

401. The Symmetrical Dianthryls. Part IV.

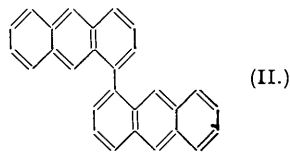
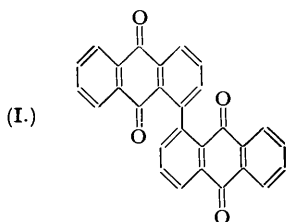
By F. BELL and W. H. D. MORGAN.

1 : 1'-Dianthraquinonyl-4 : 4'-dicarboxylic acid has been resolved into optically active forms. Negative results were obtained on attempting the resolution of naphthidine, 1 : 1'-naphthyl-4 : 4'-dicarboxylic acid, and 8 : 8'-diquinoyl.

Some attempts to prepare further compounds exhibiting intramolecular overcrowding are outlined.

STANLEY and ADAMS (*J. Amer. Chem. Soc.*, 1931, **53**, 2364) attempted the resolution of 1 : 1'-dianthraquinonyl-4 : 4'-dicarboxylic acid. They report that "it was impossible to fractionate the alkaloid salts . . . due to their insolubility," but evidence is given for the uniformity of the quinine salt and also of the dimethyl ester. The acid was regarded as non-resolvable and a tentative explanation of the result was advanced.

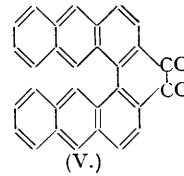
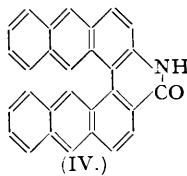
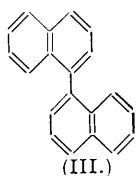
Although the distance between the *meso*-carbon atoms in anthraquinone may be slightly less than that between the *meso*-carbon atoms in anthracene it can scarcely be doubted that the opposition to planarity in 1 : 1'-dianthraquinonyl (I) is considerably greater than in 1 : 1'-dianthryl



(II). In Part II (*J.*, 1949, 1579) it was shown that 1 : 1'-dianthryl exists in enantiomorphous forms of moderate stability. It follows, therefore, that 1 : 1'-dianthraquinonyl and any of its derivatives should exist in enantiomorphous forms, and we were led to repeat the work of Stanley and Adams.

Rather surprisingly the quinidine, morphine, and cocaine salts of 1 : 1'-dianthraquinonyl-4 : 4'-dicarboxylic acid were found to be excessively soluble. The brucine salt could be crystallised from alcohol and slow, but definite, resolution was observed. With cinchonine and cinchonidine, on the other hand, resolution was a facile process and no difficulty was experienced in securing the enantiomorphous forms of the acid with $[\alpha]_D +428^\circ$ and -443° . The optical activity of the acid dissolved in sodium hydroxide was very slowly lost at room temperature, but more rapidly on boiling (complete loss in somewhat over 1 hour's heating). Racemisation was usually made apparent by the sodium salt crystallising from the 1% solution of the acid in 0.1N-sodium hydroxide; the sodium salts of the active forms are much more soluble. The active acids were attacked only slowly by hot thionyl chloride and the resultant chloride was optically inactive. It was, therefore, not possible to prepare the diastereoisomeric menthyl esters.

1 : 1'-Dinaphthyl (III) and 1 : 1'-dianthryl (II) are stereochemically closely related. If normal covalent radii are used the hydrogen atom in position 2 is barely in contact with the



hydrogen atom in position 8' (neglecting the van der Waals envelope). Two factors would be likely to render 1 : 1'-dinaphthyl less optically stable than 1 : 1'-dianthryl, *viz.*, the weight factor, for the heavier the moving parts of the molecule the less easy the oscillations about the 1 : 1'-linkage, and, secondly, the buttressing factor, for the presence of the third nucleus must hinder the outward movement of the 9 : 9'-hydrogen atoms in a dianthryl. Nevertheless it appears possible that 1 : 1'-dinaphthyl might be obtained in enantiomorphous forms. The most direct route to such optically active dinaphthyls appeared to be the elimination of the amino-groups from the optically active 2 : 2'-diamino-1 : 1'-dinaphthyls already described (Kuhn and Goldfinger, *Annalen*, 1929, **470**, 183). This, however, did not prove to be the case as conditions could not be found for smooth elimination. Next, resolution of 4 : 4'-diamino-1 : 1'-dinaphthyl by (+)-camphorsulphonic acid and of 1 : 1'-dinaphthyl-4 : 4'-dicarboxylic acid by brucine was attempted. The results were completely negative and, therefore, the resolvability of 1 : 1'-dinaphthyl must remain an open question.

