STEREOCHEMISTRY OF BIARYLS.

Thesis presented by STANLEY ARTHUR RIDGWELL
in requirement for the Degree of Doctor of
Philosophy in The University of London.

The author wishes to express his thanks to Professor E.E. Turner, F.R.S. for his continued help and encouragement, to Drs. D.M. Hall and M.M. Harris for valuable discussion, and to the Department of Scientific and Industrial Research for a Maintenance Allowance.

Abstract.

Hydrogen atoms attached to an aromatic nucleus have been found to be particularly effective in causing hindrance to free rotation about the inter-nuclear bond of certain biaryls. In order to investigate the limits of this effect, some substituted phenylnaphthalenes and dinaphthyls have been synthesised by means of the Ullmann reaction and their stereochemical properties investigated. In some cases the compounds have been obtained in optically active forms, while others were shown to be incapable of optical activation, even at low temperatures. The optically active compounds have been racemised under controlled conditions and accurate values for their optical half-lives have thus been obtained.

During the course of the work, it was observed that optically active biaryls in which there are two adjacent carboxyl groups (e.g. 1-phenylnaphthalene-2':8-dicarboxylic acid ; 1:1'-dinaphthyl-8:8'-dicarboxylic acid), racemise more quickly in sodium hydroxide solution than in a non-polar solvent. It has further been shown that the rate of racemisation of such compounds in chloroform is sensitive to the percentage of ethyl alcohol present. Thus it appears that the presence of two adjacent carboxylate ions in a compound decreases the optical half-life. Experimental data obtained from the literature supports

this conclusion.

The ultra-violet absorption spectra of the compounds under investigation have been measured and an attempt has been made to correlate the degree of conjugation between the two rings, as inferred from the spectra, with the optical half-lives of the compounds concerned.

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PART I.

INVESTIGATION OF THE OPTICAL STABILITIES OF SOME BIARYLS.

Section 1. Introduction to the Stereochemistry of Biaryls.

After the collapse of the evidence for the Kaufler formula of diphenyl which required a non-coaxial arrangement of the two rings, it was necessary to postulate some reason for the observed optical activity of 6:6'-dinitrodiphenic acid, which Christie and Kenner (J., 1922, 121, 614) had described as existing in an optically labile form. (It was later shown to be relatively optically stable.)

The need for a theory explaining the optical isomerism in this series became even more urgent when several other substituted diphenic acids were shown to be resolvable (e.g. 6-nitrodiphenic acid; 4:6-dinitrodiphenic acid and 4:4':6:6'-tetranitrodiphenic acid), while compounds exhibiting structural similarity (e.g. diphenic acid; 4-nitrodiphenic acid and 4:4'-dinitrodiphenic acid) could not be obtained in an optically active form.

The foundations of the modern view, which requires a co-axial but non-coplanar molecule, were embodied in three explanations which were almost simultaneously presented.

Turner and Le Fèvre (Chem. and Ind., 1926, 45, 831 and 833) explained the experimental results, including the reported optical instability of the Kenner Acid, by proposing a diphenyl molecule in which the two aryl nuclei were co-axial and in which an attraction existed between the 2:2'- carbon atoms because of a Thiele residual affinity effect.

Such an attraction would tend to stabilise a coplanar form. It was considered that groups in the 2:2' or 6:6' positions would have an opposite effect, either owing to their bulk, or to their electrical properties.

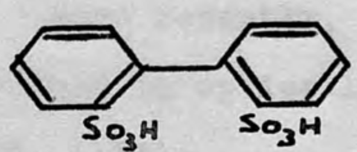
Bell and Kenyon (Chem. and Ind., 1926, 45, 864) considered that groups in a 2:6- position owing to their size or electrical properties would act as an obstacle to any other substituent in the 2'- position.

Mills (Chem. and Ind., 1926, 45, 884 and 905) ignored the possibility of electrical effects and considered only the bulk of groups in the *ortho* positions.

The fundamental idea of these theories was supported by the fact that all the compounds so far resolved had at least three groups substituted in the ortho positions, while those which could not be obtained in an optically active form contained not more than two groups in the collision position.

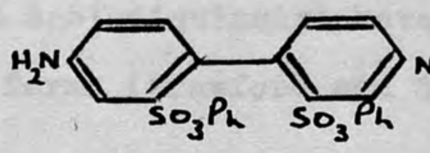
A considerable amount of experimental support for the obstacle theory was forthcoming and it soon became the generally accepted explanation of this new stereochemical phenomenon. It was obvious that in addition to the non-coplanarity of the molecule it was necessary that both rings should be unsymmetrically substituted if the mirror images were to be non-superimposable.

Once the idea of hindrance to free rotation was established, it became evident that a well defined division of diphenyl compounds into optically stable and optically inactive classes was not possible. Between the two extremes of the non-racemisable and the non-resolvable was discovered a multitude of compounds varying widely in optical stability. The minimum amount of substitution in the 2:2' and 6:6'-positions necessary to produce optically active substances, was investigated by Lesslie, Shaw and Turner, who obtained the following compounds in an active form:-

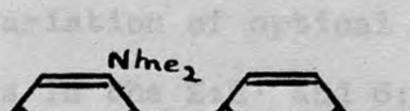


Lesslie and Turner

<u>J</u>., 1932, 2394

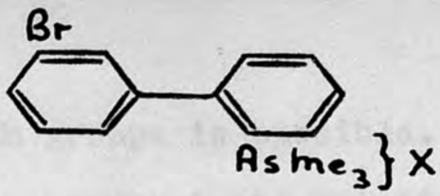


idem, ibid., p.2021



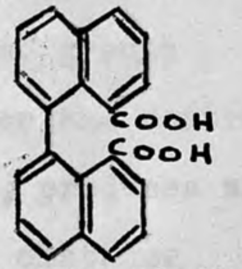
Shaw and Turner, <u>ibid</u>., 1933, 135

The only known case of optical activity in a monosubstituted diphenyl was reported when Lesslie and Turner, (<u>J</u>., 1933, 1588)

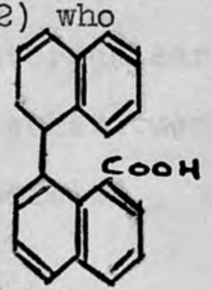


obtained a mutarotation with 3'-bromodiphenyl-2-trimethyl arsonium iodide and (+)-camphorsulphonic acid. Other cases of optically active di-substituted diphenyls were reported.

1:1'-Dinaphthyl-8:8'-dicarboxylic acid



was resolved by Stanley (J.Amer. Chem. Soc., 1931, 53, 3104) and also by Corbellini (Atti accad. Lincei, 1931, 13, 702) and Meisenheimer and Beisswenger (Ber., 1932, 65. 32) who also resolved 1:1'-dinaphthyl-8-carboxylic acid.



More recently, 4:4'- and 5:5'-diquinolyl have been obtained in optically active forms (Crawford and Smyth, J., 1952, 4133).

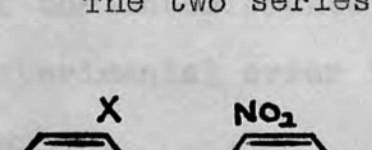
Adams and his co-workers commenced a long term investigation into the variation of optical activity with the size of the substituents in the 2:2' and 6:6'- positions. An application of the results was made to predictions of resolvability and even in certain cases to the degree of optical stability to be expected.

On the basis of the obstacle theory it was apparent that the amount of interference would be directly related to the size of the substituent group. No direct measurement of the overlap of two such groups is possible. However by making certain assumptions, approximate relative values of the degree of interference can be derived.

An adjustment of the aliphatic internuclear carbon to substituent distance is made in order to obtain a value applicable to the aromatic series. In the case of groups such as CH_3 and NO_2, an addition to this value for the centre atom, in order to account for the attached atoms, produces an acceptable figure for the group as a whole. The distance between the 2- and 2'- carbon atoms has been measured by Dhar (*Indian J. Physics*, 1932, *7*, 43) and shown to be 2.90 Å. The difference between this value and the sum of the internuclear distances between the 2:2'- carbon atoms and their substituents was called the 'interference value' and was the predicted relative degree of interference.

Adams and his school carried out extensive experiments in order to determine the accuracy of the interference values in predicting the relative optical stability of certain substituted diphenyls.

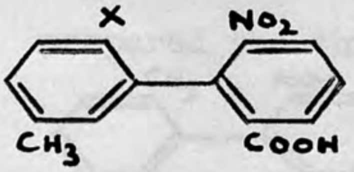
The two series of compounds



$X = OCH_3$ Stoughton and Adams, *J. Amer. Chem. Soc.*, 1932, *54*, 4426.

$X = CH_3$: COOH : NO_2

Adams and Hale, *ibid.*, 1939, *61*, 2825.



X= F : Cl : Br

Yuan and Adams, ibid., 1932, 54, 4426

were prepared. Evidence was obtained that the 5'- methyl group in the second series had little effect on the racemisation rate and hence measurement of optical half-lives of the compounds provided a direct experimental comparison between the effective interference of the substituents.

The results indicated the order of relative intereference to be:-

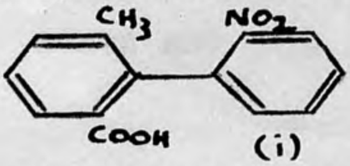
$Br > CH_3 > Cl > NO_2 > COOH > OCH_3 > F$

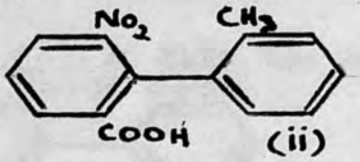
Adams ("Organic Chemistry", Ed., Gilman, 1943, 2nd. edn., Vol. 1, 363, New York, Wiley and Sons) pointed out that:- "------ the order from first to last parallels the decrease in size of the groups as determined by X-ray data."

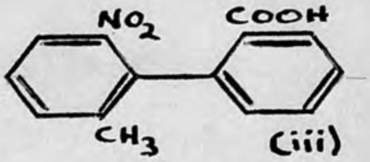
However a discrepancy was noted (Adams, Chem. Rev., 1933, 12, 261) between the half-lives and calculated interference values of the nitro and methyl or chlorine groups. Adams attributed this either to an error in the calculation of the interference value of the methyl group, or to an experimental error in the determination of the half-life period.

It was demonstrated however, that the prediction of relative optical stability based on calculated interference values was not always reliable. Adams and Hale (loc. cit.)

prepared the three acids


(i)


(ii)


(iii)

and determined their half-life periods. If it is assumed (idem., loc. cit.) that the order of the group size is $NO_2 > CH_3 > COOH$, the acids (ii) and (iii) should be more easily racemisable than (i), as in the latter case the larger NO_2 group collides with both CH_3 and COOH, whereas with (ii) and (iii) only one collision between NO_2 and another substituent (CH_3 or COOH) is possible. The experimental results placed the optical stabilities in the order:-

(iii) > (i) > (ii)

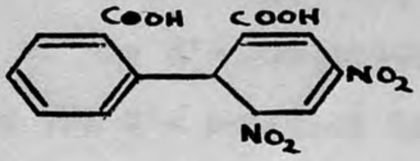
The actual racemisation rates depended on the solvent used and in view of this fact it was suggested that the blocking power of the groups depended on their solvation.

Identical experiments were carried out by Adams and Finger, (ibid., p.2828) with three acids in which the methyl group in the previous series was replaced by a methoxyl group. Similar anomalous results were obtained.

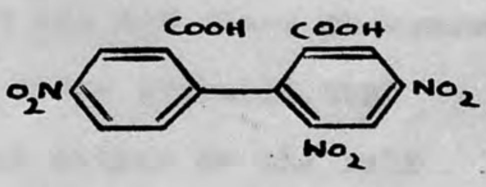
A further phenomenon for which there is yet no accepted explanation is the effect on the half-life period of groups substituted in positions other than the 2;2';6;6'.

Kuhn and Albrecht synthesised:-

(a)



(b)

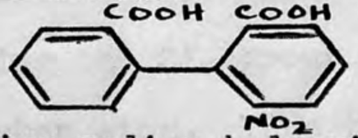


Annalen, 1927, 455, 272

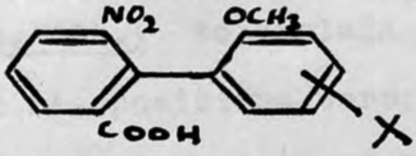
ibid., 1927, 458, 221

and showed the half-life periods in 2N sodium hydroxide at 98° to be (a) 18 mins. (b) 50 mins.

Adams and Hale (loc. cit.) give the half life of



in (presumably) boiling sodium hydroxide solution as 4.6 mins.. The results are inexplicable if the bulk of the 2,2',6,6' groups is the only factor affecting the stability of such a molecule. Adams (et alia) investigated the series of acids:-



$X = OCH_3; CH_3; Cl; Br; NO_2; H$

in which a variety of groups were substituted in the 3', 4' and 5' positions.

The active compounds in which the 3'- position was substituted (Chien and Adams, ibid, 1934, 56, 1787) were without exception more stable (of the order of 20 times) than the acids containing 4'- or 5'- groups. On the whole, the 4'- substituted compounds (Hanford and Adams, ibid, 1935, 57, 1592) are rather less resistant to racemisation than the 5'- compounds (Yuan and Adams, ibid., 1932, 54, 4434). In addition it was found that, within each series of acids, the effects of the substituents on the relative optical stabilities fell in the same order.

$$H < OCH_3 < CH_3 < Cl < Br < NO_2$$

A variety of attempts have been made to explain these phenomena. In the case of the 3'- substituents it seems probable that the group in the 2'- position is crowded either by the bulk or the electrical effects of the 3'- substituent, with the result that a displacement of the 2'- carbon to substituent bond occurs, bringing the 2'- group nearer to that situated on the 2- or 6- carbon atom. Thus the blocking power of the 2'- substituent is increased and the so called 'buttressing effect' results.

Among the other mechanisms postulated (Yuan and Adams, loc. cit.) to explain the effects of groups in the 3', 4' and 5'- positions were:-

(i) A change in bond length of the 2'- carbon to substituent link.

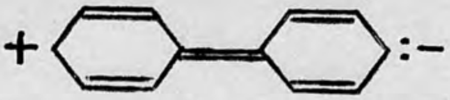
(ii) A slowing down of the simi-circular oscillations of the benzene rings by the substituent groups, with a resulting decrease in the chance of complete rotation.

(iii) A change in length of the internuclear bond.

(iv) The bending of the pivot bond in such a way that the rings are no longer co-axial.

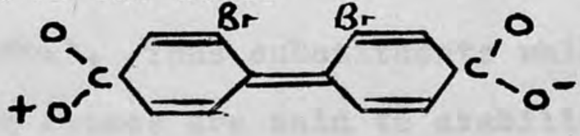
Adams conducted experiments in which an atom in one ring was replaced by another of similar polarity but of different weight. In both cases an identical effect on the rate of racemisation was observed and from this result it was concluded that factor (ii) could be discounted.

With regard to factor (iii), Calvin (J. Org. Chem., 1939, $\underline{4}$,256) pointed out that as the repulsive forces between the substituents increases very rapidly as the inter-atomic distance decreases, any contribution of a state



to the ground state of diphenyl, would result in a shortening of the 1:1'- bond with a consequent increases in the repulsive forces between groups in the collision positions.

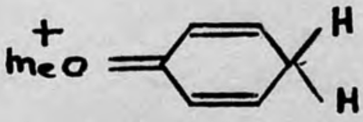
This argument has been employed to explain the fact that 4:4'-diamino-2:2'-dibromodiphenyl is non-resolvable, while 2:2'-dibromodiphenyl-4:4'-dicarboxylic acid can be obtained in an active form of half-life 5-10 mins. at 0°. It was suggested that the two amino groups are incapable of accepting electrons, while although the carboxyl group is generally an electron accepting group, it is not impossible that it should function as a source of electrons as well, when the contribution of the state



to the ground state of the molecule will be promoted.

Baddeley (Nature, 1946, 57, 694) discussed the possibility of the deformation of the pivot bond (factor iv) involving a non-coaxial structure. Models showed that restriction to rotation becomes significantly less when the bond joining the two rings is displaced from theplane of one of them by introduction of a tetrahedral carbon at position 1. The formation of this tetrahedral structure depends on the ability of the carbon atom at which it occurs to acquire a negative charge (Baddeley, loc. cit.), thus the displacement should occur in the ring of greater electron density. If it is assumed that the effect of the carboxyl group is to lower the electron density more than the combined effects of nitro- and methyl, or nitro- and methoxyl, in those compounds investigated by Adams and Hale (<u>loc. cit.</u>) and Adams and Finger (<u>loc. cit.</u>), the electron densities in one ring are in the same order as the rates of racemisation.

More recently (Crawford and Smyth, <u>Chem. and Ind.</u>, 1954, 346), Baddeley's idea has been extended by the suggestion that the varying optical stabilities of Adams compounds and other sterically hindered biaryls can be accounted for in terms of electrophilic attack by hydrogen. It is suggested that hydrogen exchange will take place through a transition state, in which the carbon atom being attacked becomes tetrahedral. Thus substituents which are activating to electrophilic attack are said to stabilise the transition state as in the case of:-



On the other hand the deactivating influence of groups such as NO_2 and COOH will minimise electrophilic attack. Thus in the case of optically active diphenyls, the tetrahedral transition state achieved during hydrogen exchange would facilitate racemisation. Following this argument, the rate of racemisation would be increased by substitution in the ring of groups which aid electrophilic attack, and decreased by the presence of deactivating groups. It is pointed out that such a reaction should be of the second order, but in view of the solvent participation it would constitute a pseudo first order reaction.

Section 2. Introduction to Asymmetric Transformations.

The first recorded use of the term asymmetric transformation was by Leuchs and Wutke (*Ber.*, 1913, *46*, 2420), who found that a solution of brucine and (+)-2-*o*-carboxybenzyl-α-hydrindone in acetone deposited the solid brucine (+)-acid salt in a yield which represented nearly 100% of the solid in solution. On removal of the alkaloid, an optically unstable acid was produced.

A different phenomenon was recorded when several workers (Read and McMath, *J.*, 1925, *127*,1572, Mills and Elliot, *ibid.*, 1928, 1291 and Kuhn, *Ber.*, 1932, *65*, 49) observed mutarotations on formation of salts in solution between alkaloids and racemic acids.

This phenomenon was explained as the setting up of an equilibrium

$$(-)\text{-Base-}(-)\text{-Acid} \rightleftharpoons (-)\text{-Base-}(+)\text{-Acid}$$

in which one form of the salt predominates.

Kuhn (loc. cit.) described this behaviour as "asymmetrische Umlagerung erster Art", referring to an optical activation which ceased when the activating agent was removed. The expression was translated as "asymmetric transformation of the first order".

He further proposed that the phenomenon in which an alkaloidal salt of the active acid is isolated as a <u>solid phase</u> representing more than 50% of the solid in solution be known as "asymmetric transformation of the second order". Kuhn's definition of first order asymmetric transformation rests on the criterion that the optical activation ceases when the activating agent (i.e. the alkaloid) is removed. This definition may under certain conditions be invalidated, as with compounds of intermediate optical stability, the kinetics of the racemisation of the active acid may be followed when the alkaloid is removed.

Thus the use of a revised definition was suggested by Jamison and Turner:- (J., 1942, 437)

"A configuratively unstable substance in solution (or liquid state) consists of equal quantities of d and l forms. On addition of a second (but optically stable) d (or l) compound which combines with the first substance to form a pair of diastereoisomerides, an equilibrium is set up in which one diastereoisomeride predominates to a greater or lesser extent. The setting up of this equilibrium we have called a first order transformation......."

The position with regard to second order asymmetric transformations was made clear in the same paper:-

".... Second order transformation in any case in which inter-conversion of diastereoisomerides is possible (first order transformation) and crystallisation can be induced, may be expected to be almost quantitatively realisable and to give one diastereoisomeride in an optically pure condition. That the optical activity of the configuratively unstable compound, when this is removed from combination with the optical stable substance, should be detectable by a physical measurement, is immaterial for the purpose of definition of terms, although it was mainly on this arbitrary point that Kuhn based his distinction between the two types of isomerism."

It is evident that the observed mutarotation is the setting up of an equilibrium, where at the time of mixing we have:-

$$\underset{50\%}{\text{Base }(+)\text{-Acid}} \rightleftharpoons \underset{50\%}{\text{Base }(-)\text{-Acid}}$$

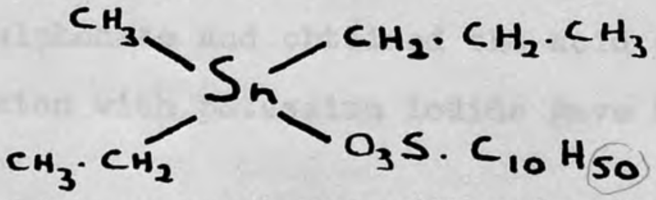
and at the time of equilibrium we have:-

$$\underset{x\%}{\text{Base }(+)\text{-Acid}} \rightleftharpoons \underset{(100 - x)\%}{\text{Base }(-)\text{-Acid}}$$

Thus for a first order change to occur, the real existence of diastereoisomerides in solution is essential and it would not be expected to take place in ionising solvents. However in the case of a second order asymmetric transformation, the diastereoisomerides may, or may not exist in the dissociated form, provided that crystallisation occurs. The first positive proof that the mutarotation observed in a first order change is due to formation of an excess of one diastereoisomeride, was provided by Mills and Elliot (loc.cit.). A mutarotation was observed on mixing chloroform solutions of N-benzenesulphonyl-8-nitro-1-naphthylglycine and brucine. After attainment of equilibrium, the brucine was removed and the resulting solution was found to have a positive rotation which changed rapidly to zero. Thus it was evident that the equilibrium solution contained an excess of one brucine salt.

Only compounds which readily undergo optical inversion will take part in these asymmetric transformations. Such optical instability can be conferred on a molecule in various ways.

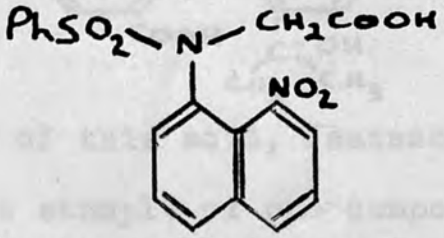
Pope and Peachey (Proc. Roy. Soc., 1900, 16, 42) obtained only one salt on crystallisation of methyl-ethyl-n-propyl tin (+)-camphorsulphonate



from water, which on treatment with potassium iodide gave (+)-methyl-ethyl-n-propyl tin iodide. In this case it is presumed that inversion involves a flat tin cation.

Enantiomorphism due to restriction of rotation about a single bond has provided a field in which many examples of both types of isomerism are to be found. In these cases optical instability occurs because of only partial hindrance to rotation.

Mills and Elliot (loc. cit.) showed that the brucine salt of N-benzenesulphonyl-8-nitro-1-naphthylglycine



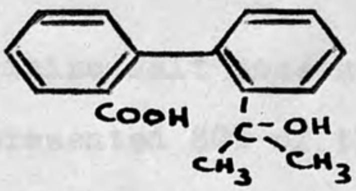
underwent what is now called second order asymmetric transformation in two directions, depending on the solvent used. Both the (+)- and (-)-acids were obtained from the salts which crystallised. This was the first example of two active forms of one compound being obtained by asymmetric transformation.

Other cases of transformations in the peri-substituted naphthalene series are known.

Mills and Breckenridge (*ibid.*, 1932, 2209), crystallised 8-benzenesulphonethylamino-1-ethyl quinolinium (+)-α-bromo-camphor-π-sulphonate and obtained the acid (+)-base, which on decompasition with potassium iodide gave the (+)-quinolinium iodide.

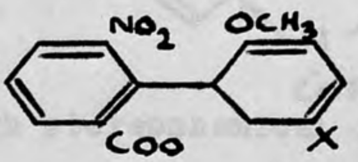
Extensive work on the diphenyl series compounds has produced a variety of examples of optically labile compounds and as might be expected many instances of first and second order asymmetric transformations.

2'- (α -Hydroxy*iso*propyl) diphenyl-2-carboxylic acid was reported by Corbellini and Angeletti (*Atti R. Accad. Lincei*, 1932, *15*, 968) to undergo a second order asymmetric transformation with brucine in ethyl alcohol solution.



On re-examination of this acid, Jamison and Turner (loc. cit.) provided the first example of one compound undergoing both first and second order transformations with the same alkaloid (brucine) without a change of solvent (chloroform). Thus for the first time the van't Hoff-Dimroth rule (Dimroth, Annalen, 1910, 377, 127; ibid., 1913, 399, 91) could be applied to asymmetric transformation. The results obtained were found to agree with the prediction that "the stable form is the more soluble".

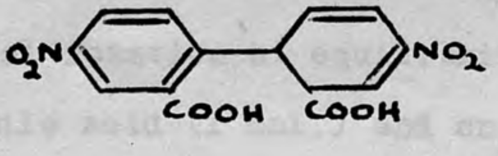
A series of 2-nitro-2'-methoxydiphenyl-6-carboxylic acids



X = CH_3, Cl, Br, NO_2

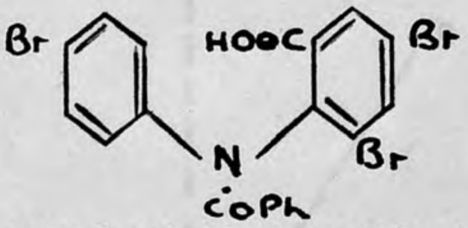
examined by Yuan and Adams (loc. cit.) was shown from the experimental results to take part in what are obviously second order transformations. However in this case as in many other instances, no attempt was made to distinguish between an asymmetric transformation and a resolution.

An interesting case in which a second order change was claimed to have occured, was that of 4:4'-dinitrodiphenic acid.



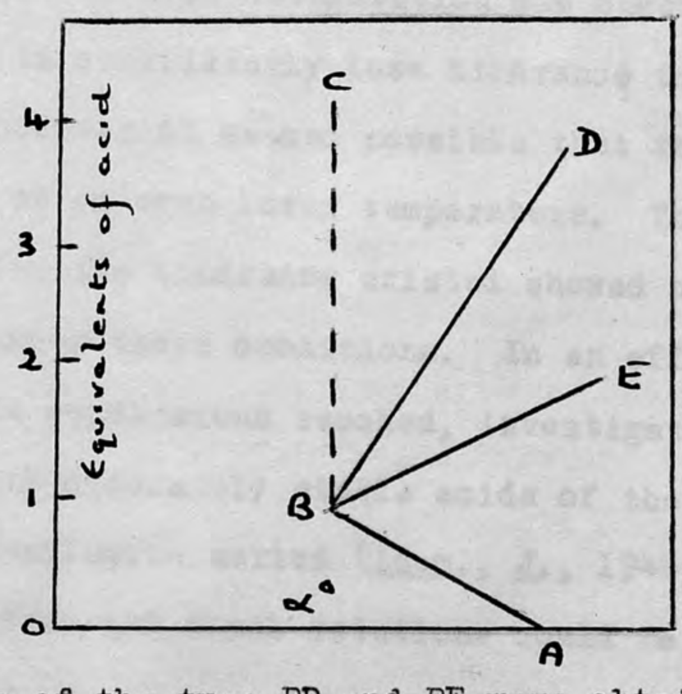
Kuhn and Albrecht (Annalen, 1927, 435, 272) obtained two crops of the quinine salt possessing the same rotation and m.p., which represented 80% of the theoretical yield. However on removal of the alkaloid, an acid was obtained which showed no optical activity.

