JOC The Journal of Organic Chemistry

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Synthesis of Aliphatic Sulfur Pentafluorides by Oxidation of SF_5-Containing Anisole, Phenols, and Anilines

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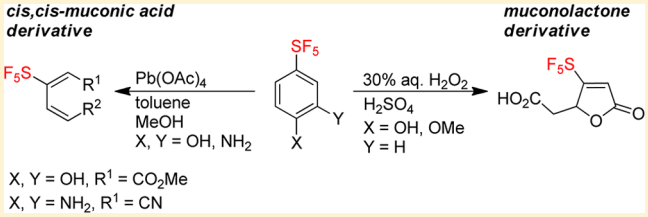
Supporting Information

ABSTRACT: 4-(Pentafluorosulfanyl)catechol, 2-amino-4-(pentafluorosulfanyl)phenol, and 2-amino-5-(pentafluorosulfanyl)phenol undergo oxidation by lead tetraacetate at ambient temperature leading to dearomatization and the formation of SF_5-substituted nitriles and esters of *cis,cis*-hexa-2,4-dienedioic (muconic) acid in good yields. 4-(Pentafluorosulfanyl)phenol and 4-(pentafluorosulfanyl)anisole are oxidized by 30% aqueous hydrogen peroxide in concentrated sulfuric acid to provide 2-(5-oxo-3-(pentafluorosulfanyl)-2,5-dihydrofuran-2-yl)acetic acid [3-(pentafluorosulfanyl)-muconolactone] and small amounts of side products—SF_5-containing maleic and succinic acids. The methods presented are the first examples of the practical synthesis of aliphatic SF_5-containing compounds from readily available aromatic ones.

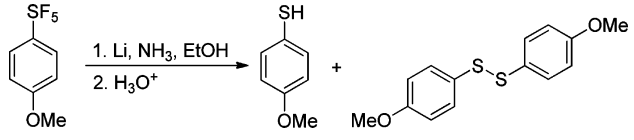


The most common fluorinated, electron-acceptor, highly stable, and lipophilic group used to modify properties of molecules in the development of new drugs, agrochemicals, and functional materials is the trifluoromethyl group. The unique physicochemical properties that are exerted by the trifluoromethyl group in molecules are even more pronounced in the case of the pentafluorosulfanyl (SF_5) group.[1−7] However, pentafluorosulfanyl-containing compounds remain a much less developed class of compounds due to the lack of availability of key building blocks. Synthetic methods toward aliphatic SF_5 compounds are mainly based on free radical addition of SF_5Cl and SF_5Br to unsaturated compounds.[8−10] However, SF_5Cl is a very expensive and toxic gas and SF_5Br is not commercially available at the moment. The synthesis of both reagents in the laboratory is not at all straightforward.[11,12] Thus, there are several commercial aliphatic SF_5 compounds available at prices that reflect the challenges in their synthesis. The situation with the availability of aromatic SF_5 compounds is much better. Large-scale direct fluorination (with F_2) of bis(nitrophenyl)-disulfides provides 3- and 4-nitro(pentafluorosulfanyl)-benzenes,[13−15] and two-step synthesis from diaryl disulfides or aromatic thiols affords substituted (pentafluorosulfanyl)-benzenes.[16,17]

With the aim of improving the availability of aliphatic SF_5 compounds, we envisioned a synthetic strategy in which aliphatic SF_5 compounds could be accessed from readily available aromatic ones. This process requires overcoming the resonance energy of the aromatic ring; with this goal, we investigated classical reduction pathways such as hydrogenation in the presence of heterogeneous transition-metal catalysts or Birch reduction; however, it was the oxidation strategy[18] that provided the best results.

Heterogeneous catalytic hydrogenation of aromatics is a straightforward route to saturated cyclic compounds such as cyclohexanes. For example, recently published PtO_2-mediated hydrogenation of 2-, 3-, or 4-(trifluoromethyl)anilines with H_2 (1 bar) at ambient temperature afforded (trifluoromethyl)-cyclohexylamines in good yields.[19] However, when similar conditions (PtO_2, Pd/C, or Rh/C catalysts, H_2 1−50 bar, TFA or EtOH, rt) were tested with 3-(pentafluorosulfanyl)aniline, 4-(pentafluorosulfanyl)phenol, or 4-(pentafluorosulfanyl)-anisole,[20] no SF_5-containing aliphatic products were detected in the reaction mixtures. Another type of reduction of aromatics to aliphatic compounds, Birch reduction,[21−23] was applied to 4-(pentafluorosulfanyl)anisole providing a mixture of 4-methoxybenzenethiol and 1,2-bis(4-methoxyphenyl)disulfide and no SF_5-containing aliphatics (Scheme 1). Similarly, the attempted reduction of 1-nitro-4-(pentafluorosulfanyl)benzene afforded only 4,4′-disulfanediyldianiline (Scheme 2).

Scheme 1. Attempted Birch Reduction of 4-(Pentafluorosulfanyl)anisole

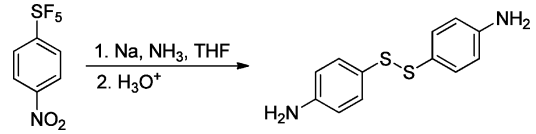


Thus, the attention was turned toward oxidation. Selective oxidation methods of aromatics, especially those bearing electron-acceptor groups, are scarce in the literature. Oxidation of 4-(pentafluorosulfanyl)benzene-1,2-diamine available in two steps from 1-nitro-4-(pentafluorosulfanyl)benzene[24] (Scheme 3) using sodium periodate[25] or the O_2/CuCl system[26,27] did

Received: July 14, 2014
Published: August 19, 2014

   dx.doi.org/10.1021/jo501562z | J. Org. Chem. 2014, 79, 8906−8911

Scheme 2. Attempted Birch Reduction of 1-Nitro-4-(pentafluorosulfanyl)benzene



not provide the expected muconononitrile **1**, but a mixture of the corresponding azo product and a complicated product mixture, respectively. Finally, reaction with lead tetraacetate (3 equiv)[28] in toluene afforded benzotriazole **2** in moderate yield and SF_5-substituted muconononitrile **1** in low yield (Scheme 3).

