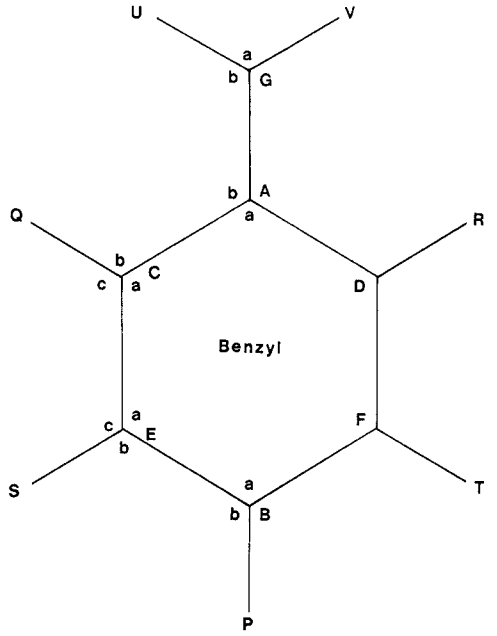

Figure 2. Structure and definitions of bond lengths and bond angles of the benzyl radical.

Table III. Expectation Values $\langle H \rangle$ of the Hamiltonian H_{op} and Expectation Values $\langle S^2 \rangle$ of the Spin Operator S^2 with Respect to the Wave Functions Ψ_{UHF} and Ψ_{ROHF} of the Phenyl and Benzyl Radicals

	phenyl	benzyl
$\langle H \rangle_{UHF}$	-229.988346	-268.761460
$\langle H \rangle_{ROHF}$	-229.725501	-265.837128
$\langle S^2 \rangle_{UHF}$	1.4970	1.4194
$\langle S^2 \rangle_{ROHF}$	0.7500	0.7500

in Table II. The bond lengths are expressed in terms of angstroms and the bond angles are expressed in terms of degrees. The bond lengths and bond angles of the phenyl radical are defined in Figure 1, and the corresponding quantities of the benzyl radical are defined in Figure 2.

Experimental data on the structures of the phenyl and benzyl radicals do not seem to be available, and it is not possible to decide which of the two sets of theoretical results, UHF or ROHF, are closer to experiment. On the other hand, the two sets of theoretical values are fairly similar. The root mean square deviation of the bond lengths is 0.014 Å for the phenyl radical, and it is 0.018 Å for the benzyl radical. The largest discrepancy is 0.04 Å for the CC bond length AG between the ring and the methyl group in the benzyl radical. The UHF bond lengths are generally a bit longer than the ROHF bond lengths, which is consistent with the results derived by Farnell, Pople, and Radom.[3] It follows also from the data in Tables I and II that the difference between the UHF and the ROHF bond angle predictions are quite small, especially if we bear in mind that the margin of error in the computed bond angles is usually taken as 0.1 or 0.2°. We feel that the agreement between the two sets of geometry predictions is good enough to encourage the use of the UHF method in those situations where the ROHF method is not feasible.

In Table III we list the expectation values $\langle H \rangle$ and $\langle S^2 \rangle$ of the Hamiltonian operator H_{op} and of the spin operator S^2 with respect to the UHF wave functions. It follows from the variational principle that the UHF energy should always be lower than the corresponding ROHF energy. In the case of the phenyl radical, we use a slightly better basis set than Pacansky, Liu, and DeFrees[1] (6-31G versus 4-31G), and our energy is somewhat lower than theirs. In the case of the benzyl radical, we used the same basis set as Pacansky, Liu, and DeFrees,[1] namely 4-31G, and we were surprised to find that our UHF energy was lower by more than 3 hartree. We rechecked our result, and we also found that it is consistent with previously obtained 3-21G results so that we have no further explanation for this large discrepancy.

The spin contamination of the UHF wave functions may not be quite as bad as it seems from the data reported in Table III. According to a simple argument, similar to a recent analysis by Schlegel,[4] we may expand Ψ_{UHF} as

$$\Psi_{UHF} = {}^2\Psi + {}^4\Psi + {}^6\Psi + {}^8\Psi + \ldots \quad (1)$$

We define the normalization integrals

$$N_k = \langle {}^k\Psi | {}^k\Psi \rangle \quad (2)$$

and we have

$$1 = N_2 + N_4 + N_6 + \ldots \quad (3)$$

since Ψ_{UHF} is normalized to unity. The expectation value $\langle S^2 \rangle_{UHF}$ is then given by

$$\langle S^2 \rangle_{UHF} = \langle \Psi_{UHF} | S^2 | \Psi_{UHF} \rangle = {}^3/_4 N_2 + {}^{15}/_4 N_4 + {}^{35}/_4 N_6 + \ldots = {}^3/_4 + 3N_4 + 8N_6 + \ldots \quad (4)$$

It is easily derived from the $\langle S^2 \rangle_{UHF}$ values for phenyl and benzyl in Table III that the spin contamination is at worst 25% for phenyl and 22% for benzyl if all of the spin contamination is concentrated in the quartet spin state.

