Reaction of 2-lithio-3.4-bis(trifluoromethyl)furan with electrophiles

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Abstract

2-Substituted-3,4-bis(trifluoromethyl)furans $\overline{CH=C(CF_3)C(CF_3)=CR-O}$ [R = CO_2H (and hence R = CO_2Me and CO_2Et), CHO, CHPhOH, CHMeOH, $CH(OH)CH=CH_2$] are obtained in good yield by treatment of the corresponding 2-lithiofuran with the appropriate electrophile. With methyl acrylate, initial attack occurs at carbonyl carbon but the resulting ketone (R = $COCH=CH_2$) undergoes Michael addition with an excess of the lithium salt. From the reaction with dichloromaleic anhydride, 5,5-bis[3,4-bis(trifluoromethyl)-2-furyl]-3,4-dichloro-2-furanone is formed in 85% yield.

Introduction

There are a number of reports on the use of the lithio derivatives of non-fluorinated furans in synthesis, but the only report involving 2-lithio-3,4-bis(trifluoromethyl)furan (**1**) covered its preparation and reaction with 1,1-dichlorodifluoroethylene to provide a precursor to the 2-ethynyl derivative, a monomer required for polymerisation studies [1].

In the present work, as part of a study of the chemistry of the parent 3,4-bis(trifluoromethyl)furan [2], the reactions of the lithium salt **1** with a variety of electrophiles have been investigated.

Experimental

General techniques

Reaction product mixtures were separated by dry column 'flash' chromatography (DCFC) using silica gel (60H Merck GF_{256}) purchased from BDH Chemicals, Ltd.

^1H nuclear magnetic resonance (NMR) spectra were run either on Perkin–Elmer R34 (220 MHz) or Bruker AC (300 MHz) FT spectrometers, ^{13}C broad band decoupled NMR spectra were recorded on the Bruker AC machine and ^{19}F NMR spectra were recorded on a Perkin–Elmer R32 (84.6

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MHz) spectrometer. Internal tetramethylsilane (TMS) and external trifluoroacetic acid (TFA) were used as the respective references and chemical shifts to low field of reference are designated positive.

Infrared (IR) spectra were recorded on a Perkin–Elmer 783 spectrometer using KBr discs for solid samples and CsI plates for liquid films.

Low-resolution (electron impact) mass spectra were run on Kratos MS 45 or MS 25 instruments operating at 70 eV and high-resolution spectra were recorded on a Kratos Concept mass spectrometer.

Melting points are uncorrected.

Elemental analyses (for C, H, F and Cl) were carried out by the Departmental analytical service using standard methods.

Starting material

3,4-Bis(trifluoromethyl)furan $CF_3\overline{C=CH-O-CH=C}CF_3$ (**16**) [3], was prepared in *ca.* 65% overall yield by Diels–Alder reaction of hexafluorobut-2-yne with furan followed by hydrogenation (catalyst, 10% Pd on C) and then retro-cleavage of ethylene at 200 °C, a procedure previously used for the synthesis of dimethyl furan-3,4-dicarboxylate and related compounds [4].

2-Lithio-3,4-bis(trifluoromethyl)furan (**1**) was generated from furan (**16**) by treatment of a stirred solution in diethyl ether (10 cm^3) with a slight excess of a solution of n-butyl-lithium in hexane added from a syringe at −70 °C, as reported previously [1]. The addition (and subsequent reaction) was carried out under nitrogen in a reaction flask fitted with a septum cap, a dropping funnel, a nitrogen inlet and a cold finger (cooled to −78 °C) surmounted by a condenser leading to a nitrogen outlet. The solution was stirred for *ca.* 0.5 h before reaction with the electrophile was carried out.

Reactions of 2-lithio-3,4-bis(trifluoromethyl)furan (1)

