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Unusual Reaction of Chloramine-T with Araldoximes

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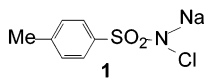
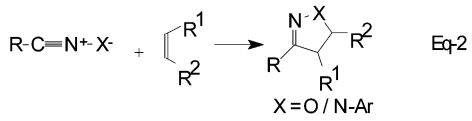
Abstract: Reaction of araldoximes with 4 equiv of chloramine-T in refluxing methanol produces *N*-(*p*-tolyl)-*N*-(*p*-tosyl)benzamides via addition of 2 equiv of chloramine-T to the intermediate nitrile oxide followed by extrusion of sulfur dioxide.

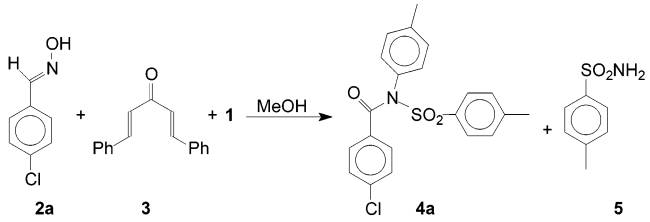
Chloramine-T (**1**), a representative example of *N*-halogeno-*N*-metallosulfonamides, is a versatile reagent in organic synthesis.[1,2] It is established that in solution chloramine-T exhibits a series of equilibria. It reacts with a wide variety of functional groups effecting an array of transformations because of its ability to act as source of different species, such as (a) chloronium ion; (b) hypochlorite; (c) N-anions, which act both as bases and nucleophiles; (d) tosylnitrene, etc.[1] One of the most commonly exploited reactions of chloramine-T is oxidation, as it is a very good oxidizing agent in both acidic and basic media.[2] Chloramine-T has been used for the in situ oxidation of oximes and hydrazones of aldehydes to generate the nitrile oxides and nitrile imines (eq 1), respectively.[3] Synthesis of a variety of isoxazolines and pyrazolines have been developed via the 1,3-dipolar cycloadditions of olefins with the in situ generated nitrile oxides and nitrile imines (eq 2).[4] In 1989, Hassner and Rai[5] reported an improved procedure via preformation of a stable nitrile oxide from the corresponding oxime and 1 equiv of chloramine-T in ethanol and subsequent reaction with olefins. As a continuation of our interest in the generation of multi-heterocyclic systems via 1,3-dipolar cycloaddition reactions of nitrile oxides and nitrile imines to a variety of olefins,[6] we have investigated the reaction of araldoxime **2a** and 1,5-diphenyl-1,4-pentadien-3-one (**3**) in the presence of an excess of chloramine-T. However, in contrast to the expected isoxazoline, it resulted in the formation of an unusual product,[7] and herein we describe the details of these investigations.

Reaction of *p*-chlorobenzaldoxime (**2a**) with 2 equiv of chloramine-T (**1**) in the presence of dienone **3** in refluxing methanol for 48 h followed by purification on a silica gel column furnished two compounds, **4a** and **5** (Scheme 1).





SCHEME 1



The polar compound **5** was readily identified as *p*-toluenesulfonamide, the common end product in the oxidation reactions with chloramine-T.

Spectral analysis of the less polar compound **4a** readily indicated the absence of incorporation of the dienone **3** in the product. To substantiate further, the reaction was carried out in the absence of any olefin, which also generated the same mixture of compounds **4a** and **5**. It was found that presence of 4 equiv of chloramine-T furnishes optimal yield of **4a**. The IR spectrum of **4a** exhibited the presence of tosyl and amide groups. The ^{1}H and ^{13}C NMR spectra clearly showed the presence of three 1,4-disubstituted benzene moieties. Presence of two aromatic methyl groups (δ 2.45 and 2.32 ppm) in the ^{1}H NMR spectrum suggested the incorporation of two molecules of chloramine-T and one molecule of oxime in the product **4a**, which is further supported from its elemental analysis. The presence of an amide group was further supported by the presence of the carbonyl carbon resonance at δ 168.6 ppm in the ^{13}C NMR spectrum. Presence of an upfield AB quartet at δ 7.07 and 6.97 ppm due to one of the benzene rings suggested a deep-seated change. Hence, the structure of the product **4a** was solved by X-ray analysis. Good single crystals of **4a** were grown

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‡ Punjab University.