In using the GAUSSIAN 82 program package[2] for computations on organic radicals, we have found[5] that the UHF computations converge more readily than the corresponding ROHF computations. It is therefore useful to have some information about the relation between geometry predictions derived from UHF and from ROHF computations. Even though the amount of information that we present here is rather limited, it encourages us to use the UHF procedure for geometry predictions of aromatic radicals and radical anions in situations where the ROHF procedure does not converge.

Acknowledgment. I thank D. Norman Heimer for some stimulating discussions and helpful suggestions. I also express my gratitude to the Air Force Office of Scientific Research for supporting the work described here.

Registry No. Phenyl radical, 2396-01-2; benzyl radical, 2154-56-5.

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Reaction of Organometallic Reagents with Ethyl Trifluoroacetate and Diethyl Oxalate. Formation of Trifluoromethyl Ketones and α-Keto Esters via Stable Tetrahedral Adducts

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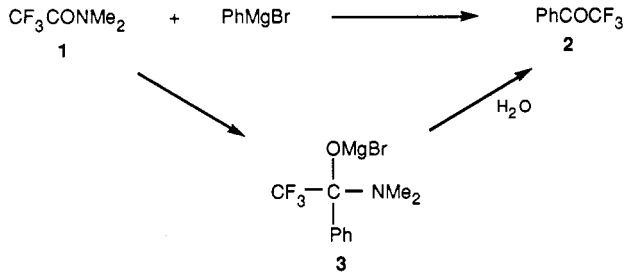
Received May 13, 1987

In conjunction with our studies designed to evaluate the effect of the trifluoromethyl group on free radical stabilities, we had need for a variety of trifluoromethyl ketones, $RCOCF_3$. The primary method for preparation of these

0022-3263/87/1952-5026$01.50/0

substrates involves reaction of the appropriate Grignard reagent with trifluoroacetic acid.[1] This reaction requires an equivalent of Grignard reagent to form the salt of trifluoroacetic acid and an additional equivalent of the Grignard to form the ketone. In practice, 3 mol of Grignard result in highest yields. A modification of this procedure,[2] in which preformed lithium trifluoroacetate is reacted with the Grignard reagent, circumvents the need for using such large excesses of the reagent. This modification, although successful, lacks some of the convenience of a simple Grignard reaction. We therefore sought a simple and convenient method for the preparation of trifluoromethyl ketones, $RCOCF_3$, which was not wasteful in terms of the group R.

Trifluoromethyl ketones have also been produced by reaction of *N,N*-diethyltrifluoroacetamide with organometallic reagents.[3] This type of reaction of amides with organometallic reagents is known to give ketones.[4] By a similar procedure, we have prepared trifluoroacetophenone, **2**, in 74% yield by the reaction of *N,N*-dimethyltrifluoroacetamide, **1**, with PhMgBr. The reaction owes its success presumably to the fact that the tetrahedral intermediates **3** is stable under the reaction conditions. The ketone product is presumably not formed until all of the Grignard reagent in consumed and water is added. While this reaction requires only 1 mol of Grignard reagent, the disadvantages of this method lies in the fact that CF_3CONMe_2 and CF_3CONEt_2 are not commercially available.



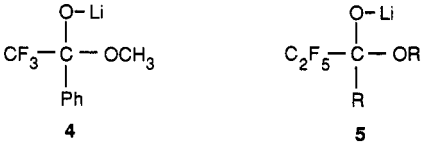
Attention was therefore turned to the use of the commercially available and inexpensive ester CF_3CO_2Et as a source of the trifluoroacetyl group. The reaction of Grignard reagents and organolithium reagents with esters constitutes a classic synthesis of tertiary alcohols. The intermediate ketones generally cannot be isolated. Despite these facts it was hoped that the electron-withdrawing CF_3 group would stabilize the initial tetrahedral adduct between the Grignard reagent and CF_3CO_2Et. Indeed, varying mixtures of fluorinated ketones, R_fCOR, and carbinols, $R_fC(OH)R_2$ could be prepared by reaction of RLi with $R_fCO_2CH_3$.[5] McGrath and Levine also noted in passing that PhMgBr reacted with methyl trifluoroacetate to give a 67% yield of $PhCOCF_3$ but this reaction was not further pursued as a general synthetic method.[5] Chen et al.[6] have

