OPTICAL STUDIES OF 2-t-BUTYL-2'-SUBSTITUTED BIPHENYLS.

By:

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for the degree of Doctor of Philosophy.

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ABSTRACT.

Several 2-t-butyl-2'-substituted biphenyls have been prepared and resolved. The synthesis of these compounds was effected by heating with copper bronze a mixture of o-iodo-t-butylbenzene (or a derivative) and the appropriately substituted halogeno-benzene (or naphthalene) (Ullmann reaction). Large quantities of o-iodo-t-butylbenzene and methyl (or ethyl) 3-iodo-4-t-butylbenzoate have therefore been prepared.

6,6'-Di-t-butylbiphenyl-3,3'-dicarboxylic acid was resolved through the brucine salt, and optically active 2,2'-di-t-butylbiphenyl has been obtained by decarboxylation of the optically active acid. 2',6'-Di-t-butylbiphenyl-3-carboxylic acid has been resolved through its strychnine salt and found to show high optical stability.

An unsuccessful attempt was made to prepare 2'-nitro-6-t-butylbiphenyl-3-carboxylic acid, however, the synthesis of 2'-t-butyl-6-nitrobiphenyl-4-carboxylic acid succeeded and it was found that its strychnine salt underwent second-order asymmetric transformation in ethanol, and racemised in boiling chloroform solution. Racemisation

of the optically active acid was studied at several temperatures between 51° and 75° and from the rates of racemisation the energy of activation was found to be 25.4 kcal.mole^{-1}.

Methyl 8-(2'-t-butylphenyl)-l-naphthoate was prepared by heating equimolecular proportions of o-iodo-t-butylbenzene and methyl 8-bromo-l-naphthoate. The acid obtained by hydrolysis of this ester was resolved through its strychnine salt, and racemisation of the optically active acid was studied. An attempt to prepare (2'-t-butylphenyl)-l-naphthalene from 8-(2'-t-butylphenyl)-l-naphthoic acid by the Schmidt reaction resulted in the formation of the cyclisation product, 7-oxo-ll-t-butylbenz[d e]anthracene. The benzanthracene obtained from the optically active acid was inactive.

The author is indebted to Dr. M. S. Lesslie for her constant help and encouragement, and wishes to thank Professor E. E. Turner, F.R.S., Professor P.B.D. de la Mare and all the Chemistry Department at Bedford College for their interest and advice.

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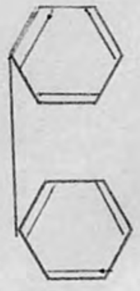
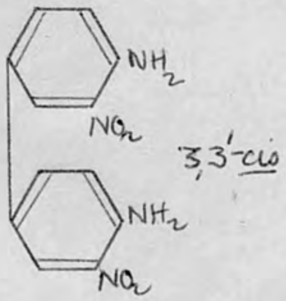
CONTENTS.

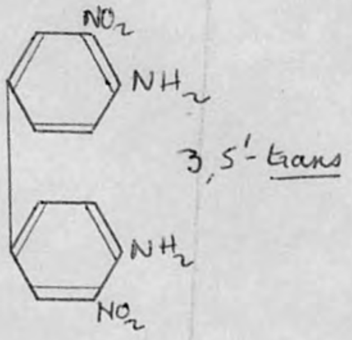
INTRODUCTION.

The optical resolution by Christie and Kenner (1922) of 6,6'-dinitrodiphenic acid opened an entirely new field of stereochemistry. Until 1907, it was generally considered that the two benzene rings in biphenyl and its derivatives were extended and coplanar; in that year, however, Kaufler proposed a more or less rigid folded space formula for biphenyl (I) to account for the existence and ease of formation of cyclic derivatives of benzidine, which were described in the earlier literature in organic chemistry. He concluded from this survey that the two amino-groups in the base must be almost as near together as they are in an aromatic o-diamine. This folded structure was adopted by Cain (1912) to explain the existence of two isomers, conventionally inexplicable, of 3,3'-dinitrobenzidine (IIA and IIB) and, later, of two pairs of geometric isomers of the m-dinitro-o-tolidines.


I

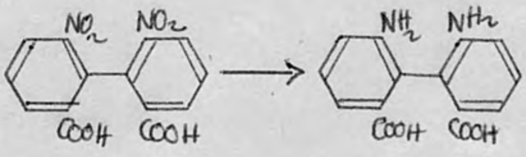


IIA

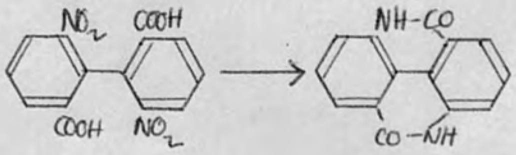


IIB

In 1921, Kenner and Stubbings (J., 1921, 593) prepared 6,6'-dinitrodiphenic acid by heating ethyl 2-chloro-3-nitrobenzoate with copper bronze and hydrolysing the product. They found that their acid differed in chemical and physical properties from the dinitrodiphenic acid prepared by the oxidation of the nitration products of phenanthaquinone and also by direct nitration of diphenic acid (Schultz, Annalen, 1880, 203, 95), and which was believed to be 6,6'-dinitrodiphenic acid (Schmidt and Kämpf, Ber., 1903, 36, 3745). On reduction, Kenner's acid very readily produced an internal dilactam, whereas Schultz's acid yielded the corresponding diamino-acid. Kenner & Stubbings concluded that these acids constituted another pair of geometric isomers and assumed that their acid was the trans form and Schultz's acid was the cis.

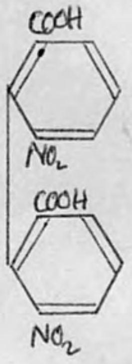


SCHULTZ'S ACID

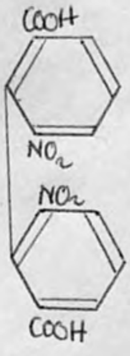


KENNER'S ACID

King (<u>Proc.Chem.Soc.</u>, 1914, <u>30</u>, 249) was the first to point out the possibility of optical activity in one of the dinitrobenzidines (IIB) if the Kaufler formula were correct. Thorpe (<u>J.</u>, 1921, 535) also noted a similar possibility in one of the above dinitrodiphenic acids, and Christie and Kenner (<u>J.</u>, 1922, 614) discussed further in some detail, the stereochemistry of the two dinitrodiphenic acids. On the basis of the extended coplanar formula for biphenyl the <u>cis</u> acid has a plane of symmetry and the <u>trans</u> form has a centre of symmetry, hence neither acid should be resolvable into optical antipodes. On the basis of the Kaufler formula, however, the <u>cis</u> form has a plane of symmetry whereas the <u>trans</u> has not, and should therefore be resolvable.



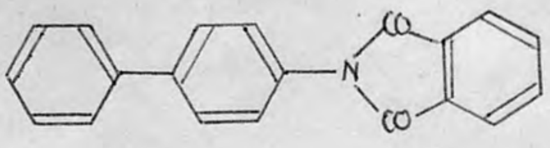
<u>cis</u>



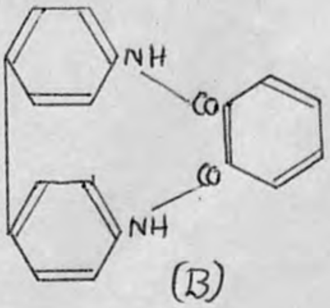
<u>trans</u>

On the basis of formulae with a common axis for the two benzene rings but with the rings non-coplanar both acids should be resolvable. By the successful resolution of their dinitrodiphenic acid, the supposed <u>trans</u> acid, Christie and Kenner provided very convincing support for Kaufler's space formula, and soon after their discovery five more diphenic acids of the same type were resolved.

Meanwhile Brady (1923), re-investigating the isomeric dinitrobenzidines, suggested that the isomerism might be structural. This was clearly established as a correct view when Le Fèvre and Turner (1926) confirmed Brady's result that Cain's 3,5'-dinitrobenzidine was symmetrically substituted, and also showed that the 3,3'-dinitrobenzidine was, in fact, unsymmetrically substituted and was 2,3'-dinitrobenzidine. It was further shown that several of the Kaufler condensation products of benzidine contained free amino-groups; for example monophthalylbenzidine, the most fully investigated of the Kaufler compounds, was (A) and not (B). There was therefore no justification for retaining the Kaufler formula.



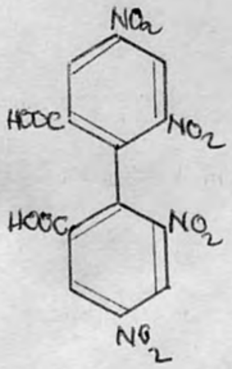
(A)



(B)

The only evidence in its favour which remained was Kenner's optical resolutions. (It is interesting to reflect on the outcome if Kenner had attempted the resolution of the Schultz acid in 1922). The problem now was to discover the cause of the peculiar optical isomerism in biphenyls.

By 1926, the following biphenyls had been resolved.



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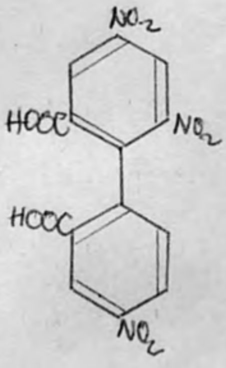

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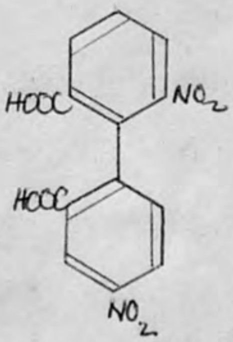
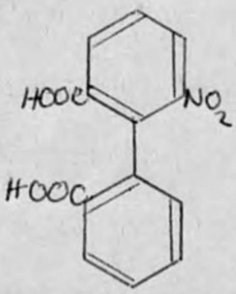
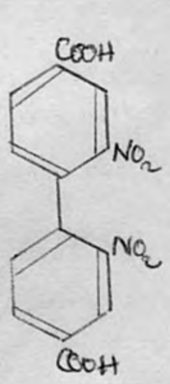


V

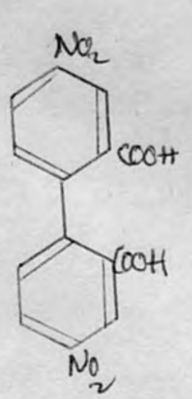


VI

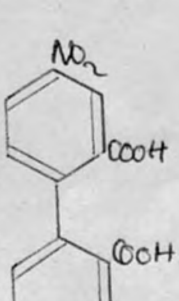
At the same time, however, many compounds chemically and structurally closely related to the above biphenyls were found to be non-resolvable (VII - XI).



VII



VIII



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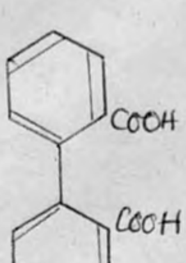
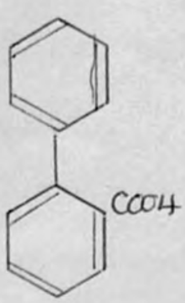


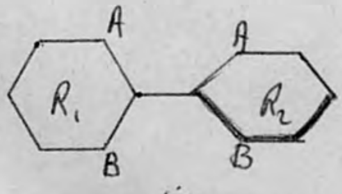
X



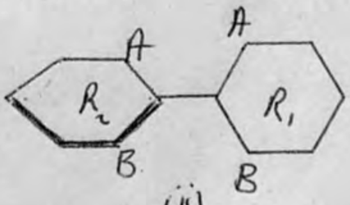
XI

That no specific effect of the $-NO_2$ or -COOH groups was involved was shown by the resolution of 6,6'-dichlorodiphenic acid (Christie, James and Kenner, J., 1923, 1948) and by the resolution of 2,2'-dimethyl-6,6'-diaminobiphenyl (Meisenheimer and Höring, Ber., 1927, 60, 1425). It thus became apparent that the isomerism was not due to the specific effect of any particular group in the ring.

The theory, put forward by Christie and Kenner (J., 1922, 121, 614), that the two rings in optically active biphenyl molecules were co-axial but non-coplanar, was generally accepted. It was assumed that the rings were at an angle to each other and diagrams (i) and (ii) represent two active forms of a substituted biphenyl which are mirror images but non-superimposable.



(i)

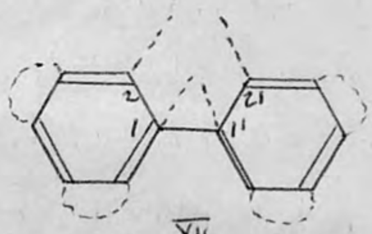


(ii)

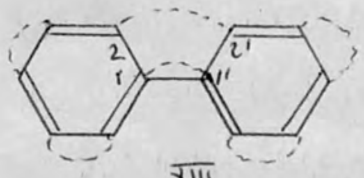
This theory, however, is not sufficient to explain the phenomenon since, if rotation about the single bond joining the two rings takes place, then the two rings could swing into a coplanar configuration and so destroy the asymmetry of the molecule. The rotation must therefore be restricted, a condition which was implied by Kenner.

It is a fundamental assumption in organic chemistry that two atoms joined by a single bond can have complete free rotation about the bond as an axis and yet, without restricted rotation, Kenner's view of a coaxial-noncoplanar model for substituted biphenyls is impossible. Inspection of compounds resolved by 1926 showed that all of them have three or four substituents in the 2,2',6,6' positions, whereas the non-resolvable compounds have two or less. This led to the theory of restricted rotation put forward almost simultaneously, in slightly different forms, by Turner and Le Fèvre (<u>Chem.and Ind</u>., 1926, <u>45</u>, 831), Bell and Kenyon (<u>ibid</u>., 1926, <u>45</u>, 864) and Mills (<u>ibid</u>., 1926, <u>45</u>, 884 and 905). The theory stated that substituents in the 2,2',6,6' positions in a biphenyl molecule can, by their interference, restrict the free rotation of the two nuclei around the common axis, and so prevent them from becoming coplanar.

The nature of the interference was attributed to various causes. Turner and Le Fèvre suggested that the cause was the electrical nature of the substituents, the residual affinity on each ring, and the internuclear forces. According to them, each carbon atom in the molecule possessed a certain amount of residual affinity. Carbon atoms 3,4,5, 6 and 3',4',5'6' would be mutually saturated in the Thiele sense as shown in XII. Since there was no reason to suppose that the distance between 1 and 1' was greater than that between atoms 1 and 2, some mutual saturation may occur between 1 and 1'. In this way the bond 1-1' became of the type existing in the benzene ring and the tendency for rotation somewhat restricted. Carbon atoms 2 and 2' would possess free affinity and this would tend to stabilise the planar configuration as shown in XIII



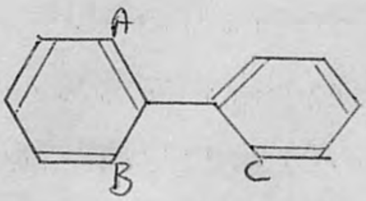
XII

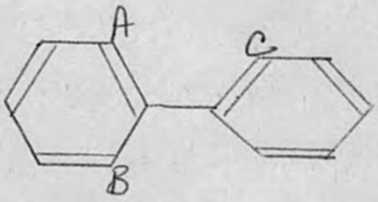


XIII

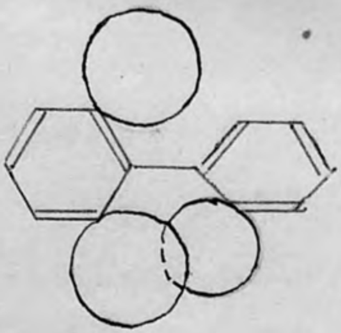
With a compound with mutually repelling forces, provided the repulsion is greater than the original attracting force between carbon atoms 2 and 2', distortion of the planar configuration may occur. One benzene ring would rotate about the common axis through an angle whose magnitude would be a function of the repulsive force.

Bell and Kenyon suggested that owing to their electrical characteristics or their size, or to both, two ortho groups A and B acted as "obstacles" to the passage of a third ortho group C on the other nucleus, thus preventing interconversion of the optical isomers.



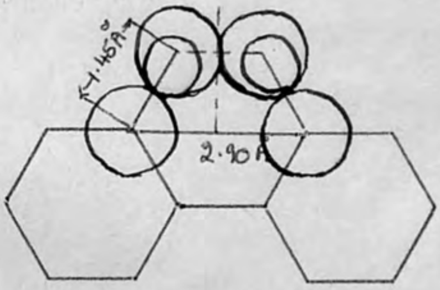


Mills, on the other hand, accepted the mechanical idea of steric hindrance caused by the bulk of the ortho-substituents alone. A model built up from the usual tetrahedra and drawn to scale, indicated that two bulky ortho substituents in the one ring would interfere with the free rotation of the second ring owing to collisions between them and the third substituent in the second ring. The obstacle or mechanical theory received

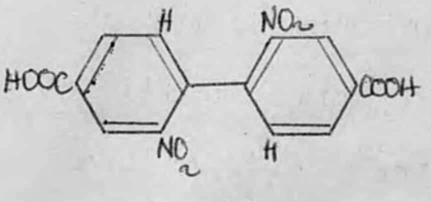


support from Kuhn, Mascarelli, Adams and others, and is now the generally accepted view.

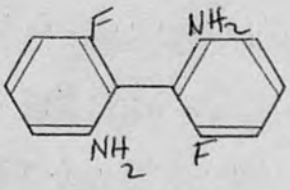
Data intended to permit definite predictions concerning the resolvability of biphenyls were first presented by Stanley and Adams (J.Amer.Chem.Soc., 1930, 52, 1200). On the obstacle theory, the amount of interference will be determined by the size of the substituent atoms or groups. This magnitude cannot be directly measured, but with the aid of certain assumptions it is possible to derive values which give a relative measure of the degree of interference. From X-ray data, internuclear distances between carbon and other atoms or groups were known, and these "slightly adjusted to bring them into line with aromatic compounds" were used by Adams.



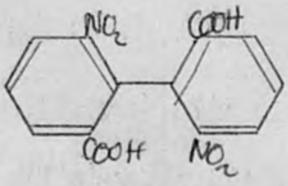
When a coplanar biphenyl molecule is drawn to scale, the distance between the 2 and 2' carbon atoms is found to be 2.90Å. The difference between this value, and the sum of the internuclear distances of the atoms or groups attached to the 2,2' carbon atoms was called the "Interference Value." Thus, a negative interference value would indicate a non-resolvable biphenyl; a small positive value, a resolvable but easily racemised compound, and a large interference value should indicate a compound which is resolvable but not easily racemised.



XIV



XV

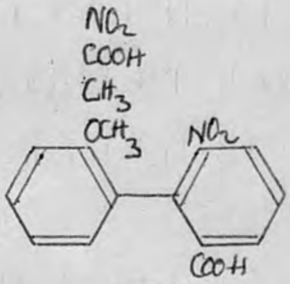


XVI

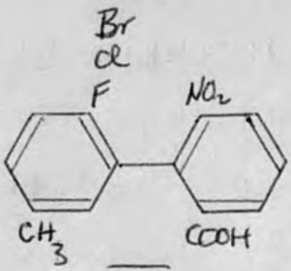
In the above compounds XIV was found to be non-resolvable, XV resolvable but easily racemised and XVI resolvable and non-racemisable. The interference value for each is -0.04, +0.05, +0.58 respectively.

Lesslie and Turner (J., 1932, 2021) predicted the resolvability of biphenyls by using models in which the atoms are drawn to scale as spheres. The models show that if an atom or group X of radius 1.18Å is present in both 2- and 2'-positions, the model can be arranged so that the two benzene nuclei are co-planar as well as co-axial. But X is then in contact with the hydrogen atom in position 6 and 6' which is only possible in a model but not in a molecule. Therefore, if X is of radius 1.18Å the molecule is non-planar and resolvable. Planar configuration would also be prevented if X were less than 1.18Å, e.g. 1.10Å, because it is unlikely that X would come within 0.1Å of the hydrogen atom.

In order to determine the relative interference of several groups in the ortho position, Adams and his students synthesised two sets of compounds, the 2-methoxy-methyl-, carboxyl- and nitro- derivatives of 2'-nitrobiphenyl-6'-carboxylic acid XVII and the 2-fluoro-chloro- and bromo-derivatives of 5-methyl-2'-nitrobiphenyl-6'-carboxylic acid XVIII.



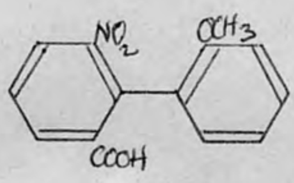
XVII



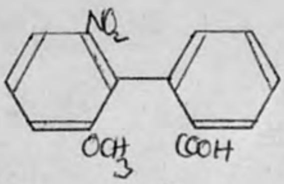
XVIII

[Hale & Adams, Unpublished results quoted by Yuan and Adams, Chem.Rev., 1933, XII, 261; Stoughton and Adams, J.Amer.Chem. Soc., 1932, 54, 4426]. They assumed that the methyl group in the 5-position would have little effect on the optical stability of the compounds and that a direct comparison of the two sets of compounds, on a semi-quantitative basis, was therefore permissible. Only one brucine salt of the methoxy- and fluoro-compounds was obtained, and both underwent mutarotation (the mutarotation of the fluoro-compound was not detected at room temperature, but at 0° it had a half-life period of 42 minutes.) The other five compounds were resolved, and the rates of racemisation determined on the active acids. From the half-life periods it appeared that the relative interference of these groups would be in the order $Br > CH_3 > Cl > NO_2 > COOH > OCH_3 > F$.

The relative size of the ortho-groups does not seem to be the only factor affecting the optical stability of the biphenyl compounds. From experiments, by Adams and his co-workers, it appeared that the positions of the groups relative to each other affected the optical stability. Adams and Finger (J.Amer.Chem.Soc., 1939, 61, 2828) prepared the three compounds, XIX-XXI, and resolved them.



