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Cycloaddition reactions of furan derivatives with trifluoroethene

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Abstract

The cycloaddition reaction of trifluoroethene with furan and a number of derivatives to give the unreported 1,1,2-trifluoro-7-oxa-bicyclo[2.2.1]hept-4-ene, and derivatives has been investigated. Reactions were carried out in stainless steel autoclaves at 200°C under autogenous pressure using an excess of trifluoroethene. Reactions were found to proceed with furan and derivatives with methyl groups in the 2 and/or 5 positions. Electron-withdrawing substituents in these positions prevented reaction however. Attempted dehydrofluorination of 1,1,2-trifluoro-7-oxa-bicyclo[2.2.1]hept-4-ene using a variety of bases gave no reaction, however use of LDA led to the preparation in 25% yield of 2,3-difluoro phenol. © 2000 Elsevier Science S.A. All rights reserved.

Keywords: Trifluoroethene; Furan; Cycloaddition

1. Introduction

With the advent of 'HFCs', particularly 134a, i.e. CF_3CH_2F (**1**), there is an increasing interest in trifluoroethene (3FE, **2**), which can be obtained from **1** by elimination of hydrogen fluoride, Scheme 1 [1].

Various cycloaddition reactions of trifluoroethene have been described previously, including 2+2 thermal dimerisation [2], addition to a fluorinated oxaziridine [3], and to trifluoronitrosomethane [4]. However, Diels–Alder (4+2) processes are limited to minor components in the reactions of 3FE with butadiene [5], and with isoprene, 2,3-dimethyl butadiene, *cis*-1,3-pentadiene and *trans*-1,3-pentadiene [6]. It is only in the reaction with cyclopentadiene [7] that the 4+2 process predominates. It seemed reasonable that furan and derivatives, as cyclic, π-electron rich systems, could also give Diels–Alder products and we have now demonstrated that this is indeed the case.

2. Results and discussion

A mixture containing furan and excess 3FE, sealed under vacuum in an autoclave, was heated to ca. 200°C and, under these conditions, we obtained 36% conversion to a mixture of isomers **4a** and **4b**, (Scheme 2). The use of tetrahydrofuran as solvent, led to a cleaner product without significant reduction in conversion. Product characterisation was achieved by elemental analysis and NMR, while mass-spectrometry led essentially to retro Diels–Alder reaction in the instrument, with parent peaks arising from the two original reactants. The isomers **4a** and **4b** were identified by observing the J_{HH} and J_{FH} values in the ^1H and ^{19}F NMR spectra of the *exo*- and *endo*-hydrogen in **4a** and **4b** respectively, as indicated in Scheme 2. The *exo*-hydrogen on C2 in **4a** and the *exo*-fluorine in **4b** couple to the hydrogen on C3 and give rise to coupling constants of 4.4 and 7.7 Hz, respectively. Coupling between the hydrogen on C3 and *endo*-hydrogen or *endo*-fluorine on C2 is too small to be observed.

We attempted to convert the product to the diene (**8**) by elimination of hydrogen fluoride but, using a variety of procedures, e.g. heating to higher temperatures and treating with the bases (25 M KOH, DBU, sodium methoxide, sodium hydride, and potassium *t*-butoxide) no reaction was obtained. However, with LDA the mixture of **4a** and **4b** reacted to give 2,3-difluorophenol (**7**), which was characterised as the tosylate, together with substantial amounts of an uncharacterised polymer. The latter material is soluble in solvents such as acetone and ether but the resonance in the ^1H and ^{19}F NMR spectra, subsequently obtained from these solutions, were extremely broad and yielded no useful structural information. The most likely explanation for these observations is that the endoxides **4a, 4b**, react with base to

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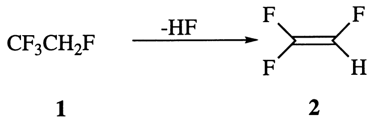


Scheme 1

form anion (**5**), which could lose fluoride ion but, more likely, ring-opening occurs to give **6** which loses fluoride to yield the phenol (**7**) (Scheme 3).