Oxidation with lead tetraacetate was mainly previously used for catechols.[29−31] In the presence of methanol, muconic acid methyl esters were formed. When we applied oxidation with lead tetraacetate to 4-(pentafluorosulfanyl)catechol (**3**), the expected muconic acid ester **4** was formed in good yield (Scheme 4).

Oxidation of aminophenols **5** and **6** afforded muconic acid derivatives **7** and **8**, respectively, in good yields (Schemes 5 and 6).

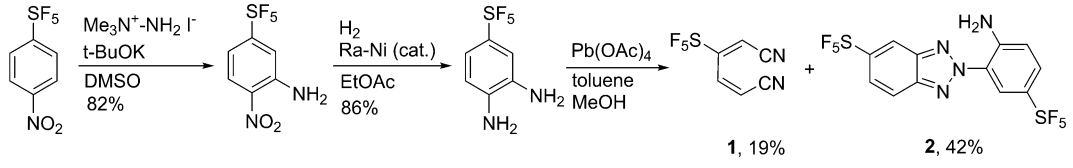
Muconic acid derivatives **1**, **4**, **7**, and **8** were formed exclusively with the *cis,cis*-stereochemistry. Despite relatively good yields of oxidations with lead tetraacetate, we continued to search for alternative reaction conditions that do not use heavy metals.

It is well-known that catechols and *ortho*-quinones are oxidized by peroxoacids, initially to oxepine-2,7-dione (Baeyer−Villiger oxidation product), which is then further converted to muconic acid, muconolactone, and other oxidation products.[18,33,34] Additionally, some electron-rich phenols and catechols were found to undergo oxidation with hydrogen peroxide in the presence of a diaryl diselenide catalyst to provide muconic acids and muconolactones.[35] However, conditions described for the oxidation of catechols (peroxyacetic acid in acetic acid, 0−25 °C) were not effective in the reaction with 4-(pentafluorosulfanyl)phenol or 4-(pentafluorosulfanyl)anisole. Therefore, a more powerful oxidant was needed. A particularly effective oxidant is trifluoroperacetic acid (PTFA)[36] or a mixture of hydrogen peroxide with trifluoroacetic acid (TFA) or trifluoroacetic anhydride (TFAA), which initiate the oxidation of aromatics by electrophilic aromatic hydroxylation. The reaction does not stop in mono- or dihydroxylation; for example, with PTFA, toluene is converted to acetic and hexa-2,4-dienedioic acids.[36] We discovered that reactions of 4-(pentafluorosulfanyl)anisole with hydrogen peroxide (aqueous solution or complex with urea, UHP) in TFA or 98% sulfuric acid provided oxidation products **9**−**13**. Optimization results are shown in Table 1. With UHP in TFA under the conditions in entry 1, the major product was phenol **9**, which was characterized (NMR, GCMS, and HRMS); however, with aqueous hydrogen peroxide, muconic acid **10** and its lactone **11** were predominant products (entry 2). The highest NMR yield of lactone **11** was achieved with 30% hydrogen peroxide in TFA at 80 °C (entry 3). The employment of peroxides at higher concentrations did not afford any improvements (entry 4). A more economical alternative to TFA in which the oxidation could be successfully performed was found to be concentrated sulfuric acid. After some experimentation with peroxide concentrations and the amount of solvent, it was found that about 8 equiv of H_2O_2 as well as 3 vol equiv of sulfuric acid were necessary for optimal conversion to lactone **11**. With sulfuric acid, only traces of the initial oxidation products **9** and **10** were observed. The amount of sulfuric acid needed in the reaction was about 2.5 mL when 30% hydrogen peroxide was used per 1 mmol of starting anisole. This amount could be reduced to about one-half when 57% hydrogen peroxide was employed. However, the use of peroxide at a higher concentration did not provide higher product yields and was found to be more exothermic and potentially dangerous. For these reasons, further oxidations and preparative experiments were conducted with 30% peroxide solution. The highest yield was achieved when the reaction was started at 0 °C and slowly warmed up to ambient temperature (entry 11). Under these conditions, the formation of SF_5-maleic and succinic acids were suppressed.

In analogy to 4-(pentafluorosulfanyl)anisole, 4-(pentafluorosulfanyl)phenol was found to undergo oxidation, but this time, no hydroxylation product (SF_5-catechol) could be observed (Table 2). The muconic acid derivative **10** was isolated in 10% yield from the reaction of 4-(pentafluorosulfanyl)phenol with UHP in TFA. Employment of 4-(pentafluorosulfanyl)phenol provided a higher NMR yield of **11** under optimized conditions (entry 5) compared to reactions starting from 4-(pentafluorosulfanyl)anisole. New maleic and succinic acids **12** and **13** were isolated and fully characterized. The stereochemistry of acid **12** was determined by X-ray analysis confirming the expected *cis* configuration of the carboxylic groups (CCDC 1011378, Figure S1).