Another series of compounds in which the optical activity is due to restriction to rotation within the molecule is the substituted benzoyl diphenylamines. These compounds have afforded many examples of asymmetric transformations of both types. Jamison and Turner (J., 1938, 1646) submitted N-benzoyl-4:6:4'-tribromodiphenylamine-2-carboxylic acid



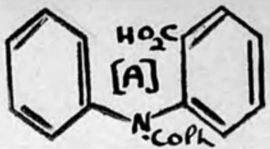
to a thorough stereochemical investigation. With cinchonidine it was found to undergo first and second order transformation and resolution, depending on the conditions of the experiment. On decomposition of the active cinchonidine salt the (+)-acid was obtained. A variety of other labile acids in this series were investigated by Jamison and Turner (J., 1940, 264) and shown to be capable of optical activation by various alkaloids.

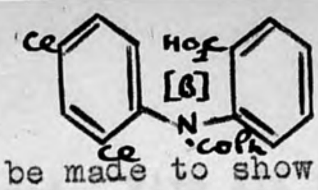
These workers observed (J., 1938, 1646) that the optical rotation at equilibrium of a solution containing a labile acid (1 mol.) and an alkaloid (1 mol.) was extremely sensitive to the addition of an excess of the racemic acid. After examining a number of these compounds it was found that the rotation at equilibrium underwent a change only in the case of those compounds in which optical activity might be expected from structural considerations. With molecules whose structure indicated a complete lack of hindrance to rotation, the equilibrium rotation was largely unaffected by addition of further acid. Thus on plotting equivalents of acid against rotation, the following types of 'addition curves' were obtained.

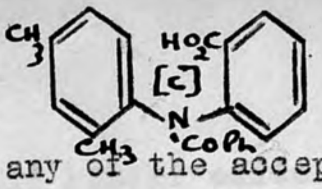


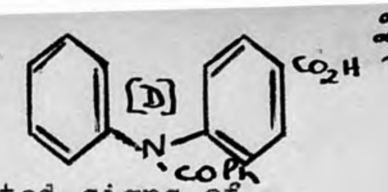
Curves of the type BD and BE were obtained with molecules which were expected to show restricted rotation, while compounds in which no restriction was apparent give results similar to BC. It was suggested (idem., loc.cit) that the phenomenon might be employed to detect potential optical activity in certain cases.

The series of acids:-

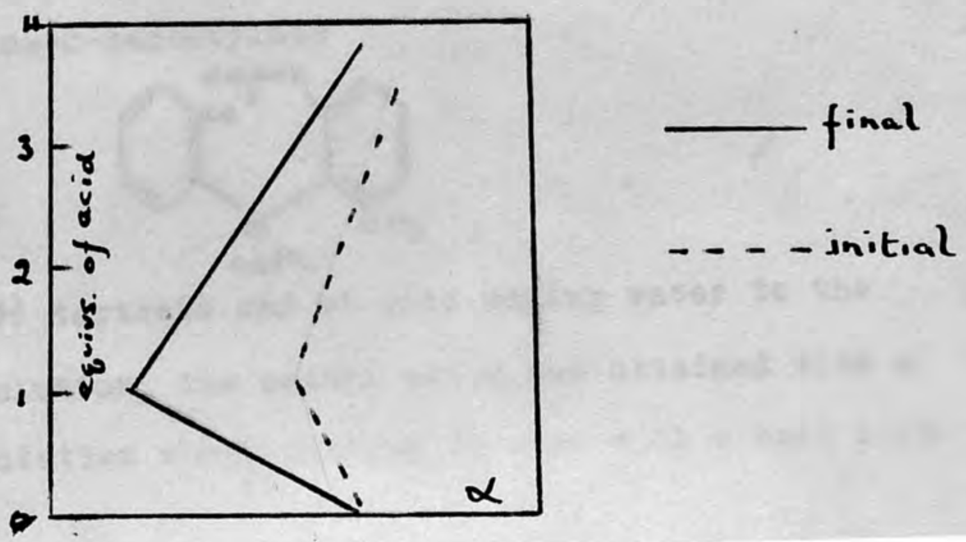




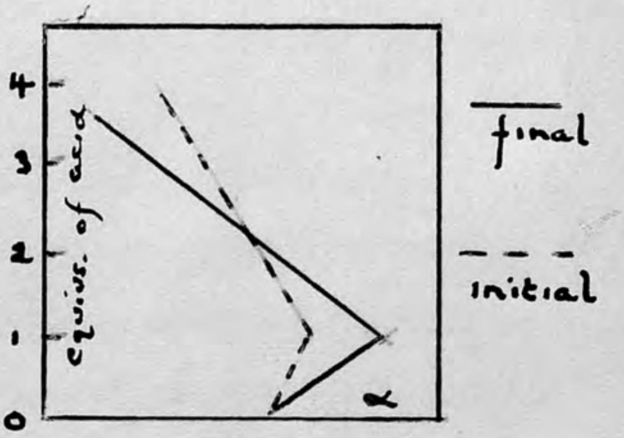




could not be made to show any of the accepted signs of optical activity at normal temperatures. However on plotting addition curves, changes in rotation with excess acid were observed with A, B and C. With D, the curve deviated only slightly from the vertical after the one equivalent point had been reached. Work carried out at -31° showed that both the acids B and C exhibited a definite mutarotation of measurable half-life with nor-(+)-ψ-ephedrine. No such mutarotation was observed with A in which there is considerably less hindrance to rotation than in B or C; however it seemed possible that that a mutarotation might occur at an even lower temperature. The acid D in which no effective hindrance existed showed no optical activation under these conditions. In an effort to substantiate the conclusions reached, investigations were conducted with moderately stable acids of the substituted benzoyl diphenylamine series (*Idem.*, *J.*, 1940, 264) Here both the initial and final rotations could be plotted and results of the type:-

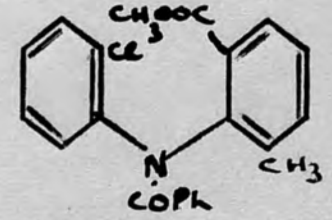


were obtained. With all the labile acids used, not only was the position of equilibrium changed, but in addition, the rate of attainment of equilibrium was increased, with the number of equivalents of acid used. Cases of some interest were those in which the initial and final curves crossed over.



The mechanism of this 'excess acid' effect has not been elucidated. It seems that no formal bond is necessary between the acid and optically active base in order that optical activation shall occur. This has been demonstrated by the optical activation of a racemic compound by an optically active solvent.

On dissolving methyl N-benzoyl-2'-chloro-6-methyl diphenylamine-2-carboxylate

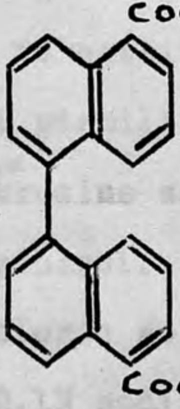


in ethyl (+) tartrate and at once adding water to the filtered solution, the methyl ester was obtained with a negative rotation which changed to zero with a half life of 9 mins. (Glazer, Harris and Turner, J., 1950, 1753; Buchanan and Graham, J., 1950, 500) By this method, 8-nitro-N-benzene sulphonyl-N-(2-hydroxyethyl)-1-naphthylamine was obtained in an optically active form for the first time. (idem., loc. cit.)

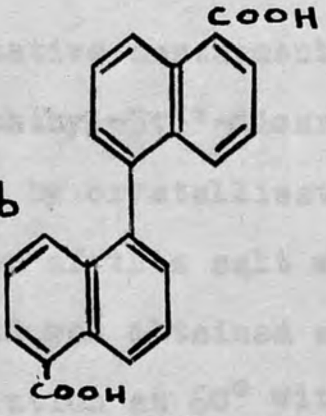
Section 3. Stereochemical Study of Substituted 1-Phenylnaphthalenes and 1:1'-Dinaphthyls.

Diphenic acid has been shown to undergo rapid optical activation at -30° in chloroform solution in the presence of nor-(+)-ψ-ephedrine (Lesslie, Turner and Winton, J., 1941, 257), but the free acid has never been obtained in an optically active form. Bell, Morgan and Smyth (Chem. and Ind., 1951, 634), recorded the isolation of optically active 1:1'-dinaphthyl-5:5'-dicarboxylic acid (Ia and Ib) with $[\alpha]_D$ +60° in 0.1N sodium hydroxide solution. The activity was lost when the solution was boiled for an hour. Although no quantitative value for the half-life of racemisation was given, a relatively high optical stability is implied. Such a high optical stability is surprising, since although the 8:8'- carbon atoms clearly cannot pass each other without great distortion of the main structure (Ia), very little interference would hitherto have been expected between the

Ia



Ib

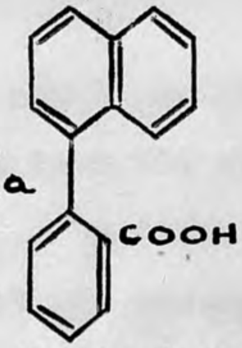


hydrogen atoms in the 2 and 8' or in the 2' and 8 positions (Ib). Bell and his co-workers (*loc. cit.*; Crawford and Smyth, *J.*, 1952, 4133) also obtained 4:4'-diquinolyl and 5:5'-diquinolyl in optically active, but less optically stable forms. They associated the optical activity observed in these three compounds with steric hindrance between the van der Waals envelopes of the 2 and 8' hydrogens. More recently it has been proposed by Crawford and Smyth (*Chem. and Ind.*, 1954, 346) that the racemisation of these and similar compounds may take place by a mechanism involving electrophilic attack by hydrogen. (For a more complete discussion see p. 11)

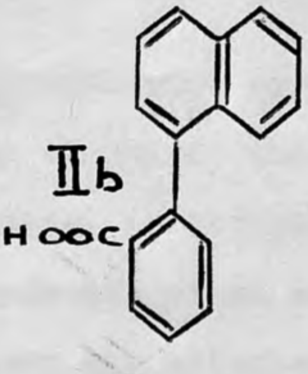
In order to obtain a more quantitative assessment of the optical stability of 1:1'-dinaphthyl-5:5'-dicarboxylic acid, the brucine salt was obtained by crystallisation from 2-ethoxyethanol. On decomposition of this salt with dilute hydrochloric acid, the (+)-acid was obtained and racemised in 0.1*N* sodium hydroxide solution at 60° with a half-life period of 33 minutes.

An acid intermediate in structure between diphenic acid and 1:1'-dinaphthyl-5:5'-dicarboxylic acid would be expected to exhibit optical activity. Such an acid, 1-phenylnaphthalene-2'-carboxylic acid (IIa and IIb) has

IIa



IIb

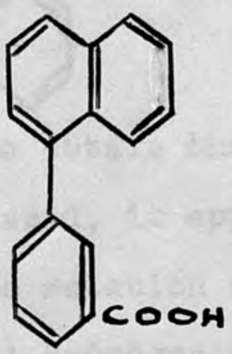


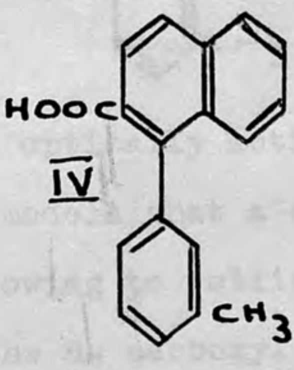
been synthesised and examined.

In acetone solution, second order asymmetric transformation was realised with cinchonidine and with brucine. The brucine (+)- acid salt obtained had a half-life period of 0.6 minutes in chloroform solution at 20°. From the brucine salt, (+)-1-phenylnaphthalene-2'-carboxylic acid was obtained by careful decomposition with cold formic acid. The (+)-acid racemised rapidly in chloroform at 20°, with a half-life of 2 minutes. Optical activation of the acid was observed with cinchonidine, quinidine and brucine. Quantitative determinations of the rates of mutarotation of the acid with brucine and cinchonidine were attempted. Owing to the small and rapid change in the observed angle, the results were of no quantitative value, but a log. plot of the readings obtained gave a straight line, approximately parallel to that obtained for the mutarotation of the alkaloid salts obtained by second order asymmetric transformations. Attempts to activate the acid in acetone solution were unsuccessful.

For one position of the phenyl nucleus (IIa), rotation about the 1:1'- bond is effectively prevented by interference between the carboxyl group and the 8- CH grouping. In the other position (IIb), however, hindrance to rotation arises from the slight overlap of the 2' and 8 hydrogen atoms. The results of the optical investigation therefore support the assumption that hydrogen atoms are capable of impeding free rotation when they are attached to an aromatic nucleus.

In order to investigate some of the limits of this effect, 1-phenylnaphthalene-3'-carboxylic acid (III) and 3'-methyl-1-phenylnaphthalene-2-carboxylic acid (IV) were prepared and examined.


III

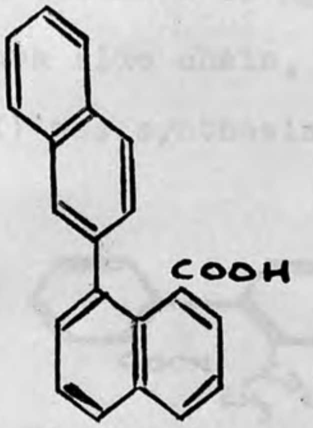

IV

With both of these compounds, the maximum blocking is provided by the slight overlap of the 2' (or 6') and 8-hydrogen atoms. In neither case could evidence of optical activity be obtained. Attempted optical activation of both acids by brucine at 5° was unsuccessful and "addition curves" (Jamison and Turner, J., 1938, 1646; ibid., 1940, 264), constructed by plotting the rotation of solutions containing brucine (or cinchonidine) and excess acid, against the equivalents of acid used, gave no indication of potential optical activity.

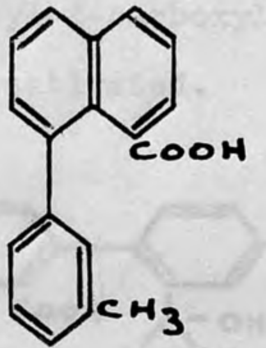
Attempts to bring about a second order asymmetric transformation of either acid with brucine were unsuccessful; decomposition of the alkaloidal salts obtained gave in both instances an inactive acid.

Meisenheimer and Beisswenger (<u>loc. cit.</u>) prepared 1:2'-dinaphthyl-8-carboxylic acid (V) and unsuccessfully

V



VI



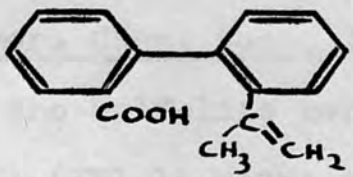
attempted to obtain the acid in an optically active form. In such an acid, it appeared from models that a considerable hindrance to rotation might exist owing to collision between the 1' or 3'-hydrogen atoms with the 8- carboxyl group. If such were the case, optical activity (although probably of an unstable type) should be detectable.

In view of these conclusions, together with the experimental results obtained with related acids, it was considered of interest to re-investigate the compound. Meisenheimer and Beisswenger synthesised the substance from ethyl 1-chloro-8-naphthoate and 2-chloronaphthalene, by means of an Ullmann reaction. Repeated attempts to obtain the acid by the Ullmann reaction starting with available methyl 8-bromo-1-naphthoate and 2-bromonaphthalene were unsuccessful. As an alternative an attempt was made to prepare 3'-methyl-1-

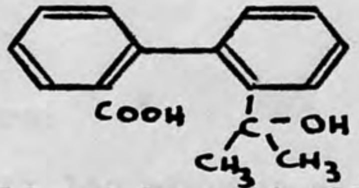
phenylnaphthalene-8-carboxylic acid. A product was obtained from an unsymmetrical Ullmann reaction in a very low yield (3% of Theory) and with poor analysis results. The attempts at preparation were discontinued.

In order to discover whether the efficient blocking properties apparently possessed by the nuclear hydrogen atoms were extended to hydrogen atoms attached to an unsaturated carbon side chain, 2'-isopropenyldiphenyl-2-carboxylic acid (VII) was synthesised and optically investigated.

VII



VIII

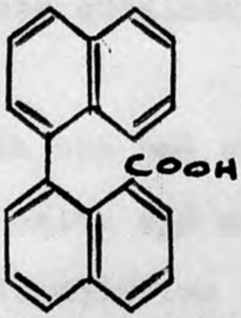


It was shown that the acid could not be optically activated either by brucine or cinchonidine. Addition curves were constructed with both these alkaloids, but no evidence of potential optical activity could be deduced, although the related acid (VIII) had been obtained in an optically active form (Corbellini and Angeletti, *loc. cit.* ; Jamison and Turner, *J.*, 1942, 437).

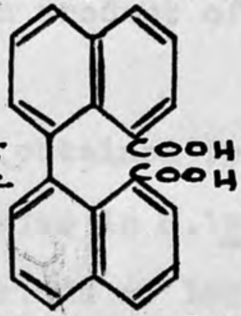
It is evident, in the series of compounds so far discussed, that while collision between nuclear hydrogen atoms is extremely efficient in preventing free rotation about the inter-nuclear bond, such a collision between only two such atoms, without supporting collisions between other groups in the molecule, does not hinder rotation about the 1:1'-bond sufficiently for it to give rise to observable activity.

A comparative study of the relative optical stabilities of 1:1'-dinaphthyl-5:5'-dicarboxylic acid (Ia and Ib), 1:1'-dinaphthyl-8-carboxylic acid (IX) and 1:1'-dinaphthyl-8:8'-dicarboxylic acid (X) reveals an apparent anomaly.

IX



X



Meisenheimer and Beisswenger (loc. cit.) resolved (IX) and (X) and determined the rates of racemisation of the acids in aqueous sodium hydroxide solution (see also, Stanley, J. Amer. Chem. Soc., 1931, 53, 3104).

The half-life periods found were:

(IX) 15 hours at 20° and (X) 160 minutes at 20°,

so that the order of stabilities would appear to be,

$$(IX) > (I) > (X).$$

(The half-life period of (I) at 20° is not known, but an estimation from the value at 60° indicates that it will be between 300 and 700 minutes.)

This order is obviously contrary to that expected from consideration of the number of substituents in the 'blocking positions'. It was therefore decided to re-investigate (X). The acid was synthesised from methyl 8-bromo-1-naphthoate by an Ullmann reaction, the 8-bromo-1-naphthoic acid being prepared from naphthalene-1:8-dicarboxylic acid (Rule, Pursell and Brown, J., 1934, 168). Thus the structure of (X) was established, precluding the possibility that the acid obtained by Meisenheimer and Beisswenger was an isomer having the

COOH- groups in positions other than the 8:8'.

(Meisenheimer prepared the acid from ethyl 8-chloro-1-naphthoate obtained via the nitration product of 1-naphthoic acid.)

Both the (+) and (-) acids were obtained from the brucine salts and were found to racemise in 0.1N sodium hydroxide solution with half-life periods of 163 and 165 minutes respectively; values which agree closely with those of Meisenheimer.

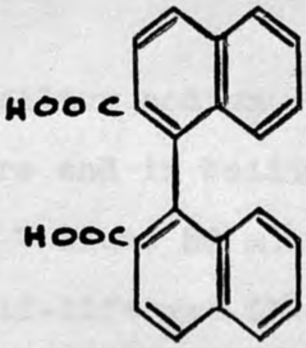
The explanation of the apparently anomalous order of stabilities is seen if the stability of the mono-ethyl ester of (X) is considered. Meisenheimer et. al. (loc. cit.) showed this compound to possess a half-life of 28 hours in aqueous sodium hydroxide solution at 18°. We thus have for the stability order:

mono-ethyl ester (x) $>$ (IX) $>$ (I)

i.e. the order expected from structural considerations.

It appears to follow that the relatively low optical stability of the disodium salt of (X) is due to the presence in the molecule of two adjacent charged carboxylate ion groups. Even so, it is difficult to see why (X) or its mono-ethyl ester should racemise at all readily. From the consideration of accurately constructed models, it appears that the considerable interference with free rotation about the 1:1'-bond in 1:1'-dinaphthyl-8:8'-dicarboxylic acid (X) is similar to that in 1:1'-dinaphthyl-2:2'-dicarboxylic acid (XI).

XI

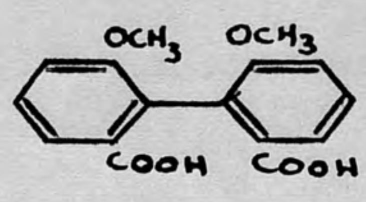


The latter compound is highly optically stable. Kuhn and Albrecht (Annalen, 1928, 465, 282) failed to racemise the active compound by heating a solution in aqueous sodium hydroxide for 4.5 hours on a boiling water bath. Hall and Turner (Chem. and Ind., 1953, 1177) resolved the acid and confirmed this result. The rotation of the acid was unchanged after boiling in 0.1 N sodium hydroxide solution for 10 hours, followed by heating in a sealed tube for 5 hours.

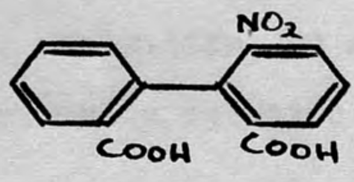
In support of the theory associating the presence of adjacent carboxylate ions with an increase in the rate of racemisation, it may be noted that certain active substituted diphenic acids are known for which the rate of racemisation in aqueous sodium hydroxide is greater than that in an organic solvent.

Stanley, McMahon and Adams (J. Amer. Chem. Soc., 1953, 55, 706) observed that 6:6'-dimethoxydiphenic acid (XII)

XII



XIII



racemised in boiling sodium ethoxide solution with a half-life of 11 hours and in boiling 0.1N sodium hydroxide with a half-life of 7 hours 50 minutes, whilst in boiling ethyl alcohol the half-life was 61.5 hours.

Adams and Hale (ibid., 1939, 61,2825) recorded that whilst 6-nitrodiphenic acid (XIII) racemised in boiling 0.1N sodium hydroxide with a half-life of 4.6 minutes, the half-life of the acid in boiling n -butyl alcohol was 101 or 107 minutes.

The theory that adjacent carboxylate ions affect the rate of racemisation may possibly be extended to explain the discrepancy noted by Kuhn and Albrecht (Annalen,1927, 455, 272; ibid., 1927, 458, 221) in the rate of racemisation of 4:6-dinitrodiphenic acid and 4:4':6-trinitrodiphenic acid in 2N sodium hydroxide solution at 98°, and to correlate the rates obtained for these acids with that obtained for 6-nitrodiphenic acid by Adams and Hale (loc. cit.).

The rates for these three acids are:-

(a) 6-nitrodiphenic acid : Half-life, 4.6 mins. in boiling 0.1N sodium hydroxide solution.

(b) 4:6-dinitrodiphenic acid: Half-life, 18 minutes in 2N sodium hydroxide solution at 98°.

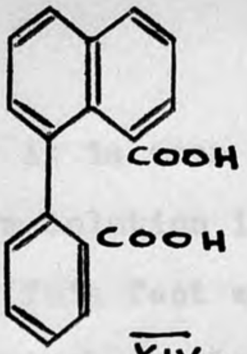
(c) 4:4':6-trinitrodiphenic acid : Half-life, 50 minutes in 2N sodium hydroxide solution at 98°.

The experimental results show that the two adjacent charged groups cause an active molecule to racemise more rapidly than the same molecule with two adjacent non-charged groups. Thus it does not seem unreasonable to suppose that the rate of racemisation would vary with the intensity of the charges on the two groups. Now in the case of 4:6-dinitrodiphenic acid (b) it seems possible that the electron withdrawing properties of the 4-nitro group will cause the charge density on the carboxylate ions to be less than that in the compound (a). Thus it might be predicted that (b) would racemise less rapidly than compound (a). In the case of 4:4':6-trinitrodiphenic acid (c) the extra 4'-nitro group will cause the total charge density on the carboxylate ions to decrease even further, when the rate of racemisation would be expected to be even slower than those of the other members of this series (a) and (b). The order of the rates of racemisation would then be,

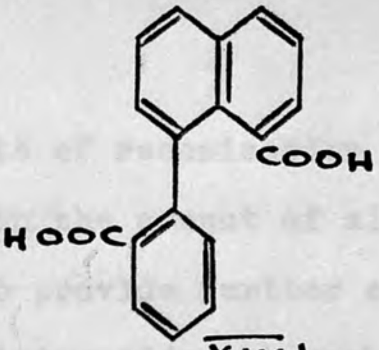
$$(a) > (b) > (c)$$

which in fact is the order found experimentally.

In an attempt to obtain more information concerning the effect of polar and non-polar solvents on the racemisation rate of a compound containing adjacent carboxyl groups, 1-phenylnaphthalene-2':8-dicarboxylic acid (XIVa and XIVb) was prepared and examined.



XIVa



XIV b

The brucine salt of this acid underwent first order asymmetric transformation in chloroform solution at 20°. With two molecules of brucine to one of acid the rate of equilibration was considerably faster than with one molecule of each. Second order transformation in benzene (and acetone) solution gave a mono-brucine (+)-acid salt (even when two equivalents of brucine were used), having a half-life of 460 minutes in chloroform solution at 20°. Racemisation of the free (+)-acid was observed in chloroform solution at 20°, when the rate of racemisation was found to be very sensitive to the amount of alcohol present. Three experiments were carried out.

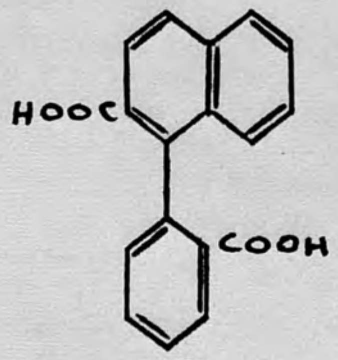
(i) In a "B.P." chloroform solution which had been washed with dilute hydrochloric acid and water, to ensure complete removal of brucine, the half-life period was 220 minutes. The washing was presumed to have removed some of the alcohol usually present in the solvent.

(ii) In "B.P." chloroform containing the usual amount of alcohol the half-life period of the acid was found to be 60 minutes.

