

Deprotection of Arenediazonium Tetrafluoroborate Ethers with BBr_3

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Table of Contents

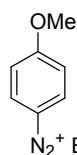
Experimental Section	S2
NMR Spectra	S9

General Information

All starting materials were obtained from commercial suppliers and used as received. Solvents were HPLC grade and were used as received. ^1H and ^{13}C spectra were recorded on a 400 MHz NMR apparatus for ^1H NMR and 100 MHz for ^{13}C NMR. Proton chemical shifts are reported in ppm downfield from TMS. Coupling constants are given in Hz. IR were recorded neat or KBr pellets using FT-IR spectrophotometer.

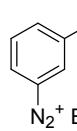
General procedure for the synthesis of arenediazonium salts 1a-8a and 10a-11a

Boron trifluoride etherate (1.5 mmol, 1.5 equiv) was added to a solution of amine (1 mmol, 1 equiv) in 3 mL of THF at an ice bath temperature. After 5 min stirring, *tert*-butyl nitrite (1.2 mmol, 1.2 equiv) was added drop wise at 0 °C. After another 15 min stirring, the precipitated was filtered and washed with diethyl ether.



4-methoxybenzenediazonium tetrafluoroborate (1a):

Prepared according to the general procedure from 4-methoxyaniline. This compound has been previously prepared and characterized.¹ White needles. Mp= 146°C (black when it is melt). IR (film): 2251, 1583, 1032, 843 cm⁻¹. ^1H NMR ((CD₃)₂CO): δ = 8.76 (d, J = 9.4 Hz, 2 H), 7.54 (d, J = 9.4 Hz, 2 H), 4.17 (s, 3 H). ^1H NMR (DMSO): δ = 8.61(d, 1H, J = 9.4Hz), 7.48(d, J = 9.4Hz), 4.01(s, 3H). ^{13}C NMR ((CD₃)₂CO): δ = 170.8, 137.1 (2 x C), 118.5 (2 x C), 103.8, 58.1. ^{19}F (DMSO): δ = -148.2. HRMS (FD+) calculated for C₇H₇N₂O [M+H]⁺ 135.0558, found 135.0557.

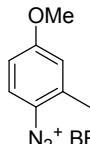


3-methoxybenzenediazonium tetrafluoroborate (2a):

Prepared according to the general procedure from 4-methoxyaniline. This compound has been previously prepared² and characterized. Brick red powder. mp = 80°C. IR (film): 2302, 1595, 1487, 1216, 1024 cm⁻¹. ^1H NMR (DMSO): δ = 8.30 (m, 2H), 7.87 (m, 2H), 3.91 (s, 3H). ^{13}C NMR (DMSO): δ = 159.5, 132.3, 128.0, 125.4, 116.4, 115.7, 56.6. ^{19}F (DMSO): δ = -148.3. HRMS (FD+) calculated for C₇H₇N₂O [M+H]⁺ 135.0550, found 135.0558.

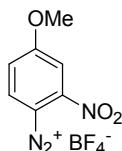
¹ Heinrich, M., R. ; Blank, O. ; Ullrich, D. ; Kirschstein, M. *J. Org. Chem.* **2007**, 72, 9609.

² Preparation of 8-(Arylsulfanyl)adenines with Diazonium Salts under Mild, Aerobic Conditions Marco A. Biamonte, Jiandong Shi, David Hurst, Kevin Hong, Marcus F. Boehm, and Srinivas R. Kasibhatla *J. Org. Chem.*; 2005; 70(2) pp 717 - 720



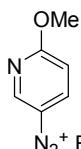
4-methoxy-2-methylbenzenediazonium tetrafluoroborate (3a):

