SHORT PAPER

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A facile and efficient method for synthesis of the aryloxyimidoyl azides†

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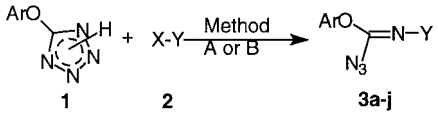
A facile and efficient synthesis is introduced for the new aryloxyimidoyl azides in a quantitative yield.

Organoazides are one of the most important synthetic intermediates for the preparation of nitrogen-containing organic compounds. The azido functionality not only reacts with nucleophiles and electrophiles but also serves as a nitrene precursor on thermolysis or photolysis.[1–6] In recent years imidoyl azides have been also used as a convenient reagent to generate the nitrenes.[7–12] Some nitrenes have been seldom used due to handling difficulties and the danger of explosion of their azide precursors, as well as their low selectivity.[1–6,10] Imidoyl azides show none of the above major difficulties.[7–12]

In connection with the synthetic value of the imidoyl azides[7–12], we have developed a new synthetic method for aryloxyimidoyl azides. A facile and efficient synthesis method is presented a quantitative yield (near 100% within the experimental error) for these compounds. The imidoyl azides are generally prepared by reaction of tetrazoles with electron-withdrawing electrophiles (such as, TsCl, Br-CN, MsCl, *etc*) in anhydrous peroxide-free THF and one equivalent of triethylamine under inert atmosphere (nitrogen or argon). The reaction mixture must be passed through column chromatography, because the reaction is not completive and quantitative (method A).[7–13] In attempts to improve the yield and eliminate the difficulties associated with this method, the following improvements were achieved; (a) No need for over purification of solvents. (b) No need for separation or purification of azides by column chromatography or other methods; and (c) Quantitative yields of azides.

It was found that the reaction was completed quantitatively in ethyl acetate, at ambient temperature with 1.3 equiv. of Et_3N, the minimum amount required (method B). After filtrating the reaction mixture, 1 equiv. of $Et_3N.HX$ salt was produced (that is %100 yield). Evaporation of the filtrated solution under vacuum at ambient temperature (evaporating along with heating can decompose small amounts of azides) gave pure azides in quantitative yield. The results are shown in Table 1 and Scheme 1.



1 **2** **3a-j**

Scheme 1

One interesting aspect of method B is the synthesis of **3i** (entry 9). This azide was not produced in method A. Furthermore, addition of THF to the reaction mixture to increase the solubility of the azide (some of the azide produced was co-precipitated with $Et_3N.HX$ salt) prevented azide formation (reaction was not completed even after two days). Method B was also examined with other electrophiles such as $PhSO_2Cl$, Br-CN (entries 2,3,10). A quantitative yield of the azides was achieved. For cases where azide is not soluble in ethyl acetate (*e.g.* entry 9) or where it is contaminated with $Et_3N.HX$ salt, two work up procedures were developed to eliminate these problems (see experimental section).

The question raised why the reaction is complete in ethyl acetate but not with THF and other solvents. This could be attributed to the equilibrium between azide and 1- or 2-substituted tetrazole, Scheme 2. In ethyl acetate the equilibrium favors the azide. Further investigations of the tetrazole-azide equilibrium are now underway.

In principle, azido/tetrazole equilibrium depends on three important factors; substituent, solvent and temperature. The electron-withdrawing groups, when the temperature increases and the solvent polarity decreases, favor formation of the azide isomer.[14–16]

In summary, we have described a facile and convenient synthesis method for a series of new aryloxyimidoyl azides in ethyl acetate. This method does not require purification or separation, most importantly by column chromatography and produces azides in quantitative yields.

