5,8-Difluoro-2,3-dihydro-1,4-benzodioxin (10). A mixture of 2-(2,3,6-trifluorophenoxy)ethanol, 4.13 g (0.0215 mol), K_2CO_3, 3.12 g (0.0226 mol), and 62 mL of DMF was refluxed overnight, cooled, and poured into H_2O. The solution was made acidic with 10% HCl and then extracted twice with Et_2O; the extracts were washed three times with H_2O, twice with 10% NaOH, and again with H_2O. The Et_2O solution was dried over $MgSO_4$ and concentrated to dryness, leaving 1.56 g (42%) of a white solid, mp 44–47 °C. An analytical sample was prepared by recrystallization from EtOH/H_2O: mp 54–57 °C; mass spectrum, m/e 172 (M^+), 157, 116, 88 (base); ^1H NMR ($CDCl_3$) δ 4.37 (s, 4, OCH_2CH_2O), 6.57 (t, 2, Ar H). Anal. Calcd for $C_8H_6F_2O_2$: C, 55.82; H, 3.51. Found: C, 55.96; H, 3.74.

3,6-Difluorocatechol. Anhydrous $AlCl_3$, 2.4 g, was added to a solution of **10**, 0.64 g (3.7 mmol), in 25 mL of toluene and then the mixture was refluxed for 4.5 h under a N_2 atmosphere. The reaction mixture was cooled, poured onto ice, and acidified with concentrated HCl and the layers were separated. The aqueous layer was extracted twice with Et_2O; the Et_2O extracts were combined with the toluene layer, washed with H_2O, dried over $MgSO_4$, and concentrated to a dark residue. Kugelrohr distillation of this residue at 15 mm and up to 105 °C afforded 0.41 g (76%) of white solid: mass spectrum, m/e 146 (M^+, base), 126, 98, 70, 69; ^1H NMR ($CDCl_3$) δ 5.50 (br s, 2, OH), 6.47 (d of d, 2, Ar H).

3,6-Difluoroveratrole (9) was obtained via methylation of 3,6-difluorocatechol. 3-6-Difluorocatechol, 0.40 g (2.7 mmol), powdered anhydrous K_2CO_3, 1.51 g (10.9 mmol), Me_2SO_4, 10.4 mL (10.9 mmol), and 6 mL of acetone were refluxed under N_2 for 1.5 h. The reaction mixture was cooled, diluted with H_2O, and extracted twice with Et_2O. After being washed twice with H_2O, the Et_2O extracts were stirred for 0.5 h with 50 mL of 1 N NH_4OH; the Et_2O layer was separated, washed twice with H_2O, dried over $MgSO_4$, and concentrated at 30 °C on the rotary evaporator to 0.43 g of a tan liquid. The liquid was chromatographed on silica, eluting with hexane containing up to 20% CH_2Cl_2, in order to remove a faster running impurity; 0.21 g (44%) of pure (TLC) colorless liquid was obtained which was identical in all respects with material prepared from *p*-difluorobenzene.

Registry No. 1, 72912-24-4; 1·HBr, 59043-74-2; 2, 75626-15-2; 2·HBr, 75626-16-3; 3, 394-64-9; 4, 456-49-5; 6, 73943-41-6; 7, 7537-08-8; 8, 75626-17-4; 9, 75626-18-5; 10, 72912-50-6; 11, 75626-19-6; 12, 75626-20-9; dimethyl 2-fluoro-6-methoxyboronate, 75626-21-0; 2-fluoro-3,4-dimethoxybenzyl chloride, 1716-43-4; 2,5-difluorophenol, 2713-31-7; *p*-difluorobenzene, 540-36-3; 3,6-difluoroguaniacol, 75626-22-1; 2-(2,3,6-trifluorophenoxy)ethanol, 72912-49-3; 1,2,3,4-tetrafluorobenzene, 551-62-2; 3,6-difluorocatechol, 75626-23-2.

1,2-Difluoroethylenes: Synthesis via Fluoro Ketones

Jacques Leroy

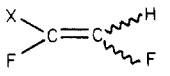
CNRS-CERCOA, 2 rue Henri Dunant, 94320 Thiais, France

Received June 20, 1980

In a previous paper,[1] we have shown that the reaction of trifluoro(fluorooxy)methane with diazo ketones led to a mixture from which only one stereoisomer of 1,2-difluoro epoxides of type 1 was detected and isolated (Scheme I).

