Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron
Tetrahedron 60 (2004) 5019–5024

Oxidative nucleophilic substitution of hydrogen in nitroarenes with trifluoromethyl carbanions. Synthesis of trifluoromethyl phenols

Marek Surowiec and Mieczysław Mąkosza*

Institute of Organic Chemistry, Polish Academy of Sciences, ul. Kasprzaka 44/52, PL-01-224 Warsaw POB 58, Poland

Received 3 February 2004; revised 18 March 2004; accepted 8 April 2004

Abstract—Trifluoromethyl carbanions generated from the Ruppert reagent and TASF add to highly electron-deficient nitroarenes to produce σ^H adducts subsequently oxidized with dimethyldioxirane to substituted trifluoromethyl phenols.

1. Introduction

Pharmaceutical and plant protection agents often contain F or CF_3 substituents and thus methods of introduction of these groups are of great interest in modern organic synthesis.[1,2] Of particular interest are arenes containing CF_3 groups. There are a few general methods of synthesis of such arenes, and the main ones are: exchange of chlorine for fluorine in CCl_3 groups of readily available trichloromethyl arenes and treatment of benzoic acids with SF_4.[3] On the other hand, the direct introduction of a CF_3 group to arenes is also possible via Cu catalyzed replacement of halogen with CF_3^- carbanion generated from the Ruppert reagent, CF_3SiMe_3, or other sources.[4] Attempts to replace halogens or the nitro group in halonitrobenzenes with CF_3^-, generated from the Ruppert reagent without a Cu catalyst, gave the expected products, trifluoromethylnitroarenes, in low yields.[5] There is also one report on oxidative nucleophilic replacement of hydrogen in trinitrobenzene with a CF_3^- anion.[6]

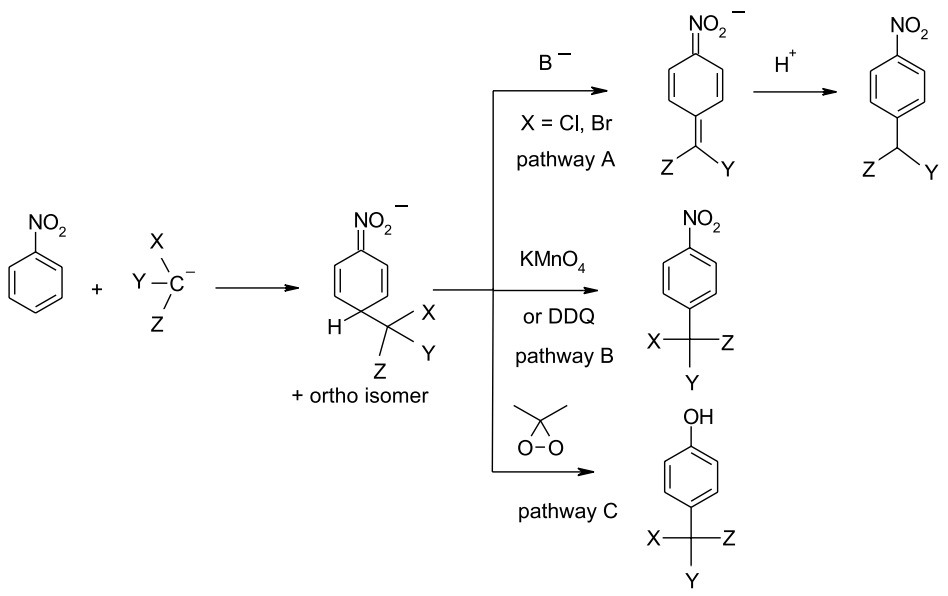
Introduction of carbon substituents into electron-deficient arenes can be efficiently executed via nucleophilic substitution of hydrogen with carbanions[7] or Grignard reagents.[8] The reaction proceeds via addition of these carbon nucleophiles to the electron-deficient rings in the *ortho*- or *para*- positions to the NO_2 group occupied with hydrogen to form σ^H adducts that are converted into the final products in many ways. When the reacting carbanions contain leaving groups X at the carbanion center, base induced β-elimination of HX from the σ^H adducts gives products of vicarious nucleophilic substitution (VNS).[9] On the other hand, oxidation of the σ^H adducts with external oxidants such as $KMnO_4$, DDQ etc. gives substituted nitroarenes, products of oxidative nucleophilic substitution[10] whereas some σ^H adducts oxidized with dimethyldioxirane (DMD) are converted into substituted phenols.[11] Trichloromethyl anions generated by deprotonation of chloroform react with nitroarenes along the VNS pathway affording nucleophilic dichloromethylation.[12] The various ways of transforming σ^H adducts of carbanions to nitroarenes into final products are shown in Scheme 1.

