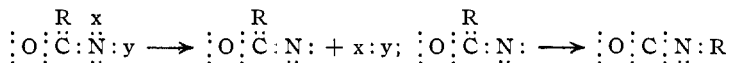


[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

## Molecular Rearrangements Involving Optically Active Radicals. IV. The Hofmann Rearrangement of the Amide of an Optically Active 2,2'-Disubstituted 6-Carboxydiphenyl<sup>1</sup>

BY EVERETT S. WALLIS AND WENDELL W. MOYER

In recent investigations<sup>2</sup> in this Laboratory on acid azides, hydroxamic acids and acid amides the nature of the products of rearrangement has been determined when the rearranging group, R, is an optically active radical.



In all the cases studied the first products of the rearrangement were found to be optically active and to have the same sign for the rotatory power as the acid amide, acid azide or hydroxamic acid from which they were prepared. It was also observed that the specific rotations of the products from the Curtius rearrangement were of the same value as the specific rotations of the same compounds prepared either from the Lossen or the Hofmann rearrangement.

The results of these experiments point to two important conclusions: (1) the radical in its migration from the carbon atom to the nitrogen atom maintains an asymmetric configuration; (2) the radical either has the same configuration as it had before rearrangement or else undergoes complete Walden inversion; partial inversion (racemization) seems unlikely. The conditions of the three rearrangements are very different and if racemization takes place it could be detected inasmuch as it is improbable that in such rearrangements the amount of inversion is the same. If we take into account the sign of the rotatory power it would appear that the radical maintains its original configuration during the rearrangement. Any theories as to the mechanism of these rearrangements must explain these conclusions.

The mechanism by means of which the radical originally attached to the carbon atom migrates to the nitrogen atom has been the subject of much discussion.<sup>2,3</sup>

In explaining their results on the rearrangement of *d*-benzyl-methylacetazide, C<sub>7</sub>H<sub>7</sub>(CH<sub>3</sub>)HCCON<sub>3</sub>, Jones and Wallis suggested two possible interpretations for the optical stability of the radical, R, during its migration

(1) This paper was presented before Section C, American Association for the Advancement of Science, at its meeting in Atlantic City, December 27-31, 1932.

(2) Jones and Wallis, *THIS JOURNAL*, **48**, 169 (1926); Wallis and Nagel, *ibid.*, **53**, 2787 (1931); Wallis and Dripps, *ibid.*, **55**, 1701 (1933).

(3) Hoogewerff and van Dorp, *Rec. trav. chim.*, **6**, 373 (1887); **8**, 173 (1889); Nef, *Ann.*, **298**, 202 (1897); **318**, 1, 137 (1901); Stieglitz, *Am. Chem. J.*, **29**, 57 (1903); *THIS JOURNAL*, **36**, 288 (1914); Hesse, see Stieglitz, *Am. Chem. J.*, **29**, 56 (1903); Jones, *ibid.*, **50**, 441 (1913); Whitmore, *THIS JOURNAL*, **54**, 3274 (1932).

from the carbon atom to the nitrogen atom. (1) It was assumed to be a positive radical. A survey of the properties of other optically active compounds described in the literature implied that under suitable conditions a positive radical of the nature of a carbonium ion might be optically stable. There are many reactions in which substitution of one group for another directly attached to an asymmetric carbon atom does not lead to racemization. They also pointed out the analogy that could be drawn between such an ion and the optically stable asymmetric sulfonium ion. However, as has been previously stated,<sup>4</sup> the sulfonium ion possesses a complete octet of electrons whereas a positive carbonium radical possesses only a sextet of valency electrons. Therefore such a radical might possess a far less rigid structure than the corresponding sulfonium ion. The stability of the radical could also have been explained on the basis of a stable negative radical.<sup>5</sup> In fact recent experimental work<sup>6</sup> has shown quite conclusively that a tervalent negative carbonium ion under suitable conditions is optically stable. Such an ion is also probably present in the sodium salts of the secondary nitroparaffins which have been prepared in enantiomorphic modification.<sup>7</sup> (2) It might be assumed that the rearranging group, R, does not exist even momentarily as a free radical, either positive or negative but that "in some way before the group actually parts company with its carbon neighbor the univalent nitrogen atom has begun already to exercise its influence on the radical in such a manner that when cleavage actually does take place a change in the configuration of the groups about the asymmetric carbon atom is prevented." Such an interpretation implies that in molecular rearrangements at no time is the rearranging group actually free and unattached.

