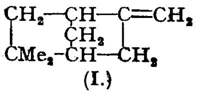
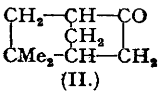
45. *Terpene Compounds. Part V. A Synthesis of* (±)-β-*Fenchocamphorone.*

By (Miss) Debi Mukherji and J. C. Bardhan.

Ethyl 2 : 2-dimethyl*cyclo*pentan-1-one-4-carboxylate (Bardhan, Banerji, and Bose, *J.*, 1935, 1128) readily condenses with ethyl cyanoacetate to give *ethyl 4-carbethoxy-2 : 2-dimethyl*cyclo*pentylidenecyanoacetate.* This on catalytic hydrogenation followed by hydrolysis affords *4-carboxy-2 : 2-dimethyl*cyclo*pentane-1-acetic acid.* The corresponding lead salt on pyrolysis furnishes (±)-β-fenchocamphorone. This synthesis establishes the correctness of the structure of β-fenchocamphorone and consequently of β-fenchene.

β-Fenchene (I) on oxidation furnishes β-fenchocamphorone (II) (Wallach, *Annalen*, 1898, **302**, 384; Komppa and Roschier, *ibid.*, 1929, **470**, 145) from which β-fenchene itself has been synthesised by the action of methylmagnesium iodide followed by dehydration of the resulting tertiary alcohol, methyl-β-fenchocamphorol (III) (Komppa and Roschier, *Ann. Acad. Sci. Fennicæ*, 1917, *A*, **10**, No. 15, 1).


(I.)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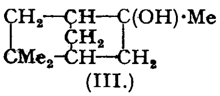
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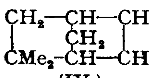
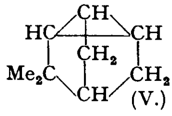

(IV.)

Nametkin and Chuchrikoff (*Annalen*, 1924, **438**, 197; Nametkin, *J. Russ. Phys. Chem. Soc.*, 1915, **47**, 425; and other publications) have apparently succeeded in preparing β-fenchocamphorone from camphenilane (IV) by successive nitration and oxidation. β-Fenchocamphorone has also been prepared, in an indirect way, from camphenilone *via apo*cyclene (V) by hydration followed by oxidation of the resulting secondary alcohol (Komppa and Roschier, *Annalen*, 1922, **429**, 175; Nametkin and Alexandroff, *ibid.*, 1928, **467**, 197). A rational synthesis of β-fenchocamphorone, however, does not appear to have been carried out hitherto. This gap has now been filled.

Ethyl 2 : 2-dimethyl*cyclo*pentan-1-one-4-carboxylate (VI) (Bardhan, Banerji, and Bose, *J.*, 1935, 1128) readily condenses with ethyl cyanoacetate in presence of ammonium acetate–acetic acid (cf. Cope *et al.*, *J. Amer. Chem. Soc.*, 1941, **63**, 3452) to give *ethyl 4-carbethoxy-2 : 2-dimethyl*cyclo*pentylidenecyanoacetate* (VII). This on hydrogenation in alcoholic solution over Adams's platinum oxide catalyst yielded *ethyl 4-carbethoxy-2 : 2-dimethyl*cyclo*pentylcyanoacetate*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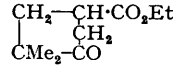
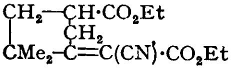
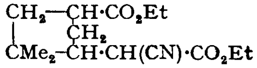
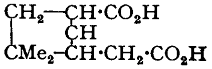
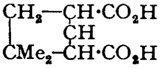

(VI.)


(VII.)


(VIII.)

