ORGANIC
LETTERS

2008
Vol. 10, No. 18
3961−3964

Unusually Stable, Versatile, and Pure Arenediazonium Tosylates: Their Preparation, Structures, and Synthetic Applicability

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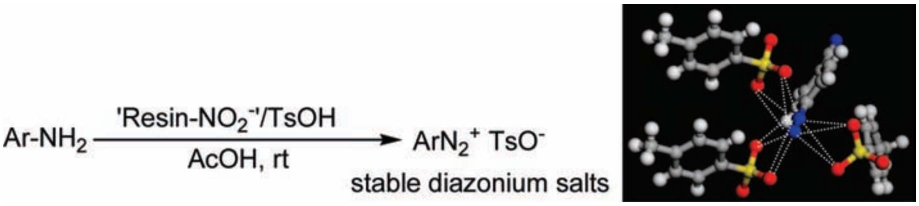
Received June 15, 2008

ABSTRACT



A new, simple, and effective method for the diazotization of a wide range of arylamines has been developed by using a polymer-supported diazotization agent in the presence of *p*-toluenesulfonic acid. Various pure arenediazonium tosylates with unusual stabilities can be easily prepared by this method. As a result, these salts are useful and versatile substrates for subsequent transformations, such as halogenation and Heck-type reactions. The unusual stabilities of arenediazonium tosylates are also preliminarily discussed with their X-ray structures.

Aromatic diazonium salts are important building blocks not only in classical organic synthesis but also in the preparation of modern organic nanocompounds and the grafting of organic molecules onto metallic or nonmetallic surfaces.[1] Despite wide applicability in the synthesis of compounds with a diazonium motif, diazonium salts have a serious drawback—their intrinsic instability and explosive nature. Because of this instability, subsequent reactions with diazonium salts must be carried out in the same medium in which they were produced. This restricts many chemists from approaching potentially important transformations of these salts.[1a] Thus, new diazonium salts that can be readily made, are stable and explosion proof in a solid state for storage, and have high versatility in organic reactions are both desirable and necessary. These properties are peculiar to aryldiazonium tetrafluoroborates,[1b] hexafluorophosphates,[1c−f] and arenediazonium *o*-benezenedisulfonimides.[2]

Other potential diazonium salts that meet these criteria are arenediazonium arylsufonates, $Ar^1N_2^+ Ar^2SO_3^-$. About half

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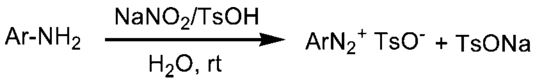
10.1021/ol8013528 CCC: $40.75

a century has passed since some of their characteristics were reported.[3] Nevertheless, little attention has been focused on them since, especially with regard to organic synthesis. They have been prepared by ionic exchange from arenediazonium chlorides $Ar^1N_2^+Cl^-$ and used only for the production of azo-dyestuffs and analytical purposes. Thus, the application of most of these salts is new in organic synthesis, and their properties and preparative synthetic methods have not been reported.

We have recently shown that *p*-toluenesulfonic acid (TsOH) serves as a mild acidic agent in one-step diazotization−iodination of arylamines via intermediate, arenediazonium tosylates ArN_2^+ TsO^-.[4] We found that a few pure arenediazonium tosylates can be prepared by diazotization of arylamines using $NaNO_2$ in a water paste (Scheme 1).[5]

Scheme 1. Diazotization of Arylamines by $NaNO_2$ in the Presence of *p*-Toluenesulfonic Acid



The similar solubility of formed arenediazonium tosylates and TsONa, however, complicates their separation and creates unwanted disposal issues of the diazonium products during the purification process. Thus, the development of a new method to circumvent this problem is necessary.

We report a new, efficient method for the production of pure arenediazonium tosylates and their physical and chemical characteristics. We have developed a new diazotization method of aminoarenes **1−18** in the presence of TsOH by using a polymer-supported diazotization reagent. The preparation of the polymer-supported nitrite ("Resin-NO_2^-") was achieved by ion exchange of porous tetramethylammonium hydroxide resin AV-17-8[6] or Amberlyst A26 with an aqueous solution of $NaNO_2$. A similar polymer-supported agent has been used for the generation of a few arenediazonium chlorides in aqueous HCl.[7]

Diazotization of various aromatic amines **1−18** (Scheme 2) was easily carried out by stirring glacial AcOH or MeOH solution with the appropriate amine, *p*-toluenesulfonic acid, and the reagent "Resin-NO_2^-" for 5−20 min at room temperature until the starting substrate disappeared (TLC). The resin was removed by filtration, and the final product, arenediazonium salts **1a−18a**, were precipitated by adding Et_2O (Table 1).