(a) With carbon dioxide

Carbon dioxide gas was bubbled over a period of 2.5 h into an ethereal solution of lithio-furan **1** [prepared from n-butyl-lithium in hexane (1.6 M, 7.30 cm^3, 11.68 mmol) and furan **16** (2.33 g, 11.42 mmol) at −70 °C (2 h)]. The cooling bath was maintained at −40 to −50 °C during this period and then allowed to rise gradually to ambient temperature. Hydrochloric acid (0.1 M, 20 cm^3) was added and stirring continued (0.5 h), and then the organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo* to give a thick yellow oil which was purified by DCFC [petroleum ether (b.p., 40–60 °C): chloroform (4:1, v/v)]. This gave a white crystalline solid (R_F, 0.70) which was identified as 3,4-bis(trifluoromethyl)furan-2-oic acid (**2**) (nc) (2.33 g, 9.40 mmol, 82%) (Found: C, 33.6; H, 0.8%; mol. wt., 248.$C_7H_2O_3F_6$ requires C, 33.9; H, 0.8%; mol. wt., 248), m.p., 124–126 °C. ^{1}H NMR 300 MHz, acetone-d_6: δ 8.2 (s, =CH) and 11.8 (s, CO_2H) ppm. ^{19}F NMR: δ +18.5 and +21.5 (2q, J = 9 Hz, $2CF_3$) ppm. ^{13}C NMR: δ 157.8 (s, CO_2H), 147.2 (q, ^3J = 6 Hz, =CH), 146.8 (q, ^3J = 4 Hz, $=CCO_2H$), 121.6 (q, ^1J = 267 Hz, CF_3), 121.2 (q, ^1J = 269 Hz, CF_3), 119.4 (q, ^2J = 43 Hz, $=CCF_3$) and 118.2 (q, ^2J = 40 Hz, $=CCF_3$) ppm. IR $\nu_{max.}$: 3200–2860 (br.,

O–H str.), 1725 (s, C=O str.), 1620 and 1585 (m, C=C str.) and 1200–1140 (s, C–F str.) cm^{-1}. Mass spectrum *m/z*: 248 (100%, M^+); 231 [51.5, $(M-OH)^+$], 229 [5.4, $(M-F)^+$], 209 [49.8, $(C_7HF_4O_3)^+$], 203 [16.8, $(M-CO_2H)^+$] and 69 [31.2, $(CF_3)^+$].

(b) With ethyl chloroformate

To a stirred solution of salt **1** [prepared from furan **16** (1.15 g, 5.64 mmol) and n-butyl-lithium in hexane (1.6 M, 4.0 cm^3, 6.4 mmol) in ether (10 cm^3) under nitrogen at −70 °C] was added ethyl chloroformate (0.8 cm^3, 8.37 mmol) dropwise from a pressure-equalizing dropping funnel. Stirring was continued (2 h) after addition was complete and the flask was allowed to warm gradually to room temperature. Stirring was maintained overnight under nitrogen and the resultant white, viscous, sweet-smelling substance was treated with distilled water (20 cm^3) and the ether layer was separated, dried ($MgSO_4$) and concentrated to give a very thick brown oil. Purification by DCFC [chloroform:hexane (2:1 v/v)] afforded colourless crystals of bis[3,4-bis(trifluoromethyl)-2-furyl]ketone (**5**) (nc) (1.20 g, 2.76 mmol, 98%) (Found: C, 36.3; H, 0.5; F, 52.1%; mol. wt., 434. $C_{13}H_2O_3F_{12}$ requires C, 35.9; H, 0.5; F, 52.5%; mol. wt., 434), m.p., 54–56 °C. ^1H NMR 300 MHz, $CDCl_3$: δ 8.0 (s, =CH) ppm. ^{19}F NMR: δ +19.5 and +21.5 (2q, $J=9$ Hz, $2CF_3$) ppm. ^{13}C NMR: δ 168.3 (s, C=O), 149.4 (q, $^3J=3$ Hz, $=CC=O$), 146.1 (q, $^3J=6$ Hz, $=CCH$), 120.0 and 118.7 (2q, $^2J=40$ Hz, 2 $=CCF_3$), 119.2 and 120.2 (2q, $^1J=269$ Hz, $2CF_3$) ppm. IR $\nu_{max.}$: 3160 (w, vinylic C–H str.), 1675 (s, C=O str.), 1605 and 1550 (m, C=C str.), and 1220–1135 (s, C–F str.) cm^{-1}. Mass spectrum *m/z*: 434 (28.9%, M^+), 415 [31.8, $(M-F)^+$], 231 [100.0, $(M-C_6HF_6O)^+$], 203 [10.0, $(C_6HF_6O)^+$] and 69 [8.1, $(CF_3)^+$].

