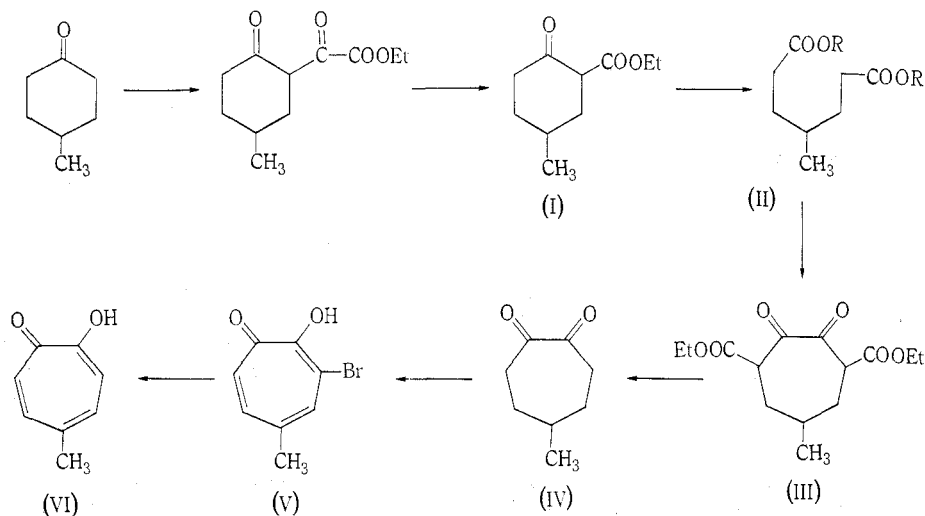


# SYNTHESIS OF 5-METHYLTROPOLONE

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In connection with studies on the photochemistry of tropolones, we required a supply of 5-methyltropolone. The only preparation of 5-methyltropolone recorded is that of Nozoe *et al.*,<sup>1</sup> using *p*-cresol as starting material. The method was long and the yields were insufficient. A new method was adopted, using 4-methylcyclohexanone as a starting material as shown in Scheme 1.



Scheme 1

Ethyl 5'-methylcyclohexyl-2-oxoacetic acid (I) was prepared by condensing 4-methylcyclohexanone and diethyl oxalate, and then hydrolysed<sup>2</sup> to 3-methylpimelic acid (II; R = H).

The conversion of diethyl 3-methylpimelate (II; R = Et) into 5-methylcycloheptane-1,2-dione (IV) was accomplished in low yields. Various research groups<sup>3-5</sup> have tried similar reactions, but their yields were generally lower than ours. Addition of a cooled mixture of the two esters to a suspension of sodium ethoxide in dry ether, followed by heating the residue and subsequent acidification, gave the cyclic ester (III) in 34% yield. The product was characterized as its dipyrazolone.

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<sup>1</sup> Nozoe, T., Mukai, T., and Muroi, T., *Sci. Rep. Tôhoku Univ.*, 1952, **35**, 242.

<sup>2</sup> Einhorn, A., and Erhurt, H., *Liebigs Ann.*, 1897, **295**, 185.

<sup>3</sup> Namov, A., and Perminova, S., *Acta Univ. Asiae mediae*, VI Fasc., 1937, 281.

<sup>4</sup> Cook, J. W., Loudon, J. D., and Steel, D. K. V., *J. chem. Soc.*, 1954, 530.

<sup>5</sup> Burnell, R. H., and Taylor, W. I., *J. chem. Soc.*, 1957, 3307.

Hydrolysis of this diester caused much difficulty. The use of concentrated hydrochloric acid, a mixture of dilute sulphuric acid and glacial acetic acid, and 95% formic acid failed to give the dione. However, the product was obtained in 20–40% yields by using 15% sulphuric acid.

Bromination of the above dione (IV) gave 3-bromo-5-methyltropolone (V). Dehydrobromination of sodium salt of (V) failed to give the desired product. Instead, an oil was obtained, which resisted crystallization. However, hydrogenation of 3-bromo-5-methyltropolone over palladium-charcoal gave a 75% yield of 5-methyltropolone (VI). Its physical constants were the same as those reported by Nozoe *et al.*<sup>1</sup>

### Experimental

#### Ethyl 5'-Methylcyclohexyl-2-oxoacetate

This compound was prepared from 4-methylcyclohexanone and diethyl oxalate by the method described by Synder *et al.*<sup>6</sup> for the preparation of ethyl cyclohexyl-2-oxoacetate. The product (71%) distilled as a colourless liquid, b.p. 140–142°/40 mm,  $n_D^{25}$  1.4634 (Found: C, 65.5; H, 8.8. Calc. for  $C_{10}H_{16}O_3$ : C, 65.2; H, 8.8%).

It reacted with phenylhydrazine in boiling ethanol to form a pyrazolone, which separated as colourless crystals, m.p. 199–200° (Found: C, 73.6; H, 7.0; N, 12.0. Calc. for  $C_{14}H_{16}N_2O$ : C, 73.6; H, 7.0; N, 12.3%).

#### 3-Methylpimelic Acid

To a hot methanolic sodium hydroxide solution (50 g dissolved in 150 ml methanol) was added ethyl 5'-methylcyclohexyl-2-oxoacetate (50 g) over a period of 2 hr with vigorous stirring. Heating and stirring were continued for an hour more; then water (330 ml) was added. Methanol was distilled off and the hot solution was neutralized with concentrated hydrochloric acid (150 ml). 3-Methylpimelic acid (36 g, 76%) was obtained as colourless crystals, m.p. 56–57° (lit.<sup>2</sup> 56–57°).