The preparative synthesis of lactone **11** under optimized conditions was performed starting either from 4-(pentafluorosulfanyl)anisole or from 4-(pentafluorosulfanyl)phenol on a 1 and 0.4 g scale, respectively (Scheme 7). The isolated yields of **11** do not seem high, but it has to be kept in mind that the final muconolactone **11** is a product of a multistep reaction sequence and the required conditions are rather harsh. The total yield of the three main products **11**−**13** was 50−60% which was considered satisfactory for the oxidative cleavage of electron-deficient phenol and anisole derivatives. The workup and isolation of lactone **11** from minor byproducts diacids **12** and **13** is straightforward, and the reaction is scalable. After the reaction, the mixture was poured into cold water; extraction into dichloromethane and recrystallization from benzene provided the pure lactone **11**. The diacids **12** and **13** (insoluble in dichloromethane) were efficiently extracted into diethyl ether. The maleic acid derivative **12** was obtained in its pure form by repeated sonication with dichloromethane, while the

Scheme 3. Synthesis of 4-(Pentafluorosulfanyl)benzene-1,2-diamine[24] and Oxidation with Lead Tetraacetate



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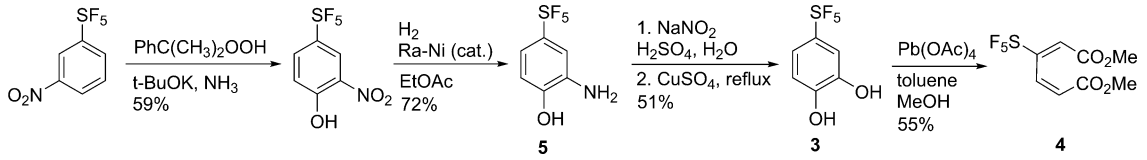
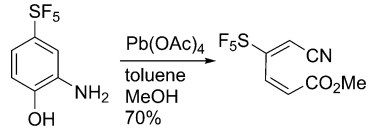
Scheme 4. Synthesis of Aminophenol 5,[32] Catechol 3, and Its Oxidation to Diester 4



Scheme 5. Oxidation of Aminophenol 5 to Muconic Acid Derivative 7



less acidic succinic acid derivative **13** was isolated by converting it to water-soluble potassium salt with aqueous K_2HPO_4, acidification to pH = 4.5, and extraction back into diethyl ether.

The structure of the observed products and literature precedent in related oxidations[18] enabled us to suggest a plausible mechanism of the reaction sequence (Scheme 8). We believe that the first step is the electrophilic aromatic hydroxylation in the position that is *ortho* to the oxygen functionality. When starting from 4-(pentafluorosulfanyl)-anisole, phenol **9** formed in the reaction with hydrogen peroxide and TFA (Table 1, entries 1 and 2). Next, demethylation with strong acid and oxidation to substituted *ortho*-quinone occurs. In the case of 4-(pentafluorosulfanyl)-phenol the intermediate catechol **3** is not observed. The substituted *ortho*-quinone undergoes Baeyer–Villiger (BV) oxidation to substituted oxepine-2,7-dione which is hydrolyzed to muconic acid **10**. Conjugate addition of one of the carboxylic acid groups to the sterically less congested double bond provides the major product muconolactone **11** (Scheme 8). The described pathway to **10** and **11** is similar to aerobic microbial degradation of aromatic compounds, which involves hydroxylating oxygenase and ring-cleaving dioxygenase enzymes.[37−41] For the formation of minor side products, maleic acid **12** and succinic acid **13**, several pathways are possible. Monohydroxylated aromatics **3** and **9** are more activated toward S_EAr than the starting SF_5 phenol or anisole, and the result of a control experiment in which **12** is not formed in the reaction of **10** or **11** with H_2O_2/H_2SO_4 suggests the formation of **12** by further S_EAr hydroxylation of **3** and **9**, oxidation, and a series of BV oxidation and hydrolytic steps. Another control experiment that showed that the diacid **13** formed in the reaction of **11** with H_2O_2/H_2SO_4 suggests the formation of **13** by unfavorable isomerization of the double bond of **11** and a series of hydrolytic and BV oxidation steps.

In conclusion, it was demonstrated that oxidation of SF_5-catechol, aminophenols, and benzenediamine with lead tetraacetate provides new SF_5-substituted nitriles and esters of *cis,cis*-hexanedioic (muconic) acid. Oxidations of SF_5-phenol and anisole with hydrogen peroxide in sulfuric acid yield new SF_5-muconolactone. These reactions are easy to perform and use bulk chemicals. The processes described are the first reports of the preparation of aliphatic SF_5 compounds from easily accessible aromatic ones.

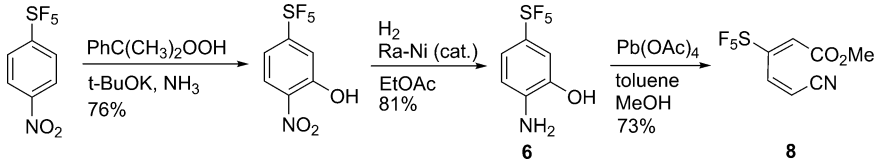
EXPERIMENTAL SECTION

General Information. NMR spectra were recorded on a 400, 500, or 600 MHz instruments. The chemical shifts (δ) are reported in parts per million (ppm), and coupling constants (J) are given in hertz. ^{13}C spectra were proton decoupled. GCMS spectra were recorded using a quadrupole mass-selective electron impact (EI) detector (70 eV). High-resolution mass spectra (HRMS) were recorded using electron impact (EI), chemical (CI), or electrospray (ESI) ionizations. Infrared spectra were measured on an FTIR instrument. Purifications of products were performed by flash chromatography using silica gel 60. TLC plates were visualized with ultraviolet light (254 nm) and/or with $KMnO_4$ staining solution.

