Journal of Fluorine Chemistry, 56 (1992) 359–371

Some reactions of 3,4-bis(trifluoromethyl)furan and its precursor, 2,3-bis(trifluoromethyl)-7-oxabicyclo[2,2,1]hepta-2,5-diene: novel isocoumarin formation from thermal reaction of the furan with ethyl propynoate*

Aliyu B. Abubakar, Brian L. Booth, Nadia N. E. Suliman (in part) and Anthony E. Tipping**
Chemistry Department, University of Manchester Institute of Science and Technology, Manchester M60 1QD (UK)

(Received August 12, 1991; accepted November 7, 1991)

Abstract

Thermolysis at 450 °C of 2,3-bis(trifluoromethyl)-7-oxabicyclo[2,2,1]hepta-2,5-diene (**2**) gives 3,4-bis(trifluoromethyl)furan (**1**). Treatment of oxanorbornadiene (**2**) with triflic acid (in CH_2Cl_2 under reflux) and then with water affords a mixture of 2,3-bis(trifluoromethyl)phenol (**4**) (6%), tris-(6-trifluoromethylsalicylide) (**5**) (45%) and 2-trifluoromethyl-6-hydroxybenzoic acid (**6**) (16%); analogous reaction with conc. sulphuric acid gives only the phenol **4** (44%).

Diels–Alder reaction either of furan **1** with dimethyl acetylenedicarboxylate (DMAD) or of dimethyl 3,4-furandicarboxylate with hexafluorobut-2-yne gives the oxanorbornadiene (**8**) (ca. 80%). In contrast, reaction of furan **1** with ethyl propynoate (EP) (1:1 molar ratio) at 150 °C affords a mixture of ethyl 6,7-bis(trifluoromethyl)isocoumarin-3-carboxylate (**12**) (52%) and its 4-carboxylate isomer **13** (9%), presumed to arise via a novel Diels–Alder cycloaddition of the dienophile EP to the C=C–C=O system of the 1:1 adduct ethyl 2,3-bis(trifluoromethyl)-7-oxabicyclo[2,2,1]hepta-2,5-diene-5-carboxylate (**14**). Diene **14** is conveniently prepared (93%) by the reaction of a large excess of hexafluorobut-2-yne with ethyl 3-furoate at room temperature, and when heated with EP (1:1 molar ratio) at 150 °C, the isocoumarin **12** (84%) is obtained; at 60 °C, however, **14** decomposes to give furan **1** and EP.

Introduction

Furans have found wide use in synthesis as the diene component in Diels–Alder cycloadditions. Oxanorbornadienes, formed by such reactions with alkynes, can be ring-opened with Lewis or protic acids to afford phenols [2, 3] or deoxygenated to give benzenes, e.g. with $LiAlH_4/Et_3N/THF$ [4]. Also certain 3- and 3,4-substituted furans, which cannot be made straightforwardly by other methods, have been synthesised from 2- and 2,3-substituted

---

*See ref. 1.

**Author to whom correspondence should be addressed.

0022-1139/92/$5.00

oxanorbornadienes by reduction of the least substituted double bond followed by thermal retrocleavage of ethene, e.g. see ref. 5.

In the present work, certain cycloaddition reactions of 3,4-bis(trifluoromethyl)furan (**1**) have been investigated and several reactions of its oxanorbornadiene precursor (**2**) have also been carried out.

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 and DEPT 135° NMR spectra were recorded on the Bruker AC machine and ^{19}F NMR spectra were recorded on a Perkin-Elmer R32 (84.6 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 spectrophotometer using KBr discs for solid samples and CsI plates for liquid films.

Low-resolution [electron impact (EI), unless stated otherwise or chemical ionisation (CI)] 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.

Single-crystal X-ray crystallographic analysis was carried out on a Rigaku Single-Crystal Diffractometer.

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

Starting materials

Ethyl 3-furoate (Aldrich), dimethyl acetylenedicarboxylate (DMAD; Aldrich), ethyl propynoate (EP; Lancaster Synthesis) and hexafluorobut-2-yne (Fluorochem Ltd.) were commercial samples.

3,4-Bis(trifluoromethyl)furan (**1**) was prepared (i) as reported [5,6] by reaction of hexafluorobut-2-yne with furan to afford 2,3-bis(trifluoromethyl)-7-oxabicyclo[2,2,1]hepta-2,5-diene (**2**) (94%), followed by reduction [H_2, Pd (10%) on C] in acetone of the least-substituted double bond (82%) and then thermolytic retrocleavage of ethene (100%), and (ii) by thermolytic retrocleavage of ethyne from the endoxide **2** as detailed below. Dimethyl 3,4-furandicarboxylate (**9**) was made analogously [5, 22] by reaction of DMAD with furan (95%), partial reduction of the resulting endoxide (86%) and then pyrolytic elimination of ethene (75%).

Reactions of 2,3-bis(trifluoromethyl)-7-oxabicyclo[2,2,1]hepta-2,5-diene (2)

(a) Pyrolysis

Endoxide **2** (4.70 g, 17.70 mmol) contained in a pressure-equalizing dropping funnel was added dropwise (0.5 h) down a silica tube (100 cm × 1 cm i.d.) inclined at an angle of ca. 30° and heated to 450 °C. The material which collected in an external trap (− 70 °C) was distilled to afford a colourless oil identified as 3,4-bis(trifluoromethyl)furan (**1**) (2.88 g, 14.12 mmol, 80%) (Analysis: Found: C, 35.2; H, 1.1; F, 55.4%. Calc. for $C_6H_2OF_6$: C, 35.3; H, 1.0; F, 55.9%.), b.p., 86 °C/760 mmHg {lit. value [6]: b.p., 88–89 °C/760 mmHg}.