XIX



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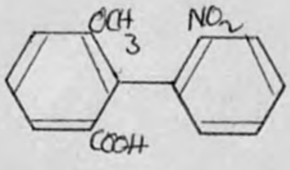
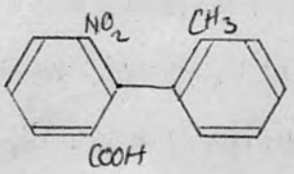
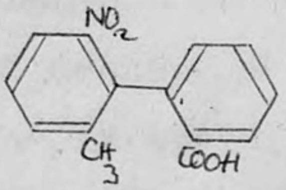


XXI

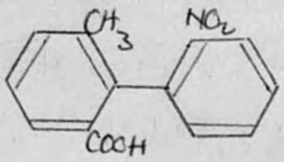
From the relative size of the substituents it was expected that XIX and XX would have approximately the same optical stability (since in each case there is collision between the two smaller substituents $-OCH_3$ and -COOH), and XXI should be the most stable. In fact XIX was found to be the least stable, whereas XX and XXI were considerably more stable. When the half-life periods were measured in absolute ethanol at 25^{o}, they were found to be 10.2, 219 and 271 minutes respectively. Similar anomalies were observed by Adams and Hale (J.Amer.Chem.Soc., 1939, 61, 2825) when they prepared XXII - XXIV. Thus, factors other than the size of the group must operate.



XXII

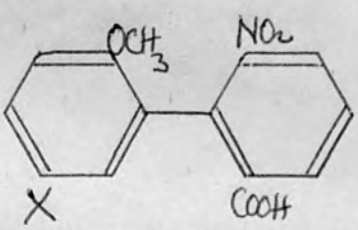


XXIII



XXIV

In order to determine the influence of substituents in positions other than the ortho, Yuan and Adams (J.Amer. Chem.Soc., 1932, 54, 4434) prepared a series of compounds of the type



where X was $-OCH_3$, $-CH_3$, -Cl, -Br or $-NO_2$. The unsubstituted 2'-methoxy-2-nitrobiphenyl-6-carboxylic acid had been resolved (Stoughton and Adams, ibid., 1932, 54, 4426) and found to have a half-life period of 9.4 minutes at 26°. Yuan and Adams now found that all the 5'-substituted acids were more stable than the unsubstituted acid, the order of stability being $NO_2 > Br > Cl > CH_3 > OCH_3$. The above authors suggested that the groups in the 5'-position in the biphenyl molecule could influence the stability of the molecule on account of one or more of the following causes:

"(1) The variation of the valency angle at which the ortho substituent on the ring is attached, thus changing the effective size of the group;

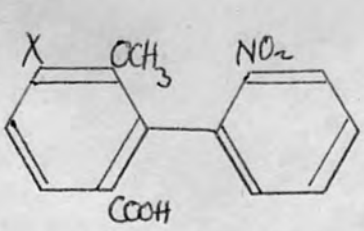
(2) the slowing down of the semi-circular oscillation of the two phenyl rings by substituents, thus diminishing the chances of the complete rotation;

(3) the modification of the distance between 1,1' carbon atoms with the nature of the substituents;

(4) the bending of the linkage between the two rings in such a way that the rings are no longer co-axial."

From the experimental results, however, it would appear that cause (2) is not a factor, since the substitution of two atoms of similar polarity but of different weight, such as chlorine and bromine, resulted in essentially identical effects on the rate of racemisation.

A similar series of compounds was prepared in which the groups were substituted in the 3'-position (Chien and Adams, J.Amer.Chem.Soc., 1934, 56, 1787).

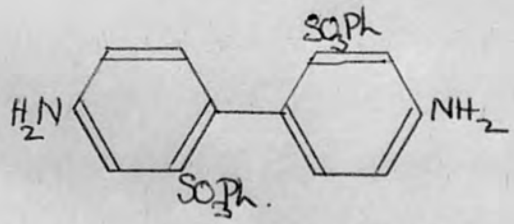


Again, X was -OCH$_3$, -CH$_3$, -Cl, -Br, -NO$_2$. The same order of stability in the 3'-substituted acids was observed, and in each case the 3'-compounds were more optically stable than the corresponding 5'-isomers. (From these experiments it was also shown that the solvent affected the rate of racemisation. The sodium salts of the 5'-substituted acids were found to be less optically stable in ethanolic solution than in aqueous solution.) The substituent in the 3'-position makes it more difficult for the methoxy group in the 2'-position to turn outwards and so more difficult for the molecule to turn through the coplanar form, which is necessary for racemisation.

2,2'-Disubstituted Biphenyls.

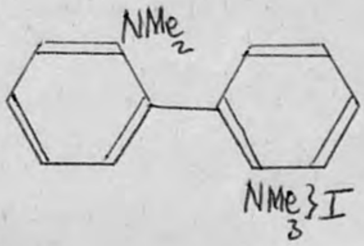
Bell and Robinson (J., 1927, 1695) pointed out the theoretical possibility of resolving 2,2'-disubstituted biphenyls as a logical consequence of the obstacle theory, and several compounds were subsequently resolved.

The first disubstituted biphenyl to be resolved was phenylbenzidine-2,2'-disulphonate (Lesslie and Turner, J., 1932, 2021). In this compound the sulphur atom attached



to the 2,2'-positions is itself attached to three other atoms. Consideration of a model of this molecule shows that if the sulphur atom carried only two oxygen atoms, these could swing away from the opposed 2'-hydrogen atom, but when there are three oxygen atoms attached to the sulphur, this cannot happen so readily, since, on an average, one of the oxygen atoms will be too close to the hydrogen atom. The asymmetry was ascribed to the "dynamic effect" of the $-SO_3Ph$ group. The same authors (J., 1932, 2394) also resolved biphenyl-2,2'-disulphonic acid. Both compounds were stable at room temperature but racemised quickly at 100°.

Another similar disubstituted biphenyl which was resolved was o-(2-dimethylaminophenyl)phenyltrimethylammonium iodide (Shaw and Turner, J., 1933, 135). Again, the asymmetry results from the dynamic effect of the $-NMe_3$ group. A cold aqueous solution of the active iodide retained its

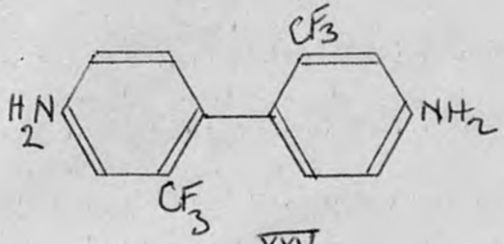


optical activity indefinitely, and at 99.5° the half-life period of racemisation was 125 minutes; it was considerably more stable than the disulphonic acid.

Among the first 2,2'-disubstituted biphenyl compounds to be studied which had single atoms as substituents, was 2,2'-diiodobiphenyl-4,4'-dicarboxylic acid (Searle and Adams, J.Amer.Chem.Soc., 1933, 1649). Using X-ray data (2.20Å for C-I distance) the "interference value" on each side of the molecule is approximately 0.12Å. The acid was resolved through its brucine salt which mutarotated in chloroform solution and had a half-life period of 70 minutes at 25°. The optically active acids racemised in dioxan with a half-life period of 91.3 minutes also at 25°.

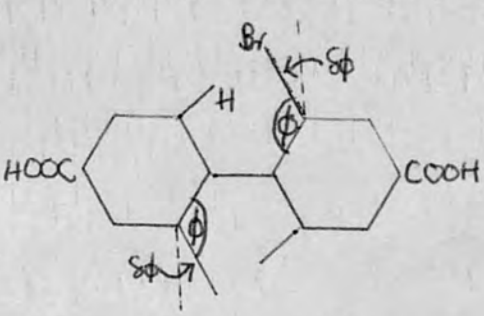
From the relative size of the atoms, it was expected that 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid (C-Br distance 2.11Å, interference value 0.075Å on each side of the molecule) should be resolvable but racemise more rapidly than the corresponding diiodo-acid. This was confirmed by the same authors (J.Amer.Chem.Soc., 1934, 2112) who resolved the dibromo-acid through the brucine salt. The optically active acids were obtained by decomposition of the salts at -65°. The mono- and di-brucine salts of the active acids, and the active acid itself had half-life periods in a 7:3 mixture of dioxan and methanol at 0° of 6.6, 8.1 and 10.7 minutes respectively. More recently rates of racemisation of this dibromo acid were determined over a range of temperatures by Harris (Proc.Chem.Soc., 1959, 367) who found the activation energy of racemisation to be 19.0 ± 0.5 k.cal/mole.

Another compound which has been investigated is 2,2'-bistrifluoromethylbenzidine (XXV) (Hall and Harris, ibid., 1959, 396). Its (+)-hydrogentartrate underwent second-order asymmetric transformation in 96% ethanolic solution, and a salt was obtained which had $[\alpha]_{5461}^{24.3}$ -20.5° in acetone. The base, obtained by decomposition of the salt with aqueous ammonia below 10°, had $[\alpha]_{5461}^{39.0}$ -0.84° (c 3.23 in ethanolic solution) and racemised at 39° with a half life period of 58.4 minutes. The authors considered that in effective size the group $-CF_3$ probably falls between $-CH_3$ and $-SO_3Ph$.



XXV

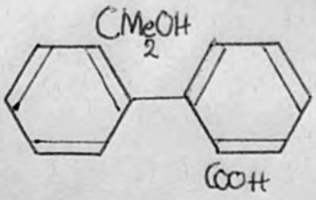
In 2,2'-disubstituted biphenyls, it has also been observed that groups in the 3- and 3'-positions affect the optical stability of a compound. Rieger and Westheimer (J.Amer.Chem.Soc., 1950, 19 and 28) resolved 2,2'-diiodo- and 2,3,2',3'-tetraiodo-5,5'-dicarboxylic acid, and compared their optical stabilities. The brucine salt of the diiodo-acid underwent second order asymmetric transformation in 95% ethanolic solution and from it the (-)-acid was obtained. From the tetraiodo-acid diastereoisomeric salts were isolated. Determination of the rates of racemisation of both acids showed that the diiodo-acid racemised 30,000 times faster than the tetraiodo-acid. The energy of activation for the diiodo- and tetraiodo-acids was found to be 21.6 and 28.5 kcal/mole respectively. The greater stability of the tetraiodo-compound was ascribed to the "buttressing effect" already observed by Adams (although he did not use this term) in the 3'-substituted 2'-methoxy-2-nitrobiphenyl-6-carboxylic acids. In calculating the activation energy of 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid theoretically, Westheimer et al.(J.Chem.Phys, 1946, 14, 733; 1947, 15, 252) included in their calculation an angle ϕ (XXVI) which increases by $\delta\phi$ to allow the molecule to become co-planar and so facilitate racemisation. They



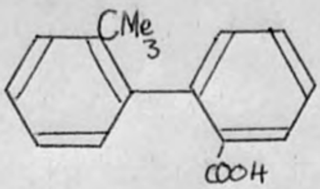
suggested that the group in the 3- and 3'-position would prevent the atom from moving through $\delta\phi$, and so make racemisation more difficult.

Similarly, attempts to resolve 2,2'-dimethylbenzidine having failed (P.Popper, Diplomarb., Hannover 1951), Theilacker and Hopp (Ber., 1959, 92, 2293) prepared 2,3,2',3'-tetramethylbenzidine and resolved it through its (+)-α-bromocamphorsulphonate. The diastereoisomeric salts showed mutarotation in 60% acetone solution and had a half-life period of 5 hours at room temperature. They determined the energy of activation and found it to be 17.7 kcal/mole. [The lowest activation energy observed for a resolvable compound is 14.9 kcal/mole obtained for 2'-fluoro-6-methyl-N-benzoylbiphenylamine-2-carboxylic acid (Brooks, Harris and Howlett, J., 1947, 2380)].

Corbellini and Angeletti (Atti.Accad.naz.Lincei, Rend.Classe Sci.fis.mat.nat., 1932, 15, 968) found that the brucine salt of 2'-(α-hydroxyisopropyl)-biphenyl-2-carboxylic acid (XXVII) underwent second-order asymmetric transformation in ethanolic solution and later Jamison and Turner (J., 1942, 437) showed that it also underwent first-order asymmetric transformation in chloroform solution. Recently, Lesslie (J., 1961, 611) prepared 2-t-butylbiphenyl-2'-carboxylic acid (XXVIII), and found that its brucine salt underwent second-order asymmetric transformation in ethanolic solution; no first-order transformation was observed. The active (-)-acid racemised in ethanolic solution at 57°, 67° and 79° with half-life periods of 35, 14.1 and 5.6 minutes respectively and the energy of activation was found to be 24 kcal./mole.



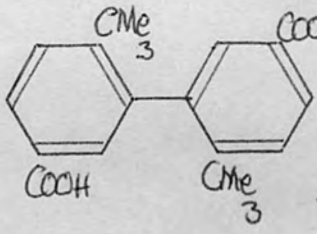
XXVII



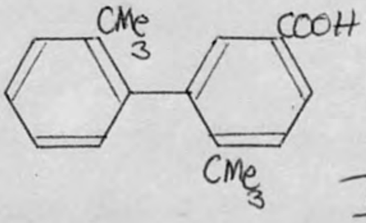
XXVIII

DISCUSSION.

The following compounds have now been prepared and resolved.



I



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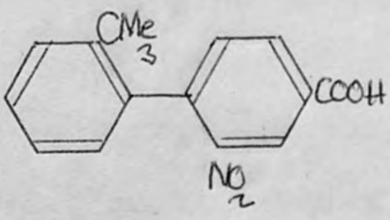
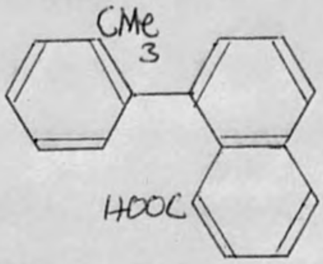
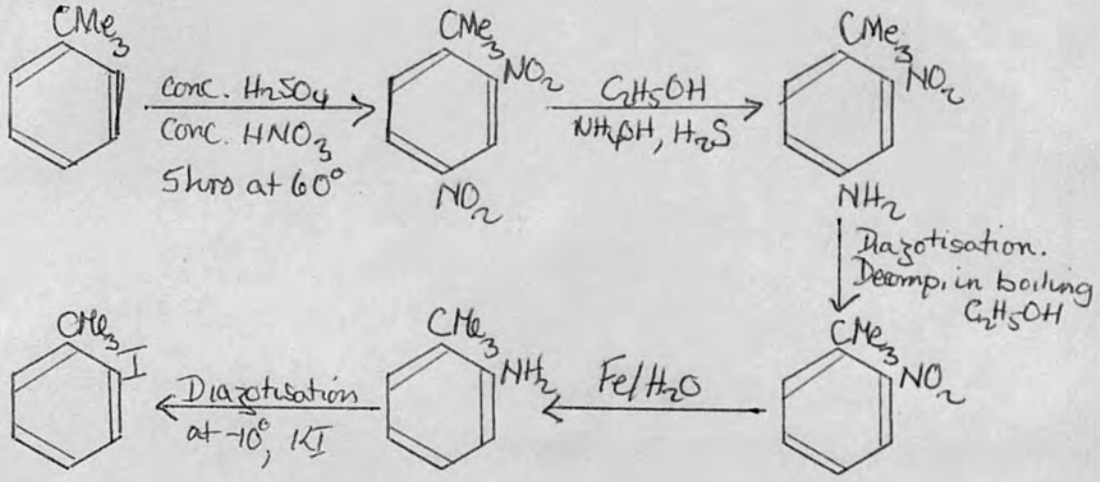


III



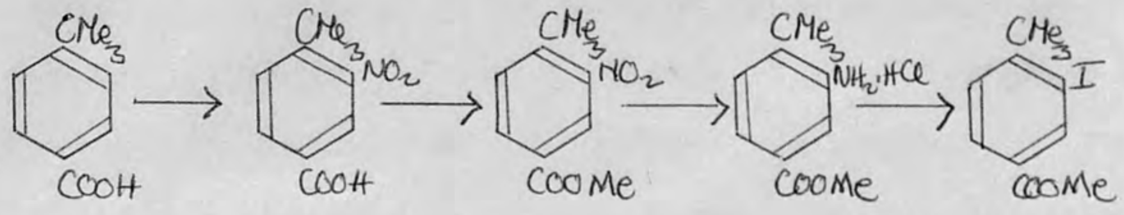
IV

The synthesis of these compounds was effected by heating with copper bronze a mixture of *o*-iodo-t-butylbenzene (or a derivative) and the appropriately substituted halogeno-benzene (or naphthalene) (the Ullmann reaction), and large quantities of *o*-iodo-t-butylbenzene and methyl (or ethyl) 3-iodo-4-t-butylbenzoate were therefore required. The former was prepared in small yield by Shoesmith amd Mackie (*J.*, 1928, 2334) by the following route:



The same route was followed in the present work but with considerable modifications which greatly enhanced the yields at each stage. t-Butylbenzene was nitrated with fuming nitric acid and after heating for 15 minutes at 60° gave 2,4-dinitro-t-butylbenzene (80%). This was reduced with an aqueous solution of sodium disulphide and the resulting nitro-amine (71%) was deaminated either by the hypophosphorous acid method (75%) or through the diazonium fluoroborate (56%). During the diazotisation of o-amino-t-butylbenzene decomposition of the diazonium sulphate set in at -8°. The diazotisation was therefore performed at -35°, the reaction mixture was allowed to warm up (in the freezing solution) to -13°, then added to aqueous potassium iodide solution. By this procedure o-iodo-t-butylbenzene was obtained in 60% yield.

Methyl 3-iodo-4-t-butylbenzoate was synthesised by the following series of reactions:



(In the early stages of the present investigation p-t-butylbenzoic acid was prepared from p-t-butylacetophenone, but later the commercial product was used). The preparation of the iodo-ester from the amine hydrochloride presented unexpected difficulty because of the instability of the diazonium salt.

The crude methyl iodo-ester was a green viscous oil: it was distilled under reduced pressure and appeared to be homogeneous. Addition of light petroleum produced a wax-like solid which crystallised from light petroleum and was actually a 1:1 molecular compound of the iodo-ester and methyl 3-hydroxy-4-t-butylbenzoate. The iodo-ester, a liquid at room temperature (m.p.~12°), was obtained from the light petroleum mother-liquors after all the molecular compound had been removed. It is surprising that the molecular compound behaved as if it were an individual substance, and that in ethereal solution it did not yield the phenolic component when extracted with cold alkali. On the other hand, when the solid compound was stirred with a cold aqueous solution of sodium hydroxide (30%) or warmed with an aqueous solution of sodium hydroxide (10%), a mixture of the iodo-ester and sodium 3-hydroxy-4-t-butylbenzoate was obtained. By this method the iodo-ester was recovered from the molecular compound. It was then hydrolysed, the iodo-acid was purified by crystallisation from methanol and then converted into its methyl ester. In later preparations the solid compound was not isolated but the oil obtained from the vacuum-distillation was stirred with successive amounts of cold concentrated sodium hydroxide solution and the sodium salt of the hydroxy-acid was removed by repeated washing with water. The iodo-ester was obtained pure by the method just described.

Ethyl 3-amino-4-t-butylbenzoate hydrochloride was also prepared. The diazonium chloride derived from it was also very unstable but there was no evidence of compound formation between the iodo- and the hydroxy-esters. Extraction with alkali failed to remove the hydroxy-ester from the ethereal solution of the crude iodo-ester, but on removal of the solvent, a mixture of the two solid esters was obtained. These were easily separated by crystallisation from ethanol in which the hydroxy-ester was very soluble.

The dimethyl and diethyl esters of 6,6'-di-t-butylbiphenyl-3,3'-dicarboxylic acid (I) were prepared by heating the appropriate iodo-esters with copper bronze at 245°, and the acid was obtained from these by hydrolysis with ethanolic potassium ethoxide.

The dicarboxylic acid was resolved through its brucine salt, which was prepared in ethanol. The salt of the (+)-acid separated as rosettes of thin rectangular plates: after concentration of the mother-liquor the (-)-acid salt was obtained as a gel. The free acids were obtained having $[\alpha]_{5791}$ $\pm 18.3^\circ$ ($\pm 0.3^\circ$) and $[\alpha]_{5461}$ $\pm 24.1^\circ$ ($\pm 0.1^\circ$) in acetone and showed high optical stability. Scale models based on known atomic radii show that in the above di-t-butylbiphenyl acid, the two tertiary butyl groups cannot pass the hydrogens in the 2,2'-positions.

Several attempts were made to decarboxylate the (±)-acid in order to obtain the hydrocarbon, 2,2'-di-t-butylbiphenyl.

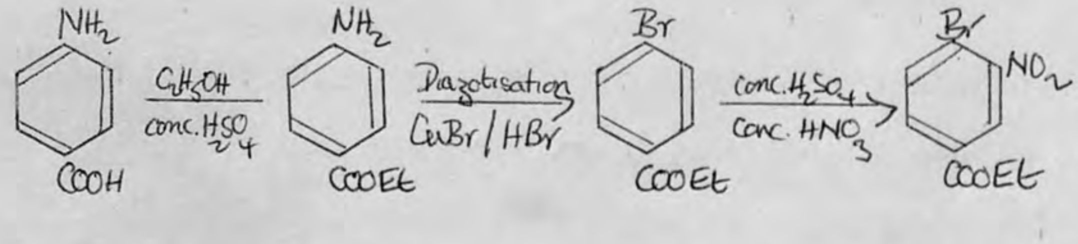
The acid was recovered unchanged after it had been heated in quinoline solution with copper bronze for several hours, and also after heating with hydroxylamine hydrochloride and polyphosphoric acid (a method suggested by Snyder, Elston and Kellan, <u>J.Amer.Chem.Soc.</u>, 1953, <u>75</u>, 2014 and which was successful in the decarboxylation of many substituted benzoic acids). Attempts to obtain the dibromo-compound from the silver salt of the (±)-acid were also unsuccessful.

