

98. *Experiments on the Synthesis of Irone.*

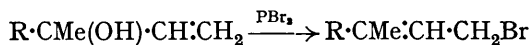
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Attempts have been made to decide between the two possible structures for irone (I and II) by the synthesis of (I). Most of the reactions which have been used for this purpose are well known and occur readily in the case of ionone, the lower homologue of (I); in the present instance the reactions proceeded normally for several stages, but unexpected difficulties then arose and (I) has not yet been obtained.

2, 182) and converted into geraniol by Barbier (*Compt. rend.*, 1893, **116**, 1200); on the other hand Rupe and Lang (*Helv. Chim. Acta*, 1929, **12**, 1133) found that dehydrolinalool (as VIII) did not give citral, but yielded a six-membered tetrahydropyran derivative which could be oxidised to α -cinenic acid (XII; R = CO₂H, R' = H) of known structure.

In the present instance *dehydro- ϵ -methyl-linalool* (VIII) was readily obtained and from it ϵ -methyl-linalool (X) : once again, however, ring closure through the oxygen atom took place with both these substances under conditions which usually bring about the isomerisations, and substances (XII; R = C:CH, R' = Me; or R = CH:CH₂, R' = Me) were obtained. We have no evidence either in this case or above of the six-ring structure of these oxides, except by analogy from the work of Rupe and Lang, and as the substances were useless from our point of view, they were not further investigated.

The method used by Goethals (*Bull. Soc. chim.*, 1937, **46**, 419) for the preparation of primary bromides from isomeric tertiary alcohols by treatment with phosphorus tribromide also failed :



Further investigations of alternative methods for the synthesis of (I) and related compounds are in progress.

EXPERIMENTAL.

α -Bromo- $\beta\gamma$ -dimethyl- Δ^{β} -butene (III).— $\beta\gamma$ -Dimethylbutadiene (60 g.), prepared from pinacol (Kyriakides, *J. Amer. Chem. Soc.*, 1914, **36**, 991. The yield of diene is diminished from 70 to 34% at the expense of pinacolone if pure redistilled pinacol is not used), was treated with hydrogen bromide (1 mol. from AnalaR bromine) ("Organic Syntheses," XV, p. 35) at 0°, and the product distilled in a vacuum; b. p. 49—52°/15 mm. Yield, 95% of the theoretical. It is essential to keep the product overnight before distillation to allow isomeric change to the stable bromide to occur (Claisen, *J. pr. Chem.*, 1922, **105**, 65).

$\beta\gamma$ -Dimethyl- Δ^{β} -hepten- ζ -one (IV).—The above bromide (15.9 g.) was added to ethyl sodioacetate (1 mol.) in alcohol during 1 hour and after heating for a similar period the product was worked up in the usual way. It had b. p. 127—130°/11 mm. Yield, 80% (Found : C, 67.9; H, 9.6. C₁₂H₂₀O₃ requires C, 67.95; H, 9.45%). This ester was hydrolysed by shaking it with twenty times its weight of cold 10% aqueous potassium hydroxide for 24 hours. The ketone was isolated by steam distillation and had b. p. 188°. It resembles methylheptenone in that it gives a red colour on a pine splint moistened with hydrochloric acid and in that it gives colours with certain aromatic aldehydes in the presence of hydrochloric acid : with salicylaldehyde, bright cherry-red; with anisaldehyde, intense red; and with *o*-nitrobenzaldehyde, yellow. The colour with anisaldehyde is detectable with an alcoholic solution of the ketone containing only one part in a million. The *semicarbazone*, crystallised from alcohol, had m. p. 160° (Found : C, 61.0; H, 9.4. C₁₀H₁₉ON₃ requires C, 60.9; H, 9.6%).

By ozonolysis in water acetylacetone, b. p. 192° (semicarbazone, m. p. and mixed m. p. 225—226°), acetone peroxide, m. p. 133°, and acetone (semicarbazone, m. p. and mixed m. p. 186°) were formed : the structure of the ketone is therefore beyond doubt.