Electron-donating groups in the furan clearly favour the Diels–Alder process because both mono- and di-methyl compounds **8** and **9** gave the corresponding cyclo-adducts (**10**) and (**11**) respectively, in good yield, (Schemes 4 and 5). However, reactions of each of these adducts with base gave polymer and no identifiable product. We also explored the ring-opening of **8** and **9** with acid and this occurred readily, but led to a very complex range of products that we have not attempted to identify.

Other furan derivatives, e.g. (R^1=CH_2OH; CH_2O-$COCH_3$; COOH, R_2=H) gave only traces of cyclo-adducts.

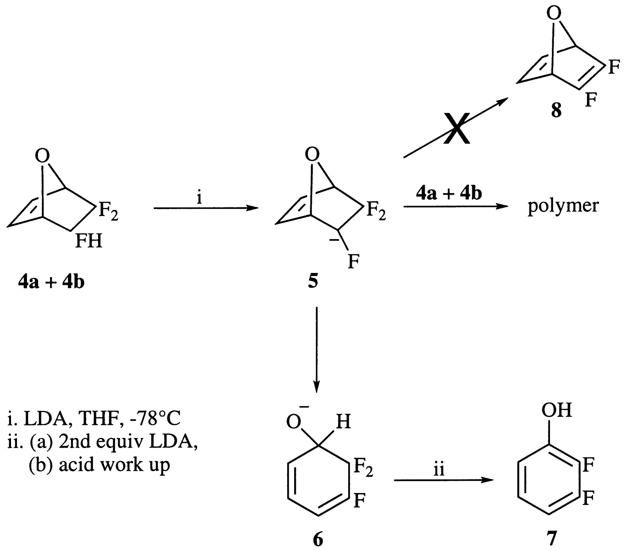
3. Experimental

Gas liquid chromatographic (GLC) Analyses were carried out using a Hewlett Packard 5890A gas liquid chromatograph equipped with a 25 m cross-linked methyl silicone capillary column. Preparative scale GLC was carried out using a Varian Aerograph Model 920 (catharometer detector) gas liquid chromatograph with a packed column (3 m 10% S.E. 30).

Elemental Analyses were obtained using a Perkin-Elmer 240 Elemental Analyser or a Carlo Erba Strumentazione 1106 Elemental Analyser.

NMR spectra were recorded on a Bruker AC 250 (250 MHz) or a Varian VXR400S (400 MHz). Chemical shifts were recorded in ppm from TMS or $CFCl_3$ in $CDCl_3$ solution.

Infrared spectra were recorded on a Perkin-Elmer 457 or 577 Grating spectrometer using KBr discs (for solid samples) or thin films between two KBr plates (for liquid samples). Gaseous samples were condensed into a cylindrical cell fitted with KBr plates.



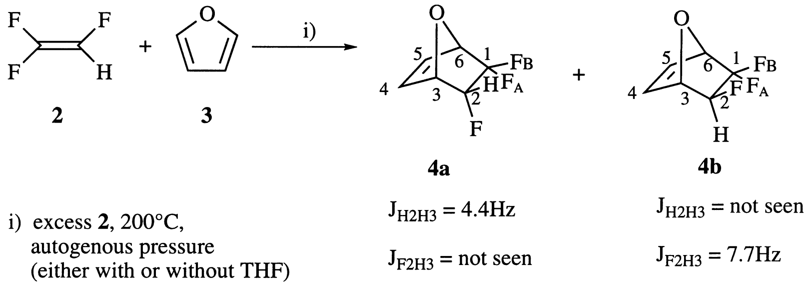
Scheme 3

Mass spectra of solid samples were recorded on a VG 7070E spectrometer. GLC mass spectra were recorded on the VG 7070E spectrometer linked to the Hewlett Packard 5790A gas chromatograph fitted with a 25 m cross-linked methyl silicone capillary column.