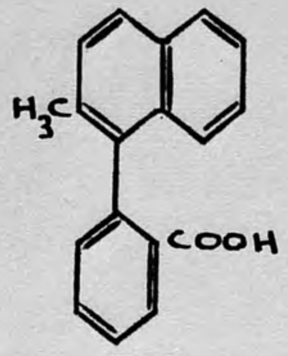
(iii) In "B.P." chloroform, to which had been added an extra 2.5% of ethanol, the half-life period was 35 minutes.

Thus it is seen that the rate of racemisation in chloroform solution increases with the amount of alcohol present. This fact would seem to provide further evidence that with such a molecule (containing adjacent carboxyl groups) the anion racemises faster than the free acid. Attempts to observe the racemisation in alkaline solution were unsuccessful. The sodium salt was found to be sparingly soluble and the acid dissolves so slowly in aqueous potassium hydroxide that polarimetric readings could not be taken until 15 minutes after wetting, by which time, racemisation was complete. This result also indicates qualitatively that the anion racemises more rapidly than the free acid, and that the acid is intermediate in optical stability between 1-phenylnaphthalene-2'-carboxylic acid and 1:1'-dinaphthyl-5:5'-dicarboxylic acid.

With a view to obtaining more date concerning the 'adjacent ion' effect, together with information about the relative optical stabilities of the phenylnaphthalene series, it was proposed to prepare and investigate 1-phenylnaphthalene -2:2'-dicarboxylic acid (XV).



XV



XVI

The preparation was attempted employing an Ullmann reaction between methyl o-iodobenzoate and methyl 1-bromo-2-naphthoate. A homogeneous product could not be obtained. In a further attempt to obtain (XV), 2'-methyl-1-phenylnaphthalene-2-carboxylic acid (XVI) was prepared, but an attempt to oxidise it proved unsuccessful.

PART II.

RELATION BETWEEN ULTRA-VIOLET ABSORPTION SPECTRA AND CONFIGURATION

Section 1. Introduction, including previous work.

Transitions of the π (unsaturation) electrons from one energy level to another can give rise to absorption in the region λ 200 - 1000 mμ, and hence it can be seen that investigation of the ultra-violet absorption spectra (λ = 200 - 400 mμ) should yield information concerning the distribution of unsaturated linkages in a molecule.

While the resultant effect on the ultra-violet spectra of two well separated ethylenic bonds in a molecule is largely additive, the result when two such chromophores are separated by only one single bond is anomalous and certain characteristic phenomena are observed which have become associated with conjugated systems. This unpredicted behaviour is parallelled in their chemical reactions (e.g. 1:4 addition) and by the optical exaltation recorded in the molecular refraction values. The chemical effects have been explained by the concept of resonance or mesomerism. The properties of compounds whose behaviour cannot be fully explained by one conventional formula are often elucidated by a consideration of several structures of similar potential energy, which differ only in the distribution of electron pairs. The individual structures have no separate existence and the molecule is regarded as a 'resonance hybrid' of the energetically permissible forms. The hybrid has a lower potential energy than any of the contributing structures, with the result that the electronic energy levels and hence the molecular spectra are affected. The energy levels are depressed and transition from one state to another requires less energy than in any of the resonating forms. From the equation $(E_I - E_{II}) = h\nu$, it can be seen that the corresponding absorption band will be at a lower frequency, i.e. at a longer wavelength. In addition the energy levels are crowded together, transitions between them become more probable and the intensity of the absorption band is increased.

With a system containing double bonds, the number of possible resonance forms and the associated spectral effects are increased by the degree of conjugation. From the foregoing conclusions, it can be predicted that as the conjugation of a system increases, the absorption bands will undergo a shift (bathochromic) to longer wavelengths and will become more intense. These predictions have been confirmed by experimental results.

Benzene exhibits two main absorption bands. The first is of high intensity (ϵ ca. 8000) in the region of 198 mμ and is consequently just outside the limit of the usual quartz spectrophotometer. This band is probably a conjugation (K-)

band similar to that found in other conjugated systems. The other main region of absorption is between 230 and 270 mμ and here the band is of low intensity (ϵ ca. 230) and exhibits considerable fine structure. The spectrum of diphenyl shows certain pronounced differences from that of benzene, which are mainly attributed to conjugation across the rings. Maximum absorption occurs at 255 mμ, the intensity is greatly increased (ϵ 18,000) and no trace of fine structure is apparent. This 'diphenyl' (conjugation) band of high intensity and lacking in fine structure, which bears no resemblance to the spectra of the partial benzenoid chromophores, is found in a variety of diphenyl compounds substituted in positions other than the 2:2' or 6:6'. On the other hand, the spectra of diphenyls which <u>are</u> substituted in the <u>ortho</u> positions tend to show a reversion to the benzenoid type.

Picket, Walter and France (<u>J. Amer. Chem. Soc.,</u> 1936, <u>58</u>, 2296) investigated the ultra-violet spectra of diphenyl compounds in which the four <u>ortho</u> positions were;
(i) substituted and (ii) unsubstituted. 2:2':4:4':6:6'-Hexachlorodiphenyl was found to have a spectrum of substantially the type observed for trichlorobenzene; while that of dimesityl was found to agree closely with that of 1:3:5-trimethylbenzene. In each case, the intensity of the main band of the diphenyl compound was greater than that of the benzene compounds owing to the combined contributions of the partial benzenoid chromophores. On the other hand, 4:4'-

dimethyldiphenyl and 4:4'-dichlorodiphenyl each exhibited an absorption band which resembled the conjugation band of diphenyl (high intensity and lack of fine structure) rather than the spectra of toluene and chlorobenzene (which show low intensity and considerable fine structure).

Certain diphenyl compounds in which only two of the four ortho positions are substituted also fail to exhibit the characteristic diphenyl band. O'Shaughnessy and Rodebush (ibid., 1940, 62, 2906) measured the spectra of 2:2'-dimethyldiphenyl and 2:2':4:4'-tetramethyldiphenyl and showed them to be of the dimesityl type, quite different from the results obtained for 3:3'- and 4:4'-dimethyldiphenyl which closely resembled the spectrum of diphenyl. See also, Beaven, Hass, Lesslie, Turner and Bird, J., 1954, 131).

Even diphenyls in which only one of the ortho positions is substituted may show a decrease in intensity of the diphenyl band. Friedel, Orchin and Reggel (ibid., 1948, 70, 199) compared the spectrum of diphenyl with those of 2-methyl-, 2-methoxy-and 2-hydroxydiphenyl. With these three compounds a decrease in intensity, together, in the last two cases, with the appearance of a long wave band was observed. Friedel et. al. (loc. cit.) also examined the cases of the isomeric dinaphthyls and certain phenylnaphthalenes.

The spectrum of 2-phenylnaphthalene bears little resemblance to that of naphthalene, however substitution of a methyl group in the 2'- position causes a reversion of the spectrum towards that of naphthalene. With 1-phenylnaphthalene which can be regarded as a monosubstituted diphenyl, the spectrum resembles that of naphthalene in spite of a slight bathochromic shift. In the case of the dinaphthyls, it was found that the spectrum of 1:1'-dinaphthyl shows the closest resemblance to that of naphthalene, while 2:2'-dinaphthyl shows a marked difference. 1:2'-dinaphthyl exhibits a spectrum between these two with a bias towards that of the 1:1'-compound.

The original explanation advanced to account for the retention or loss of the diphenyl band in the ultra-violet absorption spectra of substituted diphenyls, was based upon the belief that conjugation across the rings was only possible while a coplanar configuration was maintained. O'Shaughnessy and Rodebush (loc. cit.) stated that:-

"------- For resonance or conjugation to involve two rings as in biphenyl, it is necessary that the π orbitals of the adjacent 1:1'-carbons be parallel and this requires the coplanarity of the two rings."

Thus it was assumed that in diphenyl compounds unsubstituted in the ortho positions the rings adopted a coplanar configuration and conjugation between them was complete. As expected, a corresponding change in the spectra observed for the benzenoid chromophores is exhibited. The main absorption bands undergo a bathochromic shift, considerable increase in intensity and a loss of fine structure. However when all four ortho positions are blocked, free rotation about the 1:1'-

bond is no longer possible and a non-coplanar preferred configuration results. In such a case it was believed that interannular conjugation was no longer possible, which would explain the hypsochromic shift, decrease in intensity and increase in fine structure observed, as a reversion to the spectra of the individual benzenoid constituents.

Certain diphenyls with sufficiently large ortho substituents have been shown to be capable of resolution and are thus incapable of attaining a coplanar form. As the size of the ortho groups is decreased, the compounds become less stable and while they may be optically activable, they are no longer capable of resolution. However some compounds of the diphenyl series having such small groups in the blocking position that the compound cannot even be optically activated have spectra which imply a lack of or decrease in conjugation usually associated with a non-coplanar form. It was considered at one time that the stabilising effects of resonance in compounds of this type would tend to produce a structure in which at least the preferred configuration would be planar. Recently, however, a mass of conflicting evidence has accumulated concerning the configuration of many diphenyl compounds. It has been suggested that even with diphenyl the preferred configuration of the isolated molecule is not a coplanar one.

Dhar (loc. cit.), using X-ray crystallographic methods, showed the diphenyl molecule in the crystal to be coplanar.

Similarly, Toussaint (Acta Cryst., 1948, 1, 43) found that the rings of 3:3'-dichlorobenzidine in the crystal were approximately coplanar, the chlorine atoms having a trans relationship. However, Smare (ibid., p. 150) concluded that with 2:2'-dichlorobenzidine the rings were at an angle of 72° to each other but with the chlorine atoms cis rather than trans. A similar result was obtained for 2:2'-dimethylbenzidine dihydrochloride (Fowweather and Hargreaves, ibid., 1950, 3, 81): the rings were shown to be at an angle of 71° with the methyl groups arranged in a cis position.

These results only give information concerning the configuration in the crystal form, where the molecule is subjected to the influence of cohesive forces which are absent in solution or in the vapour state.

On the other hand, electron diffraction measurements of vapours give data concerning the isolated molecule. Using this method, Karle and Brockway (J. Amer. Chem. Soc., 1944, 66, 1974) suggested a non-coplanar form for the diphenyl molecule; the angle between the rings was given by Bastiansen (Acta Chem. Scand., 1949, 3, 408) as 45 ± 10°. In the same paper it was concluded that the rings in 3:3'-dichlorobenzidine and 3:3'-dibromodiphenyl were at angles of 52 ± 10° and 54 ± 5° respectively.

Dipole moment measurements have been employed to give information concerning the configuration of certain 2:2'-disubstituted diphenyls, and in general the results support the non-coplanar form. (e.g. Hampson and Weissberger, J. Amer. Chem. Soc., 1936, 58, 2111; Le Fevre and Vine J., 1938, 967)

Le Fèvre and Le Fèvre (ibid., 1936, 1130) measured the dipole moments of unsymmetrical 4:4'-disubstituted diphenyls and compared the results obtained with the values for the corresponding para disubstituted benzene derivative in order to obtain information concerning resonance inter-action between the two rings. It was concluded that in the case of 4-amino-4'-nitrodiphenyl some such interaction between the rings occurs.

From the foregoing results it appears that the former broad generalisations connecting conjugation (as implied from the ultra-violet spectra) with coplanarity of the rings in substituted diphenyls must be treated with some reserve.

Other apparent anomalies concerning these generalisations have been observed. The absorption spectrum of 2:2'-dimethyldiphenyl shows few of the characteristics associated with that of diphenyl (O'Shaughnessy and Rodebush, loc. cit.); however introduction of 4:4'-dinitro groups almostly completely restores the diphenyl conjugation band (Sherwood and Calvin, ibid., 1942, 64, 1340)

Thus it appears that in certain cases the interaction between a substituent and the aromatic nucleus can result in changes in the ultra-violet spectra which overshadow the steric effects. It has been shown (Williamson and Rodebush, ibid., 1941, 63, 3018) that the absorption spectrum of 3:3'-dimethoxydiphenyl exhibits a conjugation band of lower intensity than that of diphenyl and in some respects resembles the spectrum of the corresponding 2:2'- compound.

Certain diphenyls maintained in a non-coplanar configuration by bridging the 2:2'- positions, exhibit spectra which imply a coplanar structure (Beaven, Hall, Lesslie and Turner, J., 1952, 854).

Neither this phenomenon nor the non-coplanarity of certain unhindered diphenyls (as shown by electron diffraction measurements) conforms with the original theory linking the absorption spectrum with the configuration of the molecule. As already stated, this requires that conjugation between the two rings (as deduced from spectra results) could only exist in a coplanar or near coplanar molecule.

Guy (J. Chim. Phys., 1949, 46,469), claimed that calculations show that the angle between the rings in a diphenyl compound could increase from 0° to 22.5° without resonance being affected. He has further concluded that with an increase of the angle to a value between 45° and 67.5° (θ), the resonance interaction decreases to practically zero. Thus if a compound adopts a preferred configuration in which the angle has a value between 22.5° and θ, a hypsochromic shift of the first ultra-violet absorption band would be observed, the magnitude of which would depend on the angle attained. For values of the angle between the rings from θ to 90° Guy states that the resonance is completely prevented, when the observed spectrum would be that of the partial benzenoid chromophores.

Section 2. Results

The ultra-violet absorption spectra were measured using a Unicam spectrophotometer (SP/500).

In each case, the solvent used was 95% ethyl alcohol especially purified for spectroscopic measurements. The concentration of the compound in the solution under investigation was in each case, 0.125×10^{-4} g. moles/litre. The solutions were prepared using a dilution technique.

Measurements of the optical density were first carried out employing a 10 mm. cell, and subsequently checked by using a 5 mm. cell to ensure that maxima and minima were real.

The main features of the spectra measured are recorded in Tables I and II, and in Figs. I and II. For purposes of comparison, the data for 1:1'-dinaphthyl-2:2'-dicarboxylic acid has been included (Dr. D.M. Hall, unpublished results). The approximate values for the features of the necessary reference compounds are given in Table III. In this table the figures have been estimated from the published curves of log. ϵ against λ and the intensities are therefore subject to considerable error. (see Ultraviolet Spectra of Aromatic Compounds, Wiley & Sons, Inc., New York)

Table I. 1:1'-Dinaphthyls.

All in 95% EtOH and 1.25×10^{-5} M.

Compound	Shortwave band				Longwave band		
	λ max.	ϵ max.	λ min.	ϵ min.	λ max.	ϵ max.	
1:1'-Dinaphthyl-5:5'-dicarboxylic acid (I).	2216	73,400	2599	4,610	3017	15,900	Negligible fine structure.
1:1'-Dinaphthyl-8:8'-dicarboxylic acid (**X**)	2195 2395	59,600 45,600	2670	4,620	3092 3320	13,500 10,800	
1:1'-Dinaphthyl-2:2'-dicarboxylic acid (**XI**).	2245	94,400	2625	9,400	2850 2958	13,100 11,300	More fine structure than I or II.

Table II. 1-Phenylnaphthalenes.

Compound	Shortwave band				Longwave band		All in 95% EtOH and mainly 1.25 x 10-5 M.
	λ_{max}	ϵ_{max}	λ_{min}	ϵ_{min}	λ_{max}	ϵ_{max}	
1-Phenylnaphthalene-2'-carboxylic acid (II).	2223	68,900	2555	5160	2832	8800	Some fine structure - inflections on either side of longwave maximum.
Bachmann and Deno's figures. op. cit. No. 294	2220	64,600	2540	4400	2840	8900	
1-Phenylnaphthalene-3'-carboxylic acid (III).	2230	76,800	2550	6580	2885	12,100	No inflections.
1-Phenylnaphthalene-2':8-dicarboxylic acid (XIV).	2267	42,400	2666	5280	2982	9480	No inflections.
3'-Methyl-1-phenylnaphthalene-2-carboxylic acid (IV).	2327	42,600	2598	3560	2842	6730	Some fine structure.

Table III Reference Compounds.

Compound	Shortwave band				Conjugation band				Longwave band		Solvent
	λ max.	ϵ max.	λ min.	ϵ min.	λ max.	ϵ max.	λ min.	ϵ min.	λ max.	ϵ max.	
1:1'-Dinaphthyl No. 303.	2210	89,000	2490	4500					2830 2940	13,500 13,000	95% EtOH
2:2'-Dinaphthyl No. 309.	2130	40,000	2230	20,000	2540	95,500	2860	14,500	3080	19,000	95% EtOH
1-Phenylnaphthalene No. 290.	2260	63,000	2510	3850					2890	10,500	cyclo-hexane
2'-Methyl-1-phenylnaphthalene No. 291.	2230	63,000	2500	3100					2820	8700	cyclo-hexane
1-Naphthoic acid No. 250.	2200 Not observed as band but as increasing absorption.	50,000	2510	790					2940	7800	EtOH
2-Naphthoic acid No. 251.	2330	51,000	2540	2500					2780 3330	7000 1300	EtOH
Naphthalene No. 195.	2210	98,000	2350	1120					2760 3120	5750 2500	95% EtOH

Key to Figures.

Fig. I

———	1:1'-Dinaphthyl-5:5'-dicarboxylic acid
— — —	1:1'-Dinaphthyl-8:8'-dicarboxylic acid

Fig. II

———	1-Phenylnaphthalene-3'-carboxylic acid
— — —	1-Phenylnaphthalene-2'-carboxylic acid
— · — · —	3'-Methyl-1-phenylnaphthalene-2-carboxylic acid
....	1-Phenylnaphthalene-2':8-dicarboxylic acid

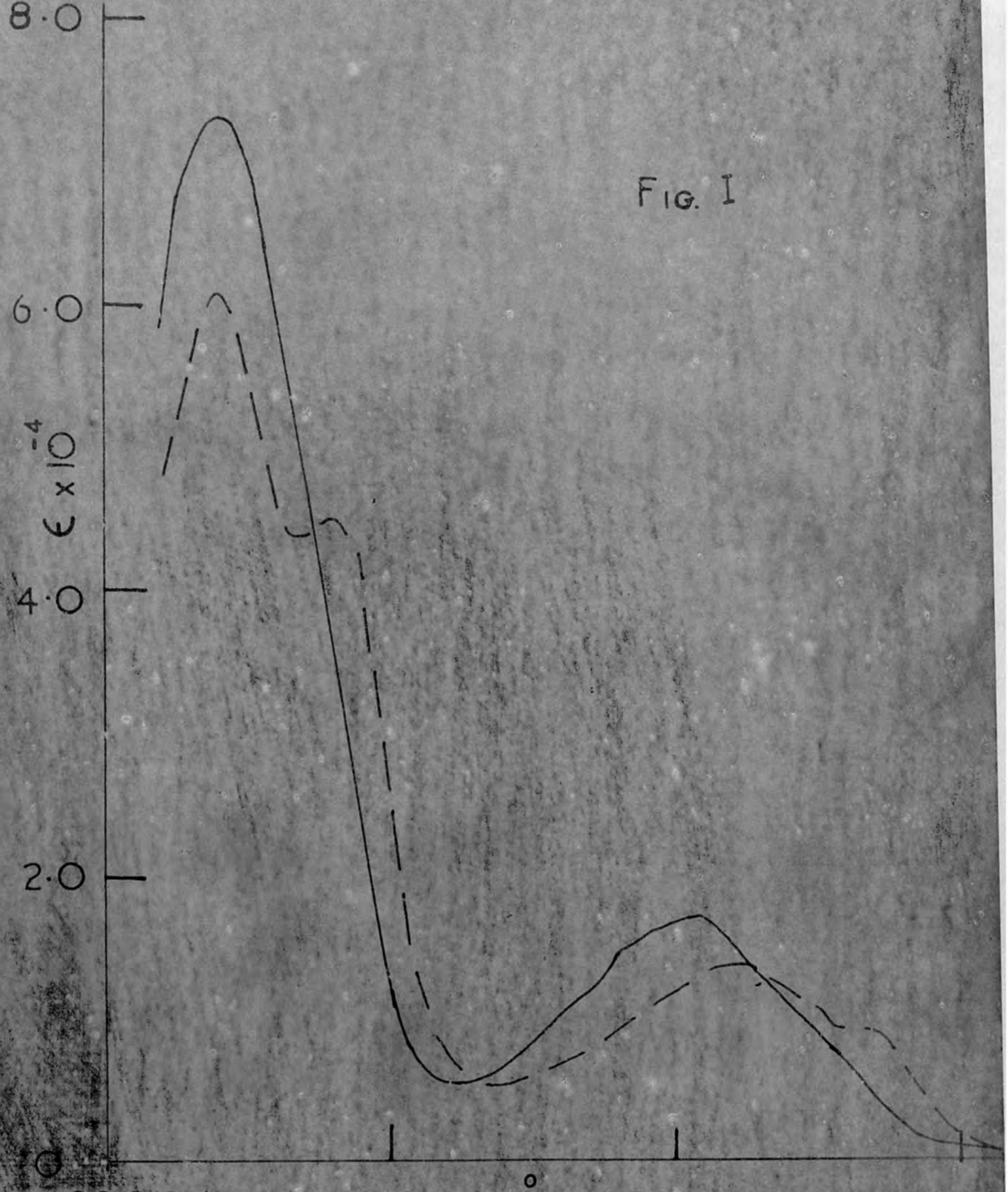
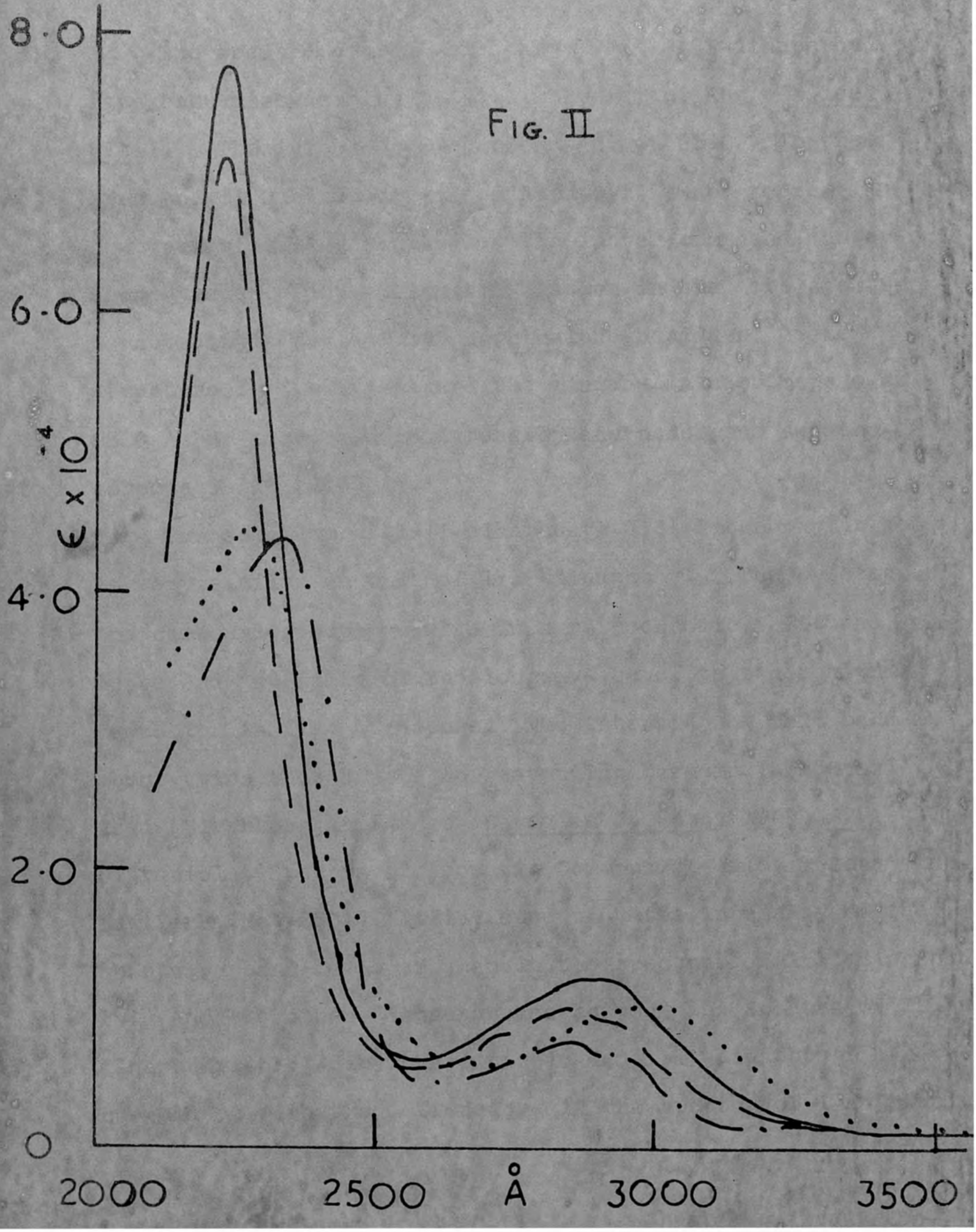


FIG. I

FIG. II



Section 3. Discussion of Results.

The spectra of 1:1'-dinaphthyl and 2:2'-dinaphthyl have been discussed by Friedel, Orchin and Reggel (loc. cit.). The intense conjugation band at 2540 Å in the spectrum of unhindered 2:2'-dinaphthyl is not present in the spectrum of 1:1'-dinaphthyl. The latter compound, however, shows traces of remaining conjugation in that its spectrum is not simply that of two naphthalene residues; fine structure is diminished and the minimum in naphthalene at 2350 Å has increased in intensity and undergone a bathochromic shift (2490 Å).

The spectrum of 1:1'-dinaphthyl-5:5'-dicarboxylic acid is very similar to that of 1:1'-dinaphthyl. The presence of the carboxyl groups results in a bathochromic shift and increased intensity of the longwave band, together with reduction in fine structure. The intensity of this band is about twice that of the corresponding band in 1-naphthoic acid (Hirshberg and Jones, Canadian J. Res., 1949, B27, 437; Ultraviolet Spectra of Aromatic Compounds, Wiley & Sons, Inc., New York, No. 250). It is found that the intensity of the shortwave band is lower than in the spectrum of 1:1'-dinaphthyl. This and the other discrepancies between the spectra of 1:1'-dinaphthyl-5:5'-dicarboxylic acid and 1:1'-dinaphthyl can be correlated with the differences in the spectra of 1-naphthoic acid and naphthalene.

In 1:1'-dinaphthyl-8:8'-dicarboxylic acid, the long wave band has shifted to a still longer wavelength, but it is less intense and more fine structure remains. The shortwave band is also reduced in intensity compared with that in the 5:5'-dicarboxylic acid, and a subsidary maximum on the longwave side is observed. Such a reduction in intensity of the shortwave band does not necessarily infer a more complete loss of conjugation across the 1:1'- bond than in the case of 1:1'-dinaphthyl-5:5'-dicarboxylic acid (as might be deduced from the greater optical stability). It may be connected with peri substitution in naphthalene since a similar reduction in intensity of the shortwave band is shown by 1:8-dimethylnaphthalene compared with 1:5-dimethylnaphthalene (op. cit., Nos 205 and 202).