Table I. Products of Reaction of Esters with Organometallic Reagents

organometallic	ester	product (% yield)[a]
PhMgBr	CF_3CO_2Et	$PhCOCF_3$ (86)
p-$CH_3C_6H_4MgBr$	CF_3CO_2Et	p-$CH_3C_6H_4COCF_3$ (68)
p-$CH_3OC_6H_4MgBr$	CF_3CO_2Et	p-$CH_3OC_6H_4COCF_3$ (69)
p-$CF_3C_6H_4MgBr$	CF_3CO_2Et	p-$CF_3C_6H_4COCF_3$ (72)
PhLi	CF_3CO_2Et	$PhCOCF_3$ (88)
p-$Me_2NC_6H_4Li$	CF_3CO_2Et	p-$Me_2NC_6H_4COCF_3$ (85)
1-naphthyl-Li	CF_3CO_2Et	1-naphthyl-$COCF_3$ (75)
p-BrC_6H_4Li	CF_3CO_2Et	p-$BrC_6H_4COCF_3$ (73)
$PhCH_2MgCl$	CF_3CO_2Et	$PhCH_2COCF_3$ (70)
cyclo-$C_6H_{11}MgCl$	CF_3CO_2Et	cyclo-$C_6H_{11}COCF_3$ (66)
n-$C_6H_{13}MgBr$	CF_3CO_2Et	n-$C_6H_{13}COCF_3$ (63)
2-thienyl-MgBr	CF_3CO_2Et	2-$C_4H_3SCOCF_3$ (51) (55)[b] $(2\text{-}C_4H_3S)_2C(OH)CF_3$ (37) (33)[b]
PhMgBr	CH_2FCO_2Et	$PhCOCH_2F$ (68) $Ph_2C(OH)CH_2F$ (28)
PhMgBr	CH_3OCH_2-CO_2Et	$PhCOCH_2OCH_3$ (29) $Ph_2C(OH)CH_2OCH_3$ (67)
PhMgBr	CH_3CO_2Et	$Ph_2C(OH)CH_3$ (96) $PhCOCH_3$ (0)
PhMgBr	n-$C_3F_7CO_2Et$	PhCO-n-C_3F_7 (trace) $Ph_2C(OH)$-n-C_3F_7 (94)

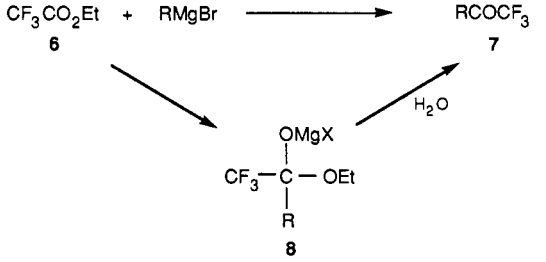
[a] Based on aryl of alkyl halide used to prepare Grignard reagent. Yields from PhMgBr and PhLi are based on measured concentration of organometallic reagent. [b] At −105 °C.

also carried out studies on the reaction of PhLi with fluorinated esters, R_fCO_2R. High yields of $PhCOCF_3$ were reported on reaction of PhLi with CF_3CO_2R. Additionally, reaction of PhLi with $CF_3CO_2CH_3$ led to the isolation of a stable solid which was identified as the tetrahedral adduct **4**. Studies by Gassman and O'Reilly[7] have also



implicated relatively stable tetrahedral adducts of type **5** in reaction of (pentafluoroethyl)lithium with various esters. Under certain conditions, this reaction gives good yields of ketones of the type $RCOC_2F_5$. The reaction of an acetylide with CF_3CO_2Et has been used to produce an intermediate trifluoromethyl ketone in the synthesis of a retinal derivative.[8] These results all suggest that esters of trifluoroacetic acid could be used quite effectively in the synthesis of trifluoromethyl ketones.

We have now reacted a variety of Grignard reagents with CF_3CO_2Et, **6**. The procedure involves addition of 1 equiv of the Grignard reagent to a solution of CF_3CO_2Et in ether at −78 °C. On warming to room temperature and an aqueous workup, good yields (Table I) of trifluoromethyl ketones **7** are formed. In most cases *no* tertiary alcohols are formed. 1-Naphthyllithium, (4-bromophenyl)lithium,



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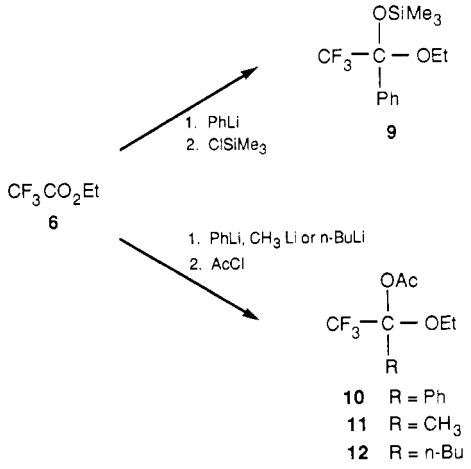
and [4-(*N*,*N*-dimethylamino)phenyl]lithium (which can be readily prepared by reaction of the corresponding bromides with *n*-butyllithium) also give good yields of trifluoromethyl ketones. These reactions are successful due to the stability of the tetrahedral intermediate **8** under the reaction as implied by previous studies.[3,6,7]

The tetrahedral adduct derived from the reaction of PhLi with CF_3CO_2Et can be silylated to give the mixed ketal **9** in 23% yield (along with $PhCOCF_3$) by addition of chlorotrimethylsilane at low temperature. Along these lines, addition of phenyllithium, methyllithium, or *n*-butyllithium to CF_3CO_2Et, followed by the addition of acetyl chloride, gave the acetates **10–12** in 40%, 46%, and 47% yields, respectively.