(c) With benzaldehyde

To an ethereal solution of salt **1** [prepared from n-butyl-lithium in hexane (1.6 M, 7.0 cm^3, 11.20 mmol) and furan **16** (2.28 g, 11.18 mmol) in diethyl ether (10 cm^3) at −70 °C] was added a solution of benzaldehyde (1.19 g, 11.22 mmol) in anhydrous ether (10 cm^3). The milky solution immediately turned yellow and was stirred at −70 °C (1.5 h) before being allowed to warm slowly to room temperature. The solution was then acidified with aqueous hydrochloric acid (0.1 M, 15 cm^3), the ether layer was separated, dried ($MgSO_4$) and concentrated to give a thick yellow oil (3.31 g) which was shown by ^1H NMR spectroscopy to consist mainly of the desired alcohol contaminated with a small amount of unreacted benzaldehyde. The mixture was purified by distillation *in vacuo* to give a yellow oil which was identified as 3,4-bis(trifluoromethyl)-2-furylbenzyl alcohol (**6**) (nc) (2.80 g, 9.03 mmol, 81%) (Found: C, 50.1; H, 2.6; F, 36.9%; mol. wt., 310. $C_{13}H_8O_2F_6$ requires C, 50.3; H, 2.6; F, 36.8%; mol. wt., 310). ^1H NMR 300 MHz, $CDCl_3$: δ 7.4 (s, =CH), 5.8 (s, =CCH), 4.2 (s, O–H) and 7.2 (mult., Ph) ppm. ^{19}F NMR: δ +19.5 and +23.0 (2q, $J=9$ Hz, $2CF_3$) ppm. ^{13}C NMR: δ 157.4 (q, $^3J=3$ Hz, $=CCH$), 143.8 (q, $^3J=6$ Hz, $=CH$), 121.5 and 121.0 (2q, $^1J=268$ Hz, $2CF_3$), 138.8, 128.8, 126.1 and 128.7 (4s, Ph), 115.9 and 110.8 (2q, $^2J=34$

Hz and 39 Hz, 2 $=CCF_3$), 67.9 (s, *C*HOH) ppm. IR $\nu_{max.}$: 3360 (m, O–H str.), 1585 (s, C=C str.) and 1200–1125 (s, C–F str.) cm^{-1}. Mass spectrum *m/z*: 310 (100.0%, M^+), 293 [26.3, $(M-OH)^+$], 292 [4.1, $(M-H_2O)^+$], 289 [22.9, $(C_{13}H_6F_5O_2)^+$], 213 [27.2, $(M-C_6H_6F)^+$], 106 [11.0, $(PhCHO)^+$], 105 [57.0, $(PhCO)^+$] and 77 [47.3, $(C_6H_5)^+$].

(d) With acetaldehyde

To an ethereal solution of salt **1** [prepared from n-butyl-lithium in hexane (1.6 M, 6.2 cm^3, 9.92 mmol) and furan **16** (2.0 g, 9.80 mmol) in diethyl ether (10 cm^3) at −70 °C] was added a solution of acetaldehyde (0.44 g, 10.0 mmol) in anhydrous ether (10 cm^3). The solution was stirred at −70 °C (1.5 h), allowed to warm slowly to room temperature and then acidified with aqueous hydrochloric acid (0.1 M, 10 cm^3). The ether layer was separated, dried ($MgSO_4$) and concentrated to give a thick yellow oil which was purified by distillation *in vacuo* and identified as 1-[3,4-bis(trifluoromethyl)-2-furyl]ethanol (**7**) (nc) (1.75 g, 7.06 mmol, 72%) (Found: mol. wt., 248.0274. $C_8H_6O_2F_6$ requires mol. wt., 248.0272). ^1H NMR 220 MHz, $CDCl_3$: δ 7.8 (s, =CH), 5.5 (q, C*H*OH), 3.0 (s, O–H) and 2.0 (d, CH_3) ppm. ^{19}F NMR: δ +19.0 and +22.5 (2q, $J=9$ Hz, $2CF_3$) ppm. Mass spectrum *m/z*: 248 (11.9%, M^+), 247 [8.1, $(M-H)^+$], 233 [44.5, $(M-CH_3)^+$], 231 [12.0, $(M-OH)^+$], 230 [2.5, $(M-H_2O)^+$], 227 [19.3, $(C_8H_4F_5O_2)^+$], 213 [100.0, $(C_7H_2F_5O_2)^+$], 185 [47.4, $(C_6H_2F_5O)^+$] and 43 [54.5, $(C_2H_3O)^+$].