In the case of 1:1'-dinaphthyl-2:2'-dicarboxylic acid, it might be expected that conjugation would be reduced to a minimum owing to the complete lack of coplanarity as deduced from the exceptional optical stability. The spectrum however, does not lead unequivocally to this conclusion. The shortwave band has undergone a slight hypsochromic shift compared to the band of 2-naphthoic acid (op. cit., No 251), although the intensity is almost double that of the band in the naphthalene partial chromophore. The increased fine structure compared to that of 1:1'-dinaphthyl-5:5'-dicarboxylic acid is comparable to that observed with 2-naphthoic and 1-naphthoic acids.

The spectra of the phenylnaphthalene series measured show differences from that of phenylnaphthalene which are, in general, consistent with the anticipated effects of the substituents on the spectra of the parent compounds(Hirshberg and Jones, loc. cit.) and on the steric hindrance to coplanarity across the 1:1'- bonds (Friedel, Orchin and Reggel, loc.cit.).

In 1-phenylnaphthalene some conjugation remains (ibid., loc.cit.). Substitution of a methyl group in the 2'-position causes a change in the spectrum of thetype associated with a decrease in conjugation, i.e. a hypsochromic shift, decreases in intensity and loss of fine structure.

The spectrum of 1-phenylnaphthalene-2'-carboxylic acid shows a resemblance to that of 2'-methyl-1-phenylnaphthalene, probably indicating a similar amount of steric hindrance.

When the carboxyl group is substituted in the 3'- position the increase in the intensity of both the long and shortwave bands, together with the decrease in fine structure indicates that a certain amount of conjugation has returned.

The interpretation of the spectra of 1-phenylnaphthalene-2':8-dicarboxylic acid and 3'-methyl-1-phenylnaphthalene-2-carboxylic acid is complicated by the additional substituents present. On the whole with the former compound there appears to be a large contribution from the 2-naphthoic acid partial chromophore, not inconsistent with a predictable lack of conjugation. With 3'-methyl-1-phenylnaphthalene-2-carboxylic acid however, the low band intensities and the shortwave shift and inflection of the longwave band seems anomalous when the complete lack of optical activity in this compound is considered.

In general throughout this series, there is poor correlation between the relative degree of conjugation across the 1:1'-bond, as inferred from the spectra and the relative optical stabilities of the active isomers. This stability seems to be determined by the gross steric hindrance to coplanarity across the 1:1'- bond, in terms of the number and location of the adjacent substituent groups. The secondary effects of the substituents on the conjugation and hence on the length of this bond, do not appear to have any further influence on the ease of rotation about it. This conclusion is contrary to the view taken by Calvin (loc. cit.), who has suggested that the shortening of the 1:1'- bond in diphenyl by resonance interaction of the appropriate 4:4'-substituents may be an important factor in determining optical stability. The lack of correlation between the spectra and optical stabilities of the compounds under discussion may perhaps be associated with the possibility that some of the compounds have non-coplanar ground states and coplanar excited states (c.f. Braude, Sondheimer and Forbes, Nature, 1954, 173, 117), so that the substituents affect the spectra by altering the transition probabilities for the excited state (and hence the intensity of the spectra), and have little influence on the ground states.

PART III.

EXPERIMENTAL.

Synthetic Work and Stereochemical Examinations.

All rotations were determined using a 2 dcm. polarimeter tube unless otherwise stated. For work in which temperature control was required, a polarimeter tube fitted with a metal jacket was employed. The temperature was maintained at a constant value by rapidly pumping water from an electrically heated thermostat through the jacket. Calibrated thermometers were placed in the inlet and outlet circuits of the system. The solution in the polarimeter tube was maintained at a constant temperature ± 0.1°.

In the experiments carried out at temperatures below 20° water was circulated through the jacket from a lagged refrigerator unit supplied with a temperature control. The temperature was maintained at a constant value ± 1°.

The mercury green line $\lambda = 5461$ was used throughout. Unless otherwise stated, the chloroform used as a solvent in polarimetric work was the commercial "B.P." product.

Purification of Alkaloids.

(i) Brucine.

The commercial product was purified following the method of Turner, (*J.*, 1951, 842). B.D.H. brucine was recrystallised from water, the crystalline tetrahydrate dried in air, dissolved in chloroform and the solution dried over anhydrous sodium sulphate. The solution was poured into dry light petroleum (b.p. 40-60°), the precipitated solid filtered off and dried to constant weight at 100°/5 mm. over phosphorus pentoxide. The product had m.p. 177-9° and $[\alpha]^{20}_{5461}$ -145° in chloroform (c = 1).

Turner (loc. cit.) gives $[\alpha]^{20}_{5461}$ -149.9° (c=1) m.p. 178-9°.

(ii) Cinchonidine.

The commercial product was recrystallised from alcohol and was found to have $[\alpha]^{20}_{5461}$ -110°, m.p. 203°.

Methods Employed.

In carrying out a first order asymmetric transformation in which a small mutarotation might take place rapidly, it was necessary to ensure that a reading of the observed angle be made as quickly as possible after wetting the acid and the alkaloid.

The alkaloid and the acid were weighed out in separate weighing bottles and a small volume of chloroform (which had been allowed to stand in the thermostat) added to each. When the solids had dissolved, one solution was introduced into the graduated flask, the other solution was rapidly added and at the same time a stop clock started. The solution was made up to the graduation mark with more chloroform, homogenity being ensured by thorough shaking. The resulting solution was filtered directly into the polarimeter tube.

Using this method thefirst reading of the observed angle could be made from 1½ - 2 minutes after mixing.

In some cases in which the acid proved difficultly soluble in chloroform, solution was brought about by shaking the solid acid with a chloroform solution of the alkaloid.

Frequently only a small amouth of the inactive acid was available in order to obtain the active alkaloid-acid salt by second order asymmetric transformation or by resolution. Both in this case and when isolating the active acid from an alkaloidal salt, filtrations were carried out on sintered glass crucibles (Grade 4), and a normal gravimetric technique was adopted.

Preparation of 1-Phenylnaphthalene-2'-carboxylic Acid.

Methyl o-iodobenzoate.

Wachter, Ber., 1893, 26, 1744

Anthranilic acid (54.8 g., 1 mol.) was suspended in 10% sulphuric acid (540 ml.) and an aqueous solution of sodium nitrite (27.5 g., 1 mol.) slowly added. The temperature of the reaction was maintained between 0 and 5°. On completion of the addition, the cold solution of the diazonium salt was slowly added with stirring to a solution of potassium iodide (100 g., 1.5 mols.) in 10% sulphuric acid (120 ml.) The reaction was completed by heating on a water-bath for two hours. The crude o-iodobenzoic acid was filtered off, washed and dried, and esterified without further purification by boiling with methyl alcohol (1.13.1.) and concentrated sulphuric acid (43.7 g.) for five hours.

Methyl o-iodobenzoate (81 g., 77%) was obtained by distillation under reduced pressure, b.p. 133-4°/11 mm.

1-Iodonaphthalene.

1-Aminonaphthalene (52 g., 1 mol.) was suspended in dilute hydrochloric acid and diazotised by adding an aqueous solution of sodium nitrite (26.5g., 1 mol.) at 0-5°. The solution of the diazonium salt was slowly added with stirring to a solution of potassium iodide (85g., 1.3 mol.) in water (200 ml.). The reaction was completed by heating on a water-bath for one hour. Free iodine was removed by addition of a little sodium metabisulphite to the reaction mixture, when crude 1-iodonaphthalene was obtained by steam distillation.

Pure 1-iodonaphthalene (55 g., 60%) was obtained by distillation under reduced pressure, b.p. 164°/ 19 mm.

1-Phenylnaphthalene-2'-carboxylic Acid.

The acid was obtained by a modification of the method of Baddar and Warren, *J.*, 1938, 401.

Freshly precipitated copper powder (30 g., 3.2 atoms), (obtained by the method of Davey and Latter, *J.*, 1948, 264) was added gradually to a stirred mixture of 1-iodonaphthalene (37.5g., 1mol.) and methyl o-iodobenzoate (38.7g., 1mol.) contained in a hard glass tube immersed in a metal bath. The temperature of the reaction was not allowed to exceed 290°, and when the addition of the copper was complete, the reaction mixture was maintained at this temperature for one hour. The temperature was then allowed to drop to 150° when the paste obtained was thoroughly extracted with *o*- dichlorobenzene. The solvent was removed from the extract by distillation and the residue was hydrolysed by boiling with an alcoholic solution of potassium hydroxide (16 g.) for two hours. The alcohol was distilled off and the solid residue was extracted with water. The aqueous solution was extracted with benzene to remove neutral compounds and then acidified with dilute hydrochloric acid. The mixture of acids which was precipitated was extracted with cold benzene. Diphenic acid remained undissolved and was filtered off. The filtrate was boiled with charcoal and evaporated to dryness. The oily residue was dissolved in boiling methyl alcohol (20 ml.). On cooling a light brown solid (4.8g., 13%) of m.p. 152-9° was obtained. The solid was recrystallised twice from methyl alcohol and a further three times from light petroleum (b.p. 100-120°).

1-Phenylnaphthalene (3.7g., 10%) was obtained as a colourless solid, crystallising in rectangular plates of m.p. 159.5-161°.

(Found: C, 81.7; H,4.7. Calc. for $C_{17}H_{12}O_2$: C, 82.2; H,4.9%)

The reaction was carried out using commercial copper-bronze in place of the precipitated copper powder; no significant change in yield was observed.

Qualitative First Order Asymmetric Transformations of 1-Phenylnaphthalene-2'-carboxylic acid with:-

(a) Brucine:

A solution of the acid (0.2020g., 1mol.) and brucine (0.3206g., 1mol.) in chloroform (25ml.) mutarotated through + 0.07°.

(b) Cinchonidine:

A solution of the acid (0.1961g., 1mol.) and cinchonidine (0.2334g., 1mol.) in chloroform (25ml.) mutarotated through -0.14°.

(c) Quinidine:

A solution of the acid (0.2014g., 1mol.) and quinidine (0.2627g., 1mol.) in chloroform (25ml.) mutarotated through +0.10°.

In the foregoing experiments no temperature control was employed.

Quantitative First Order Asymmetric Transformations:

(a) With Brucine:

A solution of the acid (0.1546g., 1mol.) and anhydrous brucine (0.2455g., 1mol.) was prepared in chloroform (20ml.) The solution was examined polarimetrically at 20°, and the first reading of the observed angle was taken 1.6 mins. after the solid had been wetted. The rotation changed from -0.40° to - 0.31° during 4 mins. (Table 1.)

A duplicate experiment was carried out, and although the mutarotation was too small and the time of change too rapid to obtain an accurate value for the rate of mutarotation, a log. plot of the combined readings (fig. 1) was consistent with a $\underline{k}$ substantially in agreement with the more accurate value derived from the second order asymmetric transformation.

(b) With Cinchonidine:

A solution of the acid (0.2462g., 1mol.) and cinchonidine (0.2942g., 1mol.) was prepared in chloroform (20ml.) at 20°. The solution was examined polarimetrically, and the change of the observed angle with time recorded (Table 2.). As with the activation with brucine, an accurate value for the rate of mutarotation could not be obtained, but a log. plot of the readings (fig. 2) was consistent with a $\underline{k}$ obtained from the mutarotation of the salt obtained by second order asymmetric transformation.

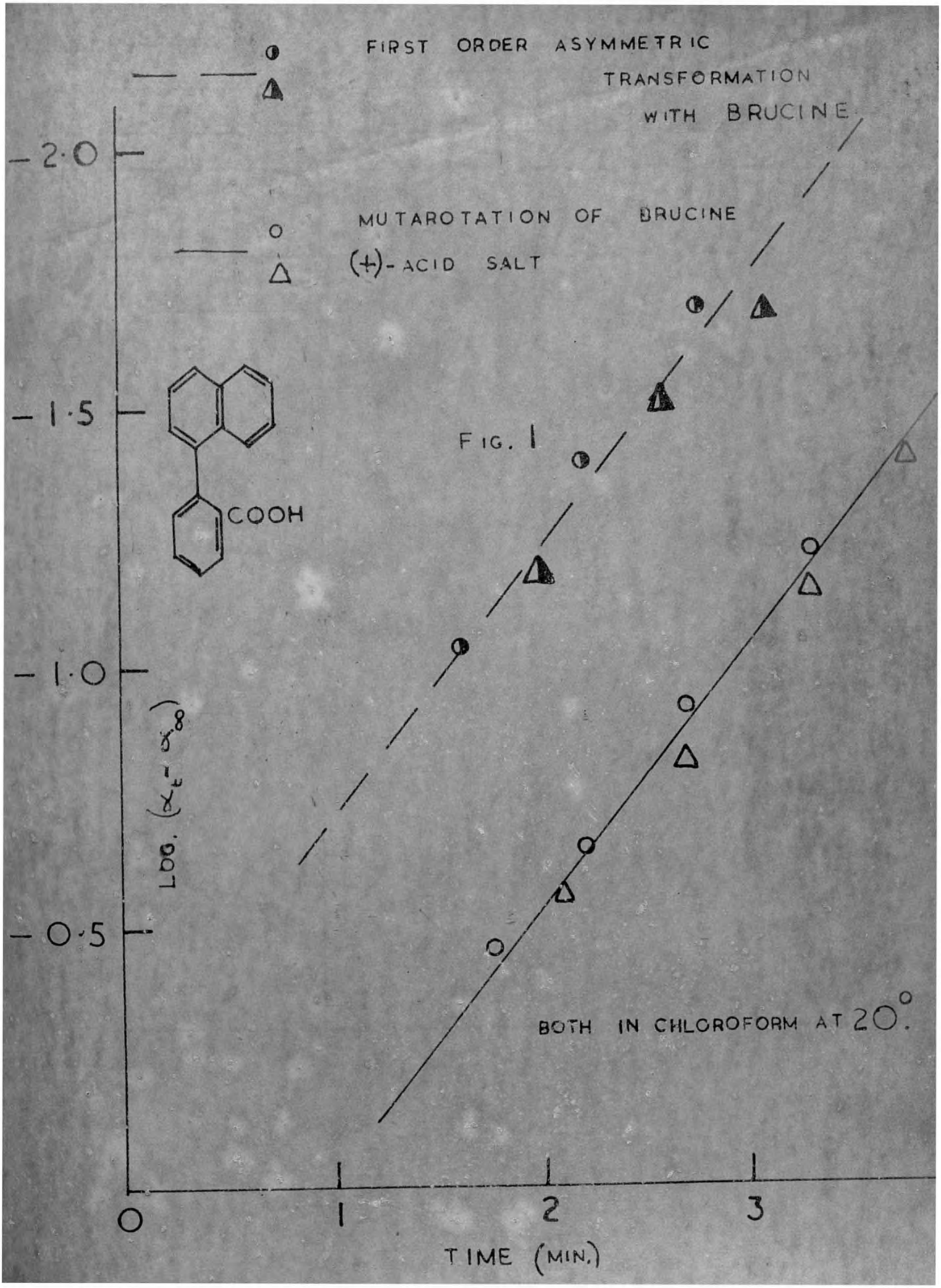


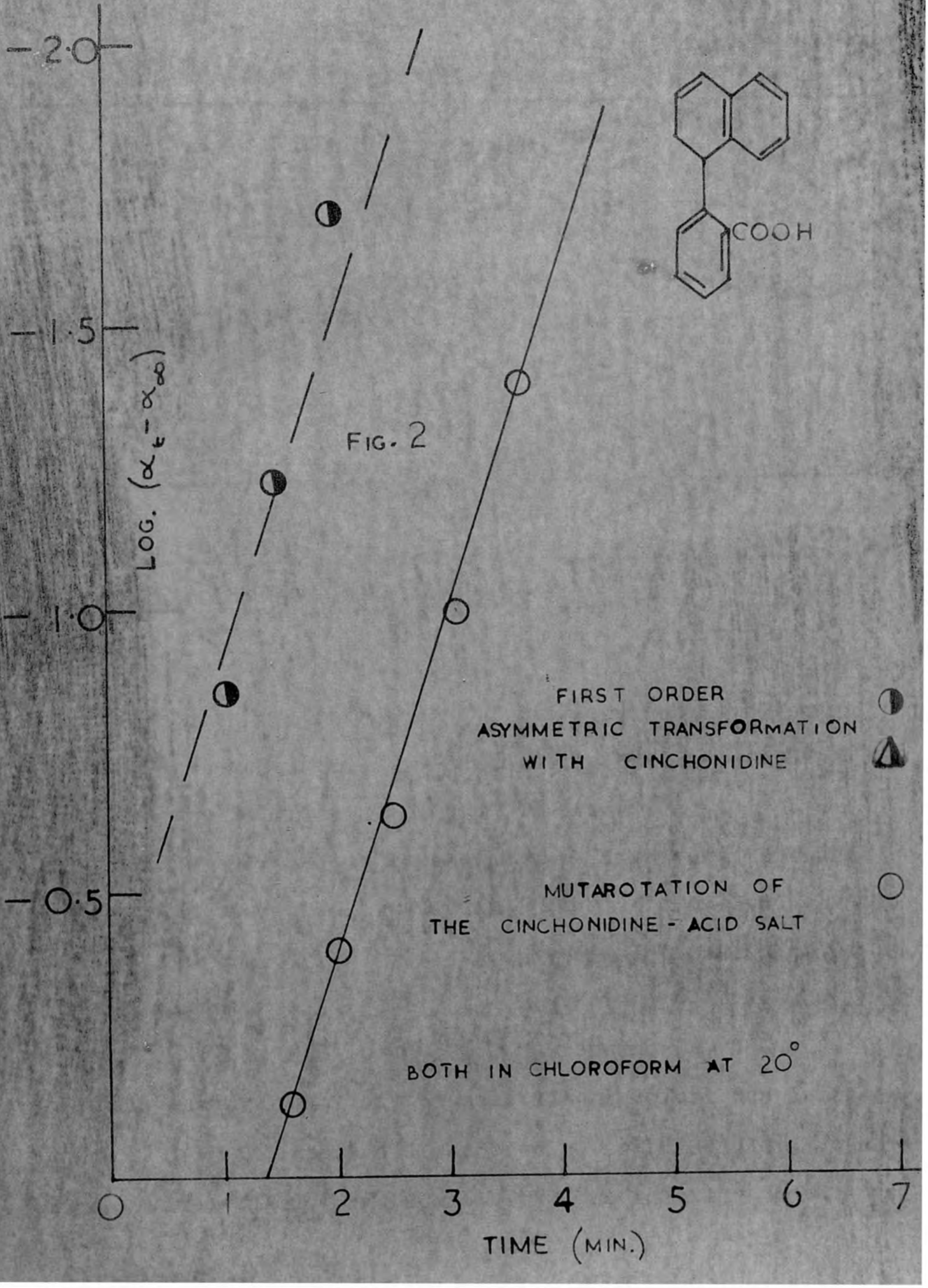
FIG. 1

FIRST ORDER ASYMMETRIC TRANSFORMATION WITH BRUCINE
MUTAROTATION OF BRUCINE (+)-ACID SALT
COOH
BOTH IN CHLOROFORM AT 20°.
LOG. $(\alpha_t - \alpha_\infty)$
−2·0
−1·5
−1·0
−0·5
0
1
2
3
TIME (MIN.)

Table 1.

First Order Asymmetric Transformation of 1-Phenylnaphthalene-2'-carboxylic Acid with Brucine in Chloroform at 20°.

Time after wetting. (min.)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k min.$^{-1}$
1st. Experiment.			
1.6	- 0.40	$\bar{2}.9542$	-
2.2	- 0.35	$\bar{2}.6021$	1.35
2.75	- 0.33	$\bar{2}.3010$	1.31
3.5	- 0.32	$\bar{2}.0000$	1.16
4.1	- 0.31	-	-
10.0	- 0.31	-	-
∞	- 0.31	-	-
2nd. Experiment.			
2.0	- 0.37	$\bar{2}.7782$	-
2.6	- 0.34	$\bar{2}.4771$	1.15
3.1	- 0.33	$\bar{2}.3010$	1.00
4.2	- 0.31	-	-
8.5	- 0.31	-	-
∞	- 0.31	-	-



COOH
-2·0
-1·5
-1·0
-0·5
LOG. $(\alpha_t - \alpha_\infty)$
0
1
2
3
4
5
6
7
TIME (MIN.)
FIRST ORDER ASYMMETRIC TRANSFORMATION WITH CINCHONIDINE ◑ △
MUTAROTATION OF THE CINCHONIDINE - ACID SALT ○
BOTH IN CHLOROFORM AT 20°

FIG. 2

Table 2.

Time after wetting. (mins.)	$\alpha^{20^\circ}_{5461}$	$[\alpha]^{20^\circ}_{5461}$	$\log_{10}(\alpha_t - \alpha_\infty)$
1.05	+4.18	+135.3	$\bar{1}.1461$
1.5	+4.26	+137.9	$\bar{2}.7782$
2.0	+4.30	+139.2	$\bar{2}.3010$
2.8	+4.32	+139.8	-
4.1	+4.32	+139.8	-
5.0	+4.32	+139.8	-
∞	+4.32	+139.8	-

Second Order Asymmetric Transformation of the Brucine Salt of (+)-1-Phenylnaphthalene-2'-carboxylic Acid from Acetone.

1-Phenylnaphthalane-2'-carboxylic acid (1.5081g., 1mol.) and anhydrous brucine (2.5100g., 1mol.) were dissolved in boiling acetone (100ml.). The solution was filtered while hot, and the filtrate evaporated to about 30ml.. The crystalline solid which separated was filtered off, washed with acetone and dried in vacuum. The yield of 3.66g. represented 91% of the total weight of solid taken. M.p. 105° (decomp.).

(Found: C, 73.2; H,6.1. $C_{40}H_{38}O_6N_2$ requires C, 74.8; H,6.0%)

The mutarotation of the salt in chloroform was followed twice. In each experiment the brucine salt (0.4010g.) was dissolved in chloroform (20ml.), and the solution examined polarimetrically at 20°. From the results (Table 3.) a log. plot was made (fig. 1) and an average value of <u>k</u> 1.13 mins^{-1} was obtained, whence the half life is 0.6 mins..

Second Order Asymmetric Transformation of the Cinchonidine Salt of 1-Phenylnaphthalene-2'-carboxylic Acid from Acetone.

The acid (0.2462g., 1mol.) and cinchonidine (0.2942g., 1mol.) were dissolved in boiling acetone (25ml.). The solution was filtered while hot and the colourless crystalline solid which was deposited on cooling was filtered off, washed, and dried in vacuum. The yield of 0.425g. represented 77% of the total solid taken. M.p. 150° (decomp.).
(Found: C, 79.7; H,6.3. $C_{36}H_{34}O_3N_2$ requires C,79.0; H,6.3%)

The salt (0.3090g.) was dissolved in chloroform (20ml.), and the solution examined polarimetrically at 20°. Readings of the observed angle with time were recorded (Table 4.). A log. plot of the results was made (fig.2) and a value of <u>k</u> 1.32 mins.$^{-1}$ was obtained whence the half life is 0.5 mins..

Table 3.

Mutarotation of the Brucine Salt of (+)-1-Phenylnaphthalene-2'-carboxylic Acid in Chloroform at 20°.

Time after wetting. (min.)	α^{20}_{5461}	log.$_{10}(\alpha_t-\alpha_\infty)$	k min.$^{-1}$
1st. Experiment.			
1.75	+0.03	$\bar{1}.5441$	-
2.2	-0.10	$\bar{1}.3424$	1.03
2.7	-0.20	$\bar{1}.0792$	1.13
3.3	-0.26	$\bar{2}.7782$	1.14
4.1	-0.30	$\bar{2}.3010$	1.22
4.75	-0.31	$\bar{2}.0000$	1.18
12.0	-0.32	-	-
∞	-0.32	-	-
2nd. Experiment.			
2.1	-0.05	$\bar{1}.4314$	-
3.3	-0.25	$\bar{2}.8451$	1.13
3.8	-0.28	$\bar{2}.6021$	1.12
4.45	-0.30	$\bar{2}.3010$	1.11
11.0	-0.32	-	-
∞	-0.32	-	-

Table 4.

Mutarotation of the Cinchonidine Salt of 1-Phenylnaphthalene -2'-carboxylic Acid in Chloroform at 20°.

Time (mins.) after 1.55 mins.	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins^{-1}
0	+5.07	$\bar{1}.8692$	-
0.5	+4.72	$\bar{1}.5911$	1.28
0.9	+4.56	$\bar{1}.3617$	1.30
1.5	+4.43	$\bar{1}.0000$	1.33
2.1	+4.37	$\bar{2}.6021$	1.38
3.05	+4.33	-	-
5.75	+4.33	-	-
∞	+4.33	-	-

(+)-1-Phenylnaphthalene-2'-carboxylic Acid.

The brucine (+)-acid salt (1.75g.) obtained from a second order asymmetric transformation was ground with a little formic acid (S.G. 1.2) at 5°. The solid did not completely dissolve and the suspension was poured into ice cold dilute hydrochloric acid. The precipitated (+)-acid (0.5g.) was filtered off, washed with water and dried in vacuo. M.P. 162°. (Found: C, 82.15; H,4.9. $C_{17}H_{12}O_2$ requires C, 82.2; H,4.9%)

Racemisation of (+)-1-Phenylnaphthalene-2'-carboxylic Acid

A solution of the acid (0.2130g.) in chloroform (20ml.) was examined polarimetrically at 20°. A duplicate experiment was carried out and a log. plot made (fig.3) of the combined results (Tables 5 and 6). The values of k obtained were: (1) 0.355 (2) 0.36 mins.$^{-1}$. Whence an average half-life of 2.0 mins. was calculated.

Attempted Activation of Methyl 1-Phenylnaphthalene -2'-carboxylate by Solvation.