(1) Campbell, M. M.; Johnson, G. *Chem. Rev.* **1978**, *78*, 65.
(2) Agarwal, M. C.; Upadhyay, S. K. *J. Sci. Ind. Res.* **1990**, *49*, 13.
(3) (a) Rai, K. M. L.; Hassner, A. *Synth. Commun.* **1997**, *27*, 467. (b) Rai, K. M. L.; Hassner, A. *Indian J. Chem.* **1997**, *36B*, 242. (c) Rai, K. M. L.; Hassner, A. *Synth. Commun.* **1989**, *19*, 2799.
(4) Peter A. W. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 4, p 1111.
(5) Hassner, A.; Rai, K. M. L. *Synthesis* **1989**, 57.
(6) (a) Padmavathi, V.; Reddy, A. V. B.; Sumathi, R. P.; Padmaja, A.; Reddy, D. B. *Indian J. Chem.* **1998**, *37B*, 1286. (b) Padmavathi, V.; Sumathi, R. P.; Reddy, A. V. B.; Reddy, D. B. *Heterocycl. Commun.* **1998**, *4*, 163. (c) Padmavathi, V.; Sumathi, R. P.; Babu, N. C. *J. Chem. Res.* **1999**, 610. (d) Padmavathi, V.; Sumathi, R. P.; Balaiah, A.; Padmaja, A.; Reddy, D. B. *Phosphorus, Sulfur Silicon* **2000**, *160*, 61. (e) Padmavathi, V.; Sumathi, R. P.; Reddy, K. V.; Reddy, A. S.; Reddy, D. B. *Synth. Commun.* **2000**, *30*, 4007. (f) Padmavathi, V.; Reddy, K. V.; Padmaja, A.; Reddy, D. B. *Synth. Commun.* **2002**, *32*, 1227; (g) Padmavathi, V.; Reddy, K. V.; Balaiah, A.; Reddy, T. V. R.; Reddy, D. B. *Heteroat. Chem.* **2002**, *13*, 6.
(7) To the best of our knowledge there is no report in the literature on the formation of such an unusual product in the reaction of oximes with chloramine-T.

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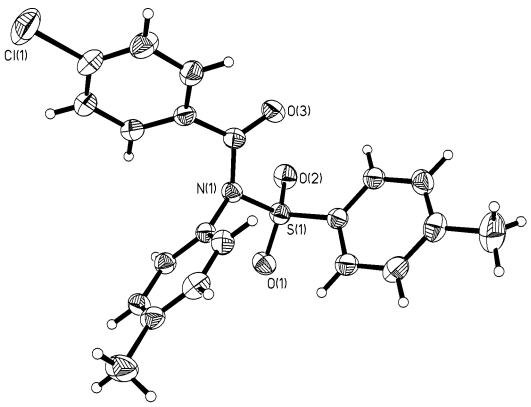
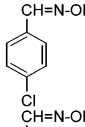
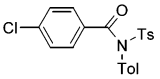
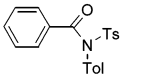
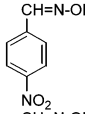
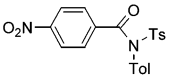
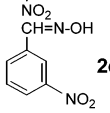
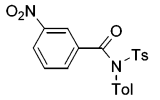
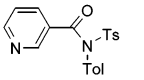
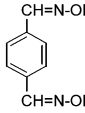
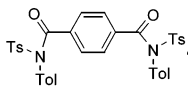
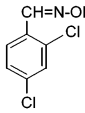
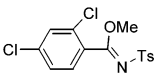
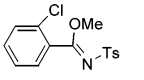


FIGURE 1. X-ray structure of **4a**.

TABLE 1.

