.	Arrhenius parameters: E kcals. mole^{-1}	logA	Transition state Functions: $\Delta H^{\ddagger}$ kcals. mole^{-1}	$\Delta S^{\ddagger}$ e.u.	$\Delta F^{\ddagger}$ at 25° kcal. mole^{-1}	Temp. range	No. of rates
1. CO_2CH_3	N,N'-DMF	104	22.3	12.4	21.7	-4.0	22.9	25.9-45.5	6
2. CO_2H	"	104	21.6	11.9	21.1	-6.1	22.9	36.2-56.2	6
3. H	"	95	20.9	11.4	20.3	-8.2	22.8	25.4-42.2	5
4. $NHCOCH_3$	"	14.5	20.6	12.0	20.0	-5.8	21.7	12.2-36.0	7
5. NH_2	"	5.3	19.9	11.9	19.4	-5.8	21.1	-0.3-+24.9	7
CO_2H	Abs.ethanol	85	21.3	11.7	20.7	-6.9	22.7	25.2-56	7
CO_2^-	N/10 NaOH	151	21.5	11.6	21.0	-7.0	23.1	30.4-60.9	7
$\overset{+}{N}H_3$	N/2aq.alc.HCl	93	22.2	12.4	21.4	-4.3	22.8	26.7-50.2	7

TABLE III.

DISCUSSION.

In the table of results, six parameters have been used to describe the optical stability of each compound. These parameters are interrelated. The Arrhenius parameters E and logA are related to the transition state theory functions $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, by the following equations:

$$E = \Delta H^{\ddagger} + RT \qquad (2)$$

$$* \log_{10} A = \frac{\Delta S^{\ddagger}}{4576} + \log T + \log_{10} \frac{ke}{h} \qquad (3)$$

The half life period $t_{\frac{1}{2}}$ at a given temperature, is a direct measure of optical stability, while $\Delta F^{\ddagger}$, the change in standard free energy accompanying the formation of the transition state from the ground state, gives the overall optical stability in terms of energy units, it too is temperature-dependent. In this discussion, E, $\Delta S^{\ddagger}$ and $t_{\frac{1}{2}}$ will be used.

E and $\Delta S^{\ddagger}$ are thermodynamic quqntities depending only upon the nature of two fixed states, in this type of optical inversion upon the ground state and the transition state. Thus, whenever these quantities are discussed, the energy or entropy of the ground state and the energy or entropy of the transition state will be considered separately

---

* $k = Ae^{\frac{-E}{RT}}$; $k = K \cdot \frac{KT}{h} \cdot e^{\frac{-\Delta H^{\ddagger}}{RT}} \cdot e^{\frac{\Delta S^{\ddagger}}{R}} = K \cdot \frac{KT}{h} \cdot e^{\frac{-(E-RT)}{RT}} \cdot e^{\frac{\Delta S^{\ddagger}}{R}}$ #

$$= K \cdot \frac{KT}{h} \cdot e \cdot e^{\frac{-E}{KT}} \cdot e^{\frac{\Delta S^{\ddagger}}{R}}$$

.. $A = K \frac{KT}{h} \cdot e \cdot e^{\frac{\Delta S^{\ddagger}}{R}}$ for $K=1$, $\log_{10} A = \log_{10} \frac{ke}{h} + \log_{10} T + \frac{\Delta S^{\ddagger}}{2.303R}$

at first.

Ground State of 2,2'-di-iodobiphenyl. Information concerning the geometry of 2,2'-di-iodobiphenyl in the vapour phase is available from electron diffraction measurements; in solution from dipole moment measurements; and in crystalline form from X-ray crystallographic studies.

The 1,1'-bond. Electron diffraction gives a value of 1.50 ± 0.03 Å for the 1,1'-bond in 2,2'-di-iodobiphenyl (Bastiansen, Acta Chem.Scand., 1950, 4, 926). This value may be compared with the value of 1.53 Å for 2,2'-dichlorobenzidine (Smare, Acta Cryst., 1948, 1, 150) and the values of 1.507 Å and 1.50(6)Å for biphenyl (planar) obtained from crystallographic studies (Trotter, Acta Cryst., 1961, 14, 1135; A. Hargreaves and Rizvi, Acta Cryst., 1962, 15, 365). These values show that the two large iodine atoms do not appear to change the length of the 1,1'-bond significantly from that of biphenyl itself and that both in the vapour phase and in the crystal, the length of the 1,1'-bond is nearer to that of an aliphatic sp^3C-sp^3C bond (1.54Å) than of an aromatic sp^2C-sp^2C bond (1.39Å). Using an atomic radius of 0.75A for the 1 and 1' carbon atoms, the π-bond order for the 1,1'-bond in biphenyl is only about 0.1 (see fig.10)

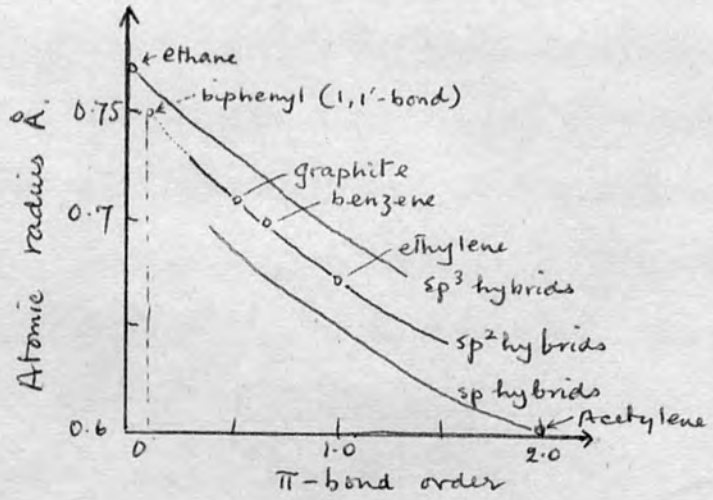


Fig. 10.

Order-length curves for carbon bonds involving sp, sp^2 and sp^3 hybridised atoms.

(Dotted line added to diagram given by Coulson in "Theoretical Organic Chemistry", The Kekule Symposium, p.51).

The Angle, θ, between the planes of the benzene rings.

The angle between the planes of the benzene rings of all four 2,2'-dihalogenobiphenyls in the vapour phase have been estimated from electron diffractions (Bastiansen, loc.cit.) and in benzene solution from dipole moment measurements (Littlejohn and Smith, J., 1954, 2552). Both methods give a cis-conformation (Hal.-Hal. contacts) rather than a trans-conformation (Hal-hydrogen contacts) for all the 2,2'-halogeno-biphenyls. Electron diffration gives $\theta = 79^{\circ} \pm 5^{\circ}$, and dipole moment measurements give $\theta = 84^{\circ}$ (value quoted by Beavan and Hall, J., 1956, 4639) for 2,2'-di-iodobiphenyl.

Individual iodobenzene units. All bonds in each benzene unit in o,o'-halogenated biphenyls have hitherto been considered as lying in one plane. In theoretical calculations for the activation energies of racemisation of these compounds, Westheimer (Mayer and Westheimer, J.Chem.Phys., 1946, 14, 733; 1947, 15, 252; Reiger and Westheimer, J.A.C.S., 1950, 72, 19) assumes that the ground states are completely free from steric strain, while Howlett (J., 1960, 1055) allows some steric interactions between the two pairs of ortho hydrogen and ortho halogen atoms in an orthogonal configuration of each o,o'-halogenated biphenyl, in which the individual halogenobenzene units are planar, with normal bond lengths and bond angles. However, a recent crystallographic study of o-chloro- and o-bromobenzoic acid reveals both in-plane and out-of-plane distortion of bonds in these compounds (Ferguson and Sim, Proc.Chem.Soc., 1961, 162; Acta Cryst., 1961, 14, 1262; 1962, 15, 346). The results for o-bromobenzoic acid show that the bromine atom is displaced 0.064 Å up out of the main plane of the molecule and the carboxyl carbon atom 0.057Å below, and that the C-C-Br angle is 4.9° and the C-C-CO_2H angle 3.4° larger than the normal bond angle of 120°.

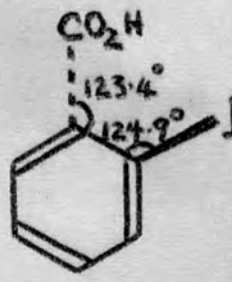


Fig. 11.

The sum of the van der Waals radii of iodine (2.15Å) and the half thickness of the phenyl ring (1.85Å) is 4.00Å, slightly larger than the value of 3.95Å given for the sum of the van der Walls radii of bromine and carboxyl carbon (Ferguson and Sim, Acta Cryst., 1962, 15, 346). It seems reasonable to suppose that the mutual distortion of an iodine atom with a phenyl ring would be at least of the order of that of a bromine atom with a carboxyl group, when each pair is situated in the o-position of a benzene ring.

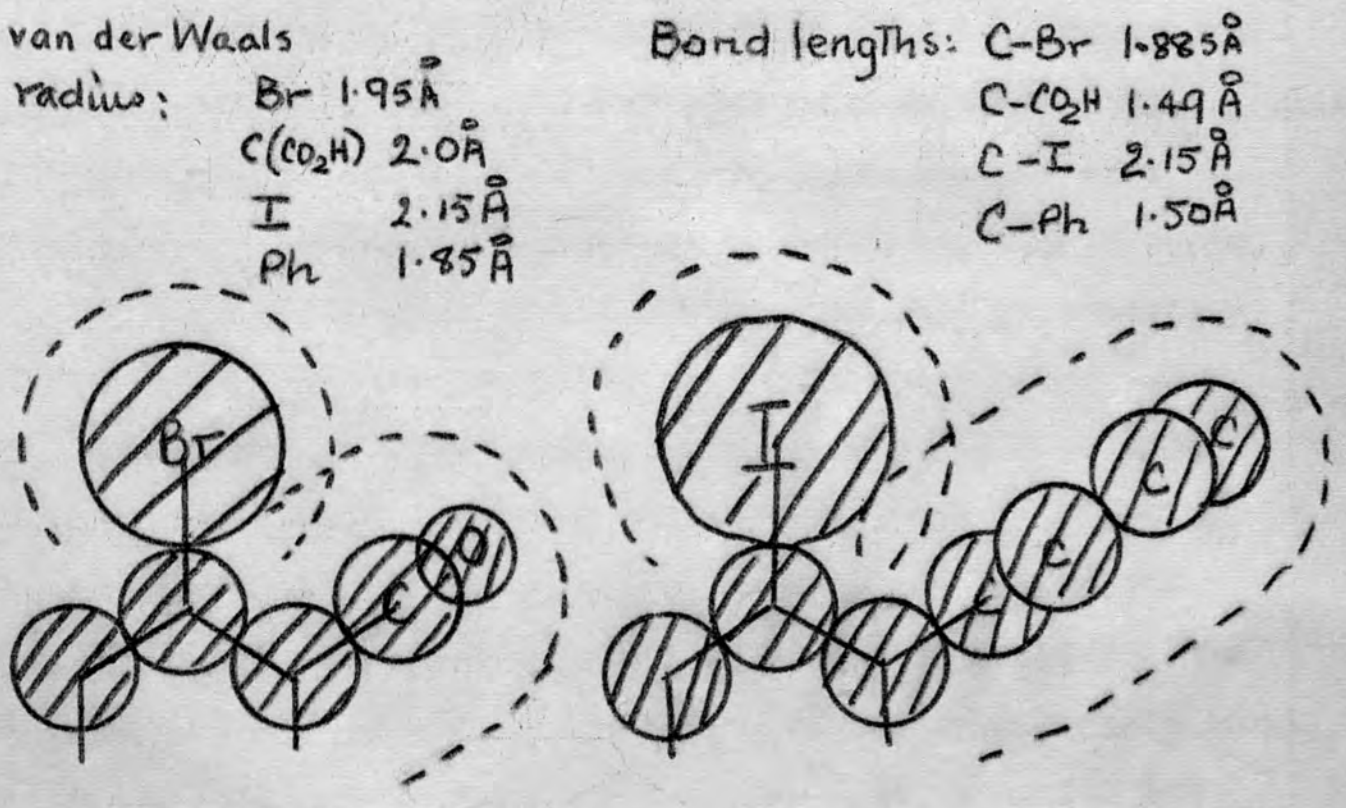


Fig.12. Sketch showing minimum interference in both cases, i.e. CO_2H and 2nd phenyl group at right angles to benzene ring.

Out-of-plane distortion is probably more marked in the gaseous phase than in the crystal, as a result of the need to pack molecules in the most efficient way in the solid. For example, biphenyl is planar in the crystal but not so in the vapour (Hargreaves and Rizvi, loc.cit.), and moreover electron diffraction in the vapour of hexachlorobenzene shows that the molecule is puckered, with the C-Cl bonds bent as much as 12° alternately up and down the mean plane of the molecule (Bastiansen, Acta Chem.Scand., 1947, 1, 489) while X-ray crystallography has not been able to detect any non-planarity in the molecule* (Tulinsky and White, Acta Cryst., 1958, 11, 7). Very little is known about the geometry of molecules in the liquid state or in solution, but it seems reasonable to suppose that the situation will be somewhere between that of the solid and that of the vapour.

It thus seems highly probable that in a solution of 2,2'-di-iodobiphenyl the individual iodobenzene units are distorted; the bond angles are strained beyond the normal values, while the C-I bond and the interannular bond point up and down out of the main plane of each benzene ring. The out-of-plane distortion is expected to be small, but insofar as it exists, gives rise to asymmetry in the iodobenzene

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* Although near ultraviolet spectrum of crystalline hexachlorobenzene suggests that the molecule is puckered (Kopelman and Schnepp, J.Chem.Phys., 1959, 30, 868).

units:

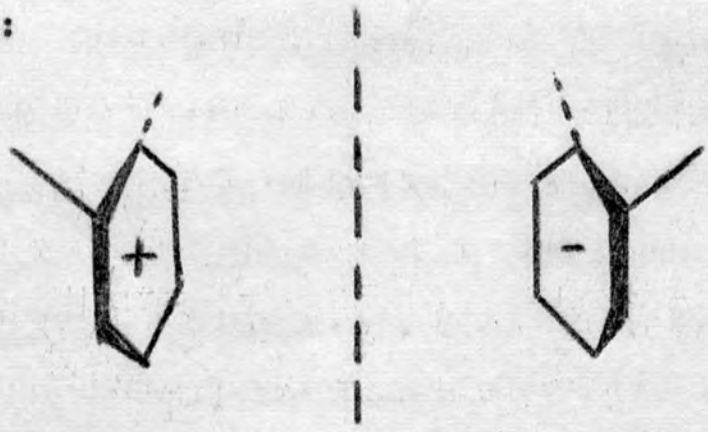

Fig.13.

The stereochemistry of 2,2'-di-iodobiphenyl can therefore be considered in a similar way to 1,1'-binaphthyl-8,8'-dicarboxylic acid. There are then three possible conformations of the 2,2'-di-iodobiphenyl molecule in its ground state, (+)(+), (+)(-), (-)(-), each of which can exist in the R or S configuration.

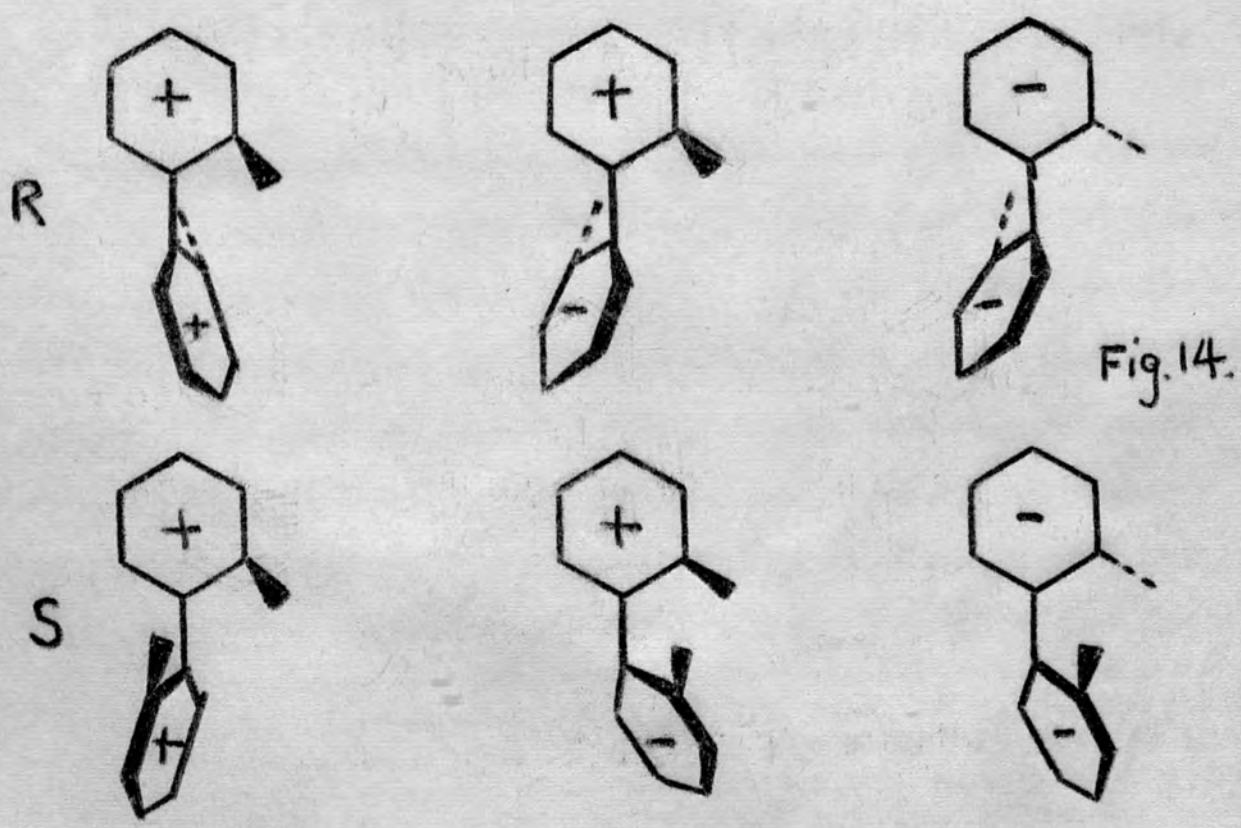

Fig.14.

The writer considers it probable that conformational inversion is fast in comparison to configurational inversion,* and each optical antipode of 2,2'-di-iodobiphenyl in solution will consist of three strained conformers in equilibrium

e.g. R(+)(+) $\rightleftharpoons$ R(+)(-) $\rightleftharpoons$ R(-)(-)

Strain energy is, however, expected to be less than that in 1,1'-binaphthyl-8,8'-dicarboxylic acid, as there is more room for the interfering groups when they are attached in the o-benzenoid positions than when they are in peri-naphthalenic positions; ultimate distortion is likely to be less for the same reason, and also because there are fewer bonds and angles among which strain can be shared.

The Transition State. Consideration of the ground states, and comparison with the case of 1,1'-binaphthyl-8,8'-dicarboxylic acid leads to the conclusion that the transition states for racemisation of 2,2'-di-iodobipheny derivatives have essentially, in the broad sense, planar benzene rings in comparison with the ground state, but with appreciable out-of-plane (as well as in-plane) distortion around the region of the interannular bond. Assuming that the forces

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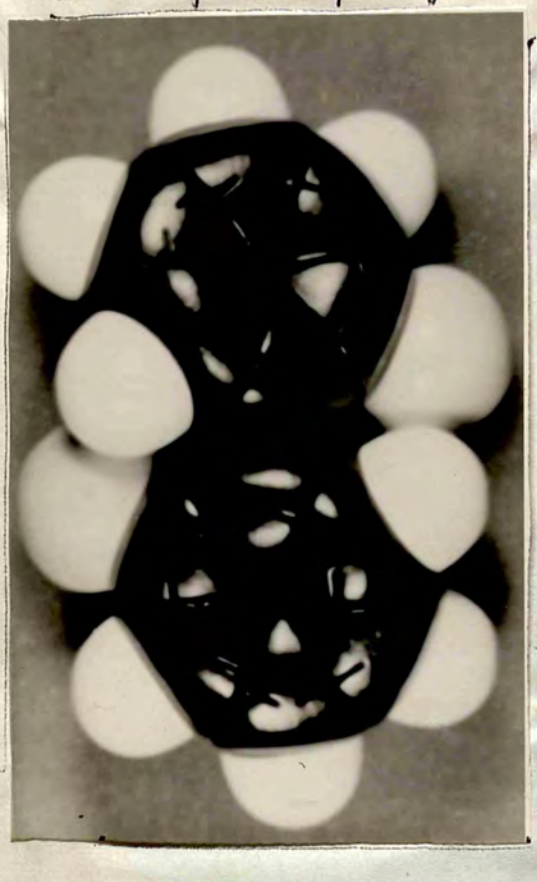
* There is evidence for this in the case of 1,1'-binaphthyl-8,8'-dicarboxylic acid: both k plots and Arrhenius plots are straight within experimental error, and racemisation experiments show complete loss of optical activity resulting in ~~resembling~~ $\alpha=0$. The loss of optical activity arising from the asymmetry of the individual naphthalenic units must therefore be much faster.

opposing racemisation are mainly steric, the transition state will be more crowded and strained than the ground state, and both in-plane and out-of-plane distortions will therefore be greater. The interannular bond will probably be slightly longer. The angle between the two benzene rings (for the mesoid transition state) will not be zero, but nearly so in comparison with the large value of θ in the ground state.

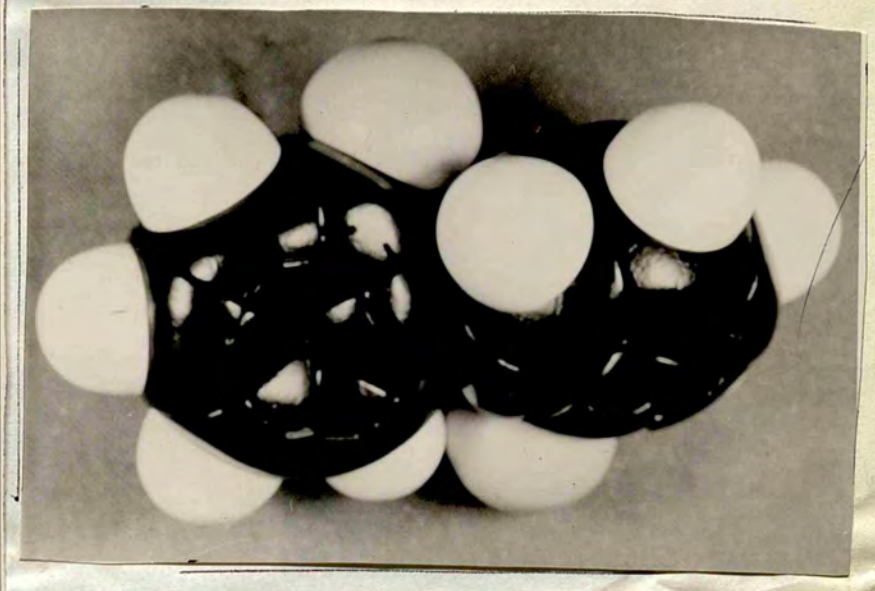
As in the case of 1,1'-binaphthyl-8,8'-dicarboxylic acid, there are two possible R $\rightleftarrows$ S transition paths, racemoid and mesoid, and the latter will be favoured in configurational inversions. The transition states and the mesoid intermediate are shown in diagram 15; the mesoid state and intermediate state are further illustrated by photographs taken on a Leybold model of 2,2'-difluoro-biphenyl. [It is not possible to use the Leybold models, which incorporate a van der Waals envelope and allow for only a small degree of departure from normal angles, to make analogous models of the dichloro- or di-iodo compounds. However, the difluoro model illustrates the steriochemical principal.] (See further discussion on pages 68 ~~and~~ 73)

Fig. 15

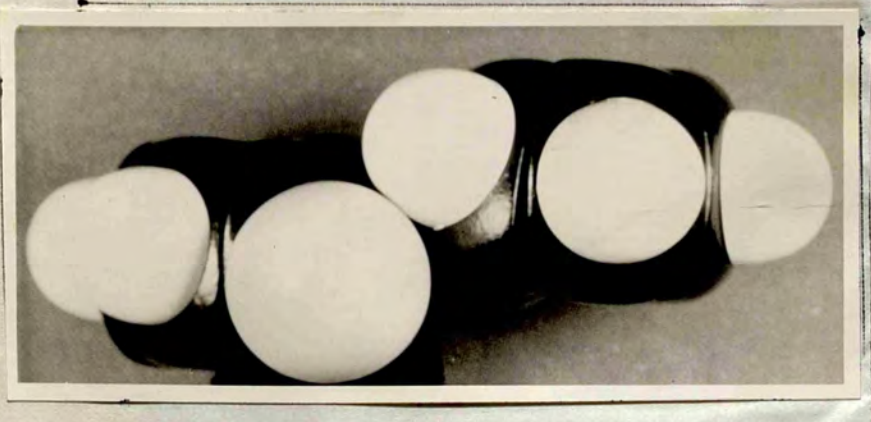
2,2'-difluorobyphenyl



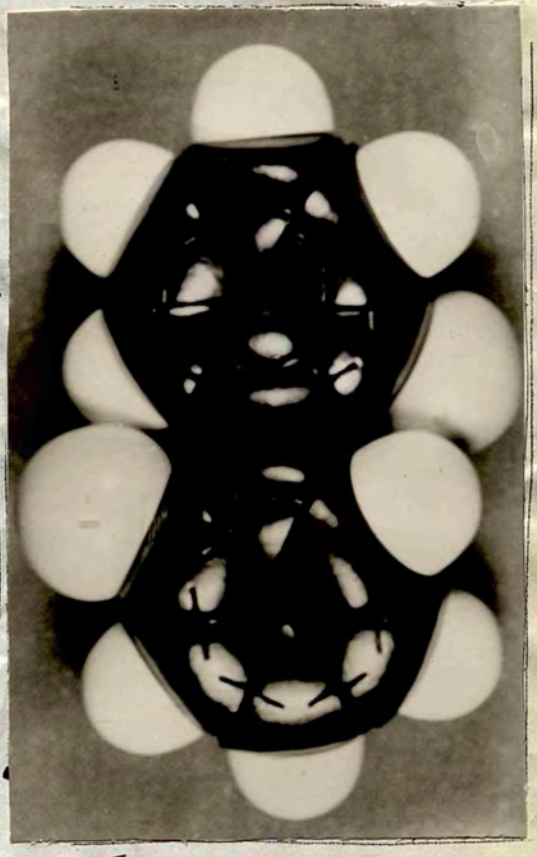
Mesoid Transition State



Side view



↑ Mesoid Intermediate →



Front view

THE ENTROPY OF ACTIVATION. Cagle and Eyring (J.A.C.S., 1951, 73, 5628) attempted the correlation of the entropy of activation for racemisation with structure, from the racemisation data of ten compounds which owed their optical activity to restricted rotation. Their approach aroused great interest. However, the data on which they based their observations were subjected to large experimental errors and were obtained by different workers under different conditions. de la Mare ("Progress in Stereochemistry", Vol.I, Butterworths, London, 1954, p.120) commented that such a correlation should await a considerable extension of the then existing information. More reliable values for the entropy of activation have now been obtained for about fifty compounds which owe their optical activity to restricted rotation, but it still seems difficult to correlate these values with structure, except in very general terms. Our understanding of the entropy of activation in the racemisation of these sterically hindered compounds is still very incomplete at the present time.

With our present knowledge of the entropy of activation, any attempt to estimate the relative entropies of the ground and transition states of 2,2'-di-iodobiphenyl will be inadequate. Such an attempt will not be made.

Experimental values for the entropy of activation are subjected to considerable errors. The entropy of

activation is given by the following equation:

$$\Delta S^{\ddagger} = 4.576 \log_{10} \frac{k}{T} + \frac{E}{T} - 49.20 \qquad (4)$$

An experimental error of $\pm$ 0.5 kcal.mole^{-1} in the energy of activation will result in an error of roughly $\pm$ 1.65 e.u. in the entropy factor, for racemisations in the temperature range 0-60°C. (the error is 1.8 e.u. at 0° and 1.5 e.u. at 60°). Small differences in entropy factors should not, therefore, be regarded as significant.

The entropies of activation for 2,2'-di-iodobiphenyl and its 4,4'-derivatives (Table IV) are of the order of -6 e.u., a value expected of such simple biphenyls (Reiger and Westheimer, J.A.C.S., 1950, 72, 19) and in agreement with those obtained for another three 2,2'-dihalogenobiphenyl derivatives: 2,2'-di-iodobiphenyl-5,5'-dicarboxylic acid, -7.7 e.u; 2,3,2',3'-tetra-iodobiphenyl-5,5'-dicarboxylic acid, -7.6 e.u; and 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid, 4.9 e.u. (Hall and Harris, J., 1960, 490).

4,4'-subs.	H	CO_2H		$NHCOCH_3$	NH_2	$\overset{+}{N}H_3$	CO_2CH_3
Solvent	DMF	aq.NaOH	EtOH	DMF	DMF	DMF	aq.alc.HCl	DMF
$\Delta S^{\ddagger}$ e.u.	-8.2	-7.0	-6.9	-6.1	-5.8	-5.8	-4.3	-4.0

Table IV.

The overall variation in entropy of activation for all the compounds is small: from -8.2 e.u. in the unsubstituted 2,2'-di-iodobiphenyl to -4.0 e.u. in the 4,4'-dicarbomethoxyl

derivative. The comparatively lower entropy factor of 2,2'-di-iodobiphenyl over all the 4,4'-derivatives (in the same solvent) may mean that 4,4'-substitution in general causes a small increase in the entropy of activation of 2,2'-dihalogenobiphenyls.

The entropy of activation for racemisation of 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid is practically the same for racemisation experiments carried out in three different solvents. Tgis indicates either that the obstacle groups (I and H in the o-positions) are not involved in solvation or, if they are, that solvation is the same in the ground state and in the transition state in all three solvents, the former explanation seems to be the most likely one.

THE ENERGY OF ACTIVATION. The difference in activation energy for racemisation of 2,2'-di-iodobiphenyl and its 4,4'-derivatives (as shown in Table III) are small: the actual activation energy values lie between 19.9 and 22,3 kcal.mole^{-1}. The energy of activation of 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid is 21.5 kcal.mole^{-1} in 0.1 aqueous sodium hydroxide, and 21.3 kcal.mole^{-1} in absolute ethanol. The first value agrees closely with the value of 21.6 kcal.mole^{-1} obtained for the racemisation of 2,2'-di-iodobiphenyl-5,5'-dicarboxylic acid in aqueous alcoholic sodium bicarbonate (Reiger and Westheimer, loc.cit.),

while the second value is surprisingly close to the value of 19.0 kcal.mole^{-1} obtained for 2,2'-dibromobiphenyl in absolute ethanol (Harris and Mitchell, loc.cit).

Theoretical calculations for the activation energy of racemisation for both 2,2'-dibromobiphenyl and 2,2'-di-iodobiphenyl have been made by Westheimer (Mayer and Westheimer, loc.cit., Reiger and Westheimer, loc.cit) and by Howlett (loc.cit.). The interaction between the interfering atoms, halogen and ortho-hydrogen was considered. Westheimer obtained the activation energy by minimising the energy of a planar transition state, expressed in terms of the van der Waals potential functions for the interactions of the interfering atoms and in terms of the energy necessary to distort the various bond lengths and angles. Howlett estimated the activation energy by finding the difference between the minimised energy of a planar transition state and the energy of an undeformed orthogonal ground state. He introduced a dipolar interaction term into the expression for the energy of the system, a resonance stabilisation energy of 6.95 kcal.mole^{-1} in the transition state, and used improved van der Waals potential functions for the compressions between the interfering atoms. Westheimer obtained a value of 18 kcal.mole^{-1} for the dibromo-compound and a value of 22.5 (21.4-23.6) kcal.mole^{-1} for the di-iodo compound. Howlett's values are 21 and 27 kcal.mole^{-1} respectively. (private communication, quoted by Cheung and Harris, loc.cit.)

