412. *Alkenylation by Use of Lithium Alkenyls. Part III. The Synthesis of Unsaturated Ketones from* iso*Butenyl-lithium.*

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*iso*Butenyl-lithium (cf. Part I, *J.*, 1950, 2000) reacts with lithium acetate, benzoate, or crotonate to give mesityl oxide, phenyl *iso*butenyl ketone, or propenyl *iso*butenyl ketone, respectively. Only poor yields of ketones are obtained from the reaction between *iso*butenyl-lithium and the acid chlorides.

Propenyl *iso*butenyl ketone, the structure of which is proved by catalytic hydrogenation, undergoes 1 : 4-addition with methylmagnesium bromide to give *iso*butyl *iso*butenyl ketone.

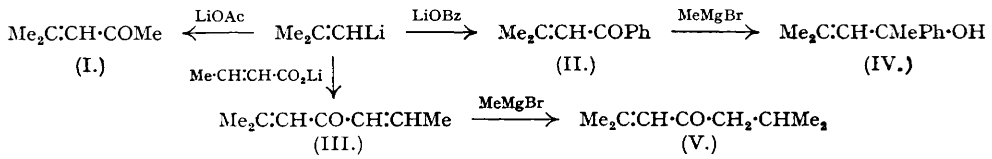
In the two preceding papers, the synthesis of unsaturated carbinols from *iso*butenyl-lithium has been described. The present work deals with the synthesis of unsaturated ketones and provides a further illustration of the usefulness of this new type of organo-metallic reagent.

A variety of carboxylic acid derivatives, including acid chlorides (Kloppenburg and Wibaut, *Rec. Trav. chim.*, 1946, **65**, 393), anhydrides (Wibaut, Kloppenburg, and Beets, *ibid.*, 1944, **63**, 134), nitriles (Ziegler *et al.*, *Annalen*, 1932, **495**, 84; 1933, **504**, 94; 1934, **512**, 164; Gilman and Kirby, *J. Amer. Chem. Soc.*, 1933, **55**, 1265), and lithium salts (Gilman and van Ess, *ibid.*, p. 1258; Arens and van Dorp, *Rec. Trav. chim.*, 1946, **65**, 338; Heilbron, Jones, and Richardson, *J.*, 1949, 287), has been employed for the synthesis of ketones from alkyl- and aryl-lithium derivatives. The last-named method appeared particularly suitable in the present case in view of the observation (Part I, *J.*, 1950, 2000) that carboxylation of *iso*butenyl-lithium affords, besides β-methylcrotonic acid, considerable proportions of phorone which must be formed by the reaction of the alkenyl-lithium with the lithium salt of the acid. An additional advantage of the use of lithium salts as secondary components is that the lithium alkenyl can be formed in their presence, thus reducing the incidence of side-reactions.

In this manner, *iso*butenyl-lithium has been condensed with lithium acetate, benzoate, or crotonate in ether to give mesityl oxide (I), phenyl *iso*butenyl ketone (II), or propenyl *iso*butenyl ketone (III). As previously (Parts I and II), appreciable amounts of the Wurtz product, 2 : 5-dimethylhexa-2 : 4-diene, are also formed, and this limits the yields of ketones to 30—40%, based on the bromide. Only small yields of ketones were obtained on treating *iso*butenyl-lithium with acetyl or crotonyl chloride, and no significant amount of ketone could be isolated after reaction with acetonitrile.

Phenyl *iso*butenyl ketone has previously been prepared by various methods (Kohler, *Amer. Chem. J.*, 1909, **42**, 398; Blaise and Herman, *Ann. Chim.*, 1911, **23**, 530; Darzens, *Compt. rend.*, 1929, **189**, 767), but the physical constants recorded for this compound are somewhat conflicting. It has now been characterised as *p*-nitrophenylhydrazone, m. p. 168°, and 2 : 4-dinitrophenylhydrazone, and was readily hydrogenated over platinum oxide to phenyl *iso*butyl ketone. The low boiling point, and the low-melting *p*-nitrophenylhydrazone (m. p. 132°) recorded by Blaise and Herman (*loc. cit.*), suggest that their product was not phenyl *iso*butenyl ketone. On treatment with methylmagnesium bromide, the ketone underwent exclusively 1 : 2-addition to give phenylmethyl*iso*butenylcarbinol (IV) (Ravier, *Compt. rend.*, 1934, **198**, 1786; Part I, *loc. cit.*). This is in contrast to the reaction with phenylmagnesium bromide which results mainly in 1 : 4-addition (Kohler, *loc. cit.*). A different behaviour of methyl- compared with ethyl- or phenyl-magnesium halide towards αβ-unsaturated carbonyl compounds has also been observed in other cases (Klages, *Ber.*, 1906, **39**, 2592; Kohler, *Amer. Chem. J.*, 1907, **38**, 529).