Prepared according to the general procedure from 4-methoxy-3-methylaniline. This compound has been previously prepared and characterized.³ White powder, mp 147°C. IR (film): 2247, 1588, 1034, 832 cm⁻¹. ¹H NMR (CD₃OD): δ = 8.48 (d, J = 9.4 Hz, 1 H), 7.35 (dd, J = 2.3, 0.5 Hz, 1 H), 7.27 (dd, J = 9.4 Hz, 2.3 Hz, 1 H), 4.08 (s, 3 H), 2.73 (d, J = 0.5 Hz, 3 H). ¹H NMR (DMSO): δ = 8.58 (d, 1H, J = 9.2Hz), 7.40 (m, 1H), 7.33 (dd, 1H, J = 9.2 and 1.5Hz), 4.03 (s, 3H), 2.68 (s, 3H). ¹³C NMR (CD₃OD): δ = 171.5, 149.8, 136.8, 119.3, 117.4, 103.9, 58.1, 18.7. ¹³C NMR (DMSO): δ = 168.6, 147.7, 135.7, 117.7, 115.8, 103.5, 57.4, 18.2. ¹⁹F (DMSO): δ = -148.3. HRMS (FD+) calculated for C₈H₉N₂O [M+H]⁺ 149.0715, found 149.0706.



4-methoxy-2-nitrobenzenediazonium tetrafluoroborate (4a):

Prepared according to the general procedure from 4-methoxy-2-nitroaniline, however there is no precipitated, and the solution is evaporated under vacuum. This compound has been previously prepared.⁴ Pale yellow needles, mp = 111°C. IR (film): 2243, 1508, 1030, 990, 851 cm⁻¹. ¹H NMR ((CD₃)₂CO): δ = 8.55 (dd, J = 9.1, 2.5 Hz, 1 H), 8.22 (d, J = 2.5 Hz, 1 H), 7.57 (d, J = 9.1 Hz, 1 H), 4.17 (s, 3 H), 3.99 (s, 3 H). ¹H NMR (DMSO): δ = 8.99 (d, 1H, J = 9.2Hz), 8.28 (d, 1H, J = 2.5Hz), 7.88 (dd, 1H, J = 9.2 and 2.5Hz), 4.19 (s, 3H). ¹³C NMR ((CD₃)₂CO): δ = 161.7, 151.2, 131.9, 114.4, 113.4, 103.2, 57.8, 57.3. ¹⁹F (DMSO): δ = -148.2. HRMS (FD+) calculated for C₇H₆N₃O₃ [M+H]⁺ 180.0388, found 180.0409.



6-methoxypyridin-3-diazonium tetrafluoroborate (5a):

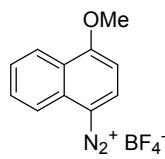
Prepared according to the general procedure from 4-methoxy-3-methylaniline. This compound has been previously prepared and characterized.⁵ White cristals, mp = 109°C. IR (film): 2283, 1578, 1031, 883, 844 cm⁻¹. ¹H NMR (CD₃OD): δ = 9.47 (d, J = 2.7 Hz, 1 H), 8.66 (dd, J = 9.3, 2.7 Hz, 1 H), 7.27 (d, J = 9.3 Hz, 1 H), 4.21 (s, 3 H). ¹H NMR (DMSO): δ = 9.56 (d, 1H, J = 2.6Hz), 8.75 (dd, 1H, J = 9.1 and 2.6Hz), 7.39 (d, 1H, J =

³ a) Schumann, P. ; Collot, V. ; Hommet, Y. ; Gsell, W. ; Dauphin, F. ; Sopkova, J. ; MacKenzie, E., T. ; Duval, D. ; Boulouard, M. ; Rault, S. *Bioorganic & Medicinal Chemistry Letters* **2001**, 11, 1153. b) Crestey, Francois; *Synthesis* **2006**, 20, 3506.

⁴ Yanxi, S. *Ranliao Gongye* **2002**, 39, 11.

