81. *5-Ethinylruban-5-ol and Related Compounds.*

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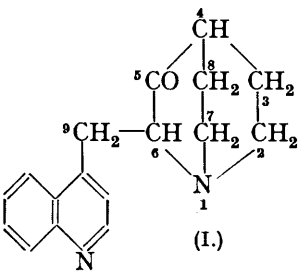
5-Ethinylruban-5-ol has been prepared by condensation of 5-ketoruban with acetylene and reduced to 5-ethylruban-5-ol. Some new and related compounds are also described.

Since 5-vinylruban-5-ol would be not only isomeric with but very closely related, structurally, to cinchonine, its preparation as an antimalarial drug was considered desirable. 5-Ketoruban (I) (J., 1939, 1241) was condensed with acetylene in the presence of sodamide or, better, by the use of a solution of potassium in *tert.*-amyl alcohol as described by Gould and Thompson (*J. Amer. Chem. Soc.*, 1935, **57**, 340). *5-Ethinylruban-5-ol* was obtained as a well-defined crystalline solid in good yield. The catalytic reduction of this compound was studied in a micro-apparatus modelled on that of Jackson (*J. Soc. Chem. Ind.*, 1938, **57**, 96). At atmospheric pressure and temperature in the presence of palladised charcoal or platinum, 5-ethinylruban-5-ol absorbed two moles of hydrogen, giving 5-ethylruban-5-ol. The absorption took place very rapidly and there was no observable change in the rate, corresponding to reduction to the vinyl stage. No definite compound was isolated from the resinous product obtained when hydrogenation was stopped after the theoretical volume calculated for reduction to the vinyl compound had been absorbed.



(I.)

5-Keto-6 : 9-rubanene also was condensed with acetylene; the product rapidly absorbed two moles of hydrogen, yielding the compound previously obtained by the action of ethylmagnesium iodide on this unsaturated ketone. Similarly, 3-keto-quinuclidine gave *3-hydroxy-3-ethinylquinuclidine*, which was smoothly hydrogenated to *3-hydroxy-3-ethylquinuclidine*. The latter compound was also prepared by the action of ethylmagnesium iodide on 3-ketoquinuclidine, but attempts to convert this into 3-ethylquinuclidine (Koenigs, *Ber.*, 1904, **37**, 3244; 1905, **38**, 3055) by dehydration and reduction have so far failed.

Experimental.

5-Ethinylruban-5-ol.—5-Ketoruban (0·5 g.), in a mixture of dry ether (10 c.c.) and *tert.*-amyl alcohol (5 c.c.), and a solution of potassium (0·5 g.) in *tert.*-amyl alcohol (15 c.c.) were simultaneously dropped during 2 hours into ether (20 c.c.) saturated with pure acetylene at − 15°; acetylene was passed with stirring during this period and for a further 12—14 hours, and the temperature was maintained at − 15° throughout. The potassium compound was decomposed by the cautious addition of ice and acetic acid, the solution evaporated under reduced pressure, the residue dissolved in a little hydrochloric acid and boiled with active charcoal, and the filtrate basified with potassium carbonate solution. The solid which separated was collected, washed with water, and dried; it crystallised from ether–ethyl acetate in large colourless prisms (0·38 g.), m. p. 213°, insoluble in water but very soluble in alcohol or benzene (Found: C, 77·7; H, 6·7. $C_{19}H_{20}ON_2$ requires C, 78·1; H, 6·9%). The mercury compound of *5-ethinylruban-5-ol*, prepared by Johnson and McEwen's process (*J. Amer. Chem. Soc.*, 1926, **48**, 471), formed small yellowish needles, m. p. 220° (darkening at 170°).

Reduction of 5-Ethinylruban-5-ol to 5-Ethylruban-5-ol.—The above acetylenic derivative (0·138 g.) was shaken with acetic acid (10 c.c.) and reduced platinum catalyst (0·02 g.) in hydrogen at atmospheric pressure. A rapid absorption of hydrogen was observed for 20 minutes (23·4 c.c., reduced to N.T.P. Calc. for 1 triple bond, 21·03 c.c.) and there was no further contraction during 2 hours. The filtered solution was basified (potassium carbonate) and the gum which separated was allowed to harden in the refrigerator, collected, washed with water, and crystallised from ethyl acetate–light petroleum (b. p. 60—80°); it formed small colourless prisms (0·05 g.), m. p. 138—139°, not depressed by admixture with 5-ethylruban-5-ol (Found: N, 9·7. Calc. for $C_{19}H_{24}ON_2$: N, 9·5%).