Table 1 Preparation of aryloxyimidoyl azides

Entry	Azide	Ar	Y	X	%Yield		mp (dec.)°C
					Method A	Method B	
1	**3a**	4-$CH_3C_6H_4$	4-$CH_3C_6H_4SO_2$	Cl	76	100[a]	92
2	**3b**	4-$CH_3C_6H_4$	$C_6H_5SO_2$	Cl	–	100[a]	97
3	**3c**	4-$CH_3C_6H_4$	CN	Br	–	100[a]	59
4	**3d**	C_6H_5	4-$CH_3C_6H_4SO_2$	Cl	76	100[a]	96
5	**3e**	2,6-$(CH_3)_2C_6H_5$	4-$CH_3C_6H_4SO_2$	Cl	87	100[a]	94
6	**3f**	4-$CH_3OC_6H_4$	4-$CH_3C_6H_4SO_2$	Cl	78	100[a]	77
7	**3g**	4-ClC_6H_4	4-$CH_3C_6H_4SO_2$	Cl	81	100[a]	98
8	**3h**	4-$O_2NC_6H_4$	4-$CH_3C_6H_4SO_2$	Cl	53	100[a]	117
9	**3i**	2,6-$(CH_3O)_2C_6H_4$	4-$CH_3C_6H_4SO_2$	Cl	0	100[a]	120
10	**3j**	2,6-$(CH_3O)_2C_6H_4$	$C_6H_5SO_2$	Cl	–	100[a]	96

[a] The yields are quantitative (within the experimental error of 2–3%).

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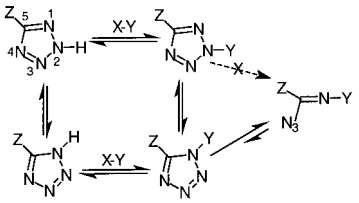
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



Scheme 2

Experimental

General.- ^{1}H-NMR spectra were recorded at Varian EM 390 (90MHz). The IR spectra were obtained on a Shimadzu Zu-435. Melting points were taken by the GallenKamp melting point apparatus and are uncorrected. The elemental analysis was performed by Research Institute of Petroleum Industries (RIPI) and Tarbiat Modarres University Research Center. All starting materials and solvents were purified with the proper purification techniques before use.[17] All reactions were followed with TLC. Tetrazoles were prepared according to literature.[8-13,18]

General procedure: Method A – To a solution of tetrazole **1** (10mmol) in 30 ml of peroxide-free anhydrous THF was added **2** (10mmol) in 10 ml THF, with cooling in an ice-salt bath under nitrogen (or argon). Triethylamine (10mmol) in 10 ml THF was added over a period of 30 min. The mixture was stirred and allowed to come to room temperature, over several h. Filtration, washing with THF, evaporation of the THF solutions, and chromatography on silica gel, gives azides. All azides recrystalize in chloroform (or dichloromethane) and petroleum ether (40–60 °C).

Method B – To a stirred solution of tetrazole **1** (10mmol) and **2** (10 mmol) in 20ml ethyl acetate, in a 50 ml flask equipped with a stopper, triethylamine (13mmol) was added drop wise over 5 min at room temprature. The mixture was stirred over 2–5h. Reaction progress was monitored by TLC. Filtrate was washed with ethyl acetate. Evaporation of the ethyl acetate solution (under vacuum and at room temperature), gave pure azides in a quantitative yield.

In cases where azide is not soluble in ethyl acetate (*e.g.* entry 9) or it is contaminated with small amounts of $Et_3N.HX$ salt, two work up procedures were developed to eliminate these problems: (a) the precipitate (after filtration), was washed several times with THF. Evaporation of THF produced azide; (b) After evaporating ethyl acetate (without filtration) the residue was washed with water and dried under vacuum to give azide.

N$^/$-(4-methylbenzenesulfonyl) (4-methylphenoxy) imidoyl azide (**3a**); mp = 92°C (dec.), ^{1}H NMR (90MHz, CD_3CN); δ (ppm) 2.36 (s, 3H), 2.42 (s, 3H), 6.94 (d, J = 9Hz, 2H), 7.15 (d, J = 9Hz, 2H), 7.25 (d, J = 7.8Hz, 2H), 7.72 (d, J = 7.8, 2H). IR (KBr); 3050(w), 3020(w), 2900(w), 2850(w), 2175(s), 2130(s), 1540–1630(vs), 1500(s), 1330(s), 1290(s), 1150(s),1090(s), 815(s), 670(m) cm^{-1} ; Anal. Calcd for $C_{15}H_{14}N_4O_3S$; C, 54.53; H, 4.27; N, 16.96; Found: C, 53.10; H, 4.2; N, 16.6.