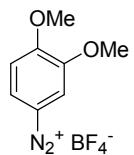
⁵ Ueda, Y. ; Connolly, T., P.; Kadow, J., F.; Meanwell, N., A.; Wang, T.; Chen, C.-P., H.; Yeung, K.-S.; Zhang, Z.; Leahy, D., K.; Pack, S., K.; Soundararajan, N.; Sirard, P.; Levesque, K.; Thoraval, D. U.S. Pat. 2005209246, 2005.

9.1Hz), 4.13 (s, 3H). ^{13}C NMR (CD₃OD): δ = 171.2, 158.4, 141.7, 115.2, 105.0, 57.1. ^{13}C NMR (DMSO): δ = 168.8, 157.0, 141.5, 113.4, 104.7, 56.3. ^{19}F (DMSO): δ = -148.2. HRMS (FD+) calculated for C₅H₆N₃O [M+H]⁺ 136.0511, found 136.0520.



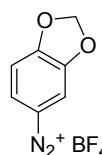
4-methoxynaphthalene-1-diazonium tetrafluoroborate (6a):

Prepared according to the general procedure from 4-methoxy-naphthalen-1-ylamine. Yellow powder, mp = 170°C. IR (film): 2207, 1584, 1382, 1047, 832 cm⁻¹. ^1H NMR (DMSO): δ = 9.20 (d, J = 9.0 Hz, 1 H), 8.47 (d, J = 8.3 Hz, 1 H), 8.36 (d, J = 8.3 Hz, 1 H), 8.10 (ddd, J = 8.3, 7.1, 1.3 Hz, 1 H), 7.91 (ddd, J = 8.3, 7.1, 1.3 Hz, 1 H), 7.59 (dd, J = 9.0, 0.3 Hz, 1 H), 4.31 (d, J = 0.3 Hz, 1 H). ^{13}C NMR (DMSO): δ = 166.9, 141.3, 132.5, 129.2, 128.7, 124.1, 122.5, 107.8, 98.1, 58.5. ^{19}F (DMSO): δ = -148.2. HRMS (FD+) calculated for C₁₁H₉N₂O.H₂O [M+H]⁺ 203.0639, found 203.0820.



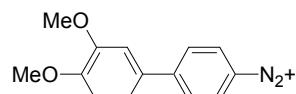
3,4-dimethoxybenzenediazonium tetrafluoroborate (7a) :

Prepared according to the general procedure from 3,4-dimethoxyaniline. This compound has been previously prepared and characterized.⁶ Brown powder, mp = 123°C. IR (film): 2243, 1508, 1030, 990, 851 cm⁻¹. ^1H NMR ((CD₃)₂CO): δ = 8.55 (dd, J = 9.1, 2.5 Hz, 1 H), 8.22 (d, J = 2.5 Hz, 1 H), 7.57 (d, J = 9.1, 1 H), 4.17 (s, 3 H), 3.99 (s, 3 H). ^{13}C NMR ((CD₃)₂CO): δ = 161.7, 151.2, 131.9, 114.4, 113.4, 103.2, 57.8, 57.3. ^{19}F (DMSO): δ = -148.2. HRMS (FD+) calculated for C₈H₉N₂O₂ [M+H]⁺ 165.0653, found 165.0664.



Benzo[d][1,3]dioxole-5-diazonium tetrafluoroborate (8a) :

Prepared according to the general procedure from benzo[1,3]dioxol-5-ylamine. This compound has been previously prepared.⁷ Brown powder, mp = 121°C. IR (film): 2248, 1501, 1024, 912, 857 cm⁻¹. ^1H NMR (CD₃OD): δ = 8.36 (dd, J = 8.8, 2.3 Hz, 1 H), 7.89 (d, J = 2.3 Hz, 1 H), 7.34 (d, J = 8.8 Hz, 1 H), 6.41 (s, 2 H). ^{13}C NMR (100 MHz): δ = 161.5, 151.0, 135.4, 112.0 (2 x C), 110.3, 107.3. ^{19}F (DMSO): δ = -148.2. HRMS (FD+) calculated for C₇H₅N₂O₂ [M+H]⁺ 149.0351, found 149.0341.