2. Results and discussion

Taking into account the expected higher nucleophilicity of CF_3^- anions, that are less stabilized by fluorine substituents than CCl_3^- anions, and low rate of elimination of HF from σ^H adducts of CF_3^- anions to nitroarenes, we expected that there is a good chance for introduction of CF_3 groups into nitroarenes via an oxidative process. Our first attempts of reaction of CF_3^- anions generated by treatment of CF_3SiMe_3, (**1**) with TASF [tris(dimethylamino)sulfonium difluorotrimethylsilicate] in THF–MeCN with nitrobenzene, 1-nitronaphthalene, 2-and 4-chloronitrobenzenes followed by oxidation with $Bu_4N^+MnO_4^-$ or DMD gave negative results. No CF_3ArNO_2 or CF_3ArOH or other aromatic products containing fluorine were found in the reaction mixtures, although the nitroarenes were partially consumed. Since in the reaction mixture we have found some amounts of nitroaryl acetonitriles it appears that the generated CF_3^- anions afforded deprotonation of acetonitrile and the produced carbanion reacts with nitroarenes. This supposition was confirmed by treatment of CF_3SiMe_3 and 2,4,6-trichloronitrobenzene in THF–MeCN with TASF

Keywords: Ruppert reagent; Nitroarenes; Carbanions; Dimethyldioxirane; Phenols.
* Corresponding author. Tel.: +48-22-6318788; fax: +48-22-6326681; e-mail address: icho-s@ich.edu.pl

0040–4020/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2004.04.022



Scheme 1.

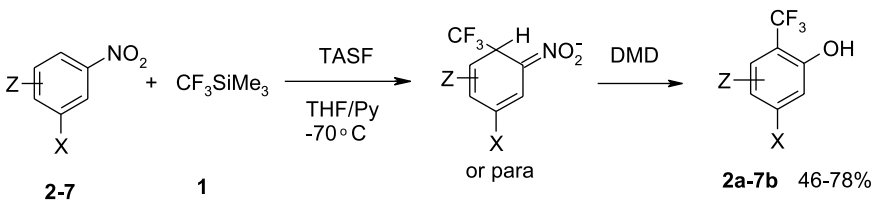
giving 3,5-dichloro-6-nitrophenylacetonitrile in a reasonable yield 46%. Thus, the THF–MeCN solvent system, widely used for reaction of aldehydes and ketones with CF_3^- anion generated from CF_3SiMe_3[13] cannot be used for its reactions with nitroarenes. Perhaps due to low rate and unfavorable equilibrium of the addition of CF_3^- to nitroarenes, the main process was acid–base equilibrium with MeCN. Thus in further studies we used the THF–pyridine solvent system, as neat THF cannot be used because it does not dissolve TASF. However, treatment of nitrobenzene and *p*-chloronitrobenzene with **1** and TASF in THF–Py (1:1) at −70 °C, followed by oxidation with $Bu_4N^+MnO_4^-$ or DMD gave negative results. Since the nitroarenes were mostly recovered we can assume that there was negligible conversion of $ArNO_2$ into σ^H adducts. Hence, we used more electrophilic nitroarenes in our further studies. The results are presented in Table 1.

When a solution of equimolar amounts of the Ruppert reagent **1**, 3-cyanonitrobenzene **2** and TASF in THF–Py (1:1) at −70 °C was treated with an acetone solution of DMD, the reaction resulted in formation of a mixture of three isomeric cyanotrifluoromethyl phenols in a reasonable overall yield 49%. The ratio of 3-cyano-2-trifluoromethyl- **2a**, 3-cyano-4-trifluoromethyl- **2b** and 3-cyano-6-trifluoromethyl phenol **2c** was 5.5:1:6. On the other hand, oxidation of this system with $Bu_4N^+MnO_4^-$ did not produce trifluoromethyl cyanonitrobenzenes, products of ONSH reaction. We have already observed that MnO_4^- oxidation of the anionic σ^H adducts is very sensitive to steric hindrance at the addition site and usually does not proceed with the σ^H adducts of carbanions in *ortho* position to the NO_2 group.[10] Interestingly the addition of CF_3 carbanions took place preferentially *ortho* to the nitro group and as a consequence oxidation of the σ^H adducts to **2** with DMD

Table 1.