Scheme 2. Diazotization of Arylamines by Using "Resin-NO_2^-" in the Presence of *p*-Toluenesulfonic Acid

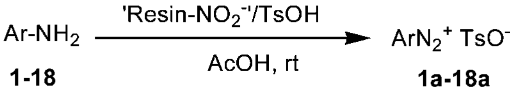


Table 1. Isolated Yields of Arenediazonium Salts **1a−18a** and Their Melting Points

entry	ArN_2^+ TsO^-	yield, %	mp, °C
1	$C_6H_5N_2^+$ (**1a**)	63[a]	224
2	2-$MeC_6H_4N_2^+$ (**2a**)	39[a], 83[b]	182
3	3-$MeC_6H_4N_2^+$ (**3a**)	42[a], 72[b]	158−161
4	4-$MeC_6H_4N_2^+$ (**4a**)	49[a], 86[b]	120
5	3,4-$Me_2C_6H_4N_2^+$ (**5a**)	82[b]	182
6	2-$MeOC_6H_4N_2^+$ (**6a**)	51[a,d]	149−151
7	4-$MeOC_6H_4N_2^+$ (**7a**)	32[a], 79[b,d]	118−120
8	4-$NH_2C_6H_4N_2^+$ (**8a**)	66[c,e]	149−151
9	2-$NO_2C_6H_4N_2^+$ (**9a**)	35[a], 95[b]	155
10	3-$NO_2C_6H_4N_2^+$ (**10a**)	54[a], 85[b]	134[f]
11	4-$NO_2C_6H_4N_2^+$ (**11a**)	39[a], 84[b]	132[g]
12	4-$NCC_6H_4N_2^+$ (**12a**)	32[a], 97[b]	124
13	2-$HO_2CC_6H_4N_2^+$ (**13a**)	82[b]	128
14	4-$HO_2CC_6H_4N_2^+$ (**14a**)	80[b]	114−115
15	4-$IC_6H_4N_2^+$ (**15a**)	60[a]	124−126
16	2,4,6-$Br_3C_6H_2N_2^+$ (**16a**)	58[a]	152
17	2-$C_{10}H_7N_2^+$ (**17a**)	84[a]	134−136
18	$^+N_2C_6H_4CH_2C_6H_4N_2^+$ (**18a**)	25[c,e]	246

[a] Diazotization occurred at rt in water for 20 min. Molar ratio of amine/"Resin-NO_2^-"/TsOH: 1:1:1. [b] Molar ratio of amine/"Resin-NO_2^-"/TsOH: 1:3:3. [c] Molar ratio of amine/"Resin-NO_2^-"/TsOH: 1:6:6. [d] Reaction time 5 min. [e] MeOH as a solvent. [f] Lit.[3c] mp 131−132 °C. [g] Lit.[3c] mp 141−142 °C.

Our new method is safer, cheaper, and more convenient than the previous diazotization with alkyl nitrites, for example, in the synthesis of stable arenediazonium *o*-benezenedisulfonimides.[2] In general, our diazotization method is applicable for various anilines with electron-donating as well as electron-accepting substituents and even for the sterically congested aniline **16**.

Isolated yields of salts **1a−18a** (Table 1) depend upon the ratio of reagents added. The optimal molar ratio of an amine/Resin-NO_2^-/TsOH is 1:3:3 in general, but for the best yield of amino salt **8a**, a ratio of 1:6:6 is necessary. Our attempts to prepare double-diazonium salt ($^+N_2C_6H_4N_2^+$, $2TsO^-$) from *p*-phenylenediamine (**8**) were unsuccessful and only resulted in **8a**. However, in the case of 4,4′-methylenedianiline (**18**) bearing two isolated NH_2 groups, it was possible to produce the double salt **18a** in a low yield. Acetic acid was an unsuitable solvent for the diazotization of

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(6) AV-17-8 is Russian analogue of Amberlyst A26 hydroxide form; 0.4−1.2 mm polystyrene beads with 16% DVB cross-linking and a loading of 4.3 mmol/g. Resin−NO_2^- reagent was prepared by the addition of resin AV-17-8 (3.5 g) into a solution of $NaNO_2$ (2.07 g, 30 mmol) in water (30 mL). The mixture was stirred at rt for 10 min. Resin−NO_2^- was filtered and washed with water until the pH of filtrate became neutral. The content of prepared Resin−NO_2^- was 3.5 mmol of NO_2^-/g.