The successful preparation of trifluoromethyl ketones from CF_3CO_2Et led us to further investigate the generality of this method for the preparation of ketones containing less potent electron-withdrawing groups. Ethyl fluoroacetate reacts with PhMgBr (–70 °C to room temperature) to give a 68% yield of α-fluoroacetophenone. Also formed is a 28% yield of the tertiary alcohol $Ph_2C(OH)CH_2F$. The formation of tertiary alcohol suggests that loss of ethoxide from the tetrahedral intermediate is more rapid due to the less potent electron-withdrawing properties of CH_2F relative to CF_3. Ethyl methoxyacetate gave only a 29% yield of the ketone $PhCOCH_2OCH_3$ with the tertiary alcohol $Ph_2C(OH)CH_2OCH_3$ being the major product (67%). Finally, in complete contrast to CF_3CO_2Et, reaction of CH_3CO_2Et with PhMgBr (1 to 1 ratio at –70 °C) gave complete tertiary alcohol formation (96%) and *no trace of acetophenone*. These trends parallel the decreasing electron-withdrawing properties of CF_3, CH_2F, CH_2OCH_3, and CH_3 with the more electronegative groups leading to greater amounts of ketone. This presumably reflects the greater stability of the tetrahedral adducts when substituted with electronegative groups.

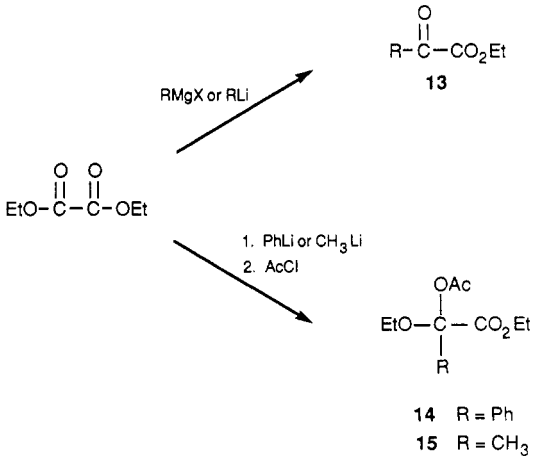
Reaction of 2-thienylmagnesium bromide with CF_3CO_2Et at –78 °C gave a substantial amount of tertiary alcohol (37%) along with the trifluoromethyl ketone (51%). The formation of trifluoromethyl ketones vs. tertiary alcohols in the reaction of Grignard reagents with CF_3CO_2Et therefore appears to be a delicate function of reaction rate of the Grignard with the ester and the rate of decomposition of the tetrahedral adduct. In the case of 2-thienylmagnesium bromide, lowering the temperature to –105 °C did not substantially change the ketone to tertiary alcohol product ratio. It therefore appears that the rate of reaction of 2-thienylmagnesium bromide with CF_3CO_2Et is comparable to the rate of decomposition of the tetrahedral adduct. This tetrahedral adduct is apparently destabilized and therefore undergoes ethoxide loss at an increased rate of because of the the electron-donating ability of the 2-thienyl group.

Table II. Yields of $RCOCO_2Et$ from Reaction of Organometallic Reagents with Diethyl Oxalate

organometallic	% yield	organometallic	% yield
PhMgBr	85	*t*-BuMgCl	83[a]
p-$CH_3C_6H_4MgBr$	72	EtMgBr	76[a]
p-$CH_3OC_6H_4MgBr$	63	CD_3MgI	46[b]
p-$CH_3SC_6H_4MgBr$	74	cyclo-$C_3H_5C_6H_4Li$	58
p-FC_6H_4MgBr	67	*p*-$CH_2CHC_6H_4Li$	60
m-FC_6H_4MgBr	65	*p*-$Me_2NC_6H_4Li$	64
p-$CF_3C_6H_4MgBr$	63	*p*-$Me_3SiC_6H_4Li$	39
m-$CF_3C_6H_4MgBr$	75	*p*-$Me_3SiCH_2C_6H_4Li$	53
2-thienyl-MgBr	83		

[a] Grignard reagent was used in 5% excess. [b] Reference 9a.

