The Reaction of Chloroacetone with Aryl Grignard Reagents.

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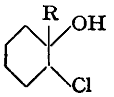
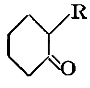
The products obtained by the reaction named in the title vary according to the nature of the aryl group.

THE reaction of 2-chloro*cyclo*hexanone with aryl Grignard reagents (Huang, *J. Org. Chem.*, in the press) proceeds by normal addition of the reagent to the carbonyl group; the resulting complex can then give rise to either the chlorohydrin (I) or the rearranged ketone (II) according to whether R is of low or high electropositivity, respectively. It seemed of interest to study the same reaction with chloroacetone, the simplest member of the chloroketones and free from steric complications.

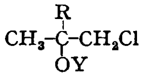
It is known that chloroacetone on reaction with phenylmagnesium bromide and subsequent hydrolysis furnishes the normal addition product, namely, the chlorohydrin (III), but that heating of the magnesium complex before hydrolysis results in a rearranged product, phenylacetone (Tiffeneau, *Ann. Chim.*, 1907, **10**, 367). The action on chloroacetone of a two-fold excess of Grignard reagent containing the typical aromatic groups has now given the following results.



(I)



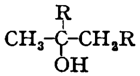
(II)



$$CH_3\text{-}\overset{R}{\underset{OY}{C}}\text{-}CH_2Cl$$

(III) Y = H

(IV) Y = MgX



$$CH_3\text{-}\overset{R}{\underset{OH}{C}}\text{-}CH_2R$$

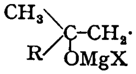
(V)

$CH_3{\cdot}CO{\cdot}CH_2R$

(VI)

$CH_3{\cdot}CR{:}CHR$

(VII)



(VIII)

(i) Strongly electron-releasing groups (*p*-ethoxyphenyl and *p*-methoxyphenyl) yield exclusively the substituted stilbenes (VII), undoubtedly derived from the alcohols (V) by dehydration. When, however, only a 0·5 mole excess of the reagent was used, the ketone (VI; R = p-MeO·C_6H_4) also was isolated in small yields. (ii) Weakly electron-releasing groups (*m*- and *p*-chlorophenyl) furnished the chlorohydrins (III) only. (iii) An *ortho*-substituted aryl group (*o*-methoxyphenyl) also yielded the chlorohydrin (III).

As with 2-chloro*cyclo*hexanone, therefore, the ultimate product of the reaction depends on the nature of the aryl group, highly electropositive groups leading to rearranged products. In the former case, however, the *cyclo*hexanone (II) was obtained, and it is not clear whether rearrangement had taken place before or after hydrolysis of the magnesium complex. With chloroacetone it appears probable that this complex had undergone rearrangement to the ketone (VI), which then reacted with more Grignard reagent to give the alcohol (V). This rearrangement might proceed *via* a free-radical intermediate such as (VIII), which could be generated from the complex (IV) by a one-electron transfer to the chlorine atom either from unchanged magnesium in the Grignard reagent, or from a component of the equilibrium $2RMgX \rightleftharpoons R_2Mg + MgX_2$. The fact that a filtered Grignard solution did not alter the course of the reaction, however, excludes the former possibility.

EXPERIMENTAL

Microanalyses were carried out in the microanalytical laboratory, Organic Chemistry Department, Imperial College of Science and Technology (Mr. F. H. Oliver), London.