The discrepancy, δE, between experimental and theoretical results is small in the dibromo compound but larger in the di-iodo compound, for both sets of theoretical values. In the following table, the activation energies for 2,2'-di-iodo and 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid in absolute ethanol are compared with the calculated values.

Table V.

2,2'-dihalogeno-biphenyl	E expt. kcal. $mole^{-1}$	Westheimer		Howlett	
		Ecal.	δE=Ecal-Eexp.	Ecal.	δE=Ecal-Eexpt.
di-iodo	21.3	22.5	+1.2	27.0	+5.7
di-bromo	19.0	18	-1	21.4	+2.4
	$\delta E_I - \delta E_{Br}$		2.2		3.3

These discrepancies may be explained, at least in part, by considering the difference between the theoretically assumed geometry of the ground states and the transition states of these 2,2'-dihalogenobiphenyls, and the geometry which is now suggested.

In the theoretical calculations, Westheimer assumed that any steric interactions in the ground state are negligible; Howlett estimated the energy of the orthogonal ground state

by considering interactions between the ortho iodine and hydrogen atoms only. (A value of 1.72 kcal. is attributed to van der Waals interactions and bond deformation, and a value of 0.1 kcal. to dipolar interactions). By analogy with the o-halogeno benzoic acids it has been shown that in the ground state of 2,2'-di-iodobiphenyl there will be considerable interaction between the 2' and 2 o-iodine atoms with the 1 and 1' carbon atoms, resulting in appreciable in-plane and out-of-plane distortion of the C-I bonds and the 1,1'-bond. The ground state energy will therefore be greater than that calculated by Howlett, and the measured activation energy of racemisation will consequently be less.

Both Westheimer and Howlett assumed a planar transition state in their theoretical calculations: the calculated energy of the transition state is minimised with respect to in-plane, but not out-of-plane, bond deformation. The deformation of bond angles calculated by Mayer and Westheimer for the transition state of 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid are given below:

Deformation of interannular C-C-C(H) angle	-3.9°
Deformation of C-C-H angle	$+5.0^{\circ}$
Deformation of C-C-Br angle	$+12.3^{\circ}$

(Steric Effects in Organic Chemistry, Wiley, 1956, p.549). It is only reasonable to suppose that steric interactions leading to an in-plane deformation of as much as 12° in bond angle will also result in out-of-plane deformation of bonds.

The energy of a transition state in which there is both in-plane and out-of-plane distortion will be lower than that of a planar transition state: it will be easier to relieve (partially) the interaction between the ortho bromine and hydrogen atoms by three dimensional bond distortion than by bond distortion restricted to one plane only. Moreover, it has already been shown that the energy of a transition state in which there is out-of-plane distortion at the interfering regions, can be further lowered by racemisation through a mesoid transition path. The postulated transition state would thus have a lower energy than that calculated for a planar one, and the experimentally determined activation energy would be smaller yet than the transition value.

The above considerations concerning strain energy in the ground state, out-of-plane distortion and a consequent mesoid transition path in the transition state, are illustrated by a schematic energy diagram for the process of optical inversion (Fig.16). Neglecting resonance stabilisation in the transition state, the discrepancy in activation energy, δE, between the theoretical and experimental values may be represented by the following equation:

$$\delta E = \delta E_{s.g.} + \delta E_{st.} + \delta E_{r.m.} \quad (5)$$ (See Fig.16)

All the terms on the right hand side of the equation will increase with the size of the 2,2'-substituents. The

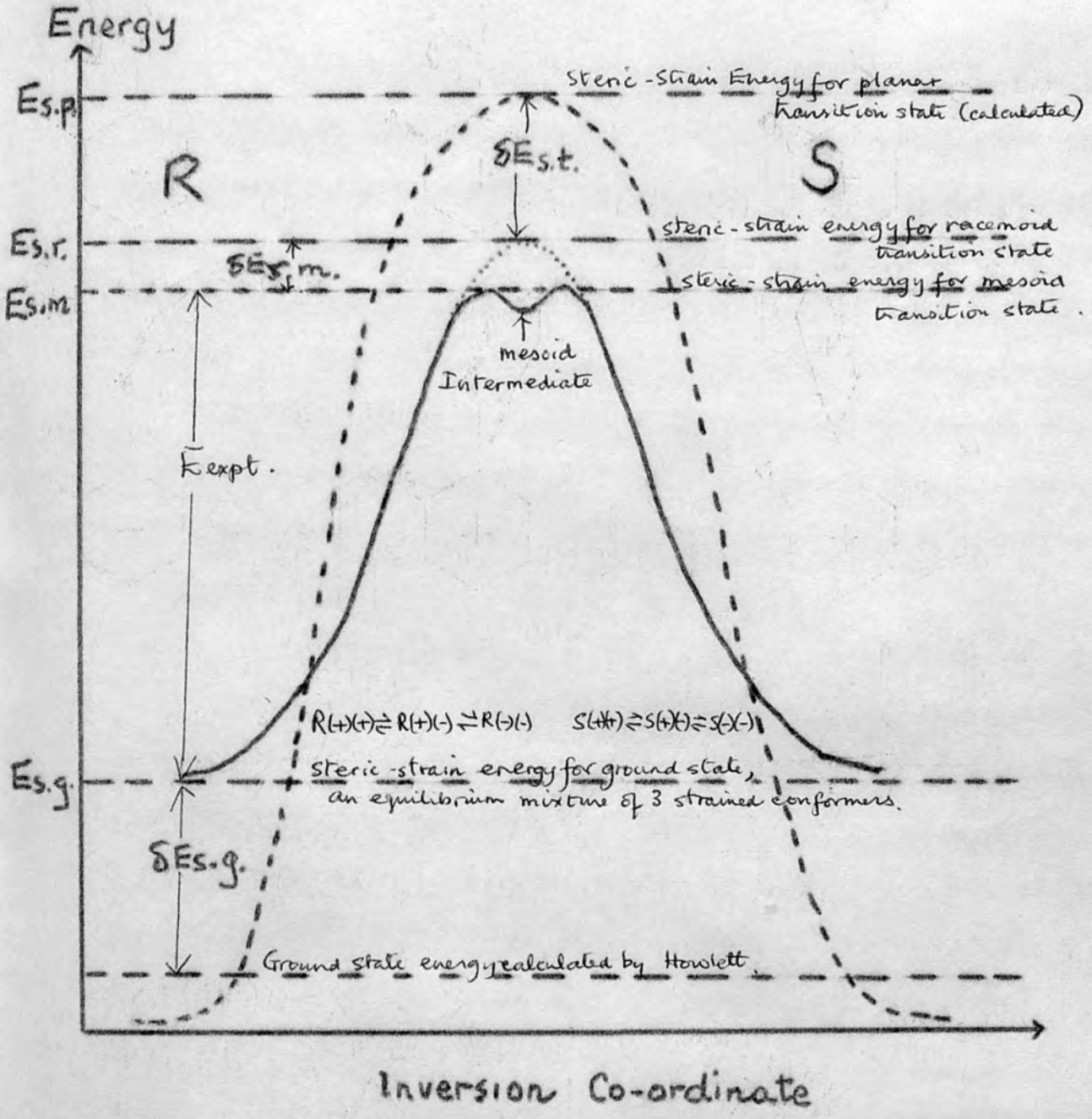


Fig.16. Schematic Energy Profile for the Iversion of 2,2'-di-iodobiphenyl.

δEs.g. = difference in energy between classical and actual ground states.
δEs.t. = " " " " planar and racemoid transition states.
δEr.m = " " " " racemoid and mesoid " ".

discrepancy between experimental and theoretical activation energies will thus be greater in 2,2'-di-iodobiphenyl than in 2,2'-dibromobiphenyl. Moreover, as this lowering of activation energy is greater in the di-iodo compound, its experimentally determined activation energy will be nearer to that of the dibromo compound than normally expected.

If it is assumed that there is some resonance stabilisation energy, Er, in the transition state, the activation energy (experimental) may be represented by the equation

$$E = Es.m. - Es.g. - Er \quad . \quad ①$$ (see p.28)

There is a small, but significant variation in the experimental activation energies of 2,2'-di-iodobiphenyl and its 4,4'-derivatives.

4,4'-substituent	Solvent	E kcal.mole^{-1}	δ'E kcal.mole^{-1}
NH_2	$HCON(CH_3)_2$	19.9	1.0
$NHCOCH_3$	"	20.6	0.3
H	"	20.9	0
CO_2H	C_2H_5OH	21.3	-0.4
$CO_2^-Na^+$	H_2O	21.5	-0.6
CO_2H	$HCON(CH_3)_2$	21.6	-0.7
$\overset{\oplus}{N}H_3Cl^{\ominus}$	H_2O/EtOH	22.2	-1.3
CO_2CH_3	$HCON(CH_3)_2$	22.3	-1.4

Table VI.

As all the racemisation experiments have been carried out by the same worker, using the same technique and the same apparatus, this variation should not be ignored.

There is a difference of 1.4 kcals. between the activation energies of 2,2'-di-iodobenzidine in dimethyl formamide and of 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid inabsolute ethanol, the latter being the more stable of the two. If the same difference in optical stability applies to the corresponding 2,2'-dibromobiphenyl derivatives, the optical stability of 2,2'-dibromobenzidine would be very low, as can be seen from the following table:

Table VII

	biphenyl-4,4'-dicarboxylic acid in abs.ethanol		-benzidine in N,N'-DMF	
	E kcal.mole^{-1}	$\Delta S^{\neq}$ e.u.	E kcal.mole^{-1}	$\Delta S^{\neq}$ e.u
2,2'-di-iodo	21.3	-6.9	19.9	-5.8
2,2'-dibromo	19.0	-4.9	(19.9-2.3=17.6)	(-5.8 + 2.0=-3.8)
	δE = +2.3	$\delta\Delta S^{\neq}$ = -2.0		

(* $t_{\frac{1}{2}}$ at -15.3° for 2,2'-dibromobenzidine is 4.4 min.)
This low optical stability of 2,2'-dibromobenzidine explains, at least in part, the repeated failures in attempting to obtain it optically active.

* $\Delta S^{\neq} = 4.576 \log_{10}\frac{k}{T} + \frac{E}{T} - 49.2$ $\quad \therefore -3.8 = 4.576 \log_{10}\frac{0.6931}{t_{\frac{1}{2}}.257.9} + \frac{17600}{257.9} - 49.2$

$$\log_{10} t_{\frac{1}{2}} = \frac{1}{4.576}\left(3.8 + \frac{17600}{257.9} - 49.2\right) + \log_{10}\frac{0.6931}{257.9} = 4.992 - 2.5706 = 2.421.$$

$$t_{\frac{1}{2}} = \frac{263}{60} \text{ mins} = 4.4 \text{ min}.$$

The variation in activation energy for the series of 4,4'-derivatives of 2,2'-di-iodobiphenyl, as shown in Table VI, shows that groups which can be electron donating decrease the activation energy when placed in the 4,4'-positions, while groups which are electron withdrawing increase it. This means that greater electron availability in the whole system decreases the activation energy for racemisation. Moreover, as 4,4'-substituents directly affect the electron availability at the 1 and 1' carbon atoms,

Fig. 17.

and configurational inversion takes place in the region of the 1,1'-bond (see fig.18), the present set of results suggests that increase in the electron availability at the 1 and 1' carbon atoms decreases the optical stability (Insofar as it decreases the activation energy for racemisation); this observation can be usefully compared with observations made by Baddeley, and by Crawford and Smyth (see p. 31)

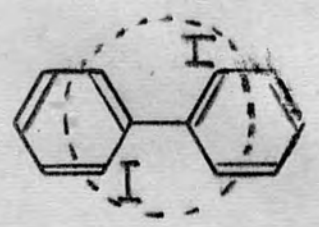


Fig. 18

It is interesting to consider the various factors which may cause this observed decrease in optical stability with increasing electron availability at the 1 and 1' carbon atoms.

One factor which should be considered is resonance involving the 1,1'-bond. Any resonance between the benzene rings in the ground state of 2,2'-di-iodobiphenyl and its derivatives may be ignored: resonance between the rings decreases with increasing angle, θ, between the planes of the benzene rings. Adrian's calculations on the variation of resonance energy with respect to θ in biphenyl show that resonance between the benzene nuclei becomes negligible when $\theta > 70^{\circ}$ (J.Chem.Phys., 1958, 608). θ in 2,2'-di-iodobiphenyl lies beyond this angle. The ultraviolet spectrum of 2,2'-di-iodobiphenyl also shows that there is no conjugation between the two benzene rings (Beaven and Hall, J., 1956, 4639). Conjugation between the benzene rings in planar biphenyl itself is thought to give rise to a resonance energy of only a few kilocalories: Guy (J.Chim.Phys., 1949, 46, 469) estimated a value of 6.95 kcal.mole^{-1} and Wheland a value of 4 kcal.mole^{-1}. Any resonance stabilisation in the transition state of 2,2'-di-iodobiphenyl will be less than these values.

If it is assumed that the steric energies of the ground and transition states, $E_{s.g}$ and $E_{s.m.}$, remain constant

for the series of 2,2'-di-iodobiphenyl derivatives, then the variation in activation energy must be attributed to variation in resonance stabilisation energy. It is worthwhile noting that since resonance between the rings would be favoured by planarity, and would be accompanied by a shortening of the 1,1'-bond, while steric energy is less when there is out-of-plane bond distortion and when the 1,1'-bond is longer, resonance between the benzene rings in the transition state of inversion of o,o'-substituted biphenyls will occur only if the increase in steric energy accompanying it is less than the resonance energy gained. It is not certain how far resonance between the benzene rings can occur in such a distorted transition state as that deduced for 2,2'-di-iodobiphenyl. If there is a resonance stabilisation of 2-3 kcal.mole^{-1} in 2,2'-di-iodobiphenyl itself, and the variations in E are attributable to this alone, then its range of variation, as observed, appears to be remarkably large.

The present set of results, when explained in terms of resonance involving the 1,1'-bond, suggests that resonance between the benzene rings in 2,2'-di-iodobiphenyl is increased by groups which would be op-directing to electrophilic reagents, but decreased by m-directing groups in the 4 and 4'-positions. It seems reasonable to make a

comparison with biphenyl derivatives which do not carry the o-halogen atoms. Conjugation of the 1,1'-bond in biphenyl has been much studied by ultra violet spectroscopy. The ultra violet spectra of biphenyl derivatives show that all 4,4'-substituents investigated, including the amino and carbethoxy groups, increase the conjugation of the 1,1'-bond (Williamson and Rodebush, J.A.C.S., 1941, 63, 3018). This has been explained in terms of the ability of all 4,4'-substituents to be involved in reasonance with the whole biphenyl nucleus.

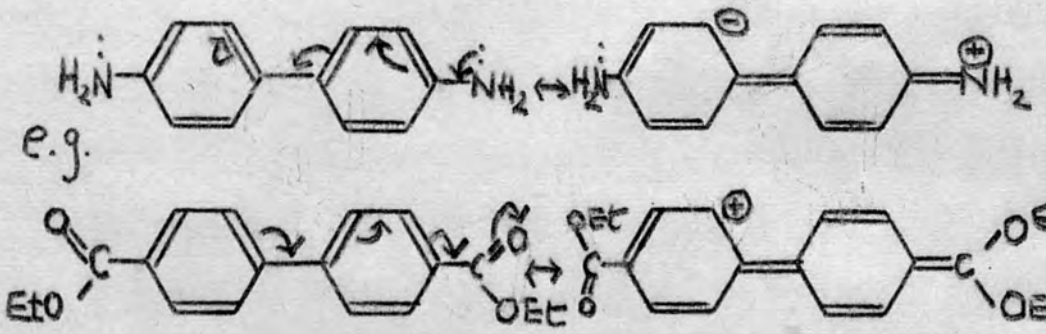


Fig. 19.

By analogy, an increase in resonance energy, in the transition state, owing to the inclusion of canonical forms of the type

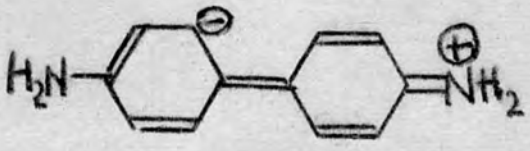


Fig. 20

does not, therefore, appear to give an adequate explanation for the observed variation in activation energy of the series of 4,4'-derivatives of 2,2'-di-iodobiphenyl studied.

In the spectra of 4,4'-biphenyl derivatives, any relationship between the op- and m-directing character of the 4,4'-substituents on the conjugation of the 1,1'-bond is marred by the overal increase in conjugation which has been described. It appears that if there be any difference in resonance energy with respect to op- and m- directing nature of substituent groups, these differences would be very small in comparison with the overall resonance energy in the 4,4'-biphenyl derivatives.

Other ultraviolet spectroscopic evidence suggests that the conjugation of the 1,1'-bond in biphenyl is related to the degree to which substituents interact with the individual benzene nuclei, rather than to the op- or m-directing character of the substituents: both ethyl and methoxy groups are op-directing, the former owing to its small positive inductive effect, while the latter to its strong mesomeric effect (which predominates over its negative inductive effect); however, the spectra of 3,3'-diethyl and 3,3'-dimethoxybiphenyl show that while the ethyl group has little effect upon the conjugation of the 1,1'-bond in biphenyl, the methoxy group greatly reduces it (Everitt, Hall, and Turner, J., 1956, 2286). The spectra of bridged biphenyls show that there is still considerable conjugation across the 1,1'-bond, even though the two benzene rings are not coplanar, but kept in a twisted position by the o,o'-bridge

(Beaven, Hall, Lesslie, and Turner, J., 1952, 854); in these compounds, two ortho methoxy groups would have little steric effect, the effect of these groups on the spectra of these compounds should be mainly electronic in character, and the effect of their op-directing nature on the 1,1'-bond, should be in the opposite direction to that of m,m'-methoxy groups; the spectra of o,o' and m,m'-dimethoxy-bridged biphenyls are, however, essentially the same, (Beaven, Hall, Lesslie, Turner and Bird, J., 1954, 131).

From the above considerations, it appears that to explain the observed variation of E in terms of resonance involving the 1,1'-bond would be inconsistent with spectroscopic evidence. An alternative explanation must be sought which accounts for the correlation between increased electron availability and lowering of the energy of activation for racemisation.

Crawford and Smyth's (loc.cit.) suggestion, that of an attack of a proton at the 1 or 1' carbon atom giving the necessary freedom for overcoming the steric barrier, would be supported were it not that it is found that 2,2'-di-iodobenzidine racemises faster in N,N'-dimethylformamide than in N/2 aqueous alcoholic hydrochloric acid, i.e. in the presence of protium cations. It may be argued that the $\overset{+}{N}H_3$ group would deactivate the aromatic nucleus, and thus decrease the rate of racemisation. However, under similar conditions,

aniline would still be highly reactive towards eletrophilic reagents, and the NH_2 group is forced to behave as the m-directing NH_3 group only under strongly acid conditions, e.g. in conc. sulphuric acid.

Baddeley's (Nature, 1946, 157, 694) suggestion that the development of a tetrahedral 1 or 1' carbon atom plays an important part in facilitating racemisation, appears to assist in the explanation of the present set of results. In an attempt to explain the relative optical stability of compounds X-XV, he wrote: "Fischer models of these diphenyl derivatives show that the rotation required for racemisation encounters much less obstruction when the bond joining the two rings is displaced from the plane of one of them by the introduction of a tetrahedral carbon atom. The displacement is shown in the diagram

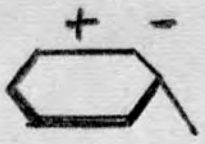


Fig 21.

and its occurrence must depend on the ability of the carbon atom at which it occurs to acquire a negative charge, for the configuration is that of a negatively charged carbon atom. If such a displacement plays a part in facilitating racemisation, the displacement will occur in the ring of greater electron density and the rate of racemisation will be related to the electron density in this ring." (ibid, quoted).

Baddeley's suggestion has been taken to mean one fully developed tetrahedral carbon atom in the transition state of racemisation (Crawford and Smyth, loc.cit.) and it seems from the above quotation that this interpretation is justified. The electron distribution in the transition state of compound X would then be represented by Fig.22.

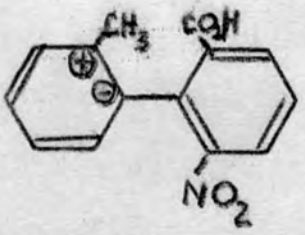


Fig.22.

In the Introduction (p. 31) it has been shown that the experimental data on which Baddeley based his theory were not really valid, owing to the large experimental errors involved, and to the presence of other factors which would affect the optical stability of the compounds concerned. However, in view of the present set of experimental results, it appears that Baddeley's idea is worth considering. The writer thinks it improbable that a fully developed tetrahedral 1 or 1' carbon atom should occur in the transition state of racemisation, but believes that racemisation is facilitated by out-of-plane bond distortion at the 1 and 1' carbon atoms (for all the optically active biphenyl derivatives - symmetrically substituted - examined on connection with the present study) which is in turn facilitated by greater

electron availability at these carbon atoms. The electron distribution in the transition state of 2,2'-di-iodobenzidine would be represented by Fig.23.

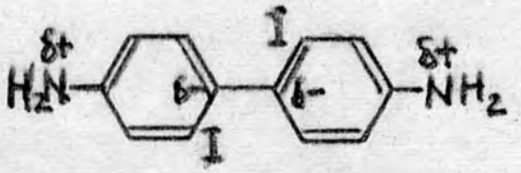


Fig. 23

These ideas are developed in the remaining section of the discussion.

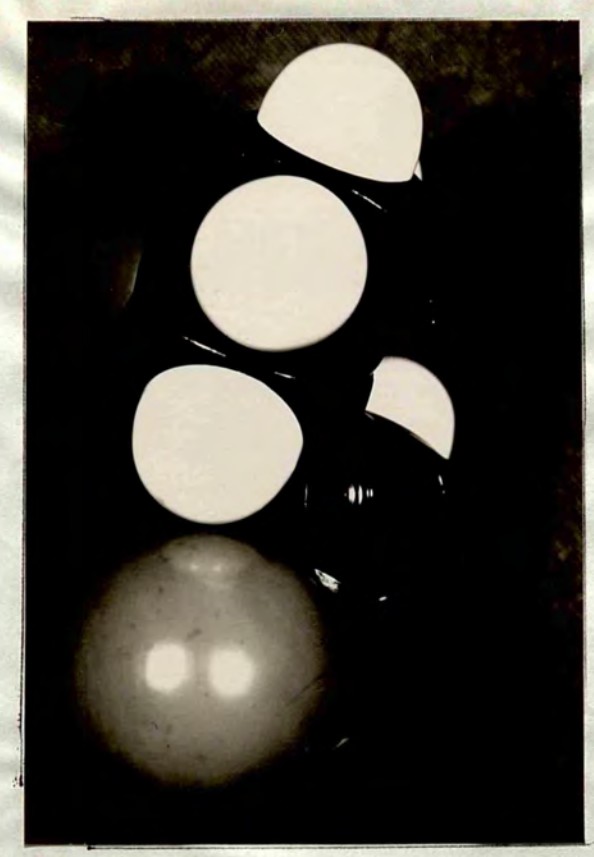
It has already been seen that in 2,2'-di-iodobiphenyl, steric interactions in the transition state would result in considerable out-of-plane (as well as in-plane) bond distortion in the region of the 1,1'-bond (bond distortion being greater than that in the ground state). This point may be further illustrated by photographs taken on Leybold models of 2,2'-di-iodobiphenyl.

(a) a model of the classical 2,2'-di-iodobiphenyl molecule is not racemisable.

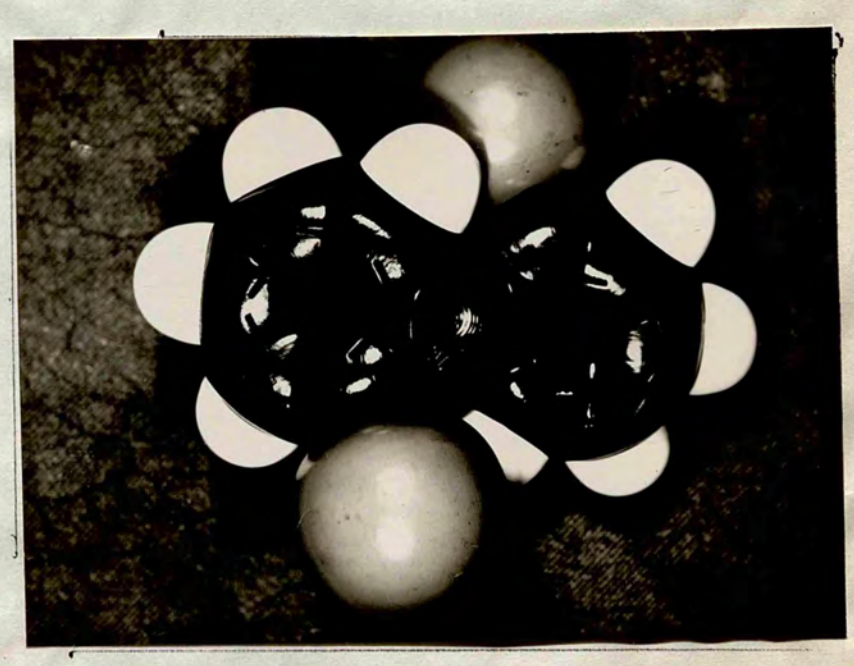
(b) a model of 2,2'-di-iodobiphenyl in which sp^3 carbon atoms are used in both the 1 and 1' positions is readily racemisable through the mesoid transition path (but not through the racemoid path).

Bond distortion in the transition state of racemisation is brought about by the severe van der Waals interaction, mainly between the ortho hydrogen and ortho

Photographs of a model of 2,2'-di-iodobiphenyl in which sp^3- C- atoms are inserted in the 1 and 1'-positions.



Mesoid
Transition State.



Mesoid
Intermediate

iodine atoms. The steric energy due to van der Waals interaction, and the strain energy due to bond distortion are interrelated: van der Waals interaction is partially relieved by bond distortion, which gives rise to a certain amount of strain energy. The transition state represents the optimum condition when the van der Waals interaction and bond distortion in the region of the 1,1'-bond are such as to give a minimum "steric strain" energy, required for the ortho hydrogen and iodine atoms to pass each other. When considerable out-of-plane bond distortion at one or more of the benzenoid carbon atoms is allowed, the consequent loss of resonance energy in the individual benzene ring(s) concerned must also be considered. For example, one fully developed sp^3 carbon atom would mean a loss of resonance energy equivalent to that of benzene.

Fig. 24

Therefore, to a first approximation, the transition state of racemisation will be one in which energy is minimised with respect to van der Waals interaction, three dimensional bond distortion, as well as loss in resonance energy.

It will be difficult to determine the exact geometry of such a transition state. However, it seems reasonable to suppose that, if out-of-plane bond distortion is allowed at the 1 and 1' carbon atoms, the configuration of these carbon atoms will lie between that of an sp^2 and that of an sp^3 carbon atom: sp^2 carbon atoms would mean very severe van der Waals interactions between the ortho hydrogen and iodine atoms in the transition state, while fully developed sp^3 1 and 1' carbon atoms would mean a loss of 2 x 36 kcals. of resonance energy.

Insofar as steric interactions between the ortho hydrogen and iodine atoms in the transition state of 2,2'-di-iodobiphenyl derivatives can bring about considerable out-of-plane bond distortion at the 1 and 1' carbon atoms, which can facilitate racemisation, increase in electron availability for the whole biphenyl system should increase the rate of racemisation: out-of-plane bond distortion at a carbon atom is associated with a certain amount of sp^3 character, and a fully developed sp^3 1 or 1' carbon atom in biphenyl is one which carries a negative charge, the energy required for out-of-plane bond distortion will be less the higher the electron availability at the carbon atom concerned.

The above arguments appear to prove a reasonable explanation for the observed decrease in activation energy with increasing electron availability at the 1 and 1' carbon

atoms in 2,2'-di-iodobiphenyl and its 4,4'-derivatives. It is interesting to note that out-of-plane bond distortion at the carbon atoms carrying the iodine atoms can also lower the energy barrier to racemisation. A Leybold model of 2,2'-di-iodobiphenyl in which the 2- and 2'- carbon atoms have an sp^3 configuration appears to be even more easily racemised than one in which the 1 and 1' carbon atoms have an sp^3 configuration. It seems reasonable to suggest that the racemisation of 2,2'-di-iodobiphenyl derivatives and similar biphenyls is facilitated by the development of some sp^3 character in the 1,1',2 and 2' carbon atoms. It would be of interest to determine the activation energies of a similar series of 5,5' derivatives of 2,2'-di-iodobiphenyl. Assuming that the negative inductive effect (Fig.25a) of the iodine atom is only small, and that its mesomeric effect (Fig.25b) does not operate to an appreciable extent during racemisation,

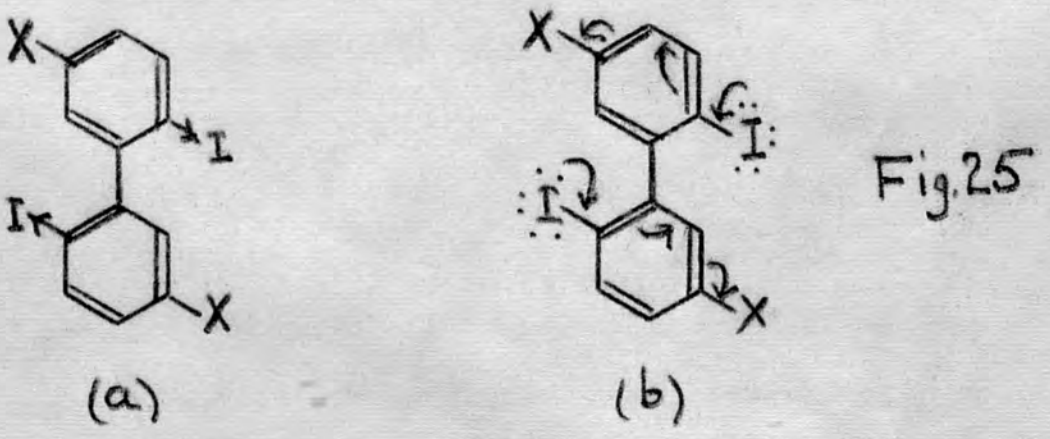
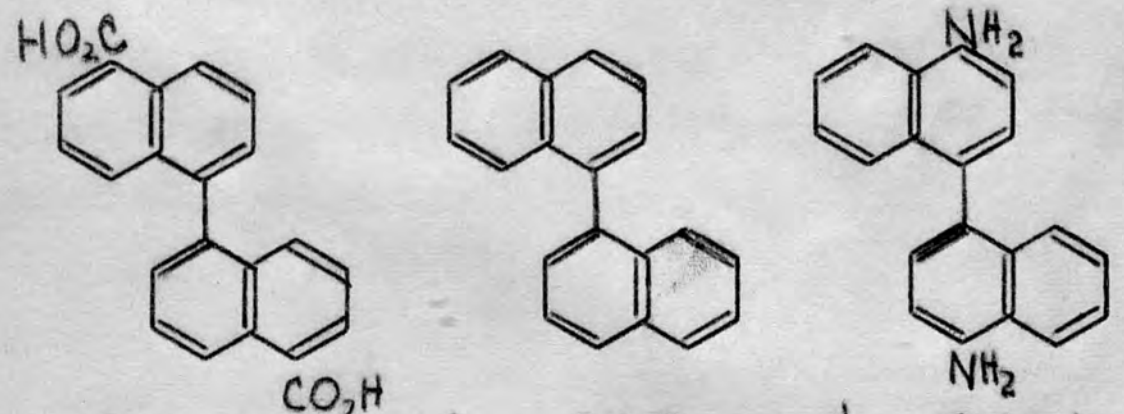


Fig.25

the variation in activation energy should be in the same order and roughly of the same (or slightly larger) magnitude

as that in the 4,4'-derivatives, if the above suggestion is correct (though complications may arise as a result of the buttressing effect of the 5 and 5' substituents on the 6 and 6' hydrogen atoms). If, on the other hand, resonance involving the 1,1'-bond is a sufficient explanation for the observed variation in activation energy with electron availability, the range of variation in the 5,5'-derivatives should be appreciably smaller, since in comparison with substituents in the 4 and 4'-positions, substituents in the 5 and 5' positions can have only little influence upon the 1,1'-bond.

