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Deprotection of Arenediazonium Tetrafluoroborate Ethers with BBr_3

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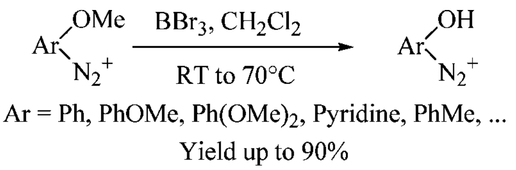
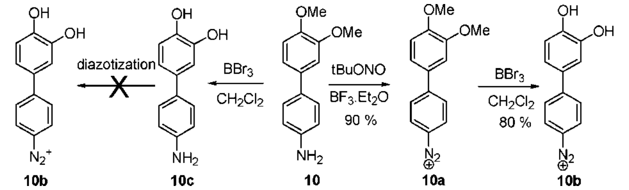


Ether cleavage was carried out on arene bearing a diazonium salt. The deprotection takes place with boron tribromide under very mild conditions in good yields without affecting the diazonium group.

Diazonium salts have always aroused much interest as intermediates in the preparation of aromatic compounds.[1] They are easily synthesized by using either organic or inorganic nitrite in the presence of an inorganic acid. Stable diazonium salts could be isolated, but in most cases, they are directly engaged in the following step due to their moderate half-life[2] depending on the arene substitution pattern and on the counteranion. The major applications of diazonium salts are their use as either an electrophile in azo-coupling to form azo dyes[3] or as a leaving group to introduce different functional groups. In the later application, a Csp^2-Csp^2 bond can be generated by a palladium cross-coupling reaction involving the arenediazonium salt as the electrophilic partner.[4] Recently, these salts also have been extensively used to modify carbon and metallic surfaces by electrochemical reduction.[5] The major advantage of this approach is the possibility to introduce numerous functional groups on different surfaces. For the use in our studies on electrode derivatization via diazonium salts electrochemistry, the aryldiazonium salt **10b** bearing a catechol moiety was prepared (Scheme 1). After ether cleavage of diphenyl **10** under classical conditions (BBr_3/CH_2Cl_2), diazotization of **10c** failed leading to a complex mixture. So, in a second approach, the diazotization was carried out on the protected catechol **10**. Surprisingly, ether group deprotection succeeded on diazonium salt **10a**.

SCHEME 1



To the best of our knowledge, the only attempts mentioned in the literature showing reactions tolerating diazonium groups were aromatic nucleophilic substitutions described by Hantzch.[6] He concluded that 4,6-dibromobenzenediazonium chloride rearranged in alcoholic solvent at room temperature to bromochlorobenzenediazonium chlorides due to the strong activating effect of the diazonium ion group.[7] Except for this observation, there are no other reports on diazonium-abiding chemistry.

The versatility and the efficiency of our original procedure were established by the use of a wide range of arene diazonium salts bearing either one, two, or three methoxy groups (Table 1). Most of the diazonium salts with BF_4^- as couteranions were known and prepared by standard methods from an amine and *tert*-butyl nitrite with BF_3 etherate[8] or HBF_4[9] in THF or water. Then, ether deprotection[10] was carried out by adding boron tribromide in dichloromethane to arene diazonium salts in dichloromethane solution under inert atmosphere. Deprotection mechanisms[11] are well-known; 1 equiv of BBr_3 could theoretically cleave three ether groups. However, an excess of boron tribromide was used in each case. Infrared spectroscopy showed the expected band around 2200 cm^{-1} corresponding to the N_2^+ vibration when the arene diazonium salt was synthesized. After ether cleavage, this band was still present, demonstrating that the diazonium salt was not affected by the subsequent deprotection step. For dimethoxy and trimethoxyarenes (entries 7 and 9−11, Table 1), the reaction proceeded rapidly and could be done at room temperature while arenes substituted by one methoxy para to the diazonium group seemed more difficult to cleave and needed a high temperature and longer reaction time. In this case, the deprotection can be rationalized with the diazonium and methoxy resonance effects with the phenyl ring. The oxygen lone pair electrons are delocalized to the diazonium ion group, which is thereby stabilized (Figure 1). Oxygen electrons are less available and the reaction is slower. For the *m*-methoxybenzene diazonium salt **2a** (Figure 1), the diazonium group is not resonance stabilized, so the compound is not stable and deprotection attempts lead to degradation of the starting compound.

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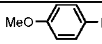
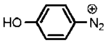
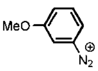
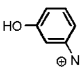
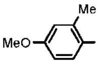
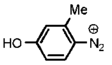
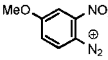
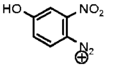
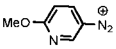
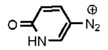
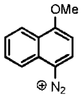
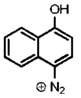
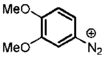
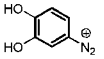
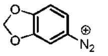
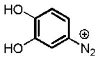
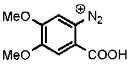
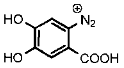
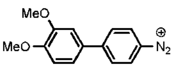
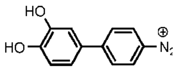
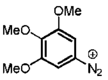
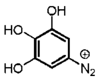
TABLE 1. Synthesis of Diazonium Salts and Ether Cleavage with BBr_3

