

mixture) was converted to the amide as described for the 2-pyridyl analog. The intermediate methyl ester distilled at 95° (2 mm.). The amide, m. p. 166–167°, was crystallized from alcohol.

*Anal.* Calcd. for  $C_8H_{10}N_2O_2$ : C, 63.98; H, 6.71. Found: C, 63.99; H, 6.90.

The following compounds were prepared as described for the 2-pyridyl analogs.

**$\beta$ -(4-Pyridyl)-ethylamine-methylurethan Hydrochloride.**—The urethan could not be obtained crystalline and decomposed on attempted distillation. The crude material was converted to the hydrochloride with dry hydrogen chloride in ethyl acetate and crystallized from methanol-ether, m. p. 132–133°.

*Anal.* Calcd. for  $C_9H_{13}O_2N_2Cl$ : Cl, 16.36. Found: Cl, 16.46.

**$\beta$ -(4-Pyridyl)-ethylamine Dihydrochloride.**—M. p. 222°.

*Anal.* Calcd. for  $C_7H_{12}N_2Cl_2$ : Cl, 36.33. Found: Cl, 36.43.

**$\beta$ -(4-Pyridyl)-ethylamine-methylurethan Methiodide.**—M. p. 121–122°.

*Anal.* Calcd. for  $C_{10}H_{15}O_2N_2I$ : I, 39.38. Found: I, 39.04.

**$\beta$ -(4-Pyridyl)-ethylamine-methochloride Hydrochloride.**—M. p. 186–187°.

*Anal.* Calcd. for  $C_8H_{14}N_2Cl_2$ . Cl, 33.91. Found: Cl, 34.05.

### Summary

The preparation as well as the chemical and pharmacological properties of some  $\beta$ -(2-, and 4-pyridylethyl and propyl)-amines have been described.

NEWARK, N. J.

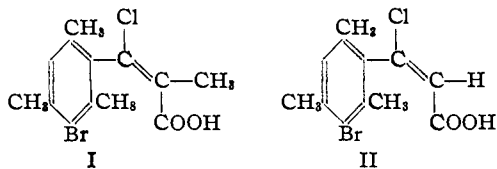
RECEIVED AUGUST 2, 1941

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

## Restricted Rotation in Aryl Olefins. III. Preparation and Resolution of $\beta$ -Chloro- $\beta$ -(2-methyl-1-naphthyl)-acrylic Acids<sup>1</sup>

BY ROGER ADAMS AND L. O. BINDER<sup>2</sup>

Among the aryl olefins with restricted rotation between the benzene ring and an acrylic acid residue reported in previous articles<sup>1,3</sup> in this series are compounds I and II.



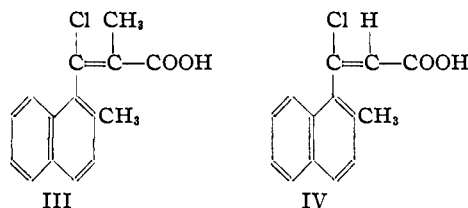
Both of these molecules were resolved readily. Compound I did not racemize in boiling *n*-butanol; compound II under similar conditions had a half-life of about two hundred minutes. Although no direct chemical proof was offered for the relative placement of the side-chain methyl and carboxyl groups in I or the hydrogen and carboxyl groups in II, by indirect deductions the structures assigned them appear to be the more likely.

A series of analogous derivatives of this type has been under investigation in order to compare the effects of various groups on the restricted rotation. The corresponding naphthalene compounds have now been synthesized and their structures are shown in formulas III and IV.

(1) For previous paper see Adams, Anderson and Miller, *THIS JOURNAL*, **63**, 1589 (1941).

(2) An abstract of a thesis submitted in partial fulfillment for the degree of Doctor of Philosophy in Chemistry.

(3) Adams and Miller, *THIS JOURNAL*, **62**, 53 (1940).



