

Dry Ice was added. After the mixture had been treated with hydrochloric acid and diluted with ether and tetrahydrofuran, the organic layer was extracted with excess aqueous sodium hydroxide. The basic solution was cooled to 0° and neutralized with cold hydrochloric acid. The yellow precipitate which formed was extracted with tetrahydrofuran with the aid of added saturated aqueous sodium chloride and then recrystallized by addition of petroleum ether. The solid obtained was filtered and washed with ether. Evaporation of the ether washings and recrystallization of the residue from benzene and ether-petroleum ether gave ferrocenecarboxylic acid (0.06 g., 0.00026 mole, 16%) which was identified by comparison with an authentic sample.

Remaining as a residue from the ether washing was 1,1'-ferrocenedicarboxylic acid (0.26 g., 0.0016 mole, 59%) which did not melt or decompose below 280°; lit.,^{2b} no melting or decomposition below 250°. The infrared spectrum of the 1,1'-ferrocenedicarboxylic acid obtained was identical with an authentic sample. The identity of the dicarboxylic acid was confirmed by esterification with methanol catalyzed by hydrochloric acid; chromatography on alumina and vacuum sublimation of the product gave dimethyl 1,1'-ferrocenedicarboxylate (73% conversion), m.p. 112–113°; lit.^{2b} m.p. 114–115°.

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[CONTRIBUTION FROM THE DOW CORNING CORP.]

Reaction of 3,3,3-Trifluoropropylmagnesium Bromide with Carbonyl Compounds

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The reaction of 3,3,3-trifluoropropylmagnesium bromide with methyl trifluoroacetate and 1,1,1,5,5,5-hexafluoro-2-pentanone in both ether and tetrahydrofuran has shown the Grignard to be only a weak reducing agent. In the case of methyl trifluoroacetate, the principal product was a solid which on hydrolysis yielded the hydrate of 1,1,1,5,5,5-hexafluoro-2-pentanone. Evidence for the structure of this solid intermediate, $\text{CF}_3\text{CH}_2\text{CH}_2\text{C}(\text{OCH}_3)(\text{OMgBr})\text{CF}_3$, and a reaction mechanism involving this intermediate are presented.

Fluorine-containing Grignard reagents have been studied extensively and, in particular, the preparation and reactions of the perfluoroalkylmagnesium halides have received much attention.¹ However, derivatives of the type $\text{R}_f\text{CH}_2\text{CH}_2\text{MgX}$ ($\text{R}_f = \text{CF}_3, \text{C}_2\text{F}_5$, etc.) have been studied only briefly in reactions of limited scope.^{2,3} In this laboratory a study was undertaken to ascertain the differences between a Grignard of the above type and a nonhalogenated Grignard in reactions in which reduction by the Grignard reagent generally occurs. For this purpose, the reaction of 3,3,3-trifluoropropylmagnesium bromide (I) with fluorine-containing carbonyl compounds was chosen.

The tendency of fluorine-containing esters to undergo reduction in preference to addition with certain Grignard reagents has been extensively discussed.^{2,4–8} In this study, the reaction of I with methyl trifluoroacetate in ether solution

formed an insoluble material which on hydrolysis and further treatment with phosphorus pentoxide gave 1,1,1,5,5,5-hexafluoro-2-pentanone (II). No reduction was observed. A similar reaction conducted in tetrahydrofuran indicated no formation of a solid precipitate and yielded II as well as 1,1,1,7,7,7-hexafluoro-4-(trifluoromethyl)-4-heptanol (III) and 1,1,1,5,5,5-hexafluoro-2-pentanol (IV). The last compound, resulting from reduction by the Grignard, was formed in only 12% yield. In an effort to increase the yield of reduction product (IV), the reaction was conducted in the presence of an excess of isopropylmagnesium bromide in ether solution.⁸ The principal product of this reaction was 1,1,1-trifluoro-3-methyl-2-butanol (V) as well as lesser amounts of II, III and IV. In contrast to the poor reducing action of I, the reaction of methyl trifluoroacetate with *n*-propylmagnesium bromide in ether was found to give only 1,1,1-trifluoro-2-pentanol (VI), the reduction product.

Addition of magnesium bromide to the methyl trifluoroacetate prior to the addition of I in tetrahydrofuran solution changed the product distribution markedly. The principal product was the ketone (II) with only trace amounts of III and IV. A similar reaction conducted in ether solution gave only II, as was the case in the absence of magnesium bromide.

The reaction of II with trifluoropropyl Grignard in ether formed the addition product (III) in good yield together with a small yield of the reduction product (IV). Addition of magnesium

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(2) O. R. Pierce, E. T. McBee, and R. E. Cline, *J. Am. Chem. Soc.*, **75**, 5618 (1958).

(3) E. T. McBee and A. Truchan, *J. Am. Chem. Soc.*, **70**, 2910 (1948).

