[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Chemistry of 1,1,1-Trifluoropropanone. II.[1] The Reactions of 4-Methyl-1,1,1,-5,5,5-hexafluoro-3-penten-2-one with Methylmagnesium Iodide[2,3]

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The Aldol condensation of 1,1,1-trifluoropropanone (I) has been studied using potassium hydroxide, sodium hydroxide, sodium amide, sodium ethoxide, pyridine and dimethylaniline as catalysts. A 56% yield of 4-hydroxy-4-methyl-1,1,1,5,5,5-hexafluoro-2-pentanone (II) was obtained using sodium amide in chloroform at −10°. Dehydration of II gave 4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one (III). Reaction of III with methylmagnesium iodide gave 2,4-dimethyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol (IV), and reduction of IV gave 2,4-dimethyl-1,1,1,5,5,5-hexafluoro-2-pentanol (V). Compound V was identical to that obtained by the reduction of compound III to give compound VI and the subsequent reaction of VI with methylmagnesium iodide, thus proving the structure of IV.

Discussion

Since the presence of a perfluoroalkyl group adjacent to a functional group modifies the chemical and physical properties of the latter, it was of interest to investigate the aldol condensation of 1,1,1-trifluoropropanone (I). Compound I was treated with basic reagents under varying conditions to determine the conditions for its self condensation; the best yields of 4-hydroxy-4-methyl-1,1,1,5,5,5-hexafluoro-2-pentanone (II) were obtained using either sodium amide in chloroform (56–65%) or sodium ethoxide in ether (58–64%) at temperatures less than 0°. Potassium hydroxide was found to be unsatisfactory because it caused subsequent hydrolysis of II to fluoroform and 3-trifluoromethyl-3-hydroxybutanoic acid; in spite of this side reaction, a 40% yield of II was obtained. When aqueous sodium hydroxide was employed, hydrolysis was the major reaction.[4] Compound II was identified by its reaction with aqueous base producing fluoroform and 3-trifluoromethyl-3-hydroxybutyric acid, which was isolated as its *p*-phenylphenacyl ester and its amide. Compound II forms a stable, solid hydrate and gives a 2,4-dinitrophenylhydrazone. Compound II was dehydrated to 4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one by sulfuric acid or phosphorus pentoxide. The dehydration of II occurred much less readily than the dehydration of diacetone alcohol and II was unchanged when treated with reagents commonly used for the formation of mesityl oxide.

The addition reactions of α,β-unsaturated ketones have been the subject of intense study during the past forty years. Some reagents add 1,2 to the carbonyl group, others add 3,4 to the ethylenic linkage, still others add 1,4 to the conjugated system and a final group of reagents adds both 1,2 to the carbonyl group and 1,4 to the conjugated system. The addition of ammonia to the olefin, 4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one, in the presence of ammonium hydroxide, takes place with greater ease than in the case of mesityl oxide.[7] The direction of addition of this anionic reagent to the double bond is undoubtedly 1,4 as is the case for mesityl oxide and ethyl 4,4,4-trifluorocrotonate.[8] The product obtained was the stable hydrate of 4-amino-4-methyl-1,1,1,5,5,5-hexafluoro-2-pentanone.

Grignard reagents may add 1,2 or 1,4 and the formation of the unsaturated alcohols is the result of 1,2-addition to the carbonyl group; the formation of saturated ketones may be due either to direct addition of the reagent to the ethylenic linkage or to 1,4-addition of the reagent to the conjugated system followed by ketonization. With the Grignard reagent the mechanism of 1,4-addition has been established and the effect of substituents on the mode of addition has been determined.[9] 4-Methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one is an α,β-unsaturated ketone possessing two trifluoromethyl groups and it was of interest to determine how this compound would add a nucleophilic reagent such as methylmagnesium iodide. This Grignard reagent possesses no β-hydrogen atoms and complications due to reduction would not be introduced.[10,11]

Colonge[12] states that in the aliphatic series addition to the conjugated system (1,4-addition) is never as important as normal addition to the carbonyl group (1,2-addition). 1,2- and 1,4-additions may be regarded as competitive, and hence the reactivity of the carbonyl group plays an important role in determining the mode of addition. In α,β-unsaturated carbonyl compounds ($RCOCR^1=CR^2R^3$) the atom or radical R— would naturally have a pronounced effect on the reactivity of the carbonyl group. The question then arises as to

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(1) Paper I in this series, E. T. McBee and T. M. Burton, THIS JOURNAL, **74**, 3902 (1952).