3',4'-dimethoxybiphenyl-4-diazonium

tetrafluoroborate

(10a) :

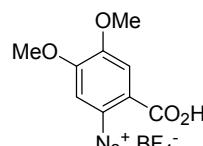
⁶ Baceta-Lizana, J., S., L.; Iyer, R.; Jackson, A., H.; Shannon, P., V., R. J. *Chem. Soc., Perkin Trans. 2* **1978**, 8, 733.

⁷ Beadle, J., R.; El'tsov, A.V. *Zh. Obshch. Khim.* **1964**, 34, 2739.

Prepared according to the general procedure from 3',4'-dimethoxybiphenyl-4-ylamine.⁸ This compound has been previously prepared and characterized.⁹ Red powder, mp = 101-102 °C. IR (film): 2243, 1573, 1037, 843 cm⁻¹. ¹H NMR ((CD₃)₂CO): δ = 8.81 (d, *J* = 9.1 Hz, 2 H), 8.37 (d, *J* = 9.1 Hz, 2 H), 7.57 (m, 2 H), 7.18 (d, *J* = 8.1, 1 H). ¹³C NMR ((CD₃)₂CO): δ = 154.0, 153.3, 151.1, 134.4 (2 x C), 129.8, 129.5 (2 x C), 122.6, 113.1, 112.0, 111.5, 56.4, 56.3. HRMS (FD+) calculated for C₁₄H₁₃N₂O₂ [M+H]⁺ 241.0977, found 241.0972.

General procedure to synthesize 9a

Amine (1 mmol, 1 equiv) was added to HBF₄ 48% (5 mmol, 5 equiv) and water (3 mL). After heating to dissolve amine, the solution was cooled to 0° C and *tert*-butyl nitrite (1.2 mmol, 1.2 equiv) was added drop wise. After 15min stirring, the precipitated was filtered and washed with diethyl ether.



2-carboxy-4,5-dimethoxybenzenediazonium tetrafluoroborate (9a):

Prepared according to the general procedure from biphenyl. This compound has been previously prepared.¹⁰ Yellow powder, mp = 107°C. IR (film): 3558, 2250, 1707, 1525, 1030, 883, 751 cm⁻¹. ¹H NMR (CD₃OD): δ = 8.28 (s, 1 H), 7.89 (s, 1 H), 4.16 (s, 3 H), 4.04 (s, 3 H). ¹³C NMR (50 MHz): δ = 163.4, 160.9, 154.2, 131.3, 116.1, 115.7, 104.5, 58.5, 58.0. ¹⁹F (DMSO): δ = -148.2. HRMS (FD+) calculated for C₉H₉N₂O₄ [M+H]⁺ 209.0562, found 209.0562.

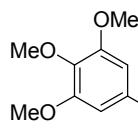
General procedure to synthesize 11a

HBF₄ 48% (5 mmol, 5 equiv) was added to a solution of amine **12** (1 mmol, 1 equiv) in 3 mL of THF at an ice bath temperature. Then *tert*-butyl nitrite (1.2 mmol, 1.2 equiv) was added drop wise at 0 °C. After 15 min stirring, the precipitated was filtered and washed with diethyl ether.

⁸ Usso, H.; Pietsch, H. *Chem. Ber.* **1967**, *100*, 2854.

⁹ Klandermen, B. H.; Criswell, T. R. *J. Org. Chem.* **1969**, *34*, 3426-3430.

¹⁰ Klandermen, B. H.; Criswell, T. R. *J. Org. Chem.* **1969**, *34*, 3426-3430.

