265. *Optical Studies of 2′-Substituted 2-t-Butylbiphenyls. Part II.*[1] *2-Nitro-2′-t-butylbiphenyl-4-carboxylic Acid and 8-o-t-Butylphenyl-1-naphthoic Acid.*

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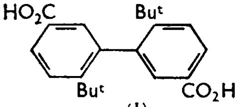
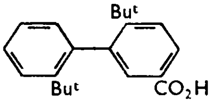
The strychnine salt of the nitro-acid named in the title underwent second-order asymmetric transformation in ethanol and gave (+)-acid, $[\alpha]_{5791}$ +33·4°. The naphthoic acid has been resolved and has $[\alpha]_{5791}$ ±44·5°. The optical stability of the two acids is contrasted with that of 2′-t-butylbiphenyl-2-carboxylic acid. The enantiomers of 2,2′-di-t-butylbiphenyl have been obtained, with $[\alpha]_{5791}$ ±18·0° (±0·2°).

In Part I[1] the preparation and high optical stability of two 2,2′-di-t-butylbiphenyl acids (I) and (II) were described. These acids could not be racemised under any conditions whereas 2′-t-butylbiphenyl-2-carboxylic acid (III) was optically labile and its strychnine and brucine salts underwent asymmetric transformation in ethanol. It therefore seemed of interest to examine the optical stability of other 2-t-butylbiphenyls in which the 2′-position was occupied by substituents more effective as blocking groups than the carboxyl group and we have now prepared compounds (IV) and (V).



(I)



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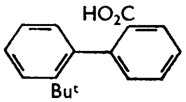

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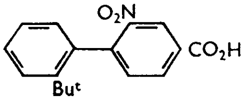

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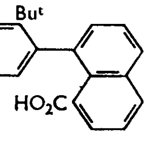

(V)

We first prepared methyl 2′-nitro-6-t-butylbiphenyl-3-carboxylate by heating *o*-chloronitrobenzene and methyl 3-iodo-4-t-butylbenzoate in presence of copper bronze but the yield was extremely small. The synthesis of the ethyl ester of acid (IV) from ethyl 3-nitro-4-bromobenzoate and *o*-iodo-t-butylbenzene was more successful. The methyl ester of

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[1] The paper by Lesslie and Mayer, *J.*, 1961, 611, is considered to be Part I.

the naphthoic acid (V) was similarly prepared by interaction of *o*-iodo-t-butylbenzene and methyl 8-bromo-1-naphthoate.

The nitro-acid (IV) gave a uniform strychnine salt which in chloroform solution racemised at room temperature during 14 days or at the boiling point in 2 hr. In contrast, the strychnine salt of acid (III) racemised at room temperature during 2 days or at the boiling point in 2 min.

The (+)-acid (IV) had $[\alpha]_{5791}$ +33·4° and $[\alpha]_{5461}$ +40·5° in chloroform. Its racemisation in toluene was studied at various temperatures between 51° and 75·2°; between these limits the half-life fell from 200 to 14·5 min., whereas between 57° and 79° the half-life of the (—)-acid (III) fell from 35 to 5·6 min.[1] The activation energy of the nitro-acid was 25·4 kcal. mole^{-1}.

8-*o*-t-Butylphenyl-1-naphthoic acid (V) was resolved through its strychnine salt. The two diastereoisomers had $[\alpha]_{5791}$ —14·5° and $[\alpha]_{5791}$ —87·7° respectively in chloroform. The active acids had $[\alpha]_{5791}$ ±44·5° (±0·1°) in chloroform. Preliminary racemisation experiments had indicated that this acid was more optically stable than the acids (III) and (IV) and rates of racemisation were therefore determined in ethylbenzene at temperatures between 121° and 136°. Between these limits the half-life fell from 183 to 44·4 min. The acid racemised completely at its melting point (145°) in contrast to the di-t-butyl acid (II) which retained its activity after melting (192°).[1] The energy of activation was found to be 29 kcal. mole^{-1}.

In an attempt to prepare the parent hydrocarbon from the above naphthoic acid by the Schmidt reaction the (±)-acid (V) was dissolved in ice-cold concentrated sulphuric acid but it cyclised immediately to 7-oxo-11-t-butylbenz[*de*]anthracene.

