Wilbur J. Doran for the micro-chemical nitrogen analyses reported in this investigation, and for his assistance in the preparation of some of the products.

Conclusion

1. Alkenylethylbarbituric acids containing the unsaturated secondary pentyl or hexyl group have less hypnotic action than corresponding barbituric acids with saturated alkyl groups and cause convulsions at low doses.

2. Two propargylalkylbarbituric acids were investigated and found to have hypnotic action which was not more effective than the corresponding barbituric acids containing the allyl or propyl group.

3. The following new products were prepared—isoamylpropargylmalonic ester, 1-methylbutenyl-2-ethylmalonic ester, 1-ethylbutenyl-2-ethylmalonic ester, 1-ethylbutylethylmalonic ester, *sec*-butyl-*n*-propylmalonic ester, *sec*-butylpropargylbarbituric acid, isoamylpropargylbarbituric acid, 1-methylbutenyl-2-ethylbarbituric acid, 1-ethylbutenyl-2-ethylbarbituric acid, 1-ethylbutylethylbarbituric acid and *sec*-butyl-*n*-propylbarbituric acid.

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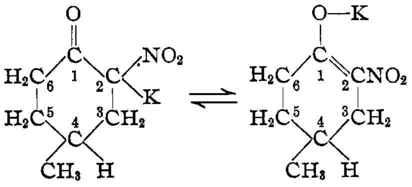
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

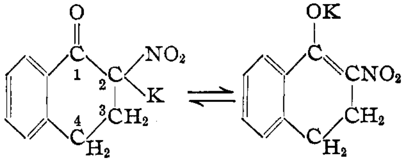
Asymmetric Syntheses. III. The Action of Optically Active Nitrates on α-Tetralone

BY W. H. HORNE AND R. L. SHRINER

The formation of an optically active product as the result of the reaction between 4-methylcyclohexanone and *d* or *l*-2-octyl nitrate[1] left undecided the location of the optically active center of the molecule and the exact structure of the salts of these nitro compounds. The presence of the asymmetric carbon atom at position 4 prevents any distinction between structures I and II since both forms would be optically active.



I II



III IV

In order to avoid the complicating effect of the asymmetric carbon atom at position 4, a study was made of the action of *d*- and *l*-2-octyl nitrates

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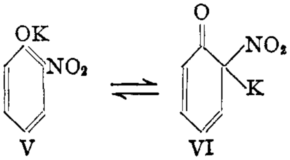
(1) Shriner and Parker, THIS JOURNAL, **55**, 766 (1933).

on another cyclic ketone, α-tetralone. If the potassium salt of the β-nitro-α-tetralone possesses the structure III, then any optical activity must be due to carbon number 2 and the salt is analogous to other optically active salts of secondary nitro compounds.[2] On the other hand, structure IV contains no asymmetric carbon atoms and would be optically inactive.

Treatment of α-tetralone with *d*- or *l*-2-octyl nitrates in the presence of potassium ethylate yielded potassium salts of β-nitro-α-tetralone which were optically inactive in every case. The reaction was carried out at 40, 22 and 0° but no activity could be observed. Immediate treatment of the potassium salt with acid gave the free β-nitro-α-tetralone, which was also optically inactive.

The optical inactivity of these compounds indicates that the structure of the salts of these nitro ketones is of the type shown by II and IV. Compounds of this type would be expected to resemble the salts of *o*-nitrophenol, most of whose reactions and properties indicate that they are derived from the enolic form (V) rather than the tautomeric keto form (VI)



V VI

Experimental

Phenylethyl Bromide.—By the action of 500 g. of 48% hydrobromic acid, 270 g. of concentrated sulfuric acid and 305 g. of phenylethyl alcohol there was obtained 375 g. (81.1%) of phenylethyl bromide, b. p. 77–80° at 3 mm.; 107–108° at 17 mm.