4-(Pentafluorosulfanyl)catechol (3). 2-Amino-4-(pentafluorosulfanyl)phenol[32] (517 mg, 2.20 mmol) was added to a mixture of water (2 mL) and 98% H_2SO_4 (2 mL). The suspension was cooled with ice, and $NaNO_2$ (151 mg, 2.19 mmol) in water (0.6 mL) was added. The mixture was stirred for 10 min, and urea (50 mg, 0.8 mmol) was then added to remove the eventual excess of HNO_2. Then the mixture was added to a boiling solution of $CuSO_4$ (10 g) in water (25 mL). After cooling, the product was extracted with Et_2O. Column chromatography on silica gel (hexane–EtOAc, 55:45) and repeated addition and removal of benzene and CH_2Cl_2 under reduced pressure gave **3** (264 mg, 51%) as a red semisolid; R_f 0.30 (hexane–Et_2O, 1:1); ^1H NMR (400 MHz, DMSO-d_6): δ 6.86 (d, 1H, J = 8.8 Hz), 7.15 (dd, 1H, J = 8.8, 2.8 Hz), 7.19 (d, 1H, J = 2.8 Hz), 9.89 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 113.8 (quin, J = 4.6 Hz), 114.4, 119.6 (quin, J = 4.8 Hz), 142.4, 145.9, 146.6 (quin, J = 18.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 63.7 (d, 4F, J = 150.2 Hz), 84.6–86.3 (m, 1F); HRMS (ESI$^-$) m/z calcd for $C_6H_4F_5O_2S$ $[M - H]^-$ 234.9858, found 234.9857.

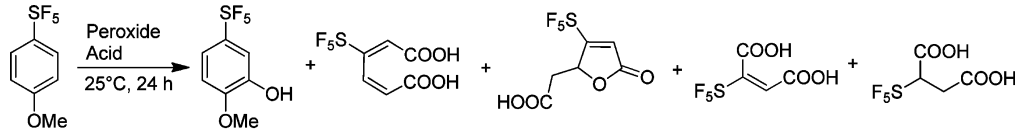
(2*E*,4*Z*)-3-(Pentafluorosulfanyl)hexa-2,4-dienedinitrile (1) and 2-(2-Amino-5-(pentafluorosulfanyl)phenyl)-5-(pentafluorosulfanyl)-2*H*-benzotriazole (2). Lead tetraacetate was recrystallized from glacial acetic acid with a few drops of acetic anhydride (7 mL acetic acid per 1 g of $Pb(OAc)_4$) and dried under vacuum for 2 h. $Pb(OAc)_4$ (2.27 g, 5.1 mmol) was suspended in a mixture of toluene (5 mL) and MeOH (5 mL) under argon at room temperature. Then 4-(pentafluorosulfanyl)benzene-1,2-diamine[24] (400 mg, 1.7 mmol) dissolved in a mixture of toluene (1.5 mL) and MeOH (1.5 mL) was added. After the mixture was stirred for 1 h, aqueous NH_4Cl was added and the mixture was extracted with EtOAc. Column chromatography on silica gel (hexane–CH_2Cl_2, 1:1) gave **1** (76 mg, 19%) as a yellow oil; R_f 0.20 (hexane–CH_2Cl_2, 1:1); ^1H NMR (400

Scheme 6. Synthesis of Aminophenol 6[32] and Its Oxidation to Muconic Acid Derivative 8



dx.doi.org/10.1021/jo501562z | J. Org. Chem. 2014, 79, 8906–8911

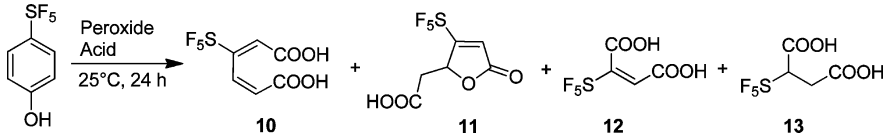
Table 1. Optimization of Oxidation of 4-(Pentafluorosulfanyl)anisole with Hydrogen Peroxide Sources in Acidic Media



entry	peroxide (equiv)	acid (vol/vol H_2O_2)	**9**, yield[a] (%)	**10**, yield[a] (%)	**11**, yield[a] (%)	**12**, yield[a] (%)	**13**, yield[a] (%)
1	UHP (8)	TFA (2:1)[b]	16	4	3	0	1
2	30% H_2O_2 (8)	TFA (7:1)	6	13	28	1	2
3[c]	30% H_2O_2 (8)	TFA (7:1)	0	2	**41**	3	9
4	57% H_2O_2 (8)	TFA (7:1)	0	19	26	2	2
5	30% H_2O_2 (8)	H_2SO_4 (1:1)	0	0	0	0	0
6	30% H_2O_2 (8)	H_2SO_4 (2:1)	2	0	29	5	2
7	30% H_2O_2 (8)	H_2SO_4 (3:1)	0	0	39	16	6
8	30% H_2O_2 (8)	H_2SO_4 (4:1)	0	0	33	19	6
9	30% H_2O_2 (4)	H_2SO_4 (3:1)	0	0	20	0	0
10	30% H_2O_2 (12)	H_2SO_4 (3:1)	0	0	35	22	7
11[d]	30% H_2O_2 (8)	H_2SO_4 (3:1)	0	0	**42**	11	2
12	57% H_2O_2 (8)	H_2SO_4 (2:1)	0	0	23	12	6
13	57% H_2O_2 (8)	H_2SO_4 (3:1)	0	0	32	18	5
14	57% H_2O_2 (12)	H_2SO_4 (2:1)	0	0	28	17	10

[a] ^{19}F NMR yield using 1-nitro-4-(pentafluorosulfanyl)benzene as an internal standard. [b] TFA/UHP molar ratio. [c] The reaction was performed at 80 °C for 1 h. [d] The reaction was performed at 0−25 °C.