(e) With dichloromaleic anhydride (DCMA)

To the salt **1** [prepared from furan **16** (2.0 g, 9.80 mmol) and n-butyl-lithium in hexane (1.6 M, 6.20 cm^3, 9.92 mmol)] was added a solution of dichloromaleic anhydride (DCMA) (1.63 g, 9.76 mmol) in anhydrous ether (15 cm^3) over 5 min at −70 °C. The cloudy solution turned pale yellow and was stirred at −70 °C (1 h), allowed to warm to room temperature and then stirred further (2 h). The resulting white suspension was removed by filtration to give a yellowish solid (2.49 g), which was purified by DCFC [chloroform:pentane (3:1 v/v)] to give colourless crystals (R_F, 0.70) identified as 5,5-bis[3,4-bis(trifluoromethyl)-2-furyl]-3,4-dichloro-2-furanone (**9**) (nc) (2.31 g, 4.15 mmol, 85%) (Found: C, 34.8; H, 0.5; Cl, 13.0%; mol. wt., 557. $C_{16}H_2O_4F_{12}Cl_2$ requires: C, 34.5; H, 0.4; Cl, 12.9%; mol. wt., 557), m.p., 118–120 °C. ^1H NMR 300 MHz, $CDCl_3$: δ 7.9 (s, =CH) ppm. ^{19}F NMR: δ +19.5 and +22.5 (2q, $J=9$ Hz, $2CF_3$) ppm. ^{13}C NMR: δ 161.8 (s, C=O), 148.2 (s, $=C$Cl), 147.4 (q, $^3J=4$ Hz, $=C$), 144.6 (q, $^3J=6$ Hz, =CH), 120.0 and 120.2 (2q, $^1J=269$ Hz, $2CF_3$), 115.3 and 118.4 (2q, $^2J=41$ Hz, 2 $=CCF_3$), 124.8 (s, $=C$ClC=O) and 80.8 (s, $\geq$C–) ppm. IR $\nu_{max.}$: 3160 (w, vinylic C–H str.), 1820 (s, γ-lactone C=O str.), 1640 and 1570 (m, C=C str.), 1310 (s, C–O str.) and 1220–1135 (s, C–F str.) cm^{-1}. Mass spectrum *m/z*: 556, 558 and 560 (14.1%, M^+), 537, 539 and 541 [20.0, $(M-F)^+$], 521 and 523 [46.0, $(M-Cl)^+$], 512, 514 and 516 [12.4, $(M-CO_2)^+$], 477 and 479 [36.9, $(M-CO_2Cl)^+$], 353, 355 and 357 [10.5, $(C_{10}HF_6O_3Cl_2)^+$], 325, 327 and 329 [7.8, $(C_9HF_6O_2Cl_2)^+$], 309, 311 and 313 [39.1,

$(C_9HF_6OCl_2)^+$], 231 [100.0, $(C_7HF_6O_2)^+$], 203 [15.3, $(C_6HF_6O)^+$], 122, 124 and 126 [82.8, $(C_3OCl_2)^+$], 69 [93.3, $(CF_3)^+$] and 44 [36.4, $(CO_2)^+$].