Conversion of the symmetrical di-t-butylbiphenyldicarboxylic acid (I) into 2,2′-di-t-butylbiphenyl was not readily achieved. The acid was unaffected when boiled in quinoline in the presence of copper bronze for several hours and when heated with hydroxylamine hydrochloride and polyphosphoric acid.[2] The diamide, readily formed from the acid chloride, failed to undergo the Hofmann reaction and several of its modifications. However, the Schmidt reaction succeeded and 3,3′-diamino-6,6′-di-t-butylbiphenyl was isolated and then deaminated by the action of hypophosphorous acid on the tetrazotised diamine. From the active acids the enantiomers of 2,2′-di-t-butylbiphenyl were obtained and had $[\alpha]_{5791}$ ±18·0° (±0·2°) in acetone; like the parent acids they showed high optical stability.

EXPERIMENTAL

2′-Nitro-6-t-butylbiphenyl-3-carboxylic Acid.—A mixture of *o*-chloronitrobenzene (13 g.) and methyl 3-iodo-4-t-butylbenzoate[1] (32 g.) was heated at 235° (bath) with copper bronze. A vigorous reaction ensued and was complete after 30 min. The product was extracted with chlorobenzene and after removal of most of the solvent dimethyl 6,6′-di-t-butylbiphenyl-3,3′-dicarboxylate crystallised (3·5 g.) and was filtered off. The filtrate was distilled *in vacuo* and a fraction (10 g.) was collected, b. p. 96—110°/3 mm., which was a mixture of *o*-chloronitrobenzene and methyl *p*-t-butylbenzoate. The residue was a brown oil (10 g.) and was hydrolysed with ethanolic potassium ethoxide. A mixture of three acids was obtained, the symmetrical di-t-butylbiphenyl-3,3′-dicarboxylic acid, *p*-t-butylbenzoic acid, and the required nitro-acid. The butylbenzoic acid was removed by extraction with boiling light petroleum (b. p. 80—100°), and the residue was crystallised from glacial acetic acid. The symmetrical biphenyldicarboxylic acid separated first and was filtered off; from the mother-liquor the *nitro-acid* was obtained after concentration. From six similar preparations the yield of nitro-acid was only 2 g. *2′-Nitro-6-t-butylbiphenyl-3-carboxylic acid* crystallised in 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%).

6-nitro-2′-t-Butylbiphenyl-4-carboxylic Acid.—A mixture of *o*-iodo-t-butylbenzene[1] (20 g.) and ethyl 3-nitro-4-bromobenzoate (21 g.) (prepared from *p*-aminobenzoic acid by a route similar to that used by Searle and Adams[3] for the preparation of the corresponding iodo-ester)

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[2] Snyder, Elston, and Kellom, *J. Amer. Chem. Soc.*, 1953, **75**, 2014.

[3] Searle and Adams, *J. Amer. Chem. Soc.*, 1933, **55**, 1649.

was heated in a bath at 170° and copper bronze then added at such a rate that the temperature of the mixture did not exceed 240°. The product was extracted with chloroform, and the chloroform solutions from four similar preparations were combined; after removal of the solvent the residual oil was distilled under reduced pressure. The lower fractions contained *o*-iodo-t-butylbenzene, 2,2′-di-t-butylbiphenyl and ethyl *m*-nitrobenzoate. The residual oil was hydrolysed with ethanolic potassium ethoxide and a mixture of the mononitro- and symmetrical dinitro-acids was obtained. These were separated by extraction of the mononitro-acid with benzene (Soxhlet). The benzene solution was then passed through a column of silica gel and eluted with benzene. Removal of the solvent gave 6-*nitro*-2′-*t*-*butylbiphenyl*-4-*carboxylic acid* (5·8 g.) that crystallised from light petroleum (b. p. 40—60°) as yellow rods, m. p. 150—151° (Found: C, 68·3; H, 5·6. $C_{17}H_{17}NO_4$ requires C, 68·2; H, 5·7%).