N$^/$-(benzenesulfonyl) (4-methylphenoxy) imidoyl azide (**3b**); mp = 97 °C (dec.), ^{1}HNMR (90MHz, $CDCl_3$); δ (ppm) 2.33 (s, 3H), 6.94 (d, J = 9Hz, 2H), 7.15 (d, J = 9Hz, 2H), 7.6 (m, 3H), 8.1 (dd, J = 6Hz, J ≅ 3Hz, 2H). IR (KBr); 3080(w), 3020(w), 2910(w), 2170(s), 2130(s), 1605(vs), 1595–1540(vs), 1500(s), 1440(m), 1330(vs), 1300–1280(vs), 1240(w), 1200(s), 1180–1140(vs), 1080(s), 1020(w), 1000–980(m), 880(m), 820(s), 760(w), 740–730(m), 690(m), 610(m), 570(m) cm^{-1}.

N$^/$-(Cyano) (4-methylphenoxy) imidoyl azide (**3c**); mp = 59°C (dec.), ^{1}H NMR (90MHz, $CDCl_3$); δ (ppm) 2.4 (s, 3H), 7.05 (d, J = 9Hz, 2H), 7.25 (d, J = 9Hz, 2H). IR (KBr); 3010(w), 2950(w), 2900(w), 2190(s), 2160(s), 1640–1600(s), 1600–1580(s), 1560(m), 1500(m), 136–1320(m), 1250(m), 1240–1200(s), 1100(m), 840–800(m) cm^{-1}.

N$^/$-(4-methylbenzenesulfonyl) (phenoxy) imidoyl azide (**3d**); mp = 96°C (dec.), ^{1}H NMR (90MHz, CD_3CN); δ (ppm) 2.42 (s, 3H), 7.1–7.4 (m, 7H), 7.77 (d, J = 7.8, 2H). IR (KBr); 3050(w), 3000(w), 2850(w), 2175(m), 2125(m), 1610(s), 1575(s), 1490(m), 1335(s), 1280(m), 1210(m), 1150(s), 1050(m), 880(m), 770(m), 690(m), 680(m) cm^{-1}; Anal. Calcd for $C_{14}H_{12}N_4O_3S$; C, 53.15; H, 3.82; N, 17.71; Found: C, 51.50; H, 3.80; N, 17.10.

N$^/$-(4-methylbenzenesulfonyl) (2,6-methylphenoxy) imidoyl azide (**3e**); mp = 94°C (dec.), ^{1}H NMR (90MHz, CD_3CN); δ (ppm) 2.08 (s, 6H), 2.42 (s, 3H), 7.09 (s, 3H), 7.3 (d, J = 7.8Hz, 2H), 7.85 (d, J = 7.8, 2H). IR (KBr); 3050(w), 3000(w), 2910(w), 2850(w), 2200(s), 2150(s), 2120(s), 1660–1440(s), 1330(vs), 1290(s), 1195(s), 1150(s), 1090(s), 815(m), 770(s), 735(s), 690(s), 660(m) cm^{-1}.

N$^/$-(4-methylbenzenesulfonyl) (4-methoxyphenoxy) imidoyl azide (**3f**); mp = 77°C (dec.), ^{1}H NMR (90MHz, CD_3CN); δ (ppm) 2.42 (s, 3H), 3.80 (s, 3H), 6.85(d, J = 10.5Hz, 2H), 7.05 (d, J = 10.5Hz, 2H), 7.3 (d, J = 7.8Hz, 2H), 7.8 (d, J = 7.8Hz, 2H). IR (KBr); 3060(w), 2950(w), 2900(w), 2850(w), 2170(m), 2150(m), 2120(m), 1440–1660(s), 1330(s), 1300(s), 1250(s), 1200(s), 1150(s), 1090(s), 830(m), 810(m), 730(m) cm^{-1}.