Subsequent pyrolysis reactions using this method did not give consistent results and so furan **1** was prepared routinely by thermal decomposition of the monoene **3** formed from partial hydrogenation of endoxide **2**.

(b) With trifluoromethanesulphonic acid

To endoxide **2** (5.00 g, 21.74 mmol) and anhydrous dichloromethane (8 cm^3), contained in a round-bottomed flask (50 cm^3) and cooled (0 °C), was added triflic acid (3.26 g, 21.74 mmol). The mixture was heated under reflux (1 h), cooled to room temperature and distilled water (35 cm^3) then added with stirring (0.5 h) to afford solid material and two liquid layers. The solid was filtered off, recrystallized (Me_2CO) and identified as tris-(6-trifluoromethylsalicylide) (**5**) (n.c.) (1.82 g, 3.23 mmol, 45%) (Analysis: Found: C, 50.9; H, 1.4; F, 30.6%; M^+, 564. $C_{24}H_9O_6F_9$ requires C, 51.1; H, 1.6; F, 30.3%; M, 564.); m.p., 184–186 °C; δ_H (300 MHz, acetone-d_6) 8.2 and 7.9 (mult., arom.) ppm; δ_F + 20.0 (s, CF_3) ppm; δ_C 163.4 (s, C=O); 148.6 (s, ring=C−O); 134.8 and 128.8 (2s, 2 ring =CH); 125.4 (q, *C*C=O, $^3J = 2$ Hz); 126.8 (q, ring=CH, $^3J = 5$ Hz); 130.1 (qm *C*CF_3, $^2J = 33$ Hz); and 124.5 (q, CF_3, $^1J = 274$ Hz) ppm; $\nu_{max.}$ 3120w (Ar C−H str.); 1775s (C=O str.); 1615 and 1590m (Ar C=C str.); 1465s (C−O str.); and 1180 and 1135s (C−F str.) cm^{-1}; *m/z* 564 (13.8%, M^+); 376 [27.0, $(C_{16}H_6O_4F_9)^+$]; 357 [3.1, $(C_{16}H_6O_4F_5)^+$]; 188 [100.0, $(C_8H_3O_2F_3)^+$]; 160 [26.9, $(C_7H_3OF_3)^+$]; 132 [26.0, $(C_6H_3F_3]^+$]; and 113 [2.6, $(C_6H_3F_2)^+$].

The organic phase was dried ($MgSO_4$) and found by TLC [CH_2Cl_2: petroleum ether (b.p., 40–60 °C) 2:1 v/v] to contain two components (R_F, 0.80 and 0.55) which were separated by DCFC (same eluant) to afford (i) 2-trifluoromethyl-6-hydroxybenzoic acid (**6**) (n.c.) (0.73 g, 3.54 mmol, 16%) (Analysis: Found: C, 46.7; H, 2.4; F, 27.9%; M^+, 206. $C_8H_5O_3F_3$ requires C, 46.6; H, 2.4; F, 27.7%; M, 206.); m.p., 156–158 °C; δ_H (220 MHz, $CDCl_3$) 10.5 (s, 1H, CO_2H); 7.2–7.8 (mult., 3H, C_6H_3); and 5.5 (s, 1H, O−H) ppm; δ_F + 18.5 (s, CF_3) ppm; $\nu_{max.}$ 3110–2530m (H-bonded O−H str.); 1660s (C=O str.); 1600m (Ar C=C str.); 1445s (C−O str.); and 1160 and 1130s (C−F str.) cm^{-1}; *m/z* 206 (20.3%, M^+); 189 [49.2, $(M-OH)^+$]; 188 [100.0, $(M-H_2O)^+$]; 167 [10.6, $(C_8H_4O_3F)^+$]; 160 [71.7, $(M-HCO_2H)^+$]; 141 [18.6, $(C_7H_3OF_3)^+$]; 132 [77.7, $(C_6H_3F_3)^+$]; 75 [3.5, $(C_6H_3)^+$]; 69 [10.8, $(CF_3)^+$]; 45 [36.6, $(CO_2H)^+$]; and 44 [72.2, $(CO_2)^+$] and (ii) 2,3-bis(trifluoromethyl)phenol (**4**) (0.31 g, 1.35 mmol, 6%) (Analysis: Found: M^+, 230.0166. $C_8H_4OF_6$ requires M, 230.0159.); m.p., 64–66 °C; δ_H (300 MHz, $CDCl_3$) 6.5 (s, 1H, OH); 7.2, 7.4 and 7.5 (mult., 3H, C_6H_3) ppm; δ_F +18.5 and +21.5 (2q, $2CF_3$, $J = 9$ Hz) ppm; δ_C 122.8 and 123.3 (2q, $2CF_3$, $^1J = 274$ Hz); 113.9 and 129.2 (2q, $2CCF_3$, $^2J = 33$ Hz); 156.1 (q, =COH, $^3J = 2$ Hz); 119.6 (q, =CH, $^3J = 7$ Hz); 122.5 and 132.8 (2s, 2=CH) ppm; ν_{max} 3380 broad (O–H str.); 1610m (Ar C=C str.); 1300s (O–H bend); and 1200–1140s (C–F str.) cm^{-1}; *m/z* 230 (13.4%, M^+); 211 [8.0, $(M-F)^+$]; 210 [10.1, $(M-HF)^+$]; 183 [7.0, $(C_7H_4F_5)^+$]; 182 [25.2, $(C_7H_3F_5)^+$]; 161 [3.7, $(M-CF_3)^+$]; 132 [11.4, $(C_6H_3F_3)^+$]; 75 [4.3, $(C_6H_3)^+$]; and 69 [24.5, $(CF_3)^+$].