(f) With methyl acrylate

To a stirred solution of salt **1** [prepared from furan **16** (3.16 g, 15.49 mmol) and n-butyl-lithium in hexane (2.5 M, 6.20 cm^3, 15.5 mmol) in diethyl ether (10 cm^3) at −70 °C], was added methyl acrylate (1.33 g, 15.47 mmol) dropwise over 15 min and stirring was continued (1 h). Aqueous hydrochloric acid (0.1 M, 10 cm^3) was then added and the organic layer was separated, dried ($MgSO_4$) and concentrated to give a dark brown oil (2.40 g). Purification of the oil by DCFC [petroleum ether (b.p., 40–60 °C):dichloromethane (3:1 v/v)] afforded colourless crystals (R_F, 0.60), identified as 1,3-bis[3,4-bis(trifluoromethyl)-2-furyl]propan-1-one (**8**) (nc) (2.03 g, 4.39 mmol, 57%) (Found: C, 39.3; H, 1.1; F, 49.0%; mol. wt., 462. $C_{15}H_6O_3F_{12}$ requires C, 39.0; H, 1.3; F, 49.4%; mol. wt., 462), m.p., 54–56 °C. ^{1}H NMR 300 MHz, $CDCl_3$: δ 3.2 (2dt, J=7.5 Hz, $2CH_2$) and 7.6 and 7.8 (2q, J=7.5 Hz, 2 =CH) ppm. ^{19}F NMR: δ +19.0 (mult., $2CF_3$) and +21.5 (mult., $2CF_3$) ppm. ^{13}C NMR: δ 185.9 (s, C=O), 157.0 and 150.9 (2q, ^3J=4 Hz, =*C*CO and =*C*), 144.9 and 142.7 (2q, ^3J=6–7 Hz, 2 =CH), 110.2, 116.5, 117.8 and 118.8 (4q, ^2J=38–41 Hz, 4*C*CF_3), 120.0, 120.4, 121.0 and 121.7 (4q, ^1J=268–270 Hz, $4CF_3$) and 20.6 and 37.1 (2s, $2CH_2$) ppm. IR $\nu_{max.}$: 3130 (w, vinylic C−H str.), 2945 (w, alkyl C−H str.), 1715 (m, C=O str.), 1585 and 1560 (m, C=C str.) and 1180 (s, C−F str.) cm^{-1}. Mass spectrum *m/z*: 462 (7.0%, M^+), 443 [7.8, $(M-F)^+$], 442 [6.3, $(M-HF)^+$], 231 [50.2, $(C_7HF_6O_2$ and $C_8H_5F_6O)^+$], 217 [100.0, $(C_7H_3F_6O)^+$], 212 [12.2, $(C_7HF_5O_2)^+$], 211 [58.9, $(C_8H_4F_5O)^+$], 203 [10.7, $(C_6HF_6O)^+$] and 69 [44.4, $(CF_3)^+$].

(g) With acrolein

To a stirred solution of salt **1** [prepared from furan **16** (1.30 g, 6.37 mmol) and n-butyl-lithium in hexane (2.5 M, 2.55 cm^3, 6.37 mmol)] in diethyl ether (10 cm^3) at −70 °C was added dropwise acrolein (0.36 g, 6.43 mmol) in diethyl ether (5 cm^3) and the mixture was stirred at −70 °C (30 min). The flask was allowed to warm slowly to room temperature, aqueous hydrochloric acid (0.1 M, 10 cm^3) was then added and the organic layer was dried ($MgSO_4$) and concentrated to give a dark brown oil (1.14 g). This was purified by DCFC [petroleum ether (b.p., 40–60 °C):dichloromethane (3:1 v/v)] to give a yellow oil (R_F, 0.50), identified as 3-[3,4-bis(trifluoromethyl)-2-furyl]prop-1-en-3-ol (**11**) (nc) (0.98 g, 3.77 mmol, 59%) (Found: mol. wt., 260.0273. $C_9H_6O_2F_6$ requires mol. wt., 260.0272). ^{1}H NMR 300 MHz, $CDCl_3$: δ 7.8 (s, ring=CH), 2.3 (b, O−H), 5.5 [d, J=6 Hz, =CHC*H*OH], 6.1 [ddd, $J(H_b-H$ *trans*$)$=17 Hz, $J(H_a-H$ *cis*$)$=11 Hz, C*H*=CH_aH_b], 5.35 [dd, $J(H_b-H_a)$=3 Hz, =CH_a] and 5.4 (dd, =CH_b) ppm. ^{19}F NMR: δ +20.0 and +23.0 (2q, J=9 Hz, $2CF_3$) ppm. ^{13}C NMR: δ 157.1 (q, ^3J=4 Hz, ring=*C*CH), 143.4 (q, ^3J=6 Hz, ring=CH), 116.4 and 110.8 (2q, ^2J=38 Hz, 2 =*C*CF_3), 121.3 and 120.9 (2q, ^1J=268 Hz, $2CF_3$), 135.0 (s, =*C*HCHOH), 118.2 (s,

$=CH_2$) and 67.2 (s, CHO) ppm. IR $\nu_{max.}$: 3420–3340 (m, O–H str.), 2940 (w, vinylic C–H str.), 1580 (s, C=C str.) and 1200–1130 (s, C–F str.) cm^{-1}. Mass spectrum *m/z*: 260 (24.9%, M^+), 243 [5.6, $(M-OH)^+$], 241 [8.5, $(M-F)^+$], 240 [38.4 $(M-HF)^+$], 231 [16.6, $(C_7HF_6O_2)^+$], 217 [12.3, $(C_7H_3F_6O)^+$], 213 [75.2, $(C_8H_6F_5O)^+$], 212 [42.2, $(C_8H_5F_5O)^+$], 211 [30.1, $(C_8H_4F_5O)^+$], 204 [15.8, $(C_6H_2F_6O)^+$], 185 [57.3, $(C_9H_4F_3O)^+$], 69 [45.1, $(CF_3)^+$] and 57 [29.6, $(C_3H_3O)^+$].