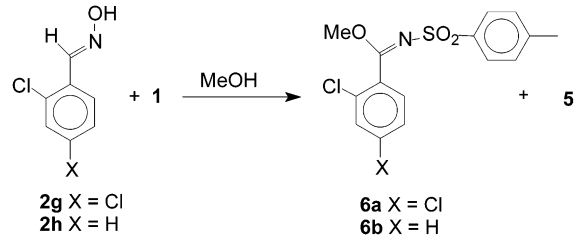
S.No	Oxime		Product[a]		Yield (%)	m.p (°C)[c]
1		**2a**		**4a**	27.2	186-187
2		**2b**		**4b**	20.0	148-150
3		**2c**		**4c**	28.4	208-209
4		**2d**		**4d**	28.4	185-187
5		**2e**		**4e**	25.0	170-171
6		**2f**[b]		**4f**	12.0	220-222
7		**2g**		**6a**	26.5	138-140
8		**2h**		**6b**	28.7	128-130

[a] Tol = 4-methylphenyl; Ts = 4-methylphenylsulfonyl. [b] Eight equivalents of **1** was employed. [c] Melting points are uncorrected.

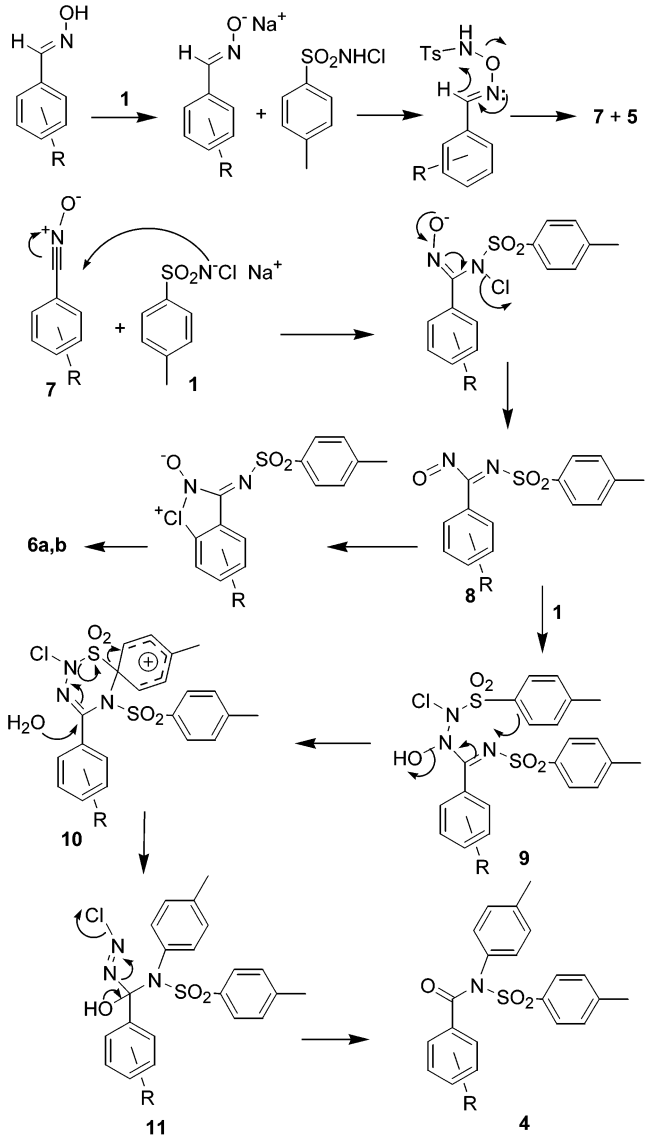
from methanol and subjected to X-ray diffraction analysis, which unambiguously established the structure of the product **4a** as *N*-(4-tolyl)-*N*-(4-toluenesulfonyl)-4-chlorobenzamide, which was totally unexpected. Perspective view of the X-ray structure of **4a** is depicted in Figure 1.

To check the generality of the reaction, various araldoximes were treated with 4 equiv of chloramine-T in refluxing methanol. The results are summarized in Table 1. The reaction proceeded more readily when electron-withdrawing groups are present in the benzene ring. It is worth noting that the reaction proceeded with both the oxime moieties of the dioxime **2f** to produce the bisamide **4f**. The reaction proceeded even with the pyridine carbaldoxime. Analogous to phenolic and anilino nitroso compounds which do not react with chloramine-T,[8] compounds containing a chloro substituent at the ortho position of the oxime group (Scheme 2) failed to produce the product **4** and instead generated the iminol ethers **6a,b**, indicating the intermediacy of a nitroso compound in the reaction.