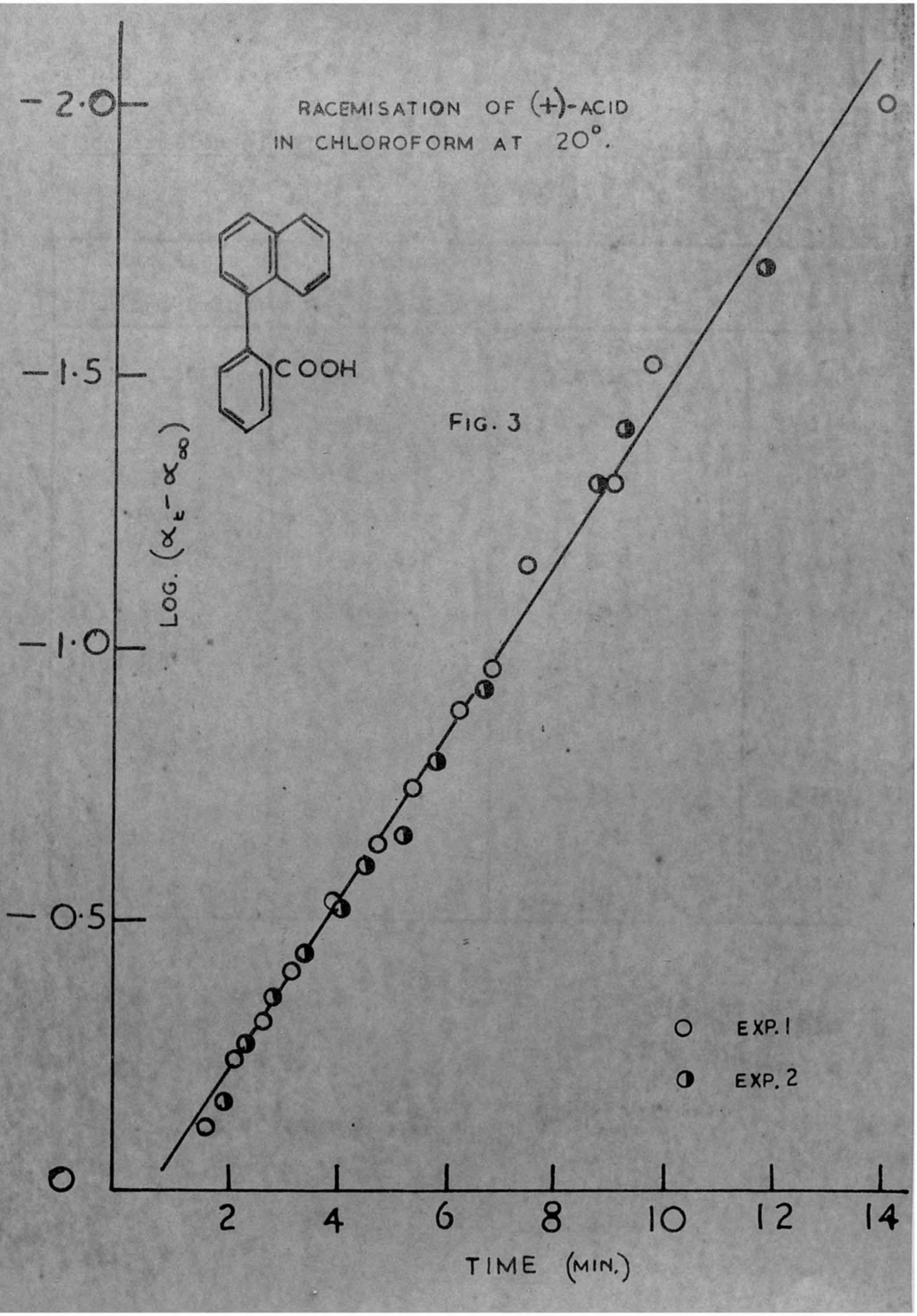
Preparation of Methyl 1-Phenylnaphthalene -2'-carboxylate.

1-Phenylnaphthalene-2'-carboxylic acid (1g.) was esterified by boiling with methyl alcohol (10ml.) and concentrated sulphuric acid (0.5g.) for three hours. The ester was crystallised from light petroleum (b.p. 80-100°) (5ml.). and had m.p. 88-9° (0.61g., 58%).

An attempt was made to activate the acid with an optically active solvent. (c.f. Glazer, Harris and Turner, J., 1950, 1753; Buchanan and Graham, J., 1950, 500.)

Methyl 1-phenylnaphthalene-2'-carboxylate (0.25g.) was dissolved in diethyl (+)-tartrate (5ml.). After standing at room temperature for an hour, ice-cold water was gradually added with stirring until the methyl ester crystallised. The solid was washed with water and dried in vacuum.

The ester (0.2000g.) was dissolved in chloroform (20ml.)



RACEMISATION OF (+)-ACID IN CHLOROFORM AT 20°.

FIG. 3

Table 5.

Racemisation of (+)-1-Phenylnaphthalene-2'-carboxylic Acid in Chloroform at 20°.

Time after wetting. (min.)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k min.$^{-1}$
2.35	+0.53	$\bar{1}.7243$	-
2.8	+0.44	$\bar{1}.6435$	0.41
3.42	+0.36	$\bar{1}.5563$	0.36
4.0	+0.30	$\bar{1}.4771$	0.35
4.45	+0.25	$\bar{1}.3979$	0.36
5.15	+0.22	$\bar{1}.3424$	0.31
5.75	+0.16	$\bar{1}.2041$	0.35
6.6	+0.12	$\bar{1}.0792$	0.35
8.7	+0.05	$\bar{2}.6990$	0.37
9.2	+0.04	$\bar{2}.6021$	0.41
11.75	+0.02	$\bar{2}.3010$	0.35
∞	0.00	-	-

Table 6.

Racemisation of (+)-1-Phenylnaphthalene-2'-carboxylic Acid in Chloroform at 20°.

Time after wetting. (min.)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k min.$^{-1}$
2.1	+0.57	$\bar{1}.7559$	-
2.62	+0.48	$\bar{1}.6812$	0.33
3.12	+0.39	$\bar{1}.5911$	0.33
3.85	+0.29	$\bar{1}.4624$	0.39
4.65	+0.23	$\bar{1}.3617$	0.36
5.3	+0.18	$\bar{1}.2553$	0.36
6.15	+0.13	$\bar{1}.1139$	0.36
6.75	+0.11	$\bar{1}.0414$	0.35
7.4	+0.07	$\bar{2}.8451$	0.35
9.0	+0.05	$\bar{2}.6990$	0.35
9.65	+0.035	$\bar{2}.4771$	0.37
∞	0.00	-	-

and examined polarimetrically at 20°. The first reading of the observed angle was made 1.5 mins. after wetting. No optical activity was observed and no mutarotation was observed.

Preparation of 1:1'-Dinaphthyl-5:5'-dicarboxylic Acid.

1-Bromonaphthalene.

A mechanically stirred solution of naphthalene (26~~.~~5g., 1.25 mols.) in dry carbon tetrachloride (90ml.) was heated to boiling and bromine (254g., 1mol.) added slowly to the reaction mixture over three hours. Heating was continued for a further two hours by which time the evolution of hydrogen bromide had ceased. The residue obtained after the bulk of the solvent had been distilled off was heated on a water bath with sodium hydroxide (20g.) for three hours. The liquid obtained was filtered through glass wool and distilled under reduced pressure, a fraction (310g.) b.p. 148-152°/20mm. was collected and redistilled. 1-Bromonaphthalene b.p. 136-7°/14mm. was obtained. (290g. 89%, calculated on the weight of bromine used.)

1-Naphthoic Acid.

A solution of 1-bromonaphthalene (207g., 1mol.) was slowly added to a mechanically stirred suspension of magnesium turnings (24.2g.) in dry ether (100 ml.). A crystal of iodine was added and the mixture gently warmed to initiate the reaction. On completion of the addition, boiling under reflux was continued for a further thirty minutes. Dry benzene (550 ml.) was added to dissolve the oil which separated and the cooled solution was poured onto crushed solid carbon dioxide (300g.). An excess of 2N sulphuric acid was added, the reaction mixture was cooled by the addition of crushed ice and stirred until two layers separated. The ether-benzene layer was extracted with aqueous sodium hydroxide. The alkaline extracts were combined and acidified, the crude 1-naphthoic acid (148g.) was washed, dried and crystallised from boiling toluene (700 ml.). Pure 1-naphthoic acid (122g., 71%) was obtained as a colourless crystalline solid of m.p. 161-162°.

5-Nitro-1-naphthoic Acid.

1-Naphthoic acid was nitrated in the main as described by Ekstrand (J. pr.Chem., 1888, [2], 38, 241). More precise conditions for the reaction were worked out.

Finely ground 1-naphthoic acid (90g.) was added gradually to concentrated nitric acid (d. 1.42, 600 ml.) at 80° with mechanical stirring. Heating was continued for a further half an hour after the addition was complete. The cooled solution was poured onto ice. A small quantity of 1-nitronaphthalene was removed by dissolving the product in sodium carbonate solution, filtering off the insoluble material, and precipitating the mixed 5- and 8-nitronaphthoic acids (105g.) with dilute hydrochloric acid. Two crystallisations from

1 litre and 500 ml. respectively of ethanol, gave pure 5-nitro-1-naphthoic acid (20g., 17.5%) as a light yellow crystalline solid m.p. 238-9°.

Ekstrand (loc. cit.) claimed that further amounts of 5-nitro-1-naphthoic acid could be obtained from the alcoholic mother liquors from the crystallisation. On esterification by passing dry hydrogen chloride through the boiling solution only ethyl 5-nitro-1-naphthoate is obtained. The 8-nitro isomer in unchanged and could be separated.. This procedure was followed, but some difficulty was experienced in attempting to hydrolyse the ester obtained. Decomposition occurred on boiling with alcoholic potassium hydroxide, while some ester remained unchanged on boiling with 70% w/w sulphuric acid.

5-Amino-1-naphthoic Acid.

(Ekstrand, loc. cit.)

An aqueous solution (1.2 l.) of hydrated ferrous sulphate (250g.) was added over a period of thirty minutes to a mechanically stirred solution of 5-nitro-1-naphthoic acid in aqueous ammonia (d. 0.880, 280 ml.). An initial red-brown precipitate was formed which later assumed a blue-black colour. The black precipitate was filtered off and the filtrate was evaporated under reduced pressure to a volume of 700 ml.. A brown crystalline solid (5g., m.p. 212-215°) separated and was filtered off and the filtrate evaporated under reduced pressure. The melting point indicated that this substance was 5-amino-1-naphthoic acid formed by dissociation of the ammonium salt. The filtrate was carefully acidified with dilute acetic acid to pH 7. After standing, the brown precipitate which formed (11.2g., m.p. 205-210°) was filtered off. The two crops of solid thus obtained (16.2g., 82%) were crystallised from ethanol (200 ml.). 5-Amino-1-naphthoic acid (11g., m.p. 214-215°, 58%) was obtained as a light brown crystalline solid. A second crop (3g.) was obtained by evaporation of the alcohol mother liquor. m.p. 210-212°.

Ekstrand (<u>loc. cit.</u>) gives m.p. 211-212°.

<u>5-Iodo-1-naphthoic Acid</u>

The acid was prepared by the method of Seer and Scholl, (<u>Annalen</u>, 1913, <u>398</u>, 82).

5-Amino-1-naphthoic acid (9g., 1mol.) was dissolved in 10% aqueous sodium hydroxide (35 ml.) and the solution was added to an aqueous solution of sodium nitrite (4g., 1.1mols.). The resultant solution was added dropwise with efficient stirring to 10% sulphuric acid (250 ml.) cooled to 0°. The turbid solution obtained was filtered into an aqueous solution (90 ml.) of potassium iodide (17g., 2.1 mols.) cooled in an ice bath. A little sodium metabisulphite was added to remove excess iodine, the crude 5-iodo-1-naphtheic acid (11g., m.p. 230-245°, 76%) was filtered off and recrystallised from glacial acetic acid (180 ml.) using a little charcoal. 5-Iodo-1-naphthoic acid (8.5g., m.p. 246-250°, 59%) was obtained as a red crystalline solid.

Seer and School (<u>loc. cit.</u>) give m.p. 253-254° after two recrystallisations.

<u>Methyl</u> 5-<u>iodo</u>-1-<u>naphthoate.</u>

5-Iodo-1-naphthoic acid (10g.) was dissolved in methyl alcohol (250 ml.) and dry hydrogen chloride was passed through the boiling solution for five hours. After pouring the reaction mixture into water and extracting with ether, the residue obtained was crystallised from methyl alcohol (50 ml.). Methyl 5-iodo-1-naphthoate (8.7g., m.p. 78-79° 83%) was obtained as a pink solid crystallising in plates.

Seer and Scholl (<u>loc. cit.</u>) give m.p. 81-82°.

1:1'-<u>Dinaphthyl</u>-5:5'-<u>dicarboxylic Acid.</u>

The acid was obtained by a modification of the method of Seer and Scholl (<u>loc. cit.</u>)

Copper bronze (5g.) was added gradually to methyl 5-iodo -1-naphthoate (5g.) contained in a hard glass tube immersed in a metal bath maintained at 250°. The reaction was carried out in an atmosphere of carbon dioxide. A rise in the initial internal temperature of 220° was observed on the addition of the copper. On completion of the addition, the reaction mixture was heated at 220° for a further fifteen minutes, allowed to cool to 120° and thoroughly extracted with o-dichlorobenzene. The solvent was distilled off and the residue was hydrolysed by boiling with 10% alcoholic potassium hydroxide (140 ml.) for three hours. The alcohol was distilled off, the residue extracted with water and insoluble material filtered off. The aqueous filtrate was boiled with charcoal, filtered and acidified with dilute hydrochloric acid, when the crude 1:1'-dinaphthyl-5:5'-dicarboxylic acid (2.1g., m.p. 344° with softening, 77%) was filtered off washed and dried. The crude acid was crystallised twice from ethanol (750 and 600 ml.), when the pure acid (1.35g., m.p. 358° (block), 50%) was obtained.

(Found: C, 75.2; H,4.0. Calc. for $C_{22}H_{14}O_4$: C, 77.2; H,4.1%)

Seer and Scholl isolated the pure dimethyl ester (75%) before obtaining the acid by hydrolysis: m.p. 359-360°.

Attempted First Order Asymmetric Transformation of 1:1'-Dinaphthyl-5:5'-dicarboxylic Acid with Brucine.

The acid was found to be sparingly soluble in chloroform. Preparation of a chloroform solution of the brucine salt was therefore carried out by dissolving anhydrous brucine (0.4607g., 2 mols.) in chloroform and shaking this solution with 1:1'-dinaphthyl-5:5'-dicarboxylic acid 0.2000g., 1 mol.) until all the solid had dissolved. The solution was made up to 20 ml. and examined polarimetrically at 20°.

Time after wetting (mins.)	$\alpha^{20^{\circ}}_{5461}$
4.75	- 2.34
7.8	- 2.34
60	- 2.34
24 hours	- 2.30

The mutarotation of 0.04° was inconclusive, and it was clearly impracticable to determine the rate of change of rotation at 20°.

Preparation of the Brucine Salt of (+)-1:1'-Dinaphthyl -5:5'-dicarboxylic Acid.

It was found impossible to crystallise the brucine salt (obtained by evaporating to dryness a chloroform solution of brucine (2 mols.) and acid (1 mol.)) from acetone, ethanol, methanol, benzene, ethyl acetate, *cyclo*hexane, *cyclo*hexanol, *cyclo*hexanone, chloroform, or tetrachlorethane. However, boiling 2-ethoxyethanol (ethyl cellosolve) dissolved the salt, and on addition of water to the boiling solution colourless prisms were deposited.

Hot water (80 ml.) was added to a solution of the acid (0.685g., 1 mol.) and anhydrous brucine (1.576g., 2 mols.) in boiling 2-ethoxyethanol (40 ml.). The hot solution was filtered and allowed to cool, when the brucine salt (1.29g., m.p. 245° (decomp.), *Crop. 1)* crystallised as colourless prisms.

The filtrate was evaporated under reduced pressure to 30 ml.. Water was added to the boiling solution, which was filtered and allowed to cool, when a further quantity of the salt (0.32g., m.p. 243° (decomp.), Crop 2.) was deposited.

A solution of the brucine salt (obtained as <u>Crop 1.</u>) in chloroform (20 ml.) was examined polarimetrically at 20°.

Time after wetting (mins.)	$\alpha^{20^\circ}_{5461}$
2.68	- 0.35
60.0	- 0.35
48 hours	- 0.38

(+)-1:1'-<u>Dinaphthyl-5:5'-dicarboxylic Acid From Crop 1.</u>

The salt obtained as the first crop was ground with ice-cold 2 <u>N</u> hydrochloric acid and then with water until the washings were free from mineral acid.

The (+)-acid obtained was dissolved in 0.1 <u>N</u> sodium hydroxide (20 ml.) and the solution was extracted with three portions of chloroform to remove traces of brucine. After a further extraction with ether the solution was made up to 25 ml. with 0.1 N sodium hydroxide and its rotation at 20° determined. $\alpha^{20^\circ}_{5461}$ + 0.51°.

The concentration of the solution (after the rate of racemisation had been determined) was found by precipitation of the acid from a known volume.

The caustic soda solution (12.4 ml.) gave 0.1027 g. of acid on precipitation with dilute hydrochloric acid. The concentration of the acid was therefore 0.8260 g./100 ml.. The acid was thus found to have $[\alpha]_{5461}^{20^\circ}$ $+27.2^\circ$ in 0.1 N sodium hydroxide solution.

After a preliminary experiment at 45° it was decided to determine the rate of racemisation of the (+)-acid at 60°.

Racemisation of (+)-1:1'-Dinaphthyl-5:5'-dicarboxylic Acid Obtained from Crop 1.

The 0.1 N sodium hydroxide solution prepared to determine the specific rotation of the acid was employed.

The solution was placed in a conical flask provided with a ground glass stopper. The flask was immersed in a water bath maintained at 60 ± 2°. After an accurately measured interval of time, the container was removed from the water bath and the racemisation rapidly stopped by immersion in a freezing mixture. The temperature of the solution was then allowed to rise to 20° and the rotation of the solution determined. The solution was then replaced in the water-bath and the procedure repeated.

In this way, an average value for k was found to be 0.024 mins.$^{-1}$, whence the half life is 29 mins. (Table 7.)

Table 7.

Racemisation of (+)-1:1'-Dinaphthyl-5:5'-dicarboxylic Acid from Crop 1 in 0.1N Sodium Hydroxide at 60°.

Time (min.)	α_{5461}^{20}	$\log_{10}(\alpha_t - \alpha_\infty)$	k min.$^{-1}$
0	+ 0.45	$\bar{1}.6532$	-
15	+ 0.31	$\bar{1}.4914$	0.025
30	+ 0.22	$\bar{1}.3424$	0.024
45	+ 0.155	$\bar{1}.1903$	0.024
60	+ 0.11	$\bar{1}.0414$	0.0235
75	+ 0.07	$\bar{2}.8451$	0.025
90	+ 0.03	$\bar{2}.4771$	-
∞	0.00	-	-

Table 8.

Racemisation of (+)-1:1'-Dinaphthyl-5:5'-dicarboxylic Acid in 0.1N Sodium Hydroxide at 60°.

Time (min.)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k min.$^{-1}$
0	+ 0.36	$\bar{1}$.5563	-
15	+ 0.27	$\bar{1}$.4314	0.020
30	+ 0.195	$\bar{1}$.2900	0.0205
45	+ 0.145	$\bar{1}$.1614	0.020
60	+ 0.11	$\bar{1}$.0414	0.020
75	+ 0.08	$\bar{2}$.9031	0.020
90	+0.05	$\bar{2}$.6990	0.022
∞	0.00	-	-

(+)-1:1'-Dinaphthyl-5:5'-dicarboxylic Acid from Crop 2.

The brucine salt (crop 2) was ground with dilute hydrochloric acid. The (+)-acid was filtered off and washed with water. The solid was dissolved in 0.1 N sodium hydroxide solution, the solution extracted with chloroform and ether and then made up to 25 ml.. The solution was found to have an initial rotation $\alpha^{20}_{5461} = +0.36^{\circ}$. Its concentration was determined by precipitation as in the first experiment.

The caustic soda solution (20.0. ml.) gave 0.0642 g. of the acid on precipitation with dilute hydrochloric acid. The concentration of the acid was therefore 0.3210 g./ 100 ml. and thus $[\alpha]^{20}_{5461} = +56.1^{\circ}$.

The rate of racemisation of the acid in 0.1 N sodium hydroxide solution at 60° was determined, using the same technique as described for the acid from crop 1. An average value $k = 0.020$ mins.$^{-1}$ was obtained (Table 8). Whence the half life is 34 mins..

Attempted Second Order Asymmetric Transformation of the Brucine Salt of 1:1'-Dinaphthyl-5:5'-dicarboxylic Acid.

At 80° the active acid is relatively unstable and it seemed possible therefore that a second order asymmetric transformation might occur if crystallisation could be induced at 80° by gradual addition of hot water to a hot solution of the (±)-acid and brucine in 2-ethoxyethanol.

The acid (0.2000 g., 1 mol.) and anhydrous brucine

(0.4606 g., 2 mols.) were dissolved in 2-ethoxyethanol at 80°. The solution was maintained at this temperature and water at 80° was added in successive 2 ml. portions at ten minute intervals. The solution was mechanically stirred throughout. After 8 ml. of water had been added, crystallisation slowly commenced and a further 4 ml. of water was introduced. The solution was stirred at 80° for an hour, when the solid (crop 1) was filtered off while the solution was still hot, washed and dried. The salt was dissolved in chloroform and its specific rotation determined. The chloroform was evaporated off (at 20°) and the residue decomposed by grinding with cold formic acid and pouring the suspension into dilute hydrochloric acid and ice. The (+)-acid was filtered off, washed, dried and dissolved in 0.1 N sodium hydroxide solution. The specific rotation of the solution was determined (the concentration was obtained by precipitation) and the rate of racemisation of the acid investigated at 60°, (Table 9, fig., 4) using the same method as in the previous experiments.

The ethyl cellosolve-water filtrate from the first crystallisation was heated to 80° and an attempt was made to induce crystallisation by the addition of water as in the first experiment. No crystals were obtained after a total of 34 ml. of hot water were added, and the solution was allowed to cool. The second crop of brucine salt which was deposited was filtered off. The specific rotation of the salt in chloroform was determined, and the specific rotation and rate of racemisation of the active acid in 0.1 N sodium hydroxide solution was obtained (Table 9, fig. 4).

Results.

The total weight of solid (acid + brucine) taken 0.6606 g.

First Crop.

(i) Brucine Salt.

Wt. 0.3010 g. (45.5% Total Solid)

$[\alpha]^{20}_{5461}$ -16.3° in chloroform

(ii) Active Acid.

Wt. 0.0880 g. $[\alpha]^{20^{\circ}}_{5461}$ $+56.6^{\circ}$

$k = 0.019$ mins.$^{-1}$ in 0.1 N sodium hydroxide at 60°.

Second Crop.

(iii) Brucine Salt.

Wt. 0.2210 g. (33.4% Total Solid, but 61.6% of solid remaining in solution.)

$[\alpha]^{20}_{5461}$ -23.1° in chloroform

(iv) Active Acid

Wt. 0.0660 g. $[\alpha]^{20}_{5461}$ $+45.3^{\circ}$

$k = 0.020$ mins. in 0.1 N sodium hydroxide at 60°.

The average value of k obtained from all the racemisations carried out with the active acid is 0.02 mins.$^{-1}$, whence the half life is ca. 33 minutes.

RACEMISATION OF THE [illegible]-ACID

IN 0.1N SODIUM HYDROXIDE AT 60°.

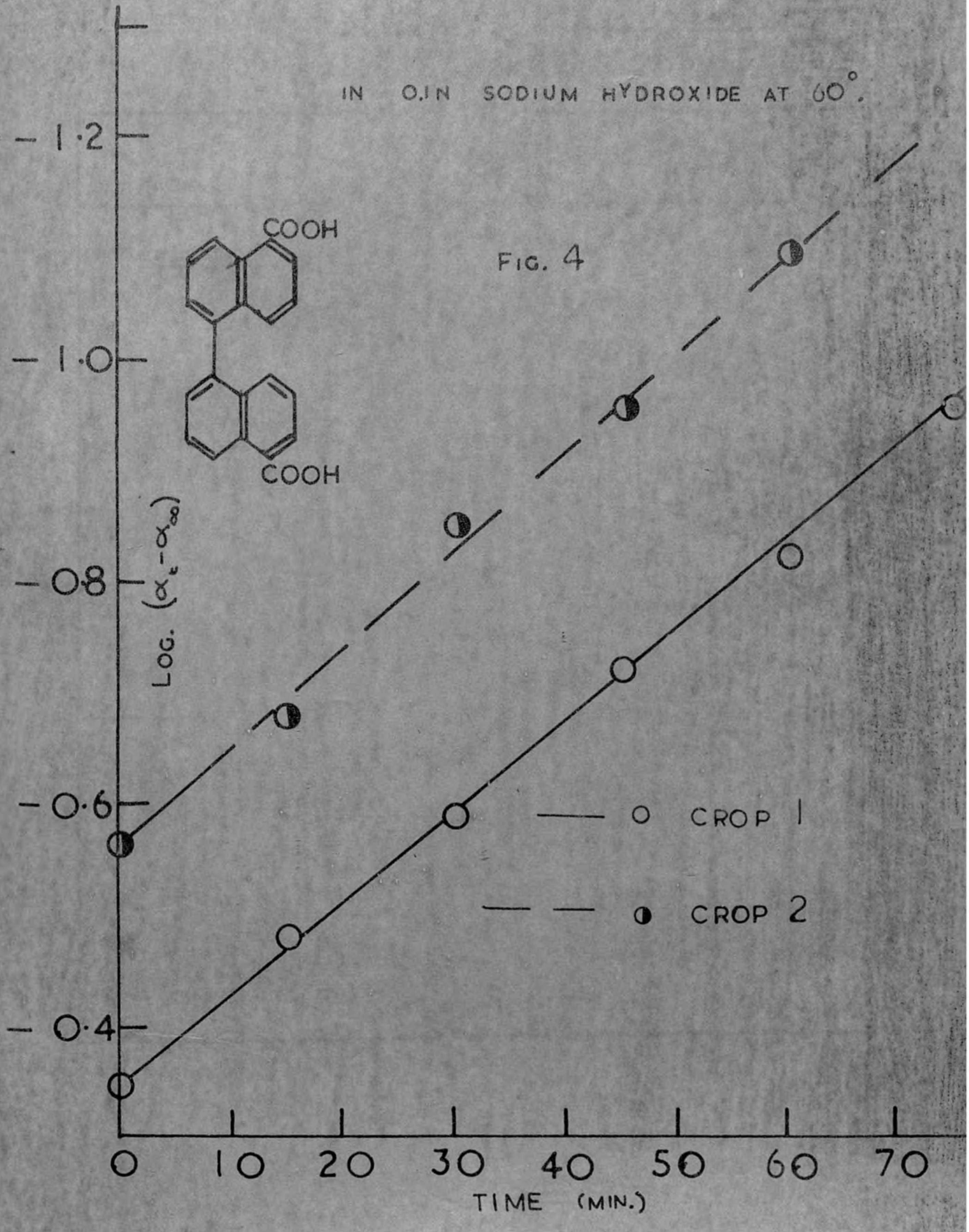


FIG. 4

Table 9.