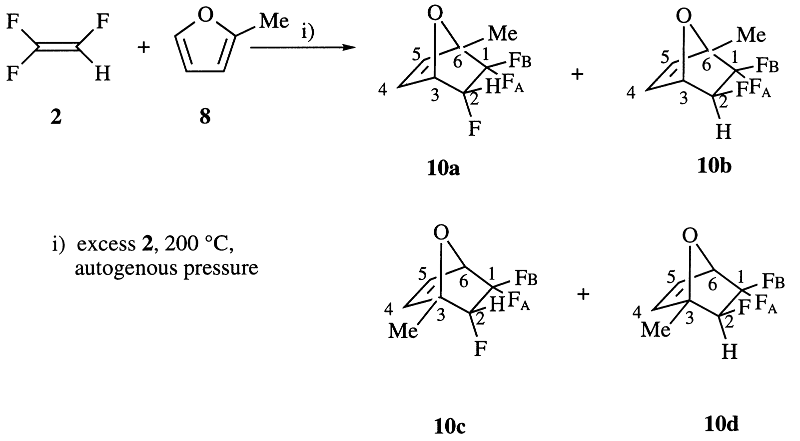
Fractional distillation of product mixtures was carried out using a Fischer Spahltrohr MMS255 small concentric tube apparatus. Melting points were carried out at atmospheric pressure and are uncorrected. Unless otherwise stated, reagents were used as supplied. Solvents were dried by standard methods and stored over a molecular sieve (type 4A).

3.1. Preparation of 1,1,2-trifluoro-7-oxabicyclo[2.2.1] hept-4-ene (4) without solvent

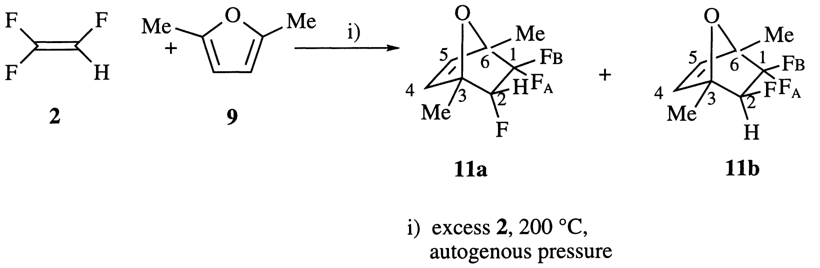
An autoclave (140 ml) was charged with trifluoroethene (36 g, 0.443 mol), furan (6.2 g, 91.6 mmol) and dipentene (0.5 ml) and then heated in a rocking furnace at 200°C for 24 h. After cooling, volatile material was transferred from the tube under reduced pressure. Distillation gave furan (3.9g, 37% conversion) and 1,1,2-trifluoro-7-oxabicyclo[2.2.1]hept-4-ene (**4**) (nc) (4.4 g, 87% yield), as a mix-