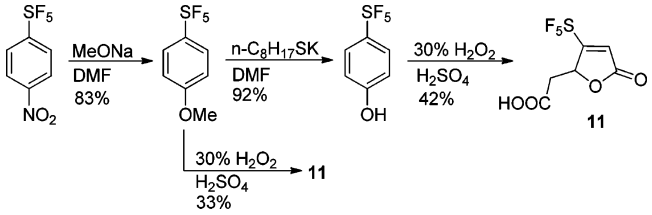
Table 2. Optimization of Oxidation of 4-(Pentafluorosulfanyl)phenol with Hydrogen Peroxide Sources in Acidic Media



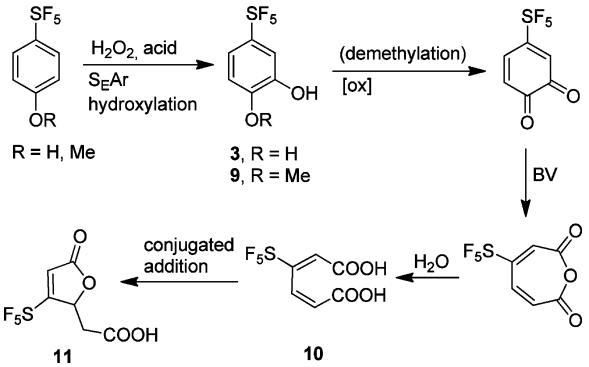
entry	peroxide[a]	acid (vol/vol H_2O_2)	**10**, yield[b] (%)	**11**, yield[b] (%)	**12**, yield[b] (%)	**13**, yield[b] (%)
1	UHP	TFA (2:1)[c]	22	19	0	2
2	30% H_2O_2	H_2SO_4 (1:1)	0	7	0	0
3	30% H_2O_2	H_2SO_4 (2:1)	0	48	9	6
4	30% H_2O_2	H_2SO_4 (3:1)	0	42	14	9
5[d]	30% H_2O_2	H_2SO_4 (3:1)	0	**55**	9	5

[a] Peroxide (8 equiv) was used. [b] ^{19}F NMR yield using 1-nitro-4-(pentafluorosulfanyl)benzene as an internal standard. [c] TFA/UHP molar ratio. [d] The reaction was performed at 0−25 °C.

Scheme 7. Synthesis of 4-(Pentafluorosulfanyl)anisole, 4-(Pentafluorosulfanyl)phenol,[20] and Preparative Oxidation to SF_5-Muconolactone 11



Scheme 8. Plausible Mechanism of Oxidation of SF_5-Phenol and Anisole to Muconolactone 11



MHz, $CDCl_3$): δ 6.07 (d, 1H, J = 11.7 Hz), 6.47 (s, 1H), 7.02 (d, 1H, J = 11.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 109.2 (quin, J = 6.2 Hz), 110.9, 111.8, 113.2, 138.2 (quin, J = 3.0 Hz), 164.3−165.2 (m); ^{19}F NMR (376 MHz, $CDCl_3$): δ 60.8 (d, 4F, J = 150.3 Hz), 74.5−76.2 (m, 1F); MS (EI) m/z (rel. int.) 230 (24) $[M]^+$, 127 (17), 122 (36), 103 (100), 95 (49), 89 (50), 76 (90), 75 (24), 71 (11), 70 (10), 64 (10), 52 (19), 51 (17), 50 (10); HRMS (CI) m/z calcd for $C_6H_4F_5N_2S$ $[M + H]^+$ 231.0015, found 231.0022; and **2** as an orange solid (165 mg, 42%); R_f 0.31 (hexane-CH_2Cl_2, 2:1); mp 162−166 °C; FTIR (film) ν_{max} (cm^{-1}) 3503, 3372, 1621, 1593, 1568, 1504, 1408, 1323, 1296, 1258, 1175, 1118, 1089, 858, 841, 821, 813, 695, 623, 596, 586, 574;

^{1}H NMR (600 MHz, DMSO-d_6): δ 7.12 (d, 1H, J = 9.2 Hz), 7.27 (br s, 2H), 7.77 (dd, 1H, J = 9.2, 2.7 Hz), 7.98 (dd, 1H, J = 9.4, 2.1 Hz), 8.27 (d, 1H, J = 9.4 Hz), 8.42 (d, 1H, J = 2.7 Hz), 8.85 (dd, 1H, J = 2.1, 0.8 Hz); ^{13}C NMR (151 MHz, DMSO-d_6): δ 116.9, 118.3 (quin, J = 4.9 Hz), 119.4, 121.2, 122.5 (quin, J = 4.5 Hz), 123.8 (quin, J = 3.8 Hz), 127.9 (quin, J = 3.4 Hz), 140.0 (quin, J = 17.7 Hz), 142.0, 143.7,

dx.doi.org/10.1021/jo501562z | J. Org. Chem. 2014, 79, 8906−8911

144.6, 151.4 (quin, J = 16.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 63.5 (d, 4F, J = 150.2 Hz), 64.0 (d, 4F, J = 150.8 Hz), 82.4−84.1 (m, 1F), 84.3−86.0 (m, 1F); MS (EI) m/z (rel. int.) 464 (10), 463 (13), 462 (100) $[M]^+$, 354 (7), 335 (14), 199 (8), 124 (8), 105 (21), 78 (14); HRMS (CI) m/z calcd for $C_{12}H_9F_{10}N_4S_2$ $[M + H]^+$ 463.0109, found 463.0090.