Kuhn and Albrecht (*ibid.*, 1928, **464**, 91) resolved 1 : 1'-dianthraquinonyl-2 : 2'-dicarboxylic acid by means of quinine. It is now found that this resolution is more easily accomplished by use of quinidine. The exceptionally high optical stability of the enantiomorphous forms is confirmed. In this compound the carboxyl groups must form almost insuperable obstacles to the opposed carbonyl groups. This opposition is of course lacking in the isomeric 1 : 1'-dianthraquinonyl-4 : 4'-dicarboxylic acid.

The optical stability and high rotatory power of these compounds renders them promising starting materials for the preparation of systems such as (IV) and (V) which might be expected to be non-planar owing to intramolecular overcrowding. Compound (IV) might arise from a Hofmann reaction on the amide derived from the anhydride of 1 : 1'-dianthryl-2 : 2'-dicarboxylic acid. We failed to prepare the requisite anhydride. A compound of type (V) might be formed by the interaction of the chloride of 1 : 1'-dianthryl-2 : 2'-dicarboxylic acid with metals, or of the ester with sodium (acyloin condensation) or 2 : 2'-diformyl-1 : 1'-dianthryl with potassium cyanide. The results of experiments along these lines were negative.

EXPERIMENTAL.

(M. p.s are uncorrected.)

1 : 1'-Dianthraquinonyl-4 : 4'-dicarboxylic acid was prepared from 1-chloro-4-benzamidoanthraquinone by the method of Stanley and Adams (*loc. cit.*), and formed a pale yellow powder, m. p. 418° . The resolution with brucine was unsatisfactory but, nevertheless, that part of the salt which was least soluble in absolute alcohol gave an acid of small levorotation, and the more soluble salt gave an acid of small dextrorotation. Resolution was however readily accomplished by use of cinchonine, which gave a less soluble salt of the (–)-acid, or cinchonidine, which gave a less soluble salt of the (+)-acid. The following is a typical experiment. Cinchonine (6 g., 2 mols.) was added to a suspension of the acid (5 g., 1 mol.) in boiling absolute alcohol (500 c.c.). About half of the acid rapidly dissolved but to get the remainder into solution required the addition of a further 3 g. of cinchonine. No crystallisation occurred on cooling of the solution and for this it was necessary to reduce the volume to about 100 c.c.

The first crop consisted of almost pure cinchonine (3 g.), the second crop of bright yellow crystals (6 g.), and the filtrate from this was decomposed by pouring it into boiling dilute hydrochloric acid. The recovered acid ($[\alpha]_D$ about $+350^\circ$ in 0.1N-sodium hydroxide) was purified by combination with cinchonidine (below).

The crop of cinchonine salt was recrystallised from alcohol until of constant rotatory power, $[\alpha]_D^{21} + 20^\circ$ (c, 1.01 in chloroform), and then had m. p. 207° (decomp.). Decomposition gave (–)-1 : 1'-dianthraquinonyl-4 : 4'-dicarboxylic acid, m. p. 395° , $[\alpha]_D - 443^\circ$ (c, 1.02 in 0.1N-sodium hydroxide).

The (+)-acid (3.15 g., 1 mol.; see above) was added to a boiling solution of cinchonidine (5.7 g., 3 mols.) in absolute alcohol (250 c.c.). The liquid immediately filled with a heavy crystalline deposit of the cinchonidine salt. This was purified by repeated extraction with hot alcohol. The purified salt, m. p. 234° (decomp.), furnished (+)-1 : 1'-dianthraquinonyl-4 : 4'-dicarboxylic acid, m. p. 390° , $[\alpha]_D + 428^\circ$ (c, 1.04 in 0.1N-sodium hydroxide).