Scheme 2



Scheme 4



Scheme 5

ture of *exo*-H **4a** and *endo*-H **4b** isomers. (Found: C, 48.1; H, 3.2. Calc. for $C_6F_3H_5O$: C, 48.0; H, 3.3%). Preparative scale GLC (50°C) allowed separation of the isomers. The *exo*-H isomer **4a** gave: δ_H (400 MHz) 4.8 (1H, m, 3H), 4.9 (1H, ddd, $^2J_{H_2F_2}$=54.7, $^3J_{H_2FB}$=15.6, $^3J_{H_2H_3}$=4.4, 2H), 5.0 (1H, m, 6H), 6.57 (1H, J_{AB}=5.8, 4H or 5H), 6.62 (1H, J_{AB}=5.8, 4H or 5H); δ_F (400 MHz) −108.8 (1F, J_{AB}=232.0 dd $^3J_{FBH_2}$=15.6, $^3J_{FBH_6}$=5.8, 1BF), and −112.9 (1F, J_{AB}=232.0 dd, $^3J_{FAF_2}$=6.3, $^3J_{FAF_2}$=1.8, 1A-F), −192.1 (1F, dd, $^2J_{F_2H_2}$=54.2, $^3J_{F_2FB}$=6.4, 2F); δ_C (400 MHz) 78.27 (ddd, $^2J_{CF}$=22.7, $^3J_{CF}$=3.6, $^3J_{CF}$=1.7, 3C), 80.9 (td, $^2J_{CF}$=27.1, $^3J_{CF}$=1.7, 6C), 87.2 (ddd, $^1J_{CF}$=204.7, $^2J_{CF}$=33.2, $^2J_{CF}$=15.1, 2C), 121.1 (ddd, $^1J_{CF}$=265.1, $^1J_{CF}$=257.2, $^2J_{CF}$=15.1, 1C), 133.1 (dd, $^3J_{CF}$=4.9, $^3J_{CF}$=1.9, 5C), 136.1 (m, 4C). The *endo*-H isomer **4b**: δ_H (400 MHz) 4.6 (1H, dd, $^2J_{H_2F_2}$= 54.2, $^3J_{H_2FA}$=7.4, 2H), 4.8 (1H, m, 3H), 5.07 (1H, m, 6H), 6.50 (1H, J_{AB}=6.0, d, J=2.0, 4H or 5H), 6.57 (1H, J_{AB}=6.0, 4H or 5H); δ_F (400 MHz) −106.2 (1F, J_{AB}=233.1, dd, $^3J_{FAH_2}$=7.4, $^3J_{FAH_6}$=1.5, 1A-F) and −120.3 (1F, J_{AB}=233.1, ddd, $^3J_{FBF_2}$=12.3, $^3J_{FBH_6}$=5.1, $^3J_{FBH_2}$=2.5, 1B-F), −198.1 (1F, ddd, $^2J_{F_2H_2}$=54.4, $^3J_{F_2FB}$ 12.2, $^3J_{F_2H_3}$=7.7, 2F); δ_C (250 MHz) 79.1 (t, $^2J_{CF}$=27.6, 6C), 83.2 (dd, $^2J_{CF}$=22.5, $^3J_{CF}$ 7.4, 3C), 88.9 (ddd, $^1J_{CF}$=209.0, $^2J_{CF}$=29.4, $^2J_{CF}$=15.5, 2C), 120.9 (ddd, $^1J_{CF}$=270.2, $^1J_{CF}$ 258.3, $^2J_{CF}$=14.3, 1C), 134.4 (d, $^3J_{CF}$=4.6, 4C or 5C), 134.7 (d, $^3J_{CF}$=5.8, 4C or 5C).

*3.2. Preparation of 1,1,2-trifluoro-7-oxabicyclo[2.2.1]hept-4-ene (**4**) with solvent*

An autoclave (500 ml) was charged with trifluoroethene (126.8 g, 1.547 mol), furan (20.9 g, 0.307 mol), THF (50 ml) and dipentene (0.5 ml) and heated in a rocking furnace at 200°C for 24 h. Volatile material was transferred from the tube under reduced pressure. Distillation gave trifluoroethene, furan (5.2 g, 75% conversion), THF and product fractions including a fraction (14.3 g) containing mostly *endo*-(H)-1,1,2-trifluoro-7-oxabicyclo[2.2.1]hept-4-ene **4b**, together with some of the *exo*-(H) isomer **4a** and a fraction (1.52 g) containing only the *exo*-(H) isomer **4a**. Total isolated yield of **4a, b** was 45%, (Found: C, 48.0; H, 3.5; Calc. for $C_6F_3H_5O$: C, 48.0; H, 3.3%); ^{19}F, ^1H and ^{13}C NMR spectra were identical with those of the material prepared previously without added THF (see Section 3.1).

