

**314.** *Researches on Acetylenic Compounds. Part XIII. The Reaction Between Epichlorohydrin and Sodium Acetylide. A Novel Route to the Ethynyl-ethylenic Alcohol, Pent-2-en-4-yn-1-ol.\**

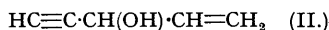
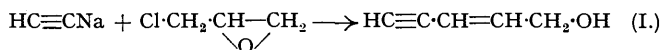
By L. J. HAYNES, SIR IAN HEILBRON, E. R. H. JONES, and F. SONDEHEIMER.

Condensation between epichlorohydrin and sodium acetylide in liquid ammonia gives, rather unexpectedly, the ethynyl-ethylenic primary alcohol, pentenynol (I). Evidence is adduced to show that this reaction proceeds *via* the ethynyl oxide (III); in particular, it is demonstrated that 1:2-epoxy-3-phenylpropane ( $\text{Ph}\cdot\text{CH}_2\cdot\underset{\text{O}}{\text{C}}\text{H}\text{-CH}_2$ ) is isomerised to cinnamyl

alcohol by treatment with sodamide in liquid ammonia. Analogous condensations with the sodio-derivatives of 1-hexyne and phenylacetylene give similar products, albeit in poorer yields.

In connexion with the synthesis of various types of acetylenic hydroxy-acids and the derived unsaturated lactones (Haynes and Jones, *J.*, 1946, 503 and 954) the condensation of various oxides or epoxy-compounds with sodium acetylide in liquid ammonia has been investigated. This paper describes some rather unexpected results which were obtained when epichlorohydrin was employed in such reactions. There is only one instance in the literature of the reaction of epichlorohydrin with an acetylenic compound, namely phenylacetylenylmagnesium bromide (Iotsitch, *J. Russ. Phys. Chem. Soc.*, 1903, **35**, 554), when a normal addition product, either  $\text{Ph}\cdot\text{C}\equiv\text{C}\cdot\text{CH}_2\cdot\text{CH}(\text{OH})\cdot\text{CH}_2\text{Cl}$  or  $\text{Ph}\cdot\text{C}\equiv\text{C}\cdot\text{CH}(\text{CH}_2\text{Cl})\cdot\text{CH}_2\cdot\text{OH}$ , was obtained in poor yield.

When epichlorohydrin reacts with sodium acetylide in liquid ammonia, the sole product, obtained in about 40% yield, is the ethynylethylenic alcohol, pent-2-en-4-yn-1-ol (I). This substance had already been prepared in these laboratories in extremely poor overall yield from

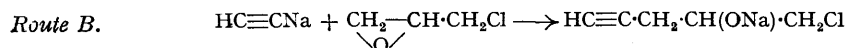
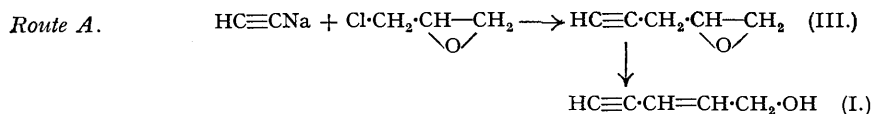


acetaldehyde *via* vinyl ethynylcarbinol (II) (Heilbron, Jones, Lacey, McCombie, and Raphael, *J.*, 1945, 77). The yield of the primary alcohol, based on the epichlorohydrin, is markedly dependent on the quantity of sodium acetylide employed. Thus with equimolar quantities of chlorohydrin and sodium under standard conditions, the yield is only 16%, but it is not improved beyond 40% when more than two moles of sodium to one of chlorohydrin are employed. Varying the reaction time from 5 to 18 hours has no appreciable effect upon the yield, and this was considerably reduced in an experiment in which the reaction mixture was kept under pressure at room temperature for 18 hours. When epibromohydrin is used under the optimum conditions found for the chlorohydrin, only a 25% yield of pentenynol is obtained. With sodium acetylide in liquid ammonia epi-iodohydrin yields mainly di-iodoacetylene.

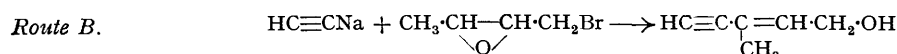
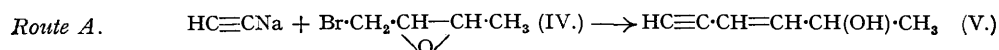
The formation of pentenynol (I) from epichlorohydrin can conceivably take place by either of two routes, *A* and *B*, depending upon whether the initial reaction step is one of substitution or

\* Patent application pending.