The sodium salts of the active acids were very much more soluble than was the sodium salt of the inactive acid, a 1% solution of which tended to crystallise in the polarimeter tube. At room temperature the solutions of the sodium salts slowly lost activity (the observed rotation had fallen to about one-third after 70 hours); at the b. p. the same loss was attained in somewhat under 1 hour. The active acid required some 6 hours' heating with thionyl chloride for complete dissolution. The chloride left after removal of the excess of thionyl chloride was insoluble in benzene, chloroform, carbon tetrachloride, acetone, *o*-dichlorobenzene, or methyl ethyl ketone, and was inactive in pyridine (c, 0.99).

Resolution of 1 : 1'-Dianthraquinonyl-2 : 2'-dicarboxylic Acid.—Quinidine (36.5 g.) was added to the acid (24.5 g.) in boiling alcohol (1600 c.c.). The mixture, after boiling for 1 hour, was allowed to cool overnight and the crystalline crop filtered off and well washed with alcohol. The residue (23.7 g.) was repeatedly extracted with hot alcohol to remove more soluble materials, and the final residue (21.2 g.) decomposed by trituration with dilute hydrochloric acid. The material so obtained crystallised from acetic acid in compact orange-red prisms, $[\alpha]_{579.1} - 318^\circ$ (c, 2.6 in 0.1N-sodium hydroxide). The alcoholic filtrate from this salt was evaporated to about one-eighth bulk and the crop (4.8 g.) obtained on cooling filtered off. The alcoholic filtrate was poured slowly into boiling dilute hydrochloric acid whereupon there was obtained the (+)-acid, $[\alpha]_{579.1} + 304^\circ$ (c, 2.5 in 0.1N-sodium hydroxide).

The acid was not decarboxylated when it was boiled with quinoline for 4 hours.

The acid was converted by thionyl chloride into the chloride which was used in the following experiments.

(i) The chloride [from 2 g. of (–)-acid], benzene (40 c.c.), and sodium azide (3 g.) were heated under reflux for 6 hours. Sodium hydroxide (3 g. in 25 c.c. of water) was then added and the heating continued for 2 hours. The benzene was removed in steam, and the residual solution filtered from a black highly insoluble material. The filtrate on acidification gave 1.7 g. of acid, $[\alpha]_{579.1} - 310^\circ$ (c, 2.6 in 0.1N-sodium hydroxide).

(ii) Sodium (0.8 g.) was added to the chloride (from 3.4 g. of acid) in boiling xylene. The sodium became covered by a black layer and little action appeared to take place. The majority of the acid was recovered unchanged after alkaline decomposition.

(iii) A similar experiment with zinc gave equally negative results.

1 : 1'-Dianthryl-2 : 2'-dicarboxylic Acid.—This was not decarboxylated by boiling it with quinoline for 4 hours. The acid chloride in boiling xylene with copper powder or finely divided silver gave *amphi-isopyranthrone* as the only product of change.

The (–)-acid (1 g.) in acetic anhydride was boiled for 1 hour. The solution did not crystallise on cooling, so all the acetic anhydride was removed under reduced pressure. The residual bright yellow scales, darkening at 230° and almost black at 250° , could not be purified by crystallisation. Only the original acid was recovered by treatment with aqueous ammonia (*d* 0.880); the acid had undergone considerable racemisation. The (–)-acid was converted through the chloride into the ethyl ester, which crystallised from ethanol in yellow flocks, m. p. $177-180^\circ$, $[\alpha]_D - 373^\circ$ (c, 1 in chloroform). The ester (3.5 g.) was added to powdered sodium (1 g.) in xylene, and the mixture boiled for 1 hour. The sodium almost immediately became black but otherwise little reaction occurred. After decomposition the majority of the ester was recovered as the fully active (–)-acid, whilst the blue-black residue had the appearance of *amphi-isopyranthrone*.

8 : 8'-Diquinolyl.—This was prepared by the method of Niementowski and Seifert (*Ber.*, 1905, **38**, 762). The base (1 mol.) did not dissolve in tartaric acid (1 mol.) in ethanol. With tartaric acid (2 mols.) a non-crystallising solution was obtained.

