

THE SYNTHESIS OF *p*-MENTHA-1,3,8-TRIENE

By A. J. BIRCH* and G. SUBBA RAO*

[Manuscript received March 21, 1969]

p-Mentha-1,3,8-triene (I) has been identified¹ as one of the constituents of Yugoslavian parsley (*Petroselinum sativum* Hoff.). The assigned structure was supported by spectroscopic data² and degradations.

We now describe the first synthesis of (I) and of its isomer (II), by several methods.

Synthesis

p-Alkoxyacetophenones, and the corresponding carbinols, undergo metal-ammonia reductions of the ring with slight, or no, loss of the side-chain oxygen by hydrogenolysis, e.g.³ It has also been briefly noted⁴ that *p*-alkylacetophenones can be reduced in the ring with some, but incomplete, loss of the side-chain oxygen.

Reduction of (III) gave (IV) (80%) and (V) (20%), the structures being supported by the p.m.r. spectrum, and the proportions by g.l.c. analysis. Attempted Oppenauer oxidation of the carbinol to the ketone resulted in production of 4-methylacetophenone, but carefully controlled oxidation with chromium trioxide in acetone under nitrogen gave a mixture of (VI) and (VII), as shown by spectra (λ_{\max} 250, 280 m μ (ϵ 3800, 9200); ν_{\max} 1670, 1640, 1620 cm⁻¹) and by g.l.c. analysis. Reaction with sodium methoxide in methanol converted the mixture into (VII), slightly contaminated (5%) with 4-methylacetophenone. The structure of (VII) was based on analysis and spectra [λ_{\max} 285 m μ (ϵ 10850), $\alpha,\beta,\gamma,\delta$ -unsaturated system; ν_{\max} 1665, 1635, 1610 cm⁻¹; τ 4.85 (d, 1H), 5.1 (m, 1H), 7.8 (m, 4H), 8.0 (s, 3H), 8.2 (s, 3H)], and was further confirmed by an alternative synthesis.

4-Methylcyclohex-3-enone (VIII) was treated with acetone cyanohydrin and base to give the cyanohydrin (IX) which was dehydrated to a mixture of (X) and (XI). The nature of the mixture was again based on spectra. Reaction of this mixture with methylmagnesium iodide gave (VII) in 65% yield, identical with that obtained previously.

Reaction of (VII) with methyltriphenylphosphonium bromide under Wittig conditions gave a mixture of (I) and (II) and *p*-cymene. The major product (I) (70%) was separated by preparative g.l.c. and identified as *p*-mentha-1,3,8-triene; its spectra correspond to those reported for the natural product.²

* Research School of Chemistry, Australian National University, Canberra, A.C.T. 2600.

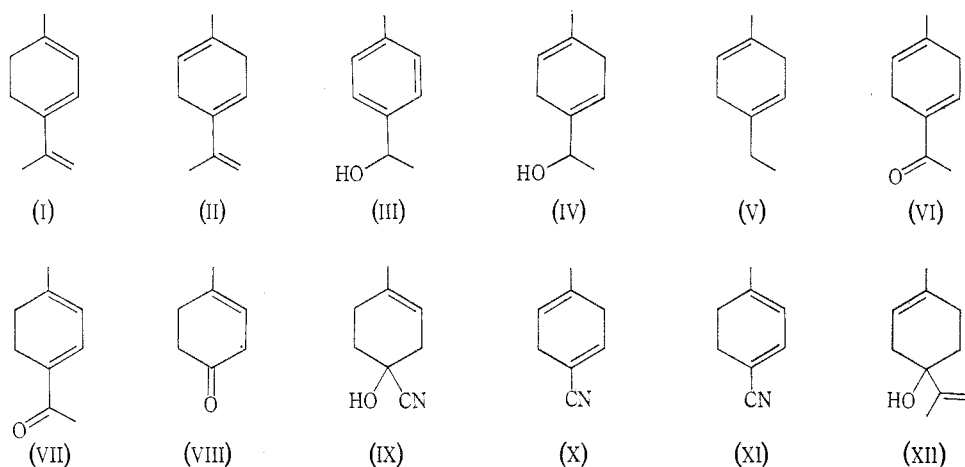
¹ Garnerio, J., Benezet, L., Peyron, L., and Chretien Bessiere, Y., *Bull. Soc. chim. Fr.*, 1967, 4679.