All of these epoxides were thought to have the same configuration since they all exhibited a fluorine–fluorine coupling constant close to 35 Hz. Unfortunately, owing to the lack of significant NMR data, this configuration could not be determined unambiguously.[2]

On the other hand, various 1,2-difluoroalkenes **2** were described, the substituent X being a proton, a halogen, or



2

an alkoxy group.[3,4] For all these compounds, the coupling constant between the two fluorine atoms lies in the range 8 to 18 Hz for a cis arrangement of fluorine atoms and varies from about 130 to 140 Hz for the trans isomer. Thus, there could not be any ambiguity with respect to their stereochemistry if the epoxides **1** proceeded from epoxidation of known alkenes of type **6** (Scheme II). This paper deals with the synthesis of such compounds.

No general and simple synthetic method was suited to the preparation of olefins **6**, i.e., olefins bearing any substituent (alkyl, cycloalkyl, phenyl, etc.). Neither Burton's olefination method[5] (terminal vinyl fluorides were obtained from ketones and aldehydes) nor addition of organolithium compounds to trifluoroethylene[6] (since metalation occurs) were applicable. Radiation-induced radical addition of ethers to 1,2-dichloro-1,2-difluoroethylene, leading to compounds such as **2**, has been used[4] but is not generally applicable. An alternative procedure has described the preparation of α,β-difluorostyrene,[7] starting from α,α-difluoroacetophenone. Here also, general applicability was not to be expected since difluoromethyl ketones are not always easily accessible. Finally, we have developed the sequence outlined in Scheme II.

Results

Preparation of Fluoromethyl Ketones. Many of the hitherto reported methods for preparing fluoromethyl ketones **4** involve the exchange of a halogen atom by a fluorine one, the latter being provided by a metallic fluoride. Among them, silver fluoride[8] is costly whereas potassium hydrogen fluoride needs relatively drastic conditions[9] (high-boiling polar solvent, high temperatures). The attractive dediazonative hydrofluorination of diazo ketones[10] seems not to be convenient for large-scale preparations. Other routes, involving the action of a Grignard reagent upon fluoroacetonitrile[11] or α-fluoro esters,[12] lead to low or moderate yields of fluoromethyl ketones.

We found that, under the conditions first described by Liotta and Harris,[13] the direct exchange of bromine by fluorine into bromomethyl ketones works with good yields (≥75%). Potassium fluoride is used as the fluoride ion source (2 mol per mole of ketone) and it is activated by 18-crown-6 ether (about 18 mol % per mole of ketone). Refluxing benzene is commonly used as the solvent. Such conditions allow particularly clean and mild exchanges.

It appeared that exchanges are yet possible if we replace the crown ether by the same quantity (in moles) of polyethylene glycol 1000 (PEG 1000) dissolved in benzene.

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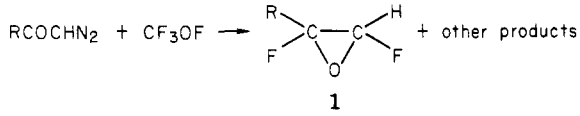
Scheme I



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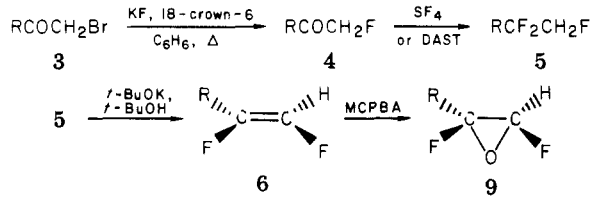
R = alkyl, cycloalkyl

Scheme II



3 4 5 6 9

a, R = 1-adamantyl; b, R = cyclohexyl; c, R = *tert*-butyl; d, R = phenyl

With bromo ketone **3b** as starting material, 100% conversion is reached within 48 h of heating, i.e., rather slower than with the crown ether. Yields in fluoro ketone **4b** (volatile liquid) are fair whereas starting from bromo ketone **3a** some difficulties were encountered in isolating solid **4a** from the reaction medium. Nevertheless, the use of cheap polyethylene glycol as a solid–liquid phase-transfer catalyst is promising, as suggested by several recent reports.[14]

Attempts to prepare phenacyl fluoride by direct exchange in acceptable yields failed because of the strong basic media, leading to side reactions. So, Bergmann's method[15] (acylation of benzene by fluoroacetyl chloride) was used.