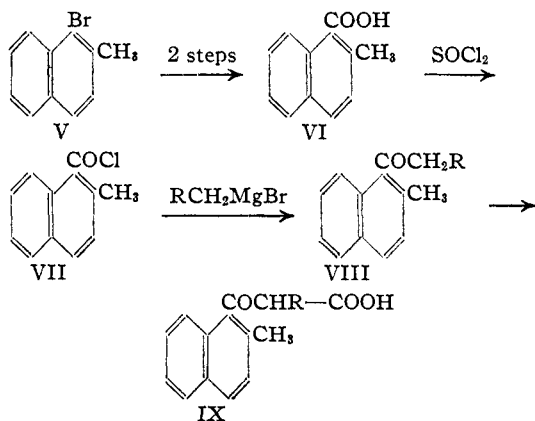
Compounds III and IV are assumed to have the same geometric configuration as compounds I and II since they were formed from the appropriate ketones by exactly the same process used for the benzene derivatives.

Evidence deduced from previous work in this field would lead to the conclusion that the two methyls adjacent to the acrylic acid side-chain in I and II and the methyl and the aromatic grouping —CH= adjacent to the side-chain in III and IV represent the bulk of the hindrance contributed by the aromatic part of the molecules. A direct comparison of the steric effect of the methyl and —CH= groups is thus possible. Although many substituted binaphthyls and biphenyls have been prepared and resolved, none has been synthesized which allows a direct comparison of these groups just mentioned.

Compound III had a half-life in boiling *n*-butanol of seventy hours in contrast to compound I which did not racemize at all in boiling *n*-butanol. Compound IV had a half-life of about seventy

minutes in the same solvent whereas compound II had a half-life of two hundred minutes. These experiments establish beyond a doubt the greater interference effect of a methyl group as compared with the  $-\text{CH}=\text{}$  group of an aromatic nucleus.

The introduction of an acyl group into the  $\alpha$ -position of  $\beta$ -methyl-naphthalene is not possible by a Friedel-Crafts reaction. An indirect synthesis was sought. The most satisfactory procedure found is shown in formulas V-VIII.  $\beta$ -Methyl-



naphthalene brominated in the  $\alpha$ -position to yield 1-bromo-2-methylnaphthalene (V). This was converted to the corresponding Grignard reagent and carbonated to give 2-methyl-1-naphthoic acid (VI). Formation of the acid chloride (VII) and treatment with an appropriate Grignard gave satisfactory yields of the desired ketones (VIII). Ethylmagnesium bromide with the ketones followed by carbon dioxide gave the ketonic acids (IX) which were transformed to compounds III and IV by means of phosphorus pentachloride in phosphorus oxychloride as a solvent. Resolution was effected readily.

### Experimental

**1-Bromo-2-methylnaphthalene.**—To a solution of 142 g. of 2-methylnaphthalene (1.0 mole) in 300 cc. of carbon tetrachloride were added a crystal of iodine and a pinch of iron powder and the flask and contents were cooled to  $0^\circ$ . The flask was covered with a towel to exclude light and 160 g. (1.0 mole) of bromine in 300 cc. of carbon tetrachloride was added with mechanical stirring over a period of eight hours without allowing the temperature to rise above  $5^\circ$ . After standing overnight, the carbon tetrachloride solution was washed thoroughly with 10% aqueous sodium hydroxide, then with water and dried over calcium chloride. The product had a b. p. of  $152\text{--}156^\circ$  (14 mm.); yield, 186 g. (84%). Meyer reports  $166^\circ$  (13 mm.).<sup>4</sup>

(4) Meyer and Steglitz, *Ber.*, **55**, 1835 (1922).

**2-Methyl-1-naphthoic Acid.**—A mixture of 26 g. of magnesium and about 40 g. of 1-bromo-2-methylnaphthalene was covered with dry ether and the reaction initiated by addition of a few drops of ethylmagnesium bromide and gentle warming. After the reaction started more of the bromide to total 240 g. (1.09 moles) in 300 cc. of dry ether was added with stirring. The reaction mixture was allowed to reflux on a hot-plate for thirty minutes after all the bromide had been added. The white precipitate which formed was dissolved by the addition of 250 cc. of dry benzene, the flask and contents were cooled and the reaction mixture then poured over 700 g. of powdered solid carbon dioxide. When the lumpy mass which formed had reached, upon warming, a semi-liquid state, dilute hydrochloric acid was added in sufficient quantity to bring all the material into solution. The ether-benzene layer was separated and extracted with 5% aqueous sodium hydroxide. On acidification of this extract the product separated as an oil which gradually crystallized. The crude product was dried and used directly for conversion to the acid chloride: yield, 140 g. (70%). Crystallized from benzene it formed white crystals, m. p.  $126\text{--}127^\circ$  (cor.). Meyer<sup>4</sup> reports  $127^\circ$ .