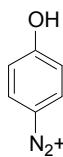


3,4,5-trimethoxybenzenediazonium tetrafluoroborate (11a):

This compound has been previously prepared and characterized.¹¹ Yellow powder, mp = 143°C. IR (film): 2270, 1589, 847 cm⁻¹. ¹H NMR (DMSO): δ = 8.19 (s, 2 H), 4.03 (s, 3 H), 3.90 (s, 6 H). ¹³C NMR (DMSO): δ = 152.5 (2 x C), 149.2, 110.9 (2 x C), 106.3, 61.6, 57.1 (2 x C). ¹⁹F (DMSO): δ = -148.2. HRMS (FD+) calculated for C₉H₁₁N₂O₃ [M+H]⁺ 195.0791, found 195.0770.

General method for ether cleavage of 1a:

The methoxyarene diazonium salt (1 mmol, 1 equiv) was dissolved in toluene (3 mL) under nitrogen atmosphere. Then 1 M boron tribromide in CH₂Cl₂ (3 mmol, 3 equiv) was slowly added at room temperature and the solution (or suspension) was stirred for 3 days at 70°C. After cooling, MeOH (1 mL) was added. The mixture was stirred for an other 5 min and concentrated under reduced pressure to give a dark residue, which was recrystallized from methanol/ether.



4-hydroxybenzenediazonium tetrafluoroborate (1b):

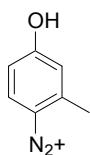
Prepared according to the general procedure from 1a. This compound has been previously prepared.¹² IR (film): 3024, 2224, 1559, 1085, 840 cm⁻¹. ¹H NMR (CD₃OD): δ = 8.48 (d, J = 9.1 Hz, 2 H), 7.22 (d, J = 9.1 Hz, 2 H), 4.10 (s, 3 H). ¹³C NMR (CD₃OD): δ = 171.4, 137.6 (2 x C), 120.1 (2 x C), 100.7. HRMS (FD+) calculated for C₆H₅N₂O [M+H]⁺ 120.0324, found 120.0331

General method for ether cleavage of 3a-11a:

The methoxyarene diazonium salt (1 mmol, 1 equiv), under nitrogen atmosphere, was dissolved in 3 mL of toluene solely if the mixture is heated. Then 1 M boron tribromide in CH₂Cl₂ (3 mmol, 3 equiv) was slowly added at room temperature to the solution (or solid) and the mixture was stirred for time and temperature indicated in table 1. After cooling, MeOH (1mL) was added. The mixture was stirred for an other 5 min and concentrated under reduced pressure to give a dark residue, which was recrystallized from methanol/ether.

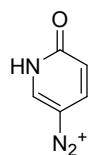
¹¹ Fukuda, Y.; Furuta, H.; Kusama, Y.; Ebisu, H.; Oomori, Y.; Terashima, S. *J. Med. Chem.* **1999**, *42*, 1448.

¹² Besse, J. ; Schwartz, W. ; Zollinger, H. *Helv. Chim. Acta*. **1981**, *64*, 504.



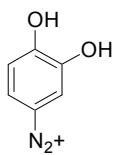
4-hydroxy-3-methylbenzenediazonium tetrafluoroborate (3b):

Prepared according to the general procedure from **3a**. This compound has been previously prepared.¹³ Violet powder, mp = 134-135°C. IR (film): 3047, 2245, 850 cm⁻¹. ¹H NMR (CD₃OD): δ = 8.50 (d, J = 9.1 Hz, 1 H), 7.12 (dd, J = 2.3 and 0.5 Hz, 1 H), 7.08 (dd, J = 9.1 and 2.3 Hz, 1 H), 2.71 (d, J = 0.5 Hz, 3 H). ¹³C NMR (CD₃OD): δ = 171.0, 149.8, 137.3, 120.7, 118.4, 101.1, 19.1. HRMS (FD+) calculated for C₇H₇N₂O [M+H]⁺ 134.0480, found. 134.0472.



