357. *Derivatives of* 1-*Methyltropane.*

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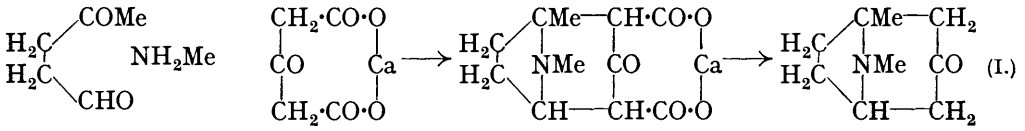
The succindialdehyde–tropinone synthesis does not succeed when the dialdehyde is replaced by a diketone such as acetonylacetone: the only product isolated in an attempted condensation with calcium acetonedicarboxylate and methylamine was 1 : 2 : 5-trimethylpyrrole. On the other hand, we have now found that a typical keto-aldehyde, namely, lævulinaldehyde, may be used for the synthesis of a homologue (I) of tropinone according to the scheme :—



(I.)

Unlike tropinone itself, ψ-pelletierine and other bases of this type, the new *methyltropinone* does not yield characteristic diarylidene derivatives. Undoubtedly this is due to the influence of the methyl group on the neighbouring keto-methylene system and a close analogy is available in the observation that 3-methyl*cyclo*hexanone affords only a monobenzylidene derivative with facility (Ruzicka, *Helv. Chim. Acta*, 1926, **9**, 101. Compare Borsche and Frank, *Ber.*, 1924, **57**, 1373, for the similar behaviour of dehydrocholic acid, and Gulland, J., 1928, 702, in connexion with hindrance phenomena in the morphine group). The methyltropinone has been converted into the corresponding 1-*methyl-ψ-tropine* and its *benzoate* (methyltropacocaine). The pharmacological properties of the latter are being examined by Professor Gunn and a colleague of the University Department of Pharmacology.

An application of Criegee's lead tetra-acetate method of oxidation to the glycol derived from methylheptenone has led to an improvement in the preparation of lævulinaldehyde.

Experimental.

Lævulinaldehyde.—Lead tetra-acetate (22·2 g.) was added gradually during 15 minutes to methylheptenone glycol (Harries, *Ber.*, 1902, **35**, 1181) (8 g.) in dry benzene (40 c.c.) kept below 40°. After 10 minutes, the lead acetate which had separated was collected, the benzene evaporated in a vacuum, and the residual oil distilled. The fraction, b. p. 45—85°/15 mm. (5·0 g.), was used in the next stage.

1-*Methyltropinone.*—Crude lævulinaldehyde (5 g.) in water (30 c.c.) was added to a solution of calcium acetonedicarboxylate (from 15 g. of the acid, 17 g. of precipitated chalk, and 100 c.c. of water), and aqueous methylamine (50 c.c. of 33%) dropped in with stirring during 30 minutes. After 24 hours the basic material was isolated in the manner previously described (Blount and Robinson, J., 1932, 1429), dissolved in acetone (10 c.c.), and mixed with a solution of picric acid (10 g.) in the same solvent (10 c.c.). The *picrate* separated at once, and a further small quantity was obtained from the mother-liquor (total yield, 12·5 g.; 65%, calculated on the methylheptenone glycol used). Recrystallisation from water afforded yellow needles (8 g.), m. p. 201° (decomp.) (Found: C, 47·2; H, 4·8; N, 14·7. $C_{15}H_{18}O_8N_4$ requires C, 47·1; H, 4·7; N, 14·7%).

1-*Methyltropinone*, regenerated from the picrate, was obtained as a colourless oil, b. p. 124°/27 mm. (Found: C, 70·3; H, 9·9; N, 9·0. $C_9H_{15}ON$ requires C, 70·6; H, 9·8; N, 9·1%). In moist air this base forms a crystalline hydrate, which liquefies when kept in a desiccator.

The *methiodide* crystallised from water in cube-like crystals, m. p. 273° to 282° (decomp.) according to the rate of heating (Found: C, 40·9; H, 6·0; I, 43·5. $C_{10}H_{18}ONI$ requires C, 40·7; H, 6·1; I, 43·1%).

Attempts to prepare a dipiperonylidene derivative in the usual way were unsuccessful. The product was an orange-coloured resin, which gave the colour reactions of a monopiperonylidene derivative.

1-*Methyl-ψ-tropine.*—Methyltropinone, from the recrystallised picrate (7 g.), was reduced by means of sodium (10 g.) and *n*-butyl alcohol (150 c.c.). After acidification and removal of the butyl alcohol in steam, the base was extracted and distilled, b. p. 138°/15 mm. It solidified on cooling, and crystallisation from petroleum (b. p. 60—80°) furnished pure 1-*methyl-ψ-tropine*,

m. p. 71° (Found : C, 69·3; H, 11·2; N, 8·6. $C_9H_{17}ON$ requires C, 69·7; H, 11·0; N, 9·0%) (yield, 1·6 g. or 56%).

In another experiment 11 g. of unrecrystallised picrate yielded 3·1 g. of distilled and 2·4 g. of recrystallised l-methyl-ψ-tropine (54%).

l-*Methyl-ψ-tropine picrate*, prepared in alcohol, formed small yellow prisms, which exploded at 280°, after previous discoloration (Found : C, 47·1; H, 5·1; N, 14·7. $C_{15}H_{20}O_8N_4$ requires C, 46·9; H, 5·2; N, 14·6%).

l-*Methyl-ψ-tropine hydrobromide* crystallised from alcohol, on addition of ether, in rhombohedra approximating to cubes, m. p. 286° (decomp.) (Found : C, 45·8; H, 7·4; Br, 33·9. $C_9H_{18}ONBr$ requires C, 45·7; H, 7·6; Br, 33·9%).

Benzoyl l-*Methyl-ψ-tropine* (*Methyltropacocaine*).—A mixture of l-methyl-ψ-tropine (1·5 g.), water (0·5 c.c.), and benzoic anhydride (3 g.) was gently refluxed for 4 hours, during which time a further quantity (5 g.) of benzoic anhydride was gradually added. The product was dissolved in ether and dilute hydrochloric acid, and the aqueous layer was separated, diluted, basified, and extracted with half its volume of ether : the greater part of the unchanged methyl-ψ-tropine remained in the aqueous layer. After evaporation of the ethereal solution, the residual base, dissolved in alcohol (50 c.c.), was treated with picric acid (rather more than 1 equiv.) in the same solvent (50 c.c.). The sparingly soluble *picrate*, which was precipitated, crystallised from alcohol in rosettes of small yellow needles, m. p. 163—164° (Found : C, 54·2; H, 5·1; N. 11·5. $C_{22}H_{24}O_9N_4$ requires C, 54·1; H, 4·9; N, 11·5%) (yield, 2·6 g. or 55%).

Methyltropacocaine, regenerated from the picrate, distilled as a colourless oil at 210°/15 mm. (Found : C, 74·2; H, 8·3. $C_{16}H_{21}O_2N$ requires C, 74·1; H, 8·1%). Crystalline salts of this base, other than the picrate, could not be obtained.

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