² Kenney, R. L., and Fisher, G. S., *J. Gas Chromat.*, 1963, 1, 19.

³ Birch, A. J., *Proc. R. Soc. N.S.W.*, 1950, 83, 245.

⁴ Birch, A. J., and Subba Rao, G. S. R., *Aust. J. Chem.*, 1969, 22, in press.

The minor component had λ_{\max} 232 $m\mu$ (ϵ 10000) to be expected of (II), and its structure is supported by the alternative preparation below.



Reaction of 2-propenylmagnesium bromide with (VIII) gave (XII). Attempted dehydration of this with several acidic reagents gave chiefly *p*-cymene, but the action of phosphorus oxychloride and pyridine at 0° under nitrogen produced a mixture of hydrocarbons, g.l.c. analysis of which indicated the presence of *p*-cymene (30%), (I) (25%), and (II) (40%). Methanesulphonyl chloride and pyridine on (XII) gave a better yield of (I) (60%).

The triene (I) was very unstable, apparently to oxygen, and attempts to purify it further met with no success.

Experimental

Melting points and boiling points are uncorrected. U.v. spectra were recorded on a Unicam SP800 instrument in ethanol; i.r. spectra were examined as liquid films on a Perkin-Elmer 251 instrument. P.m.r. spectra were examined in $CDCl_3$ in a Varian HA100 instrument. G.l.c. analyses were carried out using a Perkin-Elmer 881 gas chromatograph.

Reduction of 1-(*p*-Tolyl)ethanol

The starting material was prepared by the reduction of 4-methylacetophenone with sodium borohydride. The alcohol (10 g) in ethanol (25 ml) and ammonia (300 ml) was treated with sodium (8 g) over 2 hr. Worked up as usual, the product, b.p. 80–90°/20 mm, was analysed by g.l.c. on a Carbowax column at 100° and showed two peaks at R_t 1 min (15–20%) and R_t 2.1 min (80–85%). It has ν_{\max} 3450 cm^{-1} , τ 4.55 (t, 2H); 6.0 (m, 1H); 7.35 (s, 4H); 7.98 (s, 3H); 8.7 (d, 3H).

1-Acetyl-4-methylcyclohexa-1,3-diene

The reduced carbinol above (5 g) in acetone was cooled to 0° and to it was slowly added excess of Jones reagent under nitrogen. Methanol was added to decompose excess reagent. The product (2.8 g) had ν_{\max} 1670, 1640, 1620 cm^{-1} ; λ_{\max} 250, 280 $m\mu$ (ϵ 3800, 9200); it could not be distilled because of major conversion into 4-methylacetophenone. G.l.c. analysis on an XE60 column at 100° showed two components: R_t 2.2 min (40%) and R_t 2.8 min (60%). The mixture (2.5 g) and sodium methoxide (100 mg) in methanol (15 ml) was refluxed under nitrogen for 30

min. The product was a pale yellow liquid; b.p. 70–75°/11 mm; λ_{\max} 285 m μ (ϵ 10850); ν_{\max} 1665, 1635, 1610 cm⁻¹; τ 4.85 (d, 1H); 5.1 (m, 1H); 7.8 (m, 4H); 8.0 (s, 3H); 8.2 (s, 3H) (Found: C, 80.1; H, 8.7. C₉H₁₀O requires C, 79.5; H, 8.8%). The 2,4-dinitrophenylhydrazone, λ_{\max} 395 m μ , had m.p. 150°. G.l.c. analysis on an XE60 column showed one major component (95%), R_t 2.8 min, and 4-methylacetophenone (5%), R_t 3.2 min.