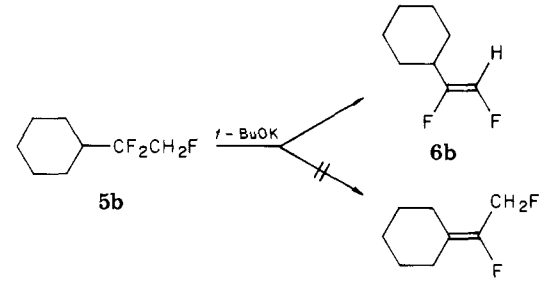
Preparation of Trifluoroalkanes. Conversion of the fluorinated ketones **4** to substituted 1,2,2-trifluoroethanes **5** was achieved at room temperature (19–20 °C) with sulfur tetrafluoride. The reaction is clean, giving good yields, except when **4c** is used. In this case, untractable byproducts, probably due to transpositions occurring at the *tert*-butyl group, are produced along with a low yield of **5c**.

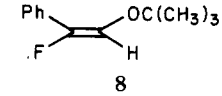
In place of gaseous sulfur tetrafluoride, liquid (diethylamino)sulfur trifluoride[16] was also used successfully albeit it was less reactive (gentle heating was needed) and gave slightly lower yields.

1,2-Difluoroethylenes and Their Epoxides. Among various weakly nucleophic basic reagents commonly used, potassium *tert*-butoxide was found to be the most appropriate for clean dehydrofluorination of the trifluoroalkanes **5**. Nevertheless, quantitative elimination needs prolonged heating at 90–100 °C. With **5b** as starting material, only the less substituted alkene **6b** is produced by dehydrofluorination instead of the alkene **7**, despite the presumed inability of fluorine to stabilize carbanions[17] (Scheme III).

Probably such an orientation can be ascribed, at least in part, to I strain[18] appearing in the conversion of **5b** into **7**. With alkane **5d** as starting material, dehydrofluorination by the *tert*-butoxide anion is complicated by subsequent addition of this anion to the difluoro olefin (*Z*)-**6d** followed by the loss of a fluoride ion, giving (*E*)-1-fluoro-1-phenyl-2-(*tert*-butyloxy)ethylene **8**.

Scheme III





8

The assigned stereochemistry of **8** is based upon a coupling constant ($^3J_{HF}$) of 21 Hz since in such fluoroethylenes $^3J_{HF}$ (cis) $\simeq$ 20 Hz whereas $^3J_{HF}$(trans) $\simeq$ 50 Hz.[3]

It is noteworthy that the difluoroalkenes **6** are always of *Z* configuration, based on the fact that the coupling constant $^3J_{FF}$ is always close to 11 Hz. The same result is obtained even if the nature of the base is quite different. Thus, tri-*n*-butylmethylfluorophosphorane[19] [$(n\text{-}C_4H_9)_3P(CH_3)F$], acting as a source of naked fluoride ion, is able to promote dehydrofluorination on heating of **5c**, leading once more to (*Z*)-**6c**. It has been well established[20] that the cis isomer of 1,2-difluoroethylene is more stable than the trans isomer. This greater stability would probably also account for the specificity of dehydrofluorination in the compounds **5**.

Epoxidation of the difluoroethylenes **6a–c** works cleanly with *m*-chloroperoxybenzoic acid but does not with basic hydrogen peroxide. The knowledge of the starting stereochemistry of the alkenes led us to that of the corresponding epoxides **9a–c** which, consequently, have a cis configuration. These epoxides seem to be much more stable than monofluoroepoxides, particularly upon heating.[21] Nevertheless, in the case of styrene **6d**, neither epoxide nor other tractable fluorinated compound can be detected (although rapid formation of insoluble *m*-chlorobenzoic acid is observed).

All the characteristics of the epoxides **9b** and **9c** are in full agreement with those of previously described epoxides.[1] On this basis, it appears that the formation of *cis*-epoxides **1** by trifluoro(fluorooxy)methane[1] and of (*Z*)-difluoroethylenes **6** by basic dehydrofluorination occurs probably through transition states looking like the presumably more stable *cis*-**1** and (*Z*)-**6**.

Experimental Section

Caution: It has been reported recently that DAST can decompose violently upon contact with water or by heating at temperatures higher than about 50 °C.[22] Suitable safety precautions must be observed in working with this reagent. Sulfur tetrafluoride and hydrogen fluoride are toxic and corrosive

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chemicals. Fluorinations should be carried out in an efficient fume hood.

