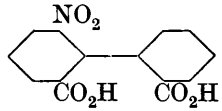
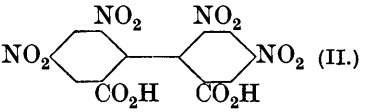
CCXCVIII.—*Investigations in the Diphenyl Series. Part VII. The Relative Stability of Optically Active Diphenic Acids.*

By Frank Bell and Percy Harry Robinson.

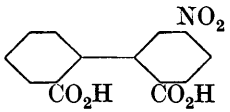
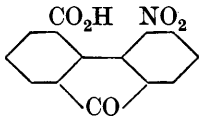
The theory advanced to account for the asymmetry of certain diphenyl derivatives (Part VI, this vol., p. 1695; *J. Soc. Chem. Ind.*, 1926, **45**, 864) definitely indicates that the optical activity

of such compounds should gain in permanence with an increase in the number of groups in the central positions. Up to the present, it has not proved possible to prepare in an optically active condition a compound with only two central groups, although some of the alkaloidal salts of "non-resolvable" acids show marked heterogeneity (compare Christie and Kenner, J., 1923, **123**, 779; 1926, 470).

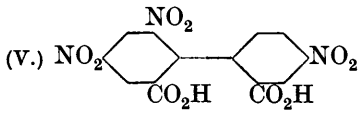
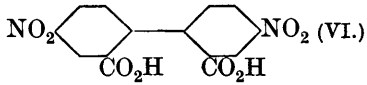
It is now found that 6-nitrodiphenic acid (I) is very much less optically stable than 4 : 4′ : 6 : 6′-tetranitrodiphenic acid (II). Thus

(I.)  (II.) 

an aqueous solution of the sodium salt of the former acid steadily falls in rotatory power, whilst no such change can be perceived in the case of the latter acid. Further, boiling acetic anhydride racemises 6-nitrodiphenic acid in a very short time, whilst 4 : 4′ : 6 : 6′-tetranitrodiphenic acid loses only 25% of its activity after boiling with acetic anhydride for 10 hours. The failure which has attended attempts to resolve 5-nitrodiphenic acid (III) and 2 : 2′-dinitrodiphenyl-4 : 4′-dicarboxylic acid could have been anticipated from

(III.)   (IV.)

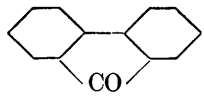
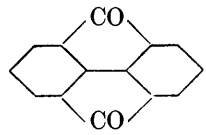
the "obstacle" theory. It may be noted that 5-nitrodiphenic acid readily forms an *anhydride*, and with sulphuric acid easily undergoes condensation to form a *fluorenone* derivative, in marked contrast to 4 : 4′ : 6′-trinitrodiphenic acid (V) which is unaffected

(V.)   (VI.)

by sulphuric acid at 160°. 4 : 4′-Dinitrodiphenic acid (VI) also does not undergo fluorenone formation (Underwood and Kochmann, *J. Amer. Chem. Soc.*, 1924, **46**, 2069).

Although the failure to resolve fluorenone-4-carboxylic acid has been already reported by Mills, Palmer, and Tomkinson (J., 1924, **125**, 2365), it appeared possible that the introduction of a nitro-group in position 5 might stabilise the enantiomorphous forms which arise if the fluorene system is non-planar. However, 5-nitrofluorenone-4-carboxylic acid (IV) was not resolved by crystallisation of its morphine or quinidine salts, and this result can be interpreted

as indicating that the 4 : 5-positions of fluorene are farther apart than are the 6 : 6′-positions in a diphenic acid. This conclusion agrees with the fact that, although such systems as (VII) are readily formed, attempts to prepare compounds of type (VIII) have repeatedly failed (see Meyer, Meyer, and Taeger, *Ber.*, 1920, **53**, 2034).

(VII.)  (VIII.) 

Experimental.

d- *and* l-6-*Nitrodiphenic Acids*.—The normal quinine salt of 6-nitrodiphenic acid was systematically crystallised from alcohol until it was separated into a slightly less soluble salt, $[\alpha]_{5461}$ + 286·6° (c = 2·5 in chloroform), and a slightly more soluble salt, $[\alpha]_{5461}$ − 122·4° (c = 2·5 in chloroform). The former on decomposition gave the *d*-acid with $[\alpha]_{5461}$ + 65·2° (c = 3·01 in ethyl alcohol), whilst the latter gave the *l*-acid with $[\alpha]_{5461}$ − 66·4° (c = 4·91 in ethyl alcohol). The *l*-acid had $[\alpha]_{5461}$ + 433° (c = 4·69 in 0·261*N*-sodium hydroxide), whilst the *d*-acid, obtained from its morphine salt, had $[\alpha]_{5461}$ − 434° (c = 4·73 in 0·426*N*-sodium hydroxide).

