524. *Allylic Bromination of Unsaturated Terpene Hydrocarbons, and the Synthesis of αβ-Unsaturated Alcohols.*

By A. KILLEN MACBETH, B. MILLIGAN, and J. S. SHANNON.

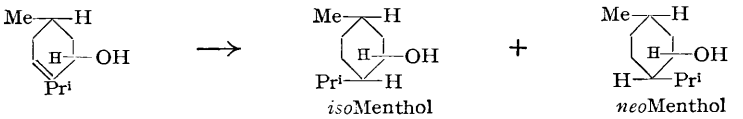
A synthesis of αβ-unsaturated terpene alcohols has been developed, consisting of allylic bromination of unsaturated hydrocarbons by *N*-bromosuccinimide and conversion of the resultant bromides into the alcohols through the formates. (+)-*p*-Menth-3-ene gave (±)-*trans*-*p*-menth-3-en-5-ol, and a (±)-carvotanacetol was obtained from (±)-*p*-menth-1-ene. The yields obtained are inferior to those produced by Treibs and Bast's reaction (*Annalen*, 1948, **561**, 165) using mercuric acetate.

αβ-UNSATURATED terpene alcohols have been prepared conveniently from the unsaturated aldehydes or ketones by reduction by the Ponndorf method, or with lithium aluminium hydride, the latter giving especially good yields. Other methods are required when the parent aldehyde or ketone is not available, and Treibs and Bast (*loc. cit.*) have shown that the reaction of mercuric acetate with an unsaturated terpene hydrocarbon yields the acetate of an αβ-unsaturated alcohol, which is readily hydrolysed. Allylic bromination with *N*-bromosuccinimide (Wohl–Ziegler reaction; *Annalen*, 1942, **551**, 80) has been widely used in steroid chemistry with good results, and the synthesis of an αβ-unsaturated bromide from an unsaturated terpene hydrocarbon for the production of the precursor of an αβ-unsaturated alcohol has now been examined as an alternative to Treibs and Bast's reaction.

Although the bromination by *N*-bromosuccinimide of methylene groups adjacent to unsaturated centres usually gives excellent yields we found that the yields were poor with the two terpene hydrocarbons *p*-menth-1-ene and *p*-menth-3-ene in carbon tetrachloride. Somewhat better yields were obtained in chloroform, and irradiation with ultra-violet light approximately doubled them.

p-Menth-3-ene, obtained by the pyrolysis of methyl (−)-menthylxanthate (Malcolm and Read, *J.*, 1939, 1037; Hückel, Tappe, and Legutke, *Annalen*, 1940, **543**, 191) and

repeatedly fractionated over sodium, when irradiated and brominated gave a product which was converted into the alcohol through the formoyloxy-compound (Henbest, *J.*, 1951, 1074). Since *N*-bromosuccinimide effects allylic bromination the resultant alcohol may be the *cis*- or the *trans*-modification of *p*-menth-3-en-2- or -5-ol. Its identity was established as (±)-*trans*-*p*-menth-3-en-5-ol as catalytic hydrogenation under controlled conditions gave a menthol mixture from which the 3 : 5-dinitrobenzoate of (±)-*iso*menthol was isolated. A 2-hydroxy-group is therefore excluded, and the *trans*-configuration of the unsaturated alcohol is indicated by the *iso*menthol relationship :



The isolation of an inactive alcohol from the lævorotatory hydrocarbon is explained by the ready racemisation of *p*-menth-3-ene under acidic conditions (Hückel *et al.*, *loc. cit.*), the succinimide formed in the initial bromination evidently being sufficiently acidic to effect the change.