(4) K. N. Campbell, J. O. Knoblock and Barbara K. Campbell, *J. Am. Chem. Soc.*, **72**, 4380 (1950).

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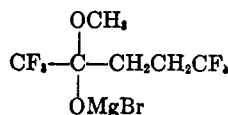
(6) E. T. McBee, O. R. Pierce, and J. F. Higgins, *J. Am. Chem. Soc.*, **74**, 1736 (1952).

(7) E. T. McBee, O. R. Pierce, and M. C. Chen, *J. Am. Chem. Soc.*, **75**, 2324 (1953).

(8) O. R. Pierce, J. C. Siegle, and E. T. McBee, *J. Am. Chem. Soc.*, **75**, 6324 (1953).

bromide to the solution decreased the amount of reduction as would be expected.^{9,10} However, a corresponding increase in addition product was not obtained.

The nature of the solid obtained in reactions conducted in ether solution was briefly examined. Hydrolysis gave a mixture of the hydrate of II, methanol and ether. No 1,1,1-trifluoropropane, arising from the hydrolysis of the Grignard, could be detected. These facts together with elemental analysis suggest the material is the ether solvated form of the following:



EXPERIMENTAL

Starting materials. 1,1,1-Trifluoro-3-bromopropane¹¹ was available in research quantities. Trifluoroacetic acid was purchased from the Minnesota Mining and Manufacturing Co. and esterified by conventional methods.

Technique. The reactions were conducted in three necked flasks equipped with a condenser, mercury-sealed stirrer and additional funnel. A Dry Ice-cooled trap was connected to the condenser. The Grignard reagent was prepared separately in a conventional manner and filtered through a glass wool plug under a nitrogen atmosphere into the reaction flask. In most cases, the carbonyl compound was added to the Grignard. All reactions were cooled by an ice bath.

After reaction was complete (usually a 2-hr. period), the mixture was hydrolyzed by adding 10% sulfuric acid. The organic layer was washed three times with water and the combined aqueous phases were extracted with three 50 ml. portions of ether. The various solvent solutions were combined, dried with Drierite, and distilled using a Todd fractional distillation apparatus.

Reaction of I with methyl trifluoroacetate (a) Ether solution. Methyl trifluoroacetate (64 g., 0.5 mole) was added with stirring to a solution of I prepared from 1,1,1-trifluoro-3-bromopropane (194.7 g., 1.1 moles) and magnesium (24.3 g., 1.0 g.-atom) in 600 ml. of diethyl ether. A heavy precipitate was noted at the end of the addition. Hydrolysis and fractionation of the reaction mixture gave an impure product containing water and boiling at 74–76° in approximately 70% yield. A small amount of 1,1,1-trifluoropropane, formed by the hydrolysis of I, was observed in the cold trap.

The product from several experiments was combined (392.0 g.) and cooled to 0°C. in a flask. Phosphorus pentoxide (339.0 g., 2.3 moles) was added in small portions with shaking to form a smooth paste. The flask was fitted with a Vigreux column, condenser, and receiver and the mixture heated slowly to 120° at which point a material distilled smoothly. Fractional distillation of this material gave 1,1,1,5,5,5-hexafluoro-2-pentanone (II) (374.0 g., 1.93 moles).¹²

(b) **Tetrahydrofuran solution.** Methyl trifluoroacetate (384.0 g., 3.0 moles) was added to a solution of I prepared from 1,1,1-trifluoro-3-bromopropane (1080 g., 6.1 moles)

and magnesium (145.8 g., 6.1 g.-atoms) in 3600 ml. of tetrahydrofuran. Much less precipitate was noted than in the case of an ether solvent. Hydrolysis and fractionation gave impure II (132 g.), b.p. 74–82° (approximately 23% yield), 1,1,1,5,5,5-hexafluoro-2-pentanol (IV) (72 g., 0.37 mole, 12% yield), b.p. 118°, n_D^{25} 1.3518, and 1,1,1,7,7,7-hexafluoro-4-(trifluoromethyl)-4-heptanol (III), b.p. 77° at 30 mm. n_D^{25} 1.3328 (464 g., 1.59 moles, 53% yield).

Anal. Calcd. for $\text{C}_8\text{H}_8\text{F}_8\text{O}$: C, 30.6; F, 58.2. Found: C, 31.1; F, 57.9. Calcd. for $\text{C}_8\text{H}_8\text{F}_7\text{O}$: C, 32.8; H, 3.3; F, 58.5. Found: C, 33.1; H, 3.8; F, 58.3.