(VIII). The latter on hydrolysis with excess of concentrated hydrochloric acid afforded *4-carboxy-2 : 2-dimethyl*cyclo*pentaneacetic acid* (*homo*apo*fenchocamphoric acid*) (IX) as a crystalline solid, m. p. 138·5°. The corresponding lead salt on distillation in a current of carbon dioxide gave a liquid, having a characteristic camphoraceous odour, which readily yielded a semicarbazone. The pure ketone on regeneration from the semicarbazone formed a white camphor-like solid. Although no natural (±)-β-fenchocamphorone was available for direct comparison, there can be little doubt from m. p. evidence that it and its semicarbazone are identical with the synthetic products.

(IX.)



(X.)

The synthetic ketone on oxidation with potassium permanganate gave, as the sole product, *cis*-(±)-*apo*fenchocamphoric acid (X), which was identified by direct comparison with a synthetic specimen prepared for this purpose by one of us (Mukherji, *Science and Culture*, 1948, XIII, 388; cf. also Komppa and Roschier, *Ann. Acad. Sci. Fennicæ*, 1917, *A*, **10**, No. 15, 1; Roschier, *ibid.*, 1916, *A*, **10**, No. 1, 1; Komppa and Roschier, *Annalen*, 1922, **429**, 175; Nametkin, *loc. cit.*).

The above synthesis of (±)-β-fenchocamphorone also implies a synthesis of β-fenchene, the structure of which may, therefore, be regarded as firmly established.

EXPERIMENTAL.

*Ethyl 4-Carbethoxy-2 : 2-dimethyl*cyclo*pentylidenecyanoacetate* (VII).—Ethyl 2 : 2-dimethyl*cyclo*pentan-1-one-4-carboxylate (VI) was prepared according to the method of Bardhan, Banerji, and Bose (*loc. cit.*). The corresponding keto-acid melts at 103° (Found: C, 61·4; H, 7·6. Calc. for $C_8H_{12}O_3$: C, 61·5; H, 7·6%); the m. p. 93° recorded before is evidently a misprint. The *semicarbazone* is readily formed, and on recrystallisation from dilute alcohol (charcoal) forms minute prisms, m. p. 216° (Found: C, 50·8; H, 6·8. $C_9H_{15}O_3N_3$ requires C, 50·7; H, 7·0%).

Ethyl 2 : 2-dimethyl*cyclo*pentan-1-one-4-carboxylate (40 g.), ethyl cyanoacetate (25 g.), ammonium acetate (3·5 g.), acetic acid (12 c.c.), and benzene (50 c.c.) were refluxed for 2 hours in an oil-bath at 150—155° in an apparatus essentially that described by Cope and his co-workers (*loc. cit.*). After cooling, the benzene layer was separated, washed with a little water, dried, and the solvent removed. The residue on distillation under reduced pressure gave at first 30—40% of unchanged material followed by *ethyl 4-carbethoxy-2 : 2-dimethyl*cyclo*pentylidenecyanoacetate* (32 g.) which formed an almost colourless oil, b. p. 175—176°/4 mm. (Found: C, 64·5; H, 7·6. $C_{15}H_{21}O_4N$ requires C, 64·5; H, 7·5%).

*Ethyl 4-Carbethoxy-2 : 2-dimethyl*cyclo*pentylcyanoacetate* (VIII).—The unsaturated cyano-ester (VII) (39·6 g.) dissolved in pure alcohol (50 c.c.) was shaken in an atmosphere of hydrogen in the presence of platinum oxide catalyst (0·1 g.) for 18 hours, by which time the calculated amount of hydrogen (3750 c.c. at 26·5°/764 mm.) had been absorbed. The solution was filtered, excess of alcohol removed, and the residual oil purified by distillation. *Ethyl 4-carbethoxy-2 : 2-dimethyl*cyclo*pentylcyanoacetate*, which was saturated towards the usual reagents, formed a colourless liquid (37·5 g.), b. p. 166°/4 mm. (Found: C, 64·0; H, 8·1. $C_{15}H_{23}O_4N$ requires C, 64·0; H, 8·1%).