**2-Methyl-1-naphthoyl Chloride.**—A mixture of 140 g. of 2-methyl-1-naphthoic acid and 270 g. of thionyl chloride was allowed to stand at room temperature for twenty-four hours. After removal of excess thionyl chloride at the water pump, the product was distilled, b. p.  $145^\circ$  (7 mm.); yield, 140 g. (91%).

**1-Aceto-2-methylnaphthalene.**—To Grignard reagent from 18 g. of magnesium and 110 g. of methyl iodide was added with stirring 50 g. (0.25 mole) of acid chloride in 300 cc. of dry ether at such a rate that moderate reflux was maintained. The reaction was refluxed on a hot-plate for thirty minutes and then cooled and decomposed with chilled aqueous ammonium chloride solution. The product had a b. p. of  $125\text{--}130^\circ$  (3-4 mm.);  $n_D^{20}$  1.6037;  $d_4^{20}$  1.084; yield, 40 g. (89%).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{12}\text{O}$ : C, 84.74; H, 6.57. Found: C, 84.69; H, 6.74.

**$\beta$ -Keto- $\beta$ -(2-methyl-1-naphthyl)-propionic Acid.**—A solution of 14 g. of 1-aceto-2-methylnaphthalene in 100 cc. of dry ether was added to a slight molar excess of ethylmagnesium bromide in 100 cc. of dry ether. The mixture was refluxed for thirty minutes, during which time the magnesium enolate precipitated out as a heavy, white, crystalline sludge. The mixture was transferred to a pressure bottle and thoroughly cooled in an ice-calcium chloride bath. Carbon dioxide at a pressure of three atmospheres was admitted to the bottle with occasional shaking from a catalytic hydrogenation machine until equilibrium was reached. The bottle was then removed from the bath and placed on the shaker for twelve hours. The bottle was once more cooled, removed from the machine, and the reaction mixture decomposed with iced hydrochloric acid. The ether layer was extracted with ice-cold 10% aqueous sodium hydroxide and the alkaline extract immediately acidified with cold hydrochloric acid. The product separated as an oil which, on rubbing, crystallized in fine, nearly white crystals. Upon drying it had a m. p. of  $107^\circ$  (cor.) with decomposition; yield, 8.5 g. (46%).

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{12}\text{O}_3$ : C, 73.65; H, 5.30. Found: C, 73.88; H, 5.36.

**$\beta$ -Chloro- $\beta$ -(2-methyl-1-naphthyl)-acrylic Acid.**—A solution of 9 g. of  $\beta$ -keto- $\beta$ -(2-methyl-1-naphthyl)-propionic acid in 18 cc. of phosphorus oxychloride was chilled and to it was added 18 g. of phosphorus pentachloride with care to avoid a violent reaction. The mixture was allowed to warm slowly to room temperature, and when the reaction subsided the temperature was gradually raised to 60° where it was maintained for fifty minutes. Decomposition of the reaction was brought about by pouring it over cracked ice and stirring very vigorously until the red, oily substance first obtained changed to a yellow, semi-solid mass. The gummy product was taken up with ether and the ether solution extracted with 5% aqueous sodium hydroxide. The alkaline solution was acidified and extracted with ether, the ether solution dried with anhydrous sodium sulfate and the ether removed from the product by means of an air stream. The black residue was extracted repeatedly with petroleum ether (b. p. 60–110°) and the combined extracts evaporated to dryness. The residue, which was deep orange, was crystallized from the smallest possible volume of carbon tetrachloride, which retained nearly all of the colored impurities in solution, and finally the acid was recrystallized, using decolorizing charcoal, from petroleum ether (b. p. 60–110°); white crystals, m. p. 184° (cor.); yield, 2 g. (21%).

*Anal.* Calcd. for  $C_{14}H_{11}O_2Cl$ : C, 68.15; H, 4.50. Found: C, 68.15; H, 4.65.

**Resolution of  $\beta$ -Chloro- $\beta$ -(2-methyl-1-naphthyl)-acrylic Acid.**—A solution of 2 g. of  $\beta$ -chloro- $\beta$ -(2-methyl-1-naphthyl)-acrylic acid in 75 cc. of warm ethyl acetate and 1 g. of *d*- $\alpha$ -phenylethylamine on cooling resulted in a voluminous precipitate of fine white needles. These were allowed to stand in the liquor overnight to complete precipitation. The salt weighed 1.3 g. This was dissolved in ethyl acetate and the solution allowed to evaporate. Four successive fractions gave identical rotations; white crystals, m. p. 158–160° (cor.) with decomposition.