(h) With dimethyl formamide (DMF)

A stirred solution of salt **1** [prepared from the furan **16** (1.09 g, 5.34 mmol) and n-butyl-lithium in hexane (1.6 M, 3.40 cm^3, 5.44 mmol) in diethyl ether (5 cm^3) at −70 °C] was treated dropwise with an ethereal solution of DMF (0.39 g, 5.34 mmol) over 15 min and stirring was continued (1 h). After warming to room temperature, the resulting material was treated with aqueous hydrochloric acid (0.1 M, 10 cm^3) and the organic layer was separated, dried ($MgSO_4$) and the solvent removed under high vacuum (*ca.* 10^{-3} mm Hg), through an external trap (−78 °C), to give a brown liquid which was identified as 3,4-bis(trifluoromethyl)-2-furancarbaldehyde (**10**) (nc) (0.67 g, 2.89 mmol, 54%) (Found: mol. wt., 232.0001. $C_7H_2O_2F_6$ requires mol. wt., 231.9959). ^1H NMR 220 MHz, $CDCl_3$: δ 8.2 (s, =CH) and 10.5 (s, CHO) ppm. ^{19}F NMR: δ +19.2 and +22.5 (2q, $J=9$ Hz, $2CF_3$) ppm. IR $\nu_{max.}$: 3160 (m, vinylic C–H str.), 2990 (w, aldehydic C–H str.), 1690 (s, C=O str.) and 1200–1130 (s, C–F str.) cm^{-1}. Mass spectrum *m/z*: 232 (100.0%, M^+), 213 [18.8, $(M-F)^+$], 203 [8.6, $(M-CHO)^+$], 185 [10.1, $(C_6H_2F_5O)^+$], 156 [19.0, $(C_7H_2F_2O_2)^+$], 69 [15.0, $(CF_3)^+$] and 29 [15.6, $(CHO)^+$].

Reactions of 3,4-bis(trifluoromethyl)furan-2-oic acid (2)

(a) With diazomethane

To a stirred, ice-cold solution of the acid **2** (1.46 g, 5.89 mmol) in ether (20 cm^3) was added a large excess of an ethereal solution of diazomethane and the temperature was maintained at 0 °C (*ca.* 3 h). The solution was allowed to warm to room temperature and stirred overnight. The ether was evaporated *in vacuo* to give a yellow oil (1.43 g) which was purified by DCFC (eluant $CHCl_3$) to give a major component (R_F, 0.50) identified as methyl 3,4-bis(trifluoromethyl)furan-2-oate (**4**) (nc) (1.21 g, 4.62 mmol, 78%) (Found: C, 36.3; H, 1.6; F, 43.6%; mol. wt., 262. $C_8H_4O_3F_6$ requires C, 36.6; H, 1.5; F, 43.5%; mol. wt., 262). ^1H NMR 300 MHz, $CDCl_3$: δ 3.9 (s, CH_3) and 7.9 (s, =CH) ppm. ^{19}F NMR δ +18.6 and +21.5 (2q, $J=9$ Hz, $2CF_3$) ppm. ^{13}C NMR: δ 156.5 (s, C=O), 145.6 (q, $^3J=6$ Hz, =CH), 145.3 (q, $^3J=4$ Hz, $=CCO_2Me$), 120.5 and 120.1 (2q, $^1J=269$ and 268 Hz, $2CF_3$), 118.9 and 117.8 (2q, $^2J=40$ and 38 Hz, 2 $=CCF_3$) and 52.8 (s, OCH_3) ppm. IR $\nu_{max.}$: 3160 (w, vinylic C–H str.), 2970 (m, alkyl C–H str.), 1750 (s, C=O str.) and 1220–1130 (s, C–F str.) cm^{-1}. Mass spectrum *m/z*: 262 (31.7%, M^+), 243 [12.6, $(M-F)^+$], 231 [100, $(M-OCH_3)^+$], 203 [13.1, $(M-CO_2Me)^+$] and 69 [4.7, $(CF_3)^+$].