Reaction of methyl trifluoroacetate with I and isopropylmagnesium bromide. A mixture of I and isopropylmagnesium bromide was prepared from 1,1,1-trifluoro-3-bromopropane (194.7 g., 1.1 moles), 2-bromopropane (170 g., 1.5 moles) and magnesium (60 g., 2.5 g.-atoms) in 2 l. of ether. Methyl trifluoroacetate (128 g., 1.0 mole) was added with stirring. Hydrolysis and fractionation gave 1,1,1-trifluoro-3-methyl-2-butanol⁸ (70 g., 0.5 mole, n_D^{25} 1.3518, 50% yield), IV (10 g., 0.05 mole, 5% yield), III (48 g., 0.18 mole, 18% yield) and impure II (approximately 30% yield). Propene (24 g., 0.55 mole) and 1,1,1-trifluoropropane (29 g., 0.3 mole) were found in the cold trap.

Reaction of methyl trifluoroacetate with *n*-propylmagnesium bromide. Methyl trifluoroacetate (64.0 g., 0.5 mole) was added to a solution of *n*-propylmagnesium bromide prepared from *n*-propyl bromide (135.3 g., 1.1 moles) and magnesium (24.3 g., 1.0 g.-atom) in 600 ml. of ether. Hydrolysis and fractional distillation gave 1,1,1-trifluoro-2-pentanol (50.0 g., 0.36 mole, b.p. 110°, 72% yield).¹³ Propene (13 g., 0.32 mole) was recovered from the trap.

Reaction of II with trifluoropropylmagnesium bromide. II (194.0 g., 1.0 mole) was added to a solution of Grignard reagent prepared from trifluorobromopropane (194.7 g., 1.1 moles) and magnesium in 600 ml. of ether. Hydrolysis and fractional distillation gave the impure II, yield ca. 15%, IV in 31% yield and III in 45% yield. Trifluoropropene (17 g., 0.18 mole) and trifluoropropane (7 g., 0.08 mole) were recovered from the trap.

Reactions in the presence of magnesium bromide (a) Methyl trifluoroacetate (64 g., 0.5 mole) was mixed with magnesium bromide (prepared from 0.6 mole of magnesium and 0.6 mole of bromine in tetrahydrofuran solvent⁹) and added to a tetrahydrofuran solution of I (194.7 g., 1.1 moles of $\text{CF}_3\text{CH}_2\text{CH}_2\text{Br}$, and 24 g., 1.0 mole of magnesium in 500 ml. of tetrahydrofuran). After hydrolysis and fractionation there was obtained impure II (about 61% yield), unchanged methyl trifluoroacetate (10% yield), trifluoroacetic acid (28%) and trace amounts of III and IV.

(b) An ether solution of I (97 g., 0.55 mole of 3-bromo-1,1,1-trifluoropropane, magnesium, 12 g., 0.5 g.-atom, and 350 ml. of diethyl ether) was added to an ether solution of II (97 g., 0.5 mole) and magnesium bromide (92 g., 0.5 mole). Hydrolysis and fractionation gave impure II (approximately 52% recovery) and III (54 g., 0.18 mole, 36% yield). No 3,3,3-trifluoro-1-propene was observed.

Studies of Grignard-ester complex. The solid formed on reaction of methyl trifluoroacetate with I in diethyl ether was treated as follows:

(a) The reaction mixture was hydrolyzed and the major part of the ether was removed by distillation. Phosphorus pentoxide (50.0 g.) was added and the fractionation was continued. II (167 g., 0.86 mole) was isolated in 86% yield.

(b) As soon as addition was complete, the solid was removed by filtration, rinsed with fresh ether, dried *in vacuo* for 30 min. at room temperature and analyzed immediately.

(c) After drying, the solid was suspended in fresh ether and hydrolyzed. No trifluoropropane or trifluoropropene was recovered. Fractional distillation gave impure II in approximately 62% yield. The ether solution remaining after

(9) C. G. Swain and H. B. Boyles, *J. Am. Chem. Soc.*, **73**, 870 (1951).

(10) E. T. McBee, O. R. Pierce, and D. D. Meyer, *J. Am. Chem. Soc.*, **77**, 83 (1955).

(11) O. W. Steward and O. R. Pierce, *J. Am. Chem. Soc.*, **81**, 1983 (1959).

(12) E. T. McBee, A. E. Kelly, and E. Rapkin, *J. Am. Chem. Soc.*, **72**, 5071 (1950).

(13) K. T. Dishart and R. Levine, *J. Am. Chem. Soc.*, **78**, 2268 (1956).

the solid had been removed was hydrolyzed. A trace of trifluoropropane was evolved. Fractional distillation yielded a trace of II.

When a similar run was made using a 2:1 ratio of trifluoropropylmagnesium bromide to methyl trifluoroacetate, hydrolysis of the solid gave equivalent results. Hydrolysis of the ether phase gave trifluoropropane in an amount corresponding to the excess Grignard reagent.

(d) After drying, the solid was hydrolyzed in the absence of solvent. Fractional distillation of the hydrolysis mixture gave ether (21 g., 0.28 mole) and methanol, isolated as an azeotropic mixture with II in low (15–20%) yield.