Strychnine 6-*Nitro*-2′-*t*-*butylbiphenyl*-4-*carboxylate*.—All rotations were measured in chloroform at room temperature ($c \sim 1·0$) in 2 dm. tubes unless otherwise stated. The acid (4·5 g.) and strychnine (5·0 g.) were dissolved in boiling ethanol (250 c.c.) and kept overnight at +4°. The first fraction of salt separated (4·5 g.) in rectangular plates, $[\alpha]_{5791}$ +14·6°. Evaporation of the mother-liquor gave successive crops which had approximately the same specific rotation. A portion of salt, on decomposition, gave an acid of $[\alpha]_{5791}$ +33·4°. 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 gave a (−)-acid. The (+)-acid salt was recrystallised three times from ethanol. *Strychnine* (+)-6-*nitro*-2′-*t*-*butylbiphenyl*-4-*carboxylate* crystallised in pale yellow 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%). In chloroform solution it racemised slowly at room temperature (14 days); the " partial racemate " had $[\alpha]_{5791}$ −2·8°, $[\alpha]_{5461}$ −4·1°. When the chloroform solution was boiled under reflux for 2 hr. racemisation was complete.

(+)6-*Nitro*-2′-*t*-*butylbiphenyl*-4-*carboxylic acid*, obtained by decomposition at 0° of the above strychnine salt, had m. p. 148—149°, $[\alpha]_{5791}$ +33·4°, $[\alpha]_{5461}$ +40·5° (Found: C, 68·4; H, 5·8. $C_{17}H_{17}NO_4$ requires C, 68·2; H, 5·7%).

Racemisation of (+)-*Acid*.—Racemisation of the (+)-acid in toluene was followed in a water-jacketed polarimeter tube thermostatically controlled, with the following results:

Temp.	51·0°	55·8°	60·5°	64·2°	70·1°	75·2°
10^3k (min.$^{-1}$)	3·47	6·31	9·49	15·2	28·1	47·8
Half-life (min.)	200	110	73·0	45·5	24·6	14·5

The activation energy was found to be 25·4 kcal. mole^{-1}.

8-o-*t*-*Butylphenyl*-1-*naphthoic Acid*.—A mixture of *o*-iodo-t-butylbenzene (20 g.) and methyl 8-bromo-1-naphthoate [4] (21 g.) reacted vigorously with copper bronze at 240° (bath). The reaction was complete after ½ hr. and the product was extracted with chlorobenzene. After removal of some of the solvent dimethyl 1,1′-binaphthyl-8,8′-dicarboxylate separated from the residual solution. It was filtered off and the filtrate was distilled under reduced pressure. The distillate was mainly methyl 1-naphthoate (6·5 g.) b. p. 80—82°/4 mm. The residue was a dark brown glass which crystallised on addition of acetone (2·3 g.). *Methyl* 8-o-*t*-*butylphenyl*-1-*naphthoate* crystallised from methanol 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 recovered after 3 hours' boiling in ethanolic potassium ethoxide solution but underwent hydrolysis in alkaline pentyl alcohol solution (3 hr.). 8-o-*t*-*Butylphenyl*-1-*naphthoic acid* crystallised from methanol in rhombic plates, m. p. 236—237° (Found: C, 82·7; H, 6·4. $C_{21}H_{20}O_2$ requires C, 82·9; H, 6·6%).

Resolution of 8-o-*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 (6·5 g.) and strychnine (7·2 g.) were dissolved in boiling ethanol (300 c.c.) and kept overnight at room temperature. The first fraction of salt (2·9 g.) separated as rectangular plates and had $[\alpha]_{5791}$ −22·2°, $[\alpha]_{5461}$ −31·4°. The second fraction (2·8 g.), which separated after concentration of the mother-liquor, had $[\alpha]_{5791}$ −43·7°, $[\alpha]_{5461}$ −62·2°. Evaporation of the mother-liquor to dryness gave a solid which had $[\alpha]_{5791}$ −94·7°, $[\alpha]_{5461}$ −126·3°. This fraction, the (−)-acid salt, was recrystallised from acetone until it was optically pure. The first two fractions were combined and recrystallised from ethanol. *Strychnine* (+)-8-o-*t*-*butylphenyl*-1-*naphthoate* crystallised from ethanol in hexagonal plates, m. p. 213—214° with loss of solvent at 101°,

[4] Rule and Barnett, *J.*, 1932, 175; Rule, Pursell, and Brown, *J.*, 1934, 168.