The acid reacted readily with thionyl chloride to give the acid chloride and this with ammonia gave the diamide. Conversion of the diamide into the diamine by the Hofmann reaction could not be achieved. The diamide was recovered unchanged after heating it in potassium hypobromite solution for 45 minutes at 75°, and also after heating under reflux with sodium hypobromite or sodium hypochlorite solution. It did not react with sodium methoxide and bromine to give the mrethane (a variation of the Hofmann reaction). The Schmidt reaction, however, performed on the acid was successful and the crude diamine was extracted with benzene from the reaction mixture, and purified by passing the solution through a column of alumina. The diamine was then tetrazotised and deaminated with hypophosphorous acid and the hydrocarbon obtained. The specific rotations of the hydrocarbon obtained from the optically active acids were $[\alpha]_{5791}$ $\pm 18.0^\circ$ ($\pm 0.2^\circ$) and $[\alpha]_{5461}$ $\pm 22.0^\circ$($\pm 0.3^\circ$) in acetone solution.

The methyl ester of 2'6-di-t-butylbiphenyl-3-carboxylic acid (II) was prepared by heating equi-molecular proportions of methyl 3-iodo-4-t-butylbenzoate and *o*-iodo-t-butylbenzene with copper bronze. The products were partially separated by distillation under reduced pressure, the main fraction consisting of a mixture of 2,2'-di-t-butylbiphenyl and the required ester. This was hydrolysed with ethanolic potassium ethoxide and the hydrocarbon removed by extraction with ether. The unsymmetrical acid was then obtained on acidification of the alkaline solution in 9.2% yield. It was converted into its strychnine salt and the two diastereoisomers were separated by crystallisation from ethanol. The (+)-acid salt was crystalline and was readily obtained optically pure, whereas the (-)-acid salt was an oil. The (±)-acid, however, was more sparingly soluble than the active acids, and the crude (-)-acid obtained from the oil was isolated optically pure by fractional crystallisation from methanol. The acids had $[\alpha]_{5791}$ $\pm 25.6^\circ (\pm 0.2^\circ)$ and $[\alpha]_{5461}$ $\pm 28.3^\circ (\pm 0.1^\circ)$ in chloroform. The optically active acid had high optical stability and retained its activity after sublimation at 130°/1 mm. and even after melting.

Attempts were made to prepare 2'-nitro-6-t-butylbiphenyl-3-carboxylic acid by heating with copper bronze equimolecular amounts of methyl 3-iodo-4-t-butylbenzoate and o-chloronitrobenzene, but it was obtained in very low yields. One probable explanation for this result was the extreme ease with which the methyl ester underwent dehalogenation by the copper bronze to give methyl p-t-butylbenzoate. This was easily removed by distillation under reduced pressure of the Ullmann reaction product but the esters of the symmetrical di-t-butylbiphenyl acid and the required unsymmetrical acid could not be separated. The mixture of esters was therefore hydrolysed and the acids were eventually separated by fractional crystallisation from glacial acetic acid, but it was a wasteful process as the difference in solubility of the two acids was very slight. From 180g. of the iodo-ester, less than 2g. of the pure acid were obtained and this synthesis was therefore abandoned.

In order to obtain a similar biphenyl compound with a nitro-group in the ortho-position ethyl 3-nitro-4-bromobenzoate was prepared by the following route:



This synthesis was parallel to that used by Searle and Adams (J.Amer.Chem.Soc., 1933, 55, 1649) for the preparation of ethyl 3-nitro-4-iodobenzoate. The ethyl ester of the bromo-nitro-acid was heated with an equimolecular proportion of o-iodo-t-butylbenzene and copper bronze, and the products were partially separated by vacuum-distillation. The residue of the distillation was hydrolysed and was a mixture of the required acid 2'-t-butyl-6-nitrobiphenyl-4-carboxylic acid (III), and the symmetrical dinitro-acid. The mixture was extracted in a Soxhlet apparatus with benzene, in which the symmetrical dinitro-acid was insoluble. The benzene solution was passed through a column of silica gel and eluted with benzene. The solvent was removed from the eluates collected, and a pale yellow solid was obtained which, on recrystallisation from light petroleum (b.p. 40-60°), gave the required acid, m.p. 150-151° in 6% yield. A negligible amount of this acid was obtained if the temperature of the Ullmann reaction mixture was allowed to rise above 240°, since above that temperature partial reduction of the $-NO_2$ group by the copper bronze occurred (Fuson and Cleveland, Org.Synth., 1940, 20, 45).

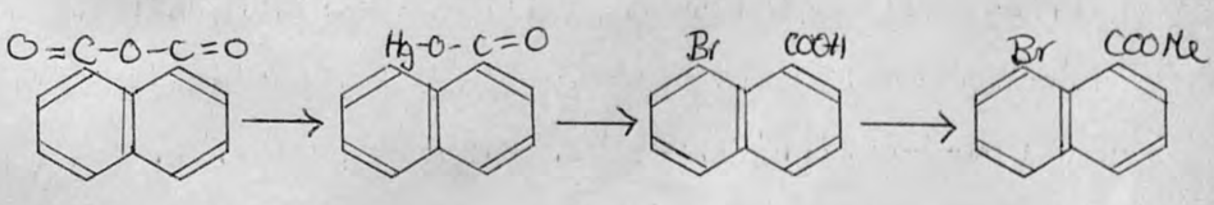
The strychnine salt of 2'-t-butyl-6-nitrobiphenyl-4-carboxylic acid was prepared in ethanol and a series of crops was obtained whose rotations in chloroform were $[\alpha]_{5791} +14.7^\circ$, and $[\alpha]_{5461} +18.7^\circ$ ($\pm 0.5^\circ$). The acid recovered from these salts was dextrorotatory and it was thus apparent that the strychnine salt had undergone second-order asymmetric transformation. The salt mutarotated in boiling chloroform solution during 2 hours and slowly at room temperature during 14 days to give the partial racemate, $[\alpha]_{5791} -2.8^\circ$ and $[\alpha]_{5461} -4.1^\circ$.

Racemisation of the (+)-acid in toluene was studied at several temperatures, between 51° and 75°, and from the rates of racemisation, the energy of activation (E) was found to be 25.4 kcal.mole^{-1}. The half-life periods at these temperatures are given in the table below:

Temperature	51.0°	55.8°	60.5°	64.2°	70.1°	75.2°
Half-life period in minutes	199.7	109.8	73.0	45.5	24.6	14.5

Methyl 8-(2'-t-butylphenyl)-1-naphthoate was prepared by heating an equimolecular mixture of methyl 8-bromo-1-naphthoate and *o*-iodo-t-butylbenzene with copper bronze at 220°.

Methyl 8-bromo-1-naphthoate was prepared by the method of Rule *et al*. (*J*., 1932, 175; *ibid*., 1934, 168).



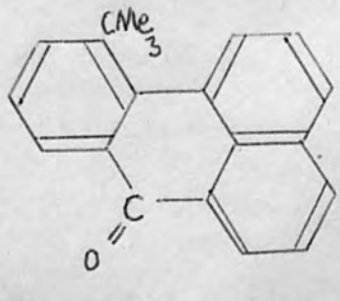
Naphthalic anhydride in a solution of aqueous sodium hydroxide was heated under reflux for 15 minutes. A solution of mercuric oxide in acetic acid was then added to the alkaline solution, the mixture was acidified with acetic acid and then heated under reflux for 80 hours.

To a suspension of the mercurihydroxy-compound in acetic acid was added a solution of bromine in aqueous sodium bromide solution, and the bromo-acid so formed was esterified through the acid chloride.

The products of the Ullmann reaction were extracted with chlorobenzene, and after the solvent had been removed, crude dimethyl 1,1'-binaphthyl-8,8'-dicarboxylate crystallised. This was filtered off and the residue was distilled under reduced pressure. The residue of the vacuum distillation contained the required ester. This was hydrolysed with a solution of potassium hydroxide in amyl alcohol, since the ester was recovered unchanged after heating with ethanolic potassium ethoxide solution for 3 hours.

8-(2'-t-butylphenyl)-1-naphthoic acid (IV) was resolved through its strychnine salt. The salt was formed in ethanol from which the (+)-acid salt crystallised in rosettes of rectangular plates, $[\alpha]_{5791}$ -14.5° and $[\alpha]_{5461}$ -19.9° in chloroform. On evaporation of the mother-liquor to dryness a solid was obtained which was recrystallised from acetone and gave the (-)-acid salt, $[\alpha]_{5791}$ -87.7° and $[\alpha]_{5461}$ -100.7° in chloroform. The free acids were obtained having $[\alpha]_{5791}$ $\pm 44.5^\circ$ and $[\alpha]_{5461}$ $\pm 49.8^\circ$ ($\pm 0.2^\circ$) in chloroform. Racemisation of the optically active acids was studied at temperatures between 121° and 136° in ethylbenzene, and from these the energy of activation E, was found to be 29 kcal.mole^{-1}. It is interesting to note how very much more stable this acid was than the 2'-t-butylbiphenyl-2-carboxylic acid which was investigated by Lesslie (J., 1961, 61). It had E = 24 kcal.mole^{-1}.

In an attempt to decarboxylate the above naphthoic acid by the Schmidt reaction, it was observed that as soon as the acid was dissolved in ice-cold concentrated sulphuric acid, a red solution was obtained. When this sulphuric acid solution was poured on ice a yellow solid was precipitated, which was 7-oxo-11-t-butylbenz[de]anthracene (V) cyclisation having occurred.



V

The reaction was repeated on the (+)-acid and the product was found to be optically inactive, thus showing that in (V) the molecule is quite flat.

EXPERIMENTAL.

Preparation of o-Iodo-t-butylbenzene.

2,4-Dinitro-t-butylbenzene.

t-Butylbenzene (100g.) was slowly added, with stirring, to fuming nitric acid (d. 1.51, 500 ml.) at 0° within 45 minutes. The temperature of the reaction mixture was kept below 40° during the addition. The solution was then heated on a water-bath at 60-65° for 15 minutes and poured on crushed ice. The crude dinitro-compound was filtered off, melted under boiling water (3 l.), and cooled quickly with vigorous stirring. The solid was filtered off and after crystallisation from ethanol, the dinitro-t-butylbenzene was obtained (134g., 80%), m.p. 61-63°.

3-Nitro-4-t-butylaniline.

A solution of sodium disulphide was prepared by adding sulphur (26g.) to a boiling solution of sodium sulphide (96g.) in water (200 ml.), boiling the mixture until the solution was clear. It was then added to a vigorously stirred suspension of 2,4-dinitro-t-butylbenzene (44.8g.) in boiling water (500 ml.). The mixture was boiled with stirring for a further 1½ hours, the volume of the water being maintained, and then filtered hot. The filtrate was cooled in ice and the crude nitro-amine filtered off. It was boiled with concentrated hydrochloric acid and sufficient hot water added to dissolve the precipitated hydrochloride. The hot solution was filtered and allowed to cool, when the hydrochloride crystallised. It was filtered off, washed with ether and dried at 100°. The mother-liquor of the hydrochloride was washed with ether several times, the ethereal solution dried, and the solvent removed. Unchanged dinitro-compound was recovered (6g.).

The crystalline hydrochloride was dissolved in hot water and concentrated aqueous ammonia added, and the amine was precipitated. More of the amine was obtained by adding ammonia to the hydrochloride mother-liquor. The crude amine was crystallised from ethanol from which it separated as small yellow plates (27.5g., 71%), m.p.56-57°.

o-Nitro-butylbenzene.

(a) 3-Nitro-4-t-butylaniline (66g.) was diazotised in concentrated hydrochloric acid, between -5° and 2°, and the solution allowed to stand for one hour at 2° (this was essential otherwise diazotisation was incomplete). The diazonium solution was then filtered and excess hydrogen fluoroborate was added. The precipitated diazonium fluoroborate was filtered off, washed with ether, and dried *in vacuo* over calcium chloride.

To decompose the fluoroborate (80g.), it was added gradually to a boiling mixture of concentrated sulphuric acid (32g.) and ethanol (160g.) and boiled under reflux until the reaction was complete. The mixture was then poured into a large excess of water, and the nitrohydrocarbon extracted with ether. The ethereal extract was washed with aqueous sodium hydroxide solution (10%) and with water, then dried over calcium chloride. The ether was removed and the residue distilled. o-Nitro-t-butylbenzene was obtained, b.p. 94-98°/2mm. (34.2g., 56%).

(b) The nitroaniline (60g.) was diazotised as above and the filtered diazonium solution was added, with stirring, to hypophosphorous acid (600 ml.) at 0°, the temperature being maintained below 5°. The mixture was left to stand overnight at 4°, and the nitro-compound was then extracted with ether. The ethereal solution was washed with aqueous sodium hydroxide solution (10%) and with water, then dried over calcium chloride. After the solvent had been removed the residue was distilled and the o-nitro-t-butylbenzene was obtained (45.7g., 75%).

o-t-Butylaniline.

o-Nitro-t-butylbenzene (35g.) was added slowly to a suspension of iron filings (35g.) in boiling water containing a little acetic acid. The mixture was boiled under reflux for $5\frac{1}{2}$ hours, after which time the reaction was complete. The amine was extracted with boiling ethanol (containing a little ammonia) which was then removed by distillation from the filtered extract. The residue was poured into concentrated hydrochloric acid and diluted with sufficient water to dissolve the precipitated amine-hydrochloride. The solution was washed with ether to remove any unchanged nitro-compound, and the base was liberated as an oil by the addition of concentrated aqueous ammonia. The amine was extracted with ether, the ethereal extract was washed with water, and dried over potassium carbonate. After removal of the ether, the amine was distilled under reduced pressure and obtained as a yellow oil, b.p. $80-86^{\circ}$/2mm. (23g., 79%).

o-Iodo-t-butylbenzene.

o-t-Butylaniline (22g.) was dissolved in dilute sulphuric acid (*d* 1.2, 120 ml.) and the solution cooled to -35° in a freezing solution (carbon dioxide and ethanol). A concentrated aqueous solution of sodium nitrite (10.4g.) was added within 10 minutes and the reaction mixture allowed to warm up to -15° in the freezing solution. The resultant gelatinous mixture was added to aqueous potassium iodide solution (20g. in 40 ml. water), and then allowed to stand until decomposition of the diazonium iodide was complete. The mixture was made alkaline with sodium hydroxide solution and the crude iodo-hydrocarbon from two similar experiments was steam-distilled. The distillate was extracted with ether, and the ethereal extract was washed successively with dilute hydrochloric acid, sodium metabisulphite solution and with water, then dried over calcium chloride. The ether was removed and the residue was distilled under reduced pressure. o-Iodo-t-butylbenzene was obtained, b.p. 104-111°/9mm. (46g., 60%).

Preparation of Methyl-3-Iodo-4-t-butylbenzoate.

p-t-Butylacetophenone.

(Mowry, Renoll and Huber, J.Amer.Chem.Soc., 1946, 68, 1105).

To a suspension of anhydrous aluminium chloride (150g.) and dry carbon tetrachloride (1000ml.) cooled in ice, acetyl chloride (73g.) was added during 15 minutes, with vigorous stirring. The t-butylbenzene (121g.) was added dropwise over a period of $2\frac{1}{2}$ hours, keeping the temperature below 5°. The stirring was continued for a further $2\frac{1}{2}$ hours after the addition was complete. Hydrolysis of the product was effected by adding the reaction mixture to ice and hydrochloric acid. The carbon tetrachloride solution was washed successively with dilute hydrochloric acid, aqueous sodium carbonate solution and water, and dried over calcium chloride. It was then distilled through a 50cm. Vigreux column, the carbon tetrachloride was removed, and the p-t-butylacetophenone was collected, b.p. 84-86°/4mm. (117g., 74%).

p-t-Butylbenzoic acid.

(Price and Lincoln, J.Amer.Chem.Soc., 1951, 73, 5836)

p-t-Butylacetophenone (116g.) was addėd dropwise to a well-stirred solution of potassium hypochlorite which was prepared as follows. To calcium hypochlorite (667g.) dissolved in water (2667 ml.) was added a mixture of potassium hydroxide (133g.) and potassium carbonate (467g.) dissolved in water (1333 ml.). The precipitated calcium carbonate was filtered off and the hypochlorite solution used at once. The ketone reacted vigorously and when addition was complete the acid was precipitated by acidification with dilute hydrochloric acid. It was purified by crystallisation from aqueous methanol from which it separated in colourless small prisms, m.p. 166° (72g., 61%).

3-Nitro-4-t-butylbenzoic acid.

p-t-Butylbenzoic acid (100g.) was slowly added to ice-cold fuming nitric acid (1000g., d 1.51). During the addition, the temperature of the mixture was kept between 0-5°. It was then heated on a water-bath at 55-60° for 15 minutes and poured on crushed ice. The crude nitro-acid was filtered off, and crystallised from dilute acetic acid. It separated in almost colourless small prisms, m.p.162-163° (104g., 83%). It was sensitive to light and on exposure became orange-yellow.

Methyl 3-nitro-4-t-butylbenzoate.

3-Nitro-4-t-butylbenzoic acid (100g.) in absolute methanol (1000 ml.) and concentrated sulphuric acid (50g.) was heated under reflux for six hours. When cool, the mixture was poured into water, and the precipitated ester was filtered off, washed with sodium carbonate solution and with water. It was crystallised from methanol and separated as colourless plates, m.p. 45-46°, (98g., 92%).

Occasionally the ester did not solidify when the reaction mixture was poured into the water. It was then extracted with ether from the aqueous suspension and the ethereal extracts were washed with sodium carbonate solution and with water, and dried over calcium chloride. The ether was removed, and the residue was distilled under reduced pressure to give the ester, b.p. 150°/2mm. It solidified and was purified by crystallisation from methanol.

Methyl 3-amino-4-t-butylbenzoate hydrochloride.

Methyl 3-nitro-4-t-butylbenzoate (100g.) was added slowly to a suspension of iron filings (100g.) in boiling water containing a little acetic acid. The mixture was heated on a boiling water-bath for 3½ hours, after which time the reaction was complete. The base was extracted with boiling ethanol (containing a little ammonia) and the filtered extract freed from the solvent by distillation. The residue was poured into ice-cold concentrated hydrochloric acid, and the precipitated hydrochloride filtered off, washed with ether, and dried. It crystallised readily from methanol, m.p. 198-200° but usually recrystallisation was unnecessary.

The crude hydrochloride mother-liquor was extracted with ether to remove any nitro-compound that might be present, basified with ammonia (0.88) and the precipitated amine extracted with ether. The ethereal solution was washed with water and dried over anhydrous sodium sulphate. After removal of the ether, the residue was poured into ice-cold concentrated hydrochloric acid and more of the hydrochloride was obtained. The base hydrochloride was obtained in 93% yield.

Methyl 3-iodo-4-t-butylbenzoate.

The above hydrochloride (48g.) was diazotised in concentrated hydrochloric (30 ml.) and water (30 ml.) with a concentrated aqueous solution of sodium nitrite (13.8 g.) at -20° to -10°. The diazonium solution was then added to an aqueous solution of potassium iodide (50g. in 80 ml. water), with shaking, and the mixture allowed to stand overnight. The resultant oil which contained some low-melting solid was extracted with ether, the ethereal solution was washed repeatedly with alkali, then successively with sodium metabisulphite solution, acid, and water, and dried over calcium chloride. The ether was distilled off, and the residue was distilled under reduced pressure. A green oil was obtained, b.p. 164-165°/10mm., which, on addition of a few drops of light petroleum (b.p. 40-60°) solidified to give a wax-like solid. On crystallising the solid from light petroleum it separated in fine needles, m.p. 58-59°, and was the 1:1 molecular compound of the iodo-ester and methyl 3-hydroxy-4-t-butylbenzoate. The iodo-ester was recovered from the molecular compound by stirring it with cold aqueous sodium hydroxide solution (30%) and extracting the iodo-ester with ether to separate it from the sodium t-butylhydroxybenzoate. More of the iodo-ester was obtained similarly from the residues of the crystallisation mother-liquors.

Alternatively, the green oil, obtained from the vacuum-distillation of the crude "iodo"-product, was stirred with cold alkali until free of the hydroxy-compound and the iodo-ester was extracted with ether from the mixture. After removal of the solvent, the residue was hydrolysed with ethanolic potassium ethoxide and the acid obtained was crystallised from methanol.

3-Iodo-4-t-butylbenzoic acid crystallised in colourless needles, m.p. 202-203° (Found: C, 43.5; H, 4.4. $C_{11}H_{13}IO_2$ requires C, 43.4; H, 4.3%). The pure iodo-acid was converted into its methyl-ester which had b.p. 156-158°/4mm., m.p. $\sim$ 12°.

Preparation of Ethyl 3-Iodo-4-t-butylbenzoate.

Ethyl 3-nitro-4-t-butylbenzoate.

3-Nitro-4-t-butylbenzoic acid (100g.) was heated under reflux in a solution of ethanol (500g.) and concentrated sulphuric acid (50g.) for 6 hours. After cooling, the mixture was poured into water and the oil was extracted with ether. The ethereal solution was washed with aqueous sodium carbonate solution, and with water, and then dried over calcium chloride. After removing the ether, the residue was distilled under reduced pressure.

Ethyl 3-nitro-4-t-butylbenzoate, b.p. 162-164°/5mm., crystallised from ethanol in colourless plate, m.p. 22-24° (Found: C, 62.1; H, 6.7. $C_{13}H_{17}NO_4$ requires C, 62.1; H, 6.8%).

Ethyl 3-amino-4-t-butylbenzoate hydrochloride.

The above nitro-ester (75g.) was reduced with iron filings (75g.) suspended in boiling water containing a little glacial acetic acid. On completion of the reaction, the reduction mixture was extracted with boiling ethanol, the solution was filtered, and the solvent removed. The residue was poured into ice-cold concentrated hydrochloric acid and the precipitated hydrochloride was filtered off and washed with ether. The mother-liquor was extracted with ether, basified with ammonia and the precipitated base was extracted with ether. The ethereal solution was dried over anhydrous sodium sulphate, the solvent removed by distillation and the residue distilled under reduced pressure. The amine thus obtained was converted into the hydrochloride. The total yield of the ethyl ester base hydrochloride was 57.5g. (77%).