(c) With concentrated sulphuric acid

Concentrated sulphuric acid (0.86 g, 8.78 mmol) was added dropwise to a stirred ice-cold solution of endoxide **2** (2.00 g, 8.70 mmol) in dichloromethane (10 cm^3) contained in a round-bottomed flask (50 cm^3). The mixture was allowed to warm to room temperature, heated under reflux (ca. 1 h) and then cooled to room temperature. Distilled water (10 cm^3) was added to the stirred solution to afford some dark insoluble material which was filtered off. The organic phase was separated, dried ($MgSO_4$) and purified by DCFC [petroleum ether (b.p., 40–60 °C): dichloromethane (2:1 v/v)] to give phenol **4** (0.90 g, 3.91 mmol, 44%).

(d) With concentrated hydrochloric acid

An equimolar mixture of adduct **2** (2.00 g, 8.70 mmol) and concentrated hydrochloric acid was heated under reflux and worked-up as reported in the preceding experiments, but no reaction had taken place.

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

(a) With dimethyl acetylenedicarboxylate (DMAD)

A mixture of DMAD (2.22 g, 15.63 mmol) and furan **1** (2.99 g, 14.66 mmol) was heated at 100 °C (7 d) *in vacuo* in a Rotaflo tube (ca. 250 cm^3). The resulting volatile material was removed *in vacuo* and the solid residue purified by DCFC [$CHCl_3$: n-C_6H_{14} (2:1 v/v)] to afford colourless crystals (R_F, 0.75), identified as dimethyl 2,3-bis(trifluoromethyl)-7-oxabicyclo[2,2,1]hepta-2,5-diene-5,6-dicarboxylate (**8**) (n.c.) (4.11 g, 11.88 mmol, 81%) (Analysis: Found: C, 41.7; H, 2.3; F, 32.7%; M^+, 346. $C_{12}H_8O_5F_6$ requires: C, 41.6; H, 2.3; F, 33.0%; M, 346.); m.p., 72–74 °C; δ_H (300 MHz, acetone-d_6) 5.9 (s, 2H, 2CHO–) and 3.9 (s, 6H, $2CH_3$) ppm; δ_F +17.5 (s, $2CF_3$) ppm; δ_C 120.4 (q, $2CF_3$, $^1J = 271$ Hz); 148.8 (q, $2{=}CCF_3$, $^2J = 44$ Hz); 86.1 (s, 2CHO–); 151.0 (s, 2=CC=O); 161.2 (s, 2H, CHO–); 52.9 (s, 6H, $2CH_3$) ppm; ν_{max} 3030m (bridge C–H str.); 2970m (alkyl C–H str.); 1740 and 1650 m (C=C str.); 1720s (C=O str.); and 1140 and 1100s (C–F str.) cm^{-1}; *m/z* 346 (1.0%, M^+); 316 [2.3, $(M-2CH_3)^+$]; 315 [3.1, $(M-OCH_3)^+$]; 287 [11.9, $(M-CO_2CH_3)^+$]; 284 [6.2, $(M-2OCH_3)^+$]; 277 [3.2, $(M-CF_3)^+$]; 204 [100.0, $(C_6H_2OF_6)^+$]; 69 [12.1, $(CF_3)^+$]; and 59 [54.2, $(CO_2CH_3)^+$].

(b) With ethyl propynoate (EP)

Experiment 1. A mixture of furan **1** (2.32 g, 11.37 mmol) and EP (1.18 g, 12.04 mmol), heated *in vacuo* in a Rotaflo tube (ca. 250 cm^3) at 100 °C (40 h), gave only unchanged starting materials.

Experiment 2. The reaction was repeated and a mixture of EP (1.23 g, 12.55 mmol) and furan **1** (2.51 g, 12.30 mmol), heated at 150 °C (14 d) gave volatile material identified as a mixture of unreacted furan **1** and ethanol. The solid residue in the tube was washed out with anhydrous ether and recrystallized from ethyl acetate to afford flaky crystals of ethyl 6,7-bis(trifluoromethyl)isocoumarin-3-carboxylate (**12**) (n.c.) (1.15 g, 3.25 mmol, 52%) (Analysis: Found: C, 47.2; H, 2.2; F, 32.4%; M^+, 354. $C_{14}H_8O_4F_6$ requires C, 47.5; H, 2.3; F, 32.2%; M, 354.); m.p., 192–194 °C; δ_H (300 MHz, acetone-d_6) 7.50 (s, 1H, 4-H); 8.03 (s, 1H, 5-H); 8.78 (s, 1H, 8-H); 4.40 (q, 2H, OCH_2, $J=7$ Hz); and 1.38 (t, 3H, CH_3, $J=7$ Hz) ppm; $\delta_F+18.8$ to $+20.1$ (mult., $2CF_3$) ppm; δ_C 160.0 (s, CO_2Et); 159.2 (s, C=O); 147.3 (s, OC=); 110.6 (s, OC=CH); 128.4 and 131.0 (2q, $2CF_3C{=}CH$, $^3J=6$ Hz); 131.5 and 132.1 (2q, $2CF_3C{=}$, $^2J=34$ Hz); 125.5 and 138.9 (2s, 2 arom. =C–); 123.1 and 123.2 (2q, $2CF_3$, $^1J=274$ Hz); 63.7 (s, OCH_2); and 14.8 (s, CH_3) ppm; $\nu_{max.}$ 3110–3080m (arom. and vinylic C–H str.); 3000–2960w (aliph. C–H str.); 1760s (lactone C=O str.); 1710s (ester C=O str.); 1650 and 1630w (arom. and vinylic C=C str.); and 1200 and 1155s (C–O str. and C–F str.) cm^{-1}; *m/z* 354 (49.4%, M^+); 335 [10.1, $(M-F)^+$]; 309 [1.5, $(M-OEt)^+$]; 281 [100.0, $(M-CO_2Et)^+$]; 270 [17.9, $(C_{12}H_5O_4F_3)^+$]; 225 [82.5, $(C_{11}H_4O_2F_3)^+$]; 69 [13.5, $(CF_3)^+$] and 44 [9.9, $(CO_2)^+$].