4-Methylcyclohexa-1,3-diene-1-carbonitrile

4-Methylcyclohex-3-enone (10 g) and acetone cyanohydrin (40 ml) were treated for 12 hr with saturated aqueous potassium hydroxide (2 ml) to give the cyanohydrin (13.8 g); ν_{\max} 3425, 2240 cm⁻¹. This compound (13 g) in pyridine (30 ml) was treated with phosphorus oxychloride (15 ml) at 0°, and the mixture left 12 hr. The product (10.2 g) had b.p. 98°/18 mm; λ_{\max} 293 m μ (ϵ 9600); ν_{\max} 2210, 1640, 1585 cm⁻¹; τ 3.4 (d, 1H); 4.25 (m, 1H); 7.75 (m, 4H); 8.2 (s, 3H) (Found: C, 80.4; H, 7.5. C₉H₉N requires C, 80.1; H, 7.6%). G.l.c. analysis on an XE60 column at 100° showed the presence of two compounds: R_t 1.8 min (38%) and R_t 2 min (62%). The p.m.r. spectrum can be interpreted in the light of this admixture.

The nitrile mixture (5 g) in ether was added at 0° under nitrogen to methylmagnesium iodide (from 7 g of methyl iodide). After 12 hr the mixture was refluxed for 2 hr and worked up to give 1-acetyl-4-methylcyclohexa-1,3-diene (65%), b.p. 80°/12 mm; λ_{\max} 288 m μ (ϵ 11520); ν_{\max} 1660, 1630, 1612 cm⁻¹; identical in i.r., u.v., and p.m.r. spectra, apart from minor differences probably due to impurities in the first specimen, with the 1-acetyl-4-methylcyclohexa-1,3-diene above. The g.l.c. analysis on an XE60 column at 100° showed a major peak at R_t 2.8 min (90%), corresponding to 1-acetyl-4-methylcyclohexa-1,3-diene and a minor peak due to starting material.

p-Mentha-1,8-dien-4-ol and its Dehydration

The Grignard reagent from 2-bromopropene (12.1 g) at 0° was treated with 4-methylcyclohex-3-enone (8.5 g) in ether (20 ml) for 12 hr. The product (12.8 g), isolated without the use of acidic conditions in work-up, had ν_{\max} 3440, 1640 cm⁻¹; τ 4.7 (m, 1H); 4.95 (s, 1H); 5.15 (s, 1H); 7.5–8.2 (m, 6H); 8.1 (s, 3H); 8.3 (s, 3H).

The compound (2.5 g) in pyridine (10 ml) was treated with phosphorus oxychloride (3 ml) at 0° and left for 30 min. The product had λ_{\max} 235, 302 m μ (ϵ 6000, 3800), and g.l.c. on a Carbowax column indicated three components: (1) R_t 1.8 min (40%); (2) R_t 2.2 min (25%); (3) R_t 3.5 min (30%). The last was identified as *p*-cymene. The components (1) and (2) were separated by g.l.c. on a preparative scale and had the following characteristics: (1) λ_{\max} 232 m μ (ϵ 10800), *m/e* 134, corresponding to the expected values for *p*-mentha-1,4,8-triene; (2) λ_{\max} 305 m μ (ϵ 11040), *m/e* 134, τ 4.2 (s, 1H); 4.4 (s, 1H); 5.2 (m, 2H); 7.8 (m, 4H); 8.0 (s, 3H); 8.2 (s, 3H), corresponding to the expected values for *p*-mentha-1,3,8-triene.

Dehydration with methanesulphonyl chloride in pyridine at 0° for 24 hr gave a product containing the 1,4,8-triene (40%) and the 1,3,8-triene (60%) (g.l.c.).

Conversion of 1-Acetyl-4-methylcyclohexa-1,3-diene into p-Mentha-1,3,8-triene

To a suspension of sodium hydride (1 g) in benzene (10 ml) was added methyltriphenylphosphonium bromide (4 g) in benzene (25 ml). The mixture was stirred under nitrogen until reaction had ceased, and 1-acetyl-4-methylcyclohexa-1,3-diene (1 g) was added. After stirring for 30 min the mixture was refluxed for 1 hr and worked up in the usual way. The product (0.8 g) remaining after removal of all of the solvent was shown by g.l.c. as above to contain *p*-cymene (15%, R_t 3.5 min), *p*-mentha-1,3,8-triene (65%, R_t 2.2 min), and *p*-mentha-1,4,8-triene (10%, R_t 1.8 min).