The hydrochloride was readily soluble in most organic solvents and crystallisation from dilute hydrochloric acid resulted in hydrolysis of the ester to give 3-amino-4-t-butylbenzoic acid hydrochloride, m.p. 238-239° (decomp.) (Found: C, 57.5; H, 6.8; Cl, 15.2. $C_{11}H_{16}ClNO_2$ requires C, 57.5; H, 6.9; Cl, 15.4%). Since an analytically pure sample of the ethyl ester base hydrochloride could not be obtained, a portion of it was converted into the free base.

Ethyl 3-amino-4-t-butylbenzoate was a viscous oil, b.p. 160°/4mm. (Found: C, 70.6; H, 9.3. $C_{13}H_{19}NO_2$ requires C, 70.6; H, 8.7%).

Ethyl 3-iodo-4-t-butylbenzoate.

Ethyl 3-amino-4-t-butylbenzoate hydrochloride (26g.) was diazotised in hydrochloric acid at -20°. The temperature of the mixture was allowed to rise to -10° and then poured into an aqueous solution of potassium iodide (25g. in 40 ml.water). When effervescence had ceased, the mixture was extracted with ether, and the ethereal solution was washed repeatedly with aqueous sodium hydroxide solution (10%), then successively with dilute hydrochloric acid, an aqueous solution of sodium metabisulphite, and water, and dried over calcium chloride. (A negligible amount (0.5g.) of hydroxy-acid was recovered from the sodium hydroxide solution extracts). After removing the solvent from the ethereal solution, a sticky solid was obtained, which was crystallised from ethanol.

Ethyl 3-iodo-4-t-butylbenzoate crystallised from ethanol in colourless rectangular prisms, m.p. 58-59° (Found: C, 47.1; H, 4.9. $C_{13}H_{17}IO_2$ requires C, 47.0; H, 5.2%).

Concentration of the crystallisation mother-liquors yielded more of the ethyl iodo-ester and finally the ethyl hydroxy-ester which, on treatment with cold aqueous sodium hydroxide solution (30%), followed by acidification, gave the 3-hydroxy-4-t-butylbenzoic acid, m.p. 187-188°.

Preparation of 6,6'-Di-t-butylbiphenyl-3,3'-dicarboxylic Acid.

Diethyl 6,6'-di-t-butylbiphenyl-3,3'-dicarboxylate.

Ethyl 3-iodo-4-t-butylbenzoate (18g.) was heated with copper bronze (18g.) in a bath at 230-240°. It reacted vigorously and when the reaction was complete the mixture was extracted with boiling chlorobenzene. After removal of the solvent, a viscous oil was obtained. A little ethanol was added and the crude ester crystallised, and was filtered off. It was recrystallised from ethanol (3.8g., 24.2%).

Diethyl 6,6'-di-t-butylbiphenyl-3,3'-dicarboxylate crystallised in fine needles, m.p. 144° (Found: C, 76.0; H, 8.4. $C_{26}H_{34}O_4$ requires C, 76.1; H, 8.4%).

Dimethyl 6,6'-di-t-butylbiphenyl-3,3'-dicarboxylate was similarly prepared by heating methyl 3-iodo-4-t-butylbenzoate (20g.) with copper bronze (20g.) at 235°. The dimethyl ester crystallised from methanol, from which it separated in fine needles, m.p. 202-203° (5.5g., 45.8%).

6,6'-Di-t-butylbiphenyl-3,3'-dicarboxylic acid.

The dimethyl ester (20g.) was hydrolysed with 10% ethanolic potasium ethoxide (60 ml.). After heating the mixture under reflux for three hours the ethanol was distilled off and the residue was dissolved in water. On acidification of the aqueous solution, the acid was precipitated and was purified by crystallisation from glacial acetic acid. It separated in hexagonal prisms, m.p. 345-346° (Kofler block), (18.5g., 98%).

The diethyl ester was similarly hydrolysed.

Resolution of 6,6'-di-t-butylbiphenyl-3,3'-dicarboxylic acid.

All rotations were measured in "AnalaR" acetone at room temperature ($\underline{c} \sim 0.5$) in 2 dm.tubes.

The acid (13g.) and brucine (28.8g.) were dissolved in boiling ethanol (900 ml.) and the solution kept overnight at +4°. The first fraction of salt (15.5g.) separated as rosettes of thin rectangular plates and had $[\alpha]_{5791}-42.4^{\circ}$ and $[\alpha]_{5461}-49.4^{\circ}$. The second fraction (5.5g.) which separated after concentration of the mother-liquor had $[\alpha]_{5791}-45.6^{\circ}$ and $[\alpha]_{5461}-54.4^{\circ}$. Further concentration of the mother-liquor yielded a gel which contained a small amount of crystalline salt, and since the gel was very soluble in ethanol it was possible to separate them.

Brucine (+)-6,6'-di-t-butylbiphenyl-3,3'-dicarboyxlate was obtained optically pure from the first fraction of salt after four recrystallisations from ethanol, and had $[\alpha]_{5791}-37.8^{\circ}$ $[\alpha]_{5461}-43.9^{\circ}$. The second fraction was recrystallised several times but its specific rotation remained unchanged; it was obviously an inseparable mixture of the (+)-acid salt and the partial racemate.

The optically active acids were obtained by decomposition of the brucine salts with aqueous sodium hydroxide solution in the usual manner. (+)-6,6'-Di-t-butylbiphenyl-3,3'-dicarboxylic acid crystallised from glacial acetic acid in sheaves of rectangular rods and, since it had solvent of crystallisation, it was heated _in vacuo_ at 130° for several hours. It melted at 345° (Kofler block) and had $[\alpha]_{5791}$ +18.6°, $[\alpha]_{5461}$ +24.1°. The crude (-)-acid, obtained by decomposition of the gel, was recrystallised from glacial acetic acid, and a small amount of (±)-acid separated. This was filtered off and after concentration of the mother-liquor the (-)-acid crystallised. Recrystallisation from glacial acetic acid gave the pure (-)-acid, m.p. 345° (Kofler block) and $[\alpha]_{5791}$ -18.9°, $[\alpha]_{5461}$ -24.2°.

Preparation of 2,2'-_Di-t-butylbiphenyl_.

Method I.

6,6'-Di-t-butylbiphenyl-3,3'-dicarboxylic acid (3g.) in quinoline solution, was heated under reflux with copper bronze (1g.) for three hours. The dicarboxylic acid was recovered unchanged.

Method II.

The procedure suggested by Snyder, Elston and Kellom (_J.Amer.Chem.Soc._, 1953, _75_, 2014) for the formation of amines from the corresponding aromatic carboxylic acids, was followed.

A mixture of hydroxylamine hydrochloride (1.1g.), the dicarboxylic acid (2.5g.) and polyphosphoric acid (30g.) was gradually heated to 180°, with mechanical stirring. Hydrogen chloride was evolved as the temperature approached 100°, but little effervescence was observed as the temperature was raised further. The resultant brown solution was poured on crushed ice, and unchanged dicarboxylic acid was precipitated (2g.).

Method III.

(Kleinberg, Chem.Rev., 1947, 40, 386).

Bromine (3.2g.) was slowly added to a suspension of the silver salt of 6,6'-di-t-butylbiphenyl-3,3'-dicarboxylic acid (5.6g.) in carbon tetrachloride, and the mixture was heated under reflux for 80 hours. It was then cooled and the insoluble silver bromide filtered off. The acid (2g.) was again recovered from the carbon tetrachloride solution.

Method IV.

The Hofmann reaction (Adams et al., Organic Reactions, III, 267)

6,6'-Di-t-butylbiphenyl-3,3'-dicarbonyl chloride.

The above acid (13.5g.) was heated under reflux with thionyl chloride (54g., 20 ml.) until the evolution of hydrogen chloride had ceased. After removal of the excess thionyl chloride by distillation, the residue was left overnight in vacuo over soda lime and calcium chloride (12.5g., 83.8%).

6,6'-Di-t-butylbiphenyl-3,3'-dicarbonyl chloride crystallised from light petroleum (b.p. 40-60°) in micro crystals, m.p. 120-122° (Found: C, 67.9; H, 6.2. $C_{22}H_{24}Cl_2O_2$ requires C, 67.5; H, 6.2%).

6,6'-Di-t-butylbiphenyl-3,3'-dicarbonamide.

(a) The above crude acid chloride (4g.) was added to ice-cold ammonia (d 0.88, 80 ml.), and the mixture left to stand overnight. The solid which had separated was filtered off and washed with a little water. It was crystallised from methanol (2.5g., 55%).

(b) The acid chloride (9g.) was dissolved in dry carbon tetrachloride (50 ml.) and the cold solution slowly added to ice-cooled carbon tetrachloride saturated with ammonia, and through which ammonia was bubbled continuously. When addition was complete the reaction mixture was left to stand for one hour at 0°, then allowed to warm up to room temperature. During the reaction a solid separated.

The suspension was then boiled to expel ammonia, cooled, and the solid was filtered off.

6,6'-*Di-t-butylbiphenyl*-3,3'-*dicarbonamide* crystallised from methanol in small colourless rhombic crystals, m.p. 331° (Found: C, 75.4; H, 8.4. $C_{22}H_{28}O_2$ requires C, 75.0; H, 8.0%). It was sparingly soluble in the usual organic solvents, but readily soluble in cellosolve.

[Attempts made to prepare the diamide from the dimethyl ester were unsuccessful. The ester was recovered unchanged after standing with ammonia (*d* 0.88) for two weeks, and also after ammonia had been bubbled through a solution of the ester in methanol for five hours.]

Attempts to prepare 3,3'-*diamino*-6,6'-*di-t-butylbiphenyl*.

(a) A solution of alkaline potassium hypobromite was prepared by the addition of bromine (3.2g.) to aqueous potassium hydroxide solution (8g. in 40 ml. water). The above diamide (3.5g.) was added and remained in suspension. After the mixture had been heated at 70-75° for 45 minutes, it was cooled and the unreacted diamide (2g.) filtered off. On acidification of the alkaline filtrate, a solid was precipitated (0.7g., m.p. 195-220°) which was probably a mixture of hydrolysis products of the diamide.

(b) The diamide (2.8g.) was recovered unchanged after it had been heated under reflux for seven hours with an alkaline solution of sodium hypobromite.

(c) The diamide (3g.) was also recovered unchanged after heating under reflux with alkaline sodium hypochlorite solution for one hour.

(d) Sodium methoxide solution, prepared from sodium (0.9g.) and methanol (30 ml.) was added to a solution of the diamide (3.2g.) in methanol (600 ml.). Bromine (3.2g.) was added rapidly, with mechanical stirring, and the mixture heated under reflux for one hour. The unchanged diamide (3g.) was recovered from the methanolic solution.

This was repeated by adding the sodium methoxide solution to a solution of the diamide in cellosolve (150 ml.) but this again failed to yield the urethane.

Method V.

The Schmidt reaction. (Adams et al., Organic Reactions, III, 307).

Activation of sodium azide (Nelles, Ber., 1932, 65, 1345).

Industrial sodium azide (10g.) was ground in a mortar with hydrazine hydrate (0.5 ml.). The moist powder was air-dried overnight, and then dissolved in the minimum of water. Addition of acetone to the aqueous solution caused precipitation of sodium azide, which was filtered off, washed with methanol and with ether and dried *in vacuo*.

3,3'-*Diamino*-6,6'-*di-t-butylbiphenyl*.

6,6'-Di-t-butylbiphenyl-3,3'-dicarboxylic acid (3.5g.) was dissolved in concentrated sulphuric acid (20 ml.) and to this solution benzene was added (20 ml.) The mixture was heated to $\sim 50^{\circ}$ and the activated sodium azide (2g.) was added gradually, within 45 minutes. The temperature was maintained at $\sim 50^{\circ}$ until the vigorous reaction had subsided, then it was slowly raised to 75° and maintained at that temperature until effervescence had ceased. The mixture was then ice-cooled and made alkaline with aqueous sodium hydroxide solution (30%). The precipitated sodium sulphate was dissolved by the addition of water, and the mixture was extracted with benzene. The benzene solution was washed with water, dried over anhydrous sodium sulphate, then passed through a column of alumina, and eluted with a 1:5 mixture of acetone and benzene. The solvent was removed from the eluates and a viscous yellow oil was obtained. This was heated with concentrated hydrochloric acid and the *hydrochloride* crystallised. It was recrystallised from dilute hydrochloric acid and separated in pink glistening plates, m.p. 276-278° (decomp.).

3,3'-*Diamino*-6,6'-*di-t-butylbiphenyl hydrochloride* crystallised as the tetrahydrate (Found: C, 54.6; H, 8.4. $C_{20}H_{30}Cl_2N_2.4H_2O$ requires C, 54.4; H, 8.7%). After heating the hydrate *in vacuo* at 80° for several hours the loss of weight corresponded to 4 molecules of water of crystallisation.

3,3'-*Diamino*-6,6'-*di-t-butylbiphenyl* was obtained from the hydrochloride and crystallised from light petroleum (b.p. 40-60°) in pale yellow fine needles, m.p. 104-105° (2.1g., 72%). (Found: C, 77.5 ; H, 9.3. $C_{20}H_{28}N_2$ requires C, 81.0; H, 9.5%). The analysis figures indicate that the sample was a mixture of hydrates.

2,2'-*Di-t-butylbiphenyl*.

The above diamine (2g.) was diazotised in a solution of concentrated hydrochloric acid (5 ml.) and water (5 ml.) at -20° and the temperature of the reaction mixture was allowed to rise gradually to 0°. The diazonium solution was added, with stirring, to ice-cold hypophosphorous acid (30 ml.) (the temperature being maintained below 5°), and the mixture was left to stand overnight at 4°. The crude hydrocarbon was extracted with light petroleum (b.p. 40-60°), the petroleum extract was washed with aqueous sodium hydroxide solution (10%) and with water, and dried over anhydrous sodium sulphate. The solution, which was yellow, was passed through a column of alumina and eluted with light petroleum. The residue obtained from the eluates, after removal of the solvent, was a colourless solid which crystallised from methanol and was 2,2'-di-t-butylbiphenyl, m.p. 63-64° (0.8g., 52%).

Following the above procedure, the optically active di-t-butylbiphenyls were obtained from the active acids. Rotations were measured at room temperature in 2 dm. tubes, $c \sim 0.5$.

(+)-2,2'-Di-t-butylbiphenyl.

From 3.5 g. of (+)-acid, (+)-3,3'-diamino-6,6'-di-t-butylbiphenyl (2.1g.) was obtained which crystallised from light petroleum (b.p. 60-80°) in stout yellow needles, m.p. 144-145°, and had $[\alpha]_{5791}$ +11.4° and $[\alpha]_{5461}$ +14.5° in ethanol (Found: C, 81.4; H, 9.8. $C_{20}H_{28}N_2$ requires C, 81.0; H, 9.5%)

(+)-2,2'-Di-t-butylbiphenyl crystallised from methanol in colourless rhombic plates, m.p. 73-74°, and had $[\alpha]_{5791}$ +17.8° and $[\alpha]_{5461}$ +21.6° in acetone (Found: C, 90.1; H, 9.8. $C_{20}H_{26}$ requires C, 90.2; H, 9.8%).

(-)-2,2'-Di-t-butylbiphenyl.

2.5g. of the (-)-acid were converted into the diamine hydrochloride (1.4g.) and straightway deaminated.

(-)-2,2'-Di-t-butylbiphenyl crystallised from methanol in colourless rhombic plates, m.p. 73-74°, and had $[\alpha]_{5791}$ -18.1° and $[\alpha]_{5461}$ -22.3° in acetone (Found: C, 90.0; H, 10.1 $C_{20}H_{26}$ requires C, 90.2; H, 9.8%).

Preparation of 2',6-Di-t-butylbiphenyl-3-carboxylic Acid.

A mixture of 3-iodo-4-t-butylbenzoate (32g.) and o-iodo-t-butylbenzene (26g.) was heated with copper bronze (58g.) in a bath at 220°. When the reaction was complete, the product was extracted with boiling chlorobenzene. The solvent was distilled off and an oil was obtained. On addition of methanol, a solid separated which was found to be the symmetrical ester. It was filtered off and the residue was distilled under reduced pressure. Three fractions were obtained:

(i) Almost colourless oil, b.p. 102-134°/2mm. (7g.). This was methyl p-t-butylbenzoate, presumably produced by the dehalogenation of the iodo-ester by the copper bronze.

(ii) Yellow oil, b.p. 156-180°/2mm. (7g.).

(iii) A viscous oil, b.p. 180-222°/2mm. (5g.), which solidified on adding methanol and was identified as more of the symmetrical ester.

The second fraction was hydrolysed with ethanolic potassium ethoxide. After removal of the sdvent by distillation, the residue was dissolved in water, and the solution was extracted with ether. From the ethereal extract 2,2'-di-t-butylbiphenyl was obtained, m.p. 61-63°, and on acidification of the aqueous solution, the acid was precipitated (3g.).

2',6-Di-t-butylbiphenyl-3-carboxylic acid crystallised from methanol in slender prisms, m.p. 232-233° with previous softening (Found: C, 81.1; H, 8.5. $C_{21}H_{26}O_2$ requires C, 81.2, H, 8.4%). It was sensitive to light and on exposure became slightly yellow.

Resolution of 2',6-Di-t-butylbiphenyl-3-carboxylic acid. Rotations were measured at room temperature in "AnalaR" chloroform ($c\sim1$) in 2 dm. tubes, unless otherwise stated.

The above acid (3.1g.) and strychnine (3.4g.) were dissolved in boiling ethanol (120 ml.) and the solution kept at room temperature overnight. The first crop of salt (1.4g.) separated as fine needles, $[\alpha]_{5791}$ -8.9° and $[\alpha]_{5461}$ -11.0°. Concentration of the mother-liquor gave more salt (1.2g.) with approximately the same rotation, and on further concentration an oil was obtained which could not be induced to crystallise. This was decomposed and gave crude (-)-acid, $[\alpha]_{5791}$ -22.7° and $[\alpha]_{5461}$ -24.9°. The above crystalline salt was purified by crystallisation from ethanol until the specific rotation remained constant.

Strychnine (+)-2',6-*di-t-butylbiphenyl*-3-*carboxylate* crystallised from ethanol in slender needles, m.p. 160-161° and had $[\alpha]_{5791}$ -9.5° and $[\alpha]_{5461}$ -12.6° (Found: C, 74,2; H, 7.8. $C_{21}H_{26}O_2{:}C_{21}H_{22}N_2O_2.\overset{2H_2O}{/}$requires C, 74.1; H, 7.7%) When heated *in vacuo* at 80° the salt lost weight corresponding to two molecules of water of crystallisation. The free acids were obtained from the strychnine salts by decomposition with formic acid.

(+)-2',6-*Di-t-butylbiphenyl*-3-*carboxylic acid* crystallised from methanol in needles, m.p. 181-185° and had $[\alpha]_{5791}$ +25.5° and $[\alpha]_{5461}$ +28.4° (Found: C, 80.8; H, 8.3. $C_{21}H_{26}O_2$ requires C, 81.2; H, 8.4%). In toluene its rotation was $[\alpha]_{5791}$ +45.4° and $[\alpha]_{5461}$ + 51.8°.

The crude (-)-acid was crystallised from methanol and the first crop which separated was optically inactive (0.07g.). It was filtered off and the mother-liquor was concentrated; the (-)-acid crystallised. Recrystallisation from methanol gave the pure (-)-*acid*, m.p. 181-185°, $[\alpha]_{5791}$ -25.8° and $[\alpha]_{5461}$ -28.3° (Found: C, 80.8; H, 8.6. $C_{21}H_{26}O_2$ requires C, 81.2; H, 8.4%).

The active acids melted rather indefinitely and it was suspected that they contained solvent of crystallisation since erratic analysis figures for the same sample were obtained on several occasions. The (-)-acid was therefore heated at 130°/1 mm. and under these conditions it sublimed. The sublimed acid melted at 192-193° and had $[\alpha]_{5791}$ -65.5° and $[\alpha]_{5461}$ -72.4° in toluene (Found: C, 80.9; H, 8.6%). In another experiment, a portion of the pure (-)-acid, which had $[\alpha]_{5791}$ -44.7° and $[\alpha]_{5461}$ -52.6° in toluene was melted and allowed to solidify. Its specific rotation in toluene was unchanged.

The specific rotation of the (-)-acid did not change after heating under reflux in toluene solution for 9½ hours.

Preparation of 2'-Nitro-6-t-butylbiphenyl-3-carboxylic Acid.

A mixture of o-chloronitrobenzene (12.8g.) and methyl 3-iodo-4-t-butylbenzoate (32g.) was heated to 235° (metal bath) and copper bronze (45g.) was gradually added. A vigorous reaction ensued and was complete after 30 minutes. The product was extracted with boiling chlorobenzene, the hot solution was filtered and the solvent removed. On cooling, a solid separated and was filtered off and washed with a little ether. This was identified as dimethyl 6,6'-di-t-butylbiphenyl-3,3'-dicarboxylate (3.5g.). The residue was distilled under reduced pressure and the fraction, b.p. 96-110°/3mm. (10g.) was collected. This was a mixture of o-chloronitrobenzene and methyl p-t-butylbenzoate, the latter produced by dehalogenation of the iodo-ester by copper bronze.

The residue (13g.) from the vacuum-distillation was a brown oil, and it was hydrolysed with ethanolic potassium ethoxide (10%). After heating the mixture for three hours, the ethanol was removed and the residue dissolved in water. The alkaline solution was extracted with ether, acidified with dilute hydrochloric acid and the precipitated acid filtered off and dried.