The ability of electron-withdrawing groups to stabilize the tetrahedral adducts between organometallic reagents and esters also allows facile preparation of α-keto esters of type $RCOCO_2Et$. Over the years we[9] and others[10] have prepared a variety of α-keto esters **13** by reaction of Grignard reagents and organolithium reagents with diethyl oxalate. Table II summarizes yields of α-keto esters which we have prepared in this fashion. Our original procedure employed a large excess of diethyl oxalate relative to the Grignard or organolithium reagent. We have now found that the large excess of ester is unnecessary and now routinely use only a 10% excess of diethyl oxalate. The success of this reaction is presumably due to the fact that the initial tetrahedral adduct is stabilized under the reaction conditions by the residual electron-withdrawing carbethoxy group (as is the case in the reaction of CF_3CO_2Et with organometallic reagents). In support of this presumption, the tetrahedral adduct derived from diethyl oxalate and phenyllithium or methyllithium can be trapped (albeit in low yields) with acetyl chloride to give the acetates **14** (27%) and **15** (27%).



In summary, trifluoromethyl ketones of type $RCOCF_3$ can be prepared in good yields by reaction of ethyl trifluoroacetate with Grignard or organolithium reagents at –78 °C. These reactions owe their success to the stability of the tetrahedral intermediates as a result of the electron-withdrawing CF_3 group. The tetrahedral intermediates derived from organolithium reagents can be silylated or acetylated to give isolable mixed ketals or α-ethoxy acetates, respectively. The tetrahedral intermediates in-

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volved in the synthesis of α-keto esters, $RCOCO_2Et$, by reaction of organometallic reagents with diethyl oxalate can also be acetylated with acetyl chloride to give α-ethoxy acetates.

Experimental Section

Reaction of Organometallic Reagents with Esters. General Procedure. A solution of the appropriate Grignard reagent or organolithium reagent (1 equiv) was added dropwise to a mechanically stirred solution of the appropriate ester (1.1 equiv) in ether held at −78 °C in a dry ice–acetone bath. On completion of the addition the stirred mixture was allowed to warm to between 0 °C and room temperature. Aqueous NH_4Cl solution was added followed by dilute HCl solution. The organic phase was separated, washed with saturated NaCl solution, and dried over $MgSO_4$. Solvents were removed on a rotary evaporator and the products were isolated by distillation. They were characterized by standard spectroscopic methods. Specific examples are given below.

Preparation of p-$CF_3C_6H_4COCF_3$. A Grignard reagent was prepared from 10.115 g of p-(trifluoromethyl)bromobenzene and 1.3 g of magnesium in 50 mL of ether. The Grignard reagent was transferred to an addition funnel and added dropwise to a solution of 7.04 g of ethyl trifluoroacetate in 60 mL of ether at −78 °C. The mixture was then allowed to warm to room temperature and saturated NH_4Cl solution was added followed by dilute HCl solution. After a standard workup, the ether solvent was removed on a rotary evaporator. The residue was distilled through a 20-cm Vigreux column. After a small forerun, 7.850 g of p-$CF_3C_6H_4COCF_3$ was collected, bp 63–65 °C (15 mm): NMR ($CDCl_3$) δ 8.21 and 7.83 (AA′BB′ quartet); IR (CCl_4) ν_{CO} 1730 cm^{-1}.

Preparation of p-$Me_2NC_6H_4COCF_3$. A solution of 2.093 of p-(*N*,*N*-dimethylamino)bromobenzene in 20 mL of THF was cooled to −78 °C and 6.6 mL of 1.6 M *n*-butyllithium in hexane was added dropwise to the stirred mixture. A white precipitate formed during the addition. After being stirred for 15 min at about −70 °C, this mixture was transferred by using a double-ended needle to a solution of 1.63 g of ethyl trifluoroacetate in 16 mL of ether at 78 °C. The mixture was then warmed to room temperature, water was added, and a standard aqueous workup was followed. The organic extract was dried over $MgSO_4$ and the solvents were removed on a rotary evaporator. The solid residue was slurried with cold hexanes and collected, giving 1.931 g (85%) of p-$Me_2NC_6H_4COCF_3$. Recrystallization from hexanes gave a sample, mp 74–75 °C (lit.[3b] mp 75–75.5 °C): NMR ($CDCl_3$) δ 7.95 and 6.67 (AA′BB′ quartet, 4 H), 3.11 (s, 6 H); IR (CCl_4) $\nu_{C=O}$ 1698 cm^{-1}.