SCHEME 2



SCHEME 3



(8) Parrar, W. V.; Gulland, J. M. *J. Chem. Soc.* **1944**, 368.

TABLE 2. Crystal Data and Structure Refinement for Amide 4a

identification code	sv1	
empirical formula	$C_{21}H_{18}ClNO_3S$	
formula weight	399.87	
temperature	293(2) K	
radiation used, wavelength	Mo Kα, 0.71073 Å	
crystal system, space group	monoclinic, $P2_1/c$	
unit cell dimensions	$a = 8.311(1)$ Å	$\alpha = 90°$
	$b = 10.723(1)$ Å	$\beta = 92.25(1)°$
	$c = 22.036(2)$ Å	$\gamma = 90°$
volume	1962.3(3) Å^3	
Z, calculated density	4, 1.354 Mg/m^3	
absorption coefficient	0.322 mm^{-1}	
$F(000)$	832	
crystal size	0.29 × 0.25 × 0.19 mm	
θ range for data collection	1.85−24.50°	
scan type	$2\theta-\theta$	
scan speed	variable, 2.0−60.0°/min in ω	
scan range (ω)	0.86° plus Kα separation	
background measurement	stationary crystal and stationary counter at the beginning and end of scan, each for 25.0% of total scan time	
index ranges	$0 \le h \le 9$, $-12 \le k \le 0$, $-25 \le l \le 25$	
reflections collected	3497	
independent reflections	3253 [R(int) = 0.0150]	
refinement method	full-matrix least-squares on F^2	
data/restraints/parameters	3253/0/245	
goodness-of-fit on F^2	1.024	
weighting scheme	$1/[\sigma^2(F_o^2) + (0.0447P)^2 + 0.47P]$, $P = (\max(F_o^2,0) + 2*F_c^2)/3$	
data-to-parameter ratio	13.28:1	
final R indices, 2572 reflections [$I > 2\sigma(I)$]	$R1 = 0.0360$, $wR2 = 0.0917$	
R indices (all data)	$R1 = 0.0488$, $wR2 = 0.0996$	
extinction coefficient	0.0060(7)	
largest diff. peak and hole	0.160 and −0.221 e·Å^{-3}	

A tentative mechanism, via the nitrile oxide **7**, for the formation of the product **4** is depicted in Scheme 3. First, chloramine-T oxidizes the oxime **2a** to the nitrile oxide **7**. Addition of chloramine-T to the nitrile oxide **7** followed by elimination of chloride results in the formation of the nitroso compound **8**, which is stabilized when a chloro substituent is present at ortho position and led to the formation of the iminol ethers **6**. It is well-established that chloramine-T does not add to phenolic and anilino nitroso compounds.[8] In the absence of a stabilizing group at the ortho position, addition of one more molecule of chloramine-T to the nitroso group in **8** generates the intermediate **9**,[8] which undergoes an intramolecular Friedel−Crafts type reaction leading to the formation of the intermediate **10**. Addition of water to **10** leads to chloro diazo intermediate **11** with the loss of sulfur dioxide. Finally loss of nitrogen and chloride ion transforms the intermediate **11** into **4**. A tentative mechanism for the formation of **5** is also shown in Scheme 3.

In conclusion, we have discovered an unusual reaction of chloramine-T with oximes, which is unprecedented in the literature. Reaction of an araldoxime with 4 equiv of chloramine-T furnishes *N*-(4-tolyl)-*N*-(4-tosyl)benzamide via addition of two molecules of chloramine-T to the intermediate nitrile oxide with extrusion of one molecule of sulfur dioxide. A probable mechanism based on a nitroso intermediate is proposed. Formation of the amides **4** in the present studies points to the limitation of the utility of chloramine-T as an oxidant for the generation of nitrile oxides from aldoximes.