Melting points were determined with a Mettler FP 61 melting-point instrument. ^1H nuclear magnetic resonance (NMR) spectra were recorded at 60 MHz on a Perkin-Elmer R24 spectrometer and are reported in parts per million from internal tetramethylsilane on the δ scale. ^{19}F NMR spectra were recorded at 56.4 MHz on a JEOL C-60 HL spectrometer and are reported in parts per million from internal $CFCl_3$ on the ϕ scale. Data are presented as follows: solvent, chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constants, and interpretation. Infrared spectra were taken on a Perkin-Elmer 167 spectrophotometer. Microanalyses were performed by the Service Central de Microanalyses du CNRS, Lyon. Mass spectra were recorded on a AEI-MS 30 spectrometer.

Preparation of Fluoromethyl Ketones 4. 1-Adamantyl Fluoromethyl Ketone (4a). To a solution of 2.16 g (8.2 mmol) of 18-crown-6 ether in 20 mL of anhydrous benzene was added 5.4 g (92 mmol) of dried potassium fluoride. After 15 min of stirring at room temperature, 11.8 g (46 mmol) of ketone **3a** in 15 mL of anhydrous benzene was added and the mixture heated with stirring for 8 h (sufficient time for completion with **3a** and also probably, but not checked, for **3b** and **3c**) at 80 °C (bath temperature). After cooling, the mixture was filtered off, poured into water, and then extracted with ether. The combined extracts were dried ($MgSO_4$) and concentrated by rotary evaporation, affording 8.95 g (99.5%) of crude, crystallized **4a** (practically pure). An analytical sample was obtained by sublimation: mp 80 °C; ^1H NMR ($CDCl_3$) δ 1.6–2.2 (15 H, 1-adamantyl), 5.0 (d, 2 H, $^2J_{HF}$ = 46.5 Hz, CH_2F); ^{19}F NMR ($CDCl_3$) ϕ 231.5 (t, $^2J_{FH}$ = 46.5 Hz); IR (CCl_4) 1728, 1700 cm^{-1}. Anal. Calcd for $C_{12}H_{17}FO$: C, 73.44; H, 8.73; F, 9.69. Found: C, 73.41; H, 8.60; F, 9.99.

Cyclohexyl Fluoromethyl Ketone (4b). Crown Ether Procedure. To a solution of 2.36 g (8.9 mmol) of 18-crown-6 ether in 50 mL of anhydrous benzene was added 5.8 g (0.1 mol) of dried KF. After 15 min of stirring at room temperature, 10.2 g (0.05 mol) of ketone **3b**[23] was added and the stirred mixture heated for about 24 h at 80 °C. After cooling, the solution was treated as for **4a**. Distillation of the residue afforded 5.6 g (39 mmol, 78%) of ketone **4b**: bp 82–83 °C (20 mm); ^1H NMR ($CDCl_3$) δ 0.9–2.9 (11 H, c-C_6H_{11}), 4.75 (d, 2 H, $^2J_{HF}$ = 47 Hz, CH_2F); ^{19}F NMR ($CDCl_3$) ϕ 229 (td, $^2J_{FH}$ = 47, $^4J_{FH}$ = 3.2 Hz, CH_2F); IR (CCl_4) 1732 (shoulder), 1720 cm^{-1}. Anal. Calcd for $C_8H_{13}FO$: C, 66.71; H, 9.08; F, 13.16. Found: C, 66.71; H, 9.14; F, 12.97.

Cyclohexyl Fluoromethyl Ketone (4b). Polyethylene Glycol Procedure. To a solution of 10 g (10 mmol) of PEG 1000 in 50 mL of anhydrous benzene was added 5.8 g (0.1 mol) of dried KF. The ketone **3b** (0.05 mol) was added and the mixture heated with stirring for 48 h at 95 °C. After cooling, the solvent was removed by rotary evaporation and the remaining volatile products were extracted from PEG 1000 by bulb-to-bulb distillation. Distillation (Vigreux column) afforded 4 g (56%) of ketone **4b**.

1-Fluoro-3,3-dimethyl-2-butanone (4c) was prepared from **3c** in a similar manner as was **4b** except that the solvent was removed by distillation at atmospheric pressure (74% after distillation of the residue): bp 75–77 °C (100 mm); ^1H NMR ($CDCl_3$) δ 1.15 (s, 9 H, CH_3), 4.98 (d, 2 H, $^2J_{HF}$ = 46.5 Hz, CH_2F); ^{19}F NMR ($CDCl_3$) ϕ 227.3 (t, $^2J_{FH}$ = 46.5 Hz); IR (CCl_4) 1728, 1708 cm^{-1}. Anal. Calcd for $C_6H_{11}OF$: C, 60.99; H, 9.38; F, 16.09. Found: C, 60.73; H, 9.57; F, 15.78.