The only 5,5'-derivative of 2,2'-di-iodobiphenyl that has been investigated in this way is the 5,5'-dicarboxylic acid (Reiger and Westheimer, loc.cit.). It has already been pointed out that its activation energy is close to that of the corresponding 4,4'-derivative. This appears to support the suggestion which is now put forward. The activation energies of racemisation of some 1,1'-binaphthyl derivatives appear also to support this suggestion:



E = 24.1 kcal. mole^{-1} 22.5 kcal. mole^{-1} 21.4 kcal. mole^{-1}

The effect of the 5,5'-carboxyl groups on the electron availability at the 8,8' carbon atoms (which carry the blocking hydrogen atoms) is the same as that of 4,4'-carboxyl groups on the 1 and 1' carbon atoms (Fig.26a); however, the influence exerted by the 5,5'-carboxyl groups on the conjugation of the 1,1'-bond must be less than that exerted by 4,4' carboxyl groups (Fig.26b).

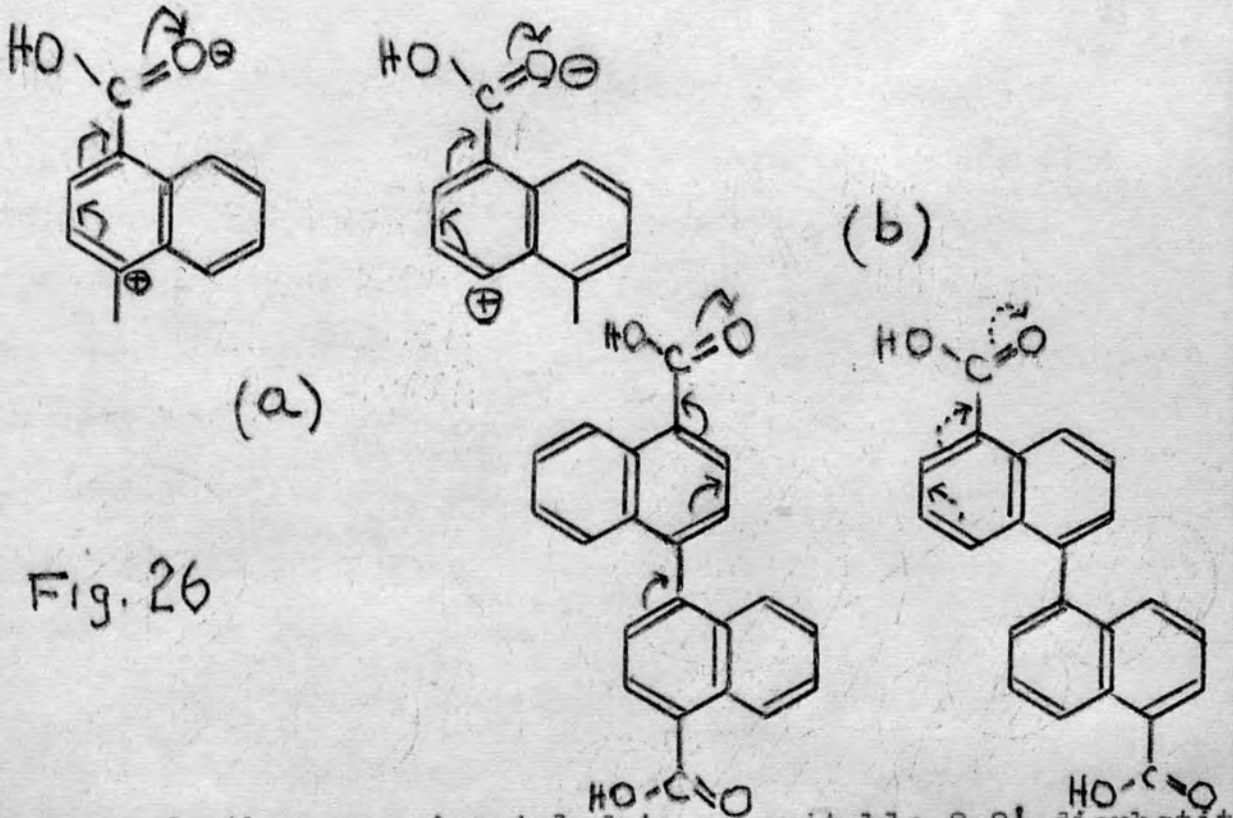


Fig. 26

However, further experimental data on suitable 2,2'-disubstituted biphenyl derivatives must be obtained before any reliable conclusions can be drawn.

OPTICAL WORK - EXPERIMENTAL.

Attempts to obtain the 2,2'-dibromobiphenyl derivatives in their optically active condition failed.

2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid was obtained optically active by second order asymmetric transformation of its dibrucine salt in ethanol (S.V.R.) and 2,2'-di-iodobenzidine by second order asymmetric transformation of its di-hydrogen tartrate in the same solvent. Appropriate reactions carried out on the optically active base and the optically active acid at low temperatures provided 2,2'-di-iodobiphenyl, its 4,4'-dicarbomethoxy and its 4,4'-diacetamido derivative in their optically active condition.

Racemisation procedure. All polarimetric readings were taken on the mercury green line 5461A.

Polarimetric measurements above 20°C were made using a 2-dm. jacketted tube: the temperature was kept constant by a fast stream of water circulated round the polarimeter tube by a Braun circotherm pump from a large Dewar flask; a standardised thermometer (-10 to 110°C), marked to 1°, was fitted into the stopper of the polarimeter tube so that the temperature of the solution could be read throughout the experiment. For temperatures below 20°C,

a specially constructed heavily lagged 2-dm. tube, described by Harris and Mitchell (J., 1960, 1905) was used; the coolant was methylated spirit pumped from a "Colora" refrigerated thermostat, and a standardised thermometer (-40 to +40°C) marked to 0.5° was used. An accurate clock marked in minutes and seconds was used for all the racemisation and mutarotation experiments.

The solvents used in the racemisation experiments include (a) absolute ethanol, (b) N,N'-dimethyl formamide, B.D.H. sample redistilled, b.p. 152-3°, (c) 0.1N aqueous sodium hydroxide solution (sufficient sodium hydroxide was present to make the full sodium salt of the acid), and (d) 0.5N aqueous alcoholic hydrochloric acid, obtained by making up 250 c.c. of N hydrochloric acid to 500 c.c. with ethanol (S.V.R.)

The optically active solid was weighed on a piece of shiny paper, (the amount of solid used varied from 0.12 to 1 g., according to the specific rotation of the sample) and added to a measured volume (about 17 c.c.) of the solvent in a conical flask. The clock was started as soon as the solid was added. The conical flask was swirled until all the solid had dissolved, and the solution filtered into the polarimeter tube, already maintained at the required temperature. Polarimeter readings were taken as soon as possible, and then at

frequent intervals throughout the experiment. An observation was made much later to ensure that the final rotation of the solution was zero for each racemisation experiment.

Calculations. To obtain the rate coefficient for racemisation at one temperature, the logarithm of the angle of rotation, α_t , was plotted against the time t.

$$k = -\frac{1}{t} \ln \left| \frac{\alpha_t - \alpha_\infty}{\alpha_0 - \alpha_\infty} \right|$$

$$= -\frac{2.303}{t} \log_{10} \left| \frac{\alpha_t - \alpha_\infty}{\alpha_0 - \alpha_\infty} \right|$$

$$\log_{10} \frac{\alpha_t - \alpha_\infty}{\alpha_0 - \alpha_\infty} = \frac{-k}{2.303} t$$

$$\log_{10} |\alpha_t - \alpha_\infty| = \frac{-k}{2.303} t + \log_{10} |\alpha_0 - \alpha_\infty|$$

The half-life period $t_{\frac{1}{2}}$ was obtained from the corresponding rate coefficient, using the equation

$$t_{\frac{1}{2}} = \frac{\ln 2}{k} = \frac{0.6931}{k}$$

Over six rate coefficients at different temperatures, covering a range of 20-30°, were obtained for the racemisation of each compound in a given solvent.

The Arrhenius parameters E and $\log_{10}A$, and the transition state theory functions $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta F^{\ddagger}$ for each racemisation process, were obtained graphically. E and $\log_{10}A$ were obtained by plotting the logarithm of the rate coefficient k against the reciprocal of the absolute temperature $^1/T°K$ (0°C is taken as 273.2°K).

$$k = A e^{\frac{-E}{RT}}$$

$$\log_{10} k = \frac{-E}{2.303R} \cdot \frac{1}{T} + \log_{10} A$$

$$\therefore E = -4.576 \times \text{gradient}$$

$\log_{10}A$ was calculated from the above equation, using any point on the graph.

$\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ & $\Delta F^{\ddagger}$ were obtained by plotting $\log_{10} k/T$ against $1/T°k$. The Glasstone, Laidler & Eyring equation gives

$$k = e \cdot \frac{kT}{h} \cdot e^{\frac{\Delta S^{\ddagger}}{R}} \cdot e^{\frac{-\Delta H^{\ddagger}}{RT}} \quad \text{(see p. 20)}$$

$$\therefore \log_{10} k = \log_{10} \frac{ke}{h} + \log_{10} T + \frac{\Delta S^{\ddagger}}{2.303R} - \frac{\Delta H^{\ddagger}}{2.303RT}$$

$$\log_{10} k/T = \frac{-\Delta H^{\ddagger}}{4.576} \cdot \frac{1}{T} + \log_{10} \frac{ke}{h} + \frac{\Delta S^{\ddagger}}{4.576}$$

$$= \frac{-\Delta H^{\ddagger}}{4.576} \cdot \frac{1}{T} + 10.319 + \frac{\Delta S^{\ddagger}}{4.576}$$ (equation given by Cagle and Eyring, J.A.C.S, 1951, 73, 5628)

$$\therefore \Delta H^{\ddagger} = -4.576 \times \text{gradient}$$

$\Delta S^{\ddagger}$ was calculated from the above equation by using any point on the graph. $\Delta F^{\ddagger}$ at a given temperature (25°C) was calculated from the equation

* $\Delta F^{\ddagger} = 47.22T - 4.576T \log_{10} k/T$ (Hall and Harris, J., 1960, 494) using the relevant point on the graph of $\log_{10} k/T$ against $\frac{1}{T^{\circ}K}$

The Arrhenius parameters were also obtained by using the method of least squares, (Hammett: Introduction to the study of Physical Chemistry, New York, McGraw-Hills; p.410) which gives for an equation of the form $y = a + bx$

$$a = \frac{\Sigma x^2 \Sigma y - \Sigma x \Sigma yx}{n\Sigma x^2 - (\Sigma x)^2} \qquad b = \frac{n\Sigma xy - \Sigma x \Sigma y}{n\Sigma x^2 - (\Sigma x)^2}$$

Writing the Arrhenius equation in this form, we have

$$\frac{1}{T} = \frac{2.303R}{E}\log_{10} A - \frac{2.303R}{E}\log_{10} k$$

where $x = \log_{10} k$, $y = \frac{1}{T}$, $b = \frac{-2.303R}{E}$ & $a = -b\log_{10} A$

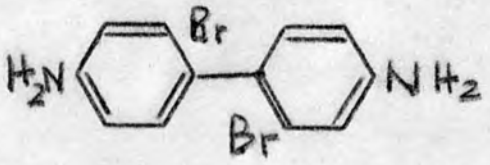
$$\therefore E = \frac{-2.303R}{b} = \frac{-4.576(n\Sigma xy - \Sigma x\Sigma y)}{n\Sigma x^2 - (\Sigma x)^2} \qquad \log_{10} A = -a/b = \left(\frac{\Sigma x^2 \Sigma y - \Sigma x \Sigma xy}{n\Sigma xy - \Sigma x \Sigma y}\right)$$

---

* $\log_{10} k/T = \frac{-\Delta H^{\ddagger}}{4.576T} + 10.319 + \frac{\Delta S^{\ddagger}}{4.576}$

$4.576 \log_{10} k/T = -\Delta H^{\ddagger} + 10319 \times 4.576T + T\Delta S^{\ddagger}$

$\therefore \Delta F^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger} = 47.22T - 4.576T \log_{10} k/T$

2,2'-dibromobenzidine. 

(A). Preparation of di-hydrogen tartrate. - 1.15 g. (1M) of 2,2'-dibromobenzidine and 1 g. (2M) of (+)-tartaric acid were dissolved in 50 c.c. of ethanol (S.V.R.) and the hot solution filtered. 1.3 g. of crystalline needles, m.p. 163-4° (decomposition) separated on standing. The analysis results were in poor agreement with those required for the di-hydrogen tartrate, but showed that the salt contained two molecules and not one molecule of tartaric acid. (Found: C, 37.1; H, 4.5; N, 4.2; Br, 24.6. $C_{20}H_{22}O_{10}N_2Br_2$ requires C, 39.4; H, 3.6; N, 4.6, Br, 26.2%)

The salt has a small specific rotation and a small temperature coefficient. $[\alpha]^{25^\circ}_{5461}$ + 0.8, $[\alpha]^{40^\circ}_{5461}$ + 1.9 in acetone; and $[\alpha]^{-25^\circ}_{5461}$ -6.1, $[\alpha]^{20^\circ}_{5461}$ 0 in N,N'-dimethyl-formamide. No- mutarotation was observed.

On concentrating the mother liquor, another 0.6 g. of crystalline needles, identical with the first crop, ~~w.r.t.~~ in melting point, and optical rotation, was obtained.

The base liberated by grinding the salt with cold aqueous ammonia has m.p. 151-3°, and was optically inactive: polarimetric readings were taken in acetone at room temperature and at -40°.

(B) Preparation of di-mandelate. (failed): - 1.15 g. (1M) of 2,2'-dibromobenzidine and 1.5 g. (2M) of (-) mandelic acid were dissolved in 20 c.c. of ethanol (S.V.R.) No salt separated after standing at room temperature for three days.

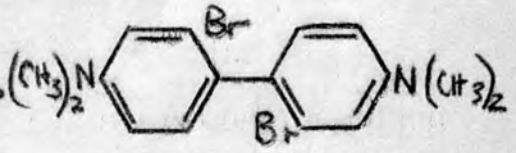
The solution was warmed and water was gradually added to effect crystallisation. The crystals which separated had m.p. 151-3°, and were found to be 2,2'-dibromobenzidine itself. The base so obtained was optically inactive at -25° in N,N'-dimethylformamide.

(C) Preparation of mono-(+)camphor-10-sulphonate. (Searle and Adams, J.A.C.S., 1934, 56, 2112). - 2,2'-dibromobenzidine (1.7 g., 1M) was dissolved in 10 c.c. of hot methanol, and the solution was added to (+)camphor-10-sulphonic acid (1.15 g., 1M) in 6 c.c. of the same solvent. 2.5 g. of fine needles, m.p. 219-220°, separated.

Recrystallisation of the salt from 50% aqueous methanol gave white silky needles, m.p. 211-215°. The rotation of this sample of the salt was taken in 75% aqueous acetone at -1°C. No mutarotation was observed.

(D) Di-(+)-α-bromocamphor-π-sulphonate: (Searle and Adams, ibid.) 2,2'-dibromobenzidine (1.7 g., 1M) was dissolved in 25 c.c. of acetone. 100 c.c. of dilute hydrochloric acid (containing 10 c.c. of 2N acid) were added, followed

immediately by the addition of a solution of ammonium-α-bromocamphor-π-sulphonate (3.3 g., 2M, in 20 c.c. of water).

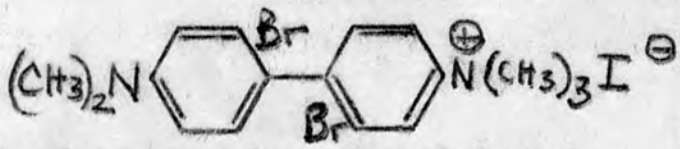
N,N'-tetramethyl-2,2'-dibromobenzidine. 

Attempts were made to obtain the di-hydrogen tartrate and the α-bromo-camphor-π-sulphonate. In both cases, the base itself crystallised out.

Experiment with (+)-tartaric acid. 0.4 g. (1M) of N,N'-tetramethyl-2,2'-dibromobenzidine were dissolved in hot ethanol (S.V.R.), and mixed with a solution containing 0.3 g. (2M) of (+) tartaric acid in the same solvent. 0.35 g. of base, melting first at 175°, and then at 183°, crystallised out as white needle-like prisms.

Experiment with ammonium (+)-α-bromo-camphor-π-sulphonate. 0.4 g. (1M) of N,N'-tetramethyl-2,2'-dibromobenzidine was warmed with 1.1 c.c. of dilute hydrochloric acid (2M), 7 c.c. of water and 25 c.c. of acetone. To this solution, 0.72 g. (2M) of ammonium-(+)-α-bromocamphor-π-sulphonate in 3 c.c. of water was added. On cooling, first at room temperature and then in the refrigerator, 0.34 g. of the base, melting first at 173°, and then at 183°, separated as greyish-white crystals.

2,2'-dibromo-4'-[N,N'-dimethylamino]-biphenyl-4-yl-trimethyl ammonium iodide.

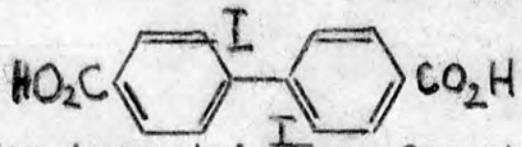


Preparation of (+)-α-bromocamphor-π-sulphonate. 0.54 g. (1M) of the methiodide was dissolved in 35 c.c. of aqueous ethanol (80% by vol. of S.V.R. ethanol and 20% by vol. of water), and a concentrated solution containing 0.42 g. (1M) of silver (+)-α-bromocamphor-π-sulphonate was added. The silver iodide which precipitated was made to coagulate by boiling the suspension for 5-10 minutes, and then filtered on a sintered glass funnel, under gentle suction. The filtrate was evaporated to dryness on a water bath. A solid glass was obtained. This solid glass was soluble in methanol, ethanol and ethyl acetate, but when treated with benzene, it first turned into a gum and then gradually solidified. 0.6 g. of solid was obtained after treatment with benzene. The solid softened at 138°, resolidified, and melted at 191°. It was soluble in methanol and ethanol, but insoluble in ethyl acetate. Attempts to recrystallise this solid from the ordinary organic solvents, including a mixture of methanol and ethyl acetate, failed.

The optical rotation of this solid was observed at +1.5° in methyl alcohol. No mutarotation was observed.

Further investigation on this compound was not carried out owing to shortage of time.

2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid.



Second Order Asymmetric Transformation of the dibrucine salt.

6 g. (1.2M) of 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid and 9.6 g. (2.4M) of anhydrous brucine were dissolved in 500 c.c. of ethanol (S.V.R.) and the solution allowed to stand at room temperature for several days. 15.4 g. of crystalline dibrucine salt, m.p.180-215° (decomp.) were obtained.

The optical rotation of the dibrucine salt was measured in solvent X (chloroform containing 2½% by vol. of ethanol) at 26.7°. Mutarotation was observed. $k^{26.7^\circ}$ = 0.014 min.$^{-1}$. The specific rotation as obtained by extrapolation of the graph of $\log_{10}\alpha_t$ against t is $[\alpha]^{26.7^\circ}_{5461}$ -33°.

To obtain the active acid,

3.35 g. of the dibrucine salt were stirred with 98% formic acid for about 2 minutes, and the solution poured with stirring into a mixture of ice and conc. hydrochloric acid. The precipitate which separated was filtered, washed with cold dilute hydrochloric acid (until free from brucine), water and then dried in vacuo over calcium chloride. 1.2 g. of white powder, m.p.333-6°, were obtained. (Found: C, 33.7; H, 1.7; I, 51.4%. $C_{14}H_8O_2I_2$ requires C, 34.0; H, 1.6; I, 51.4%).

Racemisation experiments were carried out at different temperatures in 3 different solvents: absolute ethanol, N,N'-dimethyl formamide and 0.1N aqueous sodium hydroxide.

Determination of rate coefficients for the racemisation of

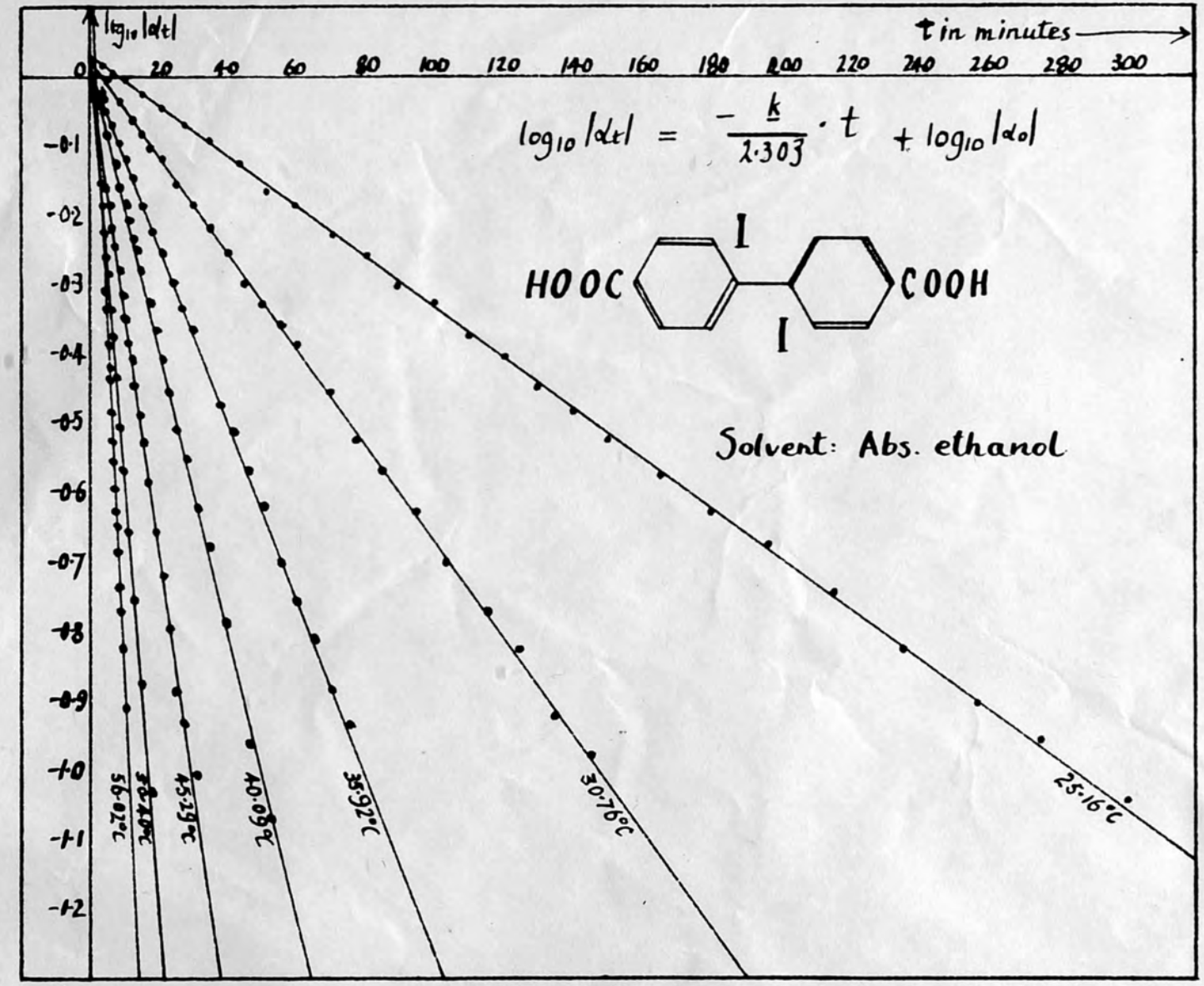
2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid.

Solvent: absolute ethanol.

Concentration: about 0.14 g. in 17 c.c. of solvent.

$[\alpha_o]_{5461}$ by extrapolation: -61^o — -67^o.

Temperature	Time of 1st reading after wetting	First Reading	No. of readings	Time during which readings were taken	$\underline{k} \times 10^{-4}$	$t_{\frac{1}{2}}$
^oC	min.	deg.		min.	$sec.^{-1}$	min.
25.16	4.0	-1.04	27	300.34	1.38	83.6
30.76	5.1	-0.99	23	144.5	2.66	43.4
35.92	4.1	-0.93	22	75.0	4.90	23.6
40.09	3.9	-0.94	20	52.8	7.84	14.7
45.29	5.1	-0.69	19	31.6	13.37	8.6
50.40	3.2	-0.71	14	18.2	22.61	5.1
56.02	3.9	-0.60	18	10.6	39.60	2.9


$\log_{10}|dx/t|$
t in minutes
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
-0·1
-0·2
-0·3
-0·4
-0·5
-0·6
-0·7
-0·8
-0·9
-1·0
-1·1
-1·2
$\log_{10}|dx/t| = -\frac{k}{2.303} \cdot t + \log_{10}|a_0|$
HOOC
I
I
COOH
Solvent: Abs. ethanol
25·16°C
30·76°C
35·92°C
40·09°C
45·39°C
50·24°C
56·02°C

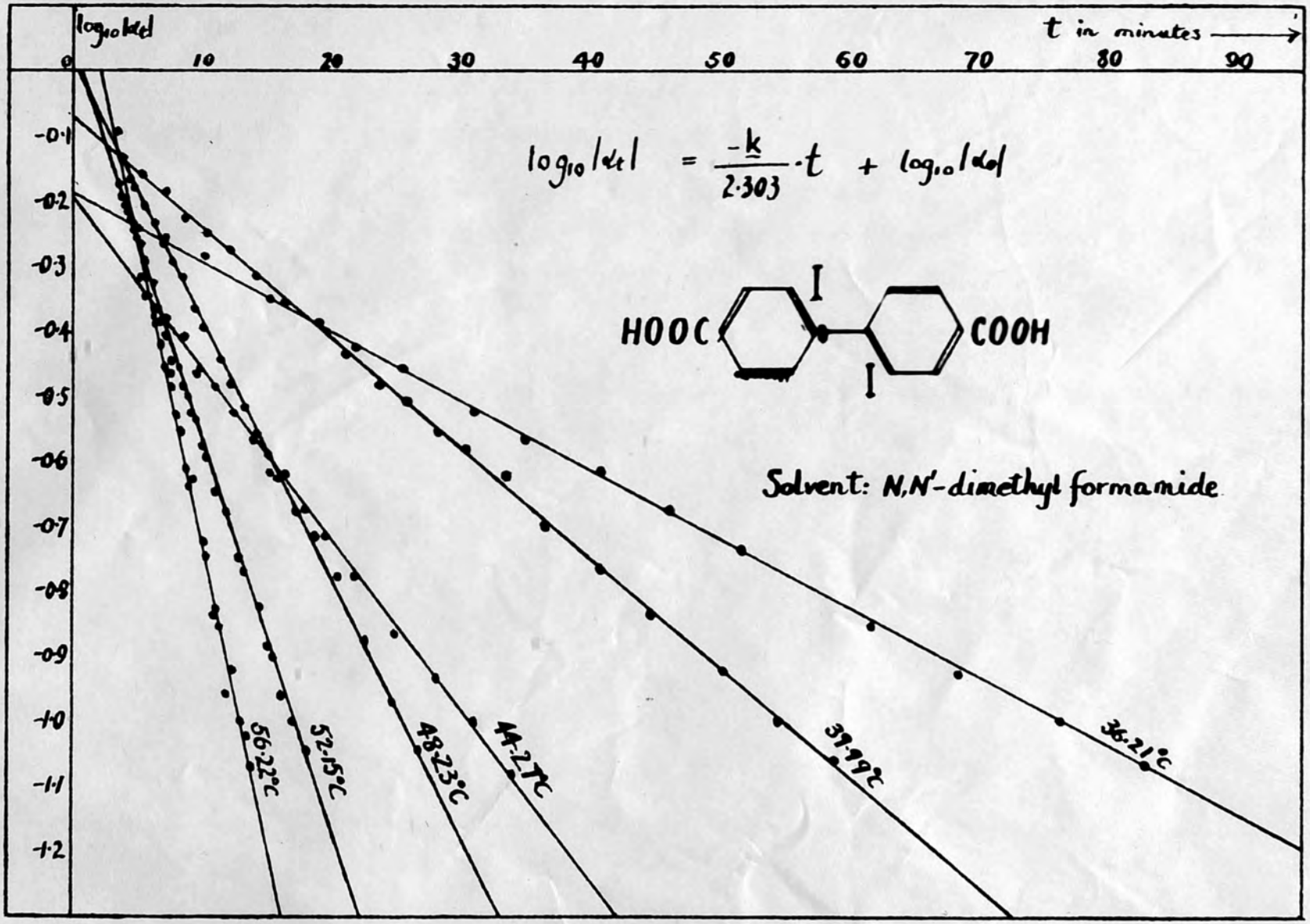
Determination of rate coefficients for the racemisation of

2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid.

Solvent: N,N'-dimethylformamide.

Concentration: 0.15-0.25 g. in 17 c.c. of solvent.

Temperature °C.	Time of 1st reading after wetting min.	First reading deg.	No. of readings	Time during which readings were taken min.	$\underline{k} \times 10^{-4}$ $sec.^{-1}$	$t_{\frac{1}{2}}$ min.
36.21	5.1	-0.57	15	82.8	4.08	28.3
39.99	5.4	-0.69	20	58.9	6.48	17.8
44.27	5.0	-0.48	18	34.0	10.00	11.6
48.23	3.9	-0.47	21	26.5	15.35	7.5
52.15	3.2	-0.73	32	18.1	23.21	5.0
56.22	3.5	-0.81	31	13.8	35.62	3.2


log10|dc/dt|
t in minutes
0
10
20
30
40
50
60
70
80
90
-0·1
-0·2
-0·3
-0·4
-0·5
-0·6
-0·7
-0·8
-0·9
-1·0
-1·1
-1·2
$\log_{10}|dc/dt| = \frac{-k}{2.303} \cdot t + \log_{10}|dc_0|$
HOOC
COOH
I
I
Solvent: N,N'-dimethyl formamide
56·22°C
52·15°C
48·23°C
44·27°C
39·99°C
36·21°C

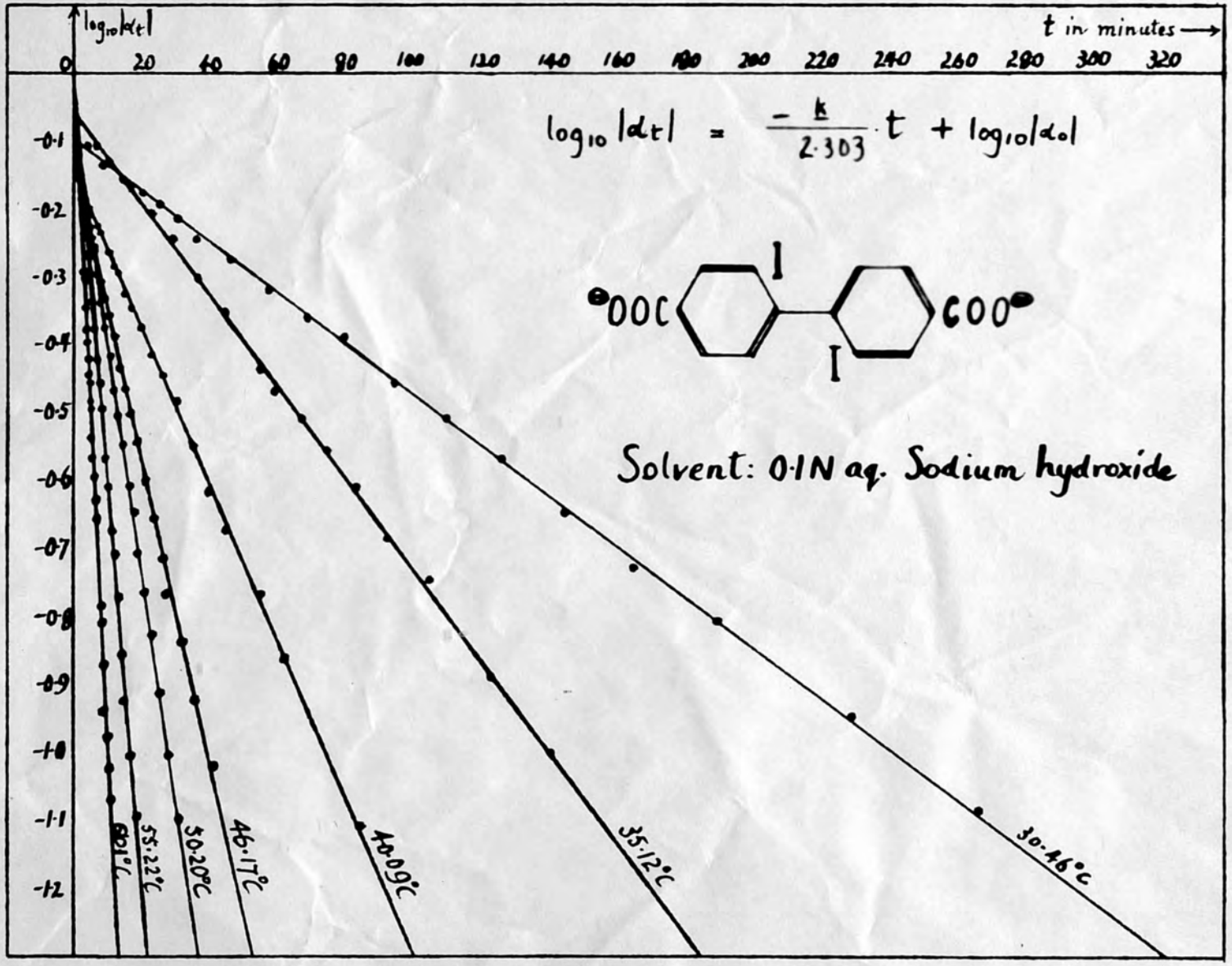
Determination of the rate coefficients for the racemisation of

2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid.