Experimental Section

General Procedure. Reaction of 4-Chlorobenzaldoxime with Chloramine-T. Chloramine-T·3H_2O (0.726 g, 2.6 mmol) was added to a solution of the oxime **2a** (0.1 g, 0.640 mmol) in methanol (25 mL) at room temperature. The reaction mixture was refluxed for 48 h, and the inorganic salts were filtered off. The filtrate was concentrated, and the residue was extracted with dichloromethane. The organic extract was washed with water and brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the residue by column chromatography (silica gel) using ethyl acetate−hexane (1:3) as eluent furnished *N*-(4-tolyl)-*N*-(4-tosyl)-4-chlorobenzamide **4a** (0.072 g, 28%) and the tosyl amide **5** (0.270 g, 61%), mp.134−136 °C (lit. 137−138 °C). **Data for 4a**: mp 186−187 °C; IR (neat) ν_{max} cm^{-1} 1696, 1363, 1260, 1185, 1168, 1083; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 7.79 (2 H, d, J = 8.4 Hz), 7.39 (2 H, d, J = 8.4 Hz), 7.29 (2 H, d, J = 8.4 Hz), 7.14 (2 H, d, J = 8.4 Hz), 7.07 (2 H, d, J = 8.1 Hz), 6.99 (2 H, d, J = 8.1 Hz), 2.45 (3 H, s), 2.32 (3 H, s); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 168.6 (C), 144.6 (C), 139.3 (C), 138.1 (C), 135.4 (C), 134.8 (C), 132.3 (C), 131.0 (2 C, CH), 130.1 (2 C, CH), 130.0 (2 C, CH), 129.7 (2 C, CH), 129.2 (2 C, CH), 128.4 (2 C, CH), 21.8 (CH_3), 21.3 (CH_3). Anal. Calcd for $C_{21}H_{18}ClNO_3S$: C 63.07; H 4.53; N 3.50. Found: C 62.95; H 4.52; N 3.22.

Reaction of 2,4-Dichlorobenzaldoxime with Chloramine-T. Chloramine-T·3H_2O (0.845 g, 3.0 mmol) was added to a solution of the oxime **2g** (0.142 g, 0.75 mmol) in methanol (25 mL) at room temperature. It was refluxed for 48 h, and the inorganic salts were filtered off. The filtrate was concentrated, and the residue was extracted with dichloromethane. The organic extract was washed with water and brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the residue by column chromatography (silica gel) using ethyl acetate−hexane (1:3) as eluent furnished the iminol ether **6a** (0.058 g, 26.5%) and the tosyl amide **5** (0.306 g, 51.2%). **Data for 6a**: mp 138−140 °C; IR (neat) ν_{max} cm^{-1} 1620, 1582, 1323, 1160, 1092, 681; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 7.70 (2 H, d, J = 8.4 Hz), 7.40 (1 H, d, J = 7.8 Hz), 7.39 (1H, s), 7.35 (1 H, d, J = 8.4 Hz), 7.24 (2 H, d, J = 7.8 Hz), 3.99 (3 H, s), 2.43 (3 H, s); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 167.8 (C), 143.4 (C), 138.3 (C), 137.3 (C), 132.2 (C), 130.7 (C), 130.2 (CH), 129.5 (CH), 129.3 (2 C, CH), 127.3 (2 C, CH), 126.9 (CH), 56.2 (CH_3), 21.7 (CH_3). Anal. Calcd for $C_{15}H_{13}Cl_2NO_3S$: C 50.29; H 3.66; N 3.91. Found: C 50.13; H 3.60; N 3.70.

X-ray Analysis of 4a. Good single crystals of **4a** were grown from methanol, and a single crystal with dimension 0.29 × 0.25 × 0.19 mm was mounted along the largest dimension and used for data collection. The intensity data were collected on a single-crystal diffractometer equipped with molybdenum sealed tube (λ = 0.71073 Å) and highly oriented graphite monochromator. The lattice parameters and standard deviations were obtained by least-squares fit to 40 reflections (10.62° < 2θ < 30.36°). The data were collected by 2θ−θ scan mode with a variable scan speed ranging from 2.0° to a maximum of 60.0°/min. The data were corrected for Lorentz and polarization factors. The structure was solved by direct methods using SHELX-97[9] package and also refined using the same. A weighting scheme of the form $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ with a = 0.0447 and b = 0.47 was used. The refinement converged to a final R value of 0.0360. Details of X-ray analysis are given in Table 2.

(9) Sheldrick, G. M. *SHELX-97*, Program for the solution and refinement of crystal structures; University of Göttingen: Göttingen, Germany, 1997.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for compounds **4a**−**f** and **6a,b** and X-ray crystallographic data for compound **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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