Ethyl β -Hydroxy- ϵ -methyl- $\alpha\beta$ -dihydrogeranate (V).—The ketone (40 g.) was condensed with ethyl bromoacetate (62 g.) in the presence of zinc (24 g.) in benzene (40 c.c.) by heating during 5 hours after the initial vigorous reaction. (The yield of product is much diminished if more than the specified amount of benzene is used.) The ester had b. p. 146—148°/15 mm. Yield, 48.4 g. (Found : C, 67.9; H, 10.4. C₁₃H₂₄O₃ requires C, 68.4; H, 10.5%. Found : double bonds by bromine absorption, 1.07 per mol., by hydrogenation, 1.08 per mol.; hydroxyl by Zerewitinoff, 1.11 per mol.). When the ester was heated during 6 hours at 200°, the b. p. gradually fell; ethyl acetate and dimethylheptenone were isolated from the product. Benzoyl chloride and caustic soda solution, and acetyl chloride and sodium acetate were without effect on the ester, and acetic anhydride and zinc chloride gave a tar. When the ester was heated with iodine, or in benzene solution with phosphoric oxide, the cyclic oxide (VII, R = Et) was formed in good yield, b. p. 121—122°/14 mm. (Found : C, 67.9; H, 10.7. C₁₃H₂₄O₃ requires C, 68.4; H, 10.5%). This ester absorbed a negligible quantity of hydrogen with either the Adams platinum oxide catalyst or the Busch-Stöwe (*Ber.*, 1916, **49**, 1064) palladium catalyst, and in a Zerewitinoff estimation only small quantities of methane were evolved; these effects probably arise from contamination with traces of the unchanged hydroxy-ester. The same oxide-ester was formed in poor yield by treating the hydroxy-ester with phosphorus tribromide

and pyridine, and with hydrogen bromide, and, mixed with the ketone (IV), by heating it with benzoyl chloride, phenyl isocyanate or with potassium hydrogen sulphate.

β -Hydroxy- ϵ -methyl- $\alpha\beta$ -dihydrogeranic acid was obtained by the hydrolysis of the foregoing ester with 10% alcoholic potash: it had b. p. $168^\circ/15$ mm. (Found: equiv. by back titration, 202.8. $C_{11}H_{20}O_3$ requires 200). That this acid was unchanged by heating with acetic anhydride and sodium acetate was shown by b. p., equivalent weight and hydrogenation experiments (double bond found, 0.98 per mol.). When it was heated with phosphoric oxide, it decomposed into dimethylheptenone and acetic acid.

A mixture of the dry barium salt of the acid, barium formate and sand was heated at 0.4 mm., first at 150° during $1\frac{1}{2}$ hours and finally with a free flame until no further distillate was obtained: the distillate was dimethylheptenone (cf. Heilbron, J., 1935, 585).

With phosphoric oxide, a cold benzene solution of the acid gave a product, b. p. 110 — $116^\circ/0.05$ mm. (equiv., 197). This substance absorbed scarcely any hydrogen and is doubtless an oxide (VII, R = H).

Ethyl β -hydroxy- $\alpha\beta$ -dihydrogeranate was prepared from methylheptenone in a similar manner to that described above for its homologue; b. p. 134 — $138^\circ/12$ — 13 mm. By heating in benzene with phosphoric oxide, an ester, b. p. $118^\circ/13$ mm., was obtained (Found: C, 66.6; H, 9.9. $C_{12}H_{22}O_3$ requires C, 67.3; H, 10.3%). This ester absorbed no hydrogen with a catalyst and is presumably a cyclic oxide analogous to (VII).

Dehydromethyl-linalool (VIII).—Solutions of potassium (2.8 g.) in *tert.*-amyl alcohol (34 g.) and of dimethylheptenone (10 g.) in ether (15 c.c.) were simultaneously run slowly into ether (15 c.c.) saturated with acetylene at -15° and stirred vigorously. The temperature was then raised to 0° while the stirring and passage of acetylene were continued during 6 hours. After standing overnight the product was shaken with dilute hydrochloric acid, and water, and fractionated. The carbinol (5.4 g.) had b. p. 97 — $99^\circ/10$ mm. [Found: C, 79.9; H, 10.9. $C_{11}H_{18}O$ requires C, 79.5; H, 10.8%. Found: hydroxyl (Zerewitinoff), 0.99 per mol.]. An explosive silver salt was precipitated in alcoholic solution by silver nitrate.

