Ring Opening of (−)-Pin-2(10)-ene with Iodine

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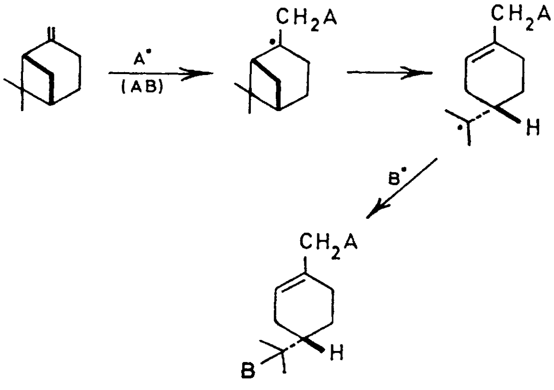
(−)-Pin-2(10)-ene reacts with iodine to give 7,8-di-iodo-*p*-menth-1-ene (II). The latter, on treatment with dimethyl sulphoxide, gives *p*-mentha-1,4(8)-dien-7-al (V), an isomer of *p*-mentha-1,8-dien-7-al (perillaldehyde) (I).

(—)-Pin-2(10)-ene reacts with halogens in such a way that the pinene skeleton is often preserved.[1] Chlorination of pin-2(10)-ene gives 10-chloropin-2-ene (myrtenyl chloride) and 2,6-*endo*-dichlorobornane.[2] Reaction with bromine is similar, but with iodine and fluorine aromatisation to *o*- and *p*-cymenes results.[3] A large number of radical additions to pin-2(10)-ene have been studied.[4,5] Reactions that led to ring opening are summarised in the Scheme. We were interested in devising a synthesis of (—)-perillaldehyde (*p*-mentha-1,8-dien-7-al) (I), based on this Scheme.

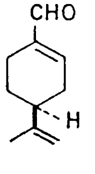


Scheme

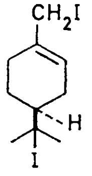
Although pin-2(10)-ene reacts under vigorous conditions with iodine to give aromatic products,[3] we felt that under mild conditions iodine could behave as iodine atoms and might afford ring-opened iodides suitably constituted for further transformation into (—)-perillaldehyde (I). In the event, pin-2(10)-ene, on treatment with iodine in benzene at room temperature (5 min), gave an extremely unstable di-iodide (II) which liberated iodine on standing (see Table in Experimental section). Conducting the iodination in ether or glyme gave a mixture of (by n.m.r.) the iodides (II), (III; X = I), and (IV; X = I), with (III; X = I) predominating.

Reduction of 7,8-di-iodo-*p*-menth-1-ene (II) with lithium aluminium hydride gave (—)-*p*-mentha-1,8-diene (IV; X = H) and *p*-mentha-1,4(8)-diene (III; X = H). G.l.c. analysis, n.m.r., and optical rotation showed that they were formed in the ratio 1 : 3.

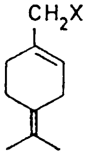
The di-iodide (II) was treated with dimethyl sulphoxide–sodium hydrogen carbonate to give the aldehyde (V) (41%) and traces of (—)-perillaldehyde (I). The aldehyde (V) was characterised as its crystalline 2,4-dinitrophenylhydrazone and oxime. The latter had zero optical rotation. In order to avoid the generation of traces of acid in the iodine reaction, pin-2(10)-ene was treated with iodine in the presence of epoxyethane. This reaction gave the iodide (VI), which was oxidised by dimethyl sulphoxide to the aldehyde (VII). We were able to prepare relatively pure aldehyde (V) from pin-2(10)-ene consistently in an overall yield of 40%.



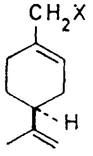
(I)



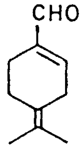
(II)



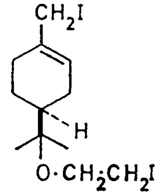
(III)



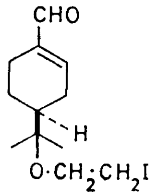
(IV)



(V)



(VI)



(VII)

EXPERIMENTAL

M.p.s were taken with a Kofler hot-stage apparatus. Unless otherwise stated i.r. spectra were measured for solutions in CHCl$_3$. U.v. spectra were measured for solutions in ethanol. N.m.r. spectra were recorded for deuteriochloroform solutions with tetramethylsilane as internal standard. Solvents were dried by standard techniques.

7,8-*Di-iodo*-p-*menth*-1-*ene* (II).—Pin-2(10)-ene (1·079 g) in

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[2] A. Kergomard, *Ann. Chim.* (*France*), 1953, **8**, 153; D. V. Tishenko and B. Matveev, *Zhur. obshchei Khim.*, 1950, **20**, 896.