Reaction of Acetylene with 5-Keto-6 : 9-rubanene.—By the same procedure 5-keto-6 : 9-

rubanene (0·5 g.) yielded a *compound* (0·35 g.), which crystallised from ethyl acetate in large, faintly yellow prisms, m. p. 238° (Found : C, 78·6; H, 6·5; N, 9·8. $C_{19}H_{18}ON_2$ requires C, 78·6; H, 6·3; N, 9·6%). The mercury derivative was a yellowish crystalline powder, m. p. 162° (decomp.). The picrate separated from alcohol as an oil which slowly solidified to a crystalline mass, m. p. 110—112°, but could not be purified.

Reduction of the above acetylene compound. The above compound (0·237 g.), m. p. 238°, in acetic acid (15 c.c.) was shaken with reduced platinum catalyst (0·02 g.) in hydrogen at atmospheric pressure. The contraction (35·1 c.c., reduced to N.T.P. Calc. for $2H_2$, 36·3 c.c.) took place smoothly during 25—30 minutes. The filtered solution was evaporated under reduced pressure, the residue dissolved in a little hydrochloric acid and boiled with active charcoal, and the filtrate basified (potassium carbonate). The oil which separated was dried in chloroform, the solvent evaporated, and the residue crystallised from light petroleum (b. p. 60—80°), forming colourless prisms (0·035 g.), m. p. 162°, identical with the compound obtained by the action of ethylmagnesium iodide on 5-keto-6 : 9-rubanene (Found : N, 9·6. Calc. for $C_{19}H_{22}ON_2$: N, 9·6%).

3-*Hydroxy*-3-*ethinylquinuclidine*.—3-Ketoquinuclidine (0·35 g.) was condensed with acetylene in the presence of a solution of potassium (0·5 g.) in *tert.*-amyl alcohol (15 c.c.) as previously described. The potassium compound was decomposed by the addition of ice and acetic acid, amyl alcohol removed in steam, and the residue basified (potassium carbonate) and extracted with chloroform. The residue from the evaporation of the dried extracts crystallised in large colourless prisms (0·15 g.), m. p. 159—160° (Found : C, 71·6; H, 8·8. $C_9H_{13}ON$ requires C, 71·5; H, 8·7%). The picrate crystallised from benzene–alcohol in deep yellow needles, m. p. 153°, very soluble in alcohol, and apparently contained solvent of crystallisation.

3-*Hydroxy*-3-*ethylquinuclidine*.—Under the conditions described, 3-hydroxy-3-ethinylquinuclidine (0·130 g.) rapidly absorbed hydrogen corresponding to complete reduction of the triple bond (39·5 c.c. at N.T.P. Calc., 38·3 c.c.). The solution was filtered, acidified (concentrated hydrochloric acid), and evaporated, the residue basified (potassium carbonate), and the base extracted with chloroform, dried, and distilled, giving 0·08 g. of a colourless oil, b. p. 97—101°/1 mm., identical with that obtained by the direct action of ethylmagnesium iodide on 3-ketoquinuclidine (below). The *picrate* crystallised in long yellow needles, m. p. 178° (Found : C, 47·3; H, 5·5. $C_9H_{17}ON,C_6H_3O_7N_3$ requires C, 46·9; H, 5·2%).

3-*Hydroxy*-3-*ethylquinuclidine*.—A solution of 3-ketoquinuclidine (0·5 g.) in ether (25 c.c.) was slowly added to a purified Grignard solution, prepared from magnesium (3 g.) and ethyl iodide (9 c.c.) in ether (25 c.c.) cooled at − 10°. The thick greyish mixture was kept overnight in a refrigerator, decomposed with ice and acetic acid, and acidified (concentrated hydrochloric acid), and the ether removed. The aqueous liquid was evaporated, the residue basified (sodium hydroxide solution), and the liberated oil extracted with chloroform, dried, and distilled. The main fraction (b. p. 131—135°/25 mm.) was treated with light petroleum (b. p. 60—80°, 5 c.c.) and ether (2 c.c.) and kept overnight at 0°. The solid was collected and crystallised from light petroleum (b. p. 60—80°), forming colourless needles (0·08 g.), m. p. 113°, soluble in water (to an alkaline solution). The picrate of this compound separated from benzene–alcohol in deep yellow leaflets, m. p. 195° (Found : C, 46·95; H, 5·0%). Consistent molecular-weight determinations could not be made on this compound, but the values obtained (600—200) indicated that it was a polymer of 3-hydroxy-3-ethylquinuclidine (*M*, 155). The filtrate from the initial crystallisation of the above substance was distilled and gave 3-*hydroxy*-3-*ethylquinuclidine* as a thick, faintly yellow oil (0·3 g.), b. p. 98—100°/1 mm., which could not be crystallised (Found : C, 70·2; H, 11·2; N, 9·2. $C_9H_{17}ON$ requires C, 69·7; H, 11·0; N, 9·0%). The picrate separated from benzene in yellow needles, m. p. 175° (Found : C, 46·8; H, 5·4. Calc. for $C_9H_{17}ON,C_6H_3O_7N_3$: C, 46·9; H, 5·2%).

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