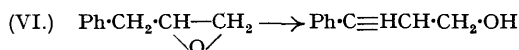
addition. Conclusive evidence has been obtained to show that route *A*, involving the intermediate formation of an ethynyl oxide (III), by elimination of sodium chloride, gives the more accurate picture of the reaction sequence. If, in the reaction with sodium acetylide, 1-bromo-2:3-epoxybutane (IV) is employed in place of epichlorohydrin, different products would be expected according as to whether the reaction proceeds by route *A* or route *B*. Both



of these possible products had already been prepared and characterised in these laboratories and it was comparatively simple to demonstrate that the product obtained in 45% yield by interaction of the bromo-compound (IV) with sodium acetylide is the straight chain secondary alcohol, hexenynol (V).



The rearrangement of the ethynyl oxide (III) to the primary alcohol (I), inherent in scheme *A*, has been shown to be highly probable by studying the action of alkaline reagents on 1:2-epoxy-3-phenylpropane (3-phenylpropylene oxide) (VI). It remains unaffected on treatment with 10% potassium hydroxide and also with sodium acetylide in liquid ammonia, but with



a molecular proportion of sodamide in this medium an 80% yield of cinnamyl alcohol is obtained. It is well known that oxides rearrange under suitable conditions to aldehydes or ketones; in the case of oxides of the type of (III) and (VI), however, it may well be that isomerisation of the ethylenic bond in the intermediate enol form is brought about by the tendency to form conjugated vinylacetylene and styrene systems respectively.

Attempts to extend the scope of the novel reaction between epichlorohydrin and sodium acetylide, by using substituted acetylenes, have not been particularly successful. Thus phenylacetylene gives only a 15% yield of the primary alcohol (5-phenylpent-2-en-4-yn-1-ol) (VII), the structure of which is confirmed by the ultra-violet absorption data and by



hydrogenation and then oxidation to  $\delta$ -phenylvaleric acid. Similarly, although a reaction time of 42 hours is necessary, 1-hexyne gives *non-2-en-4-yn-1-ol* (VIII) in 20% yield, converted into *n*-nonyl alcohol on hydrogenation.

#### EXPERIMENTAL.

Light-absorption data determined in alcohol solutions.

*Pent-2-en-4-yn-1-ol* (I).—(a) To a solution of sodium acetylide in liquid ammonia (7 l.), prepared from sodium (276 g.), using the ferric nitrate catalyst of Vaughn, Vogt, and Nieuwland (*J. Amer. Chem. Soc.*, 1934, **56**, 2120) to catalyse the formation of sodamide, epichlorohydrin (555 g.) was run in during 2 hours with stirring and cooling (alcohol-carbon dioxide). Nitrogen was introduced during the addition and during the subsequent 16 hours' stirring after which ammonium chloride (660 g.) was added during 2½ hours and the ammonia evaporated on the steam-bath. Ether (3 l.) was added, and the solid residue obtained on filtering was dissolved in water. A small quantity of tar was removed by filtration, the solution was extracted thoroughly with ether, and the combined ethereal solutions were washed with dilute sulphuric acid and water and then dried. Evaporation of the solvent and distillation gave *pent-2-en-4-yn-1-ol* (201 g.), b. p. 71–73°/19 mm.,  $n_D^{20}$  1.4972. Light absorption: Maximum, 2230 Å.;  $\epsilon = 15,000$ . Inflection, 2290 Å.;  $\epsilon = 10,000$  (Heilbron, Jones, Lacey, McCombie, and Raphael, *J.*, 1945, **77**, give b. p. 90°/50 mm.,  $n_D^{20}$  1.4933; maximum, 2230 Å.;  $\epsilon = 14,000$ ). The  $\alpha$ -naphthylurethane had m. p. 111–112°, undepressed on admixture with an authentic specimen (m. p. 110–111°).