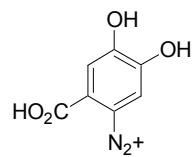
6-oxo-1,6-dihydropyridin-3-diazonium tetrafluoroborate (5b):

Prepared according to the general procedure from **5a**. This compound has been previously prepared.¹⁴ Dark powder, mp = 141°C. IR (film): 2788, 2217, 1632, 1054, 836 cm⁻¹. ¹H NMR (CD₃OD): δ = 9.41 (d, J = 2.9 Hz, 1 H), 8.07 (dd, J = 9.9 and 2.9 Hz, 1 H), 6.67 (d, J = 9.9 Hz, 1 H). ¹³C NMR (100 MHz): δ = 161.7, 156.3, 135.7, 123.0, 92.1. HRMS (FD+) calculated for C₅H₄N₃O [M+H]⁺ 121.0276, found 121.0271.



3,4-dihydroxybenzenediazonium salt (7b):

Prepared according to the general procedure from **7a**. This compound has been previously prepared. Brown powder, mp = 130°C. IR (film): 3088, 2220, 1588, 1071, 853 cm⁻¹. ¹H NMR (CD₃OD): δ = 8.21 (dd, J = 8.9 and 2.5 Hz, 1 H), 7.93 (d, J = 2.5 Hz, 1 H), 7.19 (d, J = 8.9 Hz, 1 H). ¹³C NMR (100 MHz): δ = 161.9, 148.9, 130.7, 118.9, 117.3, 100.1. HRMS (FD+) calculated for C₆H₅N₂O [M+H]⁺ 136.0273, found 136.0267.



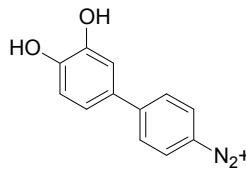
2-carboxy-4,5-dihydroxybenzene diazonium salt (9b):

Prepared according to the general procedure from **9a**. This compound has been previously prepared.¹⁵ IR (film): 2211, 1678, 1590, 1538, 1258, 1138, 1101 cm⁻¹. ¹H NMR (CD₃OD): δ = 7.69 (s, 1H), 8.02 (s, 1H). ¹³C NMR (DMSO): δ = 162.6, 158.6, 149.6, 127.8, 119.1, 119.0, 99.7. HRMS (FD+) calculated for C₇H₇N₂O [M+H]⁺ 181.0249, found 181.0247 (M+1 requires).

¹³ Abu-Eittah, R.; Abdou, M.; Hamed, M.; El Nady, Y. *Bulletin of the Chemical Society of Japan* **1997**, 70, 2631.

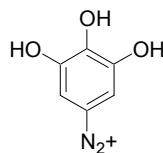
¹⁴ Thorstad, O.; Undheim, K. *Chemica Scripta* **1974**, 5, 222.

¹⁵ Yoneda, N.; Fukuhara, T. *Tetrahedron* **1996**, 52, 5223.



3',4'-hydroxybiphenyl-4-diazonium salt (10b):

Prepared according to the general procedure from **10a**. Yellow powder, mp = 134°C. IR (film): 3059, 2248, 1573, 804 cm⁻¹. ¹H NMR (DMSO): δ = 8.57 (d, J = 9.1 Hz, 2 H), 8.14 (d, J = 9.1 Hz, 2 H), 7.31 (m, 2H), 6.94 (d, J = 8.6, 1 H). ¹³C NMR (DMSO): δ = 151.3, 148.5, 145.7, 132.9 (2 x C), 127.6 (2 x C), 126.7, 119.9, 116.1, 114.4, 109.8. HRMS (FD+) calculated for C₁₂H₉N₂O₂ [M+H-N₂]⁺ 186.0681, found 186.0689.



3,4,5-trimethoxybenzenediazonium salt (11b):

Prepared according to the general procedure from **11a**. This compound could not be purified in the conditions used. IR (film): 3006, 2203, 1605, 842 cm⁻¹. ¹H NMR (CD₃OD): δ = 7.57 (s, 2 H). ¹³C NMR (CD₃OD): 151.4, 148.3 (2 x C), 112.9 (2 x C), 101.3. HRMS (FD+) calculated for C₇H₇N₂O [M+H]⁺ 153.0300, found 153.0308.

NMR Spectra