Racemisation of (+) 1:1'-Dinaphthyl -5:5'-dicarboxylic acid in 0.1 N Sodium Hydroxide Solution at 60°

Time (mins.)	$\alpha^{20^\circ}_{5461}$	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins.^{-1}
(+) acid from crop 1.			
0	+0.45	$\bar{1}.6532$	-
15	+0.33	$\bar{1}.5185$	0.021
30	+0.26	$\bar{1}.4150$	0.018
45	+0.19	$\bar{1}.2788$	0.019
60	+0.15	$\bar{1}.1761$	0.018
75	+0.11	$\bar{1}.0414$	0.019
90	+0.09	$\bar{2}.9542$	0.016
∞	+0.00	-	-
(+) acid from crop 2.			
0	+0.27	$\bar{1}.4314$	-
15	+0.21	$\bar{1}.3222$	0.017
30	+0.14	$\bar{1}.1461$	0.022
45	+0.11	$\bar{1}.0414$	0.020
60	+0.08	$\bar{2}.9031$	0.020
∞	+0.00	-	-

Preparation of 1-Phenylnaphthalene-2':8-dicarboxylic Acid.

8-Bromo-1-naphthoic Acid.

Rule, Pursell and Brown, *J.*, 1934, 168.

Naphthalene-1:8-dicarboxylic acid (48 g., 1 mol.) was dissolved in an aqueous solution (1.2 l.) of sodium hydroxide (31 g.). The solution was filtered through glass wool and boiled under reflux. After fifteen minutes, a solution of mercuric oxide (55 g., 1.1 mols.) in glacial acetic acid (40 ml.) and water (150 ml.) was added to the boiling solution, when a light brown solid separated. On acidification with acetic acid a white suspension was obtained, and was boiled under refux continuously for eighty hours. After this time a sample taken was completely soluble in sodium hydroxide solution, and no mercury was deposited on a clean copper wire immersed in the solution. These tests indicated that the reaction was complete. The hydroxy-mercuric compound was filtered off, washed with water, alcohol and ether. The dry solid was suspended in glacial acetic acid (300 ml.) and water (50 ml.) and cooled in an ice bath. A solution of bromine (34g., 1 mol.) in 50% aqueous sodium bromide (150 ml.) was slowly added with stirring over a period of an hour and a half, keeping the temperature between 0-5° throughout. At this stage the mixture became thick and difficult to stir. The reaction mixture was allowed to warm up to room temperature and then heated to 90°. The hot solution was poured into boiling water (3 l.), boiled for a short time, filtered, allowed to cool and the solid which was deposited (50 g., m.p. 159° with softening.) was filtered off. The crude acid was recrystallised from benzene (250 ml.) and pure 8-bromo-1-naphthoic acid (39.6 g., 71% m.p. 173°) was obtained in plates.

Rule (loc. cit.) give m.p. 176-179° with softening at 170°.

Methyl 8-bromo-1-naphthoate.

8-Bromo-1-naphthoic acid (39.6 g., 1 mol.) was dissolved in benzene (300 ml.) and the solution boiled under reflux. Thionyl chloride (22 g., 1.2 mols.) was slowly added to the boiling solution and the reaction mixture boiled under reflux for three and a half hours. Methyl alcohol (100 ml.) (dried over anhydrous sodium sulphate) was cautiously added to the solution which was then boiled for a further thirty minutes. The benzene solution was washed twice with water, then twice with 10% aqueous sodium carbonate solution and finally again with water. The benzene was evaporated off and the oily residue was dissolved in boiling light petroleum (b.p. 80-100°). The solution was filtered from a small amount of oily insoluble residue and on evaporation of some of the solvent, methyl 8-bromo-1-naphthoate was obtained (38 g., 90% Theory) as a cream coloured solid, m.p. 35-37°.

Rule and Barnett, (J., 1932, 175) give m.p. 33°.

Methyl 1-phenylnaphthalene-2':8-dicarboxylate.

Rule, Pursell and Barnett, J.,1935, 571.

Copper bronze (27 g., 4 atoms) was added gradually to a stirred mixture of methyl 8-bromo-1-naphthoate (29.5 g., 1 mol.) and methyl o-iodobenzoate (45 g., 1.5 mols.) contained in a hard glass tube immersed in a metal bath kept at 215°. The temperature of the reaction mexture did not rise above 225° throughout the addition. After the addition of the copper was complete, the temperature was maintained at 220° for a further two hours. The mixture was allowed to cool and then thoroughly extracted with acetone. The extracts were combined and the solvent removed, when a syrupy liquid was obtained. Ether (25 ml.) was added to the residue which solidified almost immediately. The mixture was allowed to stand, the solid filtered off and washed with a further amount of ether (30 ml.). The solid was dissolved in boiling light petroleum (b.p. 100-120°), the solution left for two hours, when the clear supernatant liquid was decanted off. The solid remaining was recrystallised from a further amount of light petroleum (165 ml.), and methyl 1-phenylnaphthalene-2':8-dicarboxylate (16 g., 45%) was obtained, m.p. 132-136°.

Rule, Pursell and Barnett, loc. cit. obtained the methyl ester with m.p. 132-133°.

1-Phenylnaphthalene-2':8-dicarboxylic Acid.

(Rule, Pursell and Barnett, loc. cit.)

The dimethyl ester (10 g.) was boiled under reflux with 30% alcoholic potassium hydroxide (100 ml.) for sixteen hours. The alcohol was evaporated off and the solid remaining extracted with water. 1-Phenylnaphthalene-2':8-dicarboxylic acid was precipitated from the filtered solution with dilute hydrochloric acid and recrystallised twice from ethanol. The pure acid (5.5 g., 60%) was obtained as a colourless solid, m.p. 230-233°.

(Found: C, 73.9; H,4.0. Calc. for $C_{18}H_{12}O_4$: C, 74.0; H,4.1%)

Rule et. al. (loc. cit.) give m.p. 231-232°.

First Order Asymmetric Transformation of 1-Phenylnaphthalene-2':8-dicarboxylic Acid.

(i) Acid (1 mol.) with Brucine (2 mols.)

A solution of the acid (0.1000 g., 1 mol.) and anhydrous brucine (0.2695 g., 2 mols.) was prepared in chloroform (20 ml.). In order to facilitate solution, ethanol (0.5 ml.) was added. The solution was examined polarimetrically at 20° and showed a mutarotation from $[\alpha]^{20}_{5461}$ -57.2° to $[\alpha]^{20}_{5461}$ -37.9 (Table 10).

Table 10.

First Order Asymmetric Transformation of (±) 1-Phenylnaphthalene 2':8-dicarboxylic acid (1 mol.) with Brucine (2 mols.).

in Chloroform at 20°.

Time (hours)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins.^{-1}
0	-2.13	$\bar{1}.8195$	-
0.5	-2.05	$\bar{1}.7634$	0.0043
1.13	-1.96	$\bar{1}.6902$	0.0044
1.5	-1.89	$\bar{1}.6232$	0.0050
2.0	-1.84	$\bar{1}.5682$	0.0048
2.5	-1.785	$\bar{1}.4983$	0.0049
4.0	-1.675	$\bar{1}.3118$	0.0050
4.5	-1.635	$\bar{1}.2175$	0.0051
5.0	-1.61	$\bar{1}.1461$	0.0052
6.0	-1.58	$\bar{1}.0414$	0.0050
∞	-1.47	-	-

Table 11.

First Order Asymmetric Transformation of (±) 1-Phenylnaphthalene 2':8-dicarboxylic acid (1 mol.) with Brucine (2 mols.). in Chloroform at 20°.

Time (hours)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins.^{-1}
0	-2.01	$\bar{1}.7853$	-
0.5	-1.94	$\bar{1}.7324$	0.0041
1.0	-1.85	$\bar{1}.6532$	0.0051
1.5	-1.79	$\bar{1}.5911$	0.0050
2.5	-1.68	$\bar{1}.4472$	0.0052
3.5	-1.62	$\bar{1}.3424$	0.0049
4.5	-1.55	$\bar{1}.1761$	0.0041
5.5	-1.505	$\bar{1}.0212$	0.0053
6.75	-1.47	$\bar{2}.8451$	0.0053
∞	-1.40	-	-

A duplicate experiment was carried out (Table 11,) and two values for k were obtained, (i) 0.0049 (ii) 0.0049 mins.$^{-1}$, whence the half life is 140 minutes.

(ii) Acid (1 mol.) with Brucine (1 mol.)

A solution of the acid (0.1000 g., 1 mol.) and anhydrous brucine (0.1347 g., 1 mol.) was prepared in chloroform (20 ml.). Ethanol (0.5 ml.) was added to facilitate solution. The solution was examined polarimetrically at 20°, and showed a mutarotation from $[\alpha]^{20}_{5461}$ -16.3° to $[\alpha]^{20}_{5461}$ $+13.0^\circ$ (Table 12,). A duplicate experiment was carried out (Table 13,) and the values for k were obtained, (i) 0.0012 (ii) 0.0013 mins.$^{-1}$, thus the half life is 550 minutes.

Preliminary Second Order Asymmetric Transformations of 1-Phenylnaphthalene-2':8-dicarboxylic Acid with Brucine.

(i) From Benzene.

The acid (0.3000g., 1 mol.) and anhydrous brucine (0.8085 g., 2 mols.) were dissolved in boiling benzene (10 ml.). A colourless solid (0.541 g.) crystallised in needles, m.p. 205°. A solution of the salt in chloroform was examined polarimetrically at 20°. The rotation was found to change from $[\alpha]^{20}_{5461}$ $+41^\circ$ to $[\alpha]^{20}_{5461}$ $+12^\circ$.

Table 12.

First Order Asymmetric Transformation of 1-Phenylnaphthalene 2':8-dicarboxylic acid (1 mol.) with Brucine (1 mol.) in Chloroform at 20°

Time (hours)	α_{5461}^{20}	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins^{-1}
0	-0.285	$\bar{1}.8663$	-
0.5	-0.26	$\bar{1}.8513$	0.00115
1.0	-0.23	$\bar{1}.8325$	0.0013
2.0	-0.185	$\bar{1}.8028$	0.0012
3.0	-0.145	$\bar{1}.7818$	0.0011
4.0	-0.105	$\bar{1}.7443$	0.0012
5.0	-0.06	$\bar{1}.7076$	0.0012
6.0	-0.025	$\bar{1}.6767$	0.0012
7.0.	-0.02	$\bar{1}.6335$	0.0013
8.0	+ 0.06	$\bar{1}.5911$	0.0013
9.0	+ 0.095	$\bar{1}.5502$	0.0013
10.0	+ 0.12	$\bar{1}.5185$	0.0013
11.0	+ 0.14	$\bar{1}.4914$	0.0013
12.0	+ 0.16	$\bar{1}.4624$	0.0013
∞	+ 0.45	-	-

Table 13.

First Order Asymmetric Transformation of 1-Phenylnaphthalene 2':8-dicarboxylic acid (1 mol.) with Brucine (1 mol.). in Chloroform at 20°.

Time (hours)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins^{-1}
0	-0.29	$\bar{1}.8692$	
0.5	-0.26	$\bar{1}.8513$	0.0014
1.5	-0.21	$\bar{1}.8195$	0.0013
2.5	-0.16	$\bar{1}.7853$	0.0013
3.5	-0.12	$\bar{1}.7559$	0.0012
4.5	-0.085	$\bar{1}.7284$	0.0012
5.5	-0.04	$\bar{1}.6902$	0.00125
6.5	-0.02	$\bar{1}.6721$	0.0012
7.5	+0.045	$\bar{1}.6075$	0.0013
8.5	+0.08	$\bar{1}.5682$	0.00135
9.5	+0.10	$\bar{1}.5441$	0.0013
10.5	+0.125	$\bar{1}.5119$	0.0013
11.5	+0.15	$\bar{1}.4771$	0.0013
∞	+0.45	-	-

(ii) From Acetone.

The acid (0.3000g., 1 mol.) and anhydrous brucine (0.8085g., 2 mols.) were dissolved in boiling acetone (150 ml.) and the solution evaporated to 50 ml. A colourless solid crystallised in needles. A solution of this solid in chloroform at 20° was found to mutarotate from $[\alpha]^{20}_{5461}$ $+34^{\circ}$ to $[\alpha]^{20}_{5461}$ $+14^{\circ}$.

The equilibrium values for the specific rotation of the chloroform solutions in both the above cases were unexpected as the first order asymmetric transformation shewed that for the system; acid (1 mol.) : brucine (2 mols.) the equilibrium value is $[\alpha]^{20}_{5461}$ -37.9°. However for the system: acid (1 mol.) : brucine (1 mol.) the equilibrium value was shewn to be $[\alpha]^{20}_{5461}$ $+13.0^{\circ}$

These results suggest that the salt crystallising from both benzene and acetone solutions of 1-Phenylnaphthalene-2':8-dicarboxylic acid (1 mol.) and brucine (2 mols.) is the mono brucine-acid salt. Analysis results for both the salts obtained were inconclusive. However when 0.1000g. of the salt obtained from acetone solution was dissolved in chloroform (20ml.) with ethanol (0.5ml.) and anhydrous brucine (0.0573g. 1 mol.) added, an equilibrium value of $[\alpha]^{20}_{5461}$ -38.5° was obtained. This approximated to the value of $[\alpha]^{20}_{5461}$ -37.9° obtained for the system; acid (1 mol.) : brucine (2 mol.) in chloroform, indicating that the solid obtained from acetone was in fact the mono brucine-acid salt.

Monobrucine Salt of (+)-1-Phenylnaphthalene-2':8-dicarboxylic Acid.

The acid (0.5000g., 1 mol.) and anhydrous brucine (0.6735g. 1 mol.) were dissolved in boiling benzene (150 ml.). The solution was filtered and evaporated to 30 ml. On slight cooling a colourless crystalline solid (0.9520g., m.p.205°, 75% of the total solid present) was obtained.

(Found: C,72.4;H,5.8; N4.0; calc. for $C_{41}H_{38}O_8N_2$: C,71.7;H,5.6; N,4.1%)

The salt (0.1000g.) was dissolved in chloroform, ethanol (0.5 ml.) was added and the solution made up to 20 ml. The solution was examined polarimetrically at 20°. The values obtained for the rates of equilibration in this and a duplicate experiment (Tables 14 and 15) were,

(1) 0.0015 and (2) 0.0015 $mins^{-1}$. Thus a value for the half-life of 460 mins. was obtained.

Attempted Isolation of (+)-1-Phenylnaphthalene-2':8-dicarboxylic Acid.

A variety of preliminary attempts were made to isolate the active acid from the monobrucine salt.

(i) The salt (0.3000g.) was dissolved in anhydrous formic acid (3 ml.) The solution was poured into dilute hydrochloric acid. No precipitate was formed.

(ii) A solution of the salt in pyridine was poured into dilute hydrochloric acid. No precipitate was formed.

Table 14.

Mutarotation of the Monobrucine Salt of (+) -1-Phenylnaphthalene -2':8-dicarboxylic Acid in Chloroform at 20°.

Time (hours)	$\alpha^{20^\circ}_{5461}$	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins^{-1}
0	+0.65	$\bar{1}.6702$	-
1	+0.61	$\bar{1}.6532$	0.0014
2	+0.57	$\bar{1}.6128$	0.0015
3	+0.53	$\bar{1}.5682$	0.0016
4	+0.505	$\bar{1}.5378$	0.0015
5	+0.48	$\bar{1}.5051$	0.0014
6	+0.44	$\bar{1}.4472$	0.00155
7	+0.415	$\bar{1}.4065$	0.0016
8	+0.395	$\bar{1}.3711$	0.0015
10	+0.345	$\bar{1}.2672$	0.0016
12	+0.31	$\bar{1}.1761$	0.0016
14	+0.28	$\bar{1}.0792$	0.0016
∞	+0.16	-	-

Table 15.

Mutarotation of the Monobrucine Salt of (+) -1-Phenylnaphthalene-2':8-dicarboxylic Acid in Chloroform at 20°.

Time (hours)	α^{20}_{5461}	log.$_{10}(\alpha_t - \alpha_\infty)$	k mins^{-1}
0	+0.66	$\bar{1}.6902$	-
0.5	+0.64	$\bar{1}.6721$	0.0014
1.5	+0.60(5)	$\bar{1}.6385$	0.0013
2.5	+0.57(5)	$\bar{1}.6075$	0.0013
3.5	+0.53(25)	$\bar{1}.5593$	0.0014
4.5	+0.50(5)	$\bar{1}.5250$	0.0014
5.5	+0.47	$\bar{1}.4771$	0.0015
6.5	+0.43(5)	$\bar{1}.4232$	0.0016
7.5	+0.41	$\bar{1}.3802$	0.0016
9.0	+0.39	$\bar{1}.3424$	0.0015
11	+0.34	$\bar{1}.2304$	0.0016
13	+0.30(5)	$\bar{1}.1303$	0.00165
15	+0.27(5)	$\bar{1}.0212$	0.0017
∞	+0.17	-	-

(iii) A chloroform solution of the brucine salt was extracted with two portions of 10% hydrochloric acid, washed with water and examined polarimetrically at 20°. The observed angle changed from $\alpha^{20}_{5461} + 0.66^\circ$ to $\alpha^{20}_{5461} + 0.15^\circ$.

(iv) A formic acid solution of the brucine salt was poured into dilute hydrochloric acid. The resulting aqueous solution was extracted with chloroform and the change of rotation of the chloroform solution followed with time. A mutarotation occurred from $\alpha^{20}_{5461} + 0.30^\circ$ to an equilibrium value of $\alpha^{20}_{5461} + 0.09^\circ$.

(v) A chloroform solution of the brucine salt was extracted twice with dilute hydrochloric acid, washed with water and extracted twice with 10% sodium hydroxide solution. The alkaline extract was neutralised with dilute hydrochloric acid and the solution extracted three times with chloroform (total volume 28 ml.). The solution was examined polarimetrically. The observed angle 30 mins. after dissolving the salt was found to be zero.

(vi) The brucine salt was dissolved in chloroform, extracted twice with 10% hydrochloric acid and washed with water. The chloroform solution was extracted twice with 0.1<u>N</u> aqueous sodium hydroxide solution. The alkaline solution was examined polarimetrically, and the observed angle 22 mins. after dissolution was found to be zero.

(+)-1-Phenylnaphthalene-2':8-dicarboxylic Acid.

The monobrucine (+)-acid salt was ground with dilute hydrochloric acid. The suspension was filtered off and washed with dilute hydrochloric acid and then with water and dried in a vacuum. Wt. 0.2370g.

Rates of Racemisation of (+)-Acid.

(i) A chloroform solution (20 ml.) of the (+)-acid (0.050g.) was extracted with three 25 ml. portions of dilute hydrochloric acid, washed with water, and examined polarimetrically at 20° in a 1 dcm. polarimeter tube. A duplicate experiment was carried out and from the results (Table 16, fig. 5) an average value of the rate of racemisation was obtained.

(The "B.P." chloroform contains less than the normal amount of alcohol owing to the washing with acid and water.)

k 0.0030 mins^{-1}. whence the half-life is 230 mins. ± 40 mins.

The low observed angles rendered the value for **k** subject to a considerable experimental error.

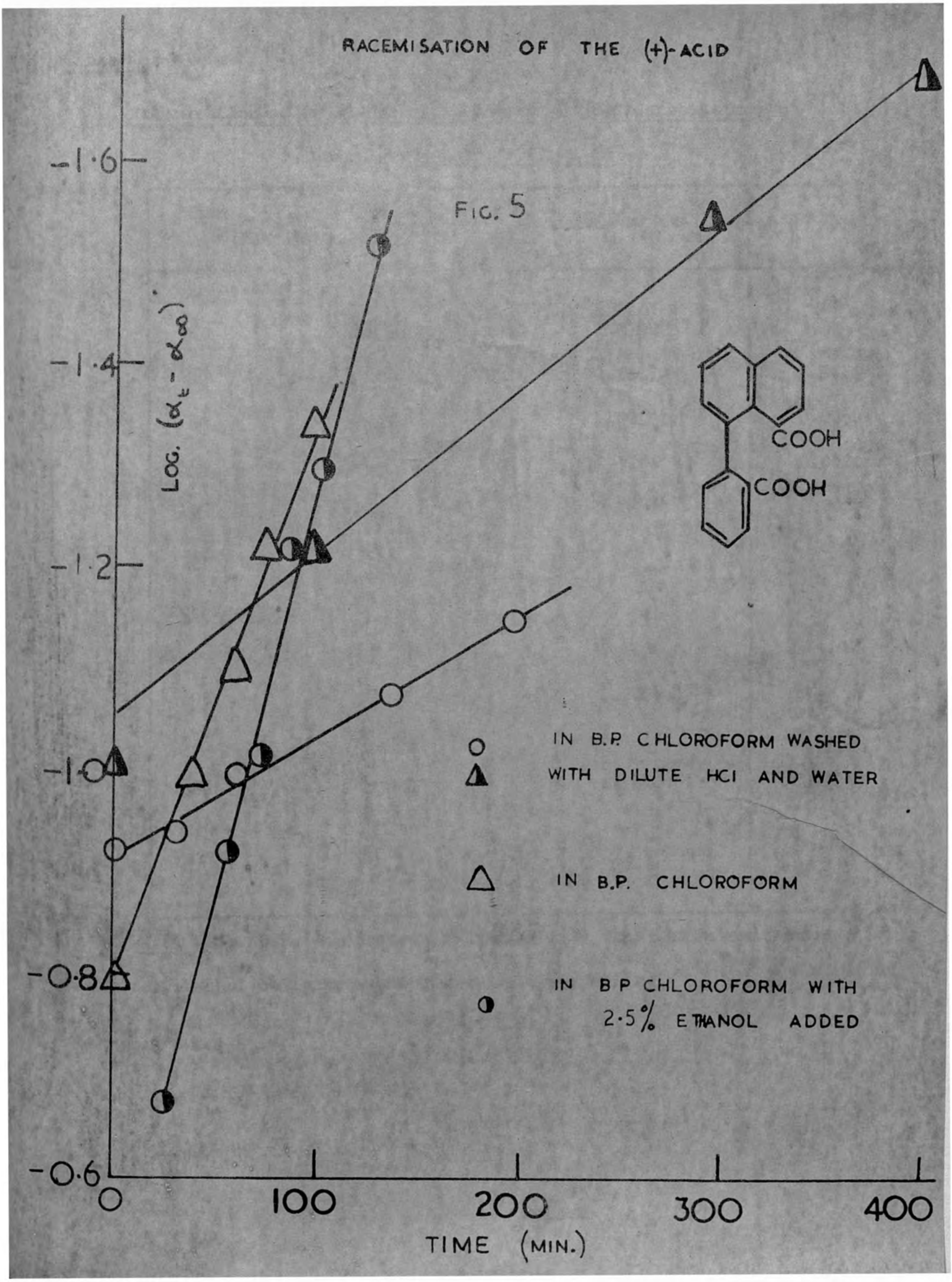
(ii) A similar racemisation experiment was carried out. The (+)-acid (0.050g.) was dissolved in chloroform (10.0ml.) The solution was examined polarimetrically at 20° in a 1 dcm. tube without washing with dilute hydrochloric acid. (i.e. the "B.P." chloroform contained the normal amount of alcohol)

A log plot was made from the results (see Table 17, fig.5) and a straight line graph was obtained.

k 0.0115 $mins^{-1}$, half-life 58±8 mins.

(iii) The (+)-acid (0.1000g.) and 0.5 ml. of ethyl alcohol were dissolved in chloroform and the volume made up to 20 ml. The solution was examined polarimetrically at 20° and from the results (see Table 18 fig. 5) a value of k 0.020 $mins^{-1}$ was obtained. Whence the half-life is 35±2 mins.

(iv) A solution (20 ml.) of the (+)-acid (0.1000g.) in 0.1 N potassium hydroxide was examined polarimetrically at 20°. No reading was possible until 15 mins. from the time of dissolution owing to the initial haziness of the solution, when the observed angle was found to be zero.



RACEMISATION OF THE (+)-ACID

FIG. 5

Table 16.

Racemisation of (+)-1-Phenylnaphthalene-2':8-dicarboxylic acid in Chloroform Solution at 20°

Time (mins.)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins.$^{-1}$
Experiment 1.			
0	+ 0.12	$\bar{1}.0792$	-
30	+ 0.11	$\bar{1}.0607$	0.0029
60	+ 0.10	$\bar{1}.0000$	0.0030
135	+ 0.085	$\bar{2}.9294$	0.0026
195	+ 0.07	$\bar{2}.8451$	0.0035
∞	0.00	-	-
Experiment 2.			
0	+ 0.085	$\bar{2}.9294$	-
95	+ 0.06	$\bar{2}.7782$	0.0037
315	+ 0.03	$\bar{2}.4771$	0.0033
390	+ 0.02	$\bar{2}.3010$	0.0037
∞	0.00	-	-

N.B. The "B.P." chloroform contained less than the normal amount of alcohol owing to washing with acid and water.

Table 17.

Racemisation of (+)-1-Phenylnaphthalene-2':8-dicarboxylic Acid in "B.P." Chloroform.

Time (mins.) after 2.5 mins.	α^{20}_{5461}	log$_{10}$ ($\alpha_t - \alpha_\infty$)	k mins.$^{-1}$
0	+ 0.16	$\bar{1}$.2040	-
37.5	+ 0.105	$\bar{1}$.0212	0.010
57.5	+ 0.08	$\bar{2}$.9031	0.012
72.5	+ 0.06	$\bar{2}$.7782	0.013
92.5	+ 0.045	$\bar{2}$.6532	0.014
∞	0.0	-	-

Table 18.

Racemisation of (+)-1-Phenylnaphthalene-2':8-dicarboxylic Acid in "B.P." Chloroform plus 2.5% Ethanol.

Time (mins.) after 4.5 mins.	α^{20}_{5461}	log$_{10}$ ($\alpha_t - \alpha_\infty$)	k mins^{-1}.
0	+ 0.35	$\bar{1}$.5441	-
11.5	+ 0.28	$\bar{1}$.4472	0.021
25.5	+ 0.21	$\bar{1}$.3222	0.020
55.5	+ 0.12	$\bar{1}$.0792	0.019
70.5	+ 0.09	$\bar{2}$.9542	0.019
85.5	+ 0.06	$\bar{2}$.7782	0.021
100.5	+ 0.05	$\bar{2}$.6990	0.019
130.5	+ 0.03	$\bar{2}$.4771	0.019
∞	+ 0.00	-	-

Preparation of 1-Phenylnaphthalene-3'-carboxylic Acid.

Methyl m-iodobenzoate.

m-Iodobenzoic acid was prepared by a method identical with that for o-iodobenzoic acid. m-Aminobenzoic acid (27.4 g.) gave crude m-iodobenzoic acid (20.2 g., m.p. 184°, 41%). The crude acid was esterified without purification by passing dry hydrogen chloride through a solution of the acid in boiling methyl alcohol for six hours. The ester (20 g.) obtained had b.p. 126°/7 mm. (94%).