$[\alpha]_{5791}$ −14·5°, $[\alpha]_{5461}$ −19·9° (Found: C, 69·3; H, 7·6. $C_{21}H_{20}O_2,C_{21}H_{22}N_2O_2,5H_2O$ requires C, 69·2; H, 7·2%). On being heated *in vacuo* at 80° for several hours the salt lost its water of crystallisation and the loss in weight corresponded to $5H_2O$. On exposure to air the salt quickly reverted to the hydrated form.

Strychnine (−)-8-o-*t-butylphenyl*-1-*naphthoate* crystallised in small rectangular plates, m. p. 192—193°, $[\alpha]_{5791}$ −87·7°, $[\alpha]_{5461}$ −100·7° (Found: C, 78·6; H, 6·7. $C_{21}H_{20}O_2,C_{21}H_{22}N_2O_2$ requires C, 79·0; H, 6·6%). The optically active acids were obtained from their strychnine salts by decomposition with aqueous sodium hydroxide solution in the usual manner. (+)-8-o-*t-Butylphenyl*-1-*naphthoic acid*, crystallised from 1 : 5 benzene–light petroleum (b. p. 60—80°), had m. p. 145—146°, $[\alpha]_{5791}$ +44·4°, $[\alpha]_{5461}$ +49·7° (Found: C, 83·1; H, 6·7. $C_{21}H_{20}O_2$ requires C, 82·9; H, 6·6%). The (−)-*acid* had m. p. 145—146° and $[\alpha]_{5791}$ −44·6°, $[\alpha]_{5461}$ −50·0° (Found: C, 83·1; H, 6·7%). When the active acid melted, the melt solidified immediately and then remelted at 236—237°, the m. p. of the racemic acid.

Racemisation of (−)-*Acid* (V).—The racemisation of the (−)-acid was studied at temperatures between 121° and 136°. The acid (~0·15 g.) was dissolved in ethylbenzene (20 c.c.) and sealed in 8 glass tubes which were heated in a thermostat-bath at the required temperature. At intervals a tube was removed and cooled rapidly and the solution examined polarimetrically (1 dm. tube) at room temperature. As racemisation proceeded the acid became less soluble in the solvent and crystallised in the tubes. The following results were obtained:

Temp.	121°	125°	131°	136°
10^3k (min.$^{-1}$)	3·79	5·38	9·48	15·62
Half-life (min.)	183	129	73·1	44·4

The energy of activation was found to be 29 kcal. mole^{-1}.

7-*Oxo*-11-*t-butylbenz*[de]*anthracene*.—The racemic t-butylphenylnaphthoic acid (0·9 g.) dissolved in concentrated sulphuric acid (10 c.c.) at 0° to give a red solution. It was left at 0° for 30 min., then poured on ice. The solid which separated was filtered off, washed with aqueous sodium carbonate solution and water, and dried (0·5 g.). From light petroleum (b. p. 60—80°) 7-*oxo*-11-*t-butylbenz*[de]*anthracene* formed yellow 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 (+)-acid likewise gave the cyclised product which was optically inactive.

6,6′-*Di-t-butylbiphenyl*-3,3′-*dicarbonyl Chloride*.—6,6′-Di-t-butylbiphenyl-3,3′-dicarboxylic acid [1] (13·5 g.) and thionyl chloride (54 g.) were heated under reflux until the reaction was complete. The excess of thionyl chloride was removed by distillation. 6,6′-*Di-t-butylbiphenyl*-3,3′-*dicarbonyl chloride*, crystallised from light petroleum (b. p. 40—60°), had 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*.—The above acid chloride (9 g.) was dissolved in dry carbon tetrachloride (50 c.c.) and added slowly to ice-cooled carbon tetrachloride which had been saturated with ammonia and through which ammonia was bubbled continuously. The mixture was then left at 0° for 1 hr., allowed to warm to room temperature, and then boiled to expel ammonia. The solid which had separated was filtered off. 6,6′-*Di-t-butylbiphenyl*-3,3′-*dicarbonamide* crystallised from methanol in rhombs, m. p. 331° (Found: C, 75·4; H, 8·4. $C_{22}H_{28}N_2O_2$ requires C, 75·0; H, 8·0%). It was sparingly soluble in most organic solvents.