Apart from phorone, only few simple dialkenyl ketones have been described in the literature (Nazarov *et al.*, *Bull. Acad. Sci., U.S.S.R., Cl. Sci. Chim.*, 1945, 505; 1946, 91, 201; 1947, 641, 647; 1948, 118, 236). Propenyl *iso*butenyl ketone (III), like its lower homologues, is a pale yellow liquid and does not form a semicarbazone under the usual conditions. It was characterised by the 2 : 4-dinitrophenylhydrazone. It readily absorbed two moles of hydrogen in the presence of platinic oxide to give propyl *iso*butyl ketone. On treatment with methylmagnesium bromide, propenyl *iso*butenyl ketone furnished as the sole product *iso*butyl *iso*butenyl ketone (dihydrophorone) (V), previously obtained by Paal (*Ber.*, 1912, **45**, 2226) by the partial hydrogenation of phorone :



$$\begin{tikzcd}
\underset{\text{(I.)}}{Me_2C{:}CH{\cdot}COMe} & Me_2C{:}CHLi \arrow[l, "LiOAc"'] \arrow[r, "LiOBz"] \arrow[d, "Me{\cdot}CH{:}CH{\cdot}CO_2Li"'] & \underset{\text{(II.)}}{Me_2C{:}CH{\cdot}COPh} \arrow[r, "MeMgBr"] & \underset{\text{(IV.)}}{Me_2C{:}CH{\cdot}CMePh{\cdot}OH} \\
 & \underset{\text{(III.)}}{Me_2C{:}CH{\cdot}CO{\cdot}CH{:}CHMe} \arrow[r, "MeMgBr"] & \underset{\text{(V.)}}{Me_2C{:}CH{\cdot}CO{\cdot}CH_2{\cdot}CHMe_2} &
\end{tikzcd}$$

It was identified by the semicarbazone, m. p. 137°, and was also characterised by the 2 : 4-dinitrophenylhydrazone. The exclusive occurrence of 1 : 4-addition to the propenyl keto-group in this case is by no means unexpected, since ethylideneacetone and other propenyl ketones undergo mainly 1 : 4-addition (Kohler, *Amer. Chem. J.*, 1907, **38**, 511), whereas only 1 : 2-addition takes place with mesityl oxide, phorone (Fellenberg, *Ber.*, 1904, **37**, 3578), and phenyl *iso*butenyl ketone (see above).

Attempts to prepare vinyl *iso*butenyl ketone by the condensation of *iso*butenyl-lithium with lithium acrylate or acrylonitrile failed owing to extensive polymerisation of the acrylic derivatives under the influence of the organo-metallic reagent (cf. Beaman, *J. Amer. Chem. Soc.*, 1948, **70**, 3115). *iso*Butenyl-lithium failed to react with lithium formate or ethyl orthoformate under the usual conditions.

EXPERIMENTAL.

(M. p.s were determined on a Kofler block and are corrected.)

iso*Butenyl-lithium*.—As the preparation of *iso*butenyl bromide from *tert.*-butanol (Braude and Timmons, *J.*, 1950, 2000) is rather tedious, an alternative route, adapted from Farrell and Bachman (*J. Amer. Chem. Soc.*, 1935, **57**, 1281), was employed. Mesityl oxide in 400-g. batches was converted into β-methylcrotonic acid (180 g.) by treatment with specially stabilised, 15% aqueous sodium hypochlorite solution (7 l.), kindly furnished by Milton Antiseptic Limited through the courtesy of Mr. P. A. Lincoln (Barbier and Leser, *Bull. Soc. chim.*, 1905, **33**, 815). The acid (360 g.) was treated with bromine (600 g.) in carbon disulphide (1·2 l.) at 0° and the crude dibromo*iso*valeric acid (m. p. 107°; 800 g.) was refluxed with sodium carbonate (660 g.) and water (2·5 l.) for 30 minutes. Steam-distillation yielded crude *iso*butenyl bromide which was dried ($CaCl_2$) and fractionated from a small piece of sodium. The pure bromide (130 g.) had b. p. 91—92°/760 mm., n_{D}^{22} 1·4610 (Farrell and Bachman, *loc. cit.*, give b. p. 90—91° , n_{D}^{20}1·4625; Braude and Timmons, *loc. cit.*, give b. p. 91·0—91·3°, n_{D}^{21} 1·4603) and reacted with finely cut lithium in sodium-dried ether after an induction period of 30 minutes. All condensations were carried out under nitrogen using the apparatus previously described.