*Anal.* Calcd. for  $C_{14}H_{11}O_2Cl \cdot C_8H_{11}N$ : C, 71.82; H, 6.03. Found: C, 71.98; H, 6.23.

*Rotation.* Less-soluble salt: 0.048 g. made up to 25 cc. with ethanol at 32° gave  $\alpha_D +0.16^\circ$ ; *l*, 2;  $[\alpha]^{25}_D +42^\circ$ .

The filtrate from the original precipitation of the less-soluble salt was evaporated partially but no more salt separated. The solvent was removed completely, leaving an oil which after twenty-four hours solidified. Attempts to find a solvent for recrystallization failed.

*Rotation.* Crude more-soluble salt: 0.051 g. made up to 25 cc. with ethanol at 32° gave  $\alpha_D -0.16^\circ$ ; *l*, 2;  $[\alpha]^{25}_D -39^\circ$ .

***d*- and *l*- $\beta$ -Chloro- $\beta$ -(2-methyl-1-naphthyl)-acrylic Acids.**—The salts were decomposed by stirring with successive portions of 10% hydrochloric acid which were removed by filtration. The product which still contained unchanged salt was dissolved in 10% aqueous sodium hydroxide, the solution extracted with chloroform and then acidified. The *d*-acid thus obtained was recrystallized from petroleum ether (b. p. 60–90°); white crystals, m. p. 191° (cor.). The *l*-acid recrystallized from petroleum ether (b. p. 60–110°); white crystals, m. p. 186° (cor.)

*Anal.* Calcd. for  $C_{14}H_{11}O_2Cl$ : C, 68.15; H, 4.50. Found: *d*-acid: C, 68.05; H, 4.75; *l*-acid: C, 68.05; H, 4.67.

*Rotation.* *d*-Acid: 0.019 g. made up to 10 cc. with ethanol at 32° gave  $\alpha_D +0.125^\circ$ ; *l*, 1;  $[\alpha]^{25}_D +66^\circ$ .

*Rotation.* (*l*-Acid) 0.019 g. made up to 10 cc. with ethanol at 32° gave  $\alpha_D -0.12^\circ$ ; *l*, 1;  $[\alpha]^{25}_D -63^\circ$ .

**Racemization of *d*- $\beta$ -Chloro- $\beta$ -(2-methyl-1-naphthyl)-acrylic Acid.**—Racemization of the active acid was carried out in boiling *n*-butanol. A weighed quantity of material was diluted to 25 cc. in a volumetric flask, a reading taken on the polarimeter and the material transferred quantitatively to a 50-cc., flat-bottomed flask with a ground joint. The solution was evaporated to about 15 cc. as rapidly as possible by drawing a stream of air over the boiling liquid, and then the solution was allowed to reflux for a suitable time, after which it was transferred to a volumetric flask, made up once more to 25 cc. and the rotation observed. By repetition of this procedure a series of readings was obtained.

*Rotation.* 0.100 g. made up to 25 cc. with *n*-butanol at 28° gave  $\alpha_D +0.42^\circ$ ; after refluxing for thirty minutes,  $+0.31^\circ$ ; sixty minutes,  $+0.23^\circ$ ; one hundred eighty minutes,  $+0.08^\circ$ ; two hundred forty minutes,  $+0.04^\circ$ . In a second trial, 0.100 g. made up to 25 cc. with *n*-butanol at 29° gave  $\alpha_D +0.42^\circ$ ; after refluxing for sixty minutes,  $+0.24^\circ$ ; ninety minutes,  $+0.17^\circ$ ; one hundred twenty minutes,  $+0.115^\circ$ ; one hundred fifty minutes,  $+0.09^\circ$ .

The half-life period calculated on the basis of a unimolecular reversible reaction is approximately sixty-seven minutes.

**1-Propio-2-methylnaphthalene.**—From 15 g. of 2-methyl-1-naphthoyl chloride and ethylmagnesium bromide the propio derivative was obtained: b. p. 143–144° (1–2 mm.);  $n^{20}_D$  1.5931;  $d^{20}_4$  1.064; yield, 13.5 g. (95%).