Preparation of 1,2,2-Trifluoroalkanes 5. Preparation with Sulfur Tetrafluoride. Typical Procedure. 1-(1-Adamantyl)-1,1,2-trifluoroethane (5a). A 0.3-L Monel autoclave was charged with 4.9 g (25 mmol) of ketone **4a**, 15 mL of methylene dichloride and 0.3 mL of water. The autoclave was closed, cooled with dry ice/acetone, and charged with 8.1 g (75 mmol) of SF_4 (quantities up to 5 equiv were commonly used although unnecessary). The resulting mixture was stirred for 24 h at room temperature. After being degassed and swept by an inert gas, the mixture was neutralized with a saturated sodium hydrogen carbonate solution and extracted with ether. The combined extracts were dried ($MgSO_4$). Rotary evaporation of the solvents afforded **5a** as a viscous oil purified by column chromatography on Merck silica gel 60 (cyclohexane as eluant, 92% from **4a**). An analytical sample was obtained by Kugelrohr distillation at ca. 70 °C (0.01 mm): ^1H NMR ($CDCl_3$) δ 1.5–2.2 (15 H, 1-adamantyl), 4.43 (dt, 2 H, $^2J_{HF}$ = 46.5 Hz, $^3J_{HF}$ = 13 Hz, CH_2F); ^{19}F NMR ($CDCl_3$) ϕ 119.2 (dt, 2 F, $^3J_{FF}$ = 14.8, J_{FH} = 13 Hz, CF_2), 228.3 (tt, 1 F, $^2J_{FH}$ = 46.5, $^3J_{FF}$ = 14.8 Hz, CH_2F). Anal. Calcd for $C_{12}H_{17}F_3$: C, 66.04; H, 7.85; F, 26.11. Found: C, 65.76; H, 7.69; F, 26.30.

1,2,2-Trifluoro-3,3-dimethylbutane (5c) was prepared from SF_4 and **5c** in a similar manner as was **5a** except that, after the extracts were dried, the mixture was submitted to bulb-to-bulb distillation in vacuo (0.1 mm). Solvents were removed from the distillate in a spinning-band column. Distillation of the residue in the same apparatus afforded **5c** (20%): bp 82–83 °C; ^1H NMR ($CDCl_3$) δ 1.07 (q, 9 H, $^4J_{HF} \simeq 1.1$, $^5J_{HF}$ = 1 Hz, CH_3), 4.45 (dt, 2 H, $^2J_{HF}$ = 46, $^3J_{HF}$ = 12.8 Hz, CH_2F); ^{19}F NMR ($CDCl_3$) ϕ 139.5 (qm, 2 F, CF_2), 229.2 (ttm, 1 F, $^2J_{FH}$ = 46, $^3J_{FF}$ = 13.7 Hz, CH_2F). Anal. Calcd for $C_6H_{11}F_3$: C, 51.42; H, 7.91. Found: C, 51.25; H, 7.91.

1-Phenyl-1,1,2-trifluoroethane (5d) was prepared from SF_4 and **4d** in a similar manner as was **5a**. Purification was accomplished by bulb-to-bulb distillation (87% from **4d**) and then distillation on a Vigreux column: bp 52 °C (12 mm); 70%; ^1H NMR ($CDCl_3$) δ 4.40 (dt, 2 H, $^2J_{HF}$ = 45.5, $^3J_{HF}$ = 12 Hz, CH_2F), 7.23 (s, 5 H, Ph); ^{19}F NMR ($CDCl_3$) ϕ 108 (dt, 2 F, $^3J_{FF}$ = 18, J_{FH} = 12 Hz, CF_2), 229 (tt, 1 F, J_{FH} = 45.5, $^3J_{FF}$ = 18 Hz, CH_2F). Anal. Calcd for $C_8H_7F_3$: C, 60.00; H, 4.40; F, 35.59. Found: C, 60.30; H, 4.48; F, 35.60.