Mesityl Oxide (I).—(a) *From lithium acetate*. To a suspension of anhydrous lithium acetate (33 g., 0·5 mol.) and lithium (6·9 g., 1 mol.) in ether (1 l.), a solution of *iso*butenyl bromide (68 g., 0·5 mol.) was added during 30 minutes. After 24 hours' stirring, the reaction mixture was cooled in a solid carbon dioxide–methanol bath and treated with excess of saturated aqueous ammonium chloride solution (500 ml.). Isolation of the products in the usual way afforded mesityl oxide (18 g., 36%) (identified by the 2 : 4-dinitrophenylhydrazone, m. p. 203°, undepressed on admixture with an authentic specimen) and 2 : 5-dimethylhexa-2 : 4-diene (7 g., 26%) (identified by the dihydrobromide, m. p. 66°; Braude and Timmons, *loc. cit.*, give m. p. 68°).

(b) *From acetyl chloride*. A solution of *iso*butenyl-lithium (from Li, 8·3 g.) in ether (1·5 l.) was filtered through glass wool under nitrogen pressure, and then added rapidly to a solution of acetyl chloride (43 ml.) in ether (50 ml.) at 0°. After 2 hours' stirring and working up in the usual way, mesityl oxide (11 g., 19%) and 2 : 5-dimethylhexa-2 : 4-diene (8 g., 30%) were obtained. No ketone was isolated from an experiment in which acetyl chloride was added directly to the *iso*butenyl-lithium solution at 0°.

(c) *From methyl cyanide*. No significant amount of mesityl oxide was obtained from the reaction between methyl cyanide (0·25 mol.) and *iso*butenyl-lithium (0·25 mol.), the main product consisting of high-boiling nitrogen-containing materials.

Phenyl iso*Butenyl Ketone* (II).—Anhydrous lithium benzoate (65 g.) was treated with *iso*butenyl-lithium (from Li, 6·9 g.) as above to give phenyl *iso*butenyl ketone (32 g., 40%), a pale yellow liquid, b. p. 120—121°/4 mm., n_{D}^{19} 1·5598 (Found : C, 82·1; H, 7·6. $C_{11}H_{12}O$ requires C, 82·5; H, 7·6%) (Kohler, *Amer. Chem. J.*, 1909, **42**, 398, gives b. p. 148°/22 mm.; Blaise and Herman, *Ann. Chim.*, 1911, **23**, 530, give b. p. 117°/10 mm., Darzens, *Compt. rend.*, 1929, **189**, 767, gives b. p. 134°/12 mm.) Light absorption in ethanol: Max. 2590 and 3410 A., ε = 19,600 and 140. The *p*-nitrophenylhydrazone crystallised from methanol in orange crystals, m. p. 168°, unchanged after chromatography on alumina using benzene–chloroform and after fusion (Found : C, 68·9; H, 6·2; N, 14·2. Calc. for $C_{17}H_{11}O_2N_3$: C, 69·1; H, 5·8; N, 14·2%) (Blaise and Herman, *loc. cit.*, give m. p. 132°). Light absorption in chloroform : Max. 3080 and 4250 A., ε = 5,300 and 35,400. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol in deep-red plates, m. p. 185—186° (Found : C, 59·9; H, 4·9; N, 16·7. $C_{17}H_{16}O_4N_4$ requires C, 60·0; H, 4·7; N, 16·5%). Light absorption in chloroform : Max. 3910 A., ε = 29,000; inflections 2560 and 2780 A., ε = 17,700 and 11,600. No semicarbazone could be obtained under the usual conditions. Hydrogenation of the ketone (3 g.) in ethyl acetate (50 ml.) in the presence of platinic oxide resulted in the uptake of 420 ml. of hydrogen at 20°/760 mm. (Calc., 420 ml.) and gave phenyl *iso*butyl ketone (2·5 g.), b. p. 108°/16 mm., n_{D}^{19} 1·5108 (Schroeter, *Ber.*, 1907, **40**, 1601, gives b. p. 128°/25 mm., n_{D}^{15} 1·5139), which was characterised by the oxime, m. p. 76—77° (Rheinboldt and Roleff, *Ber.*, 1924, **57**, 1923, give m. p. 74°), semicarbazone, m. p. 209—210° (Tiffeneau and Levy, *Compt. rend.*, 1926, **183**, 970, give 210°), and 2 : 4-*dinitrophenylhydrazone*, m. p. 136° (Found : C, 59·3; H, 5·3; N, 16·0. $C_{17}H_{18}O_4N_4$ requires C, 59·7; H, 5·3; N, 16·4%). Light absorption of the last in chloroform : Max. 3860 A., ε = 25,700.