Reaction of 2-Thienylmagnesium Bromide with Ethyl Trifluoroacetate. A Grignard reagent was prepared from 6.05 g of 2-bromothiophene and 1.0 g of magnesium in 50 mL of ether. The Grignard reagent was transferred to an addition funnel and added dropwise to a solution of 5.30 g of ethyl trifluoroacetate in 50 mL of ether at −78 °C. The mixture was then allowed to warm to room temperature. Saturated NH_4Cl solution was then added and a standard workup as previously described followed. The ether solvent was removed on a rotary evaporator and the residue was distilled through a 20-cm Vigreux column. 2-$C_4H_3SCOCF_3$[3a] (3.385 g, 51%) was collected, bp 65 °C (15 mm): NMR ($CDCl_3$) δ 7.98 (m, 1 H), 7.92 (dd, J = 5, 1 Hz, 1 H), 7.26 (dd, J = 5, 4 Hz, 1 H); IR (CCl_4) $\nu_{C=O}$ 1695 cm^{-1}. The Vigreux column was then replaced with a short-path distillation head and 1.823 g (37%) of $(2\text{-}C_4H_3S)_2C(OH)CF_3$ was then collected, bp 95–97 °C (0.05 mm): NMR ($CDCl_3$) δ 7.37 (dd, J = 5.1, 1.2 Hz, 2 H), 7.23 (dt, J = 3.6, 1 Hz, 2 H), 7.03 (dd, J = 5.1, 3.9 Hz, 2 H), 3.22 (s, 1 H); IR (CCl_4) ν_{OH} 3580 cm^{-1}.

Reaction of Phenylmagnesium Bromide with Ethyl Fluoroacetate. A solution of 1.53 g of ethyl monofluoroacetate in 20 mL of ether was cooled to −78 °C and 8.5 mL of 1.5 M PhMgBr was added dropwise. The mixture was warmed to 5 °C and quenched with NH_4Cl solution. After a standard aqueous workup, the organic extract was dried over $MgSO_4$. The solvents were removed on a rotary evaporator. The residue was distilled by using a short path distillation head and collected in two fractions. α-Fluoroacetophenone[11] (1.200 g, 68%), bp 86–89 °C (3 mm), was collected in fraction 1: NMR ($CDCl_3$) δ 7.89 (m, 2 H, ortho hydrogens), 7.63 (m, 1 H, para hydrogen), 7.49 (m, 2 H, meta hydrogens), 5.54 (d, J = 47 Hz, 2 H); IR (CCl_4) $\nu_{C=O}$ 1719, 1693 cm^{-1}. The pressure was then reduced to 0.05 mm and 0.358 g (28%) of $Ph_2C(OH)CH_2F$ was then collected: NMR ($CDCl_3$) δ 7.48–7.22 (m, 10 H), 4.85 (d, J = 48 Hz, 2 H), 2.95 (br s, 1 H).

Reaction of Phenylmagnesium Bromide with Diethyl Oxalate. A Grignard reagent prepared from 5.00 g of bromobenzene and 0.85 g of magnesium in 50 mL of ether was added dropwise to a solution of 5.11 g of diethyl oxalate in 50 mL of ether at −78 °C. The mixture was warmed to 10 °C and quenched with NH_4Cl solution. After a standard aqueous workup, the organic extract was dried over $MgSO_4$. The solvents were removed on a rotary evaporator and the residue was distilled by using a 20-cm Vigreux column. After a small forerun of diethyl oxalate, 4.94 g of $PhCOCO_2Et$, which codistilled with a small amount of biphenyl, was collected, bp 76–80 °C (0.05 mm). Biphenyl was removed by chromatographing 1.00 g of the distillate on 12 g of silica gel and eluting with ether in hexanes. The α-keto ester $PhCOCO_2Et$ (970 mg) (which was spectrally identical with previously prepared samples[9b]) eluted with 8% ether in hexanes. The yield of $PhCOCO_2Et$ was therefore 85%.

Preparation of Acetate 12. A solution of 2.03 g of ethyl trifluoroacetate in 20 mL of ether was cooled to −78 °C and 8.8 mL of 1.6 M *n*-BuLi in hexane was added dropwise. After 15 min at −78 °C, 1.10 g of acetyl chloride in 2 mL of ether was added. The mixture was allowed to warm to room temperature and after 30 min, 50 mg of Et_3N was added. Water was then added and a standard aqueous workup followed. The organic phase was dried over $MgSO_4$ and the solvents were removed on a rotary evaporator. The residue was distilled on a short-path distillation head and collected in two fractions. Fraction 1, bp 30–54 °C (15 mm) (0.585 g) contained $CH_3CH_2CH_2CH{=}C(OAc)CF_3$ and acetate **12** in a 1:1.95 ratio as determined by NMR. Pure samples of these products in fraction 1 could be isolated by preparative gas chromatography. Fraction 2, bp 54–55 °C (15 mm) (1.200 g, 35%), contained the acetate **12**. The combined yield of acetate **12** in both fractions was therefore 47%: NMR ($CDCl_3$) δ 3.77 (m, 2 H), 2.27 (m, 2 H), 2.12 (s, 3 H), 1.34 (m, 4 H), 1.21 (t, J = 7 Hz, 3 H), 0.90 (t, J = 7 Hz, 3 H); IR (CCl_4) ν_{CO} 1758 cm^{-1}. Anal. Calcd for $C_{10}H_{17}F_3O_3$: C, 49.58; H, 7.07. Found: C, 49.88; H, 7.38.