*4-Carboxy-2 : 2-dimethyl*cyclo*pentaneacetic acid* (*Homo*apo*fenchocamphoric Acid*) (IX).—The foregoing saturated cyano-ester (VIII) (37·5 g.) was refluxed in an all-glass apparatus with concentrated hydrochloric acid (350 c.c.) for 28 hours. When the clear solution was left overnight a mass of crystals separated, and were collected. A further small quantity was recovered from the mother liquor. On repeated crystallisation from water (charcoal) *4-carboxy-2 : 2-dimethyl*cyclo*pentane-1-acetic acid* formed small prisms (17 g.), m. p. 138·5° (Found: C, 59·8; H, 8·0. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·0%).

An acid of this composition, prepared previously by a different method (Bardhan, Banerji, and Bose, *loc. cit.*, p. 1129), had m. p. 246°. This, however, requires clarification, and we hope to investigate the matter further.

(±)-*β-Fenchocamphorone* (II).—As a result of several trials the following method was adopted as being the most satisfactory for the ketonisation. The foregoing acid (IX) (15 g.) was dissolved in aqueous ammonia, and the somewhat warm solution was treated with a slight excess of an aqueous solution of lead acetate. The heavy white precipitate of the lead salt (26 g.) was collected, washed, and dried at 140° in an air-oven. It was then mixed with iron filings (5·2 g.) and distilled in small portions at a time from a small retort connected with a condenser and a receiver cooled in ice. The mixture was carefully heated in an air-bath, and a slow stream of dry carbon dioxide was maintained during the operation. Decomposition began at about 300°, and water together with a yellowish brown liquid distilled. The temperature was gradually raised to 340° until no more liquid distilled and there remained in the retort a small carbonaceous residue The oily distillate from 26 g. of the lead salt was collected in pure ether, washed, and dried. The solvent having been removed, the residue (7 g.) was mixed with semicarbazide hydrochloride (7 g.) and sodium acetate (15 g.) dissolved in aqueous methyl alcohol, a few drops of acetic acid were added, and the clear solution was gently warmed. The crystalline β-fenchocamphorone semicarbazone which separated was obtained in minute needles (5·8 g.), m. p. 193°, by recrystallisation from methyl alcohol (charcoal) (Found: C, 61·6; H, 8·7. Calc. for $C_{10}H_{17}ON_3$: C, 61·5; H, 8·7%) (Nametkin and Chuchrikoff, *loc. cit.*, give m. p. 192—193°; Komppa and Roschier, *loc. cit.*, give m. p. 195—196°). The ketone regenerated by heating the purified semicarbazone (5·4 g.) with excess of oxalic acid in an all-glass apparatus was recovered by distillation in steam. The colourless oil which at first collected in the receiver quickly solidified to a white mass which was collected and dried. A portion after sublimation had m. p. 64—65·5° (Found: C, 78·3; H, 10·1. Calc. for $C_9H_{14}O$: C, 78·2; H, 10·2%) (Nametkin and Chuchrikoff, *loc. cit.*, give m. p. 63—65°; Komppa and Roschier, *loc. cit.*, give m. p. 64—66°). It had a characteristic camphoraceous odour.

Oxidation to cis-apo*Fenchocamphoric Acid* (X).—The synthetic ketone (0·5 g.), potassium permanganate (1·4 g.), potassium hydroxide (4 g.), and water (33 c.c.) were shaken in a stoppered bottle at 50—60° until the colour of the permanganate was almost discharged (1—2 hours). The solution was filtered, the residue washed with hot water, and the filtrate concentrated and acidified with dilute hydrochloric acid. *cis-apo*Fenchocamphoric acid thus obtained was recrystallised from water, and then had m. p. 144—145° alone or admixed with an authentic specimen (Found: C, 58·2; H, 7·6. Calc. for $C_9H_{14}O_4$: C, 58·1; H, 7·5%) (cf Nametkin, *loc. cit.*; Short, *J.*, 1927, 961).

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