*3.3. Preparation of 6-methyl-1,1,2-trifluoro-7-oxabicyclo[2.2.1]hept-4-ene and 3-methyl-1,1,2-trifluoro-7-oxabicyclo[2.2.1]hept-4-ene (**10a–d**)*

An autoclave (140 ml) was charged with trifluoroethene (32.6 g, 0.4 mol), 2-methyl furan (7.1 g, 91.6 mmol) and dipentene (0.5 ml) and heated in a rocking furnace at 200°C for 24 h. Volatile material was transferred from the tube under reduced pressure. Distillation gave 2-methyl furan (0.35 g, 95% conversion) and adducts (**10a–d**) (nc) (9.19 g, 64%). (Found: C, 51.0; H, 4.1; Calc for $C_7H_7F_3O$ C, 51.2; H, 4.3%). Preparative scale GLC (60°C) allowed separation into two fractions each containing two of the 4 isomers. Fraction 1 consisted of the *exo*-H isomers **10a** and **10c**, while fraction 2 consisted of the *endo*-H isomers **10b** and **10d**. *exo*-H 6-methyl-1,1,2-trifluoro-7-oxabicyclo[2.2.1]-hept-4-ene (**10a**) (nc) gave δ_H (400 MHz) 1.57 (3H, s, 6-Me) 4.95 (1H, ddd, $^2J_{H_2F_2}$=55.1, $^3J_{H_2FB}$=15.3, $^3J_{H_2H_2}$=4.5, 2H), 4.97 (1H, m, 3H), 6.36 (1H, J_{AB}=5.6, 4H or 5H), 6.59 (1H, J_{AB}=5.6, 4H or 5H); δ_F (400 MHz) −114.4 (1F, J_{AB}=228.8, dd, $^3J_{FAF_2}$=6.8, 1A-F) −117.9 (1F, J_{AB}=228.8, d, $^3J_{FBH_2}$=15.3, 1B-F) −190.6 (1F, dd, $^3J_{F_2H_2}$=55.6, $^3J_{F_2FA}$=6.8, 2F); *exo*-H 3-methyl-1,1,2-trifluoro-7-oxabicyclo[2.2.1]hept-4-ene (**10c**) (nc) gave δ_H (400 MHz) 1.7 (3H, s, 3-Me), 4.56 (1H, dd, $^2J_{H_2F_2}$=54.9, $^3J_{H_2FB}$=16.0, 2H), 4.76 (1H, m, 6H), 6.41 (1H, J_{AB}=6.0, 4H or 5H), 6.53 (1H, J_{AB}=6.0, 4H or 5H); δ_F (400 MHz) −108.1 (1F, J_{AB}=230.8, dd, $^2J_{FBH_2}$=15.9, $^3J_{FBH_6}$=6.3, 1B-F), −112.1 (1F, J_{AB}=231.0, d, $^3J_{F_2FA}$=6.8, 1A-F), −191.8 (1F, dd, $^2J_{F_2H_2}$=54.7, $^2J_{F_2FA}$6.8, 2F). *endo*-H 6-methyl-1,1,2-trifluoro-7-oxabicyclo[2.2.1]hept-4-ene (**10b**) (nc) gave δ_H (400 MHz) 1.58 (3H, s, 6-Me) 4.60 (1H, dd, $^2J_{H_2F_2}$=53.8, $^3J_{H_2FA}$=7.2, 2H), 4.97 (1H, m, 3H), 6.37 (1H, J_{AB}=5.6, 4H or 5H), 6.47 (1H, J_{AB}=5.6, 4H or 5H); δ_F (400 Mhz) −107.9 (1F, J_{AB}=230.0, d, $^3J_{FAH_2}$=7.5, 1A-F), −128.7 (1F, J_{AB}=230.0, d, $^3J_{FBF_2}$=11.6, 1B-F), −195.7 (1F, ddd, $^2J_{F_2H_2}$=54.4, $^3J_{F_2FB}$=11.9, $^3J_{F_2H_3}$=8.1, 2F); *endo*-H 3-methyl-1,1,2-trifluoro-7-oxabicyclo[2.2.1]hept-4-ene (**10d**) (nc) gave δ_H (400 MHz) 1.64 (3H, s, 3-Me), 4.42 (1H, dd, $^2J_{H_2F_2}$=54.9, $^3J_{H_2FA}$=7.6, 2H), 4.68 (1H, m, 6H), 6.30 (1H, J_{AB}=5.8, 4H or 5H), 6.53 (1H, J_{AB} 5.8, 4H or 5H); δ_F (400 MHz) −105.5 (1F, J_{AB}=231.6, d, $^3J_{FAH_2}$=7.4, 1A-F), −119.4 (1F, J_{AB}=231.2, dd, $^3J_{FBF_2}$=11.9, $^3J_{FBH_6}$=5.5, 1B-F), −205.8 (1F, dd, $^2J_{F_2H_2}$=54.9, $^3J_{F_2FB}$=12.0, 2F).