γ-Phenylbutyric Acid.—Twelve grams of sodium was dissolved in 250 cc. of absolute alcohol and 78 g. of malonic ester added. With vigorous stirring 89 g. of phenylethyl bromide was added and the resulting mixture refluxed for three hours. A solution of 130 g. of potassium hydroxide in 130 cc. of water was added and as much alcohol as possible removed by distillation. An additional 100 g. of 50% potassium hydroxide solution was added during the distillation of the alcohol. The residue was poured into 800 cc. of 20% hydrochloric acid and warmed on the steam cone. The layers were separated and the aqueous layer extracted with ether. The ether was distilled and the combined dry portions of the substituted malonic acid placed in a Claisen flask and heated in an oil-bath. Carbon dioxide evolution started at 120°. The temperature was slowly raised to 200° and maintained there for ten minutes. The γ-phenylbutyric acid was then vacuum distilled. The yield was 41 g. (52%) of colorless liquid boiling at 125–130° at 3 mm. This solidified and formed crystals melting at 52°, which checked the value reported in the literature.[3]

α-Tetralone.—A solution of 30 g. of γ-phenylbutyric acid in 200 cc. of concentrated sulfuric acid was heated in a boiling water-bath for three and one-half hours. The solution was poured on cracked ice and the resulting mixture extracted with ether.

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

(3) Rupe and Proske, *Ber.*, **43**, 1233 (1910).

The ether solution was dried and the ether distilled. Vacuum distillation of the residue yielded 13 g. (48.7%) of α-tetralone; b. p. 105° at 3 mm.; 135° at 26 mm. The oxime was prepared as a derivative and found to melt at 102–102.5°, which checked the value in the literature.[4]

***dl*-, *d*- and *l*-2-Octyl Nitrates.**—These were prepared according to the method previously described.[1] *dl*-2-Octyl nitrate boiled 96–98° at 20 mm.; n^{20}_{D} 1.4299. *d*-2-Octyl nitrate boiled 140–141° at 45 mm.; $[\alpha]^{25}_{D}$ +14.59; n^{20}_{D} 1.4301. *l*-2-Octyl nitrate boiled 100–103° at 24 mm.; $[\alpha]^{25}_{D}$ −14.64; n^{20}_{D} 1.4298.

Condensation of α-Tetralone with *dl*-2-Octyl Nitrate.—A solution of 4.5 g. of *dl*-2-octyl nitrate and 7.3 g. of α-tetralone in 70 cc. of absolute ether was added to a solution of potassium ethylate prepared from 1 g. of potassium, 8 g. of absolute ethyl alcohol and 25 cc. of absolute ether. The reaction mixture was maintained at 40° by means of a water-bath, after about twenty minutes 50 cc. of dry ether was added and the mixture allowed to stand for four hours. The precipitate was filtered and thoroughly washed with dry ether and alcohol mixture in order to remove a red condensation product. The yellow powder was dried after rapidly transferring to a vacuum desiccator containing concentrated sulfuric acid and a beaker of sodium hydroxide pellets. It could be purified by solution in methyl alcohol and reprecipitation with absolute ether.

Anal. Calcd. for $C_{10}H_8O_3NK$: K, 17.07; N, 6.11. Found: K, 16.32; N, 6.40.

Condensation of α-Tetralone with *d*-2-Octyl Nitrate and *l*-2-Octyl Nitrate.—Exactly the same procedure as above was followed using *d*-2-octyl nitrate and the optical rotation of the salt in absolute ethyl alcohol was determined immediately. It was optically inactive. The condensation was repeated using temperatures of 22 and 0° instead of 40° but no activity was observed.

Anal. Calcd. for $C_{10}H_8O_3NK$: K, 17.07; N, 6.11. Found: K, 17.34; N, 6.08.

d-Octanol-2 was recovered from the reaction mixture by fractional distillation of the filtrate obtained by removal of the salt. It boiled at 86–88° at 20 mm.; $[\alpha]^{25}_{D}$ +8.8°; n^{20}_{D} 1.4298.

Modification of this procedure by use of molecular quantities of α-tetralone and optically active nitrate and by addition of an ethereal solution of potassium ethylate to an ethereal solution of the nitrate and ketone also produced an optically inactive salt. The same result was obtained using *l*-2-octyl nitrate.

Anal. Calcd. for $C_{10}H_8O_3NK$: K, 17.07; N, 6.11. Found: K, 17.24; N, 6.15.

β-Nitro-α-tetralone.—The yellow precipitate obtained by the action of dilute hydrochloric acid upon an aqueous solution of the potassium nitro salt was found to melt at 67° after recrystallization from ethyl alcohol. It was optically inactive.

Anal. Calcd. for $C_{10}H_9O_3N$: N, 7.33. Found: N, 7.44.

Summary

Treatment of α-tetralone with *d*- and *l*-2-octyl nitrates in the presence of potassium ethylate produced optically inactive salts of β-nitro-α-tetralone.

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[4] Kipping and Hill, *J. Chem. Soc.*, **75**, 144 (1899).