Solvent: 0.1N aqueous sodium hydroxide

Concentration: 0.12-0.13 g. in 17 ml. of solvent.

Temperature	Time of 1st reading	1st reading a_t	No. of readings	Time during which readings made were taken	$k \times 10^{-4}$	$t_{\frac{1}{2}}$
T°C.	min.	deg.		min.	sec^{-1}	min.
30.46	4.4	-0.78	19	267.2	1.44	81.2
35.12	6.5	-0.79	16	141.2	2.54	45.4
40.09	3.7	-0.65	19	82.4	4.45	25.9
46.17	5.2	-0.57	18	41.4	8.47	13.6
50.20	4.5	-0.62	18	31.3	12.88	9.0
55.22	3.6	-0.58	17	18.3	22.01	5.2
61.01	2.6	-0.51	22	10.9	37.44	3.1


$\log_{10}|a_t|$
t in minutes
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
-0·1
-0·2
-0·3
-0·4
-0·5
-0·6
-0·7
-0·8
-0·9
-1·0
-1·1
-1·2
$\log_{10}|a_t| = \frac{-k}{2.303} \cdot t + \log_{10}|a_0|$
$^{\ominus}OOC$
I
I
$COO^{\ominus}$
Solvent: 0·1N aq. Sodium hydroxide
55·22°C
50·20°C
46·17°C
40·09°C
35·12°C
30·46°C

Determination of Arrhenius parameters E and $\log_{10}A$ and Transition State Theory Functions $\Delta H^{\neq}$, $\Delta S^{\neq}$, and $\Delta F^{\neq}$ for the racemisation of 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid in absolute ethanol.

$T^{o}K$	$\frac{10^3}{T^{o}K} = y \times 10^3$	$k \times 10^{-4}$ sec.$^{-1}$	$\log_{10}\frac{k}{h} + x$	x^2	xy	$\log_{10}\frac{k}{T}$
298.38	3.35143	1.38180	-3.85955	14.89613	12.93501	-6.33443
303.98	3.28969	2.66103	-3.57495	12.78027	11.76048	-6.05780
309.14	3.23478	4.90453	-3.30940	10.95213	10.70518	-5.79956
313.31	3.19173	7.84175	-3.10559	9.64469	9.91220	-5.60156
318.51	3.13962	13.3712	-2.87383	8.25890	9.02273	-5.37695
323.62	3.09004	22.6062	-2.64577	7.00010	8.17554	-5.15581
329.24	3.03730	39.5955	-2.40235	5.77129	7.29666	-4.91986
	22.33459		-21.77154	69.30351	69.80780	

Graphical Methods.

$E = 21.29$ kcal.mole^{-1} $\quad \log_{10}A = 11.73$

$\Delta H^{\neq} = 20.68$ kcal.mole^{-1} $\quad \Delta S^{\neq} = 6.9$ e.u.

$\Delta F^{\neq} = 22.7$ kcal.mole^{-1} (25°C)

Mean Square Calculations.

$\Sigma x = -21.77154$ $\quad \Sigma y = 22.33459 \times 10^{-3}$ $\quad \Sigma x^2 = 69.30351$

$\Sigma xy = -69.80780 \times 10^{-3}$

$n = 7$

$n\,\Sigma xy = -0.488655$	$n\,\Sigma x^2 = 485.12457$	$\Sigma x^2 \Sigma y = 1.54787$
$-\Sigma x \Sigma y = -0.486258$	$(\Sigma x)^2 = 473.99995$	$\Sigma x \Sigma xy = 1.51982$
-0.002397	11.12462	0.02805

$$E = \frac{-4.576 \times 11.12462}{-0.002397} = 21.24 \text{ kcal.mole}^{-1}$$

$$\log_{10}A = \frac{-0.02805}{-0.002397} = 11.70$$

E 21.3 kcal.mole^{-1} $\quad \Delta H^{\neq}$ 20.7 kcal.mole^{-1} $\quad \Delta F^{\neq}$ 22.7 kcal.mole^{-1} (25°C)

$\log_{10}A$ 11.7 $\quad \Delta S^{\neq}$ -6.9 e.u.

Determination of Arrhenius Parameters E and $\log_{10}A$, and Transition State Theory Functions $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ and $\Delta F^{\ddagger}$, for the racemisation of 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid in N,N'-dimethylformamide.

$T^{o}K$	$\frac{10^3}{T^{o}K}=yx10^3$	$kx10^{-4}sec^{-1}$	$\log_{10}k=x$	x^2	xy	$\log_{10}\frac{k}{T}$
309.41	3.23300	4.07823	-3.38953	11.48891	10.95835	-5.88006
313.19	3.19295	6.48030	-3.18841	10.16596	10.18043	-5.68422
317.47	3.14990	10.0013	-2.99996	8.99976	9.44957	-5.50166
321.43	3.11110	15.3533	-2.91381	7.91753	8.75404	-5.32090
325.35	3.07361	23.2085	-2.63434	6.93979	8.09693	-5.14669
329.42	3.03564	35.6170	-2.44834	5.99437	7.43228	-4.96609
	$18.79620x10^{-3}$		-17.47439	51.50628	$54.87160x10^{-3}$	

Graphical Methods.

$E = 21.59$ kcals.mole^{-1} $\quad \log_{10}A = 11.86$

$\Delta H^{\ddagger} = 21.11$ kcal.mole^{-1} $\quad \Delta S^{\ddagger} = -6.1$ e.u.

$\Delta F^{\ddagger} = 22.9$ kcal.mole^{-1} at 25°C.

Mean Square Calculations.

$\Sigma x = -17.47439$ $\quad \Sigma y = 18.79620 \times 10^{-3}$ $\quad \Sigma x^2 = 51.50628$

$\Sigma xy = 54.87160 \times 10^{-3}$

$n = 6.$

$n\Sigma xy = -0.329230$ $\quad n\Sigma x^2 = 309.03768$ $\quad \Sigma x^2 \bar{y} = 0.96812$

$-\Sigma x \Sigma y = -0.328452$ $\quad -(\Sigma x)^2 = -305.35431$ $\quad -\Sigma x \bar{x} \bar{y} = -0.95885$

-0.000778 $\quad 3.68337$ $\quad 0.00927$

$$E = \frac{-4.576 \times 3.68337}{-0.000778} \qquad \log_{10}A = \frac{-0.00927}{-0.000778}$$

$$= 21.66 \text{ kcal.mole}^{-1} \qquad = 11.92$$

E 21.6 kcal.mole^{-1} $\quad \Delta H^{\ddagger}$ 21.1 kcal.mole^{-1} $\quad \Delta F^{\ddagger}$ (25°C) 22.9 kcal. mole^{-1}

$\log_{10}A$ 11.9 $\quad \Delta S^{\ddagger}$ -6.1 e.u.

Determination of Arrhenius Parameters E and $\log_{10}A$ and Transition State Theory Functions $\Delta H^{\neq}$, $\Delta S^{\neq}$ and $\Delta F^{\neq}$ for the racemisation of 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid in 0.1N aqueous sodium hydroxide.

$T^{o}K$	$\frac{10^3}{T^{o}k} = yx10^3$	$kx10^{-4}$ sec.$^{-1}$	$\log_{10}k_2x$	x^2	xy	$\log_{10}\frac{k}{T}$
303.68	3.29294	1.44283	-3.84078	14.75159	12.64746	-6.32320
308.34	3.24317	2.54290	-3.59477	12.92237	11.65845	-6.08380
313.31	3.19173	4.45392	-3.35126	11.23094	10.69632	-5.84723
319.39	3.13097	8.46910	-3.07216	9.43817	9.61884	-5.57648
323.42	3.09195	12.8858	-2.88989	8.35146	8.93540	-5.39966
328.44	3.04470	22.0140	-2.65730	7.06124	8.09068	-5.17376
334.23	2.99195	37.4445	-2.42661	5.88844	7.26030	-4.95066
	21.98741		-21.83277	69.64421	-68.90745	

Graphical Methods:

$E = 21.41$ kcal.mole $\qquad \log_{10}A = 11.58$

$\Delta H^{\ddagger} = 20.98$ kcal.mole $\qquad \Delta S^{\ddagger} = -7.0$ e.u.

$\Delta F^{\ddagger} = 23.1$ $(25^{\circ}C)$

Mean Square Calculations:

$\Sigma x = -21.83277 \qquad \Sigma y = 21.98741 \times 10^{-3} \qquad \Sigma x^2 = 69.64421$

$\bar{z}xy = 68.90745 \times 10^{-3}$

$n = 7$

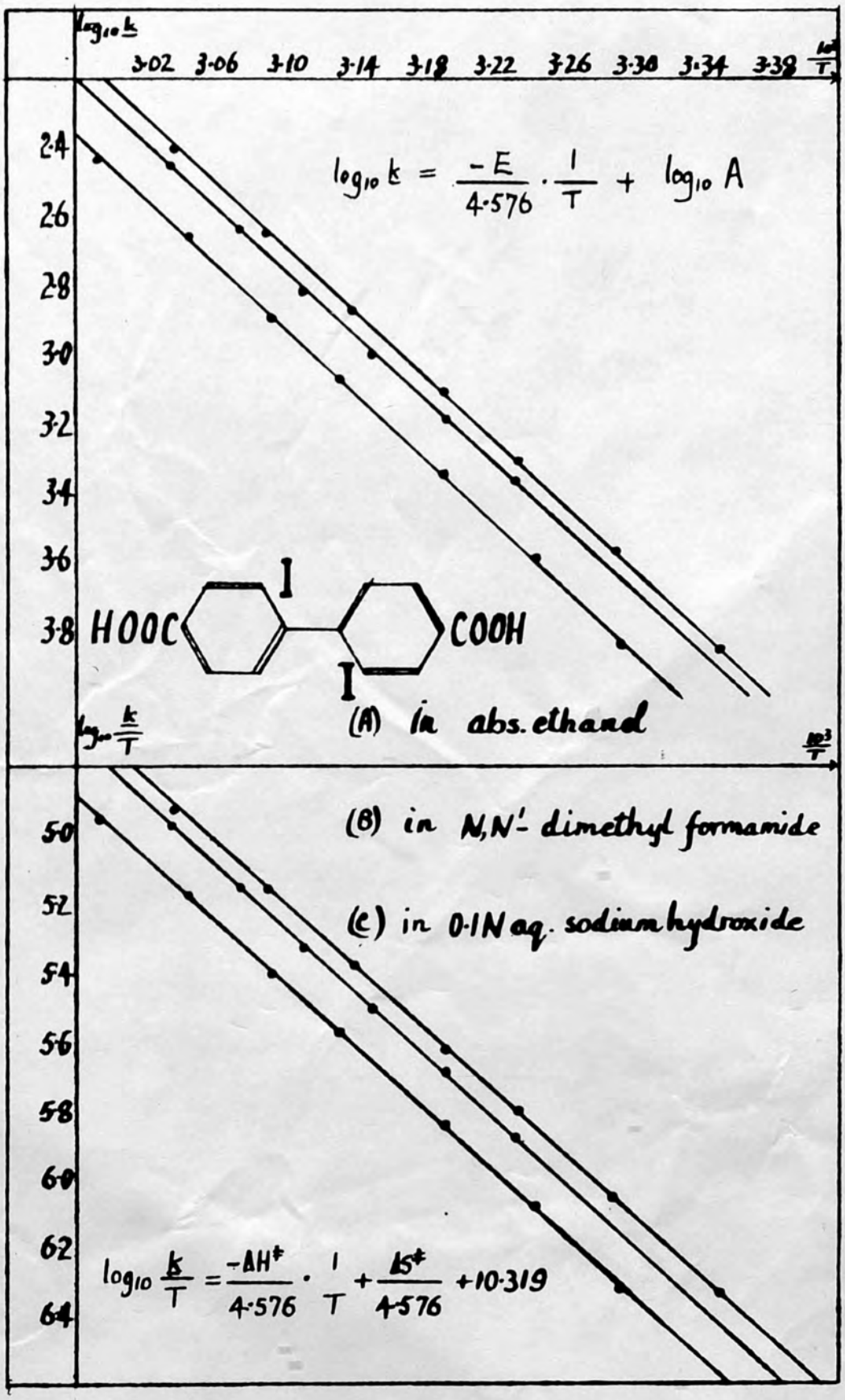
$n\Sigma xy = -0.482352$	$n\bar{z}x^2 = 487.50947$	$\Sigma x^2 zy = 1.53130$
$-\Sigma x \Sigma y = -0.480046$	$(\Sigma x)^2 = 476.66963$	$\Sigma x \Sigma xy = 1.50444$
-0.002306	10.83984	0.02686

$$E = \frac{4.576 \times 10.8398}{-0.002306} = 21.51 \text{ kcal.mole}^{-1}$$

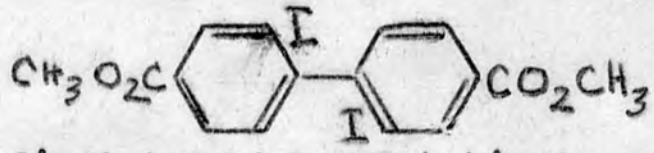
$$\log_{10}A = \frac{0.02686}{0.002306} = 11.65$$

E 21.5 kcal.mole^{-1} $\quad \Delta H^{\ddagger}$ 21.0 kcal.mole^{-1} $\quad \Delta F^{\ddagger}$ (25°C) 23.1 kcal.mole^{-1}

$\log_{10}A$ 11.6 $\quad \Delta S^{\ddagger}$ -7.0 e.u.


log10 k
3·02 3·06 3·10 3·14 3·18 3·22 3·26 3·30 3·34 3·38
10³/T
log10 k = -E/4·576 · 1/T + log10 A
2·4
2·6
2·8
3·0
3·2
3·4
3·6
3·8
HOOC
I
I
COOH
(A) in abs. ethanol
log10 k/T
10³/T
(B) in N,N'- dimethyl formamide
(C) in 0·1N aq. sodium hydroxide
5·0
5·2
5·4
5·6
5·8
6·0
6·2
6·4
log10 k/T = -ΔH‡/4·576 · 1/T + ΔS‡/4·576 + 10·319

Dimethyl 2,2'-di-iodobiphenyl-4,4'-dicarboxylate.



2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid reacted with an ethereal solution of diazomethane to give the dimethyl ester, m.p. 152-4°. The optically active ester was obtained by using the optically active acid.

Preparation of Diazomethane(Org.Syn., 1956, 36, 16)

$$p\text{-}CH_3.C_6H_4SO_2N(NO)CH_3 + ROH \xrightarrow{KOH} CH_2N_2 + p.CH_3C_6H_4SO_2OR + H_2O$$

The joints of the apparatus used were fitted with plastic sleeves to limit the possibility of an explosion.

5 g. of potassium hydroxide, 8 c.c. of water and 25 c.c. of ethanol (S.V.R.) were placed in a round bottomed distilling flask, which was partly immersed in a water bath at 65-70°. 21.5 g. of N-methyl-N-nitroso-p-toluene sulphonamide were dissolved in 130 c.c. of ether, placed in a dropping funnel fitted to the flask, and the solution gradually added to the potash solution. Ethereal diazomethane distilled over, through a water condenser into a receiver which was cooled in ice and salt, and was connected in series to a second receiver containing 40-50 c.c. of ether, which acted as a trap for any escaping diazomethane. After addition of all the N-methyl-N-nitroso-p-toluene sulphonamide solution, about 50 c.c. of ether

were gradually added and distillation continued until the distillate was colourless. The ethereal solution obtained was immediately used and was assumed to contain 2.6-2.7 g. of diazomethane.

Preparation of (-) dimethyl ester. - 10 c.c. of the ethereal solution, containing about 0.2 g. (2.4M) of diazomethane was cooled to -10°. 1 g. (1M) of (-) 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid $[\alpha]^{36°}_{5461}$ -32.5° (in N,N'-dimethyl-formamide) was gradually added, with stirring. 0.55 g. of crystals, m.p. 152-4° (1st crop) separated after 15 minutes. (Found: C, 36.5; H, 2.5; O, 12.3, I, 48.5%. $C_{16}H_{12}O_4I_2$ requires C, 36.8; H, 2.3; O, 12.3, I, 48.6%). The crystals were filtered; the filtrate was transferred into an evaporating dish and was immediately evaporated in the cold, by drawing a stream of air over its surface, with the aid of a fume cupboard. (The stream of air blew across the surface of the solution, against a sheet of cotton and wool saturated with glacial acetic acid, which absorbed any escaping diazomethane). The residue was a gum, which gradually solidified in a vacuum desiccator containing calcium chloride. 0.4 g. of solid, m.p. 151-4° (softening at 145°) was obtained (2nd crop).

The optical rotation of the dimethyl ester was measured in N,N'-dimethylformamide. It was found that the specific rotation of the first crop was very small $[\alpha]^{20°}_{5461}$ -1.4° while the second crop was more optically active $[\alpha]^{45°}_{5461}$ -19.3°.

Determination of rate coefficients for the racemisation of

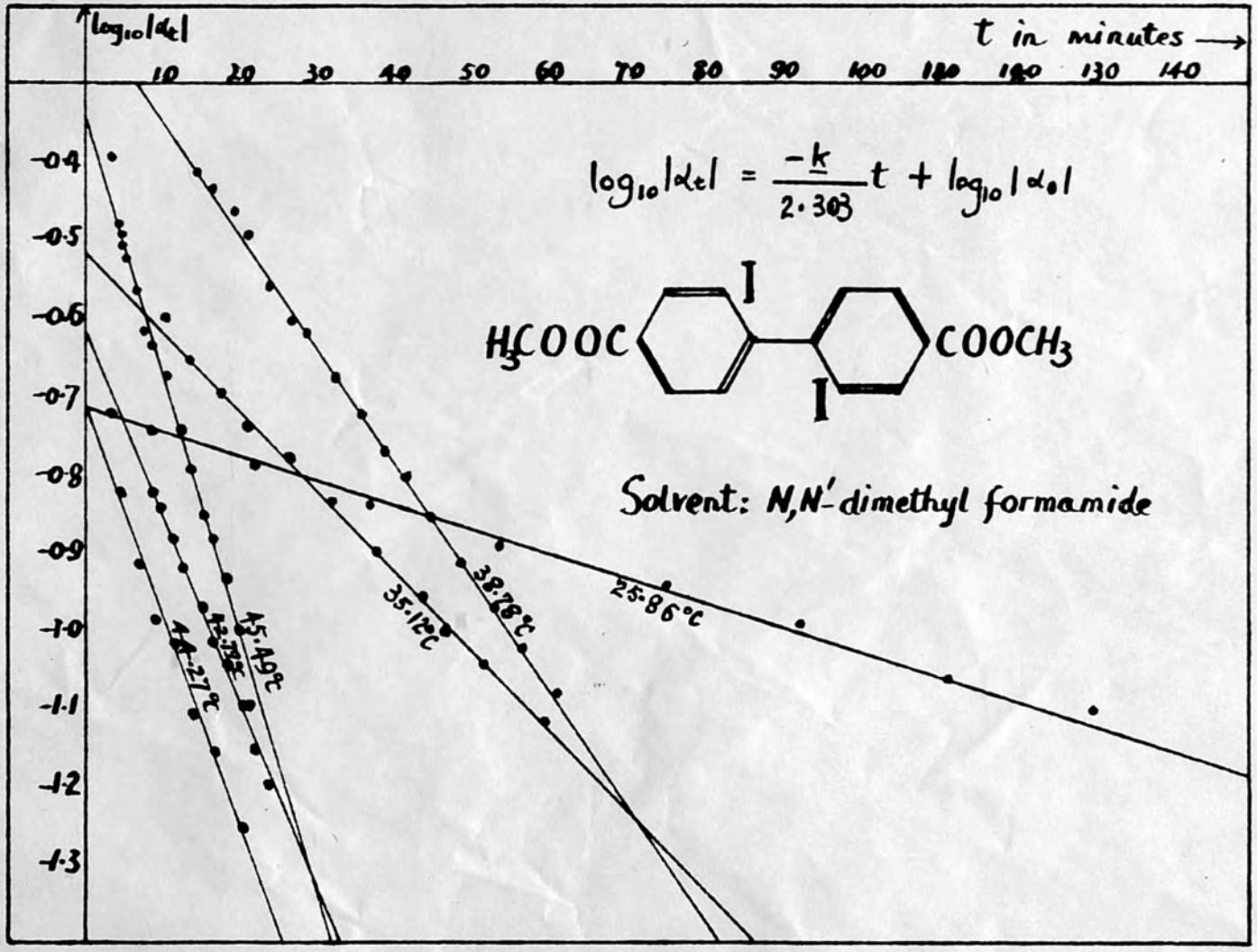
Dimethyl-2,2'-di-iodobiphenyl-4,4'-dicarboxylate.

Solvent: N,N'-dimethylformamide.

Concentration: 0.2-1 g. in 17 ml. of solvent.

* Different crops of the ester varied in optical rotation and whenever the initial rotation was too small for rate measurements the solution was poured from the polarimeter tube into a conical flask, a further amount of ester was added, and the solution again filtered into the polarimeter tube.

Temperature	Time of 1st reading	1st reading α_t	No. of readings	Time during which readings made were taken.	$\underline{k} \times 10^{-4}$	$t_{\frac{1}{2}}$
$T^{o}C$	min.	deg.		min.	$sec.^{-1}$	min.
25.86	3.4	-0.19	9	130.7	1.21	95.7
35.12	*10.4	-0.25	11	60.0	3.95	29.3
38.78	*13.5	-0.39	16	60.5	5.57	20.7
42.79	* 8.8	-0.15	10	23.6	9.49	12.2
44.27	4.7	-0.15	7	20.3	10.69	10.8
45.49	3.5	-0.40	16	21.1	12.68	9.1


log10|αt|
t in minutes →
10 20 30 40 50 60 70 80 90 100 110 120 130 140
-0·4
-0·5
-0·6
-0·7
-0·8
-0·9
-1·0
-1·1
-1·2
-1·3
log10|αt| = (-k/2·303) t + log10|α0|
I
H3COOC
COOCH3
I
Solvent: N,N'-dimethyl formamide
25·86°C
35·12°C
38·78°C
45·49°C

Determination of Arrhenius parameters E and $\log_{10}A$ and Transition State Theory Functions ΔH, ΔS, and ΔF for the racemisation of dimethyl-2,2'-di-iodobiphenyl-4,4' dicarboxylate in N,N'-dimethylformamide.

$T^{\circ}K$	$\frac{10^3}{T^{\circ}K} = yx10^3$	$kx10^{-4}sec^{-1}$	$\log_{10}k=x$	x^2	xy	$\log_{10}\frac{k}{T}$
299.06	3.3438	1.20722	-3.9182	15.38229	13.10168	-6.3940
308.32	3.2434	3.94800	-3.4036	11.58449	11.03924	-5.8926
311.98	3.2053	5.57177	-3.2540	10.58852	10.43005	-5.7481
315.99	3.1647	9.49265	-3.0226	9.13611	9.56562	-5.5223
317.47	3.1499	10.6925	-2.9709	9.82625	9.35804	-5.4726
318.69	3.1378	12.6771	-2.8970	8.39261	9.09021	-5.4006
	19.2449		-19.4663	63.88027	62.58484	

ral

Graphical Methods.

$E = 22.30$ kcal.mole^{-1} $\log_{10}A = 12.37$

$\Delta H^{\neq} = 21.66$ kcal.mole^{-1} $\Delta S^{\neq} = 4.0$ e.u.

$\Delta F^{\neq} = 22.9$ kcal.mole^{-1}

Mean Square Calculations.

$\Sigma x = -19.4664$ $\Sigma y = 19.2449 \times 10^{-3}$ $\Sigma x^2 = 63.88027$ $\Sigma xy = 62.58584 \times 10^{-3}$

$n = 6$

$n\,\Sigma xy = -0.37551$ $n\,\Sigma x^2 = 383.28162$ $\Sigma x^2 \Sigma y = 1.22942$

$-\Sigma x \Sigma y = -0.37463$ $-(\Sigma x)^2 = 378.93684$ $-\Sigma x \Sigma y = 1.21830$

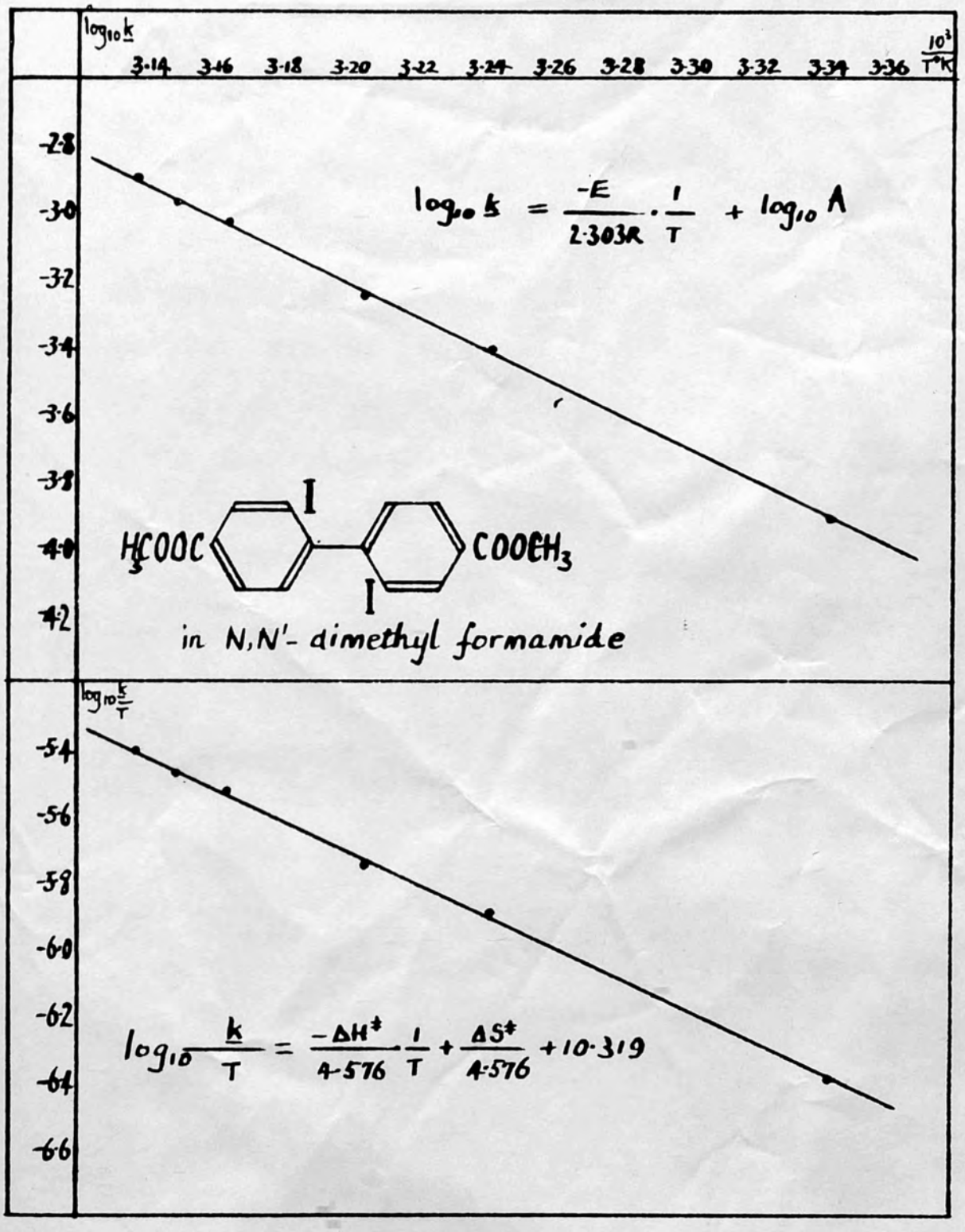
-0.00088 4.34478 0.01112

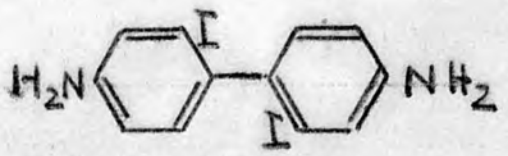
$$E = \frac{-4.567 \times 4.34478}{-0.00088} \text{ cal.mole}^{-1} = 22.59 \text{ kcal.mole}^{-1}$$

$$\log_{10}A = \frac{0.01112}{0.00088} = 12.64$$

E 22.4 kcal.mole^{-1} $\Delta H^{\neq}$ 21.7 kcal.mole^{-1}

$\Delta F^{\neq}$ 22.9 kcal.mole^{-1} $\log_{10}A$ 12.5 $\Delta S^{\neq}$ -4 e.u.


log10 k
3·14 3·16 3·18 3·20 3·22 3·24 3·26 3·28 3·30 3·32 3·34 3·36
10³/T°K
-28
-30
-32
-34
-36
-38
-40
-42
log10 k = -E/2·303R · 1/T + log10 A
I
HCOOC
COOCH3
I
in N,N'- dimethyl formamide
log10 k/T
-54
-56
-58
-60
-62
-64
-66
log10 k/T = -ΔH‡/4·576 · 1/T + ΔS‡/4·576 + 10·319

2,2'-di-iodobenzidine. 

Second Order Asymmetric Transformation of the di-hydrogen tartrate. 8.7 g. (1M) of 2,2'-di-iodobenzidine and 6.0 g. (2M) of (+)-tartaric acid were dissolved in 250 c.c. of boiling ethanol (S.V.R.), and the solution allowed to stand at room temperature. 11.7 g. of straw coloured needles, m.p. 182° (decomp.) were obtained. Another 3 g. of crystals, m.p.182° (decomp.) were obtained by concentrating the mother liquor. The analysis results were in poor agreement with those required for the di-hydrogen tartrate, but showed that the compound contained two molecules, and not one molecule of tartaric acid. (Found: C, 32.3; H, 3.7; N, 3.2; I, 32.3%. $C_{20}H_{22}O_{12}N_2I_2$ requires C, 32.6; H, 3.0; N, 3.8; I, 34.5%).

Over ten experiments were carried out for the preparation of the di-hydrogen tartrate. The optical rotations of several of the specimens obtained have been measured in acetone, dimethyl formamide and methanol. Mutarotation was observed in all cases, but the specific rotation of the salt varied from specimen to specimen. Specimens of base obtained from different specimens of the di-hydrogen tartrate also differ in specific rotation, both in sign and in magnitude. (See Table VIII)

TABLE.

