AN ABBREVIATED ROUTE TO DIFLUOROMALEIC ANHYDRIDE [1]

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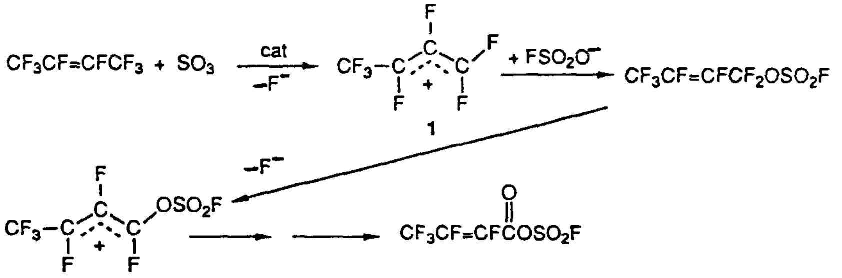
SUMMARY

Difluoromaleic anhydride is obtained in good yield by reaction of either hexafluoro-2, 5-dihydrofuran or hexafluoro-2, 5-dihydrothiophene with sulfur trioxide. Hexafluoro-2, 5-dihydrothiophene is prepared from sulfur and commercially available hexafluorocyclobutene, so its conversion to difluoromaleic anhydride in one step makes the latter readily available as well.

INTRODUCTION

Sulfur trioxide was found earlier [2] to insert into allylic C-F bonds in a reaction very effectively catalyzed by B (III) compounds. Some cases in which forcing conditions were required for acceptable conversions were found to give carbonyl compounds as by-products, apparently the result of attack at a second allylic fluorine atom. Equation (1) illustrates the chemistry involved.

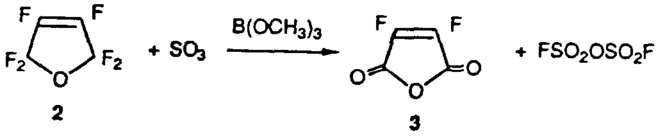


(1)

The need for forcing conditions in this case can be attributed to the presence of a trifluoromethyl group, a strongly destabilizing influence in the carbocation **1**. It might be expected, however, that a structure such as **2**, which is not only cyclic but also has no fluoroalkyl groups attached to the allylic positions, would react with excess sulfur trioxide readily to form difluoromaleic anhydride (**3**) as the end product. Such was found to be the case.

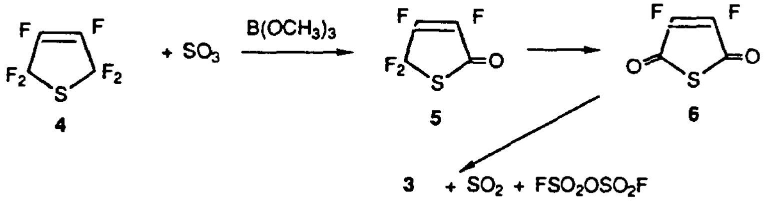
RESULTS AND DISCUSSION

Treatment of hexafluoro-2, 5-dihydrofuran (**2**) with excess sulfur trioxide and trimethyl borate catalyst gave redistilled, pure anhydride **3** in 53% yield. Since **2** is prepared in two steps from furan [3], this synthesis of **3** proceeds in three steps from readily available starting materials. The original synthesis of **3** required six rather laborious steps [4].



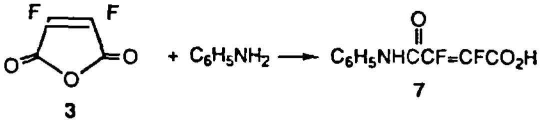
(2)

An even shorter route to **3** was unexpectedly found in the reaction of hexafluoro-2, 5-dihydrothiophene (**4**) with sulfur trioxide. Since **4** is obtainable in good yield from elemental sulfur and hexafluorocyclobutene at elevated temperatures [5], this is a two-step synthesis. The reaction has been shown to proceed in stepwise fashion via intermediates **5** and **6** by the use of reduced amounts of sulfur trioxide to allow their isolation.



(3)

Identification of difluoromaleic anhydride was by preparation of the known [4] anilide **7** as well as by spectral characterization.



$$+ \ C_6H_5NH_2 \longrightarrow C_6H_5NH\overset{O}{\overset{\|}{C}}CF{=}CFCO_2H \qquad (4)$$

3

7

Anhydride **3** is a reactive Diels - Alder partner [4] and is potentially a suitable partner for photoactivated cycloadditions. Its ready availability now makes **3** an important intermediate to consider for such reactions, as well as for other chemistry of the double bond and anhydride functions.

EXPERIMENTAL

IR spectra were recorded on 10% solutions unless otherwise indicated. NMR spectra were taken on 20% solutions with trichlorofluoromethane as internal reference; downfield shift directions were taken as positive.

Preparation of Difluoromaleic Anhydride (3) from Hexafluoro-2, 5-dihydrofuran (2).