Entry	Diazonium Salts a		Yield (%)[a]	$\bar{\nu}_{N_2}$ (cm^{-1})	Diazonium Salts b[d]		Conditions	Yield (%)[a]	$\bar{\nu}_{N_2}$ (cm^{-1})
1	**1a**		92	2251	**1b**		3d at 70°C	75	2224
2	**2a**		70	2302	**2b**			-[b]	
3	**3a**		90	2247	**3b**		1d at 40°C	85	2245
4	**4a**		75	2243	**4b**		4h at 70°C	-[b]	
5	**5a**		80	2283	**5b**		16h at 40°C	80	2217
6	**6a**		85	2207	**6b**		7d at 80°C	-[b]	
7	**7a**		80	2243	**7b**		1h at 40°C	87	2220
8	**8a**		85	2248	**8b**		6h at 40°C	90	2220
9	**9a**		95	2250	**9b**		21h at 45°C	90[c]	2211
10	**10a**		90	2243	**10b**		30min at RT	80	2248
11	**11a**		90	2270	**11b**		30min at RT	90[c]	2203

[a] Yield of isolated compounds. [b] Compound not obtained (degradation). [c] Crude yield. [d] The counterion BF_4^- has been exchanged with Br^-.

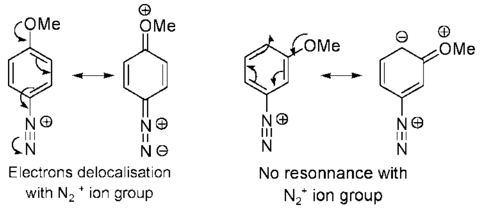
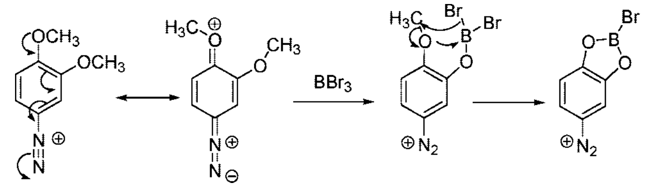


FIGURE 1. Resonance structure of *p*- and *m*-methoxybenzenediazonium salts.

The participation degree of the diazonium group with the ring resonance could be analyzed by IR spectroscopy since the N−N triple bond order is frequency dependent.[12,13] A lower IR frequency will indicate a lower N_2 triple bond[14] character and a stronger resonance stabilization. All the vibrational band frequencies of the diazonium group of **1a**,**b** to **11a**,**b** have been collected in Table 1.

In the case of **5a**, the nitrogen of the pyridine is electronegative, which raises the diazonium IR band frequency ($\bar{v} = 2283$ cm^{-1}). After deprotection, analysis confirmed the lactam formation and in IR spectroscopy, a spectacular frequency shift was observed due to the resonance between N_2^+ and lactam. We also point out that the diazonium group of the naphthalene derivative **6a** showed a low-frequency IR. This shift in the N_2^+ frequency indicates that the oxygen lone pairs are unavailable for reaction with boron tribromide. The starting material was completely recovered after one day at 40 °C while in the literature, it is specified that methoxynaphthalene led to naphthol in 35 min at room temperature with 1 equiv of BBr_3.[15] An increase in temperature to 70 °C did not lead to the naphthol derivative and proton NMR showed the appearance of unidentified products. Another limitation of the reaction is that the presence of electron-withdrawing groups such as nitro or acid functions (entries 4 and 9) makes the diazonium salt unstable and the expected compounds were not obtained or had low yields.

SCHEME 2



Boron tribromide seems to react more easily with dimethoxy- or trimethoxyarenediazonium salts (entries 7 and 11). We can suppose that the first reaction with BBr_3 takes place with the *m*-methoxy not involved in resonance with the diazonium group (Scheme 2). Then the close proximity of the boron moiety and the *p*-methoxy afforded the benzobromodioxoborole, which can be hydrolyzed.

Application of this deprotection method to methylenedioxy (entry 8) worked similarly to methyl ether cleavage (entry 7)

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but needed a longer reaction time at 40 °C. For nonconjugated methoxy groups (entry 10) deprotection takes place under very mild conditions.

In conclusion, we have shown that arenediazonium tetrafluoroborate ethers can be deprotected efficiently by BBr_3 under mild conditions in good yields without affecting diazonium salts.

Experimental Section

General Procedure: For Ether Cleavage of 3a−11a. The methoxyarene diazonium salt (1 mmol, 1 equiv) in 3 mL of CH_2Cl_2 and 3 mL of toluene was placed in a flask. Then 1 M boron tribromide in CH_2Cl_2 (3 mmol, 3 equiv) was slowly added at room temperature and the solution (or suspension) was stirred for the time and temperature indicated in Table 1. After cooling, MeOH (1 mL) was added. The mixture was stirred for another 5 min and concentrated under reduced pressure to give a dark residue, which was recrystallized from methanol/ether.

3′,4′-Dihydroxybiphenyl-4-diazonium Salt (10b). 10b was 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, $J = 8.6$ Hz, 1 H). ^{13}C NMR (DMSO) δ 151.3, 148.5, 145.7, 132.9 (2 × C), 127.6 (2 × C), 126.7, 119.9, 116.1, 114.4, 109.8.

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Supporting Information Available: General information, characterization data for compounds **1a−11a**, **1b**, **3b**, **5b**, and **7b−11b** along with copies of ^1H and ^{13}C NMR of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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