The analysis of the solid complex is given subsequently.

DISCUSSION

In the following discussion the structure of the Grignard reagent is written as RMgX , although it has been shown^{14,15} that the composition of a Grignard solution is probably closer to $\text{R}_2\text{Mg} + \text{MgX}_2 \rightleftharpoons 2 \text{RMgX}$. However, it has been pointed out¹⁶ that all forms of the Grignard reagent show the same reactivity and that the structure RMgX adequately describes the average composition of the mixture. All species are assumed to be solvated, but no attempt has been made to show the nature of the bonding between the Grignard reagent and the solvent molecule.

The mechanism of the reduction of a carbonyl compound by a Grignard has been well defined¹⁷ and probably applies in this case. The low amount of reduction obtained can be explained by the inability of I to release a pair of electrons due to the inductive effect of the trifluoromethyl grouping. As a consequence, the effect of magnesium bromide on the relative amounts of addition and reduction products was small in the case of II. However, in the case of methyl trifluoroacetate, magnesium bromide can interfere with the formation of a complex between the ester and I. Thus the subsequent intermolecular shift involved in the formation of the tertiary alcohol (III) would be minimized, accounting for the change in the product distribution.

The mechanism of the addition of a Grignard reagent to a carbonyl group is less clear, particularly in reactions involving an ester. It appears that the reaction sequence proposed by Grignard¹⁸ and supported by others^{19,20} is applicable to the reaction of I with methyl trifluoroacetate.

The alternate mechanism involving a free ketone intermediate^{21–23} is less attractive since the ketone

(14) Abegg, *Ber.*, **38**, 4112 (1905).

(15) Schlenk and Schlenk, *Ber.*, **62B**, 920 (1929).

(16) E. E. Royals, *Advanced Organic Chemistry*, Prentice-Hall, New York, 1954, p. 681.

(17) F. S. Whitmore, paper presented at 105th National Meeting, Amer. Chem. Soc., April, 1943, Atlantic City, N. J.

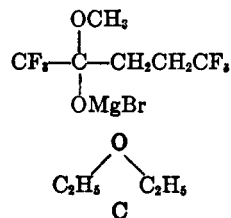
(18) V. Grignard, *Compt. rend.*, **132**, 336 (1901).

(19) A. A. Morton and L. V. Peakes, Jr., *J. Am. Chem. Soc.*, **55**, 2110 (1933).

(20) M. S. Kharash and O. Reinmuth, *Grignard Reactions of Non-metallic Substances*, Prentice-Hall, New York, 1954, p. 550.

(II) was found to react normally with I in both the free state and when complexed with magnesium bromide.

Further evidence for an intermediate similar to that proposed by Grignard, *i.e.*,



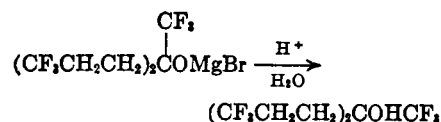
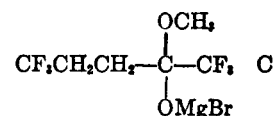
was found in the analysis of the solid. A complex such as this, when isolated from a reaction mixture and analyzed without further purification would not be expected to be a pure species. This is indicated by the analytical data.

Anal. Calcd. for C: C, 29.7; H, 4.2; F, 28.3; Mg, 5.9; Br, 19.9; Or — see text. Found: C, 26.3; F, 25.6; H, 4.3; Mg, 5.5; Br, 22.0; OR, 23.8.

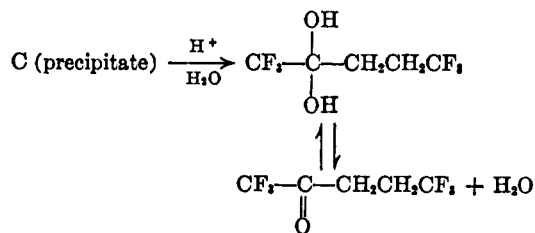
The theoretical methoxy content of C is 7.6%. However, the ether would also react with the reagents used in this determination. If the ether is assumed to react quantitatively, the value would be approximately three times this figure. A more precise calculation would not be valid and was not attempted.

In view of the evidence for an intermediate such as C, together with the semi-quantitative analytical data presented, the following scheme for the reaction of I with methyl trifluoroacetate is offered:

(1) in tetrahydrofuran



(2) in ether



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(21) Reformatsky, *J. Russ. Phys. Chem.*, **37**, 1905, 881.

(22) D. R. Boyd and H. H. Hatt, *J. Chem. Soc.*, **898** (1927).

(23) K. N. Campbell, J. O. Knoblock, and Barbara K. Campbell, *J. Am. Chem. Soc.*, **72**, 4380 (1950).