3.4. Preparation of 3,6-dimethyl-1,1,2-trifluoro-7-oxabicyclo{2.2.1]hept-4-ene (**11a, b**)

An autoclave (140 ml) was charged with trifluoroethene (27.3 g, 0.33 mol), 2,5-dimethyl furan (6.54 g, 68.03 mmol) and dipentene (0.5 ml) and heated in a rocking furnace at 200°C for 24 h. Volatile material was transferred from the vessel under reduced pressure. Distillation gave trifluoroethene, 2,5-dimethyl furan (2.4 g) and a mixture of *exo*- and *endo*-(H)-3,6-dimethyl-1,1,2-trifluoro-7-oxabicyclo[2.2.1]\hept-4-ene (**11a, b**) (nc), (7.6 g) (Found: C, 54.2; H, 5.1. Calc. for $C_8H_9F_3O$, C, 53.9; H, 5.05%); *exo*-H isomer **11a** (nc) gave (400 MHz) 1.52 (3H, s, Me), 1.60 (3H, s, Me), 4.56 (1H, dd, $^2J_{H_2F_2}$=54.6, $^3J_{H_2FB}$=15.4, 2H), 6.3 (2H, m, 4H and 5H); δ_F (400 MHz) −113.9 (1F, J_{AB}=228.0, d, $^3J_{FAF_2}$=7.4, 1A-F), −117.3 (1F, J_{AB}=228.0, d, $^3J_{FBH_2}$=15.6, 1B-F), −190.5 (1F, dd, $^2J_{F_2H_2}$=54.8, $^3J_{F_2FA}$=7.4, 2F); δ_C (400 MHz) 11.45 (s, Me), 13.5 (s, Me), 85.5 (ddd, $^2J_{CF_2}$=21.9, $^3J_{CF_1}$=4.1, $^3J_{CF_1}$=1.8, 3C), 87.2 (td, $^2J_{CF_1}$=25.6, $^3J_{CF_2}$=1.1, 6C), 93.0 (ddd, $^1J_{CF_2}$=207.3, $^2J_{CF_1}$=33.1, $^2J_{CF_1}$=16.7, 2C), 122.0 (ddd, $^1J_{CF_1}$=267.6, $^1J_{CF_1}$=262.3, $^2J_{CF_2}$=15.0, 1C), 137.1 (m, 4C or 5C), 139.3 (m, 4C or 5C). *endo*-H isomer **11b** (nc) gave (400 MHz) 1.52 (3H, s, Me), 1.60 (3H, s, Me), 4.56 (1H, dd, $^2J_{H_2F_2}$=54.6, $^2J_{H_2FA}$=7.4, 2H), 6.3 (2H, m, 4H and 5H); δ_F (400 MHz) −107.5 (1F, J_{AB}=229.2, d, $^3J_{FAH_2}$=7.9, 1A-F) and −127.8 (1F, J_{AB}=229.2, d, $^3J_{FBF_2}$=11.5, 1B-F), −203.4 (1F, dd, $^2J_{F_2H_2}$=54.6, $^3J_{F_2HB_2}$=11.6, 2F); δ_C (400 MHz) 11.3 (s, Me), 13.6 (s, Me), 85.7 (dd, $^2J_{CF_1}$=27.3, $^2J_{CF_1}$=25.4, 6C), 88.3 (dd, $^2J_{CF_2}$=25.4, $^3J_{CF_1}$=7.4, 3C), 91.1 (ddd, $^1J_{CF_2}$=213.6, $^2J_{CF_1}$=28.3, $^2J_{CF_1}$=16.0, 2C), 121.2 (ddd, $^1J_{CF_1}$=273.7, $^1J_{CF_1}$=259.4, $^2J_{CF_2}$=14.5, 1C), 139.0 (m, 4C or 5C), 139.4 (m, 4C or 5C).