Starting nitroarene			Yields of phenols (%)			
X	Z	No.	Total	Isomers		
CN	H	**2**	49	3-CN-2-CF_3	**2a**	22
				3-CN-4-CF_3	**2b**	4
				3-CN-6-CF_3	**2c**	23
CN	4-Cl	**3**	63	3-CN-4-Cl-2-CF_3	**3a**	47
				3-CN-4-Cl-6-CF_3	**3b**	16
NO_2	H	**4**	78	3-NO_2-2-CF_3	**4a**	47
				3-NO_2-4-CF_3	**4b**	18
				3-NO_2-6-CF_3	**4c**	13
NO_2	4-Br	**5**	46	3-NO_2-4-Br-2-CF_3	**5a**	29
				3-NO_2-6-Br-2-CF_3	**5b**	6
				3-NO_2-6-Br-4-CF_3	**5c**	11
NO_2	5-NO_2	**6**	53[a]	3,5di-NO_2-2-CF_3	**6a**	22
				3,5di-NO_2-4-CF_3	**6b**	31
2-Chloro-3-nitropyridine		**7**	57[b]	2-Cl-3-OH-4-CF_3-Py	**7a**	28
				2-Cl-3-OH-6-CF_3-Py	**7b**	29

[a] Additionally α,α,α-trifluoro-2,4,6-trinitrotoluene, 33% was obtained.
[b] Additionally 2,2′-dichloro-3,3′-dinitro-bipyridyl-4,4′, **7c**, 6% was obtained.



Scheme 2.

gave mostly **2a** and **2c**. Under similar conditions, other highly electro-deficient nitroarenes such as *m*-dinitrobenzene **3**, 3-cyano-4-chloronitrobenzene **4**, 2,4-dinitrobromobenzene **5**, 1,3,5-trinitrobenzene **6** and 2-chloro-3-nitropyridine **7** were converted into substituted trifluoromethylphenols as shown in Scheme 2. Also in the reaction of these nitroarenes with CF_3^- anions, the addition proceeded preferentially *ortho* to the nitro groups.

Oxidation of the σ^H adducts of CF_3^- anions to polynitroarenes **4**, **5** and **6** creates an interesting question: which of the negatively charged NO_2 groups is oxidized by DMD and converted into the OH group? Surprising there was not significant difference between rates of oxidation of such nitro groups located *ortho* and *para* to the addition site. For instance in the σ^H adduct of CF_3 to **4** ratio of the corresponding rates equals 0.72.

The structures of the trifluoromethyl phenols obtained by oxidation of the σ^H adducts of CF_3^- anions to nitroarenes were determined on the basis of analysis of ^1H, ^{13}C and ^{19}F NMR spectra. For this purpose, mass spectra were also very helpful. In MS of all *ortho* CF_3 phenols, there were well pronounced ions $[M-20]^+$ formed by elimination of HF.

Although yields of the trifluoromethyl phenols were rather moderate (46–78%), unreacted nitroarenes were recovered and thus there was an excellent material balance of the nitroarenes, usually above 90%. On this basis we suppose that the σ^H adducts of CF_3 anions, once formed, are efficiently oxidized by DMD to phenols. However, the degree of conversion of CF_3^- into the σ^H adducts is not very high in spite of high electrophilicity of the arenes. This is perhaps due to fast dissociation of CF_3^- to difluorocarbene.[14]

Formation of the σ^H adducts of CF_3^- to nitroarenes is accompanied with coloration of the mixture (orange, red, blue, etc) and oxidation of these adducts with DMD results in disappearance of the color. Usually, oxidation is completed within a few min. Only oxidation of σ^H adducts of **6** required a few hours for completion. Because of that, oxidation of the σ^H adducts to 1,3,5-trinitrobenzene with DMD gave, besides the expected phenols **6a** and **6b** substantial quantities of the ONSH product α,α,α-trifluorotrinitrotoluene, **6c**. Surprisingly oxidation of the corresponding σ^H adduct to 2-chloro-3-nitropyridine **7** also gave small amount of the bipyridine **7c**. This byproduct is perhaps formed via oxidation of the deprotonated pyridine by analogy to reported observations.[15] In this case, CF_3^- acted as a base abstracting a proton from the pyridine ring. This process shows that CF_3^- despite being a strong base is a weak nucleophile and can be considered as a hard nucleophile.

Oxidation of σ^H adducts of CF_3^- to **2** and **7** with other oxidants (MnO_4^-, DDQ, Br_2) failed; only when σ^H adducts to **4** were treated with Br_2 and Et_3N, one of the isomeric σ^H adducts was converted into 3,5-dinitro-4-trifluoromethylbromobenzene, **4d**.

3. Conclusion

We have shown that the CF_3^- anion generated by treatment of the Ruppert reagent with TASF adds to nitroarenes provided they show sufficiently high electron deficiency. In our hands the oxidation of such σ^H adducts proceeds satisfactorily only with dimethyldioxirane giving substituted trifluoromethyl phenols.