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(3) In part from a thesis submitted by R. J. Kennedy to the Graduate School, Purdue University, in partial fulfillment of the requirements for the degree of Master of Science, 1956.

(4) The marked effect of fluorine substitution on the chemical behavior of an organic compound is strikingly demonstrated by a comparison of the conditions under which acetone forms diacetone alcohol and 1,1,1-trifluoroacetone forms "hexafluorodiacetone alcohol." In the presence of potassium hydroxide acetone forms an equilibrium mixture containing 2 to 3% of diacetone alcohol.[5] The slow step in the reaction has been shown to be the reaction of the anion, formed by the action of the base on the ketone, with another molecule of acetone.[6] A small amount of potassium hydroxide was added to I to determine whether a similar equilibrium was formed by this fluorine-containing ketone. A vigorous reaction ensued with complete conversion of the ketone to poly-condensation products.

(5) H. Hammersten, *Ann.*, **421**, 312 (1920).

(6) V K. LaMer and M. L. Miller, THIS JOURNAL, **57**, 2674 (1935).

(7) P. R. Haesler, *ibid.*, **47**, 1195 (1925).

(8) E. T. McBee, O. R. Pierce and D. D. Smith, *ibid.*, **76**, 3725 (1954).

(9) M. S. Kharasch and P. O. Tawney, *ibid.*, **63**, 2308 (1941).

(10) E. T. McBee, J. F. Higgins and O. R. Pierce, *ibid.*, **74**, 1387, 1736 (1952).

(11) E. T. McBee, O. R. Pierce and D. D. Meyer, *ibid.*, **77**, 83 (1955).

(12) H. Colonge, *Bull. soc. chim.*, **2**, 754 (1935).

whether this effect is predominantly electronic or steric.

If the effect is predominantly electronic the reactivity of the carbonyl group should increase as the "electronegativity" of R— decreases and the chance of 1,2-addition occurring should be greatly enhanced.[13,14] If the steric factor is most important, the bulkier the group R— is the less the reactivity of the carbonyl group and the greater the inhibition of 1,2-addition. In 1,2-addition, R^2 and R^3 would be expected to exert a relatively minor electronic effect and a negligible steric effect. On the basis of the evidence now available, the steric effect would appear to be the more important one. Mesityl oxide undergoes 1,2-addition chiefly[15] whereas with benzalacetone, 1,4-addition predominates.[16]

When methylmagnesium iodide was added to 4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one (II) the product was a tertiary alcohol IV resulting from 1,2-addition (70%). This may be explained as follows: sterically, a trifluoromethyl group is approximately the same size as a methyl group, and since the non-fluorine-containing isomer, *i.e.*, mesityl oxide, yields 70–80% of a 1,2-addition product, this is what would have been expected. Electronically, the inductive effect exerted by a trifluoromethyl group must either be negligible or unimportant in relation to the steric factor involved.

The structure of IV was proven by selective hydrogenation of III to give a saturated ketone (VI) which on reaction with methylmagnesium iodide gave V. This product (V) was identical to that obtained on catalytic reduction of IV, and possessed identical infrared spectra.

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Experimental[17]

4-Hydroxy-4-methyl-1,1,1,5,5,5-hexafluoro-2-pentanone.—One gram atom of sodium sand was prepared in xylene and the xylene removed by means of a sintered-glass filter-stick. The sodium sand was washed twice with ether and covered with 200 ml. of ether. With vigorous stirring, 60 g. (1.3 moles) of absolute ethyl alcohol was added to the sodium sand during 30 min. To the well-stirred ether solution of sodium ethoxide was added 100 g. (0.89 mole) of 1,1,1-trifluoropropanone,[1,18] the temperature of the reaction mixture being kept below 0°. After the solution had been stirred for 1–2 hr. it was poured onto a mixture of 100 ml. of concentrated sulfuric acid and 1000 g. of ice. The solid hydrate was removed by filtration and the aqueous layer neutralized and extracted with ether. The ether solution, on distillation, gave 20 g. (20%) of crude condensation product, b.p. 78–94°. These liquid products will revert, on standing in air, to the solid hydrate, m.p. 80–81°. The solid product obtained from filtration of the hydrolysis mixture was recrystallized from a petroleum ether–benzene mixture and weighed 42 g. (39%), m.p. 80–81°.

Anal. Calcd. for $C_6H_3F_6O_2$: C, 32.12; H, 2.98. Found: C, 32.09; H, 2.69.