*Anal.* Calcd. for  $C_{14}H_{14}O$ : C, 84.81; H, 7.12. Found: C, 85.08; H, 7.26.

**$\beta$ -Keto- $\beta$ -(2-methyl-1-naphthyl)- $\alpha$ -methylpropionic Acid.**—By the same method used for obtaining the  $\beta$ -keto- $\beta$ -(2-methyl-1-naphthyl)-propionic acid, the product was obtained in about the same yield; white crystals, m. p. 105° (cor.) with decomposition.

*Anal.* Calcd. for  $C_{15}H_{14}O_3$ : C, 74.35; H, 5.83. Found: C, 74.90; H, 5.70.

**$\beta$ -Chloro- $\beta$ -(2-methyl-1-naphthyl)- $\alpha$ -methylacrylic Acid.**—To a solution of 4 g. of  $\beta$ -keto- $\beta$ -(2-methyl-1-naphthyl)- $\alpha$ -methylacrylic acid in 20 cc. of phosphorus oxychloride, 10 g. of phosphorus pentachloride was added slowly with stirring. The reaction was warmed in a water-bath at 98° for one hour and then decomposed by pouring onto cracked ice and stirring vigorously. When hydrolysis was complete the gummy product was taken up in ether, and the ether solution extracted with 5% sodium hydroxide. On acidification of the alkaline extract an oil appeared which crystallized on standing. The solid was collected on a filter, dried, and recrystallized from petroleum ether (b. p. 60–110°), m. p. 161–162° (cor.); yield, 2 g. (47%).

*Anal.* Calcd. for  $C_{15}H_{13}O_2Cl$ : C, 69.06; H, 5.03. Found: C, 69.39; H, 5.12.

**Resolution of  $\beta$ -Chloro- $\beta$ -(2-methyl-1-naphthyl)- $\alpha$ -methylacrylic Acid.**—To a solution of 1.5 g. of  $\beta$ -chloro- $\beta$ -(2-methyl-1-naphthyl)- $\alpha$ -methylacrylic acid in 60 cc. of hot ethyl acetate was added 2 g. of quinine. Upon cooling 1.5 g. of salt crystallized, and by evaporation of the solvent

nearly to dryness, an additional 1.7 g. of salt was obtained. These fractions were purified separately by recrystallization from ethyl acetate to constant rotation; less-soluble salt, white crystals, m. p. 194° (cor.) with decomposition; more-soluble salt, white crystals, m. p. 132° (cor.) with decomposition.

*Anal.* Calcd. for  $C_{15}H_{13}O_2Cl \cdot C_{20}H_{24}O_2N_2$ : C, 71.82; H, 6.38. Found: less-soluble salt: C, 71.54; H, 6.59; more-soluble salt: C, 71.98; H, 6.46.

*Rotations.* Less-soluble salt: 0.018 g. made up to 10 cc. with ethanol at 26° gave  $\alpha_D -0.140^\circ$ ; *l*, 1;  $[\alpha]^{26}_D -72^\circ$ . More-soluble salt: 0.017 g. made up to 10 cc. with ethanol at 26° gave  $\alpha_D -0.23^\circ$ ; *l*, 1;  $[\alpha]^{26}_D -136^\circ$ .

*d*- and *l*- $\beta$ -Chloro- $\beta$ -(2-methyl-1-naphthyl)- $\alpha$ -methylacrylic Acids.—The acids were obtained from their salts in the manner described for the  $\beta$ -chloro- $\beta$ -(2-methyl-1-naphthyl)-acrylic acids except that it was not necessary to extract aqueous solutions of their sodium salts with chloroform. Recrystallized from petroleum ether (b. p. 60–110°); *d*-acid, white crystals, m. p. 123° (cor.); *l*-acid, white crystals, m. p. 123° (cor.).

*Anal.* Calcd. for  $C_{15}H_{13}O_2Cl$ : C, 69.06; H, 5.03. Found: *d*-acid: C, 69.02; H, 5.19; *l*-acid: C, 69.41; H, 5.15.