4. Experimental

4.1. General remarks

Melting points are uncorrected. Infrared spectra were recorded on a Perkin–Elmer FT-IR spectrometer. NMR spectra were measured at 400 MHz on a Mercury-400BB or at 200 MHz on a Gemini-200BB spectrometers. Chemical shifts are reported in ppm relative to tetramethylsilane as internal standard. Mass spectra were obtained on AMD 604 Inectra GmbH instrument using EI, appropriate isotope patterns were observed. Analytical TLC was carried out on Merck alufolien sheets Kieselgel 60 F_{254}. For preparative HPLC Merck-Hitachi equipment was used with pump L-7100 detector VL-7400, using hexane and ethyl acetate as a solvent. For column chromatography silica gel 230–400 mesh, Merck was used. Solvents, nitroarenes and TASF were used as received from the manufacturers except for tetrahydrofuran that was distilled over potassium benzophenone ketyl before use. The Ruppert reagent was a gift from Dr A. Marhold (Bayer AG).

Acetone solution of DMD was prepared according to the described procedure.[16]

4.2. Reaction of the Ruppert reagent with 2,4,6-trichloronitrobenzene in the presence of TASF in THF/MeCN system

To a stirred solution of **1** (0.6 mmol) and nitroarene (0.5 mmol) in THF (5 mL) at −70 °C under argon, TASF (153 mg, 0.5 mmol) dissolved in MeCN (1 mL) was added dropwise, the mixture was stirred for 30 min and the cooling bath was removed. After 30 min of further stirring, aqueous HCl (1 mL) was added. The reaction mixture was dried over anhydrous $MgSO_4$, the solid phase was filtered off and washed with dichloromethane (20 mL). The solvents were

evaporated (25 °C, 15 Torr) and the product was purified by column chromatography using hexane–ethylacetate 20:1 as eluent.

4.2.1. 3,5-Dichloro-2-nitrophenylacetonitrile. Yield 54 mg, 46%, colorless crystals, mp 69–70 °C (EtOH). HR EIMS calcd for $C_8H_4N_2O_2^{35}Cl_2$ M=229.9650. Found: 229.9654. ^{1}H NMR (400 MHz, $CDCl_3$): 7.61–7.59 (m, 1H), 7.85–7.70 (m, 1H), 3.81–3.75 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 137.8, 132.5, 130.8, 128.3, 127.7, 125.7, 114.6, 20.3. Anal. calcd for $C_8H_4N_2O_2Cl_2$: C, 41.59; H, 1.75; N, 12.13, Cl, 30.69. Found: C, 41.68; H, 1.49; N, 12.19, Cl, 30.79.

4.3. General procedure for oxidation of the σ^H adducts of CF_3^- to nitroarenes with DMD

To a stirred solution of **1** (0.6 mmol) and nitroarene (0.5 mmol) in THF (5 mL) at −70 °C under argon, TASF (153 mg, 0.5 mmol) dissolved in pyridine (1 mL) was added dropwise and the mixture was stirred for 5 min. Water (9 μL, 0.5 mmol) and than an acetone solution of DMD (ca. 0.6 mmol, 10 mL of ca. 0.06 M) was added to the mixture. After 15 min of further additional stirring, dilute HCl (1 mL) was added and the cooling bath was removed. A mixture of isomeric trifluoromethylphenols was extracted from the reaction mixture with aqueous NaOH and after acidification of the aqueous layer was separated by preparative HPLC.

The products **7a** and **7b** were isolated in another manner. The reaction mixture was dried over anhydrous $MgSO_4$, the solid phase was filtered off and washed with acetone (20 mL). The solvents were evaporated (25 °C, 15 Torr) and the products were purified by preparative HPLC.

4.3.1. 3-Cyano-2-trifluoromethylphenol (2a). Yield 21 mg, 22%, colorless crystals, mp 157–158 °C (CH_2Cl_2). EIMS m/z (%): 187 (85), 168 (17), 167 (91), 139 (100), 138 (4), 120 (3), 112 (9). HR EIMS calcd for $C_8H_4ONF_3$ M=187.0245. Found: 187.0251. ^{1}H NMR (400 MHz, $CDCl_3$): 7.52 (m, 1H), 7.41 (d, 1H, J=7.7 Hz), 7.24 (d, 1H, J=8.3 Hz), 6.70 (s, broad, 1H). ^{19}F NMR (376 MHz, acetone-d_6): −58.1. Anal. calcd for $C_8H_4F_3NO$: C, 51.35; H, 2.15; N, 7.49. Found: C, 51.17; H, 1.89; N, 7.31.