Preparation with (Diethylamino)sulfur Trifluoride. Typical Procedure. 1-Cyclohexyl-1,1,2-Trifluoroethane (5b). To 3.1 mL (4 g, 26 mmol) of DAST was added, under N_2, with stirring 2.5 g (17 mmol) of **4b** in 10 mL of anhydrous benzene. The mixture was stirred for 17 h at 50 °C. After the mixture was cooled at 0 °C, 10 mL of water was slowly added (exothermic) and the mixture washed until neutral with a $NaHCO_3$ solution. After extraction with ether and drying of the extracts, removal of the solvents in vacuo gave crude **5b** which was purified by bulb-to-bulb distillation (86%). A second distillation (Vigreux column) afforded an analytical sample: bp 149 °C; ^1H NMR ($CDCl_3$) δ 0.6–2.5 (11 H, c-C_6H_{11}), 4.33 (dt, 2 H, $^2J_{HF}$ = 46, $^3J_{HF}$ = 12 Hz, CH_2F); ^{19}F NMR ($CDCl_3$) ϕ 115 (approximate quint, 2 F, $^3J_{FF}$ = 14.8, $^3J_{FH} \simeq 12.7$, $^3J_{FH}$ = 12 Hz, CF_2), 235.5 (ttm, 1 F, $^2J_{FH}$ = 46, $^3J_{FF}$ = 14.8 Hz, CH_2F). Anal. Calcd for $C_8H_{13}F_3$: C, 57.82; H, 7.88. Found: C, 58.2; H, 8.07.

1-(1-Adamantyl)-1,1,2-trifluoroethane (5a) was prepared from DAST and **4a** as was **5b**. Purification of the crude product was performed as in the SF_4 procedure, i.e., by chromatography on silica gel (cyclohexane as eluant). The head fraction, containing mainly **5a** mixed with a small amount of **6a**, was discarded (78% from **4a**).

1-Phenyl-1,1,2-trifluoroethane (5d) was prepared from DAST and **4d** as was **5b**. Purification of the crude product was accomplished as in the SF_4 procedure (82% from **4d** after bulb-to-bulb distillation).

Dehydrofluorination with Potassium *tert*-Butoxide. Typical Procedure. (*Z*)-1-(1-Adamantyl)-1,2-Difluoroethylene (6a). To a solution of 3.5 g (31.5 mmol) of potassium *tert*-butoxide in 11 mL of *tert*-butyl alcohol (the suspension was previously heated until dissolution of the butoxide) was added a solution of 3.45 g (15.8 mmol) of **5a** in 1 mL of *tert*-butyl alcohol. The magnetically stirred mixture was heated for 17 h at 100 °C. After cooling, the mixture was poured into water (250 mL) and then extracted with ether. The extracts were dried over $MgSO_4$. After rotary evaporation of the solvents, the last traces of *tert*-butyl alcohol were removed in vacuo (0.005 mm), leaving (*Z*)-**6a** (99% from **5a**). An analytical sample was obtained by sublimaton at 40 °C (0.005 mm): mp 52.6 °C; ^1H NMR ($CDCl_3$) δ 1.43–2.2 (15 H, 1-adamantyl), 6.1 (dd, 1 H, $^2J_{HF}$ = 74, $^3J_{HF}$ = 18 Hz, =CHF); ^{19}F NMR ($CDCl_3$) ϕ 146.3 (dd, 1 F, $^3J_{FH}$ = 18, $^3J_{FF}$ = 11.6 Hz, 1-AdCF=), 172.1 (dd, 1 F, $^2J_{FH}$ = 74, $^3J_{FF}$ = 11.6 Hz, =CHF); IR (CCl_4) 1705 cm^{-1}. Anal. Calcd for $C_{12}H_{16}F_2$: C, 72.7; H, 8.13; F, 19.17. Found: C, 72.99; H, 8.07; F, 19.24.

(*Z*)-1-Cyclohexyl-1,2-difluoroethylene (6b) was prepared from **5b** (15 mmol) in a similar manner as was **6a** except that the solvents were removed by distillation at atmospheric pressure and

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then (*Z*)-**7b** was distilled (62% from **5b**): bp 146 °C; ^{1}H NMR ($CDCl_3$) δ 0.5–2.5 (11 H, c-C_6H_{11}), 6.13 (ddd, 1 H, $^2J_{HF}$ = 74, $^3J_{HF}$ = 18, $^4J_{HH}$ = 1 Hz, =CHF); ^{19}F NMR ($CDCl_3$) ϕ 138 (m, 1 F, $^3J_{FH}$ = 18, 15, $^3J_{FF}$ = 11 Hz, c-$C_6H_{11}CF$=), 168.3 (ddd, 1 F, $^2J_{FH}$ = 74, $^3J_{FF}$ = 11, $^4J_{FH}$ = 3.8 Hz, =CHF); IR (CCl_4) 1718 cm^{-1}. Anal. Calcd for $C_8H_{12}F_2$: C, 65.73; H, 8.27; F, 25.99. Found: C, 66.06; H, 8.50; F, 26.07.