(b) The method described above using epibromohydrin (137 g.) and sodium (46 g.) in liquid ammonia (1:2 l.) gave: (i) Pent-2-en-4-yn-1-ol (21 g.), b. p. 80—81°/27 mm.,  $n_D^{20}$  1.4963, and (ii) a colourless liquid (10.6 g.), b. p. 74—75°/1.5 mm.,  $n_D^{22}$  1.4831, analysing for  $C_{10}H_{12}O_3$  (Found: C, 66.75, 66.4; H, 6.7, 6.7.  $C_{10}H_{12}O_3$  requires C, 66.65; H, 6.7%). Light absorption: Maximum, 2230 Å.;  $\epsilon = 16,000$ . Inflexion, 2310 Å.;  $\epsilon = 12,500$ . The structure of this product has not yet been ascertained.

*Hex-3-en-5-yn-2-ol* (V).—The method described above using 1-bromo-2:3-epoxybutane (77.5 g.; Delaby, *Compt. rend.*, 1923, **176**, 589) and sodium (24 g.) in liquid ammonia (600 c.c.) gave hex-3-en-5-yn-2-ol (21.3 g.), b. p. 82—84°/32 mm.,  $n_D^{15}$  1.4860 (Heilbron, Jones, Smith, and Weedon, *J.*, 1946, 54, give b. p. 79—81°/30 mm.,  $n_D^{15}$  1.4842). The phenylurethane had m. p. 83°, undepressed on admixture with an authentic specimen, m. p. 83—84° (Jones and McCombie, *J.*, 1943, 261). The  $\alpha$ -naphthylurethane separated from light petroleum (b. p. 60—80°) in clusters of needles, m. p. 83—84°, undepressed on admixture with a specimen prepared from authentic material (Found: N, 5.35.  $C_{17}H_{15}O_2N$  requires 5.3%).

As a by-product of this experiment there was obtained a substance (7.5 g.), b. p. 122—124°/32 mm., 66—67°/0.5 mm.,  $n_D^{18}$  1.4745, believed to be 2-(2:3-epoxy-1-butoxy)hex-3-en-5-yne, a colourless pleasant-smelling liquid, slowly turning yellow in air (Found: C, 71.85; H, 8.6.  $C_{10}H_{14}O_2$  requires C, 72.25; H, 8.5%). Light absorption: Maximum, 2230 Å.;  $\epsilon = 13,500$ . Inflexion, 2280 Å.;  $\epsilon = 12,500$ . Active hydrogen (Zerewitinoff): The ether (94 mg.) evolved 12.7 c.c. of methane (after heating to 90°) at 20°/772 mm. (0.95 active hydrogen atom). Hydrogenation of the ether (2.06 g.) in ethyl acetate (50 c.c.) in the presence of platinum oxide (10 mg.) (914 c.c. hydrogen absorbed at 13°/760 mm., equivalent to  $\bar{C} = 3.05$ ) gave 2-(2:3-epoxy-1-butoxy)hexane (1.5 g.), b. p. 86—88°/16 mm.,  $n_D^{15}$  1.4265 (Found: C, 69.45; H, 12.0.  $C_{10}H_{20}O_2$  requires C, 69.7; H, 11.7%). This saturated ether gave a negligible volume of methane in an active hydrogen determination.

*Cinnamyl Alcohol*.—To sodamide, prepared from sodium (1.75 g.), in liquid ammonia (100 c.c.) was added 1:2-epoxy-3-phenylpropane (10 g.; Levy and Sfras, *Bull. Soc. chim.*, 1931, **49**, 1823). After 20 hours' stirring in nitrogen, ammonium chloride (5 g.) was added, and the product was isolated with ether in the usual way. Distillation gave cinnamyl alcohol (7.8 g.), b. p. 85—87°/0.05 mm.,  $n_D^{19}$  1.5852, which rapidly solidified. After one crystallisation from ether-pentane it had m. p. 33°, not depressed on admixture with an authentic specimen (m. p. 33°). Only a 50% yield of the alcohol was obtained when the reaction time was reduced to 6 hours.