4.3.2. 3-Cyano-4-trifluoromethylphenol (2b). Yield 4 mg, 4%, colorless crystals. EIMS m/z (%): 187 (100), 168 (8), 139 (75), 120 (10). HR EIMS calcd for $C_8H_4ONF_3$ M=187.0245. Found: 187.0249. ^{1}H NMR (400 MHz, $CDCl_3$): 7.57 (d, 1H, J=8.7 Hz), 7.27 (s, 1H), 7.19 (d, 1H, J=8.7 Hz), 6.68 (s broad, 1H). ^{19}F NMR (376 MHz, acetone-d_6): −60.20.

4.3.3. 3-Cyano-6-trifluoromethylphenol (2c). Yield 22 mg, 23%, colorless crystals, mp 188–189 °C (CH_2Cl_2). EIMS m/z (%): 187 (82), 168 (18), 167 (100), 139 (90), 120 (3), 112 (8). HR EIMS calcd for $C_8H_4ONF_3$ M=187.0245. Found: 187.0249. ^{1}H NMR (400 MHz, $CDCl_3$): 7.64 (d, 1H, J=8.1 Hz), 7.30 (d, 1H, J=8.1 Hz), 7.28 (s, 1H), 6.60 (s broad, 1H). ^{19}F NMR (376 MHz, acetone-d_6): −63.0. ^{13}C NMR (100 MHz, acetone-d_6): 156.7, 128.9 (q, J=5 Hz), 124.1 (q, J=272 Hz), 123.8, 121.6 (q, J=31 Hz), 120.9, 118.0, 96.6. IR (KBr): 3234, 2259, 1980, 1591, 1473, 1316, 1268, 1148, 1108, 1041, 983, 808, 753. Anal. calcd for $C_8H_4F_3NO$: C, 51.35; H, 2.15; N, 7.49. Found: C, 50.99; H, 1.85; N, 7.20.

4.3.4. 4-Chloro-3-cyano-2-trifluoromethylphenol (3a). Yield 52 mg, 47%, yellow crystals, mp 201–202 °C (CH_2Cl_2). EIMS m/z (%): 223 (9), 221 (29), 203 (18), 201 (100), 175 (13), 173 (41). HR EIMS calcd for $C_8H_3ONF_3^{35}Cl$ M=220.9855. Found: 220.9858. ^{1}H NMR (400 MHz, acetone-d_6): 10.50 (s broad, 1H), 7.78 (d, 1H, J=8.9 Hz), 7.48 (d, 1H, J=8.9 Hz). ^{19}F NMR (376 MHz, acetone-d_6): −54.33. ^{13}C NMR (100 MHz, acetone-d_6): 156.6, 135.4, 129.2 (q, J=5 Hz), 124.6, 123.1 (q, J=274 Hz), 123.0 (q, J=30 Hz), 113.8, 96.6. Anal. calcd for $C_8H_3F_3NOCl$: C, 43.37; H, 1.36; N, 6.32. Found: C, 43.16; H, 1.12; N, 6.17.

4.3.5. 4-Chloro-3-cyano-6-trifluoromethylphenol (3b). Yield 18 mg, 16%, yellow crystals, mp 168–169 °C (CH_2Cl_2). EIMS m/z (%): 223 (18), 221 (57), 203 (34), 202 (16), 201 (100), 175 (24), 173 (70). HR EIMS calcd for $C_8H_3ONF_3^{35}Cl$ M=220.9855. Found: 220.9862. ^{1}H NMR (400 MHz, acetone-d_6): 7.84 (d, 1H, J=0.6 Hz), 7.54 (s, 1H), 3.4 (s broad, 1H). ^{19}F NMR (376 MHz, acetone-d_6): −64.5. Anal. calcd for $C_8H_3F_3NOCl$: C, 43.37; H, 1.36; N, 6.32. Found: C, 43.21; H, 1.28; N, 6.34.

4.3.6. 3-Nitro-2-trifluoromethylphenol (4a). Yield 49 mg, 47%, colorless crystals, mp 136–137 °C (CH_2Cl_2/hexane). EIMS m/z (%): 208 (9), 207 (100), 188 (4), 187 (2), 177 (13), 161 (80), 149 (28), 133 (18), 113 (43). HR EIMS calcd for $C_7H_4O_3NF_3$ M=207.0143. Found: 207.0150. ^{1}H NMR (acetone-d_6, 400 MHz): 10.36 (s, 1H), 7.73–7.67 (m, 1H), 7.38 (d, 1H, J=8.4 Hz), 7.28 (d, 1H, J=7.9 Hz). ^{19}F NMR (acetone-d_d, 376 MHz): −59.40. ^{13}C NMR (acetone-d_d, 100 MHz): 157.9, 135.3, 123.0 (q, J=271 Hz), 121.2, 115.1, 108.6 (q, J=34 Hz), 96.6. IR (KBr): 3428, 1617, 1531, 1465, 1376, 1338, 1306, 1154, 1129, 1042, 961, 823, 807, 740.