Preparation of Acetate 14. A solution of 1.71 g of diethyl oxalate in 16 mL of ether was cooled to −78 °C and 11 mL of 1.0 M phenyllithium in ether was added dropwise. The mixture was warmed to −65 °C and recooled to −78 °C, and 0.96 g of acetyl chloride in 1 mL of ether was added. The mixture was warmed to room temperature and after 30 min, 50 mg of Et_3N was added. An aqueous workup followed as described for **12**. Gas chromatographic analysis showed the presence of $PhCOCO_2Et$, biphenyl, PhCOCOPh, and the acetate **14**. The solvent was removed on a rotary evaporator and the residue was chromatographed on 25 g of silica gel and eluted with increasing amounts of ether (3–50%) in hexanes. Biphenyl, which was present in the starting phenyllithium, eluted first. A mixture of $PhCOCO_2Et$ and PhCOCOPh eluted next with 10% ether. Finally, the acetate **14** (781 mg, 27%) eluted with 30–40% ether: NMR ($CDCl_3$) δ 7.73–7.58 (m, 2 H), 7.48–7.35 (m, 3 H), 4.16 (m, 2 H), 3.41 (m, 2 H), 2.25 (s, 3 H), 1.23 (t, J = 7 Hz, 3 H), 1.17 (t, J = 7 Hz, 3 H); IR (CCl_4) $\nu_{C=O}$ 1772, 1751 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.00; H, 6.74.

Acknowledgment is made to the National Science Foundation and to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Registry No. **6**, 383-63-1; **9**, 110193-64-1; **10**, 110193-65-2; **11**, 110193-66-3; **12**, 110193-67-4; **14**, 110193-68-5; **15**, 110193-69-6; CH_2CO_2Et, 459-72-3; $MeOCH_2CO_2Et$, 3938-96-3; $MeCO_2Et$, 141-78-6; $CF_3(CF_2)_2CO_2Et$, 356-27-4; p-MeC_6H_4MgBr, 4294-57-9; p-$MeOC_6H_4MgBr$, 13139-86-1; p-$CF_3C_6H_4MgBr$, 402-51-7; PhLi, 591-51-5; p-$Me_2NC_6H_4Li$, 13190-50-6; p-BrC_6H_4Li, 22480-64-4; $PhCH_2MgCl$, 6921-34-2; c-$C_6H_{11}MgCl$, 931-51-1; $Me(CH_2)_5MgBr$, 3761-92-0; $\overline{CH{=}CHCH{=}C(MgBr)S}$, 5713-61-1; $PhCOCF_3$, 434-45-7; p-$MeC_6H_4COCF_3$, 394-59-2; p-$MeOC_6H_4COCF_3$, 711-38-6; p-$CF_3C_6H_4COCF_3$, 74853-66-0; p-$Me_2NC_6H_4COCF_3$, 2396-05-6;

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p-$BrC_6H_4COCF_3$, 16184-89-7; $PhCH_2COCF_3$, 350-92-5; c-$C_6H_{11}COCF_3$, 6302-04-1; $Me(CH_2)_5COCF_3$, 400-60-2; CH=CH-CH=C(COCF$_3$)S, 651-70-7; (2-$C_4H_3S)_2C(OH)CF_3$, 35320-32-2; $PhCOCH_2F$, 450-95-3; $Ph_2C(OH)CH_2F$, 337-72-4; $PhCOCH_2OMe$, 4079-52-1; $Ph_2C(OH)CH_2OMe$, 14704-09-7; PhC(OH)Me, 599-67-7; $Ph_2C(OH)(CF_2)_2CF_3$, 559-54-6; p-$MeSC_6H_4MgBr$, 18620-04-7; p-FC_6H_4MgBr, 352-13-6; m-FC_6H_4MgBr, 17318-03-5; m-$CF_3C_6H_4MgBr$, 402-26-6; EtO_2CCO_2Et, 95-92-1; $PhCOCO_2Et$, 1603-79-8; p-$MeC_6H_4COCO_2Et$, 5524-56-1; p-$MeOC_6H_4COCO_2Et$, 40140-16-7; p-$MeSC_6H_4COCO_2Et$, 62936-31-6; p-$FC_6H_4COCO_2Et$, 1813-94-1; m-$FC_6H_4COCO_2Et$, 110193-59-4; p-$CF_3C_6H_4COCO_2Et$, 73790-06-4; m-$CF_3C_6H_4COCO_2Et$, 110193-60-7; SCH=CHCH=CCOCO$_2$Et, 4075-58-5; $BuCOCO_2Et$, 677-22-5; CD_3MgI, 41251-37-0; c-$C_3H_5C_6H_4Li$, 110205-34-0; p-CH_2=CHC_6H_4Li, 7442-12-8; p-$Me_3SiC_6H_4Li$, 17881-54-8; p-$Me_3SiCH_2C_6H_4Li$, 110193-61-8; t-$BuCOCO_2Et$, 5333-74-4; $EtCOCO_2Et$, 15933-07-0; CD_3COCO_2Et, 66966-38-9; c-$C_3H_5C_6H_4COCO_2Et$, 110205-35-1; p-CH_2=$CHC_6H_4COCO_2Et$, 110193-62-9; p-$Me_2NC_6H_4COCO_2Et$, 41116-24-9; p-$Me_3SiC_6H_4COCO_2Et$, 110193-63-0; p-$Me_3SiCH_2C_6H_4COCO_2Et$, 109088-72-4; MeLi, 917-54-4; BuLi, 109-72-8; 1-naphthyllithium, 14474-59-0; (1-naphthylcarbonyl)trifluoromethane, 6500-37-4.