Specific rotation of H-tartrate		Specific rotation of base in N,N'-dimethylformamide	
Solvent			
acetone	$[\alpha]^{20^\circ}_{5461}$	- 12.6	$[\alpha]^{26^\circ}_{5461}$	-8.5°
acetone	$[\alpha]^{20^\circ}_{5461}$	- 17.4°	$[\alpha]^{22^\circ}_{5461}$	-9.4°
N,N'-DMF	$[\alpha]^{20.5^\circ}_{5461}$	-18.4°	$[\alpha]^{15.2^\circ}_{5461}$	-14°
N,N'-DMF	$[\alpha]^{22^\circ}_{5461}$	+12.6°	$[\alpha]^{19^\circ}$	+16.2°
Methanol	$[\alpha]^{25^\circ}_{5461}$	+35°	$[\alpha]^{7.4^\circ}$	+69.2°

Optically active 2,2'-di-iodobenzidine was obtained by grinding the di-hydrogen tartrate with cold aqueous ammonia. It was filtered, washed with ammonia, water and then dried *in vacuo* over potassium hydroxide. The base so obtained has m.p. 167-170°. (Found: C, 33.3; H, 2.6; N, 6.4; I, 58.0%. $C_{12}H_{10}N_2I_2$ requires C, 33.1; H, 2.3; N, 6.4; I, 58.2%).

Racemisation experiments were carried out in N,N'-dimethylformamide and 0.5N aqueous alcoholic hydrochloric acid.

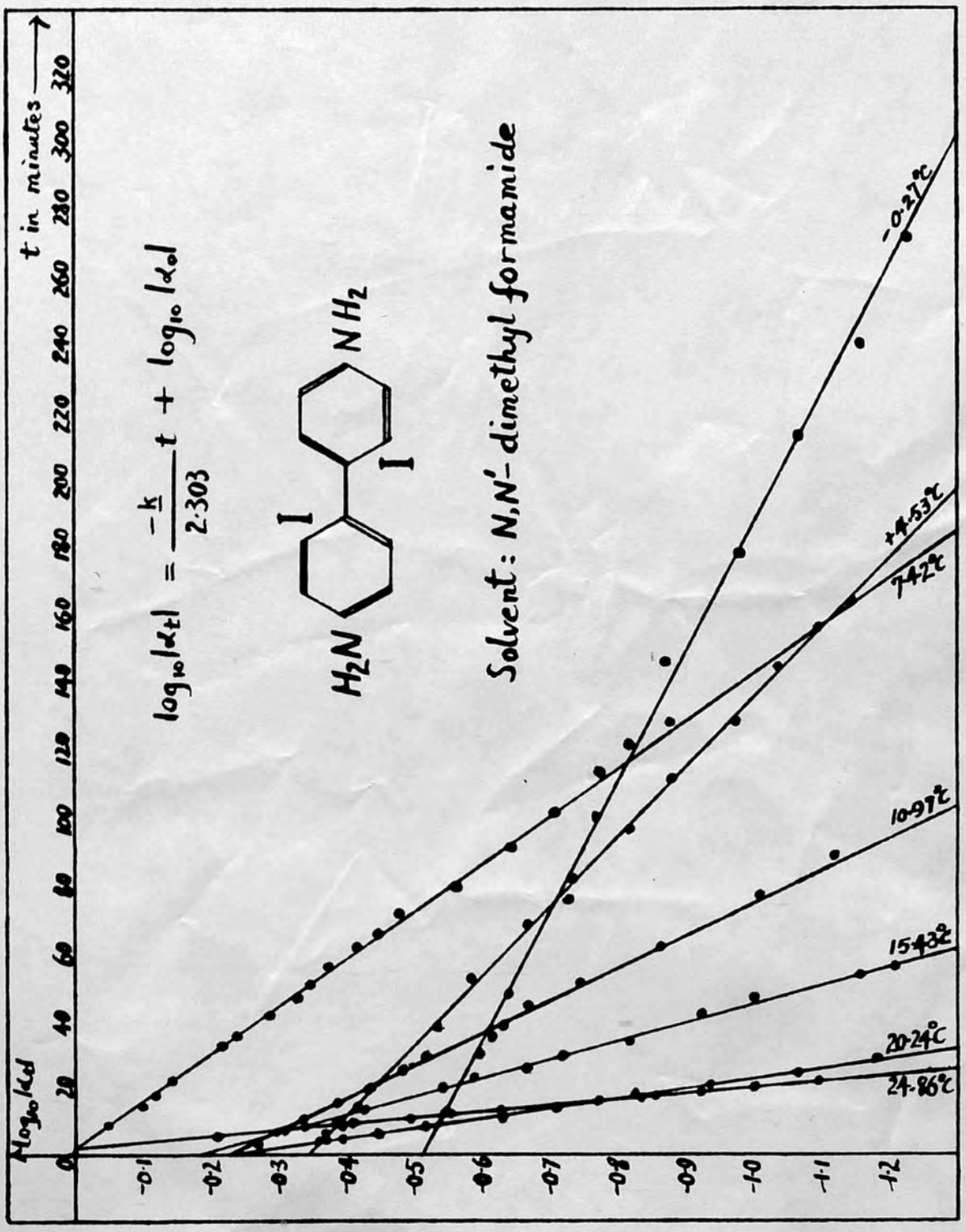
Determination of rate coefficients for the racemisation of 2,2' di-iodobenzidine.

Solvent: N,N'-dimethylformamide.

Concentration: about 1 g. in 17 ml. of solvent, except for experiment marked *, in which the concentration was 0.23 g. in 17 c.c. of solvent.

$[\alpha_o]_{5461}$ by extrapolation: $\pm 57^\circ$ to $+69.2^\circ$

Temperature	Time of 1st reading	1st reading α_t	No. of readings	Time during which readings made were taken	$\underline{k} \times 10^{-4}$	$t_{\frac{1}{2}}$
T°C	min.	deg.		min.	$sec.^{-1}$	min.
-0.27	12.4	-0.29	12	298.7	0.99	116.3
+4.53	4.2	-0.43	14	164.1	1.87	61.8
*-7.42	5.9	+0.9	19	156.6	2.69	42.9
10.97	4.4	-0.56	14	88.6	3.90	29.6
15.43	2.9	-0.54	13	55.7	6.96	16.6
20.24	1.8	-0.49	12	28.4	1.32	8.8
24.86	2.8	-0.77	12	21.6	2.16	5.36


$\log_{10}|x_t|$ = $\frac{-k}{2.303}t + \log_{10}|x_0|$
H_2N
NH_2
I
I
Solvent: N,N'-dimethyl formamide
t in minutes
$\log_{10}|x_0|$
-0·27°C
+4·53°C
7·42°C
10·97°C
15·43°C
20·24°C
24·86°C

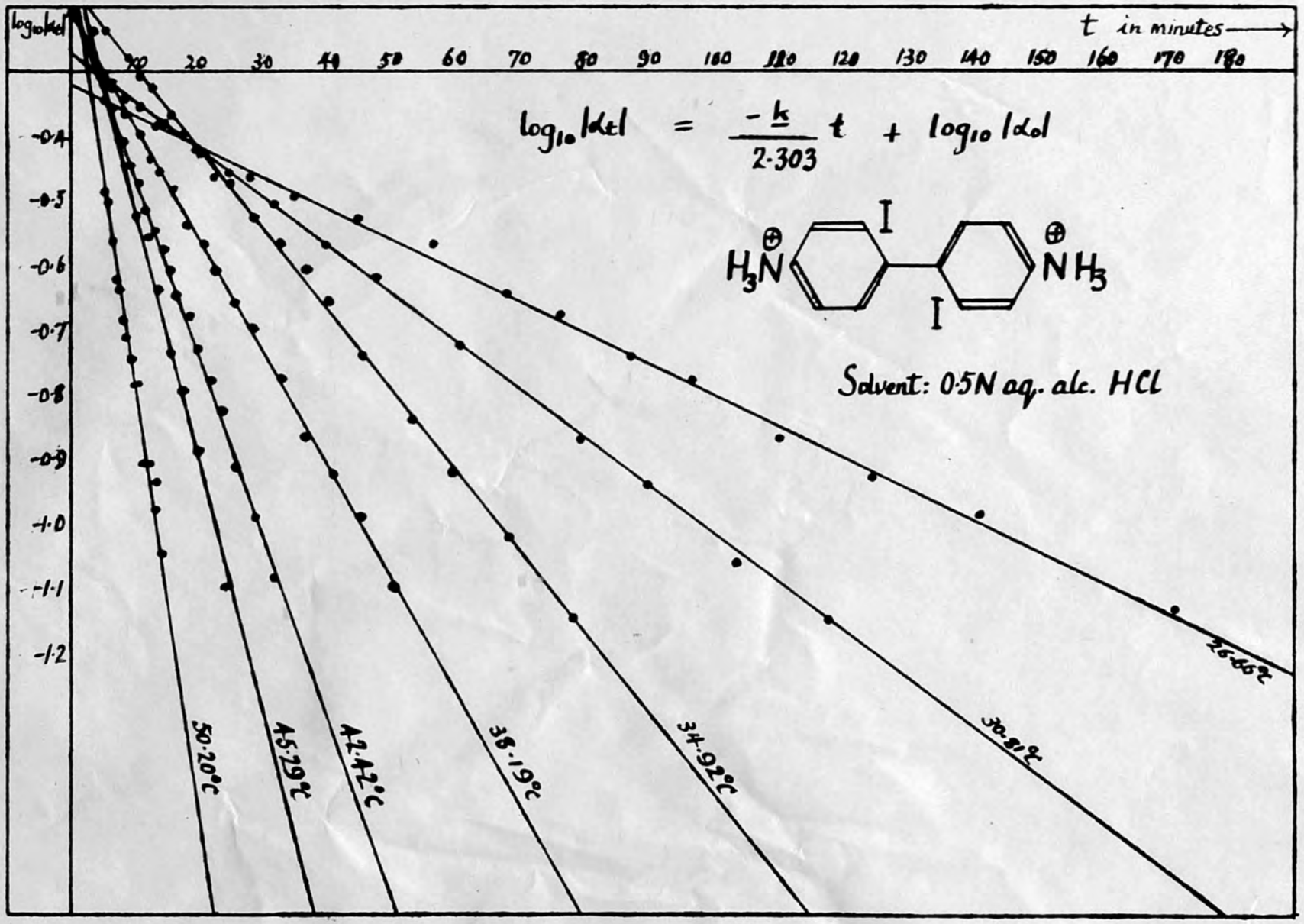
Determination of rate coefficients for racemisation of

2,2'-di-iodobenzidine.

Solvent: 0.5N aqueous alcoholic hydrochloric acid.

Concentration: 0.7-0.8 g. in 17 ml. of solvent.

Temperature	Time of 1st reading	1st reading α_t	No. of readings	Time during which readings were taken.	$k \times 10^{-4}$	$t_{\frac{1}{2}}$
T°C.	min.	deg.		min.	$sec.^{-1}$	min.
26.66	5.3	-0.45	16	171.7	1.73	66.8
30.81	6.5	+0.48	13	117.9	2.84	40.7
34.92	5.6	+0.59	19	78.1	4.78	24.2
38.19	4.9	-0.49	17	50.7	6.72	17.2
42.42	4.4	-0.53	19	34.8	10.77	10.7
45.29	3.8	+0.58	11	24.0	15.56	7.4
50.20	4.6	-0.41	19	16.6	25.34	4.6


log10|α|
t in minutes
10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180
-0·4
-0·5
-0·6
-0·7
-0·8
-0·9
-1·0
-1·1
-1·2
$\log_{10}|\alpha_t| = \frac{-k}{2.303} t + \log_{10}|\alpha_0|$
I
$H_3N^{\oplus}$
$^{\oplus}NH_3$
I
Solvent: 0·5N aq. alc. HCl
50·20°C
45·29°C
42·42°C
38·19°C
34·92°C
30·81°C
26·65°C

Determination of Arrhenius Parameters E and $\log_{10}A$ and Transition State Theory Functions $\Delta H^{\neq}$, $\Delta S^{\neq}$ and $\Delta F^{\neq}$ for the racemisation of 2,2'-di-iodobenzidine in N,N'-dimethylformamide.

$T^{o}K$	$\frac{10^3}{T^{o}K} = yx10^3$	$kx10^{-4}sec^{-1}$	$\log_{10}k = x$	x^2	xy	$\log_{10}\frac{k}{T}$
272.93	3.66394	0.99345	-4.00285	16.02281	14.66620	-6.43880
277.73	3.60062	1.96798	-3.72862	13.90261	13.42534	-6.17225
284.17	3.51902	3.90230	-3.40868	11.61910	11.99521	-5.86227
288.63	3.46464	6.96471	-3.15710	-9.96728	10.93821	-5.61744
293.44	3.40785	13.1943	-2.87962	8.29221	9.81331	-5.34713
298.06	3.35503	21.5637	-2.66627	7.10810	8.94542	-5.14058
	$21.01110x10^{-3}$		-19.843140	66.91211	$-69.78369x10^{-3}$	

Graphical Methods:

$E = 19.87$ kcal.mole^{-1} $\quad \log_{10}A = 11.90$

$\Delta H^{\ddagger} = 19.36$ kcal.mole^{-1} $\quad \Delta S^{\ddagger} = 5.81$ e.u.

$\Delta F^{\ddagger} = 31.09$ kcal.mole^{-1}

Mean Squares Calculations.

$\Sigma x = -19.84314$ $\quad \Sigma y = 21.01110 \times 10^{-3}$ $\quad \Sigma x^2 = 66.91211$

$\Sigma xy = -69.78369 \times 10^{-3}$

$n = 6.$

$n\Sigma xy = -0.418702$	$n\Sigma x^2 = 401.472660$	$\Sigma x^2 - \Sigma y = 1.405897$
$-\Sigma x\Sigma y = -0.416926$	$(\Sigma x)^2 = 393.750205$	$\Sigma x\Sigma xy = 1.384728$
-0.001776	7.722455	0.021169

$$E = \frac{-4.576 \times 7.722455}{-0.001776} \text{ cal.mole}^{-1} = 19.90 \text{ kcal.mole}^{-1}$$

$$\log_{10}A = \frac{-0.021169}{-0.001776} = 11.92$$

E 19.9 kcal.mole^{-1} $\quad \Delta H^{\ddagger}$ 19.4 kcal.mole^{-1} $\quad \Delta F^{\ddagger}$ 21.1 kcal. (25°C)mole^{-1}

$\log_{10}A$ 11.9 $\quad \Delta S^{\ddagger}$ 5.8 e.u.

Determination of Arrhenius parameters E and $\log_{10}A$ and Transition State Theory Functions $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta F^{\ddagger}$ for the racemisation of 2,2'-di-iodobenzidine in 0.5N aqueous alcoholic hydrochloric acid.

$T^{o}K$	$\frac{10^3}{T^{o}K}=yx10^3$	$kx10^4 sec^{-1}$	$\log_{10}k=x$	x^2	xy	$\log_{10}\frac{k}{T}$
299.86	3.33489	1.77776	-3.750127	14.06345	12.54624	-6.2391
304.07	3.28937	2.84037	-3.546625	12.57855	11.66616	-6.0296
308.12	3.24549	4.77538	-3.320992	11.02899	10.77825	-5.8097
311.39	3.21141	6.71708	-3.172819	10.06678	10.18922	-5.6662
315.62	3.16837	1.07687	-2.967837	8.80806	9.40321	-5.4669
318.49	3.13982	1.55581	-2.808043	7.88511	8.81675	-5.3112
323.40	3.09215	2.53374	-2.596238	6.74045	8.02796	-5.1059
	$22.48150x10^{-3}$		-22.162681	71.17139	$-71.42779x10^{-3}$	

Graphical Methods.

$E = 22.17$ kcal.mole^{-1} $\quad \log_{10}A = 12.39$

$\Delta H^{\ddagger} = 21.43$ kcal.mole^{-1} $\quad \Delta S^{\ddagger} = -4.3$ e.u.

$\Delta F^{\ddagger} = 22.8$ kcal.mole^{-1} at 25°C.

Mean Square Calculations.

$\Sigma x = -22.162681$ $\quad \Sigma y = 22.48150 \times 10^{-3}$ $\quad \Sigma x^2 = 71.17139$

$\Sigma xy = 71.42779 \times 10^{-3}$

$n = 7$

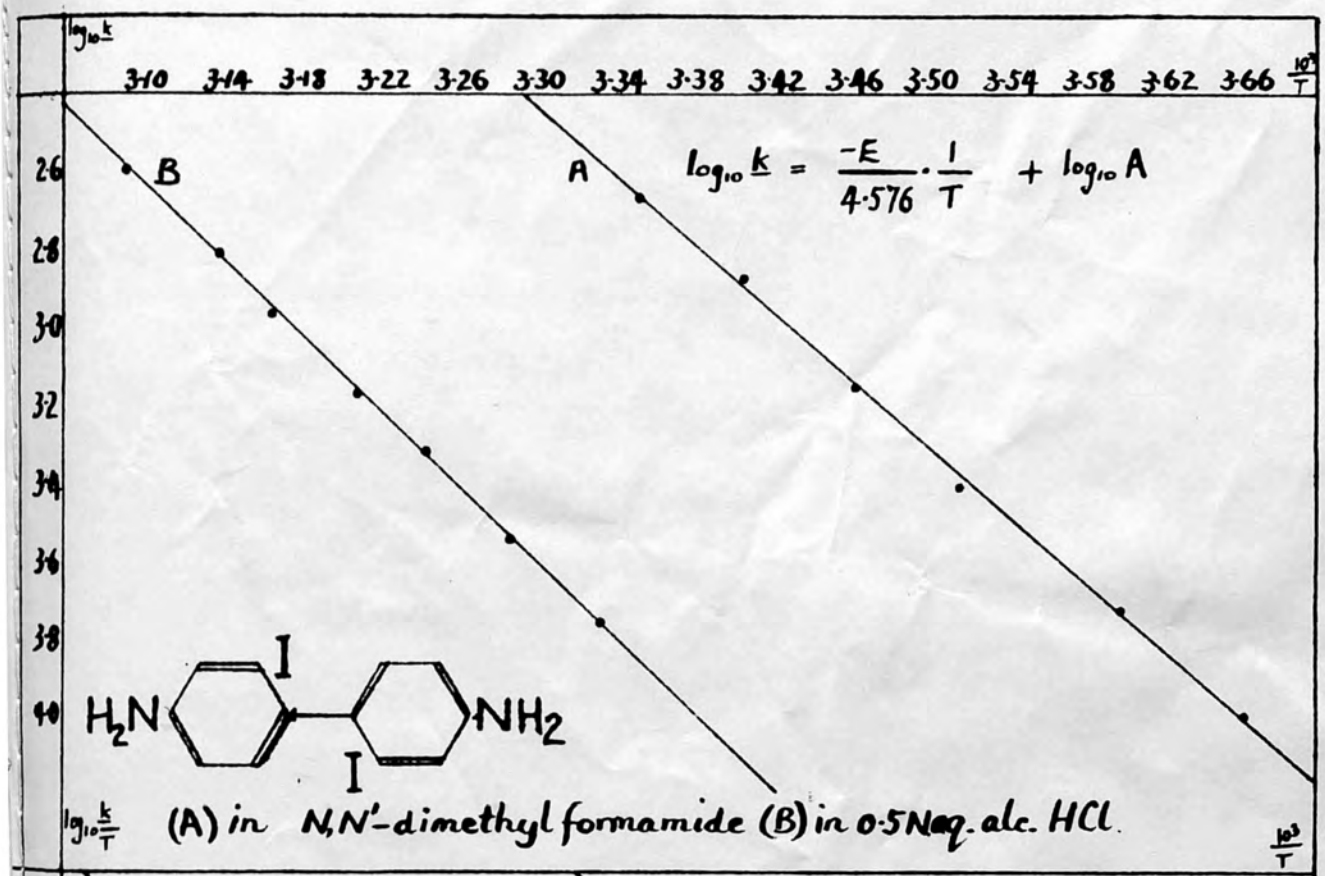
$n\Sigma xy = -0.4999945$	$n\Sigma x^2 = 498.8302$	$\Sigma x^2 \Sigma y = 1.602064$
$-\Sigma x \Sigma y = -0.4985198$	$(\Sigma x)^2 = 491.7159$	$\Sigma x \Sigma xy = 1.583888$
-0.0014747	-7.1143	0.018176

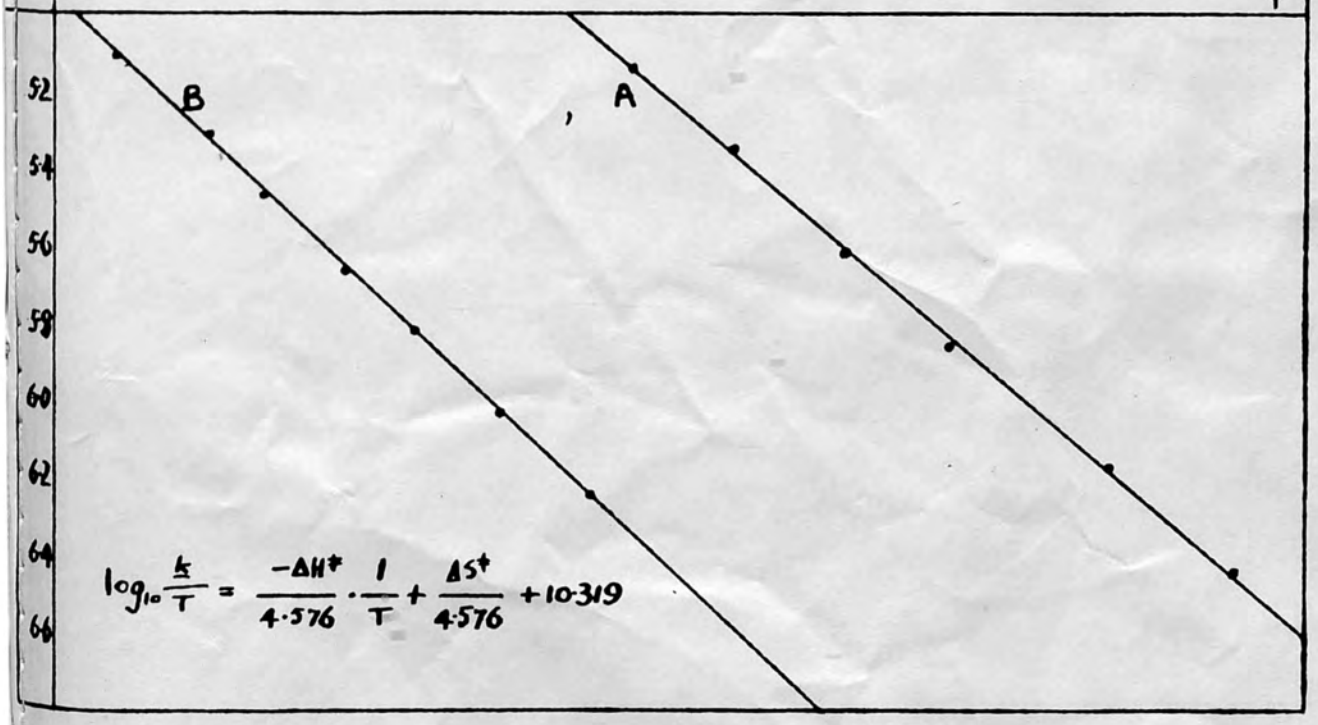
$$E = \frac{4.576 \times 7.1143}{0.0014747} \text{ cal.mole}^{-1} = 22.08 \text{ kcal.mole}^{-1}$$

$$\log_{10}A = \frac{0.018176}{0.0014747} = 12.33$$

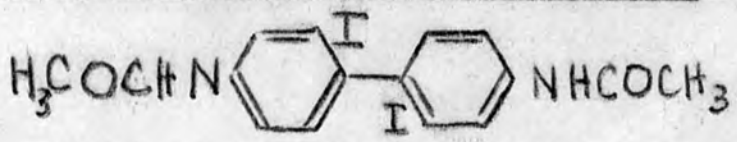
$E^{\ddagger}$ 22.1 kcal.mole^{-1} $\quad \Delta H^{\ddagger}$ 21.4 kcal.mole^{-1} $\quad \Delta F^{\ddagger}$ 22.8 kcal.mole^{-1} (25°C)

$\log_{10}A$ 12.3 $\quad \Delta S^{\ddagger}$ -4.3 e.u.

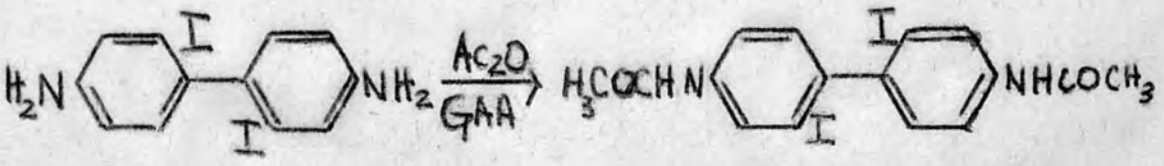

log10 k
3·10 3·14 3·18 3·22 3·26 3·30 3·34 3·38 3·42 3·46 3·50 3·54 3·58 3·62 3·66 10³/T
2·6 2·8 3·0 3·2 3·4 3·6 3·8 4·0
B
A
log10 k = −E/4·576 · 1/T + log10 A
I
H2N
NH2
I
log10 k/T
(A) in N,N'-dimethyl formamide (B) in 0·5N aq. alc. HCl.
10³/T


5·2 5·4 5·6 5·8 6·0 6·2 6·4 6·6
B
A
log10 k/T = −ΔH*/4·576 · 1/T + ΔS*/4·576 + 10·319

2,2'-di-iodo-4,4'-diacetamidobiphenyl.



2,2'-di-iodo-4,4'-diacetamidobiphenyl was obtained in optically active condition by di-acetylating 2,2'†di-iodobenzidine below -20°.



Preparation of (+) 2,2'-di-iodo-4,4'-diacetamidobiphenyl. - 4.2 g. of powdered 2,2'-di-iodobenzidine, $[\alpha]^{7.4^\circ}_{5461}$ +69.2°, in N,N'-dimethylformamide were added to a mechanically stirred mixture of 28 c.c. glacial acid and 56 c.c. of acetic anhydride, cooled below -20° in solid CO_2 and acetone. Solution took place at first, but the reaction mixture gradually became cloudy and a solid separated. (Some acetic acid also crystallised out). After half an hour, the reaction mixture was poured into 600 c.c. of ice-cold dilute hydrochloric acid, and the solid allowed to settle. After filtering, washing with water, and drying in vacuo, 5.0 g. of white powder, m.p. 293-296°, (slightly shrinking at 290°), $[\alpha]^{32^\circ}_{g}$ +25.5° were obtained (Found: C, 35.8; H, 3.0; N, 5.2; I, 48.2. $C_{16}H_{14}O_2N_2I_2,H_2O$ requires C, 35.7; H, 3.0; N, 5.2; I, 47.2%) After drying under high vacuum at 50°, (found: C, 36.9; H, 2.6; O, 6.3. $C_{16}H_{14}O_2N_2I_2$ requires C, 37.1; H, 2.7, O, 6.1%).

Determination of rate coefficients for the racemisation of

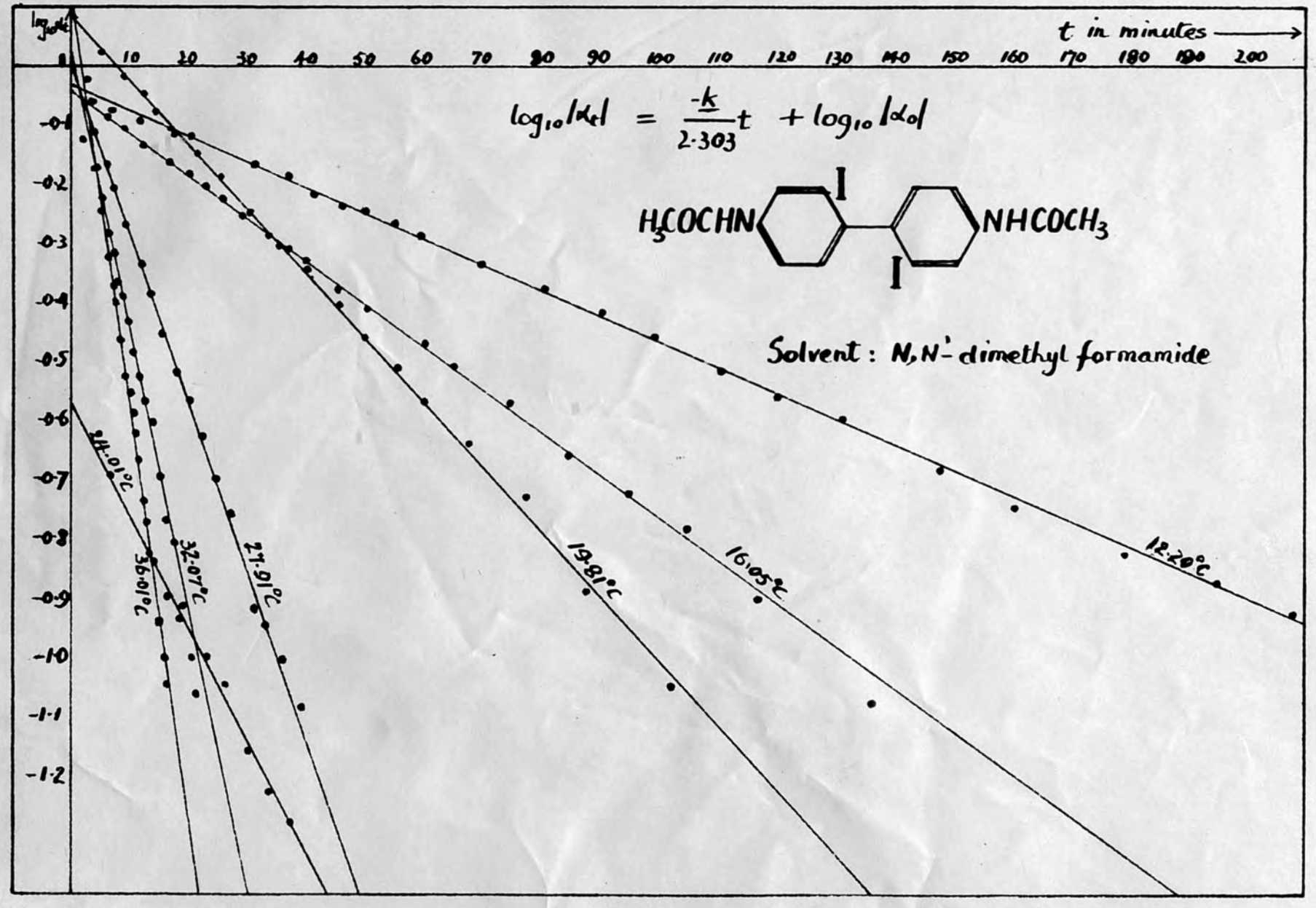
2,2'-di-iodo-4,4'-di-acetamidobiphenyl.

Solvent: N,N'-dimethylformamide.

Concentration: 0.3-0.4 g. in 17 c.c. of solvent.

$[\alpha]_{5461}$ by extrapolation $+25.2^{\circ}$-$+26^{\circ}$.

Temperature $T^{\circ}C.$	Time of first reading min.	First reading α_t deg.	No. of readings	Time during which readings were taken min.	$\underline{k} \times 10^{-4}$ $sec.^{-1}$	$t_{\frac{1}{2}}$ min.
12.20	7.05	+0.84	23	208.1	1.68	68.6
16.05	6.3	+0.82	22	136.8	2.76	41.9
19.81	5.4	+1.07	18	102.2	4.18	27.6
24.0	6.75	+0.20	9	39.4	7.26	15.9
27.91	4.0	+0.78	16	39.4	1.09	10.6
32.07	2.1	+0.75	18	21.6	1.82	6.3
36.01	2.8	+0.95	19	16.6	2.71	4.3


log |α|
t in minutes
10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200
0 -0·1 -0·2 -0·3 -0·4 -0·5 -0·6 -0·7 -0·8 -0·9 -1·0 -1·1 -1·2
$\log_{10}|\alpha_t| = \frac{-k}{2.303}t + \log_{10}|\alpha_0|$
H_3COCHN
$NHCOCH_3$
I
I
Solvent : N, N'- dimethyl formamide
44·01°C
36·01°C
32·07°C
27·91°C
19·81°C
16·05°C
12·20°C

811

Determination of Arrhenius parameters A and E, and Transition State Theory functions $\Delta H^{\neq}$, $\Delta S^{\neq}$, and $\Delta F^{\neq}$ for the racemisation of 2,2'-di-iodo-4,4'-diacetamidobiphenyl in N,N'-dimethylformamide.