*Rotations.* *d*-Acid: 0.020 g. made up to 10 cc. with ethanol at 26° gave  $\alpha_D +0.11^\circ$ ; *l*, 1;  $[\alpha]^{26}_D +55^\circ$ . *l*-Acid: 0.024 g. made up to 10 cc. with ethanol at 26° gave  $\alpha_D -0.14^\circ$ ; *l*, 1;  $[\alpha]^{26}_D -58^\circ$ .

**Racemization of *l*- $\beta$ -Chloro- $\beta$ -(2-methyl-1-naphthyl)- $\alpha$ -methylacrylic Acid.**

*Rotations.* 0.100 g. of acid made up to 25 cc. with *n*-butanol at 30° gave  $\alpha_D -0.54^\circ$ ; after refluxing for thirty-four and one-quarter hours,  $-0.38^\circ$ ; sixty-two hours,  $-0.30^\circ$ ; one hundred five hours,  $-0.225^\circ$ ; one hundred thirty-six hours,  $-0.13^\circ$ .

The half-life period calculated on the basis of a unimolecular reversible reaction is around seventy hours.

### Summary

1.  $\beta$ -Chloro- $\beta$ -(2-methyl-1-naphthyl)-acrylic acid and  $\beta$ -chloro- $\beta$ -(2-methyl-1-naphthyl)- $\alpha$ -methylacrylic acid have been prepared and resolved. The rate of racemization of the active forms was determined and the half-life values compared with those of the corresponding bromomesitylene derivatives with similar side chains. The results demonstrate that the methyl group is more effective in producing restriction than the  $-\text{CH}=\text{}$  grouping of an aromatic nucleus.

2. The  $\alpha$ -acyl- $\beta$ -methylnaphthalenes used as starting materials in the syntheses were most satisfactorily synthesized as follows:  $\alpha$ -bromo- $\beta$ -methylnaphthalene  $\rightarrow$   $\beta$ -methyl- $\alpha$ -naphthoic acid  $\rightarrow$   $\beta$ -methyl- $\alpha$ -naphthoyl chloride  $\rightarrow$   $\alpha$ -acyl- $\beta$ -methylnaphthalene.

URBANA, ILLINOIS

RECEIVED AUGUST 4, 1941

[CONTRIBUTION FROM THE GEORGE HERBERT JONES CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO]

## The Oxygen Effect in the Reaction of Bromine with Neopentane, *t*-Butylbenzene and Trimethylacetic Acid

BY M. S. KHARASCH AND MORTON Z. FINEMAN

Preliminary work in this Laboratory has shown that tertiary hydrogen atoms are more readily replaced by bromine atoms than are secondary hydrogen atoms.<sup>1</sup> Because of these observations, it was decided to investigate the bromination of compounds containing primary hydrogen atoms.

A search of the literature revealed that aliphatic compounds containing only primary hydrogen atoms have hitherto been brominated only at elevated temperatures. Most of the reactions were carried out in the gas phase.<sup>2</sup> The only reported low temperature liquid phase bromination of a compound containing only primary hydrogen atoms is that of Colibasi petroleum boiling at 0–10°; this material contained neopentane, but the range of its boiling point indicates that it was a

mixture of hydrocarbons.<sup>3</sup> Moreover, although the refractive index of the reaction product agrees with that of neopentyl bromide (prepared by Whitmore, Wittle and Harriman<sup>4</sup>), the large discrepancies in boiling point and in density suggest a mixture of brominated hydrocarbons.<sup>5</sup> Because of these discrepancies, it was decided to investigate the liquid phase bromination of neopentane, *t*-butylbenzene and trimethylacetic acid.

### Results

The results indicate that pure neopentane does not react with dilute solutions of bromine at room temperature even under optimum conditions,

(3) Poni, *Chem. Zentr.*, **77**, I, 442 (1906).

(4) Whitmore, Wittle and Harriman, *THIS JOURNAL*, **61**, 1585 (1939).

(5) Cf. the physical constants obtained by the two investigators: Poni: b. p. 89–91 (749 mm.);  $d^{20}_4$ , 1.260;  $n_D$  1.4369; Whitmore: b. p. 105 (732 mm.);  $d^{20}_4$ , 1.199;  $n_D$  1.4370.

(1) Hered, Ph.D. Dissertation, University of Chicago.

(2) (a) Egloff, Schaad and Lowry, Jr., *Chem. Rev.*, **8**, 58 (1931);

(b) Perelis, *Ind. Eng. Chem.*, **25**, 1160 (1933).