The ethereal mother liquor was purified by DCFC [CH_2Cl_2 and petroleum ether (b.p., 40–60 °C) 3:1 v/v] to afford white crystals identified as ethyl 6,7-bis(trifluoromethyl)isocoumarin-4-carboxylate (**13**) (n.c.) (0.20 g, 0.56 mmol, 9%); m.p., 192–194 °C; δ_H (300 MHz, acetone-d_6) 8.0 (s, 1H, 3-H); 8.9 (s, 1H, 8-H); 8.8 (s, 1H, 5-H); 4.4 (q, 2H, OCH_2, $J=7$ Hz); and 1.5 (t, 3H, CH_3, $J=7$ Hz) ppm; $\delta_F+18.8$ to $+20.1$ (mult., $2CF_3$) ppm; δ_C 160.5 (s, CO_2Et); 159.9 (s, ring C=O); 147.8 (s, OCH); 111.4 (s, =CCO_2Et); 130.1 and 130.7 (2q, $2CF_3C{=}CH$, $^3J=6$ Hz); 129.1 and 133.5 (2q, $2CF_3C{=}$, $^2J=34$ Hz); 126.9 and 140.6 (2s, 2 arom. =C–); 123.7 (2q, $2CF_3$, $^1J=275$ Hz); 63.6 (s, OCH_2); and 14.8 (s, CH_3) ppm; $\nu_{max.}$ 3095 and 3085m (arom. and vinylic C–H str.); 2990 and 2970w (aliph. C–H str.); 1750s (lactone C=O str.); 1710s (ester C=O str.); 1649 and 1639w (arom. and vinylic C=C str.); and 1200 and 1150s (C–O str. and C–F str.) cm^{-1}; *m/z* 354 (45.8%, M^+); 335 [15.0, $(M-F)^+$]; 326 [13.0, $(M-C_2H_4)^+$]; 281 [100.0, $(M-CO_2Et)^+$]; 270 [19.0, $(C_{12}H_5O_4F_3)^+$]; 225 [86.4, $(C_{11}H_4O_2F_3)^+$]; 156 [14.2, $(C_{10}H_4O_2)^+$]; and 44 [7.9, $(CO_2)^+$].

(c) With electron-rich dienophiles

Attempted Diels–Alder reactions carried out *in vacuo* at 50–150 °C (20 h to 7 d) with ethyl vinyl ether, but-2-yne-1,4-diol, bis(trimethylstannyl)acetylene and bis(trimethylsilyl)acetylene, both in the presence and in the absence of solvent, were unsuccessful.

(d) With electron-deficient dienophiles

Attempted Diels–Alder reactions using fumaronitrile and maleic anhydride at 100–150 °C (1–7 d) and trifluoronitrosomethane at 25–150 °C (1–7 d) carried out *in vacuo* were unsuccessful. However, reaction using tetracyanoethylene gave a small amount of unidentified product.

Reaction of ethyl 3-furoate with hexafluorobut-2-yne

A mixture of hexafluorobut-2-yne (20.83 g, 128.58 mmol) and ethyl 3-furoate (3.0 g, 21.43 mmol) in dichloromethane (ca. 12 cm^3) was shaken at room temperature (15 d) *in vacuo* in a Rotaflo tube (ca. 250 cm^3) to afford unchanged hexafluorobut-2-yne (17.82 g, 110.0 mmol, 86% recovered) and a solid residue (5.80 g) shown by TLC (CH_2Cl_2) to contain one major component (R_F, 0.86). This was purified by sublimation *in vacuo* (40 °C) to give white crystals identified as ethyl 2,3-bis(trifluoromethyl)-7-oxabicyclo[2,2,1]hepta-2,5-diene-5-carboxylate (**14**) (n.c.) (5.71 g, 18.9 mmol, 88%) (Analysis: Found: C, 43.4; H, 2.6; F, 37.8%; M$^+$, 302. $C_{11}H_8O_3F_6$ requires C, 43.7; H, 2.6; F, 37.7%; M, 302.); m.p., 38–40 °C; δ_H (300 MHz, $CDCl_3$) 7.87 (d, 1H, =CH, $J=2$ Hz); 5.1 (s, 1H, =CCH); 5.78 (s, 1H, =CHC*H*); 4.28 (q, 2H, OCH_2, $J=7$ Hz); and 1.33 (t, 3H, CH_3, $J=7$ Hz) ppm; δ_F + 15.9 and + 17.2 (2q, $2CF_3$, $J=7$ Hz) ppm; δ_C 161.5 (s, C=O); 151.1 (s, =*C*CO_2Et); 150.8 (s, =CH); 142.5 and 145.3 (2q, $2CF_3$*C*=, $^2J=33$ Hz); 120.5 and 120.8 (2q, $2CF_3$, $^1J=270$ Hz); 84.0 and 84.9 (2s, 2CHO–); 61.4 (s, OCH_2); and 14.0 (s, CH_3) ppm; $\nu_{max.}$ 3120m (vinylic C–H str.); 2965m (aliph. C–H str.); 1750s (C=O str.); 1610s (C=C str.); and 1150s (C–F str.) cm^{-1}; *m/z* (Cl, NH_3) 320 [20.0%, $(M+NH_4)^+$]; and 302 (1.2, M$^+$).