(b) With trimethylchlorosilane and ethanol

To a stirred solution of the acid **2** (0.49 g, 1.90 mmol) in diethyl ether (10 cm^3) contained in a round-bottomed flask (50 cm^3) was added trimethylchlorosilane (0.42 g, 3.89 mmol). The mixture was stirred for a further 2 h at room temperature and absolute ethanol (1 cm^3) was then added. Stirring was continued for 12 h and the excess of solvent was removed on a rotary evaporator to afford ethyl 3,4-bis(trifluoromethyl)furan-2-oate (**3**) (nc) (0.42 g, 1.52 mmol, 80%). ^1H NMR 300 MHz, $CDCl_3$: δ 1.3 (t, CH_3), 3.9 (q, CH_2), 8.0 (s, =CH) ppm. ^{19}F NMR: δ +19.4 and +22.2 (2q, $J=9$ Hz, $2CF_3$) ppm. ^{13}C NMR: δ 157.9 (s, C=O), 145.4 (q, $^3J=6$ Hz, =CH), 145.8 (q, $^3J=4$ Hz, $=CCO_2Et$), 120.5 and 120.1 (2q, $^1J=268$ and 269 Hz, $2CF_3$), 119.3 and 118.0 (2q, $^2J=42$ and 40 Hz, 2 $=CCF_3$), 66.0 (s, CH_2) and 17.3 (s, CH_3) ppm. IR $\nu_{max.}$: 3140 (w, vinylic C–H str.), 2925 (m, alkyl C–H str.), 1725 (s, C=O str.) and 1220–1160 (s, C–F str.) cm^{-1}. Mass spectrum *m/z*: 276 (3.6%, M^+), 248 [100.0, $(M-C_2H_4)^+$], 231 [95.8, $(M-OEt)^+$], 209 [52.2, $(C_7HF_4O_3)^+$], 204 [8.5, $(C_6H_2F_6O)^+$] and 203 [19.7, $(C_6HF_6O)^+$].

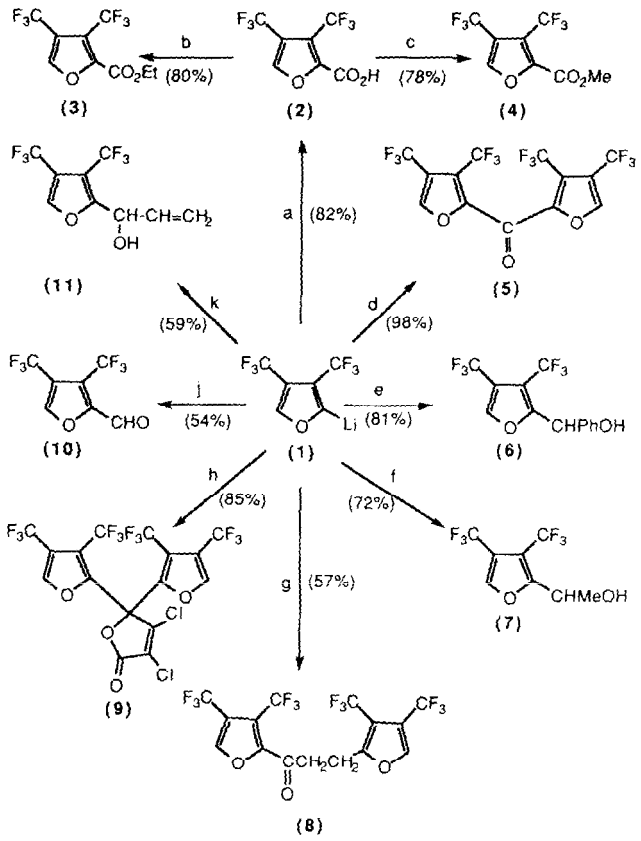
Results and discussion

Scheme 1 summarises the reactions which have been carried out. Treatment of salt **1** with carbon dioxide, benzaldehyde, acetaldehyde and dimethyl formamide proceeded as expected to afford the acid **2**, the secondary alcohols **6** and **7**, and the aldehyde **10**, respectively, in reasonable yield.