This latter viewpoint lends itself to further experimental study. It is well known that certain substituted diphenyls can be resolved into enantiomorphic modifications. This is possible because of a lack of free rotation about the axial bond. From the above point of view a study of the nature of the products of rearrangements involving molecularly asymmetric radicals is of special interest. It should give valuable information on the true nature of rearrangement processes. Of the many optically active substituted diphenyls which have been prepared and resolved only the 2,2',6-trisubstituted derivatives would be satisfactory in these investigations. For this purpose the amide of *d*-3,5-dinitro-6- $\alpha$ -naphthylbenzoic acid was prepared and the nature of the products studied, when this compound was made to undergo the Hofmann rearrangement. From the viewpoint of the two interpretations stated above two results are possible. (a) If the molecularly asymmetric radical during rearrangement actually

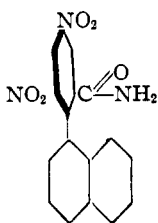
(4) Kenyon and Phillips, *J. Chem. Soc.*, **133**, 1676 (1930); Wallis, *THIS JOURNAL*, **53**, 2253 (1931).

(5) Wallis, private communication to F. C. Whitmore. See *THIS JOURNAL*, **54**, 3436 (1932).

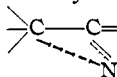
(6) Adams and Wallis, *ibid.*, **54**, 4753 (1932).

(7) Kuhn and Albrecht, *Ber.*, **60**, 1297 (1927); Shriner and Young, *THIS JOURNAL*, **52**, 3332 (1930).

parts company momentarily with its carbon neighbor either as a positive or negative radical then the blocking effect of the group might be removed and free rotation about the axial bond would then become possible. Under such conditions a racemized or at least a partially racemized product would be expected. (b) If, however, in some way the nitrogen atom begins to exercise its influence on the radical before the group actually parts company with the carbon atom, then at no time is the radical actually unattached and free rotation about the axial bond is prevented. From such a point of view the rearrangement product should be optically active and partial inversion should not take place.



Our experiments with the amide of *d*-3,5-dinitro-6- $\alpha$ -naphthylbenzoic acid show that this compound on treatment with a solution of sodium hypobromite in an aqueous solution of sodium hydroxide rearranges readily at a temperature of 70–80° to the amine, and that this amine is optically active. The specific rotation of the amide is  $[\alpha]_{5463}^{20} +37.3^\circ$ ; the amine  $[\alpha]_{5463}^{20} +398.0^\circ$ . It was also found that the specific rotation of the amine could not be changed appreciably by repeated crystallizations. This indicates that no racemization (inversion) takes place during the rearrangement. These results clearly show that at no time is the blocking effect of the —CON group removed, *i. e.*, in rearrangements of this sort the radical, R, is never free even momentarily. This is to be expected from the newer methods of considering such systems. Any idea of the formation of free radicals either of a positive or negative nature must take account of the energy required to break the bonds. No process which takes place at an appreciable rate at room temperature to 100° can involve a dissociation into radicals requiring more than 25–30 kg. calories. If there be an alternative path requiring less energy than a dissociation it will, of course, proceed in this manner. The experimental results clearly indicate that at no time in the process has there been an opportunity for rotation as there would have been if a radical had been formed. The process, therefore, seems clear enough. After the hydrogen bromide has been removed from the nitrogen atom the approximate picture of the system must be much like that indicated in the following diagram



partial valences which are beginning to form. The fact that the bonds of the carbon atom make a tetrahedral angle with each other makes the normal position of the nitrogen atom nearer the final one than would otherwise be the case. An actual calculation of the potential energy in a way that has apparently led to satisfactory results in simpler cases<sup>8</sup> would of course involve taking an account of all the possible ways bonds can be