The solution of the sodium salt was kept at room temperature, and the following observations were made :

Time (days)	0	2	9	23	36·5	51
α_{5461}	−20·51°	−18·61°	−14·42°	−8·23°	−4·00°	−1·50°

Solutions of *d*-6-nitrodiphenic acid (1 g.) in 10 c.c. of acetic acid and in 10 c.c. of acetic anhydride were boiled under similar conditions for 1 hour, and they then had α_{5461} + 11·55° and 0·0° respectively (l = 2). After the acetic acid solution had been boiled for a further period of 5 hours, it had α_{5461} + 0·94°.

d-6-Nitrodiphenic acid (1 g.) was converted into 5-nitrofluorenone-4-carboxylic acid (see below). The acid obtained was inactive (c = 2·4; l = 2).

l-6-Nitrodiphenic acid was dissolved in excess of thionyl chloride and the solution evaporated in a vacuum. The residue was crystallised from benzene–light petroleum and gave the *l* + *dl*-acid dichloride, m. p. 65—68°, $[\alpha]_{5461}$ − 209·5° (c = 5·04; l = 2), whilst the mother-liquor on evaporation gave a further crop of the dichloride with $[\alpha]_{5461}$ − 220·6° (c = 2·31; l = 2 in chloroform).

d- *and* l + dl-4 : 4′ : 6 : 6′-*Tetranitrodiphenic Acids*.—Boiling alcoholic solutions of tetranitrodiphenic acid (35·7 g. in 1 l.) and

quinidine (30·5 g. in ½ l.) were mixed, and the precipitated salt was filtered off and boiled with alcohol until the residue attained constant rotatory power $[\alpha]_{5461}$ + 243·5° (c = 2·15 in 14·7N-acetic acid); m. p. 252° (decomp.). The alcoholic filtrates were evaporated, the residue was dissolved in acetic acid, and the resultant solution poured into dilute hydrochloric acid. The liberated tetranitrodiphenic acid was extracted with ether, and the well-washed extract dried with sodium sulphate and evaporated. The residue ($[\alpha]_{5461}$ *ca.* − 50°) was boiled with benzene, and the more soluble material was repeatedly crystallised from benzene until it attained constant rotatory power. *l* + *dl*-Tetranitrodiphenic acid formed needles which, after being heated at 130° for ½ hour, melted at 224—226° and had $[\alpha]_{5461}$ − 138·5° (c = 1·7 in ethyl alcohol). The less soluble quinidine salt was decomposed (*a*) by dissolving it in acetic acid and pouring the solution into dilute hydrochloric acid, (*b*) by dissolving in pyridine and pouring the solution into dilute ammonia, (*c*) by grinding with concentrated hydrochloric acid. The acids, recovered as described above and dried at 140°, had almost the same rotatory power, showing that racemisation does not occur during the recovery process.

d-4 : 4′ : 6 : 6′-Tetranitrodiphenic acid, m. p. 226—227° (Found : equiv., 211. Calc. : 211) (0·3696 g. in 20 c.c. of ethyl alcohol in a 2 dm. tube) gave :

λ	4359	4602	5461	5790	6708
α	+16·70°	+11·64°	+5·26°	+4·12°	+2·58°

whence $[\alpha]_{5461}$ +142·3°.

0·4209 G. in 20 c.c. of 1·033N/10-NaOH in a 2 dm. tube gave :

λ	4359	4602	5106	5218	5461
α	+29—31°	+19·6—20·0°	+10·84°	+9·72°	+8·00°
λ	5790	5896	6104	6708	
α	+6·33°	+5·86°	+5·08°	+3·78°	

whence $[\alpha]_{5461}$ + 190·5°.

After 39 days, this solution had α_{5461} + 8·08°.