Reaction of oxanorbornadiene (14) with ethyl propynoate

(a) At 150 °C

A mixture of the adduct **14** (1.50 g, 4.97 mmol) and EP (0.50 g, 5.10 mmol) was heated at 150 °C (7 d) *in vacuo* in a Rotaflo tube (ca. 250 cm^3) to afford a mixture (1.80 g) which was purified by DCFC [petroleum ether (b.p., 40–60 °C): CH_2Cl_2, 1:1v/v] to give white crystals (R_F, 0.73) identified as ethyl 6,7-bis(trifluoromethyl)isocoumarin-3-carboxylate (**12**) (1.48 g, 4.18 mmol, 84%) (Analysis: Found: C, 47.8; H, 2.5; F, 31.7%; M$^+$, 354. Calc. for $C_{14}H_8O_4F_6$: C, 47.5; H, 2.3; F, 32.2%; M, 354).

(b) At 120 °C

Reaction was carried out at 120 °C (7 d) using the same quantities of reactants as in the first experiment to afford isocoumarin **12** (0.49 g, 1.39 mmol, 28%) and lower-boiling material containing furan **1**.

(c) At 60 °C

A mixture of adduct **14** (1.55 g, 5.13 mmol) and EP (0.53 g, 5.41 mmol), heated *in vacuo* in a Rotaflo tube (ca. 250 cm^3) at 60 °C (2d), gave an oil (2.0 g) which was shown (^{1}H NMR) to contain only EP and furan **1**; condensation *in vacuo* afforded furan **1** (0.50 g, 2.45 mmol, 48%).

Reaction of dimethyl furan-3,4-dicarboxylate (9) with hexafluorobut-2-yne

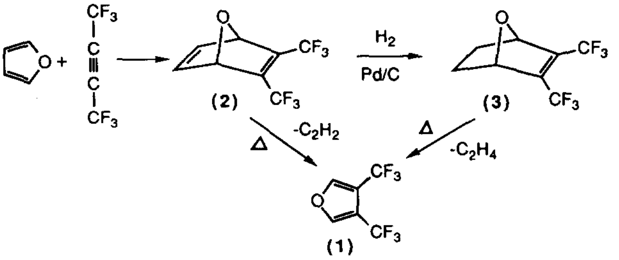
A mixture of hexafluorobut-2-yne (4.58 g, 28.27 mmol) and furan ester **9** (4.78 g, 26.0 mmol) was heated *in vacuo* in a Rotaflo tube (ca. 250 cm^3) at 115 °C (7 d). This gave yellow crystals (7.50 g) which were purified by DCFC [hexane:ethyl acetate (2:1 v/v)] to afford white crystals of dimethyl 2,3-bis(trifluoromethyl)-7-oxabicyclo[2,2,1]hepta-2,5-diene-5,6-dicarboxylate (**8**) (7.31 g, 21.13 mmol, 81%); (Analysis: Found: M$^+$, 346.0271. Calc. for $C_{12}H_8O_5F_6$: M, 346.0276); m.p., 73–76 °C.

Results and discussion

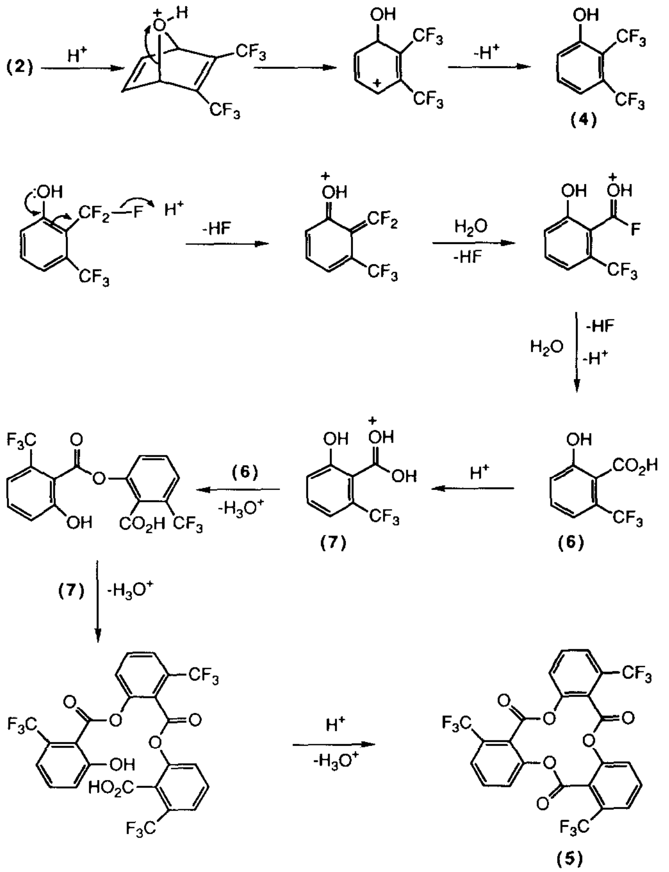
Furan **1** is best prepared by Diels–Alder reaction between hexafluorobut-2-yne and furan at 100 °C to give 2,3-bis(trifluoromethyl)-7-oxabicyclo[2,2,1]hepta-2,5-diene (**2**) [6] followed by reduction [H_2, Pd (10%) on C in Me_2CO] and thermolysis of the resulting bicyclohept-2-ene (**3**) [5]. However, a number of substituted furans can be prepared by thermal decomposition of oxanorbornadiene precursors and so diene **2** was pyrolysed in a stream of nitrogen through a silica tube heated at 450 °C. Under these conditions retrocleavage of ethyne occurred readily and furan **1** (80%) was obtained (Scheme 1), but somewhat lower yields (50–60%) were produced in subsequent experiments.