p-Menth-1-ene was initially prepared by the preferential hydrogenation of the exocyclic double bond of limonene at a palladinised charcoal catalyst, but later by an unambiguous synthesis from dihydrocryptone (4-*iso*propyl*cyclo*hexan-1-one) : this was converted by methylmagnesium iodide into 1-methyl-4-*iso*propyl*cyclo*hexan-1-ol which was dehydrated by oxalic acid. The menthene was also derived from (−)-α-phellandrene as the double bond between the two secondary carbon atoms is hydrogenated more readily than that between secondary and tertiary carbon atoms. The yields on bromination were practically the same in all three cases, but only 9% of the 3 : 5-dinitrobenzoate of the alcohol was ultimately obtained. The alcohol may be the *cis*- or the *trans*-form of either (±)-piperitol or (±)-carvotanacetol, the latter being more probable as Treibs and Bast (*loc. cit.*) obtained a carvotanacetol by the reaction of mercuric acetate on *p*-menth-1-ene. As the optically inactive carvotanacetols have not been characterised it was necessary to support the structure of the alcohol by oxidation to (±)-carvotanacetone, which was identified as the semicarbazone. The configuration of the alcohol cannot yet be established as the racemic carvomenthols which are yielded on hydrogenation have not been characterised.

Although much inferior to the Treibs and Bast reaction for the preparation of the unsaturated alcohols, the method may prove of interest for the synthesis of the corresponding amines, acids, and alkyl ethers which are not readily obtainable from the acetate.

Experimental

p-*Menth*-3-*en*-5-*ol*.—A sample of *p*-menth-3-ene prepared according to Malcolm and Read (*loc. cit.*) and thrice distilled over sodium had b. p. 82—83°/15 mm. and α_D^{15} +44·5° (homogeneous). While being irradiated with ultra-violet light the hydrocarbon (28 g.) in dry chloroform (50 ml.) was gently refluxed with freshly crystallised *N*-bromosuccinimide (22 g.). The initial vigorous exothermic reaction was controlled by external cooling and the mixture was refluxed thereafter for 10 min. Succinimide, filtered off on cooling, was washed with light petroleum (b. p. 40—60°); the combined filtrates were evaporated under reduced pressure, giving crude *p*-menth-3-en-5-yl bromide (36 g., 80% based on *p*-menth-3-ene). The crude bromide (36 g.) in dioxan (50 ml.) was stirred with sodium formate (10 g.) in formic acid (50 ml.; 98%) at room temperature for 2 hr. and after neutralisation (sodium hydrogen carbonate solution) the formate was extracted with ether. The crude *p*-menth-3-en-5-yl formate (30 g.) left on removal of the solvent was hydrolysed overnight with sodium carbonate (8 g.) in aqueous methanol (400 ml.; 50%), and the crude menthenol was extracted with light petroleum (b. p. 40—60°; 4 × 50 ml.). The combined extracts, washed with water (thrice) and dried ($MgSO_4$), were treated with pyridine (5·6 g.) and a solution of 3 : 5-dinitrobenzoyl chloride (16·5 g.) in dry benzene (50 ml.), and the ester was worked up in the usual way and crystallised from light petroleum (b. p. 60—70°), to give colourless needles of (±)-trans-p-*menth*-3-*en*-5-*yl* 3 : 5-*dinitrobenzoate* (5·0 g.), m. p. 142° (Found : C, 58·7; H, 5·75; N, 7·85. $C_{17}H_{20}O_6N_2$ requires C, 58·6; H, 5·75; N, 8·05%). Hydrolysis of the ester with methanolic potassium hydroxide (5%) gave (±)-trans-p-*menth*-3-

en-5-ol, b. p. 56°/0·7 mm. (Found : C, 77·8; H, 11·8. $C_{10}H_{18}O$ requires C, 77·8; H, 11·75%). The *phenylurethane*, needles from light petroleum, had m. p. 84·5° (Found : C, 74·85; H, 8·25; N, 5·5. $C_{17}H_{23}O_2N$ requires C, 74·7; H, 8·5; N, 5·3%). The *α-naphthylurethane* (needles) had m. p. 109° (Found : C, 77·7; H, 8·1. $C_{21}H_{25}O_2N$ requires C, 78·0; H, 7·8%).