Dimethyl (2*E*,4*Z*)-3-(Pentafluorosulfanyl)hexa-2,4-dienedioate (4). Prepared according to the procedure for **1** from **3** (81 mg, 0.34 mmol) and $Pb(OAc)_4$ (440 mg, 1.0 mmol). Chromatography on silica gel (hexane−Et_2O, 6:1) gave **4** as a pale yellow oil (56 mg, 55%); R_f 0.20 (hexane−Et_2O, 6:1); FTIR (film) ν_{max} (cm^{-1}) 2958, 1740, 1665, 1628, 1439, 1398, 1347, 1291, 1216, 1178, 893, 847, 821, 592, 573; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.72 (s, 3H), 3.75 (s, 3H), 6.23 (d, 1H, J = 11.9 Hz), 6.64 (d, 1H, J = 2.0 Hz), 6.70 (ddquin, 1H, J = 11.9, 2.0, 0.6 Hz,); ^{13}C NMR (126 MHz, $CDCl_3$): δ 51.8, 52.5, 124.9 (quin, J = 4.9 Hz), 127.5, 133.2 (quin, J = 2.2 Hz), 160.4 (quin, J = 18.0 Hz), 163.6, 164.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ 59.1 (d, 4F, J = 148.9 Hz), 78.0−79.7 (m, 1F); MS (EI) m/z (rel. int.) 281 (1), 265 (6), 237 (100), 169 (13), 138 (19), 129 (13), 79 (16), 59 (12), 51 (11); HRMS (ESI^+) m/z calcd for $C_8H_9F_5O_4SNa$ $[M + Na]^+$ 319.0034, found 319.0034.

Methyl (2*Z*,4*E*)-5-Cyano-4-(pentafluorosulfanyl)penta-2,4-dienoate (7). Prepared according to procedure for **1** from **5**[32] (200 mg, 0.85 mmol) and $Pb(OAc)_4$ (1.15 g, 2.6 mmol). Chromatography on silica gel (hexane−Et_2O, 5:1) gave **8** as a pale yellow oil (157 mg, 70%); R_f 0.39 (hexane−Et_2O, 5:1); FTIR (film) ν_{max} (cm^{-1}) 2959, 2234, 1734, 1645, 1619, 1440, 1399, 1238, 1200, 1182, 850, 823, 805, 604, 573; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3H), 6.26 (s, 1H), 6.41 (d, 1H, J = 12.0 Hz), 6.66 (dd, 1H, J = 12.0, 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.3, 106.8 (quin, J = 6.3 Hz), 112.6, 130.1, 131.6 (quin, J = 2.7 Hz), 163.6, 166.0 (quin, J = 20.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 59.9 (d, 4F, J = 150.2 Hz), 75.8−77.5 (m, 1F); MS (EI) m/z (rel. int.) 232 (18), 136 (100), 124 (21), 108 (25), 96 (29), 93 (12), 89 (12), 77 (15), 76 (30), 50 (13); HRMS (CI) m/z calcd for $C_7H_7F_5NO_2S$ $[M + H]^+$ 264.0118, found 264.0113.

Methyl (2*E*,4*Z*)-5-Cyano-3-(pentafluorosulfanyl)penta-2,4-dienoate (8). Prepared according to procedure for **1** from **6**[32] (200 mg, 0.85 mmol) and $Pb(OAc)_4$ (1.15 g, 2.6 mmol). Chromatography on silica gel (hexane−Et_2O, 4:1) gave 7 as a pale yellow oil (163 mg, 73%); R_f 0.16 (hexane−Et_2O, 4:1); FTIR (film) ν_{max} (cm^{-1}) 2960, 2229, 1741, 1655, 1607, 1439, 1386, 1343, 1290, 1220, 1185, 848, 807, 602, 573; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.84 (s, 3H), 5.85 (d, 1H, J = 11.6 Hz), 6.82 (d, 1H, J = 1.4 Hz), 7.01 (ddquin, 1H, J = 11.6, 1.4, 0.7 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 53.1, 108.4, 113.9, 127.8 (quin, J = 5.0 Hz), 139.9 (quin, J = 2.5 Hz), 158.9 (quin, J = 19.6 Hz), 162.8; ^{19}F NMR (376 MHz, $CDCl_3$): δ 60.0 (d, 4F, J = 148.8 Hz), 76.6−78.2 (m, 1F); MS (EI) m/z (rel. int.) 263 (66) $[M]^+$, 248 (85), 232 (100), 136 (77), 127 (35), 124 (25), 104 (98), 96 (65), 92 (46), 89 (39), 78 (17), 77 (83), 76 (73), 75 (24), 70 (20), 65 (27), 59 (67), 51 (32), 50 (55); HRMS (EI) m/z calcd for $C_7H_6F_5NO_2S$ $[M]^+$ 263.0039, found 263.0030.