4.3.7. 3-Nitro-4-trifluoromethylphenol (4b). Yield 19 mg, 18%, colorless crystals, mp 210–211 °C (CH_2Cl_2). EIMS m/z (%): 208 (8), 207 (100), 188 (9), 187 (79), 177 (1), 161 (32), 141 (26), 138 (33), 113 (88). HR EIMS calcd for $C_7H_4O_3NF_3$ M=207.0143. Found: 207.0137. ^{1}H NMR ($CDCl_3$, 400 MHz): 7.69 (d, 1H, J=8.7 Hz), 7.35 (d, 1H, J=2.3 Hz), 7.06–7.00 (m, 1H), 6.38 (s broad, 1H). ^{19}F NMR (acetone-d_d, 376 MHz): −59.56. ^{13}C NMR ($CDCl_3$, 100 MHz): 156.1, 134.8, 129.0, 123.9, 118.79 (q, J=31 Hz), 112.3 (q, J=207 Hz), 96.0.

4.3.8. 3-Nitro-6-trifluoromethylphenol (4c). Yield 14 mg, 13%, yellow oil. EIMS m/z (%): 208 (8), 207 (100), 189 (1), 187 (88), 161 (32), 141 (57), 113 (73). HR EIMS calcd for $C_7H_4O_3NF_3$ M=207.0143. Found: 207.0137. ^{1}H NMR (acetone-d_6, 400 MHz): 7.93–7.91 (m, 1H), 7.87 (d, 1H, J=0.5 Hz), 7.86–7.84 (m, 1H). ^{19}F NMR (acetone-d_{**d}, 376 MHz): −62.92.

4.3.9. 4-Bromo-3-nitro-2-trifluoromethylphenol (5a). Yield 42 mg, 29%, orange oil. EIMS m/z (%): 287 (98), 285 (100), 267 (45), 265 (45), 241 (33), 239 (31), 218 (22), 216 (22), 193 (42), 191 (44), 112 (57), 86 (45). HR EIMS

calcd for $C_7H_3O_3NF_3^{79}Br$ M=284.9248. Found: 284.9253. ^1H NMR (400 MHz, $CDCl_3$): 7.57 (dd, 1H, J=8.9, 0.6 Hz), 6.92 (dd, 1H, J=8.9, 0.4 Hz), 5.10 (s broad, 1H). ^{19}F NMR (376 MHz, $CDCl_3$): −59.46.

4.3.10. 6-Bromo-3-nitro-2-trifluoromethylphenol (5b). Yield 9 mg, 6%, orange oil. EIMS *m/z* (%): 287 (13), 285 (13), 267 (4), 265 (4), 241 (7), 239 (6), 86 (100). HR EIMS calcd for $C_7H_3O_3NF_3^{79}Br$ M=284.9248. Found: 284.9242. ^1H NMR (400 MHz, $CDCl_3$): 8.21 (d, 1H, J=8.8 Hz), 7.95 (d, 1H, J=8.8 Hz), 7.38 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$): −59.23.

4.3.11. 6-Bromo-3-nitro-4-trifluoromethylphenol (5c). Yield 17 mg, 11%, orange oil. EIMS *m/z* (%): 287 (13), 285 (13), 257 (4), 255 (4), 241 (7), 239 (7), 229 (4), 227 (4), 101 (23), 100 (25), 86 (100). HR EIMS calcd for $C_7H_3O_3NF_3^{79}Br$ M=284.9248. Found: 284.9257. ^1H NMR (400 MHz, $CDCl_3$): 7.85 (s, 1H), 7.34 (s, 1H), 5.6 (s broad, 1H). ^{19}F NMR (376 MHz, $CDCl_3$): −58.81.

4.3.12. 3,5-Dinitro-4-trifluoromethylphenol (6a). Yield 39 mg, 31%, colorless crystals, mp 163–165 °C (CH_2Cl_2). EIMS *m/z* (%): 253 (9), 252 (100), 183 (22), 160 (39), 159 (9), 135 (20), 132 (54). HR EIMS calcd for $C_7H_3O_5N_2F_3$ M=251.9994. Found: 251.9993. ^1H NMR (200 MHz, acetone-d_6): 7.69 (d, J=0.5 Hz). ^{19}F NMR (376 MHz, acetone-d_6): −55.8 (t, J=0.5 Hz).