The precipitated acid was a mixture of the required acid, p-t-butylbenzoic acid and the symmetrical di-t-butylbiphenyl-3,3'-dicarboxylic acid. Removal of p-t-butylbenzoic acid was effected by extraction of the crude acid with boiling light petrolum (b.p. 80-100°). The residue was then crystallised from glacial acetic acid in which the symmetrical acid was the more sparingly soluble. The nitro-acid was obtained from the acetic acid mother-liquor and was crystallised from methanol. The yield of nitro-acid was very low; from six similar preparations only 2g. of pure acid were obtained.

2'-Nitro-6-t-butylbiphenyl-4-carboxylic acid crystallised in glistening yellow plates, m.p.264-266° (Found: C, 67.8; H, 5.6. $C_{17}H_{17}NO_4$ requires C, 68.2; H, 5.7%).

Preparation of 2'-t-Butyl-6-nitrobiphenyl-4-carboxylic Acid.

Ethyl p-aminobenzoate.

A mixture of p-aminobenzoic acid (250g.), in absolute ethanol (2500 ml.) and concentrated sulphuric acid (125 ml.), was heated under reflux for 14 hours. The solution was cooled and poured into water. The precipitated ester was filtered off, washed with aqueous sodium carbonate solution and with water. It was crystallised from ethanol and separated as colourless rectangular plates, m.p.92° (251 g., 83.4%).

Ethyl p-bromobenzoate.

The above amino-ester (45.9g.) was ground finely in a mortar and made into a paste with a little water, and hydrobromic acid (d 1.5, 100 ml.) was added. The mixture was stirred mechanically and diazotised with an aqueous solution of sodium nitrite (21.3g.) at $< 2^\circ$. The mixture was then stirred for 15 minutes at room temperature and then slowly added to a solution of cuprous bromide (23g.) in hydrobromic acid (d 1.5, 35 ml.). When effervescence had ceased, the mixture was steam-distilled and the distillate extracted with ether. The ethereal solution was washed with aqueous sodium hydroxide solution, and water, and dried over calcium chloride. After removal of the solvent the residue was distilled under reduced pressure. Ethyl p-bromobenzoate was obtained as a colourless oil, b.p. 92-98°/2mm. (54g., 79%).

Ethyl 3-nitro-4-bromobenzoate.

The above bromo-ester (50.6g.) was dissolved in concentrated sulphuric acid (75 ml.) and the solution cooled at 0°. A mixture of concentrated nitric acid (30 ml.) and concentrated sulphuric acid (30 ml.) was added slowly to the above mixture, which was mechanically stirred; the temperature was kept below 5°. When the addition was complete, the mixture was stirred for a further

$2\frac{1}{2}$ hours, and the temperature allowed to rise to 10°, then poured on crushed ice. The nitro-compound was filtered off, washed well with water and crystallised from ethanol. Ethyl 3-nitro-4-bromobenzoate was obtained as cream glistening plates, m.p. 74° (46.5g., 77%).

2'-t-Butyl-6-nitrobiphenyl-4-carboxylic acid.

A mixture of o-iodo-t-butylbenzene (20g.) and ethyl 3-nitro-4-bromobenzoate (20.7g.), was heated in a metal bath to 170°, and copper bronze was added gradually; the temperature of the reaction mixture was not allowed to rise above 240°. The product was extracted with boiling chloroform, and the solution filtered. The chloroform solutions from four similar preparations were combined, the solvent removed, and the residue distilled under reduced pressure. The following fractions were obtained:

(i) Pale yellow oil (31.5g.), b.p. 80-124°/2mm. This was mainly unchanged o-iodo-t-butylbenzene.

(ii) Yellow oil containing some solid (16g.), b.p. 124-162°/2mm. which was a mixture of 2,2'-di-t-butylbiphenyl and ethyl m-nitrobenzoate.

(iii) Residue, a brown oil.

The oil was heated under reflux for three hours with alcoholic potassium ethoxide (10%), the alcohol was distilled off and the residue dissolved in water. The alkaline solution was acidified with dilute hydrochloric acid, and a brown solid was precipitated which was filtered off. It was dissolved in aqueous sodium carbonate solution, the solution was extracted with ether, and the alkaline solution then acidified. The precipitated acid was filtered off and dried, and appeared to be a mixture which contained the symmetrical dinitro-acid. It was therefore extracted in a Soxhlet apparatus with benzene in which the symmetrical acid was insoluble. The benzene solution was passed through a column of silica gel and eluted with benzene. Evaporation of the eluates gave a pale yellow solid, which on recrystallisation from light petroleum (b.p. 40-60°) gave the required acid (5.8g.). (17g. of symmetrical acid were obtained).

2'-t-Butyl-6-nitrobiphenyl-4-carboxylic acid crystallised in small pale yellow rods, m.p. 150-151°. (Found: C, 68.3; H, 5.6. $C_{17}H_{17}NO_2$ requires C, 68.2; H, 5.7%).

Resolution of 2'-t-butyl-6-nitrobiphenyl-4-carboxylic acid.

All rotations were measured in chloroform at room temperature (*c* ~ 1.0) in 2 dm. tubes unless otherwise stated.

The acid (4.5g.) and strychnine (5.0g.) were dissolved in boiling ethanol (250 ml.) and kept at 4°

overnight. The first fraction of salt (4.5g.) separated in stout rectangular plates $[\alpha]_{5791}$ +14.6° and $[\alpha]_{5461}$ +18.6°. Evaporation of the mother-liquor gave successive crops whose specific rotations were approximately the same as above. A portion of salt, on decomposition with aqueous sodium hydroxide solution, gave an acid $[\alpha]_{5791}$ +33.4°, $[\alpha]_{5461}$ +40.5°.

On one occasion only, a small amount of salt separated as fine needles from the (+)-acid salt mother-liquor. It had $[\alpha]_{5791}$ -19.1° and $[\alpha]_{5461}$ -24.6°, and gave the (-)-acid when it was decomposed.

The (+)-acid salt was recrystallised three times from ethanol and was then optically pure.

Strychnine (+)-2'-*t-butyl*-6-*nitrobiphenyl*-4-*carboxylate* crystallised in stout rectangular plates, m.p. 234-236°, $[\alpha]_{5791}$ +15.2°, $[\alpha]_{5461}$ +19.5° (Found: C, 71.7; H, 6.0. $C_{17}H_{17}NO_4.C_{21}H_{22}N_2O_2$ requires C, 72.0; H, 6.2%). The salt mutarotated in boiling chloroform solution during two hours and slowly at room temperature during 14 days to give the partial racemate $[\alpha]_{5791}$ -2.8°, $[\alpha]_{5461}$ -4.1°.

(+)-2'-*t-butyl*-6-*nitrobiphenyl*-4-*carboxylic acid* was obtained by decomposition of the above salt, m.p. 148-149°, $[\alpha]_{5791}$ +33.4° and $[\alpha]_{5461}$ +40.5° (Found: C, 68.4; H, 5.8. $C_{17}H_{17}NO_4$ requires C, 68.2; H, 5.7%).

Racemisation of the (+)-acid in toluene was studied at several temperatures, between 51° and 75°, in a polarimeter tube which was thermostatically-controlled, $\lambda = 5461$ Å.

TABLE I.

Racemisation of 2'-t-butyl-6-nitrobiphenyl-4-carboxylic acid.

$T = 51.0^{\circ}$ $\underline{c} \sim 1$ $\alpha_o = 180.08$

Time in Minutes	Observed Polarimetric Reading, α_t	$\alpha_t - \alpha_o$	$\log_{10}(\alpha_t - \alpha_o)$
2.74	180.92	0.84	$\bar{1}.9243$
3.93	180.91	0.83	$\bar{1}.9191$
7.86	180.88	0.80	$\bar{1}.9031$
12.99	180.871	0.791	$\bar{1}.8982$
25.09	180.842	0.762	$\bar{1}.8820$
39.30	180.80	0.72	$\bar{1}.8573$
55.40	180.765	0.685	$\bar{1}.8357$
71.06	180.73	0.65	$\bar{1}.8129$
85.37	180.698	0.618	$\bar{1}.7910$
110.49	180.638	0.558	$\bar{1}.7466$
152.05	180.58	0.50	$\bar{1}.6990$
171.59	180.55	0.47	$\bar{1}.6721$
195.43	180.50	0.42	$\bar{1}.6232$
215.75	180.465	0.385	$\bar{1}.5855$
249.04	180.422	0.342	$\bar{1}.5340$
284.21	180.39	0.31	$\bar{1}.4914$
315.14	180.35	0.27	$\bar{1}.4314$
393.05	180.298	0.218	$\bar{1}.3385$
447.68	180.249	0.169	$\bar{1}.2279$

$k = 0.003472 \text{ min.}^{-1}$

Half-life period = 199.7 min.

TABLE II.

Racemisation of 2'-t-butyl-6-nitrobiphenyl-4-carboxylic acid.

$T = 55.8^{o}$ $c \simeq 0.94$ $\alpha_o = 180.08$.

Time in Minutes	Observed Polarimetric Reading, α_t	$\alpha_t - \alpha_o$	$\log_{10}(\alpha_t - \alpha_o)$
2.32	180.815	0.735	$\bar{1}.8663$
4.74	180.793	0.713	$\bar{1}.8531$
10.07	180.77	0.69	$\bar{1}.8388$
13.79	180.75	0.67	$\bar{1}.8261$
20.29	180.733	0.653	$\bar{1}.8149$
25.72	180.712	0.632	$\bar{1}.8007$
36.27	180.684	0.604	$\bar{1}.7810$
48.06	180.622	0.542	$\bar{1}.7340$
66.37	180.562	0.482	$\bar{1}.6830$
79.42	180.528	0.448	$\bar{1}.6513$
100.81	180.477	0.397	$\bar{1}.5988$
121.26	180.422	0.342	$\bar{1}.5340$
145.44	180.376	0.296	$\bar{1}.4713$
169.75	180.34	0.26	$\bar{1}.4150$
189.06	180.298	0.218	$\bar{1}.3385$
220.92	180.261	0.181	$\bar{1}.2577$
248.92	180.232	0.152	$\bar{1}.1818$
287.37	180.201	0.121	$\bar{1}.0828$

$k = 0.006315 \text{ min.}^{-1}$

Half-life period = 109.8 min.

TABLE III.

Racemisation of 2'-t-butyl-6-nitrobiphenyl-4-carboxylic acid.

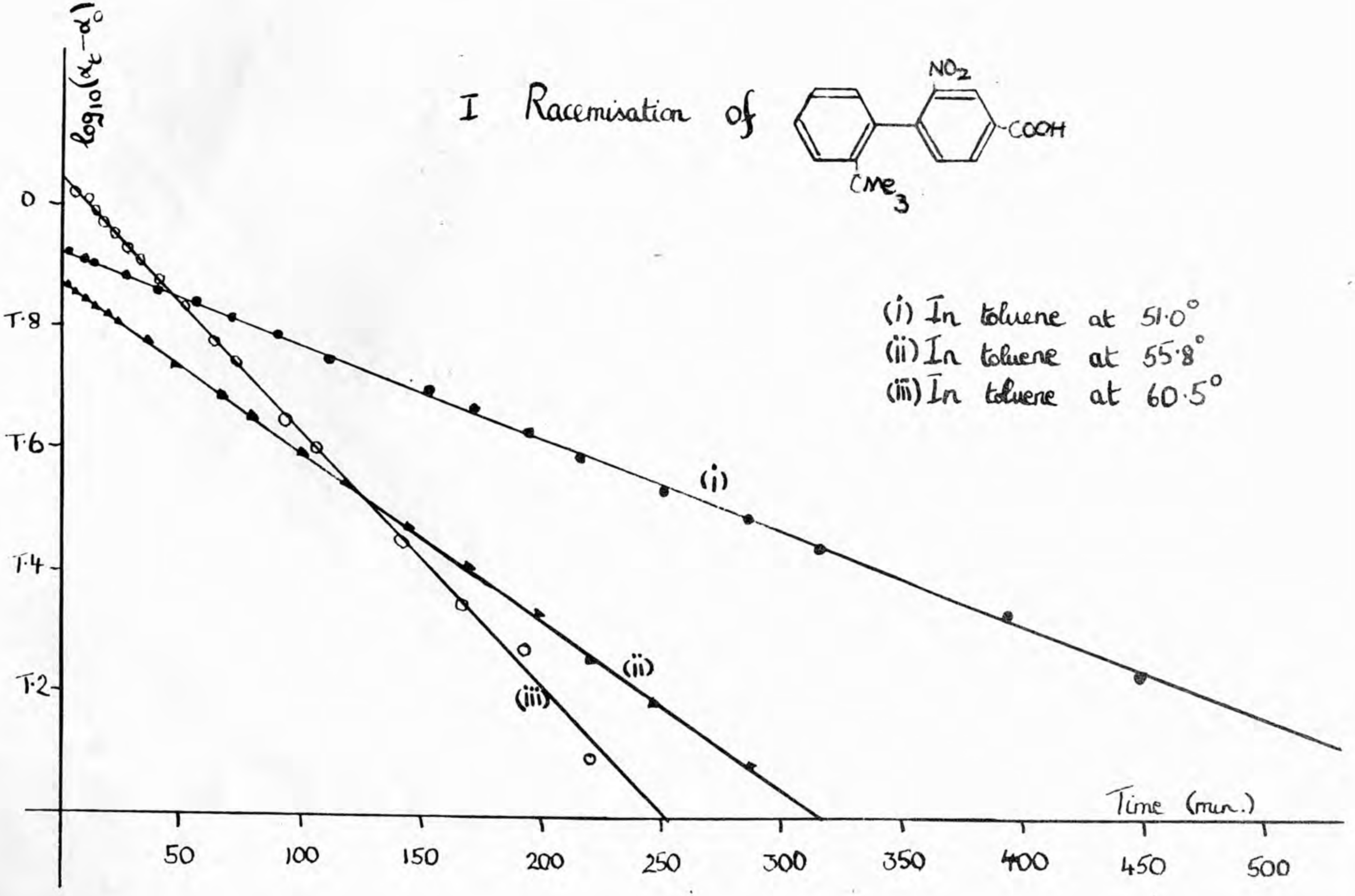
$T = 60.5^{\circ}$ $\underline{c} \sim 1.1$ $\alpha_o = 180.08$

Time in Minutes	Observed Polarimetric Reading, α_t	$\alpha_t - \alpha_o$	$\log_{10}(\alpha_t - \alpha_o)$
5.24	181.133	1.053	0.0224
9.60	181.113	1.033	0.0141
12.96	181.073	0.993	$\bar{1}.9969$
16.51	181.013	0.933	$\bar{1}.9699$
21.70	180.97	0.89	$\bar{1}.9494$
27.19	180.92	0.84	$\bar{1}.9243$
32.92	180.893	0.813	$\bar{1}.9101$
42.29	180.828	0.748	$\bar{1}.8739$
52.08	180.77	0.69	$\bar{1}.8388$
64.20	180.688	0.608	$\bar{1}.7839$
73.11	180.637	0.557	$\bar{1}.7459$
82.13	180.577	0.497	$\bar{1}.6964$
93.07	180.532	0.452	$\bar{1}.6551$
105.10	180.485	0.405	$\bar{1}.6075$
122.50	180.42	0.34	$\bar{1}.5315$
141.60	180.36	0.28	$\bar{1}.4472$
167.70	180.305	0.225	$\bar{1}.3522$
193.33	180.27	0.19	$\bar{1}.2788$
221.50	180.208	0.128	$\bar{1}.1072$

$k = 0.009491 \text{ min.}^{-1}$

Half-life period = 73.0 min.

I Racemisation of



(i) In toluene at 51·0°
(ii) In toluene at 55·8°
(iii) In toluene at 60·5°

TABLE IV.

Racemisation of 2'-*t*-*butyl*-6-*nitrobiphenyl*-4-*carboxylic acid*.

$T = 64.2^{\circ}$ $\underline{c} \sim 1.0$ $\alpha_0 = 180.08$

Time in Minutes	Observed Polarimetric Reading, α_t	$\alpha_t - \alpha_o$	$\log_{10}(\alpha_t - \alpha_o)$
1.68	180.97	0.89	$\bar{1}.9494$
2.34	180.935	0.855	$\bar{1}.9320$
4.39	180.93	0.85	$\bar{1}.9294$
6.49	180.91	0.83	$\bar{1}.9191$
9.21	180.88	0.80	$\bar{1}.9031$
11.01	180.842	0.762	$\bar{1}.8824$
14.96	180.806	0.726	$\bar{1}.8609$
18.45	180.76	0.68	$\bar{1}.8325$
22.76	180.73	0.65	$\bar{1}.8129$
26.16	180.692	0.612	$\bar{1}.7853$
30.77	180.66	0.58	$\bar{1}.7634$
37.12	180.591	0.511	$\bar{1}.7084$
42.00	180.56	0.48	$\bar{1}.6812$
46.93	180.535	0.455	$\bar{1}.6580$
51.56	180.48	0.40	$\bar{1}.6021$
57.72	180.47	0.39	$\bar{1}.5911$
65.04	180.434	0.354	$\bar{1}.5490$
75.24	180.36	0.28	$\bar{1}.4472$
85.62	180.322	0.242	$\bar{1}.3838$
98.57	180.283	0.203	$\bar{1}.3075$
112.14	180.248	0.168	$\bar{1}.2253$

$k = 0.015230 \text{ min.}^{-1}$

Half-life period = 45.5 min.

TABLE V.

Racemisation of 2'-t-butyl-6-nitrobiphenyl-4-carboxylic acid.

T = 70.1° c = 1.05 α_o = 180.08

Time in Minutes	Observed Polarimetric reading, α_t	$\alpha_t - \alpha_o$	$\log_{10}(\alpha_t - \alpha_o)$
1.61	180.876	0.796	$\bar{1}$.9009
3.14	180.847	0.767	$\bar{1}$.8848
4.53	180.831	0.751	$\bar{1}$.8756
6.13	180.807	0.727	$\bar{1}$.8615
8.71	180.748	0.668	$\bar{1}$.8248
10.75	180.738	0.658	$\bar{1}$.8182
13.80	180.66	0.58	$\bar{1}$.7634
17.61	180.617	0.537	$\bar{1}$.7292
20.59	180.563	0.483	$\bar{1}$.6839
23.99	180.517	0.437	$\bar{1}$.6405
29.80	180.461	0.381	$\bar{1}$.5809
34.86	180.418	0.338	$\bar{1}$.5289
41.30	180.352	0.272	$\bar{1}$.4346
47.20	180.313	0.233	$\bar{1}$.3674
56.33	180.27	0.19	$\bar{1}$.2788
64.30	180.208	0.128	$\bar{1}$.1072

k = 0.02813 min.-1

Half-life period = 24.6 min.

TABLE VI.

Racemisation of 2'-t-butyl-6-nitrobiphenyl-4-carboxylic acid.

$T = 75.2^{\circ}$ $\quad$ c = 0.92 $\quad$ $\alpha_o = 180.08$

Time in Minutes	Observed Polarimetric Reading, α_t	$\alpha_t - \alpha_o$	$\log_{10}(\alpha_t - \alpha_o)$
2.37	180.80	0.72	$\bar{1}.8573$
3.93	180.758	0.678	$\bar{1}.8312$
6.90	180.675	0.595	$\bar{1}.7745$
8.03	180.635	0.555	$\bar{1}.7443$
9.20	180.597	0.517	$\bar{1}.7135$
10.08	180.575	0.495	$\bar{1}.6946$
11.22	180.56	0.48	$\bar{1}.6812$
12.71	180.52	0.44	$\bar{1}.6435$
14.41	180.48	0.40	$\bar{1}.6021$
16.40	180.465	0.385	$\bar{1}.5855$
17.59	180.428	0.348	$\bar{1}.5416$
19.06	180.40	0.32	$\bar{1}.5051$
20.36	180.386	0.306	$\bar{1}.4857$
22.23	180.363	0.283	$\bar{1}.4518$
23.42	180.35	0.27	$\bar{1}.4314$
26.64	180.32	0.24	$\bar{1}.3802$
28.63	180.29	0.21	$\bar{1}.3222$
30.72	180.26	0.18	$\bar{1}.2553$
32.70	180.242	0.162	$\bar{1}.2095$
34.45	180.22	0.14	$\bar{1}.1461$
38.50	180.215	0.135	$\bar{1}.1303$
41.00	180.195	0.115	$\bar{1}.0607$
43.21	180.19	0.11	$\bar{1}.0414$

$k = 0.04777 \text{ min.}^{-1}$

Half life period = 14.5 min.

II Racemisation of 2′-nitro-biphenyl (CMe$_3$, NO$_2$, ·CO$_2$H) in toluene.