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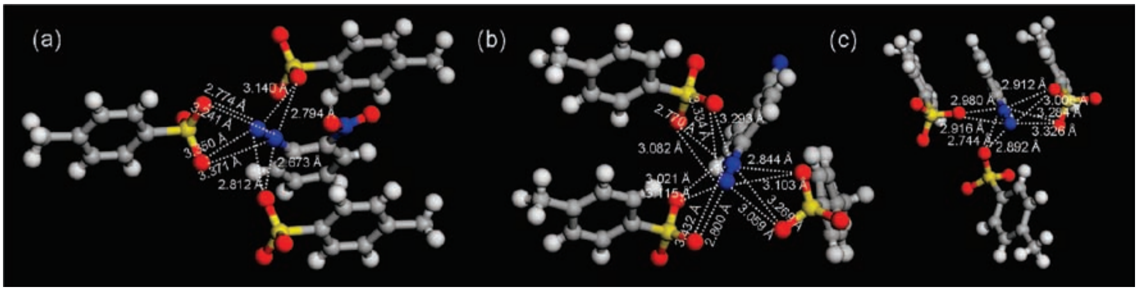


Figure 1. X-ray crystal structures of (a) **9a**, (b) **12a**, and (c) **15a** with multiple close contacts between nitrogen atoms of arenediazonium cations and oxygen atoms of tosylate anions.

strongly basic diamines **8** and **18**. On the contrary, salts **8a** and **18a** could be provided if methanol was used as a solvent instead.

The ^{1}H and ^{13}C NMR and IR spectra confirm the structures of prepared salts **1a**−**18a**, and the structures of **9a**, **12a**, and **15a** were also supported by X-ray analysis (Figure 1).

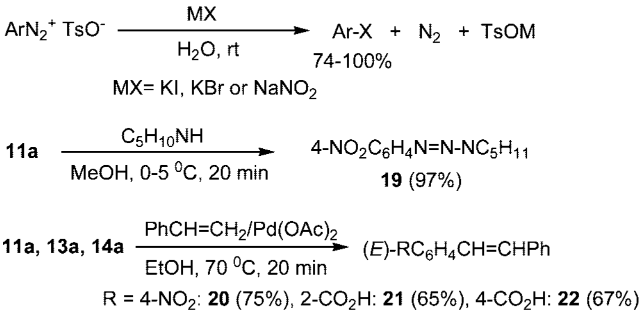
The structures and diazonium nature of **1a**−**18a** were also verified by azo-coupling reactions with 2-naphthol to give the expected (2-hydroxy-1-naphthyl)aryldiazenes in higher than 90% yields. In addition, salts **1a**−**18a** are very soluble not only in protic solvents (AcOH, MeOH, EtOH, and H_2O) but also in polar aprotic ones (DMSO, DMF, and MeCN); their good solubility is an important advantage over other arenediazonium tetrfluoroborates or hexafluoro phosphates. The prepared salts **1a**−**18a** are slightly colored solids that have well-defined melting points. One property that makes diazonium salts **1a**−**18a** very useful is their excellent stability, a feature that could lead to important synthetic developments. Pure salts **1a**−**18a** stored at room temperature in the dark for a few months underwent no changes. Even under sunlight, salt **11a** survived at room temperature without decomposition for two weeks. Thus, arenediazonium tosylates **1a**−**18a** can be stored under normal conditions like other stable organic compounds.

Thermal stabilities of **1a**−**18a** were carefully tested by DSC between 0−600 °C under a nitrogen atmosphere, and no explosive phenomenon was observed for any of the salts. The only exception is salt **9a**, in which a weak explosive phenomenon was observed at 200−205 °C during a heating process above its melting point. This result may be caused not by disintegration of **9a** but as a byproduct of its decomposition.