Sulfur trioxide (336 g. 4.2 mol) was stirred at 25°C while 83 g (0.47 mol) of hexafluoro-2, 5-dihydrofuran was distilled in. No interaction was apparent while the temperature dropped to 15°C and the SO_3 solidified. Addition of 1 g of trimethyl borate initiated reaction, which was allowed to progress overnight. Then another 42 g (0.24 mol) of hexafluoro-2, 5-dihydrofuran was added, and the mixture was refluxed for 12 hr. while the temperature rose to 92°C. Distillation afforded, after a large foreshot, 69.0 g (74%) of crude difluoromaleic anhydride, bp 100-125°C. Redistillation gave 50.0 g (53%) of **3**, bp 125-126°C. (ref. 4 reports bp 128°C). IR (1% in $CHCl_3$): 1880 (w), 1815 (s) and 1760 (m) (C=O, C=C), 1290 and 1185 cm^{-1} (C-F) NMR (acetone-d_6): ^{19}F ϕ - 141.2 (s, =CF). UV: ε isooctane/235 nm 3,176.

Anilide **7** was prepared by adding 2.9 g (0.022 mol) of **3** to a solution of 1.9 g (0.020 mol) of aniline in 100 ml of ether. The mixture was stirred for 15 min., filtered, and the filter cake dried to give 4.0 g (88%) of **7**, mp 192-193°C (ref. 4 reports mp 193-195°C). NMR (acetone-d_6): ^{19}F ϕ -124.9 (m, 1F, = CF), -132.8 (d, J_{FF}4.7 Hz, 1F, (= CF).

Preparation of 3 from Hexafluoro-2, 5-dihydrothiophene (4).

Commercial sulfur trioxide (176 g, 2.20 mol) was treated cautiously with 2.0 g of trimethyl borate, and the mixture was stirrred while 72.9 g (0.38 mol) of hexafluoro-2, 5-dihydrothiophene was added over 30 min. A mildly exothermic reaction caused reflux. The mixture was stirred 1 hr. while the temperature came down and then was heated to 60°C where a second exotherm was accompanied with pronounced gassing. A sample of the off-gases was shown by IR to be SO_2 with a minor amount of FSO_2OSO_2F present. Reaction was continued at 60-65°C until gas evolution subsided, then at reflux for 2 hr. while the pot temperature fell from 90°C to 80°C. Distillation gave a large foreshot, bp 40-100°C followed by 37.0 g (73%) of crude difluoromaleic anhydride, bp 100-125°C, nearly pure by GC. The IR spectrum was substantially the same as that of a known sample.

Isolation of Tetrafluoro -2, 5-dihydrothiophene-2-one (5) (n.c.) and Difluoro-2, 5-dihydrothiophene-2, 5-dione (6) (n.c.)

Sulfur trioxide (128.0 g, 1.60 mol) was added rapidly to 77.6 g (0.40 mol) of hexafluoro-2, 5-dihydrothiophene. After an initial exotherm, the mixture was refluxed for 30 min. and fractionated to give 121.9 g, bp 42-55°C, shown to be mainly pyrosulfuryl fluoride by ^{19}F NMR, and 29.5 g of crude **5**, bp 77-85°C. Redistillation of this product afforded 16.9 g (25%) of tetrafluoro-2, 5-dihydrothiophene-2-one, bp 83°C. IR (CCl_4): 1755 (C=O) and 1740 cm^{-1} (C=C). NMR (CCl_4): $^{19}F\phi$ -92.0 (d of d, J_{FF}14.7, 5 5 Hz, 2F,CF_2), -133.5 (q, J_{FF}14.3 Hz, 1F, CF), -144.3 (d of t, J_{FF}13.9, 5.5 Hz, 1F, CF). MS: m/e 171.9615 (M^+; calcd for C_4F_4OS, 171.9606), 143.9664 (M^+ -CO; calcd, 143 9657), 121.9641 (M^+-CF_2; calcd, 121.9638). Anal. Calcd for C_4F_4OS: C, 27.91; S, 18.63 Found: C, 28.27; S, 19.16

Further distillation of the reaction mixture afforded 32.6 g of crude **6**, bp 80-86°C (100 mm), which solidified on standing. Recrystallization from hexane/ether followed by sublimation at 45-50°C (10 mm) gave 12.7 g of nearly colorless difluoro-2, 5-dihydrothiophene-2, 5-dione, mp 57-58°C. Evaporation of the filtrate and sublimation at 40°C (10 mm) gave an additional 4.7 g of **6**, mp 52-56°C, for a total yield of 17.4 g (29%). An analytical sample, mp 58-59°C, was prepared by sublimation at 30°C (10 mm). IR (CCl_4): 1760 (w) and 1715 (s) cm^{-1} (C=O and C=C). NMR (CCl_4): $^{19}F\phi$ -132.2 (s, CF). Anal. Calcd for $C_4F_2O_2S$: C, 32.00; S, 21.36 Found: C, 32.81; S, 21.64.

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