

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CINCINNATI]

ALIPHATIC DIAZO COMPOUNDS.
A STABLE CRYSTALLINE OPTICALLY ACTIVE DIAZO
COMPOUND

BY FRANCIS EARL RAY

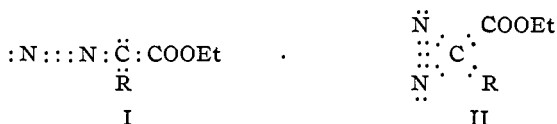
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Optically active diazo esters containing but one possible asymmetric carbon atom bound to the diazo group have been prepared by Levene and Mikeska,¹ and Chiles with Noyes² and formula I has been assigned to these compounds. The specific rotations reported, however, have been very small, of the order of one or two degrees. This small rotation together with the fact that these compounds were liquids has evoked the criticism that impurities might be the cause of the observed rotation.

Large rotations were observed in the compounds prepared by Kendall and Noyes,³ and Heubaum and Noyes.⁴ Unfortunately these compounds contained another asymmetric carbon atom and were so unstable that no direct evidence could be obtained of the activity of the carbon atom adjacent to the diazo group. Ray,⁵ from a study of the decomposition of Kendall and Noyes' methyl- γ -diazocamphonanate, concluded that the diazo group of this compound was active to the extent of about 5%.

On the other hand, the results of parachor measurements point to a ring structure, II, for the diazo esters. Analogous boiling points are adduced by Sidgwick⁶ as further evidence for the ring structure.



In an effort to reconcile these divergent viewpoints Lindemann⁷ and Ray⁸ considered that formulas I and II represented tautomeric forms. If this is the case, racemization of the active form should occur until finally no activity would be observed. It seemed, therefore, of considerable interest to synthesize a stable, optically active, crystalline diazo compound containing but one asymmetric carbon atom. This has now been successfully accomplished by the preparation of β -naphthol-phenyldiazomethane, IV, from the active forms of the amine.

The straight chain formula, I, of the diazo compounds contains two free

¹ Levene and Mikeska, *J. Biol. Chem.*, **45**, 592 (1921); **52**, 485 (1922).

² Chiles with Noyes, *THIS JOURNAL*, **44**, 1798 (1922).

³ Kendall and Noyes, *THIS JOURNAL*, **48**, 2404 (1926).

⁴ Heubaum and Noyes, *ibid.*, **52**, 5070 (1930).

⁵ Ray, *ibid.*, **52**, 3004 (1930).

⁶ Sidgwick, *J. Chem. Soc.*, 1108 (1929).

⁷ Lindemann, Wolter and Groger, *Ber.*, **63**, 702 (1930).

electrons on the asymmetric carbon atom. The presence of this pair of unshared electrons made it seem probable that an increase in negativity of the other groups would draw these electrons closer to the asymmetric carbon and contribute to the stability of the diazo compound. This proved to be the case.

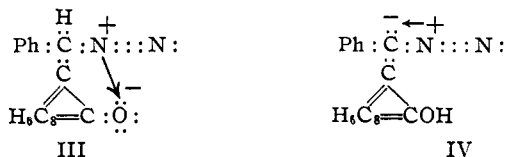
The well-known negative character of the benzenoid rings suggested their use. Betti⁸ prepared β -naphthol-phenylaminomethane some years ago and resolved it into its enantiomorphous forms and it was this compound from which the optically active diazo compound here described was prepared.

The β -naphthol-phenyldiazomethane was prepared from the active amine by treatment with nitrous acid. The light lemon-yellow compound resulting melted with vigorous decomposition at 120° and analyzed correctly. It was optically active, $[\alpha]_D^{20} = 420^\circ$, and was stable to dilute acids at room temperatures. On boiling with acids the ketazine melting at 182° was obtained. Treatment with alkali gave a brightly colored orange-red salt which decomposed with explosive violence when heated. This salt retained its optical activity.⁹ No change in rotation of an alcoholic solution could be observed after standing at room temperature (25–30°) for two weeks.