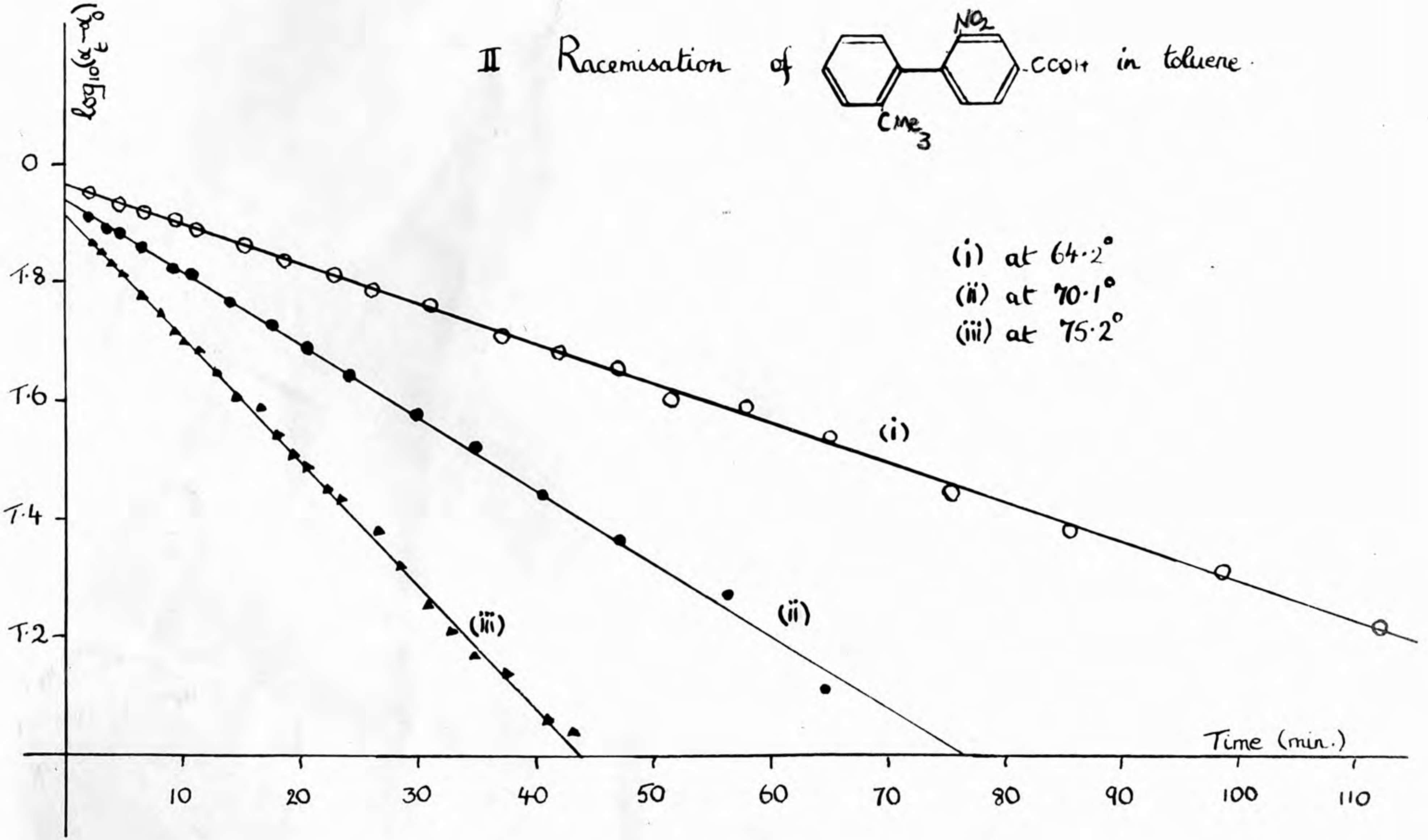
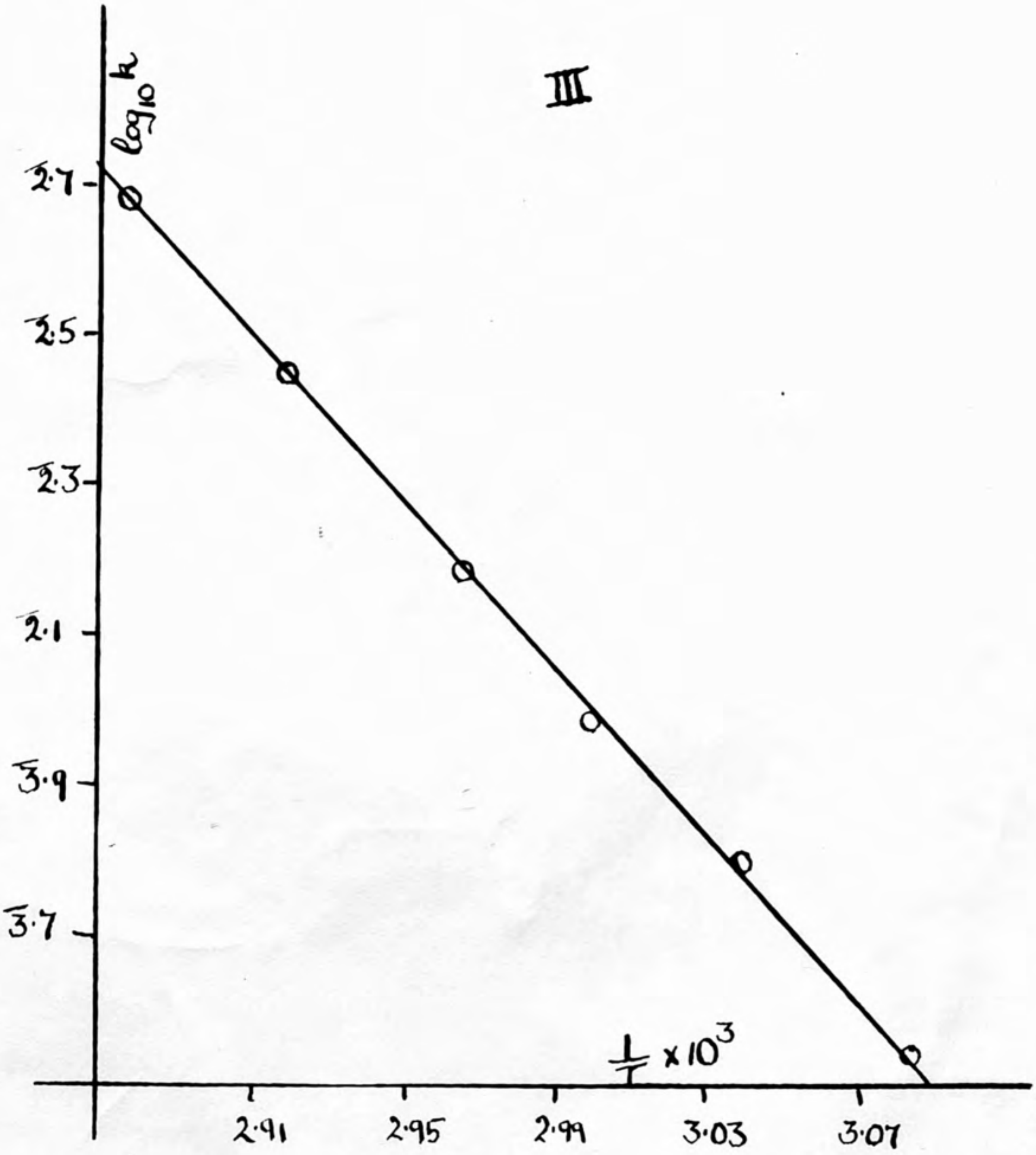


TABLE VII.

T^o	T^oK	$\frac{1}{T} \times 10^3$	k min.$^{-1}$	$\log_{10}k$
51.0	324.2	3.084	3.472×10^{-3}	$\bar{3}.5406$
55.8	329.0	3.040	6.315×10^{-3}	$\bar{3}.8003$
60.5	333.7	2.997	9.491×10^{-3}	$\bar{3}.9773$
64.2	337.4	2.963	1.523×10^{-2}	$\bar{2}.1826$
70.1	343.3	2.918	2.813×10^{-2}	$\bar{2}.4492$
75.2	348.4	2.877	4.777×10^{-2}	$\bar{2}.6791$

The straight line plot of $\log_{10}k$ against $\frac{1}{T}$ is given in graph III, and the energy of activation (E) was calculated from the gradient of the line.

$$E = 25.4 \text{ kcal.mole}^{-1}.$$


III
$\log_{10} k$
$\bar{2}.7$
$\bar{2}.5$
$\bar{2}.3$
$\bar{2}.1$
$\bar{3}.9$
$\bar{3}.7$
$\frac{1}{T} \times 10^3$
2.91
2.95
2.99
3.03
3.07

Preparation of 8-(2'-t-butylphenyl)-1-naphthoic acid.

8-Bromo-1-naphthoic acid.

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

Naphthalic anhydride (198g.) was dissolved in hot aqueous sodium hydroxide solution (124g. in 4800 ml. water) and the solution filtered through glass wool. After heating under reflux for 15 minutes, mercuric oxide (220g.), dissolved in a mixture of glacial acetic acid (160 ml.) and water (600 ml.), was added to the boiling solution; a light brown solid separated. On acidification with acetic acid a colourless suspension was obtained and this was heated under reflux continuously for 80 hours. After cooling, the hydroxy-mercuri compound was filtered off, and was washed successively with water, alcohol and ether then dried (376g.).

The hydroxymercuri-compound (94g.) was suspended in a mixture of glacial acetic acid (300 ml.) and water (50 ml.), which was cooled externally with ice. A solution of bromine (34g.) in aqueous sodium bromide solution (75g. in 150 ml.water) was added slowly, with constant stirring, the temperature being maintained at 0-5°. After the addition was complete, the mixture was heated to 90°, poured into boiling water(3 l.) then heated for a further 5 minutes and the hot solution filtered. The filtrate was cooled and the crude acid which separated was filtered off and dried.

8-Bromo-1-naphthoic acid crystallised from benzene in small fine crystals, m.p. 175-177° (125g., 50%).

Methyl 8-bromo-1-naphthoate.

(Rule and Barnett, J., 1932, 175).

The acid (39.6g.) was dissolved in benzene and the solution heated under reflux. Thionyl chloride (22g.) was added slowly to the boiling solution, and the reaction mixture was then heated for a further 3½ hours. Methanol (100 ml.) was then added slowly to the solution, and the solution was heated for another 30 minutes. The benzene solution was then cooled, washed with water, aqueous sodium carbonate solution (10%) and water, and dried over anhydrous magnesium sulphate. After removal of the solvent, the residue was distilled under reduced pressure. Methyl 8-bromo-1-naphthoate, b.p. 168-176°/3mm., m.p. 34-36°, was obtained (36g., 90.7%).

8-(2'-t-butylphenyl)-1-naphthoic acid.

A mixture of o-iodo-t-butylbenzene (20g.) and methyl 8-bromo-1-naphthoate (20.7g.) was heated in a bath at 240°, and copper bronze (40g.) added gradually during ten minutes. When the reaction was complete the product was extracted with boiling chlorobenzene. The hot solution was filtered and the solvent removed. From the residual solution a solid separated which was crude dimethyl 1,1'-binaphthyl-8,8'-dicarboxylate. It was filtered off and washed with ether. The filtrate was distilled under reduced pressure, and three fractions were obtained:

(i) Colourless oil, b.p. 80-82°/4mm. (6.5g.) which was methyl 1-naphthoate, again the product of dehalogenation of methyl 8-bromo-1-naphthoate by the copper bronze.

(ii) Yellow oil, b.p. 140-146°/4mm. (1.5g.).

(iii) A dark brown glassy residue.

On adding acetone to the residue, a solid was obtained which was the required _ester_ (2.3g.). _Methyl_ 8-(2'-_t-butylphenyl_)-1-_naphthoate_ was crystallised from methanol and separated as colourless hexagonal prisms, m.p. 111-112° (Found: C, 83.0; H, 7.1. $C_{22}H_{22}O_2$ requires C, 83.0; H, 7.0%).

The ester was unchanged after boiling with ethanolic potassium ethoxide for three hours. The hydrolysis was therefore carried out in amyl alcohol solution and the mixture was heated under reflux for three hours. The amyl alcohol was then distilled off and the residue extracted with boiling water. The alkaline solution was extracted with ether then acidified with dilute hydrochloric acid.

8-(2'-t-butylphenyl)-1-naphthoic acid crystallised from methanol as colourless rhombic plates, m.p. 236-237° (Found: C, 82.7; H, 6.4. $C_{21}H_{20}O_2$ requires C, 82.7; H, 6.6%).

Resolution of 8-(2'-t-butylphenyl)-1-naphthoic acid.

All rotations were measured in chloroform at room temperature ($c \sim 0.5$) in 2 dm. tubes unless otherwise stated.

The acid (6.5g.) and strychnine (7.14g.) were dissolved in boiling ethanol (300 ml.) and kept at room temperature overnight. The first fraction of salt (2.9g.) separated in rectangular plates and had $[\alpha]_{5791}$ -22.2° and $[\alpha]_{5461}$ -31.4°. After concentration of the mother-liquor a second fraction separated which had $[\alpha]_{5791}$ -43.7° and $[\alpha]_{5461}$ -62.2°. Evaporation to dryness of the mother-liquor yielded a solid which had $[\alpha]_{5791}$ -94.7° and $[\alpha]_{5461}$ -126.3°. This fraction was crystallised from acetone until the specific rotation remained constant. The first two fractions were combined and recrystallised from ethanol.

Strychnine (+)-8-(2'-t-butylphenyl)-1-naphthoate crystallised from ethanol in hexagonal plates, m.p. 213-214° with loss of solvent at 101°, $[\alpha]_{5791}$ -14.5°, $[\alpha]_{5461}$ -19.9° (Found: C, 69.3; H, 7.6. $C_{21}H_{20}O_2 \cdot C_{21}H_{22}N_2O_2 \cdot 5H_2O$ requires C, 69.2; H, 7.2%). On being heated in vacuo at

80° for several hours the salt lost the equivalent of five molecules of water of crystallisation. On exposure to air the anhydrous salt very quickly reverted to the hydrated form.

Strychnine (-)-8-(2'-t-butylphenyl)-1-naphthoate crystallised from acetone in small rectangular plates m.p. 192-193°, $[\alpha]_{5791}$ -87.7°, $[\alpha]_{5461}$ -100.7° (Found: C, 78.6; H, 6.7. $C_{21}H_{20}O_2 \cdot C_{21}H_{22}N_2O_2$ requires C, 79.0; H, 6.6%).

The optically active acids were obtained from the salts by decomposition with aqueous sodium hydroxide solution in the usual manner, and recrystallised from a 1:5 mixture of benzene and light petroleum (b.p. 60-80°).

(+)-8-(2'-t-butylphenyl)-1-naphthoic acid crystallised in micro crystals, m.p. 145-146°, $[\alpha]_{5791}$ +44.4°, $[\alpha]_{5461}$ +49.7° (Found: C, 83.1; H, 67. $C_{21}H_{20}O_2$ requires C, 82.9; H, 6.6%).

(-)-8-(2'-t-butylphenyl)-1-naphthoic acid crystallised in micro crystals, m.p. 145-146°, $[\alpha]_{5791}$ -44.6°, $[\alpha]_{5461}$ -50.0° (Found: C, 83.1; H, 6.7. $C_{21}H_{20}O_2$ requires C, 82.9; H, 6.6%).

On further heating, the melted active acids solidified then melted at 236-237° - the melting point of the racemic acid.

The racemisation of the optically active acid was studied at temperatures between 121° and 136°. The acid (0.15g.) was dissolved in ethyl benzene (20 ml.), sealed in 8 tubes and heated in a thermostat to the required temperature. Tubes were removed at intervals, cooled rapidly and the rotations read at room temperature. As the rotation approached zero, the (±)-acid crystallised in the polarimeter tube.

Action of concentrated sulphuric acid on (±)-8-(2'-t-butylphenyl)-1-naphthoic acid.

The substituted naphthoic acid (0.9g.) was dissolved in ice-cold concentrated sulphuric acid (10 ml.) and a red solution was obtained. This was left to stand for 30 minutes and then poured on crushed ice. A yellow solid was precipitated and was filtered off. It was washed with aqueous sodium carbonate solution and with water, and dried (0.5g., 59%).

7-Oxo-11-t-butylbenz[d e]anthracene crystallised from petroleum ether (b.p. 60-80°) in yellow micro crystals m.p. 170-171° (Found: C, 88.4; H, 6.5. $C_{21}H_{18}O$ requires C, 88.1; H, 6.3%).

The reaction was repeated on the optically active (+)-8-(2'-t-butylphenyl)-1-naphthoic acid, and the product obtained was optically inactive.

Racemisation of optically active 8-(2'-t-butylphenyl)-1-naphthoic acid.

The rates of racemisation were measured in ethylbenzene, $c \sim 0.7$, $\lambda = 5461$ Å

TABLE VIII.

Racemisation of (-)-8-(2'-t-butylphenyl)-1-naphthoic acid at 121°. Polarimetric zero, $\alpha_o = 180.08$.

Time in Minutes	Observed Polarimetric Reading, a_t	$\alpha_t - \alpha_o$	$\log_{10}(\alpha_t - \alpha_o)$
0	179.67	-0.41	$\bar{1}.6128$
20	179.70	-0.38	$\bar{1}.5798$
40	179.73	-0.35	$\bar{1}.5441$
60	179.755	-0.325	$\bar{1}.5119$
80	179.78	-0.30	$\bar{1}.4771$
100	179.80	-0.28	$\bar{1}.4472$
120	179.82	-0.26	$\bar{1}.4150$
150	179.85	-0.23	$\bar{1}.3617$
180	179.87	-0.21	$\bar{1}.3222$

$$k = 0.003793 \text{ min.}^{-1}$$

Half-life period = 182.8 min.

TABLE IX.

Racemisation of (-)-8-(2'-t-butylphenyl)-1-naphthoic acid at 125°.

Polarimetric zero $\alpha_o = 180.08$.

Time in Minutes	Observed Polarimetric Reading, α_t	$\alpha_t - \alpha_o$	$\log_{10}(\alpha_t - \alpha_o)$
0	179.60	-0.48	$\bar{1}.6812$
10	179.63	-0.45	$\bar{1}.6532$
20	179.65	-0.43	$\bar{1}.6335$
30	179.665	-0.415	$\bar{1}.6180$
46	179.70	-0.38	$\bar{1}.5798$
61	179.73	-0.35	$\bar{1}.5441$
90	179.78	-0.30	$\bar{1}.4771$
122	179.825	-0.255	$\bar{1}.4065$

$$k = 0.005385 \text{ min.}^{-1}$$

Half-life period = 128.7 min.

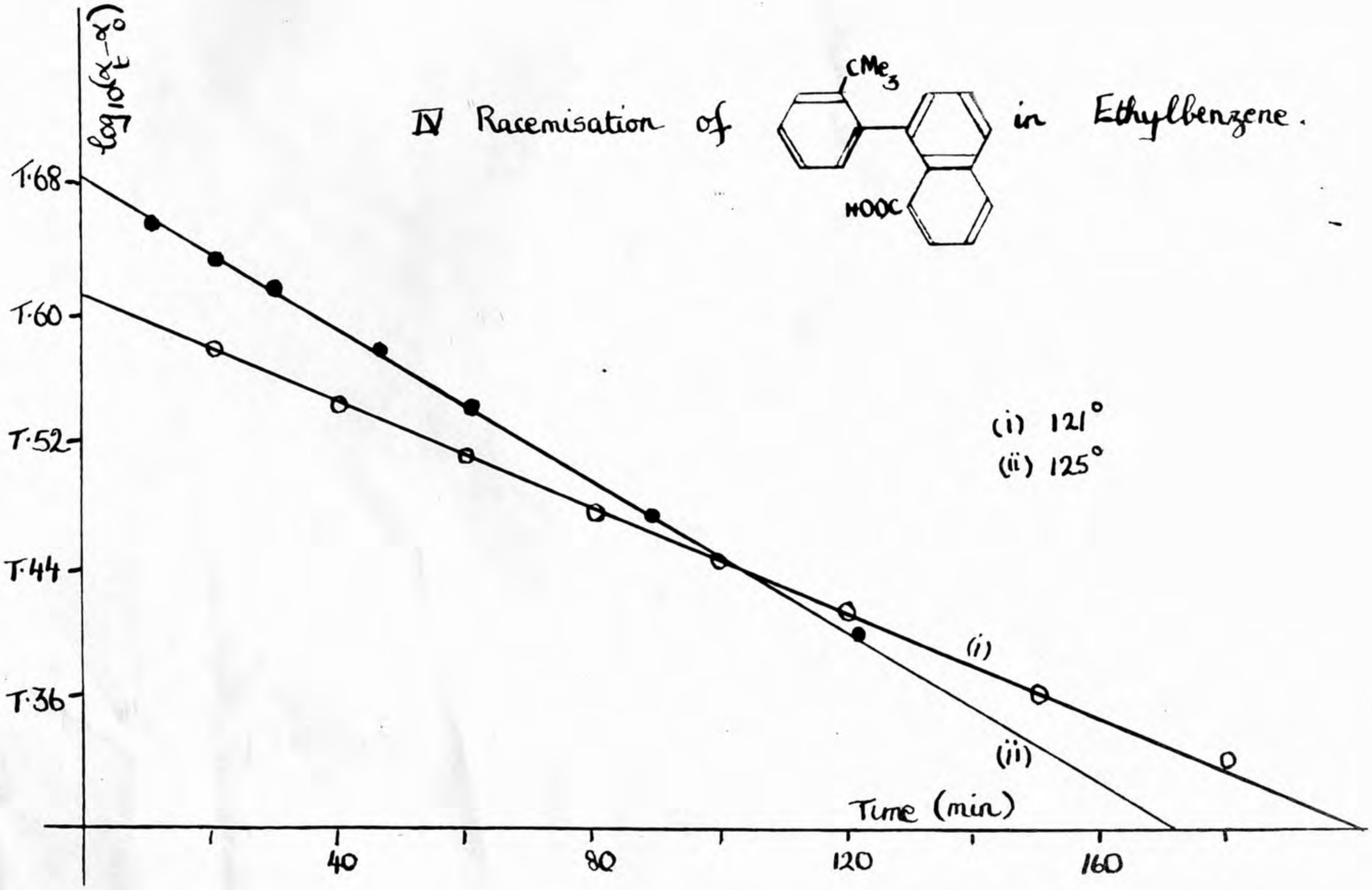

IV Racemisation of
CMe$_3$
HOOC
in Ethylbenzene.
$\log_{10}(\alpha_t - \alpha_0)$
$\bar{1}$·68
$\bar{1}$·60
$\bar{1}$·52
$\bar{1}$·44
$\bar{1}$·36
(i) 121°
(ii) 125°
(i)
(ii)
Time (min)
40
80
120
160

TABLE X.

Racemisation of (+)-8-(2'-t-butylphenyl)-1-naphthoic acid at 131°.