Addition of ethyl chloroformate to the salt **1** gave the ketone **5** in excellent yield, which indicated that the intermediate ester **3** is highly susceptible to nucleophilic attack by **1**. Further attack on the ketone **5** by salt **1** to give the salt of the corresponding tertiary alcohol is apparently not favoured, presumably for steric reasons. It is possible that the ester **3** could be prepared by the inverse addition of salt **1** to ethyl chloroformate as has been reported [5] for the reaction of 2-lithiofuran to give ethyl 2-furoate. However, ester **3** was conveniently prepared from acid **2** using the $EtOH/Me_3SiCl$ reagent recommended by Brook and Chan [6] for such a conversion and the corresponding methyl ester was made by treatment of acid **2** with diazomethane.

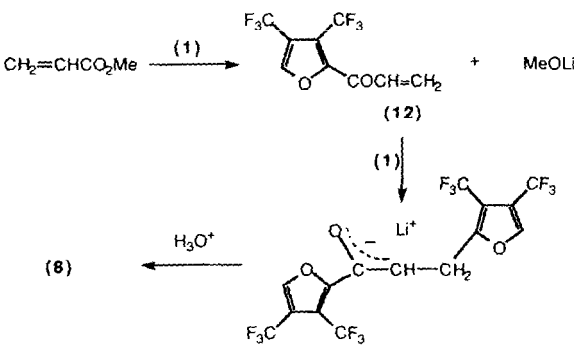
Reaction of organolithium reagents with α,β-unsaturated carbonyl compounds invariably involves nucleophilic attack at carbonyl carbon to afford alcohols after acidification, *e.g.* ref. 7. However, α,β-unsaturated aldehydes have a higher propensity to react at the carbonyl carbon than enones [8] and Locker and Seebach [9] have observed that reaction of lithium acetylides with 1,1,1-triphenylpent-3-en-2-one afforded the Michael adducts.

In the present work, reaction of salt **1** with acrolein afforded the secondary alcohol **11** via attack at carbon, but reaction involving methyl acrylate gave ketone **8** via attack at the ester carbonyl carbon followed by Michael addition to the resulting ketone **12** as shown in Scheme 2. Presumably, replacement of methoxy by the bis(trifluoromethyl)furyl group renders the carbonyl carbon

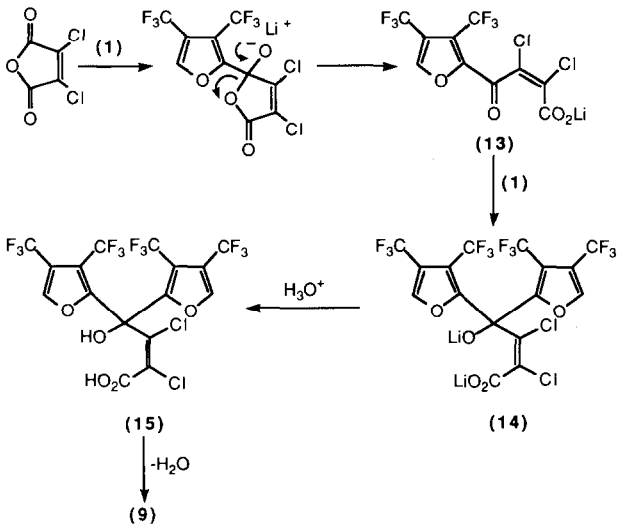


a, CO_2 then H_3O^+; (b), EtOH, Me_3SiCl; c, CH_2N_2; d, $ClCO_2Et$; e, PhCHO then H_3O^+; f, MeCHO then H_3O^+; g, $CH_2{=}CHCO_2Me$ then H_3O^+; h, $\overline{OC{-}CCl{=}CCl{-}CO{-}O}$ then H_3O^+; j, DMF then H_3O^+; k, $CH_2{=}CHCHO$ then H_3O^+.

Scheme 1.



Scheme 2.



Scheme 3.

less susceptible to nucleophilic attack by salt **1** for steric reasons, and reaction then takes place at the conjugate position.

Treatment of dichloromaleic anhydride with salt **1** resulted in opening of the anhydride ring via attack at the carbonyl carbon to give the α,β-unsaturated ketone **13**. This ketone then underwent further attack by salt **1** not at the conjugate position but at the carbonyl carbon, leading to formation of the dilithium salt **14** which on acidification gave the hydroxy acid **15** and hence the isolated lactone **9** (Scheme 3). It has been found previously that reaction of maleic anhydride with Grignard reagents gave, as intermediates, salts of keto acids which were attacked more rapidly by Grignard at the carbonyl carbon than was maleic anhydride; conjugate addition was not observed [10].

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