λ	ROTATORY DISPERSION		
	$[\alpha]^{20}$	$[\alpha]^{20}$	
656.3	- 310	+285	Red
589.3	- 420	+405	Yellow
546.3	- 518		Green
486.1	- 784		Blue
435.8	-1357		Violet

The high specific rotation of this diazo compound combined with the fact that it contains but the one asymmetric carbon atom proves beyond doubt that the carbon atom connected with the diazo group may retain its asymmetry.

There is, nevertheless, an interesting possibility existing due to the presence of the naphtholic group in the molecule. Instead of the pentad nitrogen losing an electron to the carbon atom, IV, it is possible for this electron to be transferred to the oxygen, III. This would form a ring held together by a single polar valence between nitrogen and oxygen.



⁸ Betti, *Gazz. chim. ital.*, **31**, I, 386 (1901); **36**, II, 392 (1906).

⁹ An intense violet coloration was obtained in the test for the naphtholic group with the reagent of Folin and Dennis, *J. Biol. Chem.*, **12**, 240 (1912).

If, however, a cyclic structure, III, is postulated, salt formation would destroy the ring and racemize the compound. That treatment with alkali does *not* racemize the compound must be accepted as evidence for the straight chain formula, IV. In addition, a quinoid structure is definitely eliminated by the optical activity of the compound. Staudinger¹⁰ considers all the "so-called" diazo anhydrides to have the straight chain structure. He cites examples of several equally stable diazo compounds which contain only carbon, hydrogen and nitrogen.

The study of this and related compounds is being continued.

Experimental Part

β -Naphthol-phenylaminomethane was prepared and resolved according to Betti's method.⁸ Both the *d* and *l* forms melted at 137° and gave for one gram in 50.0 cc. of ether in a one decimeter tube: $\alpha_D = 1.20^\circ$, $[\alpha]_D^{30} = 60.0 \pm 0.2^\circ$.

Anal. Calcd. for C₁₇H₁₅ON: N, 5.62. Found: N, 5.67.

β -Naphthol-phenyldiazomethane.—Five grams of the active amine was dissolved in 50.0 cc. of pyridine, the equivalent amount of aqueous sodium nitrite was added, and the solution so obtained was slowly added to an excess of concentrated hydrochloric acid cooled in a freezing mixture.¹¹ The diazo compounds separate in light flaky lemon-yellow crystals melting with decomposition at 120°. It may be recrystallized from a mixture of ether and ligroin but if the diazotization is properly carried out a pure compound results. Sometimes considerable quantities of the ketazine are formed. For some undiscovered reason the *d* diazo compound was never obtained in quite as pure a state as the *l* isomer.

Anal. Calcd. for C₁₇H₁₂ON₂: H, 4.65; C, 78.43; N, 10.8. Subs., (*d*) 0.1117: H₂O, 0.0488; CO₂, 0.3191. Found: H, 4.89; C, 77.9; N, 10.6. Subs., (*l*) 0.1112, 0.1495: H₂O, 0.0473, 0.0649; CO₂, 0.3183, 0.4289. Found: H, 4.76, 4.86; C, 78.1, 78.2; N, 10.8.

Rotation (*d*): 1.000 g. in 100.0 cc. 95% alcohol-acetone, 80–20, at 30° in a one-decimeter tube:

$$\alpha_{656.3} + 2.85^\circ, \alpha_D + 4.05^\circ, [\alpha]_{656.3}^{30} + 285^\circ, [\alpha]_D^{30} + 405^\circ$$

Rotation (*l*): 1.000 g. in 100.0 cc. 95% alcohol-acetone, 80–20, at 30° in a one-decimeter tube:

$$\alpha_{656.3} - 3.10^\circ, \alpha_D - 4.20^\circ, \alpha_{646.3} - 5.18^\circ, \alpha_{486.1} - 7.84^\circ, \alpha_{435.8} - 13.57^\circ, \alpha = 0.02^\circ, [\alpha]_{656.3}^{30} - 310^\circ, [\alpha]_D^{30} - 420^\circ, [\alpha]_{646.3}^{30} - 518^\circ, [\alpha]_{486.1}^{30} - 784^\circ, [\alpha]_{435.8}^{30} - 1357^\circ$$