(8) Eyring and Polanyi, *Z. physik. Chem.*, **12B**, 229 (1931).

formed between valence electrons. But we have sketched the more important ones. With the subsequent motion of the nitrogen<sup>9</sup> atom the bond between the two carbon atoms will grow continuously weaker and this will be accompanied by a strengthening of the dotted bonds and the appearance of an additional bond between the nitrogen and carbon atoms. The point to be emphasized is that the newer methods of considering such systems would actually enable one to construct an approximate potential energy curve which would represent the change, and that apart from the results which in themselves are clear enough one could predict that no free radical, positive or negative, would appear. Therefore an asymmetric configuration is maintained. Investigations on rearrangements are being continued which involve a change of optically active groups from oxygen to carbon, and also certain metathetical reactions applied to optically active molecules which in the racemic forms have been shown to lead to molecular rearrangement. These rearrangements may be essentially different and their study should be of interest. They will be the subject of a forthcoming paper in this series.

### Experimental Part

**Preparation of Ethyl *dl*-3,5-Dinitro-6- $\alpha$ -naphthylbenzoate.**—This compound was prepared according to the directions of Lesslie and Turner with certain modifications.<sup>10</sup> The use of a small amount of nitrobenzene as a solvent permitted a more convenient temperature control and resulted in a less darkly colored reaction mixture with no decrease in the yield of ester. The isolation of the ester by means of extraction with *o*-dichlorobenzene was found to be somewhat tedious. This was more easily achieved by direct vacuum distillation.

A mixture of 50 g. of ethyl 2-chloro-3,5-dinitrobenzoate and 50 g.  $\alpha$ -iodonaphthalene (in 70 cc. of nitrobenzene) was heated to 210° in a three-necked flask equipped with thermometer and mechanical stirrer. Fifty grams of "Naturkupfer" C was slowly added with continuous stirring. The temperature was kept at 210–215° and maintained for half an hour after all the copper had been added. The hot reaction mixture was filtered and the copper residue extracted with boiling acetone. The filtrates were combined and the acetone removed by distillation. The residual liquid was fractionally distilled under diminished pressure to separate it from the nitrobenzene and small amounts of  $\alpha,\alpha'$ -binaphthyl. The ester boiled at 244–248° at 1.5 mm. pressure without the slightest decomposition. The fraction boiling from 230–250° was collected; yield 28 g. After recrystallization from alcohol, the ester melted at 109°.

**Resolution of 3,5-Dinitro-6- $\alpha$ -naphthylbenzoic Acid.**—The acid was prepared by the hydrolysis of the pure ester according to the directions of Lesslie and Turner. The melting point of the acid was 185–187°. The brucine salt was obtained by precipitation from ethyl alcohol. The *dl*-brucine salt was found to be much more insoluble in methyl alcohol (synthetic) than reported by Lesslie and Turner, and inconveniently large volumes of methanol were required for resolution using this solvent. Methyl alcohol containing acetone or chloroform, or acetone itself effected separation of the salts

(9) Most investigators speak of migration of the radical, R. If we remember that in nature moment of momentum is conserved then in this case most of the movement will be made by the  $\text{—C=O}$  and not by the radical. Essentially the same idea has been recently expressed by Mills, *Chemistry & Industry*, 755 (1932), in a discussion of the rearrangement of oximes.  $\begin{array}{c} | \\ \text{N} \end{array}$

(10) Lesslie and Turner, *J. Chem. Soc.*, 1189 (1931).