N$^/$-(4-methylbenzenesulfonyl) (4-chlorophenoxy) imidoyl azide (**3g**); mp = 98°C (dec.), ^{1}H NMR (90MHz, CD_3CN); δ (ppm) 2.42 (s, 3H), 7.15 (d, J = 9Hz, 2H), 7.25 (d, J = 7.8Hz, 2H), 7.37(d, J = 9Hz, 2H), 7.75 (d, J = 7.8, 2H). IR (KBr); 3100(w), 3050(w), 2900(w), 2850(w), 2170(m), 2125(m), 1659–1480(s), 1330(s), 1300(s), 1205(m), 1150(s), 1080(s), 830(m), 810(m), 690(m) cm^{-1}; Anal. Calcd for $C_{14}H_{11}ClN_4O_3S$; C, 47.93; H, 3.1; N, 15.97; Found: C, 46.60; H, 3.1; N, 16.10.

N$^/$-(4-methylbenzenesulfonyl) (4-nitrophenoxy) imidoyl azide (**3h**); mp = 117°C (dec.), ^{1}H NMR (90MHz, CD_3CN); δ (ppm) 2.42 (s, 3H), 7.3 (d, J = 7.8Hz, 2H), 7.4 (d, J = 9Hz, 2H), 7.75 (d, J = 7.8Hz, 2H), 8.3 (d, J = 9Hz, 2H). IR (KBr); 3100(w), 3060(w), 3000(w), 2800(w), 2750(w), 2180(m), 2120(m), 1620–1480(s), 1330–1280(s), 1220(s), 1160(s), 1080(m), 850(m), 810(m), 690(m) cm^{-1}.

N$^/$-(4-methylbenzenesulfonyl) (2,6-dimethoxyphenoxy) imidoyl azide (**3i**); mp = 120°C (dec.), ^{1}H NMR (90MHz, $CDCl_3$); δ (ppm) 2.42 (s, 3H), 3.80 (s,6H), 6.62 (d, J = 9Hz, 2H), 7.2 (t and d, 3H), 7.9 (d, J = 9Hz, 2H). IR (KBr); 3010(w), 2972(w), 2940(w), 2840(w), 2180(s), 2140(s), 1610–1590(vs), 1580–1560(vs), 1480(s), 1440(w), 1320(s), 1310(s), 1280(s), 1260(s), 1200(w), 1180(w), 1150(s), 1110(s), 1080(s), 997(m), 890(w), 810(w), 760(m), 720(m), 697(w), 670(w), 600(w) cm^{-1}; Anal. Calcd for $C_{16}H_{16}N_4O_5S$; C, 51.05; H, 4.29; N, 14.89; Found: C, 50.07; H, 4.40; N, 15.02.

N$^/$-(benzenesulfonyl) (2,6-dimethoxyphenoxy) imidoyl azide (**3j**); mp = 96°C (dec.), ^{1}H NMR (90MHz, $CDCl_3$); δ (ppm) 3.80 (s, 6H), 6.60 (d, J = 9Hz, 2H), 7.2 (t, J = 9Hz, 1H), 7.6 (m, 3H), 8.0 (dd, J = 7.5, J = 3Hz, 2H). IR (KBr); 3050(vw), 3000(w), 2940(w), 2840(w), 2180(s), 2140(s), 1630–1590(vs), 1580–1550(vs), 1494(m), 1480(s), 1445(m), 1340–1300(vs), 1290–1280(s), 1260(vs), 1200(m), 1160(vs), 1110 (vs), 1085(s), 1022(w), 1000(w), 880(w), 780–760(m), 730(m), 685(m), 620–600(m), 580–560(m) cm^{-1}.

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