With (+)-camphorsulphonic acid a highly crystalline salt was obtained. This could be recrystallised from alcohol without change of m. p. (230°) or rotatory power $\{[\alpha]_{546.1} + 19.7^\circ$ (c, 1.22 in chloroform)}. The 8 : 8'-diquinolyl recovered from all crops was completely inactive.

4 : 4'-Diamino-1 : 1'-dinaphthyl (Naphthidine).—This amine was prepared from 1 : 1'-azonaphthalene by reduction with stannous chloride and treatment of the product with concentrated hydrochloric acid (Cohen and Oesper, *Ind. Eng. Chem., Anal.*, 1936, **8**, 306). Several attempts to prepare the compound from α -naphthylamine (Sah and Yui, *Rec. Trav. chim.*, 1939, **58**, 751) gave very unsatisfactory yields.

Naphthidine has been described as "a compound fairly soluble in organic solvents." This statement is rather misleading as the solubility is about 1% in either boiling absolute alcohol or boiling benzene, and the compound separates again on cooling. For the following experiments the naphthidine was recrystallised from absolute alcohol (1 l. for 8 g.) (charcoal).

Naphthidine did not yield a salt with tartaric acid. When (+)-camphorsulphonic acid (0.9 g., 2 mols.), dissolved in alcohol, was added to naphthidine (0.56 g., 1 mol.) dissolved in absolute alcohol (70 c.c.) an immediate pink coloured precipitate formed which was insoluble in the common solvents. This salt was repeatedly extracted with alcohol, and the residue {m. p. 263° (decomp.), $[\alpha]_D + 31.5^\circ$ (c, 2.03 in pyridine)} decomposed by trituration with dilute aqueous ammonia. The liberated base was optically inactive.

1 : 1'-Dinaphthyl-4 : 4'-dicarboxylic Acid.—This acid, m. p. 348° , was prepared from naphthidine by the method of Seer and Scholl (*Annalen*, 1913, **398**, 83), the only modification being that the 4 : 4'-di-

cyano-1 : 1'-dinaphthyl was separated from the inorganic material by extraction with chloroform and hydrolysed with ethylene glycol-potassium hydroxide (10 c.c. of 10% solution per g.) for 15 hours.

Attempts to resolve the acid using quinidine, morphine, cinchonine, and cinchonidine failed owing to the high solubilities of the salts. Brucine gave a crystalline salt which after recrystallisation from alcohol had m. p. 215°, $[\alpha]_D -17.9^\circ$ (c, 2.35 in chloroform). The brucine salt did not exhibit mutarotation; the recovered acid was completely inactive.

2 : 2'-Diamino-1 : 1'-dinaphthyl.—Deamination of the racemic compound, prepared by the method of Kuhn and Goldfinger (*loc. cit.*), was unsuccessful, using (a) the procedure applied to 2 : 2'-diamino-1 : 1'-dianthryl (*J.*, 1949, 1582), (b) alcohol, (c) sodium stannite, or (d) cuprous oxide-alcohol (Hodgson and Turner, *J.*, 1942, 748). No definite compounds were isolated (cf. previous work by Corbellini, *Atti R. Accad. Lincei*, 1931, 14, 341).

2 : 2'-Diformyl-1 : 1'-dianthraquinonyl.—Crude 2 : 2'-bisdibromomethyl-1 : 1'-dianthraquinonyl (rosettes, m. p. 336°, from *o*-dichlorobenzene) was converted as previously described (*J.*, 1949, 1580) into crude 2 : 2'-diformyl-1 : 1'-dianthraquinonyl. The reddish amorphous material (50 g.) was extracted with aqueous sodium carbonate solution (2 l. of 5%), and the residue dried (35 g.). This was dissolved in chloroform and the filtered solution evaporated to 50 c.c. The fawn-coloured dialdehyde which separated had m. p. 313°. Owing to its insolubility it was not possible to submit it to the action of potassium cyanide under favourable conditions: only tarry products were obtained.

The authors are indebted to Mr. W. Smith, F.R.I.C., and Imperial Chemical Industries Limited (Dyestuffs Division), for a gift of 1-chloro-4-benzamidoanthraquinone and to the Department of Scientific Industrial Research for a grant to one of them (W. H. D. M.).

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[Received, April 6th, 1950.]