With the intention of synthesising 2,3-bis(trifluoromethyl)phenol (**4**), oxanorbornadiene (**2**) was treated with triflic acid (1:1 molar ratio) in dichloromethane heated under reflux followed by addition of water. This gave tris-(6-trifluoromethylsalicylide) (**5**) (45%) and an organic phase from which 2-trifluoromethyl-6-hydroxybenzoic acid (**6**) (16%) and phenol **4** (6%) were obtained by DCFC.

The products are considered to be formed as shown in Scheme 2 with phenol **4** being produced initially. Hydrolysis of trifluoromethylarenes can require drastic conditions with alkaline hydrolysis needing assistance by



Scheme 1.



Scheme 2.

electron-releasing substituents *ortho* and/or *para* to the CF_3 group. However, non-activated CF_3 groups can be hydrolysed under acidic conditions using sulphuric or even hydrohalic acids [7].

In the present reaction the CF_3 group which underwent hydrolysis was activated by the *ortho*-OH group.

The major product trilactone **5** is the dehydrated trimer of the salicylic acid **6**. Telomeric salicylides have been known since 1892 [8], but considerable confusion existed in the literature until a series of papers by Wilson Baker and coworkers [9] in the early 1950s rationalised the situation and characterised bis-, tris-, tetrakis- and hexakis-salicylides and analogues including creotides and thymotides.

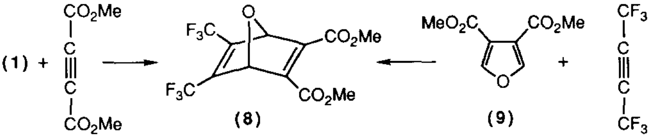
From reaction of compound **2** with concentrated sulphuric acid under comparable conditions only phenol **4** (44%) was isolated, indicating that with this weaker acid hydrolysis of the *ortho*-CF_3 group in phenol **4** is not favoured. When an even weaker acid (conc. HCl) was used reaction did not take place at all.

Thermal Diels–Alder reactions of furan and its derivatives with acetylene esters have been investigated widely since that between furan and dimethylacetylene dicarboxylate (DMAD) was first reported in 1931 [10]. Products from DMAD reactions are often temperature and reactant ratio dependent, e.g. Diels–Alder 1:1, 2:1 and 3:1 furan:DMAD adducts have been isolated and characterised [10, 11].

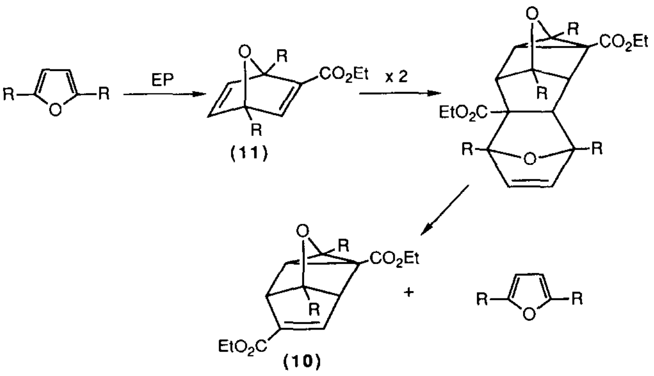
Reaction between furan **1** and DMAD at 100 °C gave the expected 1:1 adduct oxanorbornadiene (**8**) (81%), and the same compound was formed in identical yield from reaction of dimethyl 3,4-furandicarboxylate (**9**) with hexafluorobut-2-yne at 115 °C (Scheme 3). In both reactions 2:1 and/or 3:1 adducts were not detected.

In general, cycloadditions involving ethyl propynoate (EP) are less facile than those with DMAD and from reaction of furan with EP at 130 °C the sole product isolated was the 1:2 adduct **10** [12]; 2,5-dimethylfuran underwent an analogous reaction [13]. These compounds were considered to be formed via oxanorbornadiene (**11**) which then dimerised $({}_{\pi}2_s + {}_{\pi}2_s + {}_{\pi}2_s)$ followed by retrocleavage of furan or 2,5-dimethylfuran (Scheme 4; R = H or Me).