1-Phenylnaphthalene-3'-carboxylic Acid.

Copper bronze (27 g., 6 atoms.) was gradually added to a stirred mixture of 1-iodonaphthalene (18.2 g., 1 mol.) and methyl m-iodobenzoate (18.8 g., 1 mol.) contained in a hard glass tube immersed in a metal-bath maintained at 270°. On addition of the copper bronze the temperature rose to 300°. When the addition was complete, the temperature was maintained at 270° for thirty minutes. The reaction mixture was allowed to cool to 150° and extracted several times with hot o-dichlorobenzene. The extracts were combined, the solvent was distilled off and the oily residue was hydrolysed by boiling with 10% potassium hydroxide solution (200 ml.) for six hours. A residue was obtained after removal of the alcohol and was extracted with water. The insoluble material was filtered off, the aqueous solution extracted once with benzene to remove hydrocarbons and then acidified with dilute hydrochloric acid. The precipitated acids (11.5 g.) were extracted with cold benzene and the benzene solution was evaporated to dryness, when the residue was recrystallised four times from methyl alcohol. 1-Phenylnaphthalene-3'-carboxylic acid (3.2 g., 17%) was obtained as colourless prisms m.p. 185.5 - 188°.

(Found: C, 82.2; H,5.2. $C_{17}H_{12}O_2$ requires C,82.2; H,4.9%)

Attempted First Order Asymmetric Transformation of 1-Phenylnaphthalene-3'-carboxylic Acid with Brucine.

A chloroform solution (20 ml.) of the acid (0.1000 g., 1 mol.) and anhydrous brucine (0.1580 g., 1 equiv.) was examined polarimetrically at 5±1°.

Time (mins.) after wetting.	α^{5}_{5461}
2.2	-0.55
13.1	-0.56
∞	-0.55

Thus no change in the initial observed angle $[\alpha]^{5}_{5461}$ -21.3° was observed.

Attempted Optical Activation of 1-Phenylnaphthalene-3'-carboxylic Acid by Brucine.

(i) Acid (2 equivs.) : Brucine (1 equiv.)

A chloroform solution (20 ml.) of the acid (0.2000 g., 2 equivs.)

and anhydrous brucine 0.1580 g., 1 equiv.) was examined polarimetrically at 5±1°.

Time (mins.) after wetting.	α^{5}_{5461}
4.2	- 0.27
30.4	- 0.27
∞	- 0.27

(ii) Acid (3 equivs.) : Brucine (1 equiv.)

A chloroform solution (20 ml.) of the acid (0.3000 g., 3 equivs.) and anhydrous brucine (0.1580 g., 1 equiv.) was examined polarimetrically at 5°.

Time (mins.) after wetting.	α^{5}_{5461}
2.3	- 0.18
10.1	- 0.17
∞	- 0.18

Rotation of Brucine in Chloroform at 5°.

A solution of anhydrous brucine (0.1580 g.) in chloroform (20 ml.) at 5° was found to have a rotation α^{5}_{5461} - 2.28°.

From the results of these experiments an addition curve was constructed (fig. 6).

Brucine Salt of 1-Phenylnaphthalene-3'-carboxylic Acid.

The acid (0.1000 g., 1 mol.) and anhydrous brucine (0.1580g. 1 mol.) were dissolved in boiling *cyclo*hexanone (80 ml.).

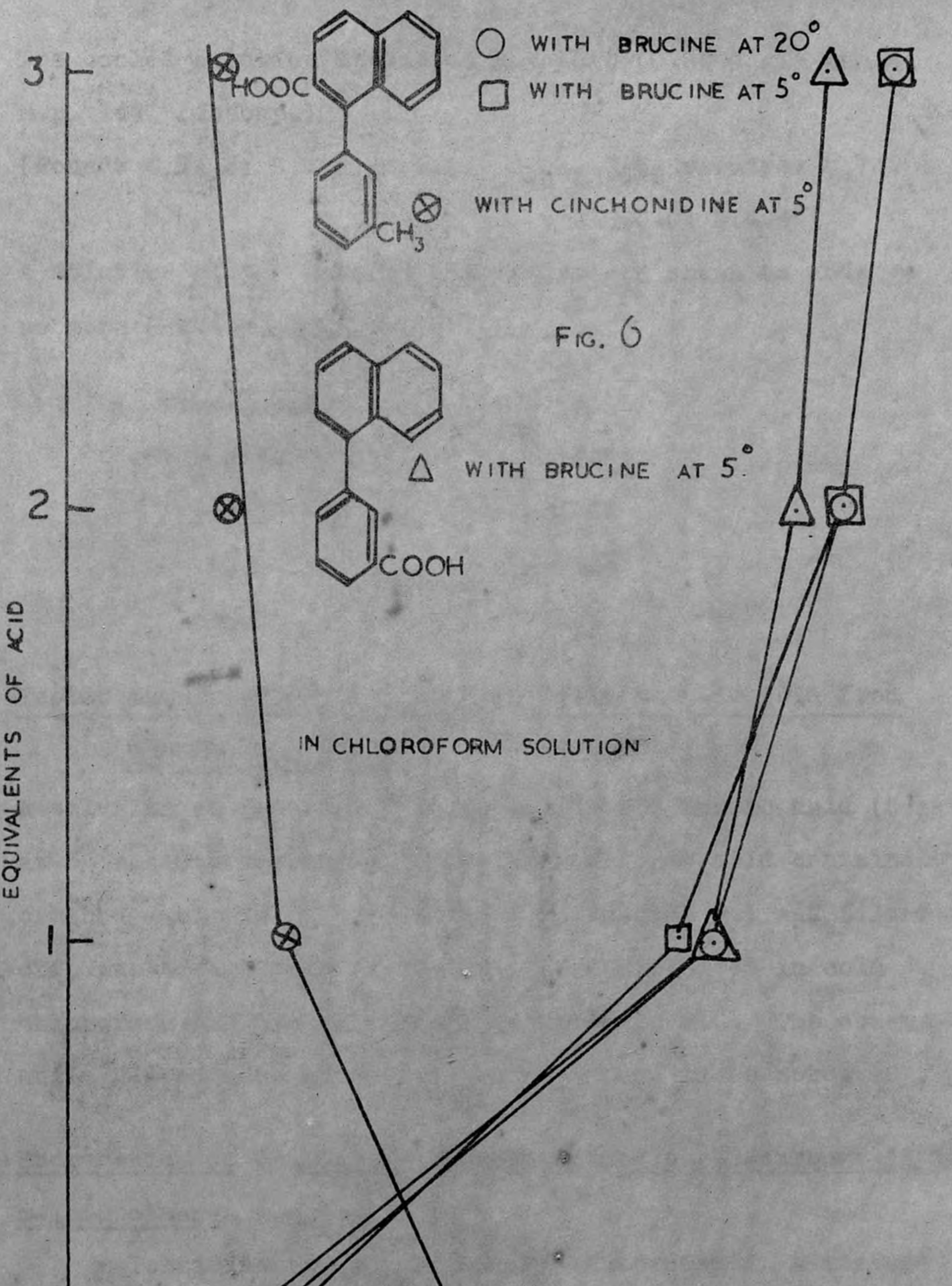


Fig. 6

HOOC
CH$_3$
COOH
○ WITH BRUCINE AT 20°
□ WITH BRUCINE AT 5°
⊗ WITH CINCHONIDINE AT 5°
△ WITH BRUCINE AT 5°
IN CHLOROFORM SOLUTION
EQUIVALENTS OF ACID
3
2
1
0
α_{5461}
-2·0°
-1·0°
0°

The cooled solution deposited the salt (0.2000 g.) of m.p. 144° (decomp.)

(Found: C,74.5; H,6.5; N,4.0. $C_{40}H_{38}O_6N_2$ requires C,74.8; H,6.0; N,4.4%)

A solution of the salt in chloroform was shown to undergo no mutarotation at 5°.

Time (mins.) after wetting.	α 5461
2.25	- 0.15
30.0	- 0.15
∞	- 0.15

Isolation of 1-Phenylnaphthalene-3'-carboxylic Acid from the Brucine Salt.

A solution of the salt (0.2000 g.) in 98% formic acid (5 ml.) at 5° was filtered into dilute hydrochloric acid containing crushed ice. The precipitated acid (0.0752 g.) was filtered off, washed and dried. The solid was dissolved in cold chloroform and the solution made up to 20 ml.. The observed angle 2.1 minutes after wetting was found to be zero.

Preparation of 3'-Methyl-1-Phenylnaphthalene-2-carboxylic Acid.

m-Iodotoluene.

m-Toluidine (53 g., 1 mol) was suspended in a mixture of concentrated sulphuric acid (100 g.) and water (500 ml.). The suspension was cooled in a freezing mixture and a solution of sodium nitrite (36 g., 1 mol.) in water slowly added with stirring, the temperature being kept below 10° throughout. When the addition was complete, the diazonium solution was added to a solution of potassium iodide (124 g., 1.5 mol.) in water (200 ml.) at 20°. The reaction mixture was allowed to stand for three hours and steam distilled. The crude product was redistilled and pure m-iodotoluene (66 g., b.p. 205 - 207°, 61%) was obtained.

Note. The reaction temperature during the coupling of the diazonium solution with the potassium iodide solution was kept at 20° to avoid separation of the explosive diazonium complex.

1-Bromo-2-methylnaphthalene.

Hall & Mitchell, J., 1951, 1375

A crystal of iodine and a little iron powder was added to a solution of 2-methylnaphthalene (212 g., 1 mol.) in carbon tetrachloride (450 ml.) cooled to 0°. A solution of bromine (240 g., 1 mol.) in carbon tetrachloride (450 ml.) was added over a period of thirty minutes with vigorous stirring, keeping the temperature below 5°. When the addition was complete, the reaction mixture was stirred for a further forty minutes. The carbon tetrachloride solution was washed first with 10% sodium hydroxide solution, then with water and dried over anhydrous calcium chloride. The solvent was evaporated off and the residue distilled in vacuo. The fraction (280 g., 84%) b.p. 160°/13 mm. was collected.

1-Bromo-2-bromomethylnaphthalene.

Newman & Kosak, *J. Org. Chem.* 1949, 14, 375

1-Bromo-2-methylnaphthalene (280 g., 1 mol.) and *N*-bromosuccinimide (214 g., 1 mol.) were dissolved in dry carbon tetrachloride (330 ml.). Benzoyl peroxide (1.3 g.) was added and the solution was boiled under reflux for three hours with occasional shaking. A further amount of dry carbon tetrachloride (330 ml.) was added and the solution was filtered while hot through a sintered glass funnel. The solution was cooled and the solid which was deposited (185 g., m.p. 107 - 115°) was filtered off. The crude material was crystallised from carbon tetrachloride (300 ml.) when 1-bromo-2-bromomethylnaphthalene (142 g., m.p. 116°) was obtained. The mother liquor was evaporated to half-volume, and a further amount of solid (75 g., m.p. 115°) was obtained. The total yield was thus 217 g. (58%).

1-Bromo-2-naphthaldehyde.

Hewett, *J.*, 1940, 293

Angyal, Morris, Tetaz & Wilson, *J.*, 1950, 2141

1-Bromo-2-bromomethylnaphthalene (90 g.) was dissolved in chloroform (400 ml.) and powdered hexamine (46.5 g.) was added to the boiling solution, when a thick paste of the hexaminium salt was obtained. The salt was filtered off, dried and boiled under reflux for an hour with 50% acetic acid (650 ml.). Concentrated hydrochloric acid (105 ml.) was added and the solution was boiled for a further five minutes. The reaction mixture was allowed to cool and the crystalline 1-bromo-2-naphthaldehyde (37 g., m.p. 123°, 53% obtained was filtered off and washed with water. On dilution of the mother-liquor with water, only a negligible amount of solid was obtained.

1-Bromo-2-naphthoic Acid

1-Bromo-2-naphthaldehyde (22 g.) was dissolved in acetone (550 ml.) and to the boiling solution kept in a water-bath at 70° was added over thirty minutes a solution of potassium permanganate (28 g.) in hot water (660 ml.). The reaction mixture was heated for thirty minutes; sulphur dioxide was passed through the solution until it became colourless. The reaction mixture was poured into 3 l. of water and when the solution was cold the/crystalline/solid was filtered off.

A further three preparations using 22g. ; 22g. and 27g. of the aldehyde were carried out, (a total of 93g. of the aldehyde was used). The products of the four batches were combined and dissolved in dilute aqueous ammonia solution. A little kieselguhr was added, the solution was filtered and acidified with dilute hydrochloric acid. The precipitated solid was centrifuged off and washed with water until the washings were neutral. Weight 78 g., m.p. 185 - 191°, 79%.

Methyl 1-bromo-2-naphthoate.

A solution of 1-bromo-2-naphthoic acid (78 g.) and concentrated sulphuric acid (78 g.) in methyl alcohol (980 ml.) was boiled under reflux for six hours. The reaction mixture was poured into water, the precipitated solid was filtered off, washed, resuspended in dilute aqueous ammonia solution and finally filtered off and washed with water. The crude product was crystallised from methyl alcohol and methyl 1-bromo-2-naphthoate (67 g., m.p. 60-62°, 81%) was obtained.

3'-Methyl-1-phenylnaphthalene-2-carboxylic Acid.

The acid was prepared by the method of Baddar and Gindy, J., 1948, 1231.

Copper bronze (15 g., 4 atoms) was gradually added to a stirred mixture of m-iodotoluene (13,3 g., 1 mol.) and methyl 1-bromo-2-naphthoate (16.2 g., 1 mol.) contained in a hard glass tube immersed in a metal-bath maintained at 230°. On completion of the addition the bath was maintained at 235° for two and a half hours. After cooling, the reaction mass was extracted with acetone. The solvent was removed, the residue was dissolved in hot ethanol (100 ml.), the solution was filtered and allowed to cool when the methyl ester of 1:1'-dinaphthyl-2:2'-dicarboxylic acid (3.8 g., m.p. 145-160°) crystallised out and was filtered off. The ethanol filtrate was boiled under reflux for six hours with potassium hydroxide (20 g.). The alcohol was evaporated off, the residue extracted with water and the insoluble 3:3'-ditolyl filtered off. After acidification of the aqueous extract the crude product was esterified by passing hydrogen chloride through the boiling methanol solution. An ether extract was washed, dried and distilled. The methyl ester of 3'-methyl-1-phenylnaphthalene-2-carboxylic acid (3.2 g.) was collected, b.p. 187 - 195°/4mm.

The ester was hydrolysed by boiling under reflux for six hours with 10% alcoholic potassium hydroxide solution (50 ml.). The crude acid obtained by precipitation of the aqueous extract with dilute hydrochloric acid was recrystallised twice from 50% aqueous ethanol. 3'-Methyl-1-phenylnaphthalene-2-carboxylic acid (1.9 g., 11%) was obtained as colourless plates, m.p. 162.5 - 165°.

(Found: C,82.6; H,5.35. Calc. for $C_{18}H_{14}O_2$: C,82.4; H,5.4%)

Attempted First Order Asymmetric Transformation of 3'-Methyl-1-phenylnaphthalene-2-carboxylic Acid with Brucine in Chloroform.

(i) A solution of the acid (0.1000 g., 1 equiv.) and anhydrous brucine (0.1502 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 20°.

Time after wetting	α_{5461}^{20}
1.3 mins.	- 0.53
17 hours	- 0.55
∞	- 0.54

No mutarotation was observed and therefore the experiment was repeated at 5°.

(ii) The acid (0.1000 g., 1 equiv.) and anhydrous brucine (0.1502 g., 1 equiv.) were dissolved in chloroform (20 ml.) and the solution examined polarimetrically at 5°.

Time after wetting	α^{20}_{5461}
1.7 mins.	- 0.66
17 hours	- 0.65
∞	- 0.65

Attempted Optical Activation of 3'-Methyl-1-phenylnaphthalene-2-carboxylic Acid with Brucine in Chloroform.

(Ia.) Acid (2 equivs.) : Brucine (1 equiv.) at 20°.

The acid (0.2000 g., 2 equivs.) and anhydrous brucine (0.1502g., 1 equiv.) were dissolved in chloroform (20 ml.) and the solution examined polarimetrically at 20°.

Time after wetting	α^{20}_{5461}
1.4 mins.	- 0.09
17 hours	- 0.11
∞	- 0.11

(Ib.) Acid (2 equivs.) : Brucine (1 equiv.) at 5°.

A solution of the acid (0.2000 g., 2 equivs.) and anhydrous brucine (0.1502 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 5°.

Time (mins.) after wetting	α^{20}_{5461}
1.9	- 0.14
13.8	- 0.12
∞	- 0.12

(IIa) Acid (3 equivs.) : Brucine (1 equiv.) at 20°.

A solution of the acid (0.3000 g., 3 equivs.) and anhydrous brucine (0.1502 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 20°.

Time (mins.) after wetting	α^{20}_{5461}
1.6	- 0.05
20.0	- 0.08
∞	- 0.07

(IIb) Acid (3 equivs.) : Brucine (1 equiv.) at 5°.

A solution of the acid (0.3000 g., 3 equivs.) and anhydrous brucine (0.1502 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 5°.

Time (mins.) after wetting	α^{20}_{5461}
1.95	+ 0.07
20.3	+ 0.07
∞	+ 0.07

Rotation of Brucine in Chloroform.

(i) Anhydrous brucine (0.1502 g.) in chloroform (20 ml.) at 20° was found to have a rotation α^{20}_{5461} - 2.2°.

(ii) Anhydrous brucine (0.1502 g.) in chloroform (20 ml.) at 5° was found to have a rotation α^{5}_{5461} - 2.11°.

From the foregoing results, two addition curves were constructed (fig. 6).

Attempted Optical Activation of 3'-Methyl-1-phenylnaphthalene-2-carboxylic Acid by Cinchonidine in Chloroform at 5°.

(i) Acid (1 equiv.) : Cinchonidine (1 equiv.)

A solution of the acid (0.1000 g., 1 equiv,) and cinchonidine (0.1120 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 5°. No mutarotation was observed.

Time (mins.) after wetting	α^{5}_{5461}
2.2	- 1.90
13.6	- 1.90
∞	- 1.90

(ii) Acid (2 equivs.) : Cinchonidine (1 equiv.)

A solution of the acid (0.2000 g., 2 equivs.) and cinchonidine (.1120 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 5°.

Time after wetting	α^{5}_{5461}
3.0 mins.	- 2.10
18 hours	- 2.10
∞	- 2.10

(iii) Acid (3 equivs.) : Cinchonidine (1 equiv.)

A solution of the acid (0.3000 g., 3 equivs.) and cinchonidine (0.1120 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 5°.

Time after wetting	α^{5}_{5461}
2.4 mins.	- 2.09
18 hours	- 2.10
∞	- 2.10

Rotation of Cinchonidine in Chloroform.

A solution of cinchonidine (0.1120 g.) in chloroform (20 ml.) at 5° was found to have a rotation α^{5}_{5461} - 1.27°.

From the foregoing results an addition curve was constructed (fig. 6).

Brucine Salt of 3'-Methyl-1-phenylnaphthalene-2-carboxylic Acid.

The acid (0.3000 g., 1 mol.) and anhydrous brucine (0.4500 g., 1 mol.) were dissolved in boiling acetone (40 ml.). Ether (80 ml.) was added to the boiling solution and on cooling a colourless solid (0.5517 g.,) crystallised in prisms, m.p.198°. (Found: C,74.4; H,6.2; N,4.0. $C_{41}H_{40}O_6N_2$ requires C,75.0; H,6.1; N, 4.4%)

(i) A solution of the brucine salt (0.1000 g.) in chloroform (20 ml.) was examined polarimetrically at 20°. An initial rotation α^{20}_{5461} - 0.30° was observed 1.25 minutes after wetting. No significant change in the observed angle was noted. The value at equilibrium was α^{20}_{5461} - 0.29°.

(ii) A solution of the brucine salt (0.1000 g.) in chloroform (20 ml.) was examined polarimetrically at 5°. An initial rotation α^{5}_{5461} - 0.29° was observed 1.8 minutes after wetting. No significant change in the observed angle was noted. The value at equilibrium was α^{5}_{5461} - 0.28°.

The brucine salt (0.2500 g.) was dissolved in cold 98% formic acid (5 ml.) and the solution poured into a mixture of dilute hydrochloric acid and ice. The precipitate obtained (0.0980 g.) was filtered off, washed and dried in a vacuum.

A solution of this acid (0.0980 g.) in chloroform (20 ml.) was examined polarimetrically at 5°. The observed angle 2.6 minutes after wetting was found to be zero.

1:1'-Dinaphthyl-8:8'-dicarboxylic Acid.

Copper bronze (10 g., 2.5 atoms) was gradually added to methyl 8-bromo-1-naphthoate (10 g., 1 mol.) contained in a hard glass tube immersed in a metal-bath maintained at 275°. During the addition the temperature of the reaction mixture rose to 310°. On completion of the addition the temperature was maintained at 290° for a further thirty minutes. The cooled mass was extracted with acetone in a soxhlet apparatus. The acetone extract was evaporated to 50 ml., when a light yellow solid (3.75 g., m.p. 155-158°, 63%) crystallised. On recrystallisation from acetone (40 ml.), methyl 1:1'-dinaphthyl-8:8'-dicarboxylate (2.93 g., m.p. 155-159°, 49%) was obtained.

(Found: C,77.8; H,5.2. $C_{24}H_{16}O_4$ requires C,77.8; H,4.9%)

A solution of the ester (1.5 g.) in a 30% solution of potassium hydroxide in methyl alcohol was placed in a hard glass tube immersed in a metal bath at 120°. When all the solvent had evaporated, the temperature of the bath was raised to 160° for one hour. The melt was extracted with water and the filtered aqueous solution was acidified with dilute hydrochloric acid. The precipitated solid (1.2 g., m.p. 300-304°) was filtered off, washed, dried and extracted with acetone in a soxhlet apparatus for ten hours. On cooling the extract a light brown solid (0.25 g., m.p. 304-305° decomp.) was obtained. The undissolved solid remaining was dissolved in boiling acetone (1.5 l.), the solution filtered and evaporated to 200 ml.. On cooling, the almost colourless 1:1'-dinaphthyl-8:8'-dicarboxylic acid (0.67 g., m.p.300-304° decomp.) crystallised. The combined weight of the two crops represented a yield of 66%.

(Found: C,76.6; H,4.0. Calc. for $C_{22}H_{14}O_4$: C,77.2;H,4.1%)

Meisenheimer and Beisswenger (<u>Ber.</u>, 1932, <u>65</u>, 32) following the method of Kalb (<u>Ber.</u>, 1914, <u>47</u>, 1726) prepared the acid by heating ethyl 8-chloro-1-naphthoate with copper bronze and hydrolysing the resulting ethyl 1:1'-dinaphthyl-8:8'-dicarboxylate with solid potassium hydroxide at 160°.

<u>Optical Resolution of</u> 1:1'-<u>Dinaphthyl</u>-8:8'-<u>dicarboxylic Acid.</u>

The brucine salts and active acids were obtained following the method of Meisenheimer and Beisswenger (<u>loc</u>. <u>cit.</u>).

1:1'-Dinaphthyl-8:8'-dicarboxylic acid (0.5000 g.) was dissolved in boiling methyl alcohol (380 ml.) and to the boiling solution was added a solution of anhydrous brucine (0.6800 g.) in methyl alcohol (20 ml.). The solution obtained was concentrated to 130 ml. and allowed to stand for two days when brucine (+)-1:1'-dinaphthyl-8:8'-dicarboxylic acid (0.4065 g.,) crystallised in colourless micro-prisms, m.p. 270-275°.

(Found: C,69.1; H,6.0; N,3.65. Calc. for $C_{45}H_{40}O_8N_2$:
C,73.3; H,5.5; N,3.8%)

The brucine (+)-acid salt in chloroform solution was found to have α^{20}_{5461} - 1.03,° whence $[\alpha]^{20}_{5461}$ -515° (c = 0.2000, l = 1)

The methyl alcohol filtrate was evaporated to dryness and the residue dissolved in boiling ethyl acetate (120 ml.). On standing, brucine (-)-1:1'-dinaphthyl-8:8'-dicarboxylic acid (0.5330 g.), crystallised in colourless long prisms, m.p. 215° with softening.

(Found: C,71.7; H,5.8; N,3.9. Calc. for $C_{45}H_{40}O_8N_2$:
C, 73.3; H,5.5; N,3.8%)

The brucine (-)-acid salt in chloroform solution was found to have α^{20}_{5461} -2.30°, whence $[\alpha]^{20}_{5461}$ -460° (c = 0.5000, l = 1).

(-)-1:1'-Dinaphthyl-8:8'-dicarboxylic Acid.

A solution of the brucine (-)-acid salt (0.20 g.) in chloroform (3 ml.) was shaken with an aqueous 0.1N sodium hydroxide solution (10 ml.) for five minutes. The alkali solution was extracted with chloroform (5 ml.), then with

ether (5 ml.) and air blown through the solution to remove traces of solvent. The racemisation of the (-)-acid in the alkali solution was followed polarimetrically at 20° in a 1 dcm. polarimeter tube. A duplicate experiment was carried out and from the results (Tables 19 & 20, fig. 7) the values of k calculated were:
(i) 0.0043 mins.^{-1} (ii) 0.0042 mins.^{-1}, whence the half life is 163 minutes.

The concentration of the acid in the 0.1N sodium hydroxide solution was determined.
7.00 ml. of the alkali solution was taken and acidified with dilute hydrochloric acid, the precipitated acid (0.0523 g.) was filtered off, washed and dried. Thus the concentration is 0.747 g./100 ml.. Hence $[\alpha]^{20^\circ}_{5461}$ -447°

(+)-1:1'-Dinaphthyl-8:8'-dicarboxylic Acid.