Polarimetric zero, α_o = 180.08

Time in Minutes	Observed Polarimetric Reading, α_t	$\alpha_t - \alpha_o$	$\log_{10}(\alpha_t - \alpha_o)$
0	180.56	0.48	$\bar{1}.6812$
5	180.545	0.465	$\bar{1}.6675$
10	180.525	0.445	$\bar{1}.6484$
15.2	180.50	0.42	$\bar{1}.6232$
20	180.48	0.40	$\bar{1}.6021$
30.5	180.44	0.36	$\bar{1}.5563$
40.2	180.41	0.33	$\bar{1}.5185$
50	180.385	0.305	$\bar{1}.4843$
60	180.355	0.275	$\bar{1}.4393$

$k = 0.009483 \text{ min.}^{-1}$

Half-life period = 73.1 min.

TABLE XI.

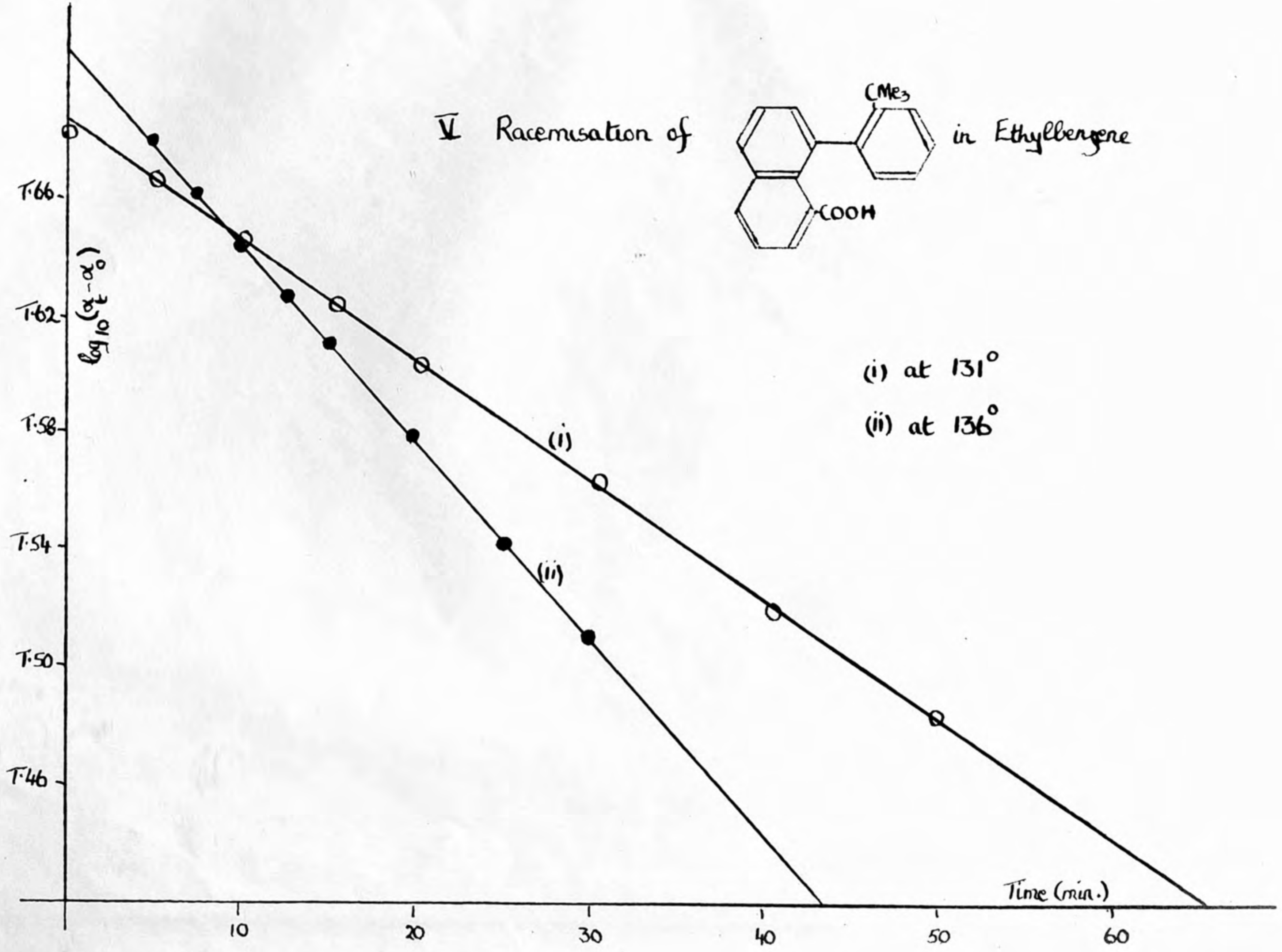
Racemisation of (-)-8-(2'-t-butylphenyl)-1-naphthoic acid at 136°.

Polarimetric zero, $\alpha_o = 180.08$

Time in Minutes	Observed Polarimetric Reading, α_t	$\alpha_t - \alpha_o$	$\log_{10}(\alpha_t - \alpha_o)$
5	179.60	-0.48	$\bar{1}.6812$
7.5	179.62	-0.46	$\bar{1}.6628$
10	179.64	-0.44	$\bar{1}.6435$
12.5	179.655	-0.425	$\bar{1}.6284$
15	179.67	-0.41	$\bar{1}.6128$
20	179.70	-0.38	$\bar{1}.5798$
25	179.73	-0.35	$\bar{1}.5441$
30	179.755	-0.325	$\bar{1}.5119$

$k = 0.015616 \text{ min.}^{-1}$

Half-life period = 44.4 min.



V Racemisation of in Ethylbenzene

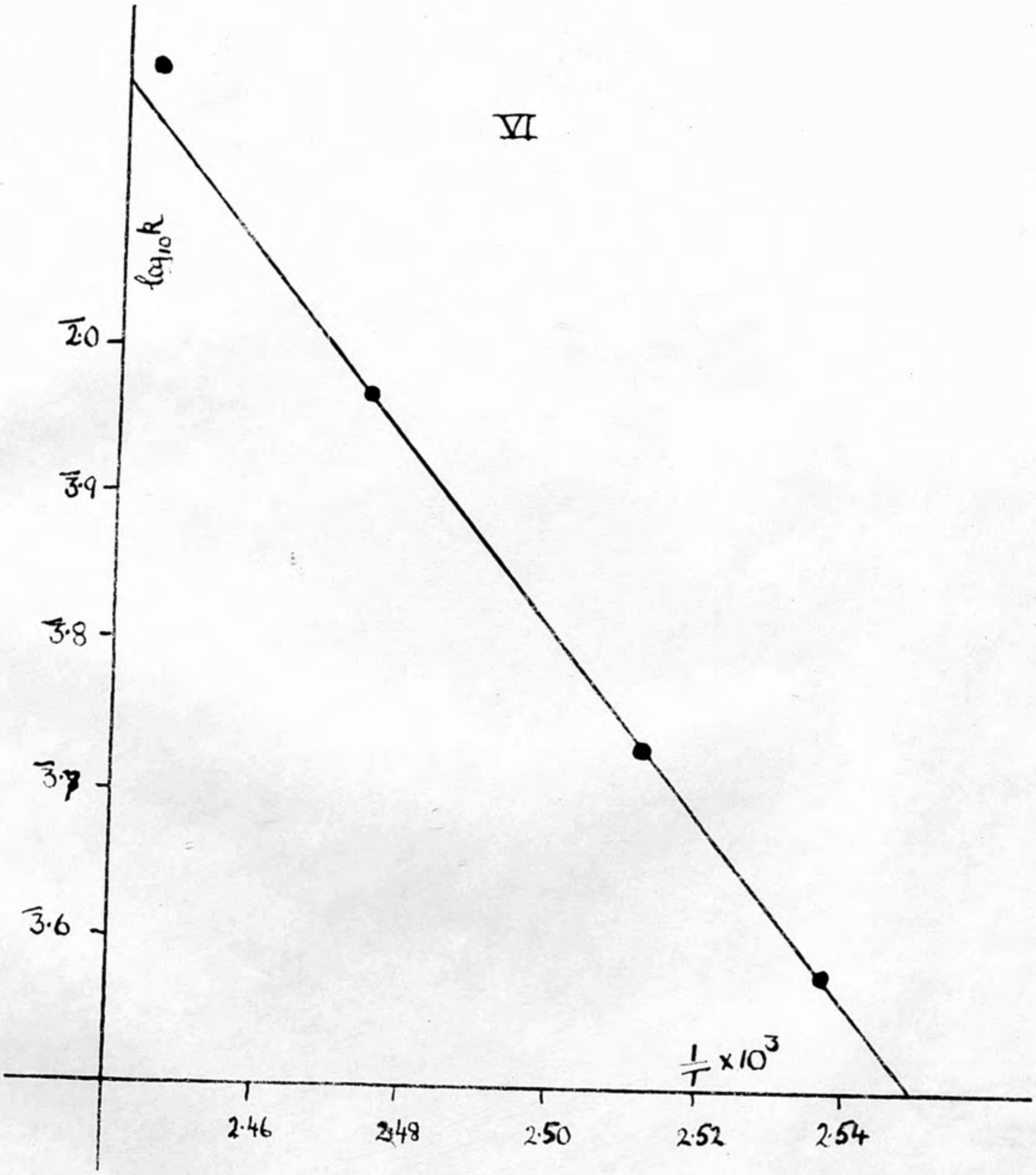
(i) at 131°

(ii) at 136°

TABLE XII.

T°	$T^{\circ}K$	$\frac{1}{T}$ x10^3	k min.$^{-1}$	$\log_{10}$ k
121°	394.2	2.537	3.793×10^{-3}	$\bar{3}.5789$
125°	398.2	2.512	5.385×10^{-3}	$\bar{3}.7312$
131°	404.2	2.474	9.483×10^{-3}	$\bar{3}.9769$
136°	409.2	2.444	1.562×10^{-2}	$\bar{2}.2337$

From the plot of $\log_{10}$k against $\frac{1}{T}$, given in graph VI, the Energy of Activation (E) was found to be 29 kcal.mole^{-1}.


VI
$\log_{10} k$
$\bar{2}$·0
$\bar{3}$·9
$\bar{3}$·8
$\bar{3}$·7
$\bar{3}$·6
$\frac{1}{T} \times 10^3$
2·46
2·48
2·50
2·52
2·54

OPTICAL STUDIES OF 2,2′-DI-t-BUTYLBIPHENYLCARBOXYLIC ACIDS AND OF 2′-t-BUTYLBIPHENYL-2-CARBOXYLIC ACID

BY
MARY S. LESSLIE
AND
URSULA J. H. MAYER

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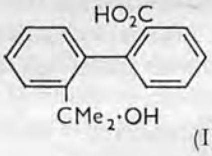
123. *Optical Studies of 2,2′-Di-t-butylbiphenylcarboxylic Acids and of 2′-t-Butylbiphenyl-2-carboxylic Acid.*

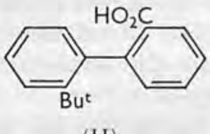
By Mary S. Lesslie and Ursula J. H. Mayer.

The synthesis of 2′-t-butylbiphenyl-2-carboxylic acid, 2′,6-di-t-butylbiphenyl-3-carboxylic acid and of 6,6′-di-t-butylbiphenyl-3,3′-dicarboxylic acid is described. The strychnine and the brucine salts of the mono-t-butylbiphenyl acid undergo second-order asymmetric transformation in ethanol. The di-t-butylbiphenyl acids have been resolved and show high optical stability.

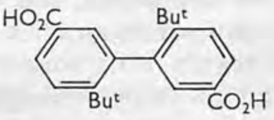
Corbellini and Angeletti[1] found that the brucine salt of the 2′-(hydroxyalkyl)biphenyl-2-carboxylic acid (I) underwent second-order asymmetric transformation in ethanol and, later, Jamison and Turner[2] showed that it also underwent first-order transformation in chloroform. We have now prepared 2′-t-butylbiphenyl-2-carboxylic acid (II) and found that its strychnine and brucine salts undergo second-order asymmetric transformation; no first-order transformation was observed. On the other hand, 6,6′-di-t-butylbiphenyl-3,3′-dicarboxylic acid (III) and 2′,6-di-t-butylbiphenyl-3-carboxylic acid (IV) were resolved and showed high optical stability.



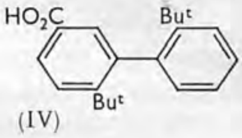
(I)



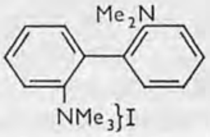
(II)



(III)



(IV)



(V)

Scale models based on known atomic radii show that in the di-t-butyl acids the two benzene rings cannot become coplanar since, owing to their volume, the two tertiary butyl groups cannot pass the hydrogens in the 2,2′-positions. Interconversion of the (+)- and (−)-forms is therefore inhibited. This is in marked contrast to the asymmetry of 2′-dimethylamino-2-biphenylyltrimethylammonium iodide (V) which arises from the " dynamic effect " of the less bulky $\cdot NMe_3^+$ group:[3] the active quaternary iodides whilst optically stable in cold aqueous solution had a half-life of 125 minutes at 99·5°.

Methyl 2′-t-butylbiphenyl-2-carboxylate (II) was prepared by heating together equimolecular proportions of methyl *o*-iodobenzoate and *o*-iodo-t-butylbenzene in presence of copper bronze. A mixture of 2,2′-di-t-butylbiphenyl, dimethyl diphenate, and methyl 2′-t-butylbiphenyl-2-carboxylate was obtained. The hydrocarbon was removed by distillation of the mixture under reduced pressure but the esters could not be separated either by distillation or by fractional crystallisation. The mixture of esters was therefore hydrolysed and the acids were eventually separated by tedious and rather wasteful crystallisations from glacial acetic acid (in which the diphenic acid was slightly less soluble) and from aqueous ethanol. *o*-Iodo-t-butyl benzene was prepared in greatly improved yield by modifications of Shoesmith and Mackie's method.[4] 2,4-Dinitro-t-butylbenzene was reduced in aqueous solution with sodium disulphide and the nitro-amine was deaminated through the diazonium fluoroborate or with hypophosphorous acid. The above authors found that during the diazotisation of *o*-amino-t-butylbenzene decomposition of the diazonium sulphate set in at −8° and we therefore performed the diazotisation at −35° and allowed the reaction mixture to warm to −13°, then added it to aqueous potassium iodide solution. This procedure resulted in greatly enhanced yields of the iodo-compound.

The dimethyl ester of the acid (III) was obtained by heating methyl 3-iodo-4-t-butylbenzoate with copper bronze. The preparation of the iodo-ester from methyl 3-amino-4-t-butylbenzoate hydrochloride (or sulphate) presented unexpected difficulty because of the instability of the diazonium salt. The crude iodo-ester was a green viscous oil; it was distilled under reduced pressure and appeared to be homogeneous Addition of light petroleum produced a wax-like solid; this crystallised from light petroleum and was found to be a 1 : 1 molecular compound of the iodo-ester and methyl 3-hydroxy-4-t-butylbenzoate. The iodo-ester is a liquid at room temperature and was obtained from the mother-liquors after all the molecular compound had been removed. It is surprising that the molecular compound distils under reduced pressure as if it were an individual substance, and in ethereal solution it did not yield the phenolic component when extracted with cold alkali. On the other hand, when the solid compound was stirred with cold 30% aqueous sodium hydroxide or warmed with a 10% solution of sodium hydroxide a mixture of the iodo-ester and sodium 3-hydroxy-t-butylbenzoate was obtained. By this means the iodo-ester was recovered from the molecular compound. In later preparations the solid compound was not isolated, but the oil obtained after vacuum-distillation was stirred with successive amounts of cold concentrated sodium hydroxide solution and the sodium salt of the hydroxy-acid was removed by repeated washing with water. The iodo-ester thus obtained was hydrolysed, and the iodo-acid was purified by crystallisation from methanol and from light petroleum, then converted into its methyl ester.

When heated with copper bronze the molecular compound gave 5,5′-dimethoxycarbonyl-2,2′-di-t-butylbiphenyl ether.

Ethyl 3-amino-4-t-butylbenzoate hydrochloride was also prepared. The diazonium chloride derived from it was very unstable but there was no evidence of compound formation between the iodo- and the hydroxy-ester. Washing with alkali failed again to remove the hydroxy-ester from the ethereal solution but on removal of the solvent a mixture of the two solid esters was obtained. These were easily separated by crystallisation from ethanol in which the hydroxy-ester was very soluble.

The methyl ester of the monocarboxylic acid (IV) was prepared by heating equimolecular amounts of methyl 3-iodo-4-t-butylbenzoate and *o*-iodo-t-butylbenzene. The products were partially separated by distillation under reduced pressure, the main fraction consisting of a mixture of 2,2′-di-t-butylbiphenyl and the required unsymmetrical ester. This was hydrolysed with ethanolic potassium ethoxide, and the hydrocarbon removed by extraction with ether. The unsymmetrical acid was then obtained on acidification of the alkaline solution.

The strychnine salt of the monocarboxylic acid (II) was prepared in ethanol, and a series of crops was obtained whose rotations in chloroform solution were approximately the same ($[\alpha]_{5791}$ $-46{\cdot}0° \pm 0{\cdot}4°$). The acid regenerated from these salts was lævorotatory and it was thus apparent that the strychnine salt had undergone second-order asymmetric transformation. Recrystallisation of the salts from methanol was more satisfactory than from ethanol since considerable dissociation into free acid and base occurred in the latter solvent. (When prepared in methanol the strychnine salt also underwent asymmetric transformation.) The purest salt had $[\alpha]_{5791}$ $-49{\cdot}9°$ in chloroform and racemised slowly during several days at room temperature. In boiling ethanol it racemised quickly. The highest rotation obtained for the acid was $[\alpha]_{5791}$ $-24{\cdot}3°$ and $[\alpha]_{5461}$ $-29{\cdot}8°$ in ethanol. Racemisation of the (—)-acid in ethanol was studied at 57°, 67°, and 79° (half-life 35, 14·1, and 5·6 minutes respectively). The activation energy was 24 kcal. mole^{-1}. The brucine salt was also prepared in ethanol and it, too, underwent second-order asymmetric transformation but to a smaller extent. The maximum rotation obtained for the recovered acid was $[\alpha]_{5791}$ $+7{\cdot}7°$ in ethanol.

6,6′-Di-t-butylbiphenyl-3,3′-dicarboxylic acid (III) was resolved through its brucine salt. The (+)-acid salt, which was the more soluble in ethanol, was a gel but it was possible to separate the two salts since their solubilities in ethanol differed considerably.

The free acids were obtained having $[\alpha]_{5791}$ ±18·6° (±0·3°) in acetone. The acids showed high optical stability and were not racemised in aqueous alkali or in pyridine at the boiling point.

2′,6-Di-t-butylbiphenyl-3-carboxylic acid (IV) was converted into its strychnine salt, and the two diastereoisomers were separated by crystallisation from ethanol. The (+)-acid salt was crystalline and was readily obtained optically pure whereas the (−)-acid salt was an oil. The (±)-acid, however, was more sparingly soluble than the active acids, and the crude (−)-acid obtained from the oil was isolated optically pure by crystallisation from methanol. The acids had $[\alpha]_{5791}$ ±25·5° and $[\alpha]_{5461}$ ±28·4° (±0·5°) in chloroform. The active acid retained its activity after sublimation at 130°/1 mm. and even after melting.

EXPERIMENTAL

2,4-*Dinitro-t-butylbenzene.*—t-Butylbenzene (100 g.) was added, with stirring, within ½ hr., to nitric acid (500 c.c.; *d* 1·51) at 0°. Then the solution was left at 60—65° for 15 min. and poured on crushed ice. The crude dinitro-compound was filtered off and was melted under boiling water (3 l.), then cooled quickly with vigorous stirring. After crystallisation from ethanol the dinitro-t-butylbenzene was obtained as white prisms which became yellow on exposure to light and had m. p. 63—64° (yield 85%).

3-*Nitro-4-t-butylaniline.*—A hot solution of sodium disulphide (2 mol.) in water (200 c.c.) was added within a few minutes to a vigorously stirred suspension of 2,4-dinitro-t-butylbenzene (45 g.) in boiling water (500 c.c.). After 1 hour's boiling, with stirring (the volume of water being maintained), the mixture was cooled and the crude nitro-amine was filtered off. After purification through its hydrochloride the base was crystallised from ethanol and from light petroleum (b. p. 40—60°). It melted at 55—56° (yield 75%).

o-*Nitro-t-butylbenzene.*—(*a*) 3-Nitro-4-t-butylaniline (60 g.) was diazotised in hydrochloric acid and the diazonium solution kept at 0—10° for 1 hr. (this was essential, otherwise much base was recovered). To the filtered solution hydrogen fluoroborate was added, and the precipitated diazonium fluoroborate was filtered off, washed with ether, and dried *in vacuo* over sulphuric acid (85 g.). It was decomposed by adding it gradually to a boiling mixture of ethanol (3 parts) and concentrated sulphuric acid (½ part). The nitro-t-butylbenzene was obtained with b. p. 102—104°/6 mm. (40 g., 72%).

(*b*) The aniline (60 g.) was diazotised as above and the filtered diazonium solution was added with stirring to hypophosphorous acid (600 c.c.) at 0°. By this method the nitro-t-butylbenzene was obtained in 75% yield.

o-*t-Butylaniline.*—The above nitro-compound (70 g.) was reduced with iron filings and water containing a little acetic acid. The base obtained (88%) had b. p. 93°/5 mm.

o-*Iodo-t-butylbenzene.*—*o*-t-Butylaniline (22 g.) was dissolved in dilute sulphuric acid (*d* 1·2; 120 c.c.) and cooled to −35°. A concentrated aqueous solution of sodium nitrite (10·5 g.) was added within 5 min. and the mixture allowed to warm in the freezing solution (carbon dioxide and ethanol) to −13° during 2 hr. The resultant brown gelatinous suspension was added to an aqueous solution of potassium iodide (75 g.). The diazonium iodide which separated decomposed readily. The mixture was made alkaline and the crude iodo-hydrocarbon from two similar experiments was steam-distilled. The distillate was extracted with ether, and the ethereal extract was washed successively with acid, sodium metabisulphite solution, acid, and water, then dried ($CaCl_2$). After removal of the solvent the residue was distilled and *o*-iodo-t-butylbenzene, b. p. 94—96°/3 mm. (68—78%), was obtained.