4-Methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one (III).—From a mixture prepared by adding 250 g. of 98% sulfuric acid to 55 g. (0.244 mole) of 4-hydroxy-4-methyl-1,1,1,-5,5,5-hexafluoro-2-pentanone hydrate there was distilled 26.6 g. (53%) of III, b.p. 76°, n^{20}_D 1.3260.

Anal. Calcd. for $C_6H_4F_6O$ (III): C, 34.90; H, 1.95. Found: C, 34.76; H, 2.13.

2,4-Dimethyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol (IV).—To a well-stirred ether solution containing 35 g. (0.21 mole) of methylmagnesium iodide was added 29.8 g. (0.21 mole) of 4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one. The solution was stirred for 1 hr. and hydrolyzed with 200 ml. of a 5% solution of hydrochloric acid. The aqueous layer was separated, neutralized with a saturated solution of sodium carbonate and extracted with two 100-ml. portions of ether. The ether washings were combined, extracted with a saturated sodium sulfite solution, and dried over anhydrous magnesium sulfate. The ether solution, on distillation, gave 26 g. (61.5%) of 2,4-dimethyl-2-hydroxy-1,1,1,5,5,5-hexafluoro-3-penten-2-ol (IV), b.p. 76° (130 mm.), n^{20}_D 1.3545, d^{25}_4 1.332.

Anal. Calcd. for $C_7H_8F_6O$: C, 37.86; H, 3.63; *MR*D, 36.42. Found: C, 37.56; H, 3.68; *MR*D, 36.28.

4-Methyl-1,1,1,5,5,5-hexafluoro-2-pentanone (V).—When 16 g. (0.077 mole) of 4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one in 50 ml. of glacial acetic acid and 0.1 g. of Adams catalyst was hydrogenated at 44 lb. pressure the uptake ceased after 45 min.; separation from the catalyst by filtration followed by distillation gave 11 g. (67%) of 4-methyl-1,1,1,5,5,5-hexafluoro-2-pentanone, b.p. 87°, n^{20}_D 1.3160, d^{25}_4 1.338.

Anal. Calcd. for $C_6H_6F_6O$: C, 34.63; H, 2.90; *MR*D, 30.76. Found: C, 34.35; H, 3.18; *MR*D, 30.48.

2,4-Dimethyl-4-hydroxyl-1,1,1,5,5,5-hexafluoro-2-pentanol (VI).—To a well-stirred ether solution containing 20.7 g. (0.125 mole) of methylmagnesium iodide was added 8 g. (0.038 mole) of 4-methyl-1,1,1,5,5,5-hexafluoro-2-pentanone. The solution was stirred for 30 min. and then hydrolyzed with 100 ml. of a 5% solution of hydrochloric acid. The ether layer was separated and combined with the ether extracts of the neutral aqueous layer. Upon distillation of the ether layer 5.8 g. (68%) of 2,4-dimethyl-4-hydroxy-1,1,1,5,5,5-hexafluoro-2-pentanol was obtained, b.p. 87° (130 mm.), n^{20}_D 1.3525, d^{25}_4 1.335.

Anal. Calcd. for $C_7H_{10}F_6O$: C, 37.53; H, 4.50; *MR*D, 36.89. Found: C, 37.71; H, 4.76; *MR*D, 36.43.

Catalytic Hydrogenation of 2,4-Dimethyl-1,1,1,5,5,5 hexafluoro-3-penten-2-ol.—When 2,4-dimethyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol in glacial acetic acid was reduced at 35 pounds hydrogen pressure with 0.1 g. of Adams catalyst the same product was obtained as when 4-methylhexafluoro-3-penten-2-one was treated with methylmagnesium iodide b.p. 87° (130 mm.), n^{20}_D 1.3526, d^{25}_4 1.335.

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(13) H. Hibbert, *J. Chem. Soc.*, **101**, 341 (1912).

(14) R. N. Lewis and J. R. Wright, This Journal, **74**, 1257 (1952).

(15) G. Dupont and L. M. Mcnut, *Bull. soc. chim.*, **6**, 1215 (1939).

(16) E. P. Kohler, *Am. Chem. J.*, **38**, 511 (1907).

(17) All temperatures are uncorrected. Infrared spectra were determined by H. Susi on a Perkin–Elmer model 21 spectrophotometer.

(18) E. T. McBee and T. M. Burton, This Journal, **74**, 3902 (1952).