To gain an insight into the thermal stability of arenediazonium tosylates, we determined crystal structures of these compounds by X-ray crystallography. After numerous unsuccessful attempts, single crystals of **9a**, **12a**, and **15a** suitable for X-ray analysis using synchrotron radiation were finally grown from an acetic acid and diethyl ether solution. The X-ray crystal structures of arenediazonium tosylates reveal that one independent arenediazonium cation is surrounded by three tosylate anions. Unlike the reported crystal structure[8] of unstable benzenediazonium chloride (N−Cl 3.22−3.56 Å in Figure S12, Supporting Information), arenediazonium tosylates in particular show multiple and close contacts between the nitrogen atoms in diazonium cations and the oxygen atoms of tosylate anions through charge−charge interactions (Figure 1). The shortest distances between the nitrogen atoms of a cation and the oxygen atoms of the corresponding tosylates in **9a**, **12a**, and **15a** are 2.673, 2.770, and 2.744 Å, respectively, which are much shorter than the sum of van der Waals radii (2.90 Å).[9] Therefore, we believe that such an intimate interaction between cations and anions might be a crucial clue for the unusual stability of arenediazonium tosylates. To our knowledge, this is the first example of the stabilization of diazonium groups by multiple and close contacts with counter tosylate anions, which is clearly elucidated by X-ray crystallography.

Despite their high thermal and aging stability, all arenediazonium tosylates **1a**−**18a** showed good reactivity in subsequent transformations. Apart from mentioned azo-coupling reactions, selected salts were tried in typical conversions of diazonium salts. These salts effectively react at room temperature with KI, KBr, or $NaNO_2$ in water to give the corresponding products of nucleophilic replacement in high yields (Scheme 3, Table 2). It is important to note that these reactions successfully proceed in the absence of cupreous salts.

Scheme 3. Selected Reactions of Arenediazonium Tosylates



$$ArN_2^+\ TsO^- \xrightarrow[H_2O,\ rt]{MX} Ar\text{-}X + N_2 + TsOM \quad 74\text{-}100\%$$

MX= KI, KBr or $NaNO_2$

$$\mathbf{11a} \xrightarrow[MeOH,\ 0\text{-}5\ ^0C,\ 20\ min]{C_5H_{10}NH} 4\text{-}NO_2C_6H_4N{=}N\text{-}NC_5H_{11}\quad \mathbf{19}\ (97\%)$$

$$\mathbf{11a, 13a, 14a} \xrightarrow[EtOH,\ 70\ ^0C,\ 20\ min]{PhCH{=}CH_2/Pd(OAc)_2} (E)\text{-}RC_6H_4CH{=}CHPh$$

R = 4-NO_2: **20** (75%), 2-CO_2H: **21** (65%), 4-CO_2H: **22** (67%)

Salt **11a** gives triazene **19** in 97% yield by the treatment with piperidine in methanol, and salts **11a**, **13a**,and **14a** are capable of styrene arylation in the presence of $Pd(OAc)_2$ to

Table 2. Reaction Results of Arenediazonium Tosylates with Nucleophilic Reagents at Room Temperature in Water

salt	reagent	time, min	product, yield (%)
7a	KI	30	*p*-MeOC_6H_4I, 80
8a	KI	50	*p*-$NH_2C_6H_4I$, 100
9a	KI	10	*o*-$NO_2C_6H_4I$, 97
11a	KI	5	*p*-$NO_2C_6H_4I$, 98
12a	KI	20	*p*-NCC_6H_4I, 64
13a	KI	200	*o*-$HO_2CC_6H_4I$, 93
14a	KI	240	*p*-$HO_2CC_6H_4I$, 91
16a	KI	10	2,4,6-$Br_3C_6H_2I$, 97
11a	KBr	60	*p*-$NO_2C_6H_4Br$, 80
12a	KBr	100	*p*-NCC_6H_4Br, 74
11a	$NaNO_2$	30	*p*-$(NO_2)_2C_6H_4$, 74

provide corresponding (*E*)-stilbenes **20**−**22** respectively (Scheme 3).

In conclusion, we have developed a new, simple, and effective method for the diazotization of a wide range of aryl amines by using a polymer-supported diazotization agent in the presence of *p*-toluenesulfonic acid. Various arenediazonium tosylates as a little-known class of diazonium salts can be easily prepared in a pure, dry state. Due to their excellent stability, they can be stored safely for a long time and be readily used for subsequent transformations. These salts reveal good solubility in many solvents and high reactivity in a typical reaction of diazonium salts. We believe that arenediazonium tosylates have good potential to be useful and versatile building blocks in organic synthesis.

Acknowledgment. We gratefully acknowledge the BK 21 program of the Korean Ministry of Education for the support of this work. X-ray diffraction experiments using synchrotron radiation were performed at the Pohang Accelerator Laboratory supported by MOST and POSTECH.

Supporting Information Available: Experimental details, ^1H and ^{13}C NMR spectral data, and X-ray crystallographic results. This material is available free of charge via the Internet at http://pubs.acs.org.

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