A solution of *d*-tetranitrodiphenic acid in acetic anhydride (1 g. in 10 c.c.), with α_{5461} + 23·15°, had after 2 hours' boiling α_{5461} + 18·14°, and after 9 hours' boiling α_{5461} + 17·12°.

l-Tetranitrodiphenic acid was dissolved in thionyl chloride by boiling for 2 hours under reflux, and the solution was evaporated in a vacuum. The residue was difficultly soluble and melted indefinitely. Though no product was isolated in a pure condition, the optical activity was preserved, since $[\alpha]_{5461}$ − 133° (c = 2 in pyridine).

5-Nitrodiphenic acid was prepared by the process described by

Schmidt and Lumpp (*Ber.*, 1908, **41**, 4315). After 1 hour's boiling with acetic anhydride, the solution on cooling deposited crystals of 5-*nitrodiphenic anhydride*, m. p. 193—195° (Found: C, 62·4; H, 2·9. $C_{14}H_7O_5N$ requires C, 62·4; H, 2·6%). 5-Nitrodiphenic acid (1·5 g.) in sulphuric acid (5 c.c.) was heated at 160° for ¼ hour, and after cooling poured into water. The precipitated 6(?)-*nitrofluorenone*-4-*carboxylic acid* melted at 282° after crystallisation from acetic acid (Found: equiv., 270·5. $C_{14}H_7O_5N$ requires equiv., 269). 5-Nitrodiphenic acid gave non-crystallisable quinine, morphine, and quinidine salts. The brucine salt on crystallisation from water gave successive crops with $[\alpha]_{5461}$ — 10·4°, — 10·9°, — 11·2°, —11·1° ($c = 2·5$; $l = 2$ in 14·7N-acetic acid), indicating that no resolution had taken place.

5-Nitrofluorenone-4-carboxylic acid was prepared by the method of Moore and Huntress (*J. Amer. Chem. Soc.*, 1927, **49**, 1324). The quinidine salt showed slight irregularity in rotatory power ($[\alpha]_{5461}$ *ca.* — 20·6°; $c = 2·5$ in chloroform) but no resolution was effected. The morphine salt was crystallised from alcohol and showed a constant rotatory power of $[\alpha]_{5461}$ — 73·5° ($c = 2$ in 14·7N-acetic acid).

2 : 5 : 7(?)-*Trinitrofluorenone*-4-*carboxylic acid*, obtained by heating 5-nitrofluorenone-4-carboxylic acid (2·5 g.) with nitric acid (*d* 1·5; 50 c.c.) at 100° for 2 hours, pouring into water, and crystallising the resulting mass from aqueous alcohol, forms glistening, pale yellow plates, m. p. 254—255° (Found: C, 46·5; H, 1·7. $C_{14}H_5O_9N_3$ requires C, 46·8; H, 1·4%).

2 : 2′-Dinitrodiphenyl-4 : 4′-dicarboxylic acid was prepared from 4-bromo-3-nitrobenzoic acid. Its excessive insolubility militated against the production of uniform normal alkaloidal salts. The brucine salt on crystallisation from water varied in rotatory power between $[\alpha]_{5461}$ — 40° and $[\alpha]_{5461}$ — 56° ($c = 2$ in pyridine), but the liberated acid was inactive when observed in 1·033N/10-sodium hydroxide.

Quinine salts of 4-*nitrodiphenic acid.* An alcoholic solution of quinine (2 mols.) and 4-nitrodiphenic acid (1 mol.) was allowed to crystallise slowly. Successive crops had $[\alpha]_{5461}$ + 94·4°, + 84·0°, + 77·2° ($c = 2·5$ in chloroform), and the mother-liquor on evaporation and desiccation gave a solid with $[\alpha]_{5461}$ + 11·9°. Recrystallisation of the intermediate crops raised the rotatory power to $[\alpha]_{5461}$ + 106·4°; m. p. 180° (indefinite) (Found: C, 66·3; H, 5·6%). The liberated 4-nitrodiphenic acid was inactive in every case. The difference in rotatory power may be attributed to: (*a*) resolution of the alkaloidal salt; (*b*) admixture of acid and normal quinine salts and quinine; (*c*) differences in the number of

molecules of solvent of crystallisation—none of the salts lost more than 0·5% by weight on drying for 1 hour at 120°, however; or (*d*) possible presence of 6-nitro- and 4 : 4′-dinitro-diphenic acids as impurities.

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