4.3.13. 3,5-Dinitro-2-trifluoromethylphenol (6b). Yield 28 mg, 22%, yellow oil. EIMS *m/z* (%): 253 (6), 252 (81), 233 (12), 232 (100), 183 (7), 160 (27), 132 (30). HR EIMS calcd for $C_7H_3O_5N_2F_3$ M=251.9994. Found: 251.9991. ^1H NMR (400 MHz, acetone-d_6): 8.18 (d, 1H, J=0.7 Hz), 7.68 (d, 1H, J=0.7 Hz). ^{19}F NMR (376 MHz, acetone-d_6): −59.2 (t, J=0.7 Hz).

4.3.14. α,α,α-Trifluoro-2,4,6-trinitrotoluene (6c). Yield 46 mg, 33%, colorless crystals, mp 88–89 °C (CH_2Cl_2) (lit.[17] 89 °C). EIMS *m/z* (%): 282 (8), 281 (100), 159 (10), 143 (68), 131 (22). HR EIMS calcd for $C_7H_2O_6N_3F_3$ M=280.9896. Found: 280.9888. ^1H NMR (200 MHz, acetone-d_6): 8.80 (s). ^{19}F NMR (376 MHz, acetone-d_6): −57.5.

4.3.15. 2-Chloro-3-hydroxy-4-trifluoromethylpyridine (7a). Yield 28 mg, 28%, yellow oil. HR EIMS calcd for $C_6H_3NOF_3^{35}Cl$ M=196.9855. Found: 196.9848. ^1H NMR (400 MHz, acetone-d_6): 8.76 (d, 1H, J=5.0 Hz), 7.77 (d, 1H, J=5.0 Hz), 7.40 (s broad, 1H). ^{19}F NMR (376 MHz, acetone-d_6): −65.09.

4.3.16. 2-Chloro-3-hydroxy-6-trifluoromethylpyridine (7b). Yield 28 mg, 28%, yellow oil. HR EIMS calcd for $C_6H_3NOF_3^{35}Cl$ M=196.9855. Found: 196.9843. ^1H NMR (400 MHz, acetone-d_6): 8.59 (s broad, 1H), 8.07 (d, 1H, J=4.8 Hz), 7.33 (d, 1H, J=4.8 Hz). ^{19}F NMR (376 MHz, acetone-d_6): −64.92.

4.3.17. 2,2′-Dichloro-3,3′-dinitro-4,4′-bipyridyl (7c). Orange crystals, mp 189–190 °C (EtOH). EIMS *m/z* (%): 316 (7), 314 (11), 270 (6), 268 (9), 242 (18), 240 (13), 177 (8), 175 (7), 153 (32), 151 (100). HR EIMS calcd for $C_{10}H_4O_4N_4^{37}Cl^{35}Cl$ M=315.9580. Found: 315.9578. ^1H NMR (400 MHz, $CDCl_3$): 8.67 (d, 2H, J=4.9 Hz), 7.32 (d, 2H, J=4.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): 151.0, 143.9, 143.4, 136.1, 122.5. Anal. calcd for $C_{10}H_4O_4N_4O_3Cl_2$: C, 38.12; H, 1.28; N, 17.78. Found: C, 38.08; H, 1.31; N, 17.47.

4.4. Oxidation of σ^H adducts of CF_3^- to *m*-dinitrobenzene with Br_2

To a stirred solution of **1** (0.6 mmol) and nitroarene (0.5 mmol) in THF (5 mL) at −70 °C under argon, TASF (153 mg, 0.5 mmol) dissolved in pyridine (1 mL) was added dropwise and the mixture was stirred for 5 min. Bromine (0.6 mmol, 97 mg) dissolved in THF (1 mL) was added to the mixture and after 5 min triethylamine (0.5 mL) was added. The cooling bath was removed. The solids were filtered off and washed with dichloromethane (20 mL). The solvents were evaporated (25 °C, 15 Torr) and the product was purified by column chromatography using hexane as an eluent. In the cases of use **2** and **7** we could not find any defined products, on GCMS we observed traces (<10%) of products of ONSH process. In case of using **4** we isolated starting nitroarene 25% and **4d** (46%).

4.4.1. 4-Bromo-2,6-dinitro-α,α,α-trifluorotoluene 4d. Yield 73 mg, 46%, yellow crystals, mp 108–109 °C (EtOH). EIMS *m/z* (%): 316 (71), 314 (72), 297 (4), 295 (4), 224 (7), 222 (7), 212 (9), 210 (9), 174 (10), 172 (8), 143 (100). HR EIMS calcd for $C_7H_2O_4N_2F_3^{79}Br$ M=313.9150. Found: 313.9156. ^1H NMR ($CDCl_3$, 400 MHz): 8.09 (d, J=0.6 Hz). ^{19}F NMR ($CDCl_3$, 376 MHz): −57.34. ^{13}C NMR ($CDCl_3$, 100 MHz): 149.8, 130.3, 129.6, 125.4 (q, J=305 Hz), 121.4, 118.7, 116.3 (q, J=36 Hz).