$T^{o}K$	$\frac{10^3}{T^{o}K} = y \times 10^3$	$k \times 10^{-4} sec^{-1}$	$\log_{10} k = x$	x^2	xy	$\log_{10} \frac{k}{T}$
285.40	3.50385	1.6846	-3.773503	14.23930	13.22178	-6.228957
289.25	3.45722	2.7576	-3.559469	12.66983	12.30587	-6.020742
293.01	3.41285	4.1795	-3.378876	11.41683	11.53161	-5.845758
297.20	3.36474	7.2617	-3.138962	9.85307	10.56178	-5.612011
301.11	3.32105	10.896	-2.962733	8.77777	9.83937	-5.441458
305.27	3.27579	18.232	-2.739166	7.50305	8.97295	-5.223850
309.21	3.23405	20.094	-2.567127	6.59016	8.30223	-5.057381
	23.56955		22.11984	71.05001	74.73559	

Graphical Methods.

$E = 20.57$ kcal.mole^{-1} $\quad \log_{10}A = 11.98$

$\Delta H = 19.92$ kcal.mole^{-1} $\quad \Delta S = -5.8$ e.u.

$\Delta F = 21.7$ kcal.mole^{-1} (25°C)

Mean Square Calculations.

$\Sigma y = +23.56955 \times 10^{-3}$ $\quad \Sigma x = -22.11984$

$\Sigma xy = -74.73559 \times 10^{-3}$ $\quad \Sigma x^2 = 71.05001$

$n = 7$

$n\Sigma xy = -0.523149$ $\quad n\Sigma x^2 = 497.3501$ $\quad \Sigma x^2 \Sigma y = 1.67462$

$-\Sigma x \Sigma y = \underline{+0.521355}$ $\quad -(\Sigma x)^2 = \underline{489.2873}$ $\quad -\Sigma x \Sigma xy = \underline{-1.65314}$

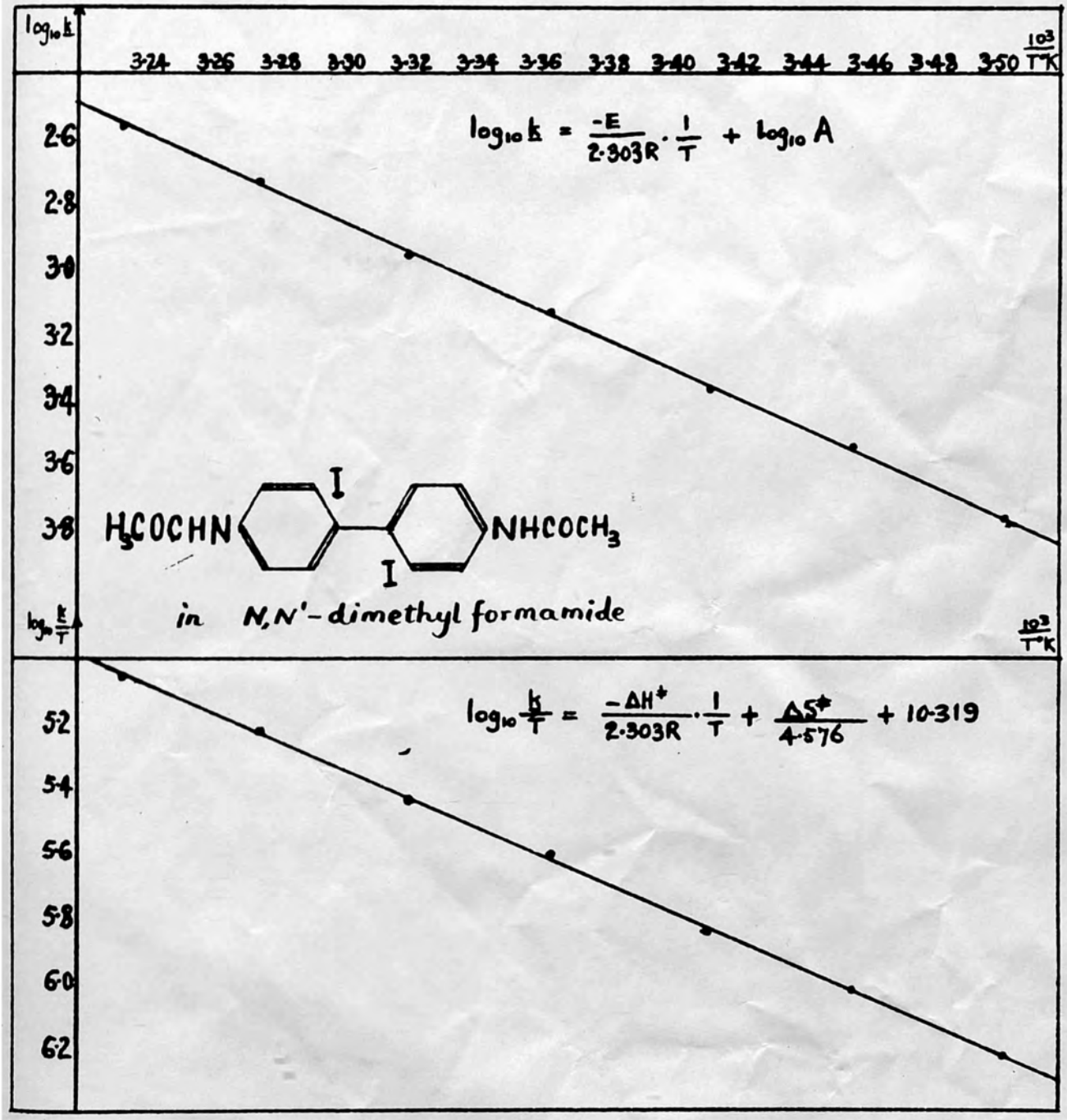
-0.001794 $\quad 8.0628$ $\quad 0.02148$

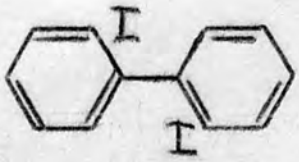
$$E = \frac{-4.576 \times 8.0628}{-0.001794} = 20.57$$

$$\log_{10}A = \frac{-0.02148}{-0.001794} = 11.97$$

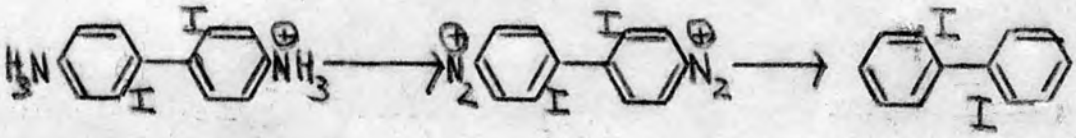
$E = 20.6$ kcal.mole^{-1} $\quad \Delta H^{\ddagger} = 19.9$ kcal mole^{-1} $\quad \Delta F^{\ddagger} = 21.7$ kcal mole^{-1}

$\log_{10}A$ 12.0 $\quad \Delta S^{\ddagger}$ -5.8


log10 k
3·24 3·26 3·28 3·30 3·32 3·34 3·36 3·38 3·40 3·42 3·44 3·46 3·48 3·50
10³/T°K
2·6
2·8
3·0
3·2
3·4
3·6
3·8
log10 k/T
log10 k = -E/2·303R · 1/T + log10 A
H3COCHN
NHCOCH3
I
I
in N,N'-dimethyl formamide
10³/T°K
5·2
5·4
5·6
5·8
6·0
6·2
log10 k/T = -ΔH‡/2·303R · 1/T + ΔS‡/4·576 + 10·319

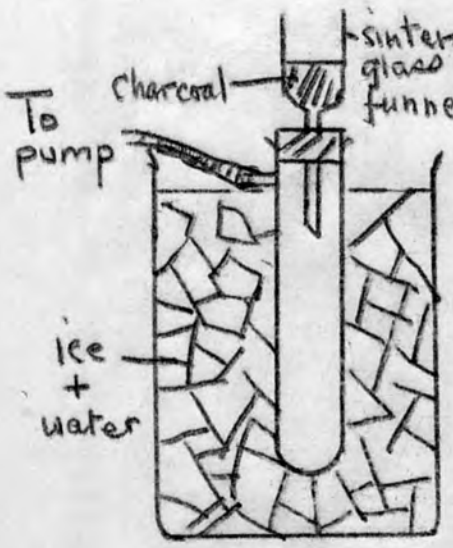
2,2'-di-iodobiphenyl. 

2,2'-di-iodobiphenyl was obtained in the optically active condition by deaminating optically active 2,2'-di-iodobenzidine at -25 to -20°.



Preparation: 1.7 g. of powdered 2,2'-di-iodobenzidine dihydrogen tartrate were placed in a small beaker immersed in a bath of acetone and solid CO_2 at -25 to -20°. 2.5 c.c. of ice-cold conc. hydrochloric acid were added with stirring. To the thick paste of 2,2'-di-iodobenzidine hydrochloride, a concentrated solution of 0.9 g. of sodium nitrite was added. The final diazo solution contained a slight yellow precipitate, but was poured without filtering into 30 ml. of mechanically stirred hypophosphorous acid contained in a beaker immersed in the same bath. Freshly prepared cuprous oxide (0.2-0.4 g.) was added from time to time to catalyse the reaction. Effervescence occurred, and after 10-30 minutes (this period varied from experiment to experiment) of stirring, vigorous frothing occurred with separation of much solid. After frothing had subsided, the solid was filtered, washed with water, cold 10% sodium hydroxide, then again with water, and dried over calcium chloride in a vacuum desiccator.

The crude product (0.85 g.) was rapidly dissolved in 15 c.c. of cold (5°) benzene and immediately filtered and washed through a short column of charcoal in cold benzene under gentle suction. (see diagram)



30 c.c. portions were collected, diluted with an equal volume of light petroleum (40-60°) and evaporated to dryness in the cold by drawing a stream of air over the surface of the solution, with the aid of a fume cupboard. The whole operation, from the solution of the crude product to obtaining the purified crystalline product, took 30-40 minutes. After drying over calcium chloride in a vacuum desiccator, 0.56 g. of white crystals, m.p. 102-106° (starting to melt slightly at 85°) were obtained. This product contained no detectable primary amine and the analysis results were good. (Found: C, 35.4; H, 1.9; I, 62.8. $C_{12}H_8I_2$ requires C, 35.5; H, 2.0; I, 62.5%).

Different specimens of 2,2'-di-iodobiphenyl obtained from the same specimen of hydrogen tartrate varied in specific rotation: from $[\alpha]_{5461}$ 2.5-4.3°; 2.5-5.0, 3.7-7.9 in N,N'-dimethylformamide, but the specimens obtained were usually the lower rotations.

Determination of rate coefficients for the racemisation of

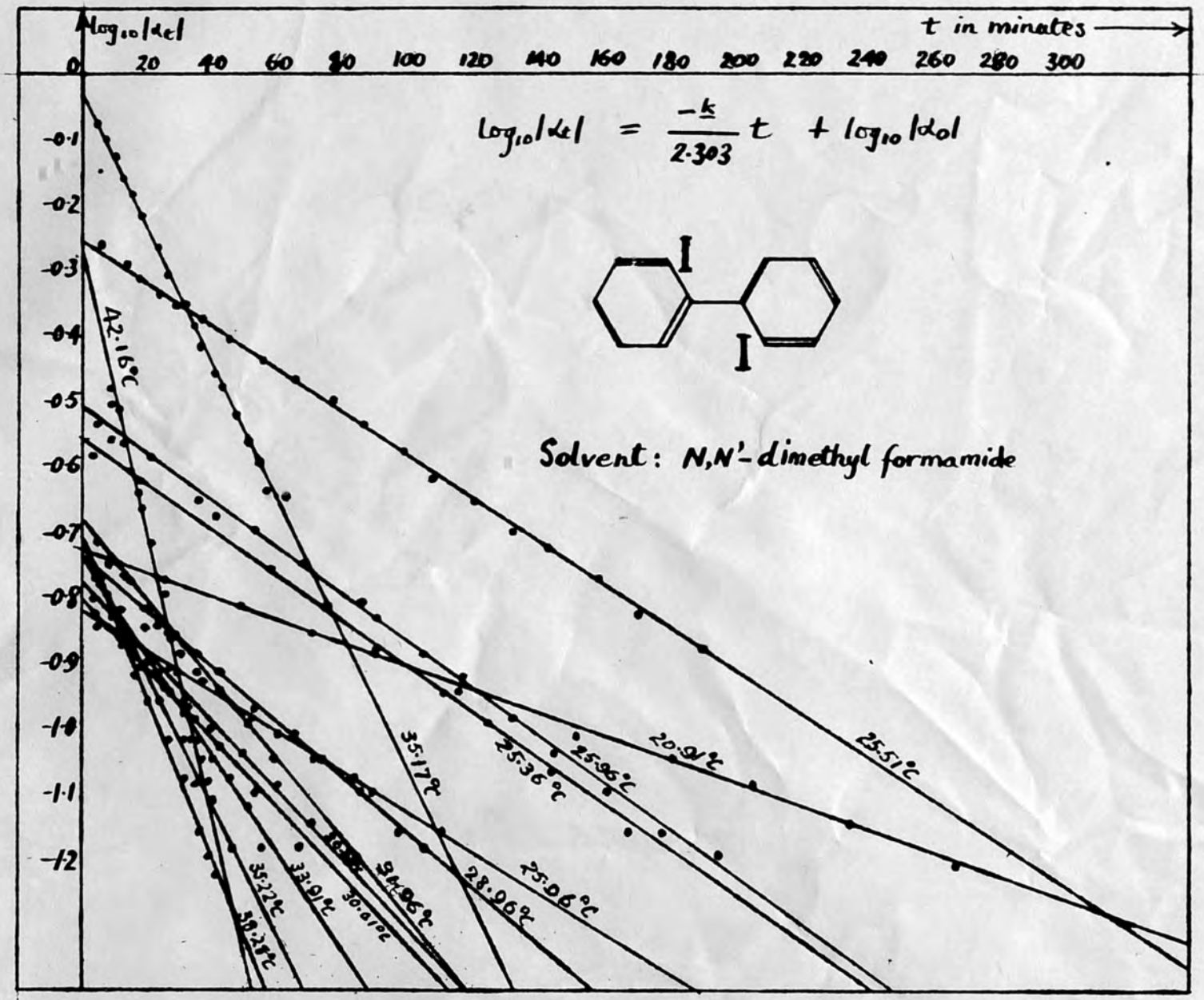
2,2'-di-iodobiphenyl.

Solvent: N,N'-dimethylformamide.

$[\alpha_o]_{5461}$ by extrapolation: -25° to -7.9°

$+2.8^\circ$ to $+15.1^\circ$

Temperature	Time of first reading		First reading α_t	Amt. of solid in 17 c.c. of solvent	No. of readings	Time during which readings were taken	$k \times 10^{-4}$	$t_{\frac{1}{2}}$
$T^\circ C.$	min.		deg.	g.		min.	$sec.^{-1}$	min.
20.91	4.5		-0.17	0.542	11	268.3	0.68	170.1
25.36	3.5	*	-0.26	0.552	10	168.1	1.34	86.5
25.51	5.5	*	-0.55	0.593	19	191.3	1.27	91.0
25.96	4.6	*	0.29	0.521	14	178.0	1.36	84.8
25.96	4.3		-0.14	0.518	10	111.6	1.19	97
28.96	8.2		-0.18	0.42	13	104.9	1.63	70.7
30.01	4.2		-0.15	0.50	10	66.6	2.12	54.5
30.36	3.6		+0.16	0.559	11	82.1	1.95	59.2
31.96	4.3		-0.17	0.458	11	58.8	2.40	36.8
33.91	5.4		-0.17	0.551	12	55.3	2.91	39.6
35.17	4.2	*	+0.83	0.517	18	62.4	3.95	29.2
35.22	4.3		+0.17	0.553	9	46.0	3.84	30.1
38.28	4.9		-0.17	0.572	10	40.7	4.71	24.5
42.16	8.4	*	+0.33	0.244	15	39.3	8.14	14.2


log10|dc|
t in minutes
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
-0·1
-0·2
-0·3
-0·4
-0·5
-0·6
-0·7
-0·8
-0·9
-1·0
-1·1
-1·2
log10|dc| = -k/2·303 t + log10|dc0|
I
I
Solvent: N,N'-dimethyl formamide
42·16°C
35·17°C
25·36°C
25·06°C
20·91°C
25·51°C
35·22°C
33·91°C
30·01°C
28·06°C
25·06°C

Determination of Arrhenius parameters E and $\log_{10}A$ and Transition State Theory Functions $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta F^{\ddagger}$ for the racemisation of 2,2'-di-iodobiphenyl in N,N-dimethylformamide.

$T^{o}K$	$\frac{10^3}{T^{o}K}$ $=yx10^3$	$kx10^{-4}$ sec.$^{-1}$	$\log_{10}k=x$	x^2	xy	$\log_{10}\frac{k}{T}$	
294.11	3.40009	0.67909	-4.16807	17.37281	14.17181		
298.56	3.34941	1.33507	-3.87449	15.01167	12.97726	-6.3495	*
298.71	3.34773	1.26985	-3.89623	15.18061	13.04353	-6.3715	*
299.16	3.34267	1.36199	-3.86582	14.94456	12.92224	-6.3417	*
299.16	3.34269	1.19121	-3.92402	15.39793	13.11678		
302.16	3.31215	1.63439	-3.78664	14.33864	12.54192		
303.21	2.29804	2.11770	-3.67414	13.49930	12.11746		
303.56	3.29424	1.95283	-3.70934	13.75920	12.21946		
305.16	3.27697	2.40477	-3.61892	13.09658	11.85909		
307.11	3.25616	2.81377	-3.53554	12.50004	11.51228		
308.37	3.24286	3.95465	-3.40289	11.57966	11.03510	-5.8920	*
308.42	3.24233	3.83833	-3.41586	11.66810	11.07535		
311.48	3.21048	4.71068	-3.32692	11.06840	10.68101		
315.36	3.17098	8.14192	-3.08274	9.50329	9.77531	-5.5815	*
	46.08682		51.28162	188.92079	169.04850		

Graphical Methods.

The data marked with * are those corresponding to experiments in which the initial αt reading is greater than 0.2° and only these 5 sets of data are used in graphical determination of E, $\log_{10}A$, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ and $\Delta F^{\ddagger}$.

$E = 20.91$ kcal.mole^{-1} $\quad\quad$ $\log_{10}A = 11.41$

$\Delta H^{\ddagger} = 20.34$ kcal.mole^{-1} $\quad\quad$ $\Delta S^{\ddagger} = 8.24$

$\Delta F^{\ddagger} = 22.8$ kcal.mole^{-}

Mean Square calculations.

$\Sigma x = -51.28162$ $\quad$ $\Sigma y = 46.08682 \times 10^{-3}$ $\quad$ $\Sigma x^2 = 188.92079$

$\Sigma xy = -169.04850 \times 10^{-3}$

$n = 14$

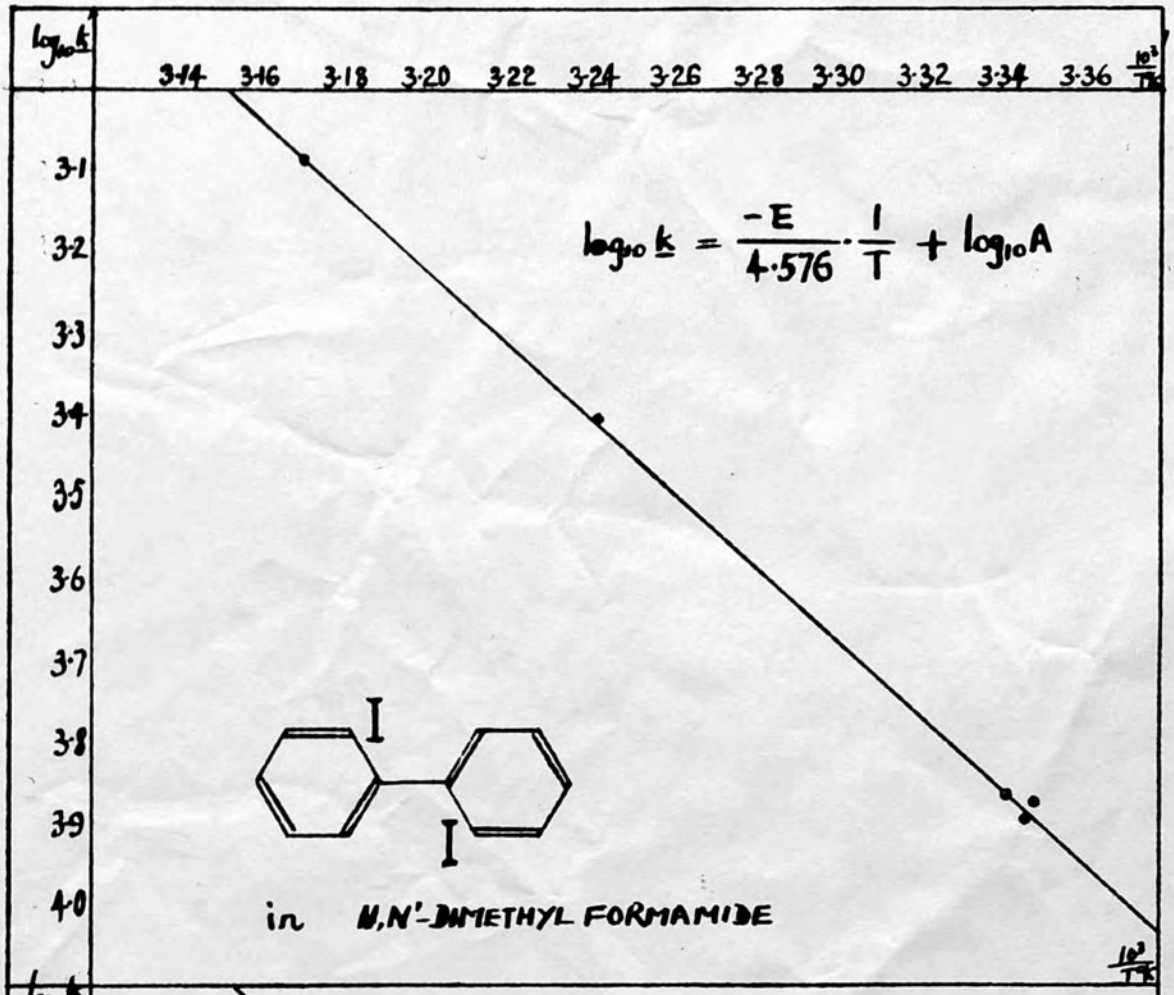
$n\Sigma xy = -2.36668$	$n\Sigma x^2 = 2644.8911$	$\Sigma x^2 \Sigma y = 8.70676$
$-\Sigma x \Sigma y = \underline{+2.36341}$	$-(\Sigma x)^2 = \underline{-2629.8045}$	$-\Sigma x \Sigma xy = \underline{-8.66908}$
-0.00327	15.0866	0.03768

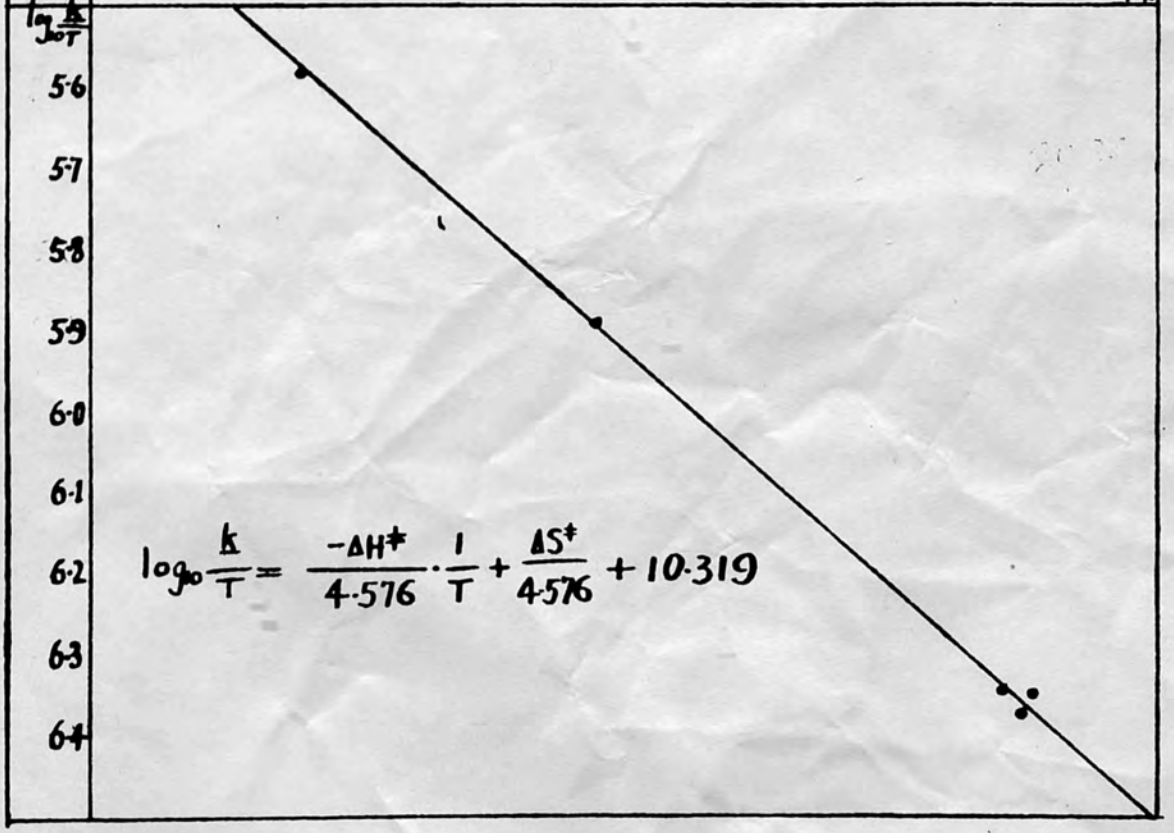
$$E = \frac{-4.576 \times 15.0866}{-0.00327} \text{ kcal.mole}^{-1} = 21.11 \text{ kcal.mole}^{-1}$$

$$\log_{10}A = \frac{-0.03768}{0.00327} = 11.52$$

E 21.0 kcal.mole^{-1} $\quad$ $\Delta H^{\ddagger}$ 20.3 kcal.mole^{-1} $\quad$ $\Delta F^{\ddagger}$ 22.8 kcal.mole^{-1} $(25^{\circ}C)$

$\log_{10}a = 11.5$ $\quad\quad$ $\Delta S^{\ddagger} = 8.2$ e.u.

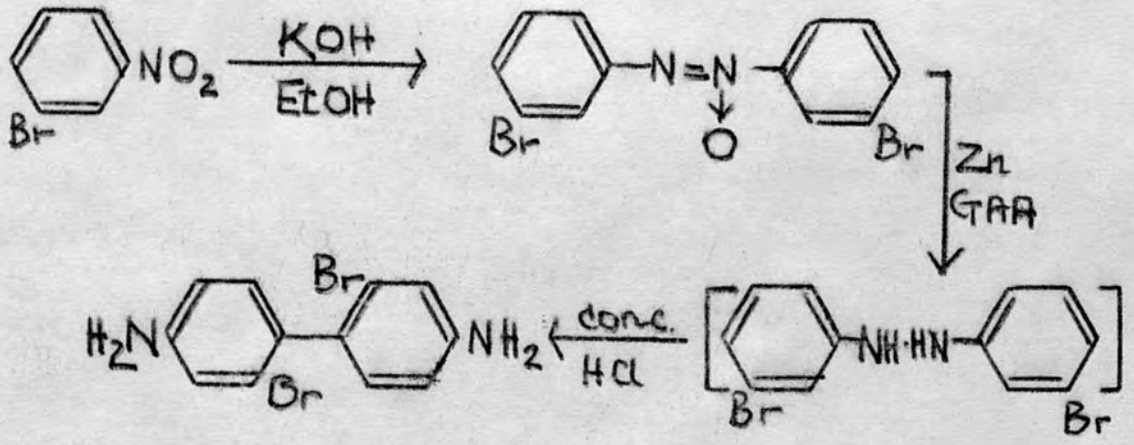

log10 k
3·14 3·16 3·18 3·20 3·22 3·24 3·26 3·28 3·30 3·32 3·34 3·36 10³/T K
3·1 3·2 3·3 3·4 3·5 3·6 3·7 3·8 3·9 4·0
log10 k = -E/4·576 · 1/T + log10 A
I
I
in N,N'-DIMETHYL FORMAMIDE
10³/T K


log k/T
5·6 5·7 5·8 5·9 6·0 6·1 6·2 6·3 6·4
log10 k/T = -ΔH‡/4·576 · 1/T + ΔS‡/4·576 + 10·319

SYNTHETIC WORK - EXPERIMENTAL.

2,2'-dibromobenzidine:

Scheme.



(i) 3,3'-dibromoazoxybenzene:- (Gabriel, Ber., 1876, 1405)

26 g. of m-bromonitrobenzene were added to a hot solution of 16 g. of potassium hydroxide in 120 c.c. of ethanol (S.V.R.) and the mixture boiled under reflux for 3/4 hr. The solution became very dark and solid gradually separated. After cooling, the solid was filtered and washed with methylated spirit, water, and then dried (20 g.). On crystallisation from glacial acetic acid containing a little conc. nitric acid, 15 g. (65.5%) of golden crystals, m.p. 111-112°, were obtained.

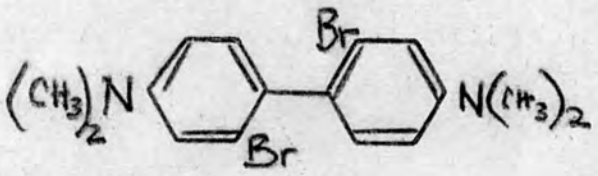
(ii) 2,2'-dibromobenzidine:

(a) 3,3'-dibromohydrazobenzene (cf. Khalifa, J., 1960, 1854). 21 g. of 3,3'-dibromoazoxybenzene, 240 g. of Zn powder and 500 c.c. of ether were warmed with mechanical stirring in a 2 L round-bottomed flask fitted with a dropping funnel and an efficient condenser. To the gently boiling solution, 15 c.c. of glacial acetic acid were added dropwise. When about half of the glacial acetic acid was added, the reaction became very vigorous and the yellow solution became orange. The vigorous reaction soon subsided and the reaction proceeded smoothly until the solution became colourless. The ethereal solution was filtered and ether was distilled off until the volume of the solution was reduced to about 80 c.c.

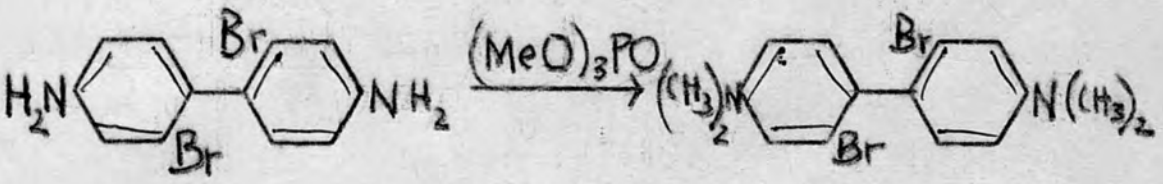
(b) Benzidine rearrangements (Searle and Adams, J.A.C.S. 1934, 2114): The ethereal solution of 3,3'-dibromohydrazobenzene was added dropwise to 140 c.c. of conc. hydrochloric acid with stirring. Heat was evolved; the acid solution became yellow and a precipitate separated gradually. The suspension was allowed to cool and the precipitate filtered, washed with a little methylated spirit and ether (which removed the orange colour) and dried (11.5 g.) This was stirred with dilute hydrochloric acid and filtered. The filtrate was treated with 0.2% NaOH solution to liberate

the base, which was filtered, washed thoroughly with water and dried (9.5 g.) Crystallisation from aqueous methylated spirit gave 7.4 g. (36.6%) of colourless crystals, m.p. 151-152.5°.