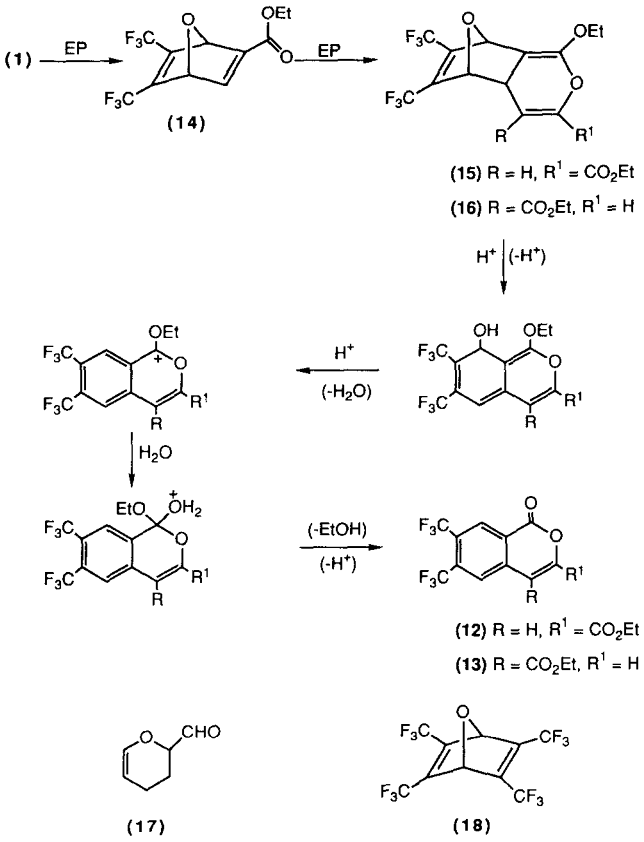
The reaction between furan **1** and EP (1:1 molar ratio) *in vacuo* at 150 °C (14 d) gave a volatile mixture of unchanged **1** and ethanol and a residue, which on treatment with diethyl ether gave solid ethyl 6,7-bis(trifluoromethyl)isocoumarin-3-carboxylate (**12**) (52%). Purification of the filtrate by DCFC after removal of the ether afforded the 4-carboxylate isomer (**13**) (9%) (Scheme 5).



Scheme 3.



Scheme 4.



Scheme 5.

These unexpected products are considered to arise by Diels–Alder cycloaddition of EP to the initial 1:1 adduct, oxanorbornadiene (**14**), in which the C=C–C=O system functions as the diene component. The 2:1 adducts **15** and **16** so formed then undergo acid-catalysed ring-opening of the oxygen bridge (presumably by traces of protons present on the walls of the Pyrex reaction tube) followed by elimination of ethanol (Scheme 5).

This result prompted the preparation of oxanorbornadiene (**14**) in order to study its reaction with EP. The diene was obtained in high yield (93%) by reaction involving a large excess of hexafluorobut-2-yne and ethyl 3-furoate (6:1 molar ratio) at room temperature. The use of a 1:1 molar ratio of reactants or elevated temperature resulted in the formation of considerable amounts of 3-furoate:butyne 2:1 adducts which have been separated and characterised [14].

A mixture of compound **14** and EP (ca. 1:1 molar ratio) when heated *in vacuo* at 150 °C (7 d) gave isocoumarin **12** (84%); isomer **13** was not detected. Slow reaction was observed to occur at 120 °C with a 28% conversion of reactants to product **12** over 7 d. However, at 60 °C oxanorbornadiene (**14**) underwent retrocleavage of EP to give furan **1**.

Therefore, since formation of oxanorbornadiene (**14**) is reversible at ≥ 60 °C, identical reactant mixtures will be present at 150 °C using furan 1 and EP (1:2 molar ratio) or oxanorbornadiene (**14**) and EP (1:1 molar ratio).

Only in the experiment in which a deficiency of EP was employed was the 4-carboxylate isomer **13** detected. This perhaps indicates that formation of the 2:1 adduct **16**, the expected kinetic isomer, is reversible under the conditions used.

Frontier orbital coefficients calculated by Houk and Strozier [15] have been used to explain the regioselectivity observed in the dimerisation of acrolein to give cycloadduct **17**, and in the reactions of acrolein and certain α, β-unsaturated ketones with various dienophiles: both HOMO (diene)/LUMO (dienophile) and LUMO (diene)/HOMO (dienophile) interactions predict the formation of the isomers observed [16]. By analogy, Diels–Alder reaction between 1:1 adduct **14** and EP would be expected to afford 2:1 adduct **15** and hence isocoumarin **12** as the major or exclusive product.

Isocoumarin **12** was identified by a single-crystal X-ray structure determination. The three low-field ^{1}H NMR absorptions at δ_H 8.8 (8-H), 8.1 (5-H) and 7.6 (4-H) ppm, were assigned as shown on the basis that (i) the two former absorptions were broad (indicating a small coupling to fluorine in an adjacent CF_3 group) and the latter sharp, and (ii) the protons which absorbed at δ_H 8.1 and 7.6 ppm were peri to each other (N.O.E. experiment); this was also consistent with structure **12** but not with **13**.

For isocoumarin **13** the broad ^{1}H NMR absorptions at δ_H 8.9 and 8.8 ppm were clearly due to the aromatic protons (probably 8-H and 5-H, respectively) and the sharp absorption at δ_H 8.0 ppm was assigned to the 3-H.

These vinylic proton assignments agree with the chemical shifts and assignments reported for the analogous protons in ethyl and methyl isocoumarin-4-carboxylates, i.e. δ_H 8.20 [17] and 8.13 [18] ppm, respectively, for H-3, and in methyl isocoumarin-3-carboxylate, i.e. δ_H 7.52 [17] ppm for H-4.