2,2′-*Di-t-butylbiphenyl.*—The above iodo-hydrocarbon (20 g.) reacted with copper bronze (20 g.) at 225° (bath). The reaction was complete after ½ hr. and the product was extracted with chlorobenzene. The solvent was removed and the residue distilled under reduced pressure. 2,2′-*Di-t-butylbiphenyl*, b. p. 140°/2 mm., was obtained. Light petroleum (b. p. 60—80°; 2 c.c.) was added to the oil, and the hydrocarbon, which crystallised, separated from ethanol as stout plates, m. p. 63—64° (Found: C, 90·2; H, 9·9. $C_{20}H_{26}$ requires C, 90·2; H, 9·8%).

2′-*t-Butylbiphenyl-2-carboxylic Acid.*—A mixture of *o*-iodo-t-butylbenzene (20 g.) and methyl *o*-iodobenzoate (20 g.) reacted with copper bronze at 210° (bath) for ½ hr. The product was extracted with chlorobenzene and after removal of the solvent the residue was distilled under reduced pressure. The lower fractions collected were liquids; the main fraction, b. p. 160—180°/5 mm. (13 g.), crystallised on addition of light petroleum (b. p. 40—60°) and was recrystallised three times from light petroleum (b. p. 40—60°). It was found to be an inseparable mixture of dimethyl diphenate and methyl 2′-t-butylbiphenyl-2-carboxylate and it was therefore hydrolysed with ethanolic potassium ethoxide. The resultant mixture of acids was separated by fractional crystallisation from glacial acetic acid followed by crystallisation from aqueous ethanol. *2′-t-Butylbiphenyl-2-carboxylic acid* crystallised from aqueous ethanol in needles, m. p. 182—183° (Found: C, 80·1; H, 7·2. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

3-Nitro-4-t-butylbenzoic Acid.—*p*-t-Butylbenzoic acid (50 g.) was added gradually to ice-cold nitric acid (500 c.c., *d* 1·51) Then the solution was kept at 60° for 15 min. and poured on ice. The acid crystallised from dilute acetic acid in small prisms, m. p. 162—163° (65%). Decarboxylation of the acid, followed by nitration of the resulting nitro-hydrocarbon, to give 2,4-dinitro-t-butylbenzene, m. p. 63—64° (Shoesmith and Mackie[4]), confirmed that the acid was the 3-nitro-isomer.

Methyl 3-Nitro-4-t-butylbenzoate.—3-Nitro-4-t-butylbenzoic acid (150 g.) was converted into its methyl ester, b. p. 162°/6 mm., plates, m. p. 45—46° (from methanol) (Found: C, 60·8; H, 6·5. Calc. for $C_{12}H_{15}NO_4$: C, 60·7; H, 6·4%). It was described as an oil by Kelbe and Pfeiffer.[5]

The *ethyl ester* had b. p. 162—165°/5 mm., m. p. 22—24° (Found: C, 62·1; H, 6·7. $C_{13}H_{17}NO_4$ requires C, 62·1; H, 6·8%).

Methyl 3-Amino-4-t-butylbenzoate Hydrochloride.—The above methyl nitro-ester (146 g.) was reduced with iron filings, water, and a little acetic acid at 100°. The mixture was extracted with hot methanol, and the filtered extract freed from the bulk of solvent by distillation. The residue was poured into an excess of concentrated hydrochloric acid at 0°. The resulting paste was filtered off and dried at 100° (121 g., 80%). The *hydrochloride* crystallised from alcohol in thin plates, m. p. 198—200° (Found: Cl, 15·0. $C_{12}H_{18}ClNO_2$ requires Cl, 14·6%).

The corresponding ethyl ester hydrochloride was similarly prepared from ethyl 3-nitro-4-t-butylbenzoate. A pure specimen was not obtained since it was too soluble in all the usual solvents. The free *base* was a viscous oil, b. p. 160°/4 mm. (Found: C, 70·6; H, 9·3. $C_{13}H_{19}NO_2$ requires C, 70·6; H, 8·7%). In attempts to crystallise this hydrochloride from dilute hydrochloric acid it was hydrolysed to *3-amino-4-t-butylbenzoic acid hydrochloride* which crystallised in prisms, m. p. 238—239° (Found: C, 57·5; H, 6·8. $C_{11}H_{16}ClNO_2$ requires C, 57·5; H, 6·9%).

3-Iodo-4-t-butylbenzoic Acid.—To the above methyl ester hydrochloride (44 g.) in concentrated hydrochloric acid at −25° the requisite amount of sodium nitrite in aqueous solution was added quickly. The mixture was left for 90 min., initially at −15°, and allowed to warm to −5°, then quickly added to aqueous potassium iodide solution (46 g.). The resultant oil which contained some low-melting solid was extracted with ether, and the ethereal solution was washed repeatedly with alkali, then successively with sodium metabisulphite solution, acid, and water, and dried. After removal of the ether the residue was distilled. The distillate was a green viscous oil, b. p. 164—168°/10 mm., which on addition of light petroleum (b. p. 40—60°) gave a wax-like solid (25·5 g.). It was recrystallised several times from light petroleum and separated as hair-like needles, m. p. 58—59° (Found: C, 54·8; H, 6·1; I, 24·1. $C_{12}H_{15}IO_2,C_{12}H_{16}O_3$ requires C, 54·8; H, 5·9; I, 24·1%).

On several occasions when the pure molecular compound was allowed to crystallise very slowly from light petroleum small rod-shaped crystals were deposited. The supernatant solution was then carefully decanted and immediately the hair-like needles of the molecular compound crystallised. The rods were identified as methyl 3-hydroxy-4-t-butylbenzoate.

The diazotisation of the base hydrochloride was repeated many times, the temperature conditions being varied and also the time allowed for the reaction to proceed. From all experiments the molecular compound was obtained in good yield; if the temperature was maintained too low or insufficient time allowed for complete diazotisation then unchanged base was recovered. The diazonium sulphate appeared to be even more unstable than the chloride and when it was added to aqueous potassium iodide the molecular compound was again the main product. The mother-liquors from the crystallisation of the molecular compound were repeatedly concentrated and cooled to −35° until no more solid compound separated. The crude liquid iodo-ester was then obtained on removal of the solvent. The iodo-ester was recovered from the molecular compound by addition of cold 30% aqueous sodium hydroxide solution. After being stirred for a few minutes the hydroxy-ester underwent hydrolysis and was easily removed as the sodium salt of the hydroxy-acid. Under these conditions no hydrolysis of the iodo-ester occurred. Alternatively, the green oil obtained from the vacuum-distillation of the crude " iodo "-product was similarly treated with cold alkali, and the iodo-ester was thus obtained free from the hydroxy-ester. The iodo-ester was hydrolysed with ethanolic potassium ethoxide to 3-*iodo-4-t-butylbenzoic acid*, needles, m. p. 202—203° (from ethanol) (Found: C, 43·5; H, 4·4. $C_{11}H_{13}IO_2$ requires C, 43·4; H, 4·3%).

The pure iodo-acid was converted into its *methyl ester*, b. p. 156—158°/4 mm., m. p. $\sim$12° (Found: C, 45·6; H, 4·8. $C_{12}H_{15}IO_2$ requires C, 45·3; H, 4·8%).

The *ethyl ester* crystallised from ethanol in cubes, m. p. 58—59° (Found: C, 47·1; H, 4·9. $C_{13}H_{17}IO_2$ requires C, 47·0; H, 5·2%).

Ethyl 3-amino-4-t-butylbenzoate hydrochloride was diazotised under the conditions employed for the methyl ester base. The product was a mixture of the iodo- and hydroxy-esters, each of which was a solid. They were readily separated by crystallisation from ethanol and the less soluble iodo-ester was obtained pure.

Methyl 3-*Hydroxy-4-t-butylbenzoate*.—Methyl 3-amino-4-t-butylbenzoate hydrochloride (12 g.) was diazotised at −15° and allowed to warm to +10° during which time decomposition with evolution of nitrogen was apparent. When the reaction was complete the solid *ester* which had separated (4·8 g.) was filtered off, dried and crystallised from light petroleum (b. p. 40—60°), forming needles, m. p. 108—109° (Found: C, 69·3; H, 7·7. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%). Hydrolysis was readily effected by stirring the ester with cold 10% aqueous sodium hydroxide. The sodium salt separated and dissolved to a clear solution when water was added. Acidification gave 3-*hydroxy-4-t-butylbenzoic acid*, rectangular needles (from aqueous ethanol), m. p. 187—188° (Found: C, 68·0; H, 7·25. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·25%).

5,5′-*Dimethoxycarbonyl-2,2′-di-t-butylbiphenyl Ether*.—The molecular compound (methyl 3-iodo-4-t-butylbenzoate, plus methyl 3-hydroxy-4-t-butylbenzoate) (45 g.) reacted with copper bronze at 240° (bath). The product was extracted with chlorobenzene and after removal of the solvent a crystalline *ether* was obtained (4·2 g.) that recrystallised from methanol as rhombohedra, m. p. 173—174° (Found: C, 72·3; H, 7·7; O, 19·3. $C_{24}H_{30}O_5$ requires C, 72·4; H, 7·6; O, 20·1%).

6,6′-*Di-t-butylbiphenyl-3,3′-dicarboxylic Acid*.—The above iodo-ester (18 g.) reacted vigorously with copper bronze at 235° (bath). The product was extracted with chlorobenzene and after removal of the solvent the crude ester crystallised and was washed with light petroleum (b. p. 40—60°). Two crystallisations from methanol gave *dimethyl* 6,6′-*di-t-butylbiphenyl*-3,3′-*dicarboxylate* as needles, m. p. 201—202° (5·5 g., 62%) (Found: C, 75·2; H, 8·0. $C_{24}H_{30}O_4$ requires C, 75·3; H, 7·9%). Ethyl 3-iodo-4-t-butylbenzoate with copper bronze at 245° similarly gave *diethyl* 6,6′-*di-t-butylbiphenyl*-3,3′-*dicarboxylate*, needles (from ethanol), m. p. 144—145° (Found: C, 76·0; H, 8·4. $C_{26}H_{34}O_4$ requires C, 76·1; H, 8·4%). Hydrolysis with ethanolic potassium ethoxide of each ester gave 6,6′-*di-t-butylbiphenyl*-3,3′-*dicarboxylic acid*, hexagonal prisms (from acetic acid), m. p. 345° (Kofler block) (Found: C, 74·4; H, 7·5. $C_{22}H_{26}O_4$ requires C, 74·5; H, 7·4%).

2′,6-*Di-t-butylbiphenyl-3-carboxylic Acid*.—A mixture of methyl 3-iodo-4-t-butylbenzoate (32 g.) and *o*-iodo-t-butylbenzene (26 g.) was heated with copper bronze in a bath at 220°. Then the mixture was extracted with chlorobenzene and after removal of the solvent an oil was obtained. On addition of methanol the symmetrical ester crystallised and was filtered off. The residue was distilled under reduced pressure and the main fraction (7 g.) was collected at 156—180°/2 mm. It was hydrolysed with ethanolic potassium ethoxide and 2,2′-di-t-butylbiphenyl was removed from the alkaline solution by extraction with ether. The acid was then precipitated on acidification of the alkaline solution. 2′,6-*Di-t-butylbiphenyl*-3-*carboxylic acid* crystallised from methanol in slender prisms, m. p. 233° with slight previous softening (Found: C, 81·1; H, 8·5. $C_{21}H_{26}O_2$ requires C, 81·2; H, 8·4%).

Alkaloid Salts of 2′-t-Butylbiphenyl-2-carboxylic Acid.—Rotations of salts were measured at room temperature for " AnalaR " chloroform solutions ($c \sim 1$) and of acid for ethanol solutions ($c \sim 1$) in 2 dm. tubes.

Strychnine salt. To a boiling solution of (±)-acid (5 g.) in ethanol (100 c.c.) strychnine (6·6 g.) was added. The salt which separated overnight at room temperature (8·0 g.) had

$[\alpha]_{5791}$ −45·6°. Evaporation of the mother-liquor gave successive crops whose specific rotations were approximately the same as above. A portion of salt on decomposition gave an acid, $[\alpha]_{5791}$ −19·9°. When prepared in more concentrated solutions of ethanol the specific rotations of the salts were lower and acids were recovered whose specific rotations varied from $[\alpha]_{5791}$ −13·5° to −18·2°. Recrystallising the salt from ethanol gave erratic results because of dissociation into free acid and base; methanol was therefore preferred and recrystallisation from this solvent was continued until the specific rotation of the salt remained constant.

Strychnine (−)-2′-*t-butylbiphenyl-2-carboxylate* crystallised from methanol in sheaves of rectangular prisms, m. p. 208—212°, $[\alpha]_{5791}$ −49·9°, $[\alpha]_{5461}$ −58·6° (Found: C, 77·3; H, 6·8. $C_{17}H_{18}O_2,C_{21}H_{22}N_2O_2$ requires C, 77·5; H, 6·8%). When it was boiled under reflux in chloroform solution for 15 min. its specific rotation fell to $[\alpha]_{5791}$ −38·2° and $[\alpha]_{5461}$ −44·8°. This salt, the " partial racemate," was always recovered from rotation solutions when the chloroform was removed by heat or by slow evaporation. When the methanol mother-liquor from recrystallisations was allowed to evaporate slowly to dryness at room temperature the residual salt yielded acid of low rotation ($[\alpha]_{5791}$ −6·3°). All salts were decomposed in the usual manner with ice-cold sodium hydroxide solution. Addition of ice-cold acid to the alkaline solution (after extraction with chloroform) gave the free acid. The purest strychnine salt gave acid, m. p. 185—187°, $[\alpha]_{5791}$ −24·3°, $[\alpha]_{5461}$ −29·8°. Crystallisation from ethanol caused complete racemisation of the acid.

Brucine salt. The (±)-acid (1 g.) and brucine (1·44 g.) were dissolved in boiling ethanol (14 c.c.). After 2 days at 4° the first crop of salt separated (1·2 g.), having $[\alpha]_{5791}$ −23·9° and $[\alpha]_{5461}$ −29·7°. From the reduced mother-liquor a second crop separated with the same rotation. After recrystallisation from ethanol the rotation was unchanged. The acid recovered from the salt had $[\alpha]_{5791}$ +7·7°. The preparation of brucine salt was repeated twice, the rotation of the recovered acids being +3·3° and +5·1°.

Racemisation of (−)-*acid.* The rate of racemisation in boiling ethanol was measured for a solution (20 c.c.) containing 0·2268 g. of (−)-acid. The temperature was rapidly raised to the b. p. (79°) and after a suitable interval the solution was rapidly cooled to room temperature. Polarimetric readings were taken at 20°. The heating and cooling processes were repeated until racemisation was complete; α_{5791} ($l = 2$) fell from −0·39° to 0°. From a logarithmic plot, k was found to be 0·00207 sec.$^{-1}$ and the half-life 5·6 min. The racemisation of the (−)-acid in ethanol was also followed at 57° and 67° in a well-lagged water-jacketed polarimeter tube ($l = 2$) thermostatically controlled. The rate constants were found to be 0·00033 and 0·00082 sec.$^{-1}$, and the half-life periods 35 and 14·1 min. respectively. From these data the activation energy was found to be 24 kcal. mole^{-1}.

Resolution of 6,6′-*Di-t-butylbiphenyl*-3,3′-*dicarboxylic Acid.*—All rotations were measured in " AnalaR " acetone at room temperature ($c \sim 0{\cdot}5$) in 2 dm. tubes. The acid (6·5 g.) and brucine (14·4 g.) were dissolved in ethanol (450 c.c.), and the solution kept overnight at +4°. The first fraction of salt (6·1 g.) separated as rosettes of thin rectangular plates and had $[\alpha]_{5791}$ −41·8°, $[\alpha]_{5461}$ −46·8°. The second fraction (1·4 g.) which separated after concentration of the mother-liquor had $[\alpha]_{5791}$ −42·4°, $[\alpha]_{5461}$ −50·2°. Further concentration of the mother-liquor yielded a gel which contained a small amount of crystalline salt and since the gel was very soluble in ethanol it was possible to separate them. The crystalline salt was recrystallised four times from ethanol and was then optically pure.

Brucine (+)-6,6′-*di-t-butylbiphenyl*-3,3′-*dicarboxylate* crystallised from ethanol as a hydrate in rosettes of long, thin rectangular plates, m. p. 210° with previous softening, $[\alpha]_{5791}$ −37·8°, $[\alpha]_{5461}$ −43·9° (Found: C, 65·3; H, 7·4. $C_{22}H_{26}O_4,2C_{23}H_{26}N_2O_4,6H_2O$ requires C, 65·3; H, 7·3%). On being heated *in vacuo* at 70° for several hours the salt lost its water of crystallisation and the loss in weight corresponded to $6H_2O$. On exposure to air the anhydrous salt very quickly reverted to the hydrated form. Decomposition of the above salt yielded (+)-acid, and from the gel the (−)-acid was obtained.

(+)-6,6′-*Di-t-butylbiphenyl*-3,3′-*dicarboxylic acid* crystallised from ethanol in glistening plates, from glacial acetic acid in sheaves of rectangular rods, and from aqueous acetic acid in plates. From these solvents it always had solvent of crystallisation which was completely removed only by heating the products *in vacuo* at 130° for several hours. From aqueous acetic acid the (+)-acid crystallised with 1 mol. of water of crystallisation, and had m. p. 345° with loss of solvent at 200° (Kofler block), $[\alpha]_{5791}$ +18·1°, $[\alpha]_{5461}$ +23·6° (Found: C, 70·9; H, 7·2. $C_{22}H_{26}O_4,H_2O$ requires C, 70·9; H, 7·6%).

The *anhydrous acid*, m. p. 345°, had $[\alpha]_{5791}$ $+18{\cdot}6°$, $[\alpha]_{5461}$ $+24{\cdot}1°$ (Found: C, 74·7; H, 7·6. $C_{22}H_{26}O_4$ requires C, 74·5; H, 7·4%).

The (−)-*acid* crystallised from glacial acetic acid with 1 mol. of acetic acid of crystallisation; it had m. p. 345° with loss of solvent at 240° (Kofler block), $[\alpha]_{5791}$ $-17{\cdot}7°$, $[\alpha]_{5461}$ $-22{\cdot}8°$ (Found: C, 69·7; H, 7·2. $C_{22}H_{26}O_4,C_2H_4O_2$ requires C, 69·6; H, 7·3%). Heating *in vacuo* at 130° for several hours gave the unsolvated acid, $[\alpha]_{5791}$ $-18{\cdot}9°$, $[\alpha]_{5461}$ $-24{\cdot}2°$.

After being boiled in sodium hydroxide or in pyridine solution for 3 hr. the active acid was recovered unchanged.

Resolution of 2′,6-Di-t-butylbiphenyl-3-carboxylic Acid.—Rotations of salts and acids were measured at room temperature in " AnalaR " chloroform ($c \sim 1$) in 2 dm. tubes unless otherwise stated.

The above acid (3·1 g.) and strychnine (3·4 g.) were dissolved in ethanol (120 c.c.) and kept at room temperature overnight. The first crop of salt (1·4 g.) separated as fine needles, $[\alpha]_{5791}$ $-8{\cdot}9°$, $[\alpha]_{5461}$ $-11{\cdot}0°$. After concentration of the mother-liquor more salt was obtained (1·2 g.) with approximately the same rotation. On further concentration an oil was obtained that did not crystallise. This was decomposed and gave the crude (−)-acid. The crystalline (+)-acid salt was purified by recrystallisation from ethanol.

Strychnine (+)-*2′,6-di-t-butylbiphenyl-3-carboxylate* crystallised from ethanol in slender needles, m. p. 160—161°, $[\alpha]_{5791}$ $-9{\cdot}5°$, $[\alpha]_{5461}$ $-12{\cdot}6°$ (Found: C, 74·2; H, 7·8. $C_{21}H_{26}O_2,C_{21}H_{22}N_2O_2,2H_2O$ requires C, 74·1; H, 7·7%). When heated *in vacuo* at 80° the salt lost 2 mols. of water of crystallisation. The free acids were obtained from the strychnine salts by decomposition with formic acid. (+)-*2′,6-Di-t-butylbiphenyl-3-carboxylic acid* crystallised from methanol in needles, m. p. 181—185°, $[\alpha]_{5791}$ $+25{\cdot}5°$, $[\alpha]_{5461}$ $+28{\cdot}4°$ (Found: C, 80·8; H, 8·3. $C_{21}H_{26}O_2$ requires C, 81·2; H, 8·4%). In toluene its rotation was $[\alpha]_{5791}$ $+45{\cdot}4°$, $[\alpha]_{5461}$ $+51{\cdot}8°$.

The crude (−)-acid was crystallised from methanol, and a small amount of (±)-acid separated. This was filtered off and the mother-liquor was concentrated: the (−)-acid crystallised. Recrystallisation from methanol gave the pure (−)-acid, m. p. 181—185°, $[\alpha]_{5791}$ $-25{\cdot}8°$ and $[\alpha]_{5461}$ $-28{\cdot}3°$.

The active acids melted rather indefinitely and it was suspected that they contained solvent of crystallisation since erratic analytical figures for the same sample were obtained on several occasions. The (−)-acid was therefore heated at 130°/1 mm. and sublimed under these conditions. The *acid* so obtained melted at 192—193° and had $[\alpha]_{5791}$ $-65{\cdot}5°$ and $[\alpha]_{5461}$ $-72{\cdot}4°$ in toluene (Found: C, 80·9; H, 8·6%). A portion of the pure (−)-acid was melted and allowed to solidify: its specific rotation in toluene was unchanged.

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