N,N'-tetramethyl-2,2'-dibromobenzidine.



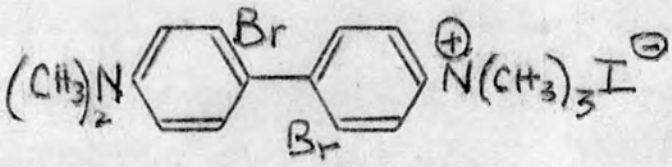
N-methylation of 2,2'-dibromobenzidine was effected by dimethyl sulphate and by trimethyl phosphate (Billman, Radike and Mundy, J.A.C.S., 1942, 64, 2977); the latter gave a better yield of N,N'-tetramethyl-2,2'-dibromobenzidine.



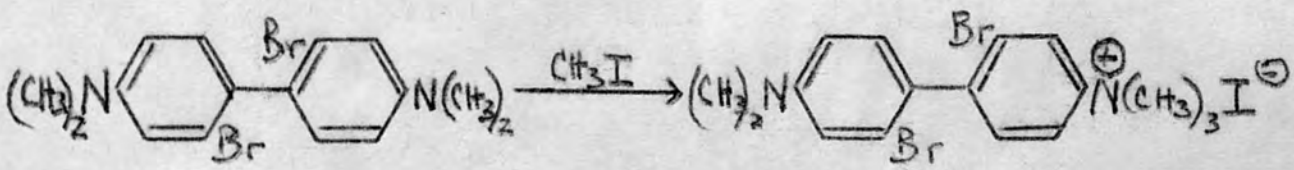
5 g. of 2,2'-dibromobenzidine and 50 c.c. of trimethyl phosphate were heated under reflux for one hour. A solution containing 60 g. of sodium hydroxide (to destroy excess trimethyl phosphate) in 200 c.c. of water was added, and heating was continued for another 2 hours. The hot reaction mixture was then filtered. The residue was stirred with 200 c.c. of hot (almost boiling) water (to remove inorganic material), filtered, and washed with hot water. The crude product (5 g.) was extracted with 120 c.c. of boiling methylated spirit and filtered (hot) on a Buchner. The residue was boiled with charcoal in methylated spirit solution, filtered and allowed to crystallise. 3.05 g. of white

prismatic needles, m.p. 184° (softening at 176°) were obtained. (Found: C, 48.3; H, 4.4; N, 7.1; Br, 40.6%. $C_{16}H_{18}N_2Br_2$ requires C, 48.3; H, 4.6; N, 7.0; Br, 40.1%). From the extract another 0.25 g. of N,N'-tetramethyl-2,2'-di-iodobenzidine was obtained. The total yield was 3.3 g. (57%).

2,2'-dibromo-4'-[N,N'-dimethylamino]-biphenyl-4-yl-trimethyl ammonium iodide.



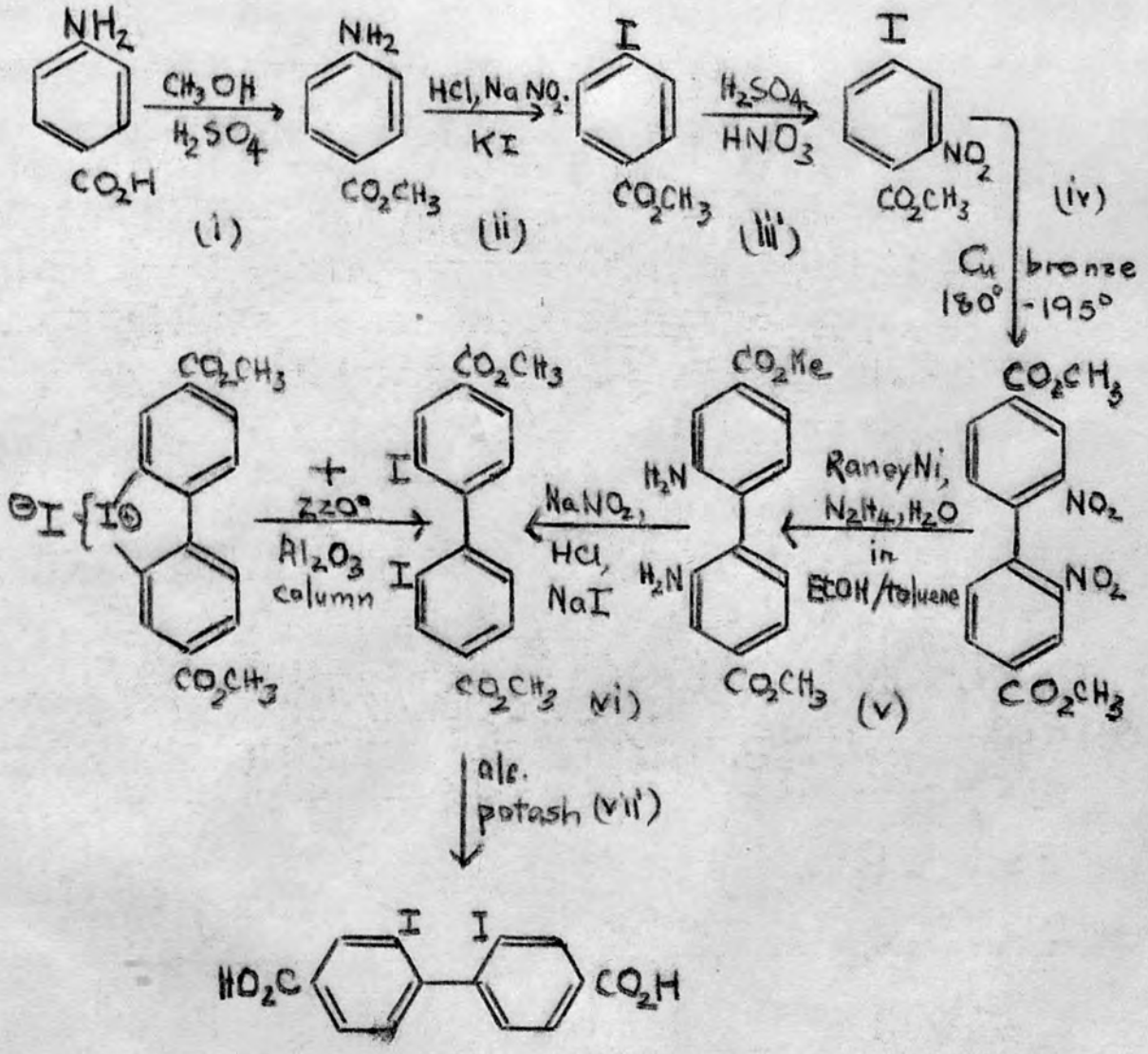
N,N'-tetramethyl-2,2'-di-bromobenzidine reacted with methyl iodide under atmospheric pressure to give the mono methiodide



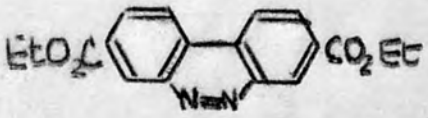
1 g. of N,N'-tetramethyl-2,2'-di-iodobenzidine and 50 c.c. of methyl iodide were heated under reflux in a water bath at 70-80°, for six hours. The resulting solution was evaporated to dryness. The crude product (1.35 g.) when crystallised from 800 c.c. of water, gave 0.61 g. of straw coloured needles, m.p. 200-213° (decomp.) varying according to the rate of heating. (Found: C, 37.7; H, 3.6; N, 5.1; Hal, 54.1%. $C_{18}H_{24}N_2Br_2I_2$ requires C, 37.8; H, 3.9; N, 5.2; Hal, 53.1%). A second crop of 0.17 g. was obtained from the mother liquor. The total yield was 0.78 g. (57.4%).

2,2'-Bi-iodobiphenyl-4,4'-dicarboxylic Acid.

The method of Searle and Adams (J.A.C.S., 1933, 56, 1951-3) was used with substantial modifications. The methyl esters were employed throughout instead of the ethyl esters used by the previous workers.



Stages (iv), (v) and (vi) of the above synthesis have been modified with improved yields. For stage (v), hydrogenation using Adams' PtO_2 catalyst yielded a product which contained the cinnolinium compound and proved difficult to purify. The cinnolinium compound



was isolated, m.p. 215-7°.
(Found: C, 66.5; H, 5.1; N, 8.6%. $C_{18}H_{16}N_2O_4$ requires C, 66.7; H, 5.0; N, 8.6%). The difficulty encountered in carrying out the above scheme of synthesis prompted attempts to obtain 2,2'-di-iodobiphenyl by direct iodination (p. 147-150)

(i) Methyl-p-aminobenzoate. - 2 Litres of methanol containing 100 c.c. of conc. sulphuric acid were added, with swirling, to 200 g. of p-aminobenzoic acid in a round-bottomed flask and the mixture heated under reflux for 10 hrs. About 1 litre of methanol was distilled off and the remainder poured into 1½ litres of cold water. A hot concentrated solution of sodium carbonate was gradually added, with stirring, until the solution was alkaline to litmus. The white solid which separated was filtered, washed with water and dried (205 g.). Crystallisation from aqueous methanol (1 litre of MeOH + 1½ litres of water) gave 184 g. (84%) of straw-coloured crystals, m.p. 110-112.5°.

(ii) Methyl-p-iodobenzoate: - 138 g. (0.92 mole) of finely powdered methyl-p-aminobenzoate were made into a paste with water. 750 c.c. of 6N hydrochloric acid (450 c.c. of conc. HCl + 300 c.c. of water) were added. The mixture was cooled with mechanical stirring below 0° and diazotised using 69 g. (1 mole) of sodium nitrite in 150 c.c. of water. The resulting solution was added, with mechanical stirring, to a solution of 250 g. (1.5 mole) of potassium iodide in 225 c.c. of water, the frothing reaction mixture warmed in hot water and stirred with sodium metabisulphite solution. The product was filtered, washed thoroughly with water and dried. Crystallisation from methanol gave 181 g.,(75.6%) of salmon-pink crystals, m.p. 112-114°. Searle and Adams quoted a yield of 68.5% for the ethyl ester.

(iii) Methyl-p-iodo-m-nitrobenzoate: - A solution of 58 g. of powdered methyl-p-iodobenzoate in 75 c.c. of conc.sulphuric acid was cooled with mechanical stirring below 5° and a mixture of 30 c.c. of conc. nitric acid and 30 c.c. of conc. sulphuric acid added dropwise, keeping the temperature below 6°. The first drop of nitrating mixture added turned the solution black and the reaction mixture became increasingly viscous until about 1/3 of the nitrating mixture had been added. Further addition was, however, accompanied by a decrease in viscosity and a gradual change of colour from black to reddish-brown. When all the nitrating mixture had

been added, the reaction mixture was stirred for a further ½ hr. and then allowed to stand in the ice + water for another 2 hours, during which time a pale yellow precipitate was gradually deposited. The mixture was poured, with stirring, on to crushed ice. The yellow solid which separated was filtered, washed thorough with water and dried. Crystallisation from methanol gave 42 g. (61.8%) of yellow crystals, m.p. 104-106°. [Note: A considerable amount of by-product was obtained from the mother liquor. This by-product, after two recrystallisations from methanol, gave pale yellow silky needles, m.p. 172-3° (decomp.) (Found: C, 33.3; H, 2.1; N, 2.4; I, 43.3%) The nitration of ethyl-p-iodobenzoate was also carried out: a similar by-product, white crystals, m.p.146-8° (decomp.) was obtained after one recrystallisation from methylated spirit. (Found: C, 35.7; H, 2.8; N, 2.8; I, 41.9%). These two by-products have not been identified.]

(iv) Dimethyl 2,2'-dinitrobiphenyl-4,4'-dicarboxylate - (Ullmann Reaction).

50 g. of Methyl 3-nitro-4-iodobenzoate were melted in a hard glass tube immersed in a metal bath heated to 180°. 40 g. of copper bronze were added, with stirring, at such a rate as to maintain the internal temperature between 180-195°, while the temperature of the bath was kept between

165-175°. When all the copper bronze had been added, the bath was raised to 190° for 15 mins. The tube was then removed from the metal bath, allowed to cool to 100° and the reaction mixture extracted several times with boiling chloroform. The extracts were filtered through a Buchner funnel, and the filtrate evaporated to dryness. Crystallisation of the crude product (29 g.) from aqueous acetone gave 22 g. of large yellow prisms, m.p. 159-161°.

The overall yield from 9 experiments using 450 g. of starting material was 207 g. (78.5%).

Notes.

(1) The procedure recommended by Searle and Adams was carried out on both the ethyl and the methyl esters. The removal of the diluent, nitrobenzene, from the product proved rather tedious; the product was difficult to obtain pure and the yields in general were rather poor (below 50%). Searle and Adams quoted a 69% yield for the ethyl ester.

(2) In carrying out the reaction without a diluent, it was found that if the internal temperature was kept above 200°, the product was much darker, and the yield poor.

(v) Dimethyl 2,2'-diaminobiphenyl-4,4'-dicarboxylate:-
The method used was described (for other compounds) by Balcom and Furst (J.A.C.S., 1953, 75, 4334) and Moore and Furst (J.Org.Chem., 1958, 23, 1504).

(a) Preparation of W-2 Raney Nickel.

This was prepared according to the procedure given in Organic Synthesis, Collective Vol.III, p.181.

(b) Reduction with hydrazine using W-2 Raney Ni as catalyst.

About 1 tablespoonful of W-2 Raney Ni was added to a hot solution of 18 g. of dimethyl 2,2'-dinitrobiphenyl-4,4'-dicarboxylate in 800 c.c. of 95% alcohol and 200 c.c. of toluene in a round bottomed flask (4L) fitted with a reflux condenser and a dropping funnel. 100% Hydrazine hydrate was added from the dropping funnel, with swirling, the rate of addition being such as to maintain a vigorous reaction without application of heat. The solution became bright yellow on colour. This colour soon disappeared, but as the reaction proceeded the colour of the solution changed from almost colourless to dark reddish brown. When the brown colour appeared, the solution was heated, more Raney Ni added, and the addition of hydrazine hydrate continued at a reduced rate until the solution became pale yellow (about 65 c.c. of hydrazine hydrate was required).

The hot solution was filtered through a pad of filter paper, concentrated to 300 c.c. by distilling off the solvent under reduced pressure, and cooled in ice.

The pale yellow crystals which separated were filtered and dried, 12.5 g; m.p. 174-6°.

Notes.

(1) Yields varied from 11 g. to 13.9 g. and m.p's from 171-4° to 174-6°. The less pure specimens were recrystallised from benzene containing a little methylated spirit. The overall yield from 204 g. of dimethyl 2,2'-dinitrobiphenyl-4,4'-dicarboxylate was 143 g. (84%). (Found: C, 64.1; H, 5.5; N, 9.4. $C_{16}H_{16}N_2O_4$ requires C, 64.0; H, 5.1; N, 9.3%).

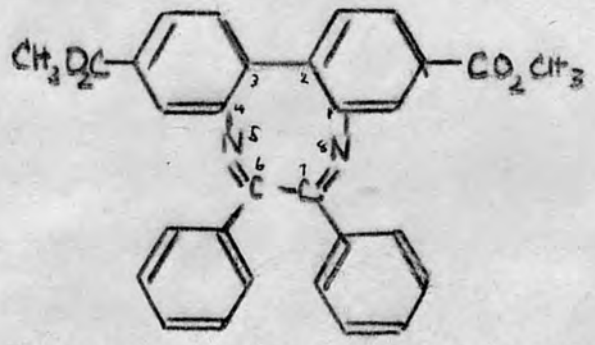
(2) Dimethyl 2,2'-diaminobiphenyl-4,4'-dicarboxylate occurs in two crystalline forms, long bright yellow needles m.p. 174.5-6°, and pale yellow rhombohedra m.p. 174-5°, mixed m.p. 174-6°. The melt of the bright yellow needles when solidified, gave the pale yellow rhombohedra; the infrared spectra of the two forms (solid) in nujol were different, but the spectrum of the solid obtained from the melt of the yellow needles was identical with that of the rhombohedra.

The reduction of the corresponding ethyl ester was also carried out. This product also crystallises in two forms, plates. m.p. 112-5°, and needles, m.p.99-100°, mixed m.p. 99-115°. The lower melting form was converted into the higher melting form by melting it and allowing the melt to solidify. The interpretation of this

phenomenon is also confirmed by the infrared spectra of the different solid samples in nujol.

(3) Searle and Adams hydrogenated 2,2'-dinitro-4,4'-dicarboethoxybiphenyl using platinum oxide catalyst and obtained a 79% yield of 2,2'-diamino-4,4'-dicarboethoxybiphenyl. This method was tried several times, but was found to be erratic, often giving an impure product, only partially reduced: the method described above was more reliable in our hands. (Searle and Adams' method has been used successfully by Dr. M. M. Harris in a previous piece of work: but in the present case it appeared that some unknown factor in the catalyst or the hydrogenator was making the results non-reproducible).

(4) Dimethyl 2,2'-diaminobiphenyl-4,4'-dicarboxylate was condensed with benzil to give dimethyl 6,7-diphenyl-5:8-diaza-1:2-3:4-dibenzocyclo-octatetraene-2,2'-dicarboxylate.



1 g. (1M) of the 2,2'-diaminobiphenyl derivative, 0.7 g. (1M) of benzil and 25 c.c. of glacial acetic acid were heated under reflux for 30 hours. Most of the glacial acetic acid was distilled off, and the viscous liquid treated with cold methanol. The solid which separated was

filtered and recrystallised from methanol. 0.46 g. (30%) of bright yellow crystals, m.p. 164-6°, were obtained. (Found: C, 76.0; H, 4.8; N, 5.8%. $C_{30}H_{22}N_2O_4$ requires C, 75.9; H, 4.7; N, 5.9%).

(vi) Dimethyl 2,2'-di-iodobiphenyl-4,4'-carboxylate: - 15 g. (0.05 mole) of finely powdered dimethyl 2,2'-diamino-biphenyl-4,4'-dicarboxylate were suspended in a mixture of 50 c.c. of conc. HCl and 50 c.c. of water. The suspension was cooled to -10° with stirring, diazotised below 0° using 8.5 g. (0.125 mole) of sodium nitrite in 12 c.c. of water. To this (slightly cloudy) solution, a solution of 22.5 g. (0.15 mole) of sodium iodide in 50 c.c. of water was slowly added, with stirring. The frothing reaction mixture was then warmed in hot water; the very dark solid which separated, decolourized with sodium metabisulphite, filtered, washed thoroughly with water and dried (22 g.)

The solid was Soxhlet extracted with 400 ml. of methylated spirit for several hours. On cooling the extract, two types of crystals were deposited, a smaller amount of light crystals together with a larger amount of heavy crystals. 9 g. of heavy crystals were separated from the lighter crystals by decantation. After boiling in ethanol (methylated spirit) with charcoal, and crystallising twice, 7 g. of straw coloured rhombic plates, m.p. 152.5-154.5, were obtained. Another 0.7 g. of the same

substance was obtained by twice recrystallising the second crop from methylated spirit.

A residue of 8.5 g. of fine pale yellow powder, m.p. 220-224° (decomp.) was obtained from the Soxhlet extraction. This was 4,4'-dicarbomethoxyldiphenylene iodonium iodide.

This compound undergoes thermal rearrangement to the corresponding 2,2'-diodobiphenyl, which can be obtained by heating the former for 3-5 minutes in a hard glass boiling tube immersed in a metal bath at 220°, extracting the product with hot benzene and running the cold extract through a column of alumina. 4,4'-dicarbomethoxy diphenylene iodonium iodide was accumulated from several experiments and 3 thermal rearrangements, each with 25 g. of the compound, were carried out. The benzene extracts were combined and run through an alumina column; on crystallising the white solid (45 g.) obtained by evaporation of the eleuent, 40 g. of white rhombic crystalline plates, m.p. 152.5-154°, were obtained.

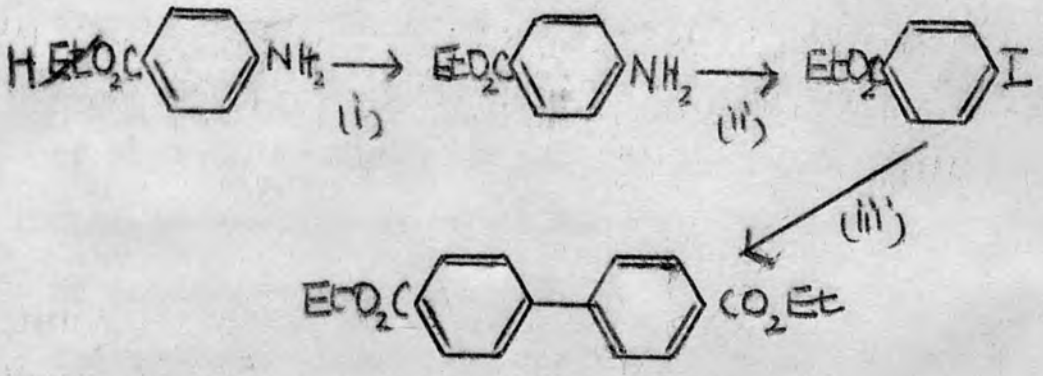
8.5 g. of the iodonium iodide would yield 4.5 g. of dimethyl-2,2'-di-iodobiphenyl-4,4'-dicarboxylate, m.p. 152.5-154°. Therefore, from 15 g. of dimethyl-2,2'-diaminobiphenyl-4,4'-dicarboxylate (7+0.7+4.5)g. ∂ 12.2 g. of dimethyl-2,2'-di-iodobiphenyl-4,4'-dicarboxylate were obtained '47%). (Found: C, 36.7; H, 2.4; I, 48.3%. $C_{16}H_{12}I_2O_4$ requires: C, 36.8; Hm 2.3; I, 48.6%),

(vii) 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid: - 10.5 g. (0.02 mole) of dimethyl 2,2'-di-iodobiphenyl-4,4'-dicarboxylate were boiled under reflux with 45 c.c. of freshly prepared 10% alcoholic potash (0.08 mole) for 15 minutes and the mixture was then poured into water. To the clear solution thus obtained, dilute hydrochloric acid was added. The white precipitate which separated was allowed to settle, filtered, washed thoroughly with water, and dried. The crude acid (9.6 g.) when recrystallied from aq. methanol yielded 7.5 g. of a white microcrystalline p powder, m.p. 330-334°, softening at 280°. When the melting point was taken on a Kaufler block, it was found that the micro-crystalline needles gradually changed into rhombohedra above 250°; the change was complete at 290°, and the rhombohedra melted at 324-6°.

Iodination of Diethylbiphenyl-4,4'-dicarboxylate.

2,2'-Dibromobiphenyl-4,4'-dicarboxylic acid was prepared through the bromination of dimethylbiphenyl-4,4'-dicarboxylate. (M.M.Harris and R·K.Mitchell, J., 1960, 1905). On carrying out the synthesis of 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid, following the method given by Searle and Adams, (J.A.C.S., 1933, 1649) difficulty was encountered in the hydrogenation of 2,2'-dinitrobiphenyl-4,4'-dicarboxylate. Attempts were therefore made to obtain the required 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid through the iodination of diethylbiphenyl-4,4'-dicarboxylate.

(A) Synthesis. Diethylbiphenyl-4,4'-dicarboxylate.



(i) Ethyl-p-aminobenzoate (benzocaine): - 100 c.c. of conc. sulphuric acid and 2 l. of absolute ethyl alcohol were carefully mixed and added to 200 g. of p-aminobenzoic acid placed in a 4 L round bottomed flask fitted with a reflux condenser carrying a calcium chloride tube. The mixture was heated for 15 hours. About 1 l. of alcohol

was then distilled off, and the rest of the solution poured into 2 l. of cold water. Concentrated sodium carbonate solution was added until the solution was alkaline to litmus. The precipitated ester was filtered, washed thoroughly with water and dried. The crude product (235 g.) when recrystallised from aqueous methylate spirit gave 204 g. (85%) of white crystals, m.p. 90-91°.

(ii) Ethyl-p-iodobenzoate. (Searle and Adams, J.A.C.S., 1933, 55, 1649)

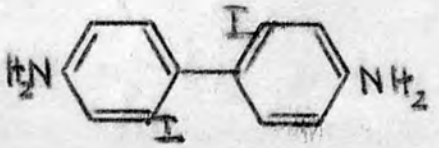
50 g. of benzocaine were made into a paste with water, and 250 c.c. of 6N hydrochloric acid (150 c.c. of conc. acid and 100 cc. of water) were added with stirring. The suspension of the base hydrochloride was cooled in an ice-salt mixture with mechanical stirring to 0° and a solution of 24.2 g. of $NaNO_2$ in 50 c.c. of water was added dropwise. When diazotisation was complete, a solution containing 80 g. of potassium iodide in 75 c.c. of water was poured into the stirred diazonium solution. A heavy black oil separated. The oil was washed with sodium metabisulphite solution, water, and then purified by distilling in super-heated steam. The steam-distillate was pale yellow. This was washed with water and dried over anhydrous magnesium sulphate. The yield was 63 g. (75%).

(iii) Diethylbiphenyl-4,4'-dicarboxylate: - This compound was obtained by Doebner through heating the silver salt of 4,4'-dicarboxybiphenyl with ethyl iodide (Ann., 1874, 172, 121). 50 g. of p-iodoethylbenzoate were heated to 220° in a metal bath. 50 g. of copper bronze were added in small portions. The addition of all the copper bronze to ½-hour. During this time the temperature of the metal bath was kept at 220-225°, while that of the reactants was between 220-250°. After all the copper bronze had been added the reaction mixture was heated for another hour at 210-220°, cooled and extracted with boiling chloroform. The brown solution was filtered through a Buchner funnel and evaporated to dryness. The crude product on recrystallising twice from acetone, gave 12 g. (44%) of straw coloured crystals, m.p.110-112°.

(B) Iodination of diethyl biphenyl-4,4'-dicarboxylate.

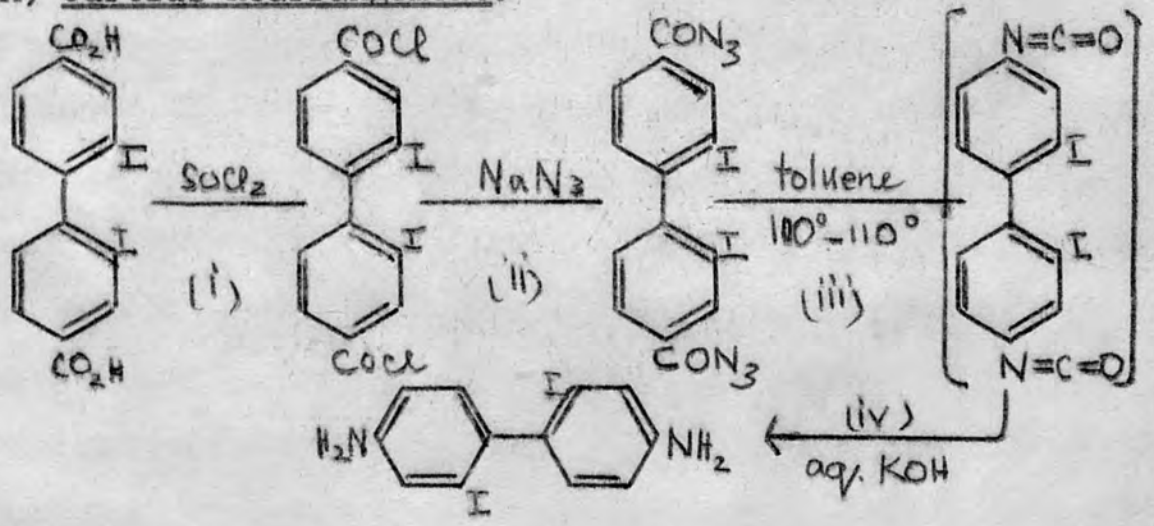
Before carrying out any experiment on the iodination of diethyl biphenyl-4,4'-dicarboxylate, three methods of iodination, described by Derbyshire and Waters (J., 1950, 3694), Trovnov and Novikov (C.A., 1954, 7483: Tomsk Polytech Zhur Obshehei Khim, 1953, 24, 1818) and by Ajeman & Boyle (J. Org. Chem. 1959, 24, 1818) were carried out on benzoic acid. In each case the yield was lower and the product less pure than described in literature.

The methods described by Ajemarw and Boyle and by Trovnov and Novikov were carried out on diethyl biphenyl-4,4'-dicarboxylate. The product obtained from the first method was very high melting and was insoluble in most organic solvents, and attempts to obtain a pure product from it failed. The second method was carried out on 30 g. of diethyl biphenyl-4,4'-dicarboxylate. The product obtained was extracted with 5% sodium hydroxide solution and filtered. The residue, (3 g.) after two recrystallisations from ethanol, yielded 1 g. of the mone-ester, m.p. 94-6°. (Found: C, 50.8; H, 3.9; I, 27.7%. $C_{18}H_{17}O_4I$ requires C, 51.0; H, 4.0; I, 29.9%) The mixture of acids obtained by acidifying the sodium hydroxide extract with dilute hydrochloric acid was Soxhlet extracted with methanol. Addition of water to the methanol extract gave 5 g. of white solid, which after several slow recrystallisations from aqueous methanol yielded 2.8 g. of crystals, m.p. 334-7°. The analysis results were in rough agreement with those required for a mono-iodo biphenyl dicarboxylic acid. (Found: C, 46.3; H, 2.8; I, 33.7%. $C_{14}H_9O_4I$ requires C, 48.8; H, 2.5; I, 34.5%).

2,2'-Di-iodobenzidine. 

2,2'-di-iodobenzidine was prepared both from 2,2'-di-iodo-4,4'-dicarboxy-biphenyl, using the Curtius rearrangement, and from m-iodo-nitrobenzene by way of a benzidine rearrangement. The first method proved very satisfactory if a reasonable quantity of 2,2'-di-iodo-4,4'-dicarboxybiphenyl were available; the second method was less satisfactory, the yield being poor in comparison with the corresponding preparation of 2,2'-dibromo-benzidine. However, the benzidine rearrangement itself was of interest.* Eight products were detected, and four were isolated (pp. 156 to 158):

(A) Curtius Rearrangement.



* It is interesting to note the recent appearance of a series of 8 papers on the mechanism of benzidine and semidine rearrangements by Banthorpe, Hughes, Ingold, Roy and Somerville. (J., 1962, 2386-2444).

(i) Acid chloride of 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid.

10 g. (0.02 mole) of powdered 2,2'-di-iodo-4,4'-dicarboxybiphenyl were quickly mixed with 30 c.c. of thionyl chloride. The mixture was heated under reflux on a steam bath for several hours under a calcium chloride tube, until a clear solution was obtained. The thionyl chloride was then distilled off under reduced pressure. The acid chloride separated as a solid, and was placed in an evacuated desiccator over soda lime, to remove the last traces of thionyl chloride. The 10.6 g. of pale yellow solid, m.p. 112-115°, were used without further crystallisation. (Theoretical yield 10.75 g.) Some of the crude product recrystallised from 80-100° light petroleum had m.p. 116-118°. (Found: C, 31.9; H, 1.5; Hal.58.0. $C_{14}H_6O_2Cl_2I_2$ requires C, 31.7; H, 1.1; Hal, 61.6%).

(ii) Azide of 2,2'-di-iodobiphenyl-4,4'-dicarboxylic acid: - The sodium azide used in this experiment was activated as follows: (Hall, Mahboob, and Turner, J., 1950, 1844; J. Nelles, Ber., 1932, 65, 1345). Industrial sodium azide was ground with a little hydrazine hydrate. The paste was spread on a watch glass and left for several hours in the fume cupboard. This was quickly dissolved in a little water and poured, with stirring, into a large quantity of acetone; the white precipitate which separated was filtered, washed with a little methanol, then ether, and finally dried in vacuo.