2-Methoxy-5-(pentafluorosulfanyl)phenol (9). Urea hydrogen peroxide adduct (0.48 g, 5.1 mmol, 8 equiv) was dissolved in TFA (0.8 mL, 10.5 mmol), 4-(pentafluorosulfanyl)anisole[20] (150 mg, 0.64 mmol) was added, and the reaction mixture was stirred for 24 h at ambient temperature. The mixture was then poured onto ice (4 g), Na_2SO_3 (0.32 g, 2.5 mmol) was added, and the aqueous layer was extracted with Et_2O (3 × 8 mL). The combined ether extract was washed with water (2 × 4 mL) as well as brine (2 mL) and dried ($MgSO_4$), and solvent was removed under reduced pressure. Column chromatography on silica gel (hexane−EtOAc, 9:1) gave **9** (12 mg, 7%) as an oil; R_f 0.14 (hexane−EtOAc, 7:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.95 (s, 3H), 5.72 (s, 1H), 6.85 (dquin, 1H, J = 8.9, 1.0 Hz), 7.28 (dd, 1H, J = 8.9, 2.7 Hz), 7.34 (d, 1H, J = 2.7 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 56.2, 109.3, 112.9 (quin, J = 4.6 Hz), 118.4 (quin, J = 4.9 Hz), 144.9, 147.0 (quin, J = 18.4 Hz), 148.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ 63.6 (d, 4F, J = 150.3 Hz), 84.4−86.1 (m, 1F); MS (EI) m/z (rel. int.) 250 (100) $[M]^+$, 235 (16), 142 (11), 127 (73), 123 (23), 108 (12), 99 (40), 89 (14), 79 (27), 51 (27); HRMS (CI) m/z calcd for $C_7H_8F_5O_2S$ $[M + H]^+$ 251.0165, found 251.0163.

(2*E*,4*Z*)-3-(Pentafluorosulfanyl)hexa-2,4-dienedioic Acid (10). Urea hydrogen peroxide adduct (1.41 g, 15.0 mmol, 8 equiv) was dissolved in TFA (2.9 mL), 4-(pentafluorosulfanyl)phenol[20] (410 mg, 1.9 mmol) was added, and the reaction mixture was stirred for 24 h at ambient temperature. The mixture was then poured onto ice (10 g), Na_2SO_3 (1.0 g, 8 mmol) was added, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The washed aqueous phase was extracted with Et_2O (3 × 10 mL). The combined ether extract was washed with water (2 × 4 mL) as well as brine (2 mL) and dried ($MgSO_4$), and the solvent was removed under reduced pressure. During isolation the product was kept below 25 °C to avoid possible decomposition or isomerization. The residuum was dried by addition of benzene and evaporation under reduced pressure. This procedure was repeated several times to provide viscous oil. CH_2Cl_2 (3 mL) was added, the mixture was sonicated for a few minutes, and the solvent was removed under reduced pressure giving solid material. Trituration with CH_2Cl_2 (2 mL) under sonication afforded **10** as a white solid (48 mg, 10%); mp 100−102 °C; FTIR (film) ν_{max} (cm^{-1}) 3299, 3097, 2557, 1713, 1664, 1626, 844, 826, 802, 598, 574; ^{1}H NMR (400 MHz, acetone-d_6): δ 6.29 (d, 1H, J = 12.0 Hz), 6.73 (d, 1H, J = 2.0 Hz), 6.88 (d, 1H, J = 12.0 Hz); ^{13}C NMR (100 MHz, acetone-d_6): δ 127.0, 129.1, 134.1−134.3 (m), 160.2−161.0 (m), 164.3, 165.3; ^{19}F NMR (376 MHz, acetone-d_6): δ 60.1 (d, 4F, J = 147.4 Hz), 80.4−82.1 (m); HRMS (ESI^-) m/z calcd for $C_6H_4F_5O_4S$ $[M - H]^-$ 266.9756, found 266.9752.

2-(5-Oxo-3-(pentafluorosulfanyl)-2,5-dihydrofuran-2-yl)-acetic Acid (11) from 4-(Pentafluorosulfanyl)anisole. To 98% H_2SO_4 (10.4 mL) cooled with ice, 30% H_2O_2 (3.5 mL, 34 mmol, 8 equiv) was added dropwise followed by the addition of 4-(pentafluorosulfanyl)anisole[20] (1.00 g, 4.27 mmol). The reaction flask was immersed in an ice/water bath and allowed to warm up to ambient temperature over several hours. After 24 h, the mixture was poured onto ice (40 g), Na_2SO_3 (2.0 g, 16 mmol) was added, and the aqueous layer was extracted with hexane (2 × 30 mL). The washed aqueous phase was extracted with CH_2Cl_2 (4 × 40 mL). The combined CH_2Cl_2 extract was washed with water (2 × 2 mL) as well as brine (2 mL) and dried ($MgSO_4$), and solvent was removed under reduced pressure. The resulting pale yellow solid (475 mg) was recrystallized from benzene (4 mL), cooled at 4 °C overnight, filtered, and washed with cold benzene (1.8 mL). After drying, **11** was obtained as a white solid (376 mg, 33%); mp 93−96 °C; FTIR (film) ν_{max} (cm^{-1}) 3507, 3132, 3040, 2636, 1786, 1764, 1725, 1632, 1407, 1291, 1272, 899, 870, 611, 589; ^{1}H NMR (500 MHz, acetone-d_6): δ 2.91 (ddquin, 1H, J = 17.4, 7.1, 0.6 Hz), 3.27 (ddquin, 1H, J = 17.4, 3.4, 0.6 Hz), 5.83 (dddquin, 1H, J = 7.1, 3.4, 2.0, 0.6 Hz), 7.07 (dquin, 1H, J = 2.0, 1.0 Hz); ^{13}C NMR (126 MHz, acetone-d_6): δ 36.4, 79.1 (quin, J = 2.9 Hz), 125.8 (quin, J = 6.0 Hz), 167.8, 169.8, 172.9 (quin, J = 20.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 64.6 (d, 4F, J = 152.4 Hz), 75.2−76.9 (m, 1F). The lactone **11** was not observed on MS (CI or ESI); therefore, its methyl ester was prepared using diazomethane: *Methyl 2-(5-oxo-3-(pentafluorosulfanyl)-2,5-dihydrofuran-2-yl)acetate*; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.76 (dd, 1H, J = 17.0, 7.7 Hz), 3.18 (ddquin, 1H, J = 17.0, 3.3, 0.8 Hz), 3.75 (s, 3H), 5.65 (dddquin, 1H, J = 7.7, 3.3, 1.9, 0.6 Hz), 6.65 (dquin, 1H, J = 1.9, 0.8 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 36.5, 52.4, 78.0 (quin, J = 2.9 Hz), 124.0 (quin, J = 5.9 Hz), 166.5, 168.2, 172.7 (quin, J = 22.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 64.6 (d, 4F, J = 152.3 Hz), 75.3−77.1 (m, 1F); MS (EI) m/z (rel. int.) 282 (7) $[M]^+$, 263 (2), 251 (30), 222 (41), 209 (56), 181 (20), 155 (100), 127 (31), 89 (52), 73 (37), 59 (66) ; HRMS (ESI^+) m/z calcd for $C_7H_7F_5O_4SNa$ $[M + Na]^+$ 304.9877, found 304.9879; the aqueous phase after extraction with CH_2Cl_2 was further extracted with Et_2O (3 × 40 mL), the combined ether phase was washed with water (2 × 2 mL) as well as brine and dried ($MgSO_4$), and the solvent was removed under reduced pressure. The resulting viscous semisolid residue was evaporated several times with benzene to remove water and Et_2O and then sonicated with CH_2Cl_2. The solvent was removed with a pipet, and the resulting solid dried under reduced pressure giving **12** as a white, slightly hygroscopic solid; *(E)-2-(Pentafluorosulfanyl)but-2-enedioic acid (**12**)*; mp 95−103 °C; FTIR (film) ν_{max} (cm^{-1}) 3502, 3097, 2582, 1728, 1424, 1410, 1256, 853, 606, 569; ^{1}H