(*Z*)-3,3-Dimethyl-1,2-difluorobutene (6c). To a solution of 2.5 g (22 mmol) of potassium *tert*-butoxide in 3 mL of dimethyl sulfoxide was added a solution of 1.7 g (12.1 mmol) of **5c** in 1 mL of Me_2SO. The mixture was heated, with stirring, for 48 h at 70 °C. After cooling, the mixture was submitted to a bulb-to-bulb distillation (room temperature, 0.01 mm). The distillate was shaken with excess water in a separatory funnel and the upper layer dried on 4-Å molecular sieves, affording (*Z*)-**6c** (45% from **5c**): bp 81–82 °C (Siwoloboff's method); ^{1}H NMR ($CDCl_3$) δ 1.07 (d, 9 H, $^4J_{HF}$ = 0.5 Hz, CH_3), 6.16 (dd, 1 H, $^2J_{HF}$ = 75, $^3J_{HF}$ = 17.5 Hz, =CHF); ^{19}F NMR ($CDCl_3$) ϕ 140 (ddm, 1 F, $^3J_{FH}$ = 17.5, $^3J_{FF}$ = 10, $^4J_{FH}$ = 0.5 Hz, *t*-BuCF=), 170.2 (dd, 1 F, $^2J_{FH}$ = 75, $^3J_{FF}$ = 10 Hz, =CHF); IR (CCl_4) 1708 cm^{-1}; no analysis; mass spectrum (70 eV), *m/e* 120.

(*Z*)-1-Phenyl-1,2-difluoroethylene (6d) was prepared from **5d** (25 mmol) in a similar manner as was **6a** except that the mixture of **5d** in *t*-BuOH–*t*-BuOK was heated only 3 h at 100 °C. The crude oil was submitted to bulb-to-bulb distillation [60 °C (0.005 mm)]. The most volatile part was distilled in a small Vigreux apparatus to afford 1.15 g (about 30% from **5d**) of (*Z*)-**6d** (contaminated by 9% **5d**): bp 86–87 °C (60 mm) [lit.[7] bp 88–90 °C (60 mm)]; ^{1}H NMR ($CDCl_3$) δ 6.78 (dd, 1 H, $^2J_{HF}$ = 71, $^3J_{HF}$ = 17 Hz, =CHF), 7.18 (s, 5 H, Ph); ^{19}F NMR ($CDCl_3$) ϕ 145.8 (dd, 1 F, $^3J_{FH}$ = 17, $^3J_{FF}$ = 11.5 Hz, PhCF=), 168.8 (dd, 1 F, $^2J_{FH}$ = 71, $^3J_{FF}$ = 11.5 Hz, =CHF); IR (CCl_4) 1693 cm^{-1}; mass spectrum (70 eV), *m/e* 140.

The residue of the bulb-to-bulb distillation was 8: ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 9 H, CH_3), 6.28 (d, 1 H, $^3J_{HF}$ = 21 Hz, =CHO-*t*-Bu), 7.12 (5 H, Ph); ^{19}F NMR ($CDCl_3$) ϕ 141.3 (d, $^3J_{FH}$ = 21 Hz, PhCF=); IR (CCl_4) 1678 cm^{-1}.

Epoxidation with *m*-Chloroperoxybenzoic Acid (MCPBA). Typical Procedure. *cis*-1-(1-Adamantyl)-1,2-difluoro-1,2-epoxyethane (9a). To a solution of 2.43 g (14 mmol) of MCPBA in 22 mL of chloroform was added 1.5 g (7.6 mmol) of **6a** in 4 mL of $CHCl_3$. The mixture was stirred overnight at room temperature (although 3 h proved to be sufficient for completion) and then filtered. The solution was washed with 2 mL of 20% sodium bisulfite solution, three 5-mL portions of saturated $NaHCO_3$ solution, and 10 mL of saturated sodium chloride solution. The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated by rotary evaporation. Bulb-to-bulb distillation of the residue (0.005 mm, bath temperature 90 °C) afforded 1.32 g of **9a**: oil (81% from **6a**); ^{1}H NMR ($CDCl_3$) δ 1.52–2.17 (15 H, 1-adamantyl), 5.33 (dd, 1 H, $^2J_{HF}$ = 82.5, $^3J_{HF}$ = 1.8 Hz, >CHF); ^{19}F NMR ($CDCl_3$) ϕ 155.8 (dd, 1 F, $^3J_{FF}$ = 36.7, $^3J_{FH} \simeq$ 1 Hz, AdCF<), 159.6 (dd, 1 F, $^2J_{FH}$ = 82.5, $^3J_{FF}$ = 36.7 Hz, >CHF). Anal. Calcd for $C_{12}H_{16}F_2O$: C, 67.26; H, 7.53; F, 17.73. Found: C, 67.15; H, 7.57; F, 17.51.