3.5. Preparation of 2,3-difluorophenol (**7**)

Lithium diisopropylamide monoTHF (1.5 M solution in hexane) (50 ml, 0.075 mol) was added dropwise over 75 min, under a dry nitrogen atmosphere, to a stirred solution of 1,1,2-trifluoro-7-oxa bicyclo[2.2.1]hept-4-ene (**4a, b**) (5 g, 33.3 mmol) in dry THF (140 ml) at −70°C. On addition, the solution turned orange/brown. The solution was maintained at −70°C for 90 min and then allowed to warm to room temperature over 2 h with stirring. The dark brown solution was filtered, then stirred with water (50 ml). Separation of the organic layer and then extraction of the aqueous layer with diethyl ether removed some of the tarry products. The pH of the aqueous layer was adjusted to 1 using conc. HCl and then extracted with diethyl ether. Volatile material was distilled from these extracts under reduced pressure to leave a tarry residue. Ether was removed from the distillate to leave a straw coloured, higher boiling liquid containing 2,3-difluorophenol (1.1 g; 25% yield), identified by comparison of its NMR and IR spectra with those of an authentic sample obtained from Aldrich.

3.6. Preparation of Tosylate of 2,3-difluorophenol

Pyridine (1.6 g, 20.3 mmol) was added dropwise to a stirred solution of *para*-toluenesulfonyl chloride (3.76 g, 19.2 mmol) and the product of the earlier reaction (Section 3.5) containing 1,2-difluorophenol (1.1 g 8.3 mmol), in dichloromethane (10 ml) at room temperature; after standing overnight (16 h) a white solid appeared. After washing with water and removal of the solvent, the remaining oil contained *p*-toluenesulphonyl chloride. The oil was therefore dissolved in pyridine (20 ml) and this solution was then dropped into vigorously stirred water (20 ml). A solid precipitate formed which was isolated by filtration and then recrystalised (ethanol/water) to give the *p*-tosylate of 1,2-difluorophenol (1.3 g, 55%), m.p. 49–50°C, (Found: C, 55.0; H, 3.45. Calc. for $C_{13}H_{10}F_2O_3S$, C, 54.9; H, 3.5%); δ_H (400 MHz) 2.47 (3H, s, Me), 7.05 (3H, m, 4H, 5H and

6H), 7.35 (2H, J_{AB}=8.2, 3′H and 5′H), 7.77 (2H, J_{AB}=8.2, 2′H and 6′H); δ_F (400 MHz) −134.5 (1F, m, 2F), −151.0 (1F, m, 3F); EI *m/z* 284 (M^+, 4.5%); CI(NH_3): *m/z* 302 ($M+18^+$, 100%).

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