[3] K. K. Sugathan and J. Verghese, *Indian J. Chem.*, 1964, **2**, 497.

[4] D. M. Olroyd, G. S. Fisher, and L. A. Goldblatt, *J. Amer. Chem. Soc.*, 1950, **72**, 2407.

[5] M. Vilkas, G. Dupont, and R. Dulon, *Bull. Soc. chim. France*, 1950, 1056; G. Dupont, R. Dulou, and G. Clement, *Compt. rend.*, 1953, **236**, 2512; G. Dupont, R. Dulou, and G. Clement, *Bull. Soc. chim. France*, 1950, 1115; M. Vilkas, G. Dupont, and R. Dulou, *ibid.*, 1955, 799; R. Lalande and M. Cazeux, *Compt. rend.*, 1964, **258**, 4567; *Bull. Soc. chim. France*, 1966, 3381; J. Moulines and R. Lalande, *ibid.*, 1966, 3387; N. O. Brace, *J. Org. Chem.*, 1962, **27**, 3027; J. A. Caisse, D. I. Davies, and L. T. Parfitt, *J. Chem. Soc.* (*C*), 1970, 258; R. Calas and E. Frainnet, *Bull. Soc. chim. France*, 1952, 241; E. Frainnet, *ibid.*, 1953, 792; R. Calas and E. Frainnet, *Compt. rend.*, 1955, **240**, 203; A. Graiffe and J. Castanet, *Compt. rend.*, *C*, 1971, **272**, 63, 96, 1012; B. Paskoff, M. Cazaux, and R. Lalande, *Bull. Soc. chim. France*, 1970, 624; D. I. Davies and S. J. Cristol, *Adv. Free-Radical Chem.*, 1966, **1**, 155.

benzene (made up to 5 ml) was treated with iodine (2·004 g) in benzene (25 ml). Aliquot portions (1 ml) were withdrawn after 5, 40, and 120 min and titrated against 0·01N-thiosulphate solution. Ether extraction of the first portion gave 7,8-di-iodo-*p*-menth-1-ene (II), τ[*] 4·0 (1H, m), 6·0 (2H, s), and 7·95 (6H, s), $\nu_{max.}$ (neat) 2900, 1640, 1460, 1440, 1160, and 1100 cm^{-1}. For further characterisation see later.

t/min	5	40	120
% Iodine consumed	80·0	71·0	65·0

*Treatment of Pin-*2(10)*-ene with Iodine in Glyme.*—Pin-2(10)-ene (1·00 g) in dry glyme (5 ml) was treated with iodine (1·81 g) in dry glyme (20 ml) at 0°. After 5 min, iodometry indicated 62% uptake of iodine. Extraction with ether and evaporation of the extract gave an oil containing the iodides (II), (III; X = I), and (IV; X = I), τ 4·05 (1H, m), 5·25 (2H, br s), 6·10 (2H, s), 8·00 (6H, d), and 8·30 (6H, d), $\nu_{max.}$ (neat) 2900, 1660, and 1640 cm^{-1}. Similarly in ether an oil was obtained that consisted of the iodides (II), (III; X = I), and (IV; X = I) (n.m.r. as above); 58% of the iodine was consumed.

Reduction of 7,8*-Di-iodo-*p*-menth-*1*-ene* (II).—Pin-2(10)-ene (5·00 g) was treated with iodine (9·35 g) in dry benzene (100 ml) at 5°. This solution was added dropwise to lithium aluminium hydride (7·50 g) in dry ether (20 ml) under nitrogen. After 3 h the excess of lithium aluminium hydride was destroyed with ethyl acetate; the mixture was poured into water and extracted with ether. The dried (Na_2SO_4) extract was evaporated to give an oil which was distilled to give a mixture (4·3 g, 86%) of *p*-mentha-1,8-diene (IX; X = H) and *p*-mentha-1,4(8)-diene (III; X = H). They were separated by g.l.c. [Carbowax (1540 on AW–DMCS) Chromosorb W, 80—100 mesh (8 : 92); column, 60°]. The retention times were identical with those of authentic samples of *p*-mentha-1,8-diene (IV; X = H) and *p*-mentha-1,4(8)-diene (III; X = H). The mixture showed absorptions at τ 4·05 (m), 5·30(br s) (ratio 1 : 2), and 8·3(s), $\nu_{max.}$ (neat) 2900, 1640, 1450, and 900 cm^{-1}, $[\alpha]_D^{20}$ −30·4° {(−)-*p*-mentha-1,8-diene, $[\alpha]_D^{20}$ −122·6°}. G.l.c. analysis of the dienes (IV; X = H) and (III; X = H) showed a ratio of 1 : 3; n.m.r. showed the ratio 1 : 3 and optical rotation measurements gave also 1 : 3.