Reaction of Chloroacetone with p-*Ethoxyphenylmagnesium Bromide.*—Chloroacetone (9·2 g., 0·10 mole) in ether (50 c.c.) was added during 0·5 hr. with stirring to the Grignard reagent prepared from *p*-bromophenetole (44 g., 0·20 mole) and magnesium (5·3 g., 0·22 mole) in ether (*ca.* 100 c.c.) with external cooling (ice and water). Stirring was then continued for 1 hr. at room temperature (28°). Next day the mixture was decomposed with concentrated aqueous ammonium chloride, and the product taken up in ether, and washed with aqueous ammonium chloride, then water; the solution was filtered from an ether-insoluble amorphous solid (*ca.* 2 g.) and dried (Na_2SO_4). The ether was evaporated, and after being heated on the steam-bath for 0·5 hr. and cooled the product solidified. It was treated with a little ethanol and filtered off, giving 4 : 4′-*diethoxy*-α-*methylstilbene* (crude, 12 g.) which crystallised from ethanol in woolly needles, m. p. 108—109° (Found: C, 80·9; H, 8·1. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·85%).

Reaction with p-*Methoxyphenylmagnesium Bromide*.—(a) *With filtered Grignard reagent.* The product from chloroacetone (7·3 g., 0·08 mole) and *p*-methoxyphenylmagnesium bromide (0·18 mole, filtered under nitrogen pressure through glass wool) was worked up as before, yielding 4 : 4′-dimethoxy-α-methylstilbene (18 g.), m. p. 124° (Found: C, 80·0; H, 7·1. Calc. for $C_{17}H_{18}O_2$: C, 80·3; H, 7·1%). Dodds, Goldberg, Grunfeld, Lawson, Saffer, and Robinson report m. p. 123—124° (*Proc. Roy. Soc.*, 1944, *B*, **132**, 83).

(b) *With* 0·5 *mole excess of the Grignard reagent.* The product from chloroacetone (13·8 g.) gave in part 4 : 4′-dimethoxy-α-methylstilbene (8·5 g.) which separated as a solid and was filtered off. The filtrate was distilled, giving (i) a yellow liquid, b. p. 102—104°/0·5 mm. (1·6 g.), which was mainly *p*-methoxyphenylacetone, and (ii) a tarry residue (12 g.). Fraction (i) quickly darkened, but readily formed *p*-methoxyphenylacetone semicarbazone, m. p. 174—176° (from ethanol) (lit., m. p. 175), and a 2 : 4-*dinitrophenylhydrazone*, orange needles (from ethanol), m. p. 104—105° (Found: C, 55·7; H, 4·5. $C_{16}H_{16}O_5N_4$ requires C, 55·7; H, 4·65%).

p-Chlorophenylmagnesium bromide (0·2 mole), on reacting with chloroacetone (9·2 g., 0·1 mole), gave, as the main product, 1-*chloro*-2-p-*chlorophenylpropan*-2-*ol* (12 g.), b. p. 100—102°/1 mm., n_D^{20} 1·5568. This appeared to be contaminated with traces of a ketone (probably VI) which could not be effectively removed by distillation. A portion (2·5 g.), treated with Girard reagent P (1 g.) in the usual manner, afforded a pure sample, b. p. 100°/1 mm., n_D^{20} 1·5554 (Found: C, 53·0; H, 5·0. $C_9H_{10}OCl_2$ requires C, 52·7; H, 4·9%). The ketonic material (<0·1 g.) extracted by the reagent gave small quantities of an orange-red 2 : 4-dinitrophenylhydrazone.

m-Chlorophenylmagnesium bromide (0·068 mole) and chloroacetone (3·1 g., 0·034 mole) gave 1-*chloro*-2-m-*chlorophenylpropan*-2-*ol* (4·2 g.), b. p. 103—105°/1 mm., n_D^{21} 1·5558 (Found: Cl, 34·2. $C_9H_{10}OCl_2$ requires Cl, 34·6%).

o-Methoxyphenylmagnesium bromide (0·20 mole) and chloroacetone (11 g., 0·12 mole) yielded 1-*chloro*-2-o-*methoxyphenylpropan*-2-*ol* (10·2 g.), b. p. 107—110°/0·5 mm., n_D^{23} 1·5442 (Found: C, 60·1; H, 6·5; Cl, 17·8. $C_{10}H_{13}O_2Cl$ requires C, 59·9; H, 6·5; Cl, 17·7%).

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