Acknowledgements

We are indebted to Dr. A. Marhold (Bayer AG) Leverkusen for the generous gift of the Ruppert reagent.

References and notes

1. Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*. Wiley: New York, 1991.
2. Hiyama, T. *Organofluorine Compounds: Chemistry and Applications*; Springer: Berlin, 2000.
3. Hudlicky, M. *Chemistry of Organic Fluorine Compounds I*; 2nd ed. Ellis Horwood: New York, 1992; pp 96–106 and 154–158. Hudlicky, M. In *Chemistry of Organic Fluorine Compounds II*; Hudlicky, M., Pavlath, A. E., Eds.; American Chemical Society: Washington, 1995; pp 178–184 and 243–249. *Houben-Weyl: Methods of Organic Chemistry*; Baasner, B., Hagemann, H., Tatlow, J. C., Eds.; Thieme: Stuttgart, 1999; Vol. E10a. Miethchen, R. pp 133–141, 348–370, Yagupolskii, L. M. pp 509–525 and Dmowski, W. pp 321–405.
4. Cottet, F.; Schlosser, M. *Eur. Org. J. Chem.* **2002**, 327. Duan, J.-X.; Su, D.-B.; Wu, J.-P.; Chem, Q.-Y. *J. Fluorine Chem.* **1994**, *66*, 167.

5. Adams, D. J.; Clark, J. H.; Hansen, L. B.; Sanders, V. C.; Stewart, J. T. *J. Chem. Soc. Perkin Trans. 1* **1998**, 3081.
6. Stahly, G. P. *J. Fluorine Chem.* **1989**, *45*, 431.
7. Terrier, F. *Chem. Rev.* **1982**, *82*, 78. Terrier, F. *Nucleophilic Aromatic Displacement*; Chemie: Weinheim, 1991. Chupakhin, O. N.; Charushin, V. N.; van der Plas, H. C. *Nucleophilic Aromatic Substitution of Hydrogen*; Academic Press: San Diego, 1994. Mąkosza, M. *Russ. Chem. Bull.* **1996**, *45*, 491.
8. Bartoli, G. *Acc. Chem. Res.* **1984**, *17*, 109. Mąkosza, M.; Surowiec, M. *J. Organometal. Chem.* **2001**, *624*, 167.
9. Mąkosza, M.; Winiarski, J. *Acc. Chem. Res.* **1987**, *20*, 289. Mąkosza, M. *Pol. J. Chem.* **1992**, *66*, 3. Mąkosza, M.; Wojciechowski, K. *Liebigs Ann. Recuil* **1997**, 1805. Mąkosza, M.; Kwast, A. *J. Phys. Org. Chem.* **1998**, *11*, 341.
10. Mąkosza, M.; Staliński, K. *Pol. J. Chem.* **1999**, *73*, 151. Mąkosza, M.; Staliński, K. *Chem. Eur. J.* **1997**, *3*, 2025. Mąkosza, M.; Staliński, K. *Synthesis* **1998**, 1631. Mąkosza, M.; Staliński, K. *Tetrahedron* **1998**, *54*, 8797.
11. Adam, W.; Mąkosza, M.; Staliński, K.; Zhao, C.-G. *J. Org. Chem.* **1998**, *63*, 4390. Adam, W.; Mąkosza, M.; Zhao, C.-G.; Surowiec, M. *J. Org. Chem.* **2000**, *65*, 1099.
12. Mąkosza, M.; Owczarczyk, Z. *J. Org. Chem.* **1989**, *54*, 5094.
13. Noyori, R.; Yokoyama, K.; Sakata, J.; Kuwajima, I.; Nakamura, E.; Shimizu, M. *J. Am. Chem. Soc.* **1977**, *99*, 1265. Nakamura, E.; Shimizu, M.; Kuwajima, I.; Sakata, J.; Yokoyama, K.; Noyori, R. *J. Org. Chem.* **1983**, *48*, 932.
14. Hine, J. *Physical Organic Chemistry*; McGraw-Hill: New York, 1962; p. 486.
15. Epsztajn, J.; Bieniek, A.; Brzeziński, J. Z.; Jóźwiak, A. *Tetrahedron Lett.* **1983**, 4735. Mongin, F.; Trécomt, F.; Queguiner, G. *Terahedron Lett.* **1999**, 5483.
16. Adam, W.; Białas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377.
17. Gray, D. N.; Schmidt, J. J. E.; Smith, C. D. *J. Chem. Soc.* **1960**, 2243.