3,3′-*Diamino*-6,6′-*di-t-butylbiphenyl*.—(*a*) Treatment of the above diamide (3·5 g.) with alkaline potassium hypobromite or hypochlorite failed to give the diamine. Attempts to prepare the urethane were also unsuccessful.

(*b*) 6,6′-Di-t-butylbiphenyl-3,3′-dicarboxylic acid (3·5 g.) was dissolved in concentrated sulphuric acid (20 c.c.), then benzene (20 c.c.) was added to the solution. The mixture was heated at ~50° and activated sodium azide [5] (2 g.) was gradually added with stirring during 45 min. A vigorous reaction ensued after each addition. The temperature was maintained at ~50° (after addition of the azide was complete) until the reaction had subsided and was then raised slowly to 75°. When effervescence had ceased the mixture was cooled in ice, made alkaline, and extracted with benzene. The benzene solution was washed with water, dried, and passed through a column of alumina. It was eluted with 1 : 5 acetone–benzene and from the eluates, after removal of the solvent, a viscous yellow oil was obtained. This was heated with concentrated hydrochloric acid. A hydrochloride crystallised.

[5] Nelles, *Ber.*, 1932, **65**, 1345.

3,3′-*Diamino*-6,6′-*di-t-butylbiphenyl hydrochloride* crystallised from dilute hydrochloric acid in pink plates, m. p. 276—278° (decomp.) (Found: C, 54·6; H, 8·4. $C_{20}H_{30}Cl_2N_2,4H_2O$ requires C, 54·4; H, 8·7%). On being heated *in vacuo* at 80° for several hours the hydrochloride lost weight corresponding to $4H_2O$. 3,3′-*Diamino*-6,6′-*di-t-butylbiphenyl* crystallised from light petroleum (b. p. 60—80°) in pale yellow needles, m. p. 125—126° (Found: C, 80·7; H, 9·4. $C_{20}H_{28}N_2$ requires C, 81·0; H, 9·5%).

2,2′-*Di-t-butylbiphenyl.*—The above diamine (2 g.) was diazotised in hydrochloric acid at −20° and the solution allowed to warm in the freezing solution (carbon dioxide and ethanol) to 0°. It was then added with stirring to hypophosphorous acid (30 c.c.) at 0° and the mixture was left overnight at 4°. The crude hydrocarbon was extracted with light petroleum (b. p. 40—60°), and the petroleum solution was washed with alkali and water, then dried. The yellow solution was passed through a column of alumina and eluted with light petroleum. After removal of the solvent from the eluates 2,2′-di-t-butylbiphenyl was obtained and, crystallised from methanol, had m. p. 63—64° (0·8 g., 52%).

Rotations were measured at room temperature in 2 dm. tubes ($c \sim 0{\cdot}5$). By the above procedure (+)-6,6′-di-t-butylbiphenyl-3,3′-dicarboxylic acid (3·5 g.) was converted into (+)-3,3′-*diamino*-6,6′-*di-t-butylbiphenyl* (2·1 g.), yellow needles [from light petroleum (b. p. 60—80°)], m. p. 144—145°, $[\alpha]_{5791}$ +11·4°, $[\alpha]_{5641}$ +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°, $[\alpha]_{5791}$ +17·8°, $[\alpha]_{5461}$ +21·6° in acetone (Found: C, 90·1; H, 9·8. $C_{20}H_{26}$ requires C, 90·2; H, 9·8%). From (−)-di-t-butylbiphenyldicarboxylic acid (2·5 g.) (−)-2,2′-*di-t-butylbiphenyl* was obtained, having m. p. 73—74°, $[\alpha]_{5791}$ −18·2°, $[\alpha]_{5461}$ −22·3° in acetone (Found: C, 90·0; H, 10·1%).

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