after repeated crystallizations. From a solution of 31 g. of the *dl*-brucine salts in 1500 cc. of boiling acetone there separated on standing 14.1 g. of orange-yellow square prisms; 0.1005 g. dissolved in chloroform and made up to a volume of 15 cc. gave  $\alpha_D^{20} +0.33^\circ$  in a 1-dc. tube;  $[\alpha_D^{20}] +49.3^\circ$ . Two more recrystallizations from acetone gave 8 g. of crystals; 0.1016 g. in a total volume of 15 cc. of chloroform gave  $\alpha_D^{20} +0.58^\circ$  in a 1-dc. tube;  $[\alpha_D^{20}] +85.6^\circ$ . A final recrystallization from 1300 cc. of methanol containing a small amount of acetone gave the pure brucine salt of the *d*-acid; 0.1006 g. in a total volume of 15 cc. of chloroform gave  $\alpha_D^{20} +0.80^\circ$  in a 1-dc. tube;  $[\alpha_D^{20}] +119.4^\circ$ . Lesslie and Turner reported  $[\alpha]_{6791}^{20} +120.1^\circ$ . The brucine salt of the *l*-acid in various degrees of resolution was obtained by concentration of the first acetone mother liquor. The corresponding free acids were prepared from their brucine salts in the usual manner, and were converted into the corresponding amides by the method previously described by Lesslie and Turner. The pure *d*-amide used in these experiments melted at  $168^\circ$ ; 0.1273 g. dissolved in benzene and the solution made up to a volume of 25 cc. gave the following rotations in a 2-dc. tube:  $\alpha_{6563}^{20} +0.25^\circ$ ;  $\alpha_{5893}^{20} +0.31^\circ$ ;  $\alpha_{5463}^{20} +0.38^\circ$ ;  $\alpha_{4861}^{20} +0.48^\circ$ ;  $[\alpha]_{6563}^{20} +24.5^\circ$ ;  $[\alpha]_{5893}^{20} +30.4^\circ$ ;  $[\alpha]_{5463}^{20} +37.3^\circ$ ;  $[\alpha]_{4861}^{20} +47.1^\circ$ . The incompletely resolved *l*-amide melted at  $172$ – $176^\circ$ ; 0.1260 g. in a total volume of 25 cc. of benzene gave  $\alpha_{5893}^{20} -0.14^\circ$  in a 2-dc. tube;  $[\alpha]_{5893}^{20} -13.8^\circ$ . The racemic amide melted sharply at  $192^\circ$ .<sup>11</sup>

**Rearrangement of *dl*-3,5-Dinitro-6- $\alpha$ -naphthylbenzamide to *dl*-3,5-Dinitro-6- $\alpha$ -naphthylaniline.**—Fifteen grams of sodium hydroxide was dissolved in 100 cc. of distilled water. The solution was cooled to  $0^\circ$  and treated with 2.0 cc. of liquid bromine. One-tenth of the volume of the solution was taken for the experiment. To this cooled solution was added 0.9 g. of the *dl*-amide, and the contents heated gently. At  $50$ – $60^\circ$  the color of the material began to change from yellow to deep orange and at  $80^\circ$  the product was a reddish-brown. Heating was continued for one to two minutes at  $100^\circ$  and then the material was cooled and filtered. The crude product was thoroughly washed and dried in a vacuum oven at  $40^\circ$ . It was then ground to a powder in a mortar and extracted with anhydrous ether. A very small amount of residue remained undissolved. The solution was filtered and treated with gaseous hydrogen bromide. Beautiful colorless needles of the hydrobromide separated out on standing in the ice box. These were filtered off and converted into the free base by treatment with cold water containing a very small amount of sodium hydroxide. The color of the crystals changed immediately to a deep yellow. The product was washed and dried and recrystallized from hot alcohol containing a small amount of water. *dl*-3,5-Dinitro-6- $\alpha$ -naphthylaniline crystallizes from hot alcohol in diamond-shaped yellow-orange plates which melt sharply at  $205.5$ – $206^\circ$ .

*Anal.* Calcd. for  $C_{16}H_{11}N_3O_4$ : N, 13.6. Found: N, 13.86.