2 : 5 : 6 : 6-Tetramethyl-2-ethyltetrahydropyran (XII; R = C \dot{C} H, R' = Me).—The above carbinol (5 g.) was heated with formic acid (38 c.c.) and water (12 c.c.) during 35 minutes. The product was cooled, an excess of caustic soda added, and the pyran extracted with ether and distilled, b. p. 64 — $66^\circ/10$ mm. (Found: C, 79.6; H, 10.9. $C_{11}H_{18}O$ requires C, 79.5; H, 10.8%). The substance formed an explosive silver salt and absorbed nearly 2 mols. of hydrogen: there is therefore little doubt of its constitution.

Hydrogenation of Dehydromethyl-linalool.—In acetic acid solution with Adams's platinum catalyst 3 mols. of hydrogen per mol. were rapidly absorbed with no break in the hydrogenation-time curve. The product was not isolated. Methyl-linalool (X) was best prepared by hydrogenation in ethyl alcohol with palladised calcium carbonate: the process was stopped after 1 mol. of hydrogen had been absorbed, a distinct break in the hydrogenation-time curve being observed at this point. The product had b. p. 98 — $102^\circ/10$ mm., and gave no silver salt. Yield, 80—90% of the theoretical. Dihydromethyl-linalool was similarly prepared in ethyl alcohol, a marked break occurring in the hydrogenation-time curve corresponding with the absorption of 2 mols. of hydrogen, rather more catalyst than previously being used. The product had b. p. 99 — $102^\circ/10$ mm. and gave no silver salt. By further hydrogenation exactly 1 mol. more of hydrogen was absorbed and by ozonolysis a steam-volatile substance was obtained which gave the iodoform reaction: there is therefore no doubt that the triple bond has been completely hydrogenated in the first case.

Attempted Conversion of Methyl-linalool into Methylgeraniol.—Methyl-linalool (10 g.) was heated with trichloroacetic acid (10 g.) and acetic acid (20 c.c.) during $2\frac{1}{2}$ hours at 65° . The product was neutralised, extracted with ether and, after removal of the ether, hydrolysed by boiling it with 10% methyl-alcoholic potash during 4 hours. A substance (2.6 g., b. p. 76 — $78^\circ/14$ mm.) was obtained having a smell and b. p. similar to those of the pyran derivative described above (geraniol has b. p. $115^\circ/12$ mm.): the remaining material distilled at 78 — $182^\circ/14$ mm. and was insoluble in methyl alcohol. As it seemed clear that methylgeraniol had not been formed, further investigation of these products was abandoned.

A solution of methyl-linalool (17.7 g.) and pyridine (3 g.) in light petroleum (30 c.c.) was slowly added to phosphorus tribromide (12 g.) and light petroleum (20 c.c.) containing pyridine (36 drops) at -15° . After stirring during $3\frac{1}{2}$ hours and standing overnight the product was washed with water and sodium bicarbonate, dried, and distilled in nitrogen: the main fraction (10.7 g.) had b. p. 116 — $118^\circ/10$ mm. (Found: Br, 32.15. $C_{11}H_{18}Br$ requires Br, 34.6%). The bromide (4 g.) was refluxed in ethereal solution with silver benzoate (7.5 g.) during 10 hours.

A yellow oil (1.1 g.), b. p. 140—142°/0.35 mm., was obtained, which was hydrolysed during 20 minutes with methyl-alcoholic potash: distillation gave 0.4 g. of product, b. p. 114—130°/13 mm. This substance was submitted to ozonolysis, and the product tested for acetylacetone with semicarbazide: no semicarbazone was produced. If the changes had proceeded normally and methylgeraniol had been formed, there should be no difficulty in recognising acetylacetone by its very sparingly soluble semicarbazone: the absence of methylgeraniol in the product may therefore be assumed. The bromide (5 g.) was heated with sodium acetate (5 g.) in acetic acid (10 c.c.) during 2 hours, and the product isolated in the obvious way: it had b. p. 73—74°/13 mm. and was clearly a pyran derivative.

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