The formation of isocoumarins in the present work contrasts markedly with the 2:1 adducts formed from the reaction of EP with furan and 2,5-dimethylfuran [12, 13].

There are very few reports in the literature concerning α,β-unsaturated esters acting as the diene components in Diels–Alder reactions. The first report was by Snider and coworkers [19] in 1979 on the reversible intramolecular cyclisation of 1-allylic-2,2-dimethylethylenetricarboxylates and this was followed by several papers by Hall *et al.* [20] covering the intermolecular reaction of a wide range of α-cyano- and α-methoxycarbonyl-$\alpha\beta$-unsaturated esters with electron-rich alkenes such as vinyl ethers. The reaction of methyl acrylate and substituted acrylates with the ynamine $Et_2NC{\equiv}CMe$ to afford

γ-pyrans has also been reported [21], but it is probable that this reaction involves two steps via a zwitterionic intermediate.

Therefore, to the best of our knowledge, this is the first report of a Diels–Alder reaction involving two α,β-unsaturated esters, one acting as the diene and the other the dienophile.

Attempted Diels–Alder reactions of furan **1** with (i) the electron-rich dienophiles $CH_2{=}CHOEt$, $HOCH_2C{\equiv}CCH_2OH$, $Me_3SnC{\equiv}CSnMe_3$ and $Me_3SiC{\equiv}CSiMe_3$, and (ii) the electron-deficient dienophiles, maleic anhydride, *trans*-$NCCH{=}CHCN$ and CF_3NO under a variety of conditions were unsuccessful. With tetracyanoethylene some reaction did take place, but the product(s) was not identified.

Previous to the present work, the only Diels–Alder reaction of furan **1** reported was that with hexafluorobut-2-yne to give the tetrakis-(trifluoromethyl)oxanorbornadiene (**18**) (86%) [6].

Further work is in progress on the reactions of furan **1** with other α,β-unsaturated esters and of other substituted furans with EP and related esters. The results will be reported in due course.

Acknowledgements

We thank the Association of Commonwealth Universities for a scholarship (to A.B.A.), the Sudanese Government for a scholarship (to N.N.E.S.) and Dr R. G. Pritchard (UMIST) for the X-ray analysis.

References

1 Reported in part in a preliminary communication; A B. Abubakar, B. L. Booth and A. E. Tipping, *J Fluorine Chem.*, *47* (1990) 353.

2 A. W. McCulloch, B. Stonovnik, D. G. Smith and A. G. McInnes, *Can J Chem*, *47* (1969) 4319.

3 E. V. Adamskaya and A. F. Oleinik, *Chem Heterocyl Comp*, *10* (1985) 1299.

4 H. N. C. Wong, *Synthesis*, (1984) 787.

5 N. Z. Huang, Y. D. Xing and D. Y. Ye, *Synthesis*, (1982) 1041.

6 C. D. Weis, *J Org Chem*, *27* (1962) 3693.

7 M. Hudlicky, *Chemistry of Organic Fluorine Compounds*, MacMillan, New York, 1962.

8 R. Anschütz, *Ber*, *25* (1892) 3506 and 3512; *Justus Liebigs Ann Chem*, *273* (1893) 73 and 97. Earlier work dating from 1853 (Gerhardt) was considered to be inconclusive.

9 W. Baker, W. D. Ollis and T. S Zealley, *J. Chem Soc*, (1951) 201; W. Baker, B. Gilbert and W. D. Ollis, *ibid*, (1952) 1443; W. Baker, J. B. Harborne, A. J. Price and A Rutt, *ibid*, (1954) 2042.

10 O. Diels and K. Alder, *Justus Liebigs Ann Chem*, *490* (1931) 143.

11 J D. Slee and E. Le Goff, *J Org Chem*, *35* (1970) 3897; A W. McCulloch, D. G Smith and A. G. McInnes, *Can. J. Chem.*, *51* (1973) 4125; Y. D. Xing and N. Z. Huang, *J. Org Chem.*, *47* (1982) 140, and references contained therein

12 A. W. McCulloch, D. G. Smith and A. G. McInnes, *Can. J Chem*, *52* (1974) 1013.

13 A. W. McCulloch and A. G. McInnes, *Can J Chem.*, *53* (1975) 1496

14 N. N. E. Suliman, *M Sc. Dissertation*, University of Manchester, 1990; M G. Barlow, N N. E. Suliman and A. E Tipping, unpublished results.

15 K. N. Houk and R. W. Strozier, *J. Am. Chem Soc.*, *95* (1973) 4094
16 I. Fleming, *Frontier Orbitals and Organic Chemical Reactions*, Wiley–Interscience, Chichester, 1989, p. 141.
17 H. Duddeck and M. Kaiser, *Spectrochim. Acta, Part A*, *41* (1985) 913
18 S. L. Spassov, I. A. Atanassova and M. A Haimova, *Org. Magn Reson.*, *22* (1984) 194.
19 B. B. Snider, D. M. Roush and T. A. Killinger, *J. Am. Chem. Soc.*, *101* (1979) 6023; B. B. Snider and D. M. Roush, *J. Org. Chem.*, *44* (1979) 4229.
20 H. K Hall Jr., A. B. Padias and S. T. Hedrick, *J. Org Chem.*, *48* (1983) 3787, and references cited therein.
21 J. Ficini and A. Krief, *Tetrahedron Lett*, (1970) 885.
22 G. Stork, E. E. Van Tamelen, L. J. Friedmann and A. W. Burgstahler, *J. Am. Chem. Soc*, *75* (1953) 384.