**Rearrangement of *d*-3,5-Dinitro-6- $\alpha$ -naphthyl Benzamide.**—This compound was allowed to rearrange under the same conditions as described above. The amine so produced was purified by means of its hydrobromide and finally the free base was crystallized from hot alcohol containing a small amount of water. It crystallized in well-defined deep yellow crystals which melted at  $157$ – $158^\circ$ . The amine was found to be strongly dextrorotatory; 0.0701 g. dissolved in ethyl alcohol (95%) and the total volume made up to 25 cc. gave the following rotations at  $20^\circ$  in a 2-dc. tube:  $\alpha_{6563}^{20} +1.15^\circ$ ;  $\alpha_{5893}^{20} +1.64^\circ$ ;  $\alpha_{5463}^{20} +2.23^\circ$ ;  $[\alpha]_{6563}^{20} +205.0^\circ$ ;  $[\alpha]_{5893}^{20} +292.4^\circ$ ;  $[\alpha]_{5463}^{20} +398^\circ$ .

*Anal.* Calcd.: N, 13.6. Found: N, 13.6.

A second recrystallization produced no appreciable change. The crystals melted at  $156.5$ – $157^\circ$ ; 0.0413 g. dissolved in ethyl alcohol (95%) and the total volume made up

(11) Lesslie and Turner reported a melting point of  $96$ – $97^\circ$ . This is undoubtedly an error in printing.

to 25 cc. gave  $\alpha_{5893}^{20} + 0.95^\circ$  in a 2-dc. tube;  $[\alpha]_{5893}^{20} + 288^\circ$ . The rearrangement of the incompletely resolved *l*-amide,  $[\alpha]_{5893}^{20} - 13.8^\circ$ , was also studied. The corresponding crystalline amine so produced melted at 201–206°; 0.0870 g. dissolved in ethyl alcohol (95%) and made up to a total volume of 25 cc. gave  $\alpha_{5893}^{20} - 0.61^\circ$  in a 2-dc. tube;  $[\alpha]_{5893}^{20} - 87.7^\circ$ .

*Anal.* Calcd.: N, 13.6. Found: N, 13.8.

### Conclusions

The Hofmann rearrangement of the amide of an optically active 2,2'-disubstituted 6-carboxydiphenyl has been studied. The corresponding amine so produced was found to be optically active, and to have the same sign for the rotatory power as the amide from which it was prepared. It was also found that the rearrangement took place in such a manner as to produce no appreciable racemization.

These results preclude the possibility of migration of the optically active group in any free form, either as a positive, negative or neutral free radical.

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## Notes

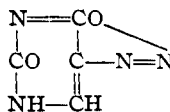
### A New Color Reaction with Sucrose

BY HARRY W. RAYBIN

In studying the chemical properties of diazo-uracil<sup>1</sup> it was observed that in alkaline sucrose solution it produced a blue-green color. Raffinose was the only other sugar found to give a similar but weaker color.

Fructose, glucose, maltose, lactose did not give this test.

Preliminary experiments were also negative (mostly yellow to brown-reds) with inulin, melezitose, turanose, as well as



for starch, glycogen, pneumococcus polysaccharide Type I, cellobiose, galactose, mannose, arabinose, lyxose, xylose, rhamnose, *l*-fucose, *d*-mannoheptose, mannoketoheptose, *d*- $\alpha$ -glucoheptose, *d*- $\alpha$ -glucoheptulose, lactulose, erythritol, adonitol, dulcitol, *d*-arabitol, perseitol, mannitol, glycerin, formaldehyde, acetone, pyruvic acid, acetoacetic ester, acetone-dicarboxylic acid.

**Experimental Procedure.**—Forty to 50 mg. of sucrose in 5 cc. of *N*/20 sodium hydroxide (10°) is shaken in a corked test-tube with 7 to 10 mg. of diazouracil until the latter dissolves. The blue-green color develops within a few minutes, the solution being kept cold. The addition of magnesium ion gives a stable blue precipitate.

An interesting reaction product with indicator properties has been isolated by salting out from neutral solution.

(1) See *Proc. Nat. Acad. Sci.*, **18**, No. 3, p. 220; *THIS JOURNAL*, **55**, 1667 (1933).