*Phenylmethyl*iso*butenylcarbinol* (2-*Phenyl*-4-*methylpent*-3-*en*-2-*ol*) (IV).—Phenyl *iso*butenyl ketone (13 g.) in ether (20 ml.) was added to methylmagnesium bromide (from Mg, 2·3 g.) in ether (250 ml.) at 0°. After 2·5 hours, the complex was decomposed with saturated ammonium chloride solution (150 ml.) to give the carbinol (13 g., 91%), b. p. 66°/10^{-4} mm., n_{D}^{20} 1·5289, $\varepsilon < 2000$ at 2580 A. (Ravier, *Compt.*

rend., 1934, **198**, 1786, gives b. p. 95°/9 mm., n_D^{20} 1·534; Braude and Timmons, *loc. cit.*, give b. p. 64°/10^{-4} mm., n_D^{17} 1·5283).

Propenyl iso*Butenyl Ketone* (III).—(a) *From lithium crotonate.* Condensation of anhydrous lithium crotonate (45 g., 0·5 mol.) with *iso*butenyl-lithium as above and fractionation of the products yielded *propenyl* iso*butenyl ketone* (17 g., 30%), a pale yellow liquid, b. p. 72°/16 mm., n_D^{21} 1·4922 (Found : C, 76·9; H, 9·9. $C_8H_{12}O$ requires C, 77·4; H, 9·8%). Light absorption in ethanol : Max. 2560 and 3450 A., ε = 16,500 and 870. The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol in deep-red plates, m. p. 141° (Found : C, 55·4; H, 5·4; N, 18·4. $C_{14}H_{16}O_4N_4$ requires C, 55·3; H, 5·3; N, 18·4%). Light absorption in chloroform : Max. 2590 and 3870 A., ε = 18,600 and 34,200. No semicarbazone could be obtained under the usual conditions. Hydrogenation of the ketone (3 g.) in ethyl acetate (50 ml.) in the presence of platinic oxide resulted in the uptake of 1100 ml. of hydrogen at 17°/766 mm. (Calc., 1150 ml.) and gave propyl *iso*butyl ketone (2·5 g.), b. p. 154°/760 mm., n_D^{20} 1·4098 (semicarbazone, m. p. 124—125°).

(b) *From crotonyl chloride.* Addition of a solution of *iso*butenyl-lithium to an ethereal solution of the chloride (48 ml.), and isolation of the products as above, afforded the ketone (6 g., 5%) (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 141°).

iso*Butyl* iso*Butenyl Ketone* (V).—Propenyl *iso*butenyl ketone (7 g.) in ether (10 ml.) was treated with methylmagnesium bromide (from Mg, 1·4 g.) in ether (150 ml.). When worked up in the usual way, iso*butyl* iso*butenyl ketone* (4·5 g., 66%) was obtained as a colourless liquid, b. p. 31°/0·1 mm., n_D^{17} 1·4534 (Found : C, 77·1; H, 11·9. $C_9H_{16}O$ requires C, 77·1; H, 11·5%). Light absorption in ethanol : Max. 2390 and 3230 A., ε = 11,200 and 530, respectively. The 2 : 4-*dinitrophenylhydrazone* was chromatographed on alumina from benzene solution and crystallised from methanol in red plates, m. p. 92° (Found : N, 17·9. $C_{15}H_{20}O_4N_4$ requires N, 17·5%). Light absorption in chloroform : Max. 3720 A., ε = 28,500. No trace of a second 2 : 4-dinitrophenylhydrazone was obtained. The semicarbazone separated from light petroleum (b. p. 100—120°), having m. p. 137—138° (Paal, *Ber.*, 1912, **45**, 2226, gives m. p. 133—134°).

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