***cis*-1-Cyclohexyl-1,2-difluoro-1,2-epoxyethane (9b)** was prepared in a similar manner as was **9a** (72% after bulb-to-bulb distillation), bp 180–182 °C (Siwoloboff's method). ^{1}H and ^{19}F NMR data are in agreement with those previously reported.[1] Anal. Calcd for $C_8H_{12}F_2O$: C, 59.25; H, 7.46. Found: C, 59.46; H, 7.61.

***cis*-3,3-Dimethyl-1,2-difluoro-1,2-epoxybutane (9c)** was prepared in the same way as was **9a** (starting from 0.3 g of **7c**) except that the whole chloroform solution was first submitted to bulb-to-bulb distillation and then the solvent was removed by distillation on a Vigreux column, leaving **9c** (55%): bp 100–101 °C (Siwoloboff's method); no analysis; mass spectrum (70 eV), *m/e* 136. ^{1}H and ^{19}F NMR data are in agreement with those previously reported.[1]

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Registry No. 3a, 5122-82-7; **3b**, 56077-28-2; **3c**, 5469-26-1; **3d**, 70-11-1; **4a**, 75600-43-0; **4b**, 768-04-7; **4c**, 4538-80-1; **4d**, 450-95-3; **5a**, 75600-44-1; **5b**, 75600-45-2; **5c**, 58384-37-5; **5d**, 75600-46-3; **6a**, 75600-47-4; **6b**, 75600-48-5; **6c**, 58384-38-6; **6d**, 15480-90-7; **8**, 75600-49-6; **9a**, 75600-50-9; **9b**, 75600-51-0; **9c**, 75600-52-1.

Remarkable Stereoselectivity in the Reaction of Nucleophilic Reagents with C(7) Carbonyl Derivatives of Functionalized Bicyclo[2.2.1]heptanes

George Majetich, Paul A. Grieco,*[1] and Shannon Bongers

Department of Chemistry, University of Pittsburgh Pittsburgh, Pennsylvania 15260

Mary G. Erman and David A. Langs*

Medical Foundation of Buffalo, Buffalo, New York 14203

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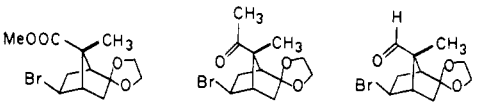
This paper describes a series of noteworthy reactions on the rigid bicyclo[2.2.1]heptane derivatives **1–3**.

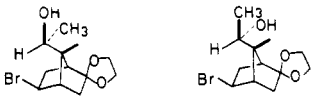


1 **2** **3**

In general, carboxylic esters react rapidly with organometallic reagents (e.g., CH_3Li, CH_3MgI) to form tertiary alcohols in high yield. There are, however, several reports in the literature describing the synthesis of ketones in good yield by the reaction of organolithium reagents with hindered esters.[2] Bulky organolithium reagents are known to react with aromatic esters to produce ketones in good yield.[3] With respect to Grignard reagents, it has been demonstrated that bulky alkylmagnesium halides in hexamethylphosphoramide react with hindered esters to afford, upon workup, modest to good yields of ketones.[4]

We have observed that treatment of bromo ketal ester **1**[5] with excess methyllithium (5.0 equiv) in ether gave rise to methyl ketone **2**: mp 70–71 °C; 94% yield. No tertiary alcohol could be detected. The presence of the bulky exo-oriented bromo substituent and the quaternary nature of the C(7) carbon atom of the bicyclo[2.2.1]heptane system are undoubtedly responsible for the observed result. The inability of sodium borohydride to reduce ketone **2** at room temperature further attests to the severe steric hindrance about the C(7) acetyl unit.

In contrast to the results with sodium borohydride, the more reactive *lithium aluminum hydride smoothly reduced ketone 2 at −20 °C, giving rise to a single crystalline diastereomer* (**4**; mp 127.0–127.5 °C) in 91% yield. NMR analysis ($CDCl_3$) of the product (**4**) revealed a three-proton



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doublet centered at δ 1.18 (J = 6 Hz) and a three-proton

(1) Address correspondence to this author at the Department of Chemistry, Indiana University, Bloomington, IN 47405.

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