#### Diethyl 3-Methylpimelate

This product was obtained by a method described by Einhorn and Erhurt.<sup>3</sup> The product distilled as a colourless liquid, b.p. 120–122°/2 mm (Found: C, 62.6; H, 9.9. Calc. for  $C_{12}H_{22}O_4$ : C, 62.6; H, 9.6%).

#### Diethyl 6-Methyl-2,3-dioxocycloheptane-1,4-dicarboxylate

To a cooled suspension of sodium ethoxide (from 4 g of atomized sodium) in dry ether (200 ml), a cooled mixture of diethyl oxalate and diethyl 3-methylpimelate (12.7 g and 20 g) was slowly added over a period of 4 hr. The resultant solution was heated under reflux for 16 hr, the ether was removed, and the residue heated under distillation conditions at 120–125° for 1 hr, then at 175–180° for 2 hr. The cooled mass was triturated with ether, and water (200 ml) was added. The insoluble sodium salt was filtered off, washed with water, ether, and finally with acetone. Acidification of this salt and extraction into ether gave diethyl 6-methyl-2,3-dioxocycloheptane-1,4-dicarboxylate (8 g, 34%) as a colourless crystalline solid, which crystallized from light petroleum (b.p. 40–60°) as colourless plates, m.p. 54–55°. Infrared spectrum (Nujol): 1650 and 1600  $cm^{-1}$ ; ultraviolet spectrum (95% ethanol):  $\lambda_{max}$  305 m $\mu$  ( $\log \epsilon$  4.18) (Found: C, 59.5; H, 7.0. Calc. for  $C_{14}H_{20}O_6$ : C, 59.2; H, 7.0%).

It reacted with phenylhydrazine in boiling ethanol to form a dipyrazolone, which separated as colourless crystals, m.p. 338–340° (dec.) (Found: C, 70.7; H, 5.3; N, 15.1. Calc. for  $C_{22}H_{20}N_4O_2$ : C, 70.9; H, 5.3; N, 15.1%). With ferric chloride, the ester gave a deep purple coloration.

<sup>6</sup> Synder, H. R., Brooks, L. A., and Shapiro, S. H., *Org. Synth.*, 1943, Coll. Vol. II, 531.

*5-Methylcycloheptane-1,2-dione*

A mixture of diethyl 6-methyl-2,3-dioxocycloheptane-1,4-dicarboxylate (10 g) and sulphuric acid (200 ml, 15%) was boiled under reflux with stirring for 12 hr. Working up in the usual manner followed by distillation of the crude product gave 5-methylcycloheptane-1,2-dione (1.8 g, 40%) as a golden yellow liquid, b.p. 101–102°/5 mm,  $n_D^{25}$  1.4779 (Found: C, 68.6; H, 8.7. Calc. for  $C_8H_{12}O_2$ : C, 68.6; H, 8.6%). It reacted with 2,4-dinitrophenylhydrazine to form a bis-hydrazone, which crystallized from glacial acetic acid in red plates, m.p. 207–208° (Found: C, 47.9; H, 3.7; N, 22.4. Calc. for  $C_{20}H_{20}N_8O_8$ : C, 48.0; H, 4.0; N, 22.4%).

*3-Bromo-5-methyltropolone*

To a cooled (0°) and stirred solution of 5-methylcycloheptane-1,2-dione (5 g) in glacial acetic acid (10 ml) was added dropwise bromine (12 g, 2.1 equiv.) in glacial acetic acid (10 ml), and the reaction mixture was set aside at room temperature for 16 hr. The resulting dark solution was then heated by steam for 1 hr. The cooled mixture was filtered and the solid was washed with a small quantity of glacial acetic acid and dried. The product was crystallized from ethanol, from which 3-bromo-5-methyltropolone (1.5 g) crystallized in pale yellow needles, m.p. 115–116° (lit.<sup>1</sup> 114–115°) (Found: C, 44.9; H, 3.5; Br, 37.4. Calc. for  $C_8H_7BrO$ : C, 44.6; H, 3.2; Br, 37.2%). A further quantity of the product (1.4 g) was obtained by evaporating the filtrate to dryness, followed by extraction with ether. The ethereal solution was shaken up with 8N sodium hydroxide and the precipitated 3-bromo-5-methyltropolone was filtered off. The overall yield of the product was 34%.

*5-Methyltropolone*

A solution of 3-bromo-5-methyltropolone (2 g) in ethanol (20 ml) was stirred under hydrogen in the presence of palladium-charcoal (200 mg, 10%) and sodium acetate (220 mg). The smooth absorption of hydrogen ceased after the uptake of one equivalent of hydrogen. The mixture was filtered and the solvent removed under reduced pressure. The residue was extracted with boiling light petroleum (b.p. 40–60°). On being cooled, the extract deposited long colourless needles of 5-methyltropolone (0.9 g, 75%), m.p. 109–110° (lit.<sup>1</sup> 109.5–110.5°) (Found: C, 70.3; H, 5.9. Calc. for  $C_8H_8O_2$ : C, 70.6; H, 5.9%).

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