dx.doi.org/10.1021/jo501562z | J. Org. Chem. 2014, 79, 8906−8911

NMR (400 MHz, acetone-d_6): δ 6.99 (s, 1H); ^{13}C NMR (126 MHz, acetone-d_6): δ 128.1 (quin, J = 6.1 Hz), 157.3 (quin, J = 17.7 Hz), 161.5, 163.5; ^{19}F NMR (376 MHz, acetone-d_6): δ 64.4 (d, 4F, J = 149.6 Hz), 78.5−80.2 (m, 1F); MS (ESI$^-$) m/z (rel. int.) 241 (10), 197 (36), 127 (100); HRMS (ESI$^-$) m/z calcd for $C_4H_2F_5O_4S$ [M − H]$^-$ 240.9599, found 240.9596.

2-(5-Oxo-3-(pentafluorosulfanyl)-2,5-dihydrofuran-2-yl)-acetic Acid (11) from 4-(Pentafluorosulfanyl)phenol. To 98% H_2SO_4 (4.4 mL) cooled with ice, 30% H_2O_2 (1.48 mL, 14 mmol, 8 equiv) was added dropwise, followed by the addition of 4-(pentafluorosulfanyl)phenol[20] (400 mg, 1.82 mmol). The reaction flask was immersed in ice/water bath and allowed to warm up to ambient temperature over several hours. After 24 h, the mixture was poured onto ice (18 g), and Na_2SO_3 (0.9 g, 7 mmol) was added, followed by extraction with CH_2Cl_2 (4 × 20 mL). The combined organic phase was washed with water (2 × 1 mL) as well as brine (1 mL) and dried ($MgSO_4$), and the solvent was removed under reduced pressure giving a pale yellow solid (265 mg). The solid was recrystallized from benzene (2.1 mL), cooled overnight at 4 °C, filtered, and washed with cold benzene (0.9 mL). After drying, pure **11** was obtained as a white solid (203 mg, 42%). The washed aqueous phase was extracted with Et_2O (3 × 20 mL), the combined organic phase was washed with water (2 × 1 mL) as wel as brine, and solvent was removed under reduced pressure. The resulting viscous residue was dissolved in aqueous K_2HPO_4 (0.3 M, 10 mL) and washed with Et_2O (10 mL). The pH of the washed aqueous phase was adjusted to 4.5 with aqueous HCl and extracted with Et_2O (2 × 10 mL). The combined ether extracts were washed with water as well as brine and dried ($MgSO_4$), and the solvent was removed under reduced pressure giving **13** as a white solid; *2-(Pentafluorosulfanyl)butanedioic acid (**13**)*; mp 140−142 °C; FTIR (film) ν_{max} (cm^{-1}) 3547, 3122, 2667, 2565, 1730, 1431, 1412, 1272, 845, 603, 569; ^{1}H NMR (400 MHz, acetone-d_6): δ 3.27 (dd, 1H, J = 17.2, 4.0 Hz), 3.35 (dd, 1H, J = 17.2, 10.9 Hz), 4.96 (dquind, 1H, J = 10.9, 6.3, 4.0 Hz); ^{13}C NMR (126 MHz, acetone-d_6): δ 34.7 (quin, J = 4.4 Hz), 81.3 (quin, J = 11.9 Hz), 165.9 (quin, J = 3.1 Hz), 170.7 (quin, J = 1.9 Hz); ^{19}F NMR (376 MHz, acetone-d_6): δ 64.1 (dd, 4F, J = 144.3, 6.3 Hz), 81.9−83.5 (m, 1F); MS (ESI$^-$) m/z (rel. int.) 243 (48), 127 (100); HRMS (ESI$^-$) m/z calcd for $C_4H_4F_5O_4S$ [M − H]$^-$ 242.9756, found 242.9752.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H, ^{13}C, ^{19}F NMR spectra of newly synthesized products and X-ray crystallographic file of **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the Academy of Sciences of the Czech Republic (Research Plan RVO: 61388963) and the Grant Agency of the Czech Republic (P207/12/0072) is gratefully acknowledged.

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