Facile Reduction of Saturated and Unsaturated Carboxylic Acids and Their Salts to Aldehydes by Thexylbromoborane–Dimethyl Sulfide[1]

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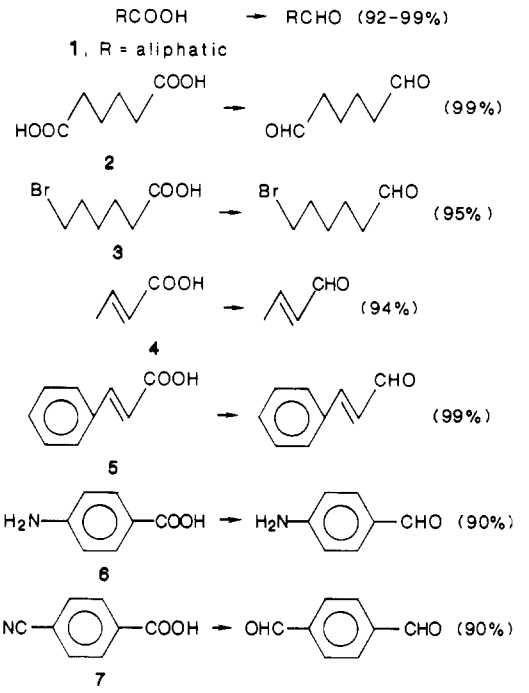
Received March 12, 1987

Thexylchloroborane–dimethyl sulfide appears to be an ideal reagent for the direct transformation of acyclic and alicyclic carboxylic acids into aldehydes so long as alkene functions are not present.[2,3] In the course of a systematic study of the reducing characteristics of thexylbromoborane–dimethyl sulfide,[4] we have found that this reagent as well selectively converts carboxylic acids and their sodium and lithium salts to the corresponding aldehydes in the presence of several functionalities, including carbon–carbon double bonds. This paper describes this facile reduction.

Results and Discussion

Thexylbromoborane–dimethyl sulfide (ThxBHBr–SMe_2) is readily prepared by hydroborating 2,3-dimethyl-2-butene (tetramethylethylene) in methylene chloride[5] with monobromoborane–dimethyl sulfide, which in turn is easily prepared by treating borane–dimethyl sulfide with $^1/_2$ equiv of bromine in carbon disulfide.[6]

Chart I



The reagent reduces aliphatic carboxylic acids **1**, regardless of structural type, to aldehydes in almost quantitative yield within 1 h at room temperature. Even aliphatic diacids **2** are converted to the dialdehydes in yields of 93–99%. The reagent tolerates many organic functionalities, viz., esters, acid chlorides, epoxides, halides, and nitro compounds. For example, halo aliphatic acids **3** provide the corresponding halo aldehydes in good yields (85–95%). However, the most useful feature of this reagent is its reluctance to hydroborate carbon–carbon double bonds, an advantage of this reagent over thexylchloroborane–dimethyl sulfide, which readily adds to alkenes. Thus, α,β-unsaturated carboxylic acids such as methacrylic, crotonic (**4**), and cinnamic (**5**) acids are readily converted to the corresponding olefinic aldehydes in yields of 94–99% (Chart I).

The rate of reduction of aromatic carboxylic acids is sluggish, requiring 3 equiv of the reagent and 9 h at room temperature. The yields are significantly lower than those in the aliphatic series and appear to be influenced by substituents on the aromatic ring. For example, the yields from both benzoic and α-naphthoic acids were ca. 50%, whereas the yields from *m*-nitro-, *o*-chloro-, *m*-chloro-, and *p*-aminobenzoic (**6**) acids were 75–93%. The reduction of terephthalic acid with 6 equiv of the reagent gave the corresponding dialdehyde in 95% yield. This reagent also reduces the nitrile function partially.[7] Thus, the reaction of *p*-cyanobenzoic acid (**7**) with 3.1 equiv of the reagent gave terephthalaldehyde in a yield of 90%. These results are summarized in Table I.

The reagent thexylbromoborane–dimethyl sulfide also reduces sodium and lithium carboxylates to the corresponding aldehydes at room temperature in high yields. This facile reduction is due to the simple substitution for

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