A solution of the brucine (+)-acid salt (0.15 g.) in chloroform (3 ml.) was shaken with an aqueous 0.1N sodium hydroxide solution (10 ml.) for five minutes. The alkali solution was extracted with chloroform (5 ml.), then with ether (5 ml.) and air was blown through the solution to remove traces of solvent. The racemisation of the (+)-acid was followed polarimetrically at 20° in a 1 dcm. polarimeter tube. A duplicate experiment was carried out, and from the results (tables 21 & 22, fig. 7) two values of k were calculated. (i) 0.0040 mins.^{-1} (ii) 0.0044 mins.^{-1},

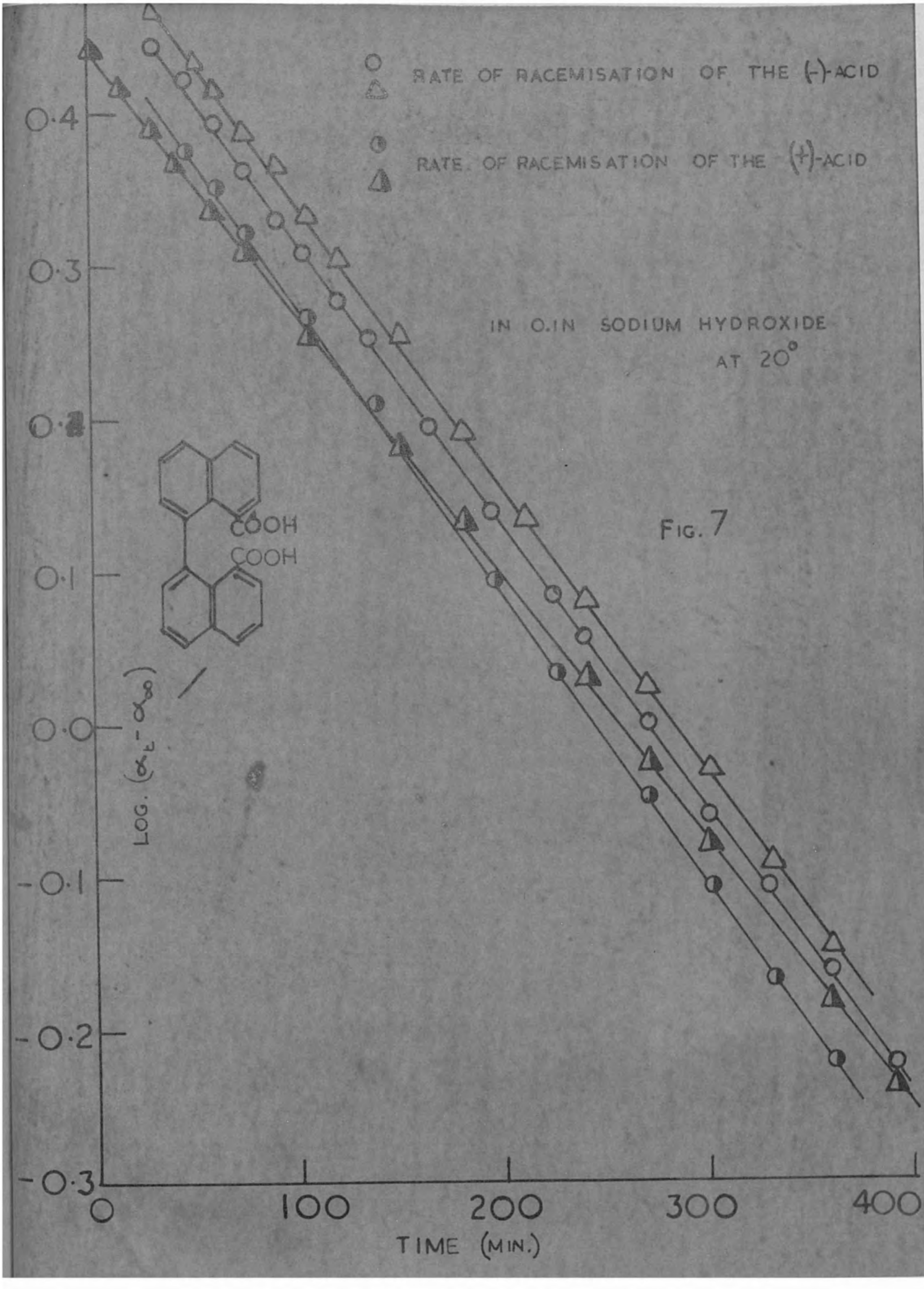

○ △ RATE OF RACEMISATION OF THE (-)-ACID
◐ ▲ RATE OF RACEMISATION OF THE (+)-ACID
IN 0.1N SODIUM HYDROXIDE AT 20°
COOH
COOH
LOG. $(\alpha_t - \alpha_\infty)$
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
-0.3
0
100
200
300
400
TIME (MIN.)

FIG. 7

Table 19.

Racemisation of (−)-1:1'-Dinaphthyl-8:8'-dicarboxylic acid in 0.1 N Sodium Hydroxide Solution at 20°.

Time (mins.)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins.$^{-1}$
0	− 3.18	0.5024	−
30	− 2.795	0.4464	0.0043
45	− 2.63	0.4200	0.0042
60	− 2.47	0.3927	0.0042
75	− 2.30	0.3617	0.0043
90	− 2.15	0.3324	0.00435
105	− 2.03	0.3075	0.0043
120	− 1.89	0.2765	0.0043
135	− 1.79	0.2529	0.0043
165	− 1.57	0.1959	0.0043
195	− 1.38	0.1399	0.0043
225	− 1.21	0.0828	0.0043
240	− 1.145	0.0588	0.0043
270	− 1.00	0.0000	0.0043
300	− 0.87	$\bar{1}.9395$	0.0043
330	− 0.78	$\bar{1}.8921$	0.0043
360	− 0.69	$\bar{1}.8388$	0.00425
390	− 0.595	$\bar{1}.7745$	0.0043
∞	0.00	−	−

Table 20.

Racemisation of (-)-1:1'-Dinaphthyl-8:8'-dicarboxylic acid in 0.1 N Sodium Hydroxide Solution at 20°.

Time (mins.)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins.$^{-1}$
0	- 3.34	0.5237	-
15	- 3.14	0.4969	0.0041
30	- 2.95	0.4698	0.00415
50	- 2.71	0.4930	0.0042
60	- 2.61	0.4166	0.0041
75	- 2.44	0.3874	0.0042
90	- 2.33	0.3674	0.0040
105	- 2.14	0.3304	0.0042
120	- 2.02	0.3054	0.0042
150	- 1.78	0.2504	0.0042
180	- 1.55	0.1903	0.0043
210	- 1.36	0.1335	0.0043
240	- 1.20	0.0792	0.0043
270	- 1.06	0.0253	0.00425
300	- 0.94	$\bar{1}.9731$	0.0042
330	- 0.82	$\bar{1}.9138$	0.0043
360	- 0.71	$\bar{1}.8513$	0.0043
∞	0.00	-	-

whence the half life is 165 minutes.

The concentration of the acid in the 0.1N sodium hydroxide solution was determined.

9.00 ml. of the alkali solution were acidified with dilute hydrochloric acid. The precipitated acid (0.0491 g.) was filtered off, washed and dried. Thus the concentration is 0.545 g./100 ml.. Hence $\left[\alpha\right]^{20}_{5461}$ $+ 534^{\circ}$

Table 21.

Racemisation of (+)-1:1'-Dinaphthyl-8:8'-dicarboxylic acid in 0.1 N Sodium Hydroxide Solution at 20°.

Time (mins.)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins.^{-1}
0	+ 2.77	0.4425	-
15	+ 2.62	0.4193	0.0037
30	+ 2.46	0.3909	0.0040
45	+ 2.31	0.3638	0.0040
60	+ 2.18	0.3385	0.0040
75	+ 2.055	0.3129	0.0040
105	+ 1.81	0.2577	0.0040
150	+ 1.52	0.1818	0.0040
180	+ 1.36	0.1335	0.0039
240	+ 1.07	0.0294	0.0040
270	+ 0.94	$\bar{1}.9731$	0.0040
300	+ 0.84	$\bar{1}.9243$	0.0040
360	+ 0.66	$\bar{1}.8195$	0.0040
390	+ 0.58	$\bar{1}.7634$	0.0040
420	+ 0.52	$\bar{1}.7160$	0.0040
450	+ 0.46	$\bar{1}.6629$	0.0040
∞	0.00	-	-

Table 22.

Racemisation of (+)-1:1'-Dinaphthyl-8:8'-dicarboxylic acid in 0.1 N Sodium Hydroxide Solution at 20°.

Time (mins.)	α^{20}_{5461}	$\log_{10}(\alpha_t - \alpha_\infty)$	k mins.$^{-1}$
0	+ 2.91	0.4639	-
30	+ 2.56	0.4082	0.0043
45	+ 2.39	0.3784	0.0044
60	+ 2.25	0.3522	0.0043
75	+ 2.11	0.3243	0.0044
105	+ 1.85	0.2672	0.0044
135	+ 1.63	0.2122	0.0043
165	+ 1.45	0.1614	0.0042
195	+ 1.25	0.0969	0.00435
225	+ 1.065	0.0274	0.0045
270	+ 0.90	$\bar{1}.9542$	0.0043
300	+ 0.78	$\bar{1}.8921$	0.0044
330	+ 0.68	$\bar{1}.8325$	0.0044
360	+ 0.60	$\bar{1}.7782$	0.0044
∞	0.00	-	-

Preparation of 2'-Isopropenyldiphenyl-2-carboxylic Acid.

2'-(α-Hydroxyisopropyl)-diphenyl-2-carboxylic Acid.

Corbellini and Angeletti, Atti R. Accad. Lincei, 1932, 15,968.
Jamison and Turner, J., 1942, 437.

A solution of methyl iodide (26.3 g., 2.8 mols.) in anhydrous ether was slowly added to a suspension of magnesium turnings (3.1 g., 2 atoms) in anhydrous ether (40 ml.). A crystal of iodine was added to initiate the reaction. On completion of the addition, all the magnesium was found to have dissolved. Solid diphenic anhydride (14 g., 1 mol.) was then added gradually to the solution of methyl magnesium iodide. The reaction proceeded smoothly and the reaction mixture was boiled under reflux for four hours after the addition had been completed. Dilute acetic acid was added in excess and the resultant solution was extracted with ether. The ether solution was washed once with water and then extracted four times with a 10% aqueous sodium carbonate solution. On acidification of the alkaline extract with dilute hydrochloric acid, a sticky, unfilterable solid was obtained. The product was isolated by extraction with ether. The residue obtained after evaporation of the solvent was boiled under reflux for one and a half hours with a 15% alcoholic sodium hydroxide solution (150 ml.) containing a little water (15 ml.). After evaporation of the alcohol, the residue was dissolved in water, the solution filtered and then acidified with dilute hydrochloric acid. The sticky solid obtained was dissolved in boiling benzene (110 ml.), a little charcoal added, the solution filtered and evaporated to 80 ml.. On cooling, 2'-(α -hydroxyisopropyl)-diphenyl-2-carboxylic acid (3.8 g., 25% Theory) crystallised as a colourless solid of m.p. 137°.

2'-Isopropenyldiphenyl-2-carboxylic Acid.

2'-(α -Hydroxyisopropyl)-diphenyl-2-carboxylic acid (3.5 g.,) and fuming hydrobrimic acid (17 ml.) (obtained by saturating 48% hydrobromic acid with hydrogen bromide at 0°.) were heated at a 100° in a sealed tube for one hour. The solid was filtered off, washed and crystallised from benzene (80 ml.). A light brown solid (0.25 g., m.p. 190-197°) was obtained which on recrystallisation from benzene (75 ml.) gave 2'-isopropenyldiphenyl-2-carboxylic acid (2 g., 62% Theory) as colourless crystalline plates m.p. 195-197.5°. (Found: C,81.1; H,5.8. $C_{16}H_{14}O_2$ requires C, 80.6; H, 5.9%)

The lactone of 2'-(α -hydroxyisopropyl)-diphenyl-2-carboxylic acid has m.p. 123°. (Corbellini and Angeletti, loc.cit.)

Attempted Alternative Preparation of 2'-Isopropenyldiphenyl -2-carboxylic Acid.

It was considered of interest to prepare the acid by an alternative method. A synthesis was proposed from methyl o-iodobenzoate and o-iodoisopropenylbenzene by means of the Ullmann reaction. However o-iodoisopropenylbenzene with copper at 235° gave a product which was not 2:2'-di*iso*propenyl benzene together with an intractable tar. It was concluded that the proposed unsymmetrical Ullmann reaction was not feasible.

o-Iodo-isopropenylbenzene.

Bergmann and Weizmann, Trans. Farad. Soc., 1936, 1327.

A solution of methyl iodide (64 g., 2.3 mols.) in anhydrous ether (200 ml.) was slowly added to a suspension of magnesium (10.4 g., 2.2 atoms) in dry ether (150 ml.). On completion of the addition, methyl *o*-iodobenzoate (52 g., 1 mol.) was gradually introduced, when a smooth reaction occurred. The reaction mixture was boiled under reflux for two hours. Dilute acetic acid was added and the solution was extracted with ether. The ether extract was washed with sodium carbonate solution, then with water and finally dried over anhydrous sodium sulphate. The residue (39 g.) obtained after removal of the ether was boiled under reflux with acetic anhydride (40 ml.) for eight hours and the resultant solution distilled under reduced pressure. *o*-Iodo-*iso*propenylbenzene (25 g., 69% Theory) b.p. 74°/2 mm. was collected.

Attempted Preparation of 2:2'-Di-isopropenyldiphenyl.

Copper bronze (15 g.) was added gradually to *o*-iodo-*iso*propenylbenzene (10 g.) maintained at 235°. The reaction mixture was maintained at 235° for one and a half hours, and on cooling was extracted with acetone. On removal of the solvent a viscous oil was obtained, which on dissolving in boiling petroleum ether (b.p. 40-60°) deposited no solid. The solvent was removed and the residue was distilled *in vacuo.* A liquid b.p. 116-120°/12 mm. was obtained, which did not solidify on cooling in ice and which was shown to contain no iodine. An intractable brown tar remained in the distilling flask.

2:2'-Di-*iso*propenyldiphenyl has a m.p. 97-98°. (Cook and Turner, *J.*, 1937, 117)

Attempted First Order Asymmetric Transformation of 2'-Isopropenyldiphenyl-2-carboxylic Acid with Brucine in Chloroform.

A solution of the acid (0.1000 g., 1 equiv.) and anhydrous brucine (0.1654 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 20°.

Time after wetting.	α^{20}_{5461}
2.4 mins.	- 0.76
5 hours	- 0.78
∞	- 0.78

No mutarotation was observed.

Attempted Optical Activation of the Acid with Brucine.

(i) The acid (0.2000 g., 2 equivs.) and anhydrous brucine (0.1654 g., 1 equiv.) were dissolved in chloroform (20 ml.) and the solution examined polarimetrically at 20°.

Time after wetting	α^{20}_{5461}
2.5 mins.	- 0.41
40.0 mins.	- 0.40
18 hours	- 0.41
∞	- 0.41

(ii) A solution of the acid (0.3000 g., 3 equivs.) and anhydrous brucine (0.1654 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 20°.

Time after wetting	α^{20}_{5461}
2.1 mins.	- 0.31
15.0 mins.	- 0.29
∞	- 0.29

Rotation of Anhydrous Brucine in Chloroform at 20°.

A solution of anhydrous brucine (0.1654 g.) in chloroform (20 ml.) at 20° was found to have a rotation α^{20}_{5461} - 2.42°.

From the foregoing results, an addition curve was plotted (fig. 8).

Attempted Optical Activation of 2'-Isopropenyldiphenyl - 2-carboxylic Acid with Cinchonidine.

(i) A solution of the acid (0.1000 g., 1 equiv.) and cinchonidine (0.1270 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 20°.

Time after wetting	α^{20}_{5461}
2.5 mins.	- 1.49
4 hours	- 1.48
∞	- 1.48

(ii) A solution of the acid (0.2000g., 2 equivs.) and cinchonidine (0.1270 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 20°.

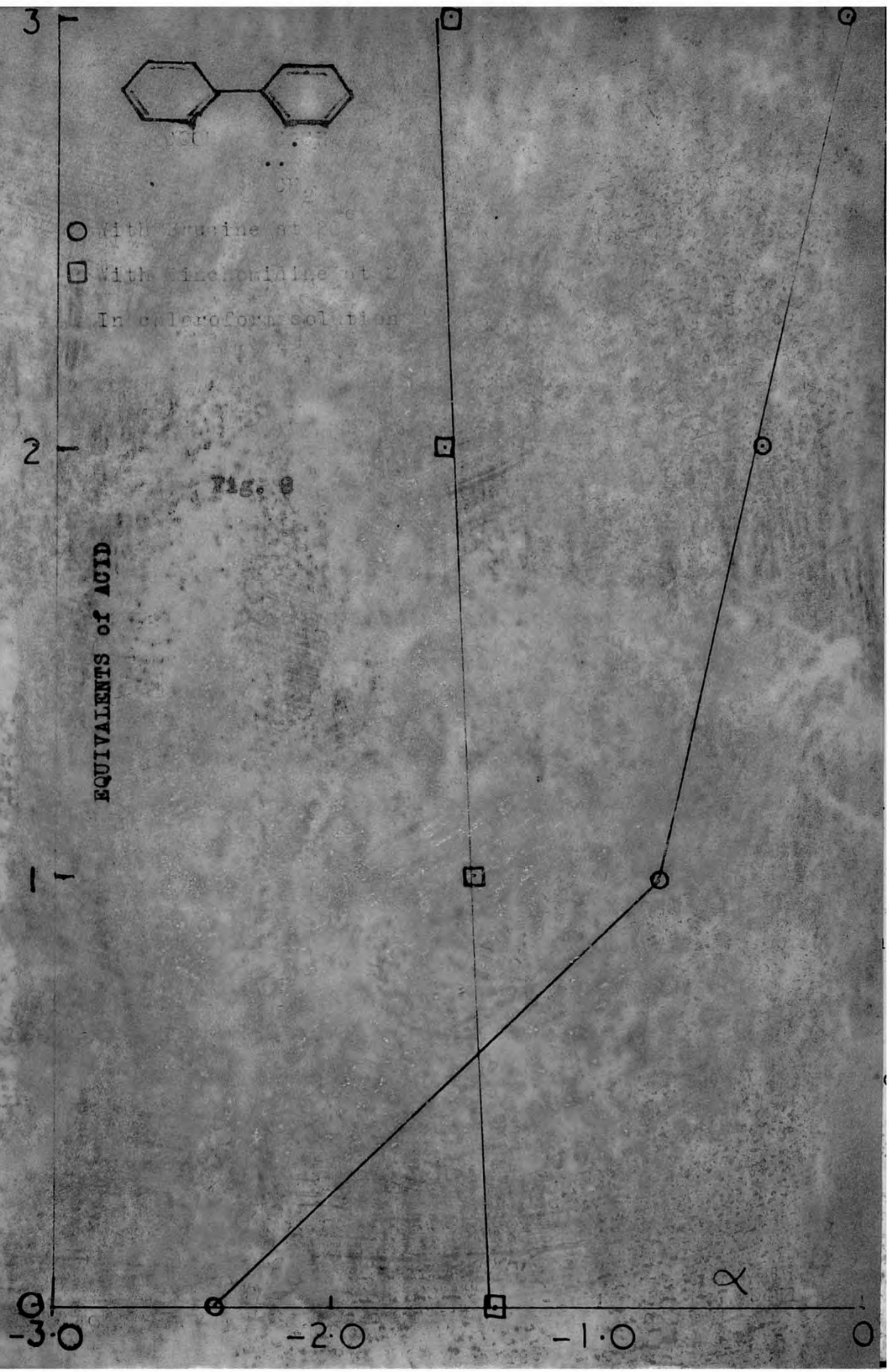
Time after wetting	α^{20}_{5461}
2.4 mins.	- 1.58
11 hours	- 1.58
∞	- 1.58

(iii) A solution of the acid (0.3000 g., 3 equivs.) and cinchonidine (0.1270 g., 1 equiv.) in chloroform (20 ml.) was examined polarimetrically at 20°.

Time after wetting.	α^{20}_{5461}
2.2 mins.	- 1.57
30.0 mins.	- 1.57
∞	- 1.57

Rotation of Cinchonidine in Chloroform at 20°.

A solution of cinchonidine (0.1270 g.) in chloroform (20 ml.) was found to have a rotation α^{20}_{5461} -1.40°.



COOH
CH2
With brucine at
With cinchonidine at
In chloroform solution
EQUIVALENTS of ACID
3
2
1
0
α
-3·0
-2·0
-1·0
0

Fig. 8

From the foregoing results an addition curve was constructed (fig. 8).

Attempted Preparation of 1-Phenylnaphthalene-2:2'-dicarboxylic Acid.

The synthesis was attempted by two methods.

(i) By an unsymmetrical Ullmann reaction between methyl *o*-iodobenzoate and methyl 1-bromo-2-naphthoate.

(ii) By the oxidation of 2-methyl-1-phenylnaphthalene-2'-carboxylic acid.

(i) Copper bronze (15 g.) was added to a mixture of methyl *o*-iodobenzoate (13.1 g., 1 mol.) and methyl 1-bromo-2-naphthoate (14.2 g., 1 mol.) maintained at a temperature of 260°. After the addition, the temperature was kept at 250° for an hour. The reaction mass was extracted with acetone and the residue, obtained after removal of the solvent, dissolved in hot alcohol (50 ml.). The solution was allowed to stand and the solid which was deposited on cooling (mainly methyl 1:1'-dinaphthyl-8:8'-dicarboxylate) was filtered off. The esters remaining in solution were hydrolysed by boiling with potassium hydroxide (10 g.) for five hours. The mixture of acids obtained by precipitation with dilute hydrochloric acid was extracted with cold benzene. Diphenic acid remained undissolved and was filtered off. The benzene solution was evaporated to dryness and the residue was recrystallised from dilute alcohol. The solid (2.3 g.) obtained melted over a wide range up to 219°. This impure acid was esterified by passing hydrogen chloride through a boiling methanol solution when a fraction (1.1 g., b.p. 200-230°/5 mm.) was collected. Hydrolysis was brought about by boiling with a 10% alcoholic potassium hydroxide solution for five hours. On precipitation of the aqueous extract a solid was obtained (0.95 g.) which melted over a wide range (100-195°). The possibility that some ester remained unchanged was considered and therefore the solid was boiled for sixteen hours with 30% alcoholic potassium hydroxide. A solid was obtained (0.79 g.) melting over the range 125-165°. This solid was heated with solid potassium hydroxide at 170° for two hours. A product (0.66 g.) was obtained m.p. 120-200°.

In order to eliminate possible solvation effects, the compound was heated at 100°/2 mm. for several hours. No significant change in the melting point was observed. A further attempt to synthesise the compound was made using a similar procedure. An end product which melted over a wide range was obtained, therefore no further attempts were made to obtain the compound by this method.

(ii) 2-Methyl-1-phenylnaphthalene-2'-carboxylic Acid.
The preparation was carried out using the method of

Baddar, J., 1939, 944.

Copper bronze (25 g.) was added to a mixture of methyl o-iodobenzoate (30 g., 2 mols.) and 1-bromo-2-methylnaphthalene (13 g., 1 mol.) maintained at 220°. The temperature rose to 245° on addition of the copper and was maintained at 230° for thirty minutes after the addition was complete. The cooled mixture was extracted with o-dichlorobenzene, and the residue obtained after removal of the solvent was hydrolysed by boiling with 10% alcoholic potassium hydroxide (100 ml.). The alcohol was removed, the residue extracted with water and the aqueous solution extracted benzene to remove hydrocarbons. On acidification of the solution with dilute hydrochloric acid a mixture of acids (13 g.) was obtained, which was extracted with cold benzene. The insoluble diphenic acid (9.6 g.) was filtered off and the extract was evaporated to dryness. The residue (3.2 g.) was crystallised from methanol (50 ml.) when 2-methyl-1-phenylnaphthalene-2'-carboxylic acid was obtained (1.8 g., 13%, m.p. 185-187.5°)

Baddar (*loc. cit.*) gives m.p. 188-189°.

Attempted Oxidation of 2-Methyl-1-phenylnaphthalene-2'-carboxylic acid.

A solution of the acid (1 g., 1 mol.) in 10% aqueous sodium hydroxide (30 ml.) was boiled with potassium permanganate (2.4 g., 4 mols.) for six hours, when the solution became decolourised. The manganese dioxide was filtered off, washed with water and the alkaline solution acidified with dilute hydrochloric acid. A solid (0.3 g.) was obtained which commenced to soften at 80° and finally melted at 115° (decomp.).

It was concluded that the product obtained was a mixture and the experiment was therefore abandoned.

Attempted Preparation of 3'-Methyl-1-phenylnaphthalene -8-carboxylic Acid.

Copper bronze (25 g.) was added to a mixture of methyl 8-bromo-1-naphthoate (13.5 g., 1 mol.) and m-iodotoluene (13 g., 1.2 mols.) at 240°. A small rise in temperature was observed on addition of the copper. The temperature was maintained at 245° for a further two hours. The reaction mixture was extracted with o-dichlorobenzene and the residue obtained after removal of the solvent was hydrolysed by boiling with 10% alcoholic potassium hydroxide (200 ml.) for three hours. After evaporation of the alcohol, the residue was extracted with water. The insoluble 3:3'-ditolyl was filtered off and the aqueous solution acidified with dilute hydrochloric acid. A gum was obtained and was extracted with ether. The solid remaining after evaporation of the ether was extracted with boiling petroleum ether (b.p. 100-120°) to remove unchanged 8-bromo-1-naphthoic acid. An insoluble solid which remained was extracted with boiling alcohol (200 ml.). The solution obtained was concentrated to 50 ml. and on cooling a solid (0.8 g.) which separated was filtered off. Two recrystallisations from ethanol gave a colourless solid (0.43 g., 3%) m.p. 232-235°.

(Found: C,76.9; H,4.7. $C_{18}H_{14}O_2$ requires C,82.4; H,5.4%)

The preparation was repeated on a slightly larger scale when a solid was obtained m.p. 218° (0.5 g.). In view of the small yield and the incorrect analysis, the experiment was discontinued.

Attempted Preparation of 1:2'-Dinaphthyl-8-carboxylic Acid. Copper bronze (25 g.) was added to a mixture of 2-bromonaphthalene (10 g., 1 mol.) and methyl 1-bromo-8-naphthoate (13.2 g., 1 mol.) maintained at 270°. The temperature rose to 285° on addition of the copper. The reaction mixture was heated for an hour and then extracted with ether in a soxhlet apparatus. The ether solution was evaporated to 30 ml. when a solid crystallised (mainly methyl 1:1'-dinaphthyl 8:8'-dicarboxylate) and was filtered off. Evaporation of the filtrate gave a residue which was steamed distilled to remove unchanged starting material. The non-volatile material was distilled and a fraction b.p. 250-265°/8 mm. was collected and solidified in the receiver. The ester was dissolved in methanol (50 ml.) and on standing, a crystalline solid was deposited (0.1 g., m.p. 186-191°) and filtered off. To the alcoholic filtrate was added potassium hydroxide (15 g.) and the solution boiled under reflux for six hours. The product obtained was found to be insoluble in aqueous alkali and was probably incompletely hydrolysed. The recovered solid was heated with solid potassium hydroxide (5 g.) at 160° for an hour. The light brown solid (1.0 g.) obtained by acidification of an aqueous extract was found to melt over a range 274-300°.

Meisenheimer and Beisswenger, (loc. cit.) obtained the acid (m.p. 189°) by an unsymmetrical Ullmann reaction between ethyl 8-chloro-1-naphthoate and 2-chloronaphthalene.