Hydrogenation of (±)-p-*Menth-3-en-5-ol*.—The alcohol (0·6 g.) in ethanol (20 ml.) was hydrogenated for 2 hr. at 100°/60 atm. in the presence of Raney nickel (0·4 g.). After filtration and removal of most of the solvent, the oil which separated on dilution of the residue was extracted with light petroleum (b. p. 40—60°), and the extract, washed and dried, was esterified with 3 : 5-dinitrobenzoyl chloride and pyridine. The crude ester (1·1 g., 81%) gave pale yellow needles having m. p. 128° [after three crystallisations from light petroleum (b. p. 40—60°)] alone or mixed with authentic (±)-*iso*menthyl 3 : 5-dinitrobenzoate.

(±)-*Carvotanacetol*.—(±)-*p*-Menth-1-ene was prepared from dihydrocryptone (105 g.) which was added dropwise to an ice-cold solution of a Grignard reagent [from methyl iodide (100 g.) and magnesium (16·8 g.) in ether (550 ml.)] during 4 hr. The mixture was refrigerated overnight and then refluxed for 0·25 hr. After filtration, washing with water, and drying ($MgSO_4$), the crude *p*-menthan-1-ol (105 g., 88%) obtained on removal of the ether was heated under reflux for 3 hr. with oxalic acid (300 g.) in water (600 ml.). Steam-distillation and extraction of the distillate with light petroleum gave a crude hydrocarbon which was fractionated over metallic sodium (yield, 75 g., 86%; b. p. 68—69°/15 mm.). A second sample was obtained by controlled hydrogenation, at room temperature and pressure, of limonene [25 g.; α_D^{17} +56° (homogeneous)] in ethanol (200 ml.) in presence of palladium–charcoal (2 g.; 10%). A third sample was obtained by controlled hydrogenation of α-phellandrene [25 g.; α_D^{21} −73° (homogeneous)] in ethanol (200 ml.) at room temperature and pressure in the presence of platinum oxide (0·25 g.).

p-Menth-1-ene (28 g.) in dry chloroform (50 ml.) was brominated with *N*-bromosuccinimide (22 g.) as described above, but the reaction was not as vigorous as in the preceding case and was readily controlled by ceasing irradiation from time to time. The crude bromide (40 g.) was stirred with a solution of sodium formate (10 g.) in formic acid (50 ml.; 98%) for 2 hr., and the crude formate was extracted with ether after neutralisation of the mixture with sodium hydrogen carbonate. The formate (30 g.) was hydrolysed overnight by a solution of sodium carbonate (8 g.) in aqueous methanol (400 ml.; 50%), and the carvotanacetol formed was extracted with light petroleum (b. p. 40—60°). After being washed and dried the extract was treated with 3 : 5-dinitrobenzoyl chloride and pyridine, and the crude dinitrobenzoate remaining after distillation with steam was recrystallised (four times) from light petroleum (b. p. 40—60°), to give (±)-*carvotanacetol* 3 : 5-*dinitrobenzoate* as needles, m. p. 94·5° (Found : C, 58·8; H, 5·85; N, 7·8. $C_{17}H_{20}O_6N_2$ requires C, 58·6; H, 5·75; N, 8·0%). The yield of ester was less than 9% based on the crude bromide used.

The dinitrobenzoate (1·8 g.) in ether (30 ml.) was hydrolysed under reflux for 10 min. with potassium hydroxide (1 g.) in methanol (10 ml.). After 1 hr. filtration and removal of most of the solvent gave an oil. This was washed in light petroleum with water and dried, and gave crude (±)-carvotanacetol (0·8 g.). The alcohol (0·8 g.) in acetic acid (15 ml.) containing chromium trioxide (0·5 g.) was kept at 35° for 1 hr. The oil which separated on dilution was extracted with light petroleum (four times), and after being washed with 5% sodium carbonate solution and then water, and dried, gave the crude ketone (0·3 g.). This was converted into the semicarbazone which twice recrystallised had m. p. 175° alone or mixed with authentic (±)-carvotanacetone semicarbazone.

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JOHNSON CHEMICAL LABORATORIES,
UNIVERSITY OF ADELAIDE.

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