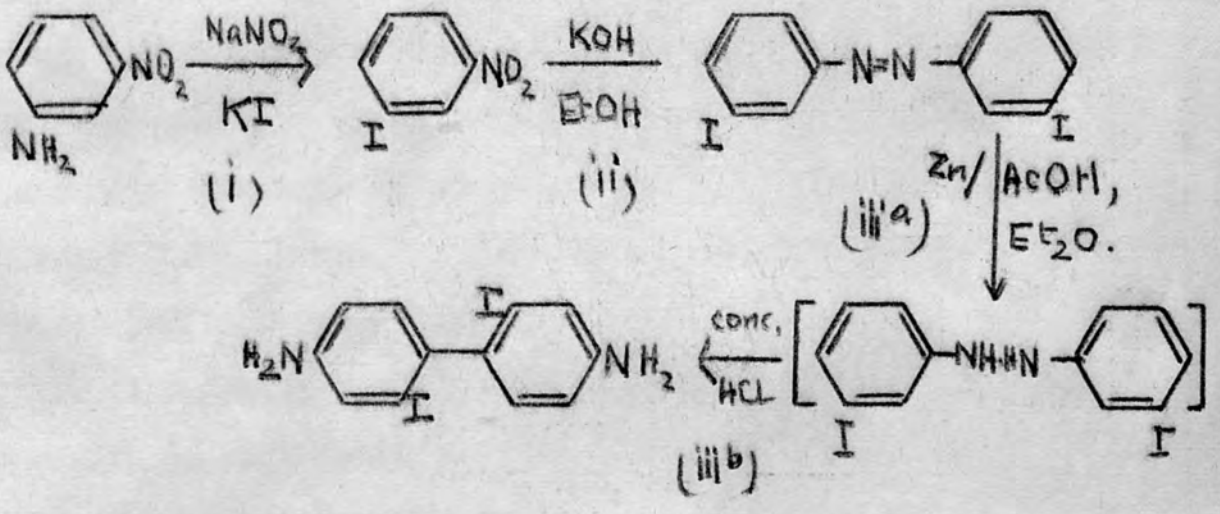
A solution of 10.6 g. of powdered acid chloride in 250 c.c. of dry acetone (A.R.) was placed in a 1 L conical flask and cooled in ice, in the fume cupboard. 3 g. (0.045 mole) of activated sodium azide was quickly dissolved in 9 c.c. of cold water and the solution immediately added to the cooled acid chloride solution with swirling. A white solid gradually separated. The reaction mixture was allowed to stand for 15 minutes, and 500 c.c. of water were slowly added to precipitate all the azide. The precipitate was filtered, washed with water and dried <u>in vacuo</u>. 10.5 g. of crude azide melting at 114° with decomposition were obtained. This was used without further crystallisation.

(iii and iv) 2,2'-di-iodobenzidine: - 10.5 g. of the azide were mixed with 15 c.c. of dry toluene and heated in an oil bath at 100-110°. The azide dissolved in the hot toluene, and nitrogen was given off. When the evolution of nitrogen had ceased, 40 ml. of hot 50% potassium hydroxide solution were added, with stirring. The base gradually separated as a white solid in the aqueous layer. The suspension was boiled for 15 minutes, removed from the oil bath and diluted with 150 ml. of water. The toluene layer was removed (with the aid of a spoon) and evaporated to dryness, while the solid in the aqueous layer was filtered. The two specimens were combined, dissolved in hot dilute

hydrochloric acid (the hydrochloride crystallised out in the cold) and the hot solution treated with aqueous ammonia. The base liberated was filtered, washed with water and dried. Crystallisation of the crude product (8.1 g.) from aqueous methanol yielded 6.6 g. straw coloured crystals, m.p. 168-170°.

From 10 g. of 2,2'-di-iodo-4,4'-dicarboxybiphenyl, 6,6 g. (74.8%) of 2,2'-di-iodobenzidine were obtained. (Found: C, 33.4; H, 2.4; N, 6.3; I, 57.8. $C_{12}H_{10}N_2I_2$ requires C, 33.1; H, 2.3; N, 6.4; I, 58.2%).

(B) Benzidine Rearrangement:



(i) m-iodonitrobenzene: - 138 g. (1 mole) of m-nitroaniline were dissolved in 750 c.c. of hot 6N hydrochloric acid (450 c.c. conc. HCl. : 300 c.c. water), and the solution rapidly cooled with stirring to below 0° and diazotised using a solution of 76 g. (1.1 mole) of sodium nitrite in 130 c.c. of water. The diazo solution was then added with mechanical stirring to 250 c.c. of freshly prepared 10% potassium iodide solution in a 5 L beaker. The dark oil which separated was washed with sodium metabisulphite and steam distilled. The m-iodo-nitrobenzene separated as a pale yellow solid. On crystallisation from light petroleum (40-60°) 175 g. (70.3%) of opaque, pale yellow flat prisms, m.p. 35-37°, were obtained.

(ii) 3,3'-di-iodoazoxybenzene: - The procedure was the same as that used for the preparation of the corresponding bromo compound. 64 g. of iodo-nitrobenzene, 30 g. of potash and 220 c.c. of ethanol (SVR) were boiled under reflux for 1½ hours. Crystallisation of the crude product (45 g.) from glacial acetic acid containing a little conc. nitric acid gave 41.5 g. (71.8%) of golden crystals, m.p. 118-120°.

(iii) 2,2'-di-iodobenzidine.

(a) 3,3'-di-iodohydrazobenzene: - The procedure for the preparation of the corresponding bromo compound was followed. 30 g. of m-iodoazoxybenzene, 130 g. of zinc

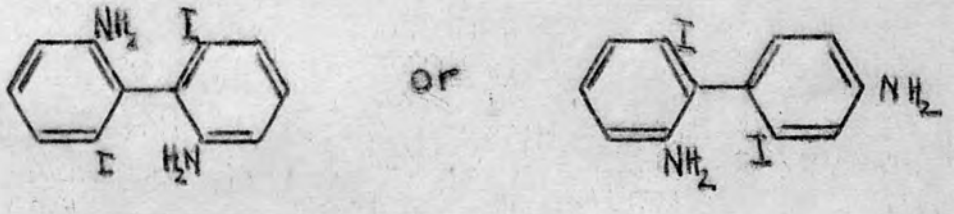
powder, 750 c.c. of ether and 24 c.c. of glacial acetic acid were used. At the end of the reaction, the colourless solution was filtered and ether was distilled off under nitrogen at reduced pressure until the volume was reduced to about 100 c.c.

(b) Benzidine rearrangement: - This ethereal solution was added dropwise to 250 c.c. of conc. HCl, which was mechanically stirred under nitrogen and cooled in ice and water. The acid solution turned very yellow and a precipitate gradually separated. After 1 hour, the precipitate was filtered and dried (13.5 g.) This was extracted with warm dilute hydrochloric acid and filtered. The residue was a yellow powder which crystallised from methylated spirit to give 0.6 g. of orange needles of the azo compound, m.p. 150-2°. The filtrate was treated with ammonia, and the base liberated was filtered, washed with water and dried (10 g.) Crystallisation from aqueous methanol gave 7.1 g. (25.6%) of mauve crystals, m.p.168-170°.

Notes.

1. Further crops of hydrochlorides were deposited from the concentrated hydrochloric acid solution. The second crop gave a mixture of bases, m.p. 55-120°, which could not be separated. The impure base obtained from the third crop of hydrochloride was washed by grinding with a little benzene, filtered and crystallised from methylated

spirit. 0.8 g. of mauve crystals, m.p. 196-8°, were obtained. The infrared spectra (solid in nujol) and mixed melting point showed that the base was different from 2,2'-di-iodobenzidine, but analysis results show that it was isomeric with the latter. (Found: C, 33.1; H, 2.4; N, 6.4; I, 58.0%. $C_{12}H_{10}N_2I_2$ requires C, 33.1; H, 2.3; N, 6.4; I, 58.2%). Deamination of the base gave 2,2'-di-iodobiphenyl, m.p. and mixed m.p. with an authentic sample, 108°. The base should therefore be either 2,2'-di-amino-6,6'-di-iodobiphenyl or 2,4'-diamino-6,6'-di-iodobiphenyl.



2. Another base was obtained from the mother liquor of crystallisation of 2,2'-di-iodobenzidine. This base was obtained as straw coloured crystals, m.p. 157.5-159.5°, after two recrystallisations from methanol. Further investigations on this compound have not been carried out owing to lack of time.

3. A mixture of all the bases (isolated and otherwise) obtained from the Benzidine Rearrangement of 3,3'-di-iodo-hydrazo-benzene was run, in benzene, on a Silica Gel G. Merk Chromatoplate (thin layer chromatography: Stahl, Die Pharmazie, 1956, **11**, 633; Chemiker-Zeitung 1958, No.82, 323; Demole, Chromatograph, **1**, 24.) Four repeated runs on a plate of $4\frac{1}{4}$" x $3\frac{1}{4}$" and 0.3 mm. thickness gave a separation of seven bases, which were detected by spraying the plate with nitrous acid, followed by alkaline β-naphthol: 6 red spots and 1 purple spot were obtained.

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Mesoid and Racemoid Transition States and the Significance of Ground State Strain in Certain Configurational Inversions

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Department of Chemistry, Bedford College, London

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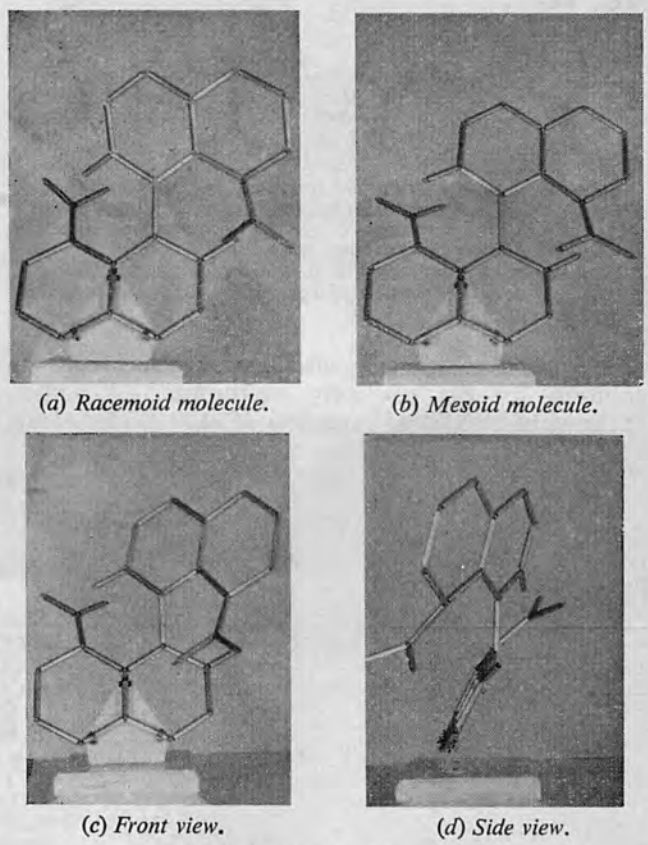
Molecular deformation in the ground state, consequent upon overcrowding, can explain why 1,1′-binaphthyl-8,8′-dicarboxylic acid is optically labile while 1,1′-binaphthyl-2,2′-dicarboxylic acid is optically stable.[1] Both in-plane and out-of-plane bond bending are postulated in the 8,8′-acid, and in all the strain conformers (+)(+), (−)(−) and (+)(−), passage from the *R* to the *S* configuration is much less obstructed than it is in the 2,2′-acid.

Construction of partially mobile molecular models of the 8,8′-acid (Fig. 1 (*a*) and (*b*)) in which bond lengths and bond angles (incorporating the estimated degree of strain) can be represented to a reasonably accurate approximation, based on *X*-ray crystallographic data, has revealed a further structural factor which can lead to lowering of the energy barrier to racemisation. If there is out-of-plane bending of the C-CO_2H bonds, inversion $R \rightleftharpoons S$, by the "*trans*" route, must go through one of three transition paths. The (+)(+) and (−)(−) transition states (racemoid) are equivalent as to energy barrier; these are states of maximum compression during the rotation of the 1,1′-bond through 180°. The (+)(−) (mesoid) path has an intermediate state, lying between energy maxima on either side.

The significant difference between the paths of inversion of the two diastereoisomeric conformations is that in case (*a*) (Fig. 2) the two barriers (2-H passing 8′-CO_2H; 2′-H passing 8-CO_2H) would be encountered simultaneously, whereas in case (*b*) (Fig. 2) they are not encountered simultaneously,



(*a*) *Racemoid molecule.* (*b*) *Mesoid molecule.*

(*c*) *Front view.* (*d*) *Side view.*

FIG. 1. *Mesoid molecule with one pair passing.*

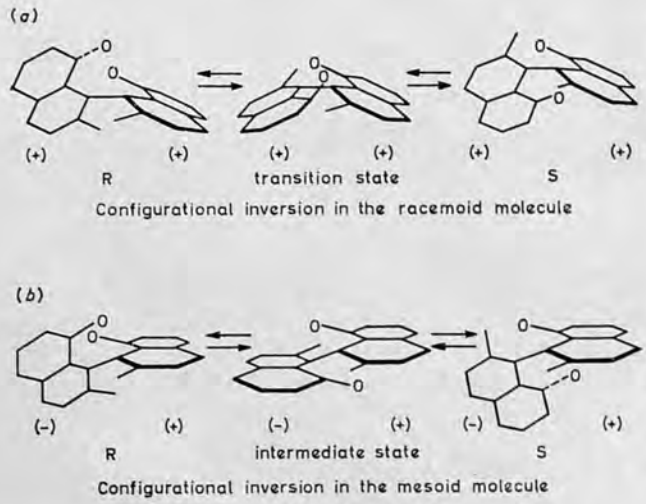


FIG. 2.

passage over them is staggered: the magnitude of the rotational interval between the two barriers depends upon the degree of out-of-plane distortion. The mesoid molecule in one passing position is illustrated in Fig. 1 (*c*) and (*d*).

In the energy profiles (Fig. 3) the dotted line

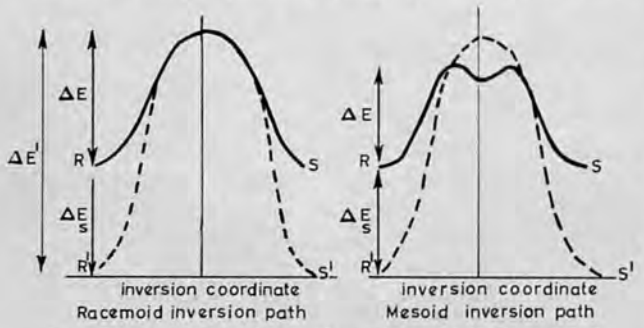


FIG. 3. *Energy Paths for Inversion of* 1,1′-*Binaphthyl* 8,8′-*dicarboxylic acid.*

$\triangle E_S$ = Strain energy in ground state.
$\triangle E$ = Experimental energy of activation for racemisation
$\triangle E'$ = Energy of activation for racemisation of relatively unstrained isomer.

represents the energy path (inaccessibly high, in solution) of the relatively unstrained 2,2′-isomer. If the conformational inversion of each naphthalenic unit, (+)⇌(−), requires very little energy in comparison with the configurational inversion $R \rightleftharpoons S$, then it would be reasonable to suppose that the mesoid path, rather than the racemoid, would be the one commonly used:

$$(+)(+)R \rightleftharpoons (+)(-)R \rightleftharpoons (-)(-)R$$
$$\Updownarrow$$
$$(+)(+)S \rightleftharpoons (+)(-)S \rightleftharpoons (-)(-)S$$

We have now prepared 2,2′-di-iodobiphenyl and several of its 4,4′-disubstituted derivatives in the optically active condition and have measured their energy barriers to racemisation in solution. These values can be compared with some previously measured[2,3] and calculated[4,5] figures see Table.

$\triangle E$ values for 2,2′-di-iodobiphenyl and its derivatives vary over only a small range but, on the whole, they vary in a manner which is consistent with the view that electron-releasing groups can make a larger contribution to the resonance energy of the transition state than can electron-withdrawing groups.

The measured values for the 2,2′-di-iodo compounds fall close to those for the 2,2′-dibromo compound, the calculated figure for the former is quite considerably higher. One explanation could be that there has been a neglected factor in our mental picture of the course of the racemisations, and thus in the geometry of the calculations, and that it is one which assumes greater importance in the iodo compounds. Ground state strain could be such a factor.

$\triangle E$ has been calculated[4,5] by finding the difference between the energy of a transition state (assumed to be planar) and an orthogonal state in which bond angles have been given their usual, unstrained values: that is, no allowance has been made for strain or compression in the orthogonal state. If the 2,2′-groups are small enough, this approximation will be justifiable, but with larger and larger groups (as in going up the series of halogens) neglect will introduce increasingly greater error.

A recent *X*-ray crystallographic study of two *o*-halogeno benzoic acids[6] leads us to think that there will be significant ground state strain in 2,2′-dibromo- and 2,2′-di-iodobiphenyl, greater in the latter. In crystalline *o*-bromobenzoic acid the angle C-C-Br is 124·9°, angle C-C-COOH is 123·4°; moreover, the bromine atom is displaced 0·064A

Table

Racemisation Data for Substituted Biphenyls

2,2′—	*Substituents* 4,4′—	5,5′—	*Solvent*	$\triangle E$ *kcal. mole*$^{-1}$ *experimental*	$log_{10}A$	$\triangle E$ *calc.*
I	—	—	$H.CONMe_2$	20·7	11·2	27·0[4]
I	NH_2	—	$H.CONMe_2$	19·9	11·9	—
I	NHAc	—	$H.CONMe_2$	20·6	12·0	—
I	CO_2H	—	(*a*) EtOH	21·4	11·8	—
			(*b*) $H.CONMe_2$	21·6	11·9	—
I	CO_2^-	—	0·1N NaOH	21·6	11·7	—
I	NH_3^+	—	HCl, EtOH, H_2O	22·1	12·3	—
I	—	CO_2H, CO_2	EtOH, H_2O, $NaHCO_3$	21·6[1]	11·5	—
Br	CO_2H	—	EtOH	19·0	12·1	—
Br	—	—	—	—	—	21·4[4]

up out of the main plane of the molecule, the carbon atom of the $-CO_2H$ group 0·057A below. It would be reasonable to suppose that the mutual distortion of an iodine atom and a phenyl group would be greater than that of a bromine atom and a carboxylic acid group in the same circumstances: two distorted units, (+) or (−), enantiomeric in so far as they are out of plane, make up 2,2′-di-iodobiphenyl. In-plane and out-of-plane angular distortion, in the *R* or in the *S* configuration, means that the ground state energy is higher than was previously imagined: and therefore the increment to be measured in racemisation is smaller. But out-of-plane distortion, in so far as it exists, provides a mesoid transition path: the two obstacles, 2-H passing 2′-I and 2′H passing 2-I, are not passed exactly simultaneously (Fig. 4). (Neither the racemoid nor the mesoid

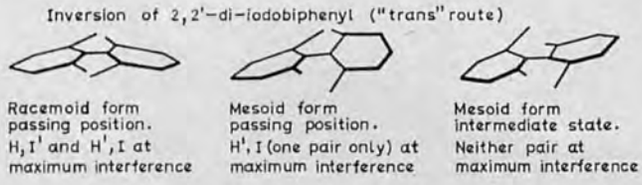
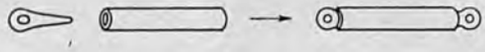


FIG. 4.

transition state is planar nor has a plane of symmetry, but the mesoid transition path goes through an intermediate which has a centre of symmetry.) In principle, the ground state strain effects are similar to those postulated for 1,1′-binaphthyl-8,8′-dicarboxylic acid, but the degree of racemoid or mesoid character is expected to be much less in the biphenyl, because the *o*-benzenoid system is likely to be less deformed than the *peri*substituted naphthalene system: there is more room for the interfering groups and the strain is shared by fewer bonds and angles.

The models illustrated are made from aluminium tubing sawn to the required lengths, to a scale of 1·5 inches to the Angstrom unit, and lined at the ends with tubular nylon sleeves. The narrow end of a brass soldering tag is forced into either end of the aluminium tube, where it is firmly gripped by the nylon sleeve. This unit is an ordinary bond: it can be joined to other bonds by a nut and a bolt, with a spring washer, through the holes in the soldering tags. In-plane angular deformation is catered for



by the adjustment of the bonds before finally tightening the screws, out-of-plane angular deformation by bending the soldering tags.

In order to make a bond about which rotation can take place, one of those just described is sawn in half and a brass rod, covered with a nylon sleeve, is inserted to form a pivot; such a bond is used for the

1,1′-bond in the binaphthyl skeleton illustrated, and for the exocyclic C-C bonds to the carboxylic acid groups.

The authors are grateful to the University of London for a Postgraduate Studentship (C.K.L.), to the University of London Central Research Fund for a polarimeter, to Dr. K. E. Howlett for permission to publish the results of his most recent calculations and to Mr. R. K. Mitchell for his assistance in the development and construction of the models.

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1 Harris, M. M. & Mellor, A. S., *Chem. & Ind.*, 1961, 557
2 Rieger, M. & Westheimer, F. H., *J. Amer. chem. Soc.*, 1950, **72**, 19; Hall, D. M. & Harris, M. M., *J. chem. Soc.*, 1960, 490
3 Harris, M. M. & Mitchell, R. K., *ibid.*, 1960, 1905
4 Howlett, K. E., *ibid.*, 1960, 1055, and personal communication, April, 1962
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References for Table II.

(i) A.S.Mellor. Ph.D. thesis submitted to University of London in March 1961. Over 7 rate measurements were carried out, covering a temperature range of about 30° for each set of results.

(ii) Bell, Morgan, and Smyth, Chem. & Ind., 1951, 634.

(iii) Theilacker and Hopp, Ber., 1959, 2299. 7 rate measurements from 10.5° to 38° for compound (4); and 5 rates from 9.3° to 30° for compound (20).

(iv) Meisenheimer and Besswenger, Ber., 1932, 65, 32.

(v) Hall, Ridgwell and Turner, J., 1954, 2498.

(vi) U.J.H.Mayer, Ph.D. Thesis submitted to University of London in July 1961. 4 rate measurements from 121° to 136° for compound (11), and 6 rates from 51° to 75° for compound (13).

(vii) Lesslie and Mayer, J., 1961, 611. 3 rate measurements at 57° 67° and 79°.

(viii) Stanley and Adams, J.A.C.S., 1930, 52, 4471.

(ix) Lesslie and Turner, J., 1932, 2394.

(x) Lesslie and Turner, J., 1932, 2021.

(xi) Hall and Harris, J., 1959, 396; and private communication (unpublished).

(xii) Shaw and Turner, Nature, 130, 315; J., 1933, 135.

(xiii) Graham and Leiffler, J.Phys.Chem., 1959, 63, 1274.

(xiv) Hall and Harris, J., 1960, 490.

(xv) Corbellini and Angeletti, Atti.acad.Lincei, 1932, 15, 968-73.

(xvi) Jamison and Turner, J., 1942, 437.

(xvii) Corbellini and Pizzi, Atti.accad.Lincei, 1932, 15, 287.

(xviii) Lesslie, Turner and Winton, J., 1941, 257.

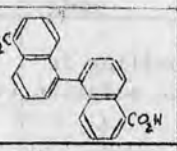
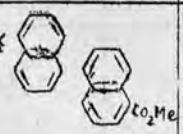
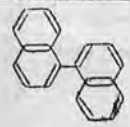
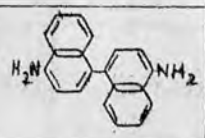
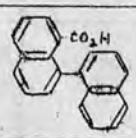
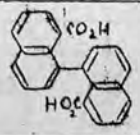
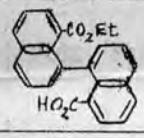
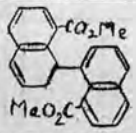
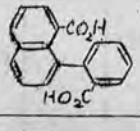
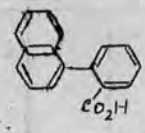
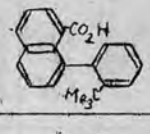
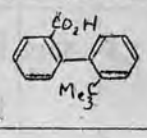
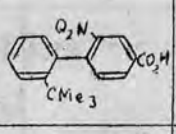
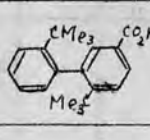
(xix) Searle and Adams, J.A.C.S., 1934, 56, 2112.

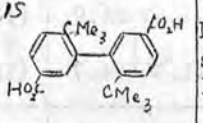
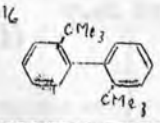
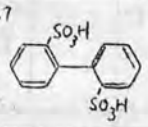
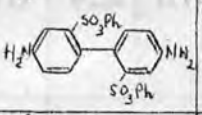
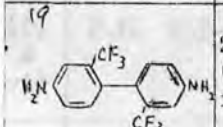
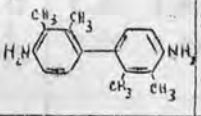
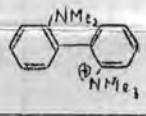
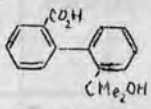
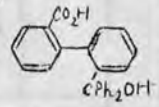
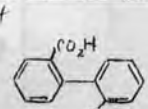
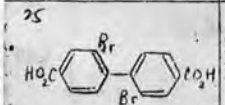
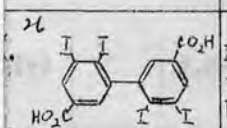
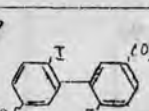
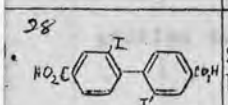
(xx) M.M.Harris, Proc.Chem.Soc., 1959, 367.

(xxi) Harris and Mitchell, J., 1960, 1905. 6 rate measurements from -20.7° to +5.6°.

(xxii) Reiger and Westheimer, J.A.C.S., 1950, 72,19. 2 rate measurements at 80.16° and 99.72° for compound (26), and 3 rates from 19.90° to 38.22° for compound (27).

(xxiii) Searle and Adams, J.A.C.S., 1933, 55, 1649.

2,2'-di-substituted Biphenyl	Methods by which optical activity was detected: resolution or optical activation.	RACEMISATION DATA							Ref
		Solvent	$t_{\frac{1}{2}}$ mins.	E kcal. mole^{-1}	logA	$\Delta H^{\ddagger}$ kcal. mole^{-1}	$\Delta S^{\ddagger}$ e.u.	$\Delta F^{\ddagger}$ kcal. mole^{-1}	
1 	Second order asymmetric transformation with brucine from aq. ethyl cellosolve.	N,N'DMF	271.5 at 50	24.1	12.3	23.5	-4.47	24.9	(i) & (ii
		$\frac{N}{10}$NaOH	94.2 at 50	24.9	12.9	24.2	-1.54	24.7	
2. 	(+) form obtained by the action of diazomethane on (+)-(1).	N,N'DMF	111.9 at 50°	23.8	12.2	23.1	-5.09	24.8	(i)
3. 	De-amination of (+)-(4) at low temperatures, using hypophosphorous acid.	N,N'DMF	14.5 at 50°	22.5	12.12		-5.17		(i)
4. 	Second ord.asym.trans. with 2 mols. of (+)- -bromo-camphor- -sulphonate, from 60% aq. ethanol.	Acetone	24.6 at 38°	21.4		20.8	-7.1	22.9	(ii
5. 	Resolved through brucine salt, from ethyl acetate.	N,N'DMF	5.5 at 50°	22.4	12.0	21.8	-5.5	23.5	(i) & (iv
6. 	Resolved through brucine salt, from methanol.	N,N'DMF	55	22.1	11.3	21.4	-9.1	24.5	(i) & (iv
		$\frac{N}{10}$NaOH	2.3 at 50°	26.01	15.2	25.4	+9.2	22.7	
7. 	Second ord,asym.trans. with brucine,from aqueous ethyl cellosolve.	N,N'DMF	17.2	21.6	11.4	20.9	-8.4	23.7	(i) & (iv
		$\frac{N}{10}$NaOH	31.1 at 50°	25.7	14.0	25.0	+3.18	24.4	
8. 	Both (+) & (-) antipodes obtained by the action of CH_2N_2 on active forms of (6).	N,N'DMF	22.7 at 50°	22.0	11.6	21.4	-7.54	23.9	(i)
9. 	Second ord.asym.tran. with brucine, from benzene. First ord.asym.trans. with brucine in chloroform.	B.P, $CHCl_3$	60 at 20°						(v)
10. 	2nd. ord.asym.trans. with brucine & cinchonidine in acetone. 1st. ord.asym. trans. with brucine, quinidine & cinchonidine in $CHCl_3$.	B.P. $CHCl_3$	2 at 20°						(v)
11. 	Resolved through strychine salt, in ethanol.	EtPh	183 at 121°	*29	*11.9		*-6.8		(vi
12. 	2nd. ord. asym. trans. with brucine & strychnine, from ethanol and methanol.	EtOH	35 at 57°	24	*12.2		*-5.6		(vii
13. 	2nd. ord.asym.trans. with strychnine, from ethanol.	CH_3Ph	110 at 55.8°	25.4	*12.9		*-1.92		(vi
14. 	Resolved through strychnine salt: fractional crystallisation from ethanol.	Activity remained unchanged after melting at 193°.							

2,2'-di-substituted Biphenyl	Methods by which optical activity was detected: resolution or optical activation.	RACEMISATION DATA: Solvent	$t_{\frac{1}{2}}$ mins.	E kcal. mole^{-1}	log A	$\Delta H^{\ddagger}$ kcal. mole^{-1}	$\Delta S^{\ddagger}$ e.u.	$\Delta F^{\ddagger}$ kcal. mole^{-1}	Ref.
15 	Resolved through brucine salt: fractional crystallisation from ethanol	Activity remained unchanged after boiling in aqueous sodium hydroxide or pyridine solution for three hours.							(vi)
16 	Both (+) &(-) forms obtained from active forms of (15) through the Schmidt reaction	Optically stable.							(vi)
17 	Resolved through mono-brucine salt by successive addition of .25mole of strychnine,HCl to the Na salt.	aqueous solution of ammonium salt racemised rapidly at 100°.							(viii) & (ix)
18 	2nd. ord.asym.trans. with (+)camphoric acid from abs. ethanol and methanol.	Pyridine solution completely racemised in ten minutes at 100°.							(x)
19 	2nd. ord.asym.trans. with (+)-tartaric acid, at 50° from ethanol.	EtOH	58.4 at 39°	19.5	9.92		-15.3		(xi)
20 	2nd.ord.asym.trans. with (+)-bromocamphor- -sulphonic acid, from 95% ethanol.	EtOAc	54.5 at 30°	17.7		17.0	-19	22.7	(iii)
21 	Resolved through (+)camphor-10-sulphonate by crystallisation from a mixture of alcohol, benzene,& light pet.	Water	125 at 99.5°	27.6	12.2	26.9	- 5.3	28.9	(xii) (xiii) & (xiv)
22 	2nd. ord.asym.trans. with brucine, from ethanol & $CHCl_3$ 1st. ord.asym.trans. in " .		26.6hr. at 25.15°						(xv) & (xvi)
23 	Resolution through brucine salt: fractional crystallisation from ethanol.	Gradually racemised at room temperature.							(xvii)
24 	Fast mutarotation with nor-(+)- -ephedrine at -30° in chloroform.								(xviii)
25 	2nd. ord.asym.trans. with brucine from ethyl acetate.	EtOH	13.4 at 1°	19.0 ±0.5	12.1 ±0.4	18.5 ±0.5	- 4.9 ±1.85	19.9 at 5.6°	(xix) (xx) (xxi)
26 	Resolution difficult: through mono- and di-brucine salts, from ethanol.	NaOH aq.		28.05	11.7	27.3	- 7.6	30.2	(xiv) & (xxii)
27 	2nd. ord.asym.trans. with 1 mole of brucine from ethanol.	aq.alc, 1% $NaHCO_3$		21.6	11.5	21.0	- 7.7	23.4	(xiv) & (xxii)
28 	2nd. ord. asym.trans. with brucine, from ethanol.	EtOAc	125,4 at 25°						(xxiii)