β -Naphtholphenoneketazine.—On heating the diazo compound to 125° until evolution of nitrogen ceased, or by boiling with dilute acids, the ketazine was obtained. It was recrystallized from alcohol and melted at 182°. Of a light color when first prepared, it soon darkened to a yellowish or reddish-brown. Imperfect diazotization also resulted in the ketazine.

Anal. Calcd. for C₂₄H₂₄O₂N₂: N, 5.69. Found: N, 5.5, 5.4.

Salt Formation.—Alcoholic 1% solutions of the active *d* compound were treated with approximately one, two and three equivalents, respectively, of 25% potassium hydroxide. Some heat was liberated and the solutions darkened considerably. No lowering in the rotation was observed. In fact a small increase seemed observable

¹⁰ Staudinger, *Ber.*, 49, 1884, 1928 (1916).

¹¹ Krishna and Bhatia, Proc. 15th Indian Sci. Congress, 1928, p. 152.

but this may have been due entirely to the darkened solution; original $\alpha_D +4.05^\circ$; after treatment with alkali: $\alpha_D +4.10^\circ, 4.15^\circ, 4.12^\circ$; average, $+4.12^\circ$.

Racemization.—An alcoholic 1% solution of the *l* compound was heated on the water-bath at $60\text{--}65^\circ$ for four hours, alcohol being added to maintain the original volume. No evolution of gas was observed; original $\alpha_D -4.20^\circ$; after heating, $\alpha_D -3.72^\circ$, a decrease of about 12%. The compound is thus somewhat stable optically. Heating to boiling caused some decomposition to the ketazine.

Summary

A stable, optically active, crystalline aliphatic diazo compound, β -naphthol-phenyldiazomethane, melting at 120° and having a high specific rotation, $[\alpha]_D^{30} = +420^\circ$, has been prepared. The rotatory dispersion is rather high, approximately 1000° between the red and violet.

On decomposition by heat or acids it forms the ketazine melting at 182° .

This shows conclusively that a carbon atom attached to the diazo group may retain its asymmetry.

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[CONTRIBUTION FROM THE PLAUT RESEARCH LABORATORY OF LEHN & FINK, INC.]

BACTERICIDAL PROPERTIES OF MONOETHERS OF DIHYDRIC PHENOLS. II. THE MONOETHERS OF HYDROQUINONE

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It has been shown in the preceding communication (Part I of this series) that among the monoethers of resorcinol there are a number of compounds which show very considerable bactericidal potency as determined with *B. typhosus* and *Staphylococcus aureus* as test organisms.¹ This bactericidal efficacy was found to depend particularly upon the length of the chain and the molecular weight of the substituting aliphatic or aromatic radical.

Continuing this series of investigations, we prepared several monoethers of hydroquinone in order to study the antibacterial effect of replacing the hydrogen atom of one hydroxyl group of this dihydric phenol by an organic radical.

Discussion

The number of hydroquinone monoethers described in the literature is comparatively small, and none appear to have been tested for their effect upon bacteria. Hydroquinone itself and some of its nucleus substituted derivatives were studied by several investigators with the aid of certain common pathogenic microbes. Thus Cooper and Woodhouse² found the phenol coefficient of hydroquinone to be 1.0 against *B. typhosus*, 1.1 against *Staphylococcus* and 0.96 against *B. coli*. Cooper and Forstner³

¹ E. Klarmann, L. W. Gatyas and V. A. Shternov, THIS JOURNAL, 53, 3397 (1931).

² E. A. Cooper and D. L. Woodhouse, *Biochem. J.*, 17, 600 (1923).

³ E. A. Cooper and G. E. Forstner, *ibid.*, 18, 940 (1924).