*5-Phenylpent-2-en-4-yn-1-ol* (VII).—To sodamide, prepared from sodium (7.7 g.) in liquid ammonia (400 c.c.) as described above, phenylacetylene (35 g.) was added during 15 minutes. After 1 hour's stirring, epichlorohydrin (30.6 g.) was run in during 15 minutes, the solution was stirred for a further 16 hours, and was then worked up in the usual manner. Distillation gave, besides some starting material, two fractions: (i) B. p. 70—72°/1 mm.,  $n_D^{16}$  1.5459 (1.8 g.); (ii) 5-phenylpent-2-en-4-yn-1-ol (6.8 g.) as a pale yellow oil, turning dark yellow on keeping, b. p. 94—96°/10<sup>-3</sup> mm.,  $n_D^{18}$  1.6173 (Found: C, 83.0; H, 6.45.  $C_{11}H_{10}O$  requires C, 83.5; H, 6.35%). There was a considerable resinous residue. Light absorption: Maxima, 2590, 2720, 2890 Å.;  $\epsilon = 19,000$ , 26,000, and 21,000 respectively. The  $\alpha$ -naphthylurethane separated from petroleum (b. p. 80—100°) in plates, m. p. 132° (Found: N, 4.25.  $C_{22}H_{17}O_2N$  requires N, 4.3%).

*5-Phenylpentan-1-ol and  $\delta$ -Phenylvaleric Acid*.—A solution of the above carbinol (1 g.) in ethyl acetate (30 c.c.) was shaken with hydrogen in the presence of platinum oxide (10 mg.) until absorption was complete. Removal of catalyst and solvent, gave on distillation 5-phenylpentan-1-ol (0.75 g.), b. p. 150—151°/18 mm.,  $n_D^{21}$  1.5170 (*v. Braun, Ber.*, 1911, **44**, 2867, gives b. p. 155°/20 mm.). Oxidation of the saturated carbinol (0.6 g.) with chromic acid in the usual way gave  $\delta$ -phenylvaleric acid (0.4 g.) which after crystallisation from water had m. p. 57.5° (Staudinger and Müller, *Ber.*, 1923, **56**, 713, give m. p. 57°).

*Non-2-en-4-yn-1-ol* (VIII).—1-Hexyne (90 g.) was caused to react with sodamide, made from sodium (23.5 g.) in liquid ammonia (1 l.), as previously described, but instead of being cooled, the reaction flask was well lagged with cork dust. Epichlorohydrin (80 g.) was dropped in during 1 hour, then the solution was stirred for 42 hours without cooling, the volume being kept constant by adding more liquid ammonia occasionally. On working up in the usual manner, distilling off starting materials, and carefully fractionating the residue through a Widmer column, there was obtained non-2-en-4-yn-1-ol (24 g.) as a pleasant-smelling colourless oil, b. p. 67°/0.1 mm.,  $n_D^{20}$  1.4920 (Found: C, 77.5; H, 10.5.  $C_9H_{14}O$  requires C, 78.2; H, 10.2%). Light absorption: Maxima, 2280, 2370 Å.;  $\epsilon = 14,000$  and 12,000 respectively. The  $\alpha$ -naphthylurethane separated from light petroleum (b. p. 40—60°) as a microcrystalline powder, m. p. 69° (Found: N, 4.75.  $C_{20}H_{21}O_2N$  requires N, 4.55%). In an experiment in which exactly the same conditions were employed as for the condensation with sodium acetylide (*viz.*, hexyne: epichlorohydrin = 2:1, reaction time 20 hours, cooling in alcohol-carbon dioxide), no appreciable amount of non-2-en-4-yn-1-ol could be detected.

*n-Nonyl Alcohol*.—Non-2-en-4-yn-1-ol (1.08 g.) in ethyl acetate (30 c.c.) was shaken in hydrogen with platinum oxide until absorption was complete. Removal of catalyst and solvent gave n-nonyl alcohol (0.8 g.), b. p. 115°/22 mm.,  $n_D^{15}$  1.4355; the p-nitrophenylurethane had m. p. 106°; the  $\alpha$ -naphthylurethane had m. p. 64°. (Ellis and Reid, *J. Amer. Chem. Soc.*, 1932, **54**, 1674, give b. p. 213.5°,  $n_D^{15}$  1.4320. Hoppenbrouwers, *Rec. Trav. chim.*, 1932, **51**, 951, gives m. p. 104° for the p-nitrophenylurethane. Adamson and Kenner, *J.*, 1934, 838, give m. p. 65.5° for the  $\alpha$ -naphthylurethane.)

The authors thank the Rockefeller Foundation for financial assistance and the University of London for Post-graduate studentships (L. J. H. and F. S.). They are indebted to Dr. E. A. Braude for the light-absorption data.