p*-Mentha-*1,4(8)*-dien-*7*-al* (V).—Pin-2(10)-ene (10·0 g) in dry benzene (20 ml) was treated with iodine (18·7 g) in benzene (200 ml) at 5°. After 5 min, the mixture was washed with aqueous sodium thiosulphate and dried (Na_2SO_4). Evaporation gave a dark oil which was dissolved in dry dimethyl sulphoxide (150 ml). Sodium hydrogen carbonate (20 g) was added to the mixture which was stirred for 20 h under nitrogen, filtered into ice-cold saturated aqueous sodium chloride solution, and extracted with ether. The dried (Na_2SO_4) extract was evaporated and the residue distilled at reduced pressure to give *p*-mentha-1,4(8)-dien-7-al (V) (4·5 g 41%), b.p. 58—62° at 1 mmHg, contaminated with *p*-mentha-1,8-dien-7-al (I) and hydrocarbons. The crude material showed absorptions at τ 3·2 (1H, m), 8·3 (6H, s), and 0·1 (1H, s), $\nu_{max.}$ (neat) 2900 and 1690 cm^{-1}.

The impure aldehyde (V) (0·20 g) was treated with 2,4-dinitrophenylhydrazine (0·40 g) in the usual way. The 2,4-*dinitrophenylhydrazone* was purified by p.l.c. to give red needles, m.p. 190—191° (from EtOAc), $\nu_{max.}$ (Nujol) 3250, 1610, 1600, and 1520 cm^{-1}, $\lambda_{max.}$ 377 nm (ε, 27 000), τ −1·2 (1H, s), 0·9 (1H, d), 1·5—2·2 (3H, m), 3·7 (1H, t), and 8·3 (6H, s) (Found: C, 58·3; H, 5·4; N, 17·2. $C_{16}H_{18}N_4O_4$ requires C, 58·2; H, 5·5; N, 17·0%).

The impure aldehyde (V) (0·5 g) in pyridine (3 ml) was treated with hydroxylamine hydrochloride (0·5 g). After 3 h, the solution was poured into water and extracted with ether. The dried (Na_2SO_4) extracts were evaporated and the residue chromatographed on silica plates. Crystallisation from light petroleum (b.p. 40—60°) gave the oxime, m.p. 98—99° (*cf.* refs. 6 and 7), $\nu_{max.}$ (Nujol) 3250 and 1650 cm^{-1}, τ 2·2 (1H, s), 4·0 (1H, t), 7·0 (2H, m), 7·7 (4H, br s), and 8·3 (6H, s), $[\alpha]_D^{20}$ 0° (Found: C, 72·6; H, 9·1; N, 8·4. $C_{10}H_{15}NO$ requires C, 72·7; H, 9·2; N, 8·5%).

8-(2*-Iodoethoxy*)-7*-iodo-*p*-menth-*1*-ene* (VI).—Pin-2(10)-ene (1·00 g) in benzene (5 ml) was treated with dry epoxyethane (5 ml) followed by iodine (1·87 g) in benzene (20 ml). After 5 min 95% of the iodine had been consumed. The solution was washed with aqueous sodium thiosulphate, dried (Na_2SO_4), and evaporated to give the iodide (VI) as a very unstable yellow oil, τ 4·05 (1H, m), 6·00 (2H, s), 6·60 (4H, m), and 8·85 (6H, s), $\nu_{max.}$ (neat) 3000 and 1660 cm^{-1}.

8-(2*-Iodoethoxy*)-p*-menth-*1*-en-*7*-al* (VII).—The crude iodide (VI) from the above reaction in dry dimethyl sulphoxide (20 ml) under nitrogen was stirred for 20 h. The mixture was filtered into ice-cold saturated aqueous sodium chloride solution and extracted with ether. The dry (Na_2SO_4) extracts were evaporated to give an oil, which was chromatographed on silica to give the aldehyde (VII) (1·41 g. 60%), $\nu_{max.}$ (neat) 3000, 1680, and 1640 cm^{-1}, τ 3·1 (1H, m), 6·5 (4H, m), and 8·8 (6H, s). Its 2,4-*dinitrophenylhydrazone* had m.p. 135—136° (from benzene), $\nu_{max.}$ (Nujol) 3250, 1620, 1600, and 1510 cm^{-1}, τ −1·3 (1H, s), 0·8 (1H, d), 1·2—2·3 (3H, m), 3·7 (1H, m), 6·5 (4H, m), and 8·8 (6H, s), $[\alpha]_D^{20}$ −72° (*c* 1·0 in $CHCl_3$) (Found: C, 42·9; H, 4·7; I, 24·9; N, 10·9. $C_{18}H_{23}IN_4O_5$ requires C, 43·0; H, 4·6; I, 25·3; N, 11·2%).

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[*] Only diagnostic signals are mentioned, the other signals are the methylene envelopes.

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