An Efficient and General Method for the Deoxygenation of Organic *N*-Oxides Using $Zn(OTf)_2$ and $Cu(OTf)_2$

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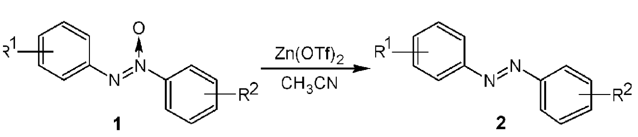
Abstract: A mild and efficient general method for the deoxygenation of organic *N*-oxides such as azoxybenzenes, *N*-arylnitrones, and *N*-heteroarene *N*-oxides using $Zn(OTf)_2$ and $Cu(OTf)_2$ in excellent yields is described.

Key words: deoxygenation, metal triflates, nitrones, *N*-heteroarene *N*-oxides, azoxybenzenes

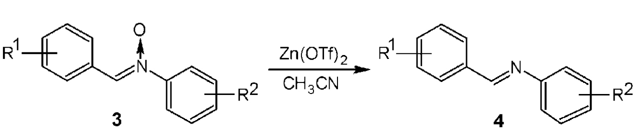
In recent years, metal triflates have attracted considerable attention.[1] This seems to be because of their advantages over conventional Lewis acids as they can be recovered and reused. Conventional Lewis acids often leave residues and their waste disposal is also critical and can cause serious environmental problems. In contrast, metal triflates are considered to be environmentally benign and are also readily accessible[2,3] commercially or they can be prepared in the laboratory and their waste/residues are not at all hazardous. These attractive properties of metal triflates seems to have encouraged a large amount of research into their application to C–C bond formation,[4] typically aldol, Mannich, and Reformatsky-type reactions. They have also been used in cycloaddition reactions,[5] oxidations,[6] as well as reductions.[7] Our interest in these unconventional Lewis acids,[8] prompted us to investigate the use of metal triflates such as $Zn(OTf)_2$ and $Cu(OTf)_2$ in the deoxygenation of organic *N*-oxides, which had previously never been used for this transformation.

Organic *N*-oxides occupy a unique position in synthetic organic chemistry;[9] they are not only excellent dipolar substrates in cycloaddition reactions,[10] they also exhibit different chemical behavior in comparison to their deoxygenated parent nitrogen bases.[11] Due to this, selective deoxygenation of *N*-oxides has attracted considerable attention[11a] and many reagents such as, NaHTe,[12] phosphorus compunds,[13a] Al/Ni alloy,[13b] Ti(0) reagents,[14c–14d] silanes,[15] $TiCl_4$–$NaBH_4$ complex,[16] organotin derivatives,[17] InX_3[18] (X = Cl, Br), PCl_5, $POCl_3$, SO_2Cl_2,[19] and very recently another complex system employing $MoO_2Cl_2(dmf)_2$[20] have been used. However, several of these methods have one drawback or another, selectivity,[21] scope, [15,17,22] rigid parameter controls, hazardous procedure,[23] unwanted halogenation of heteroarene nucleus,[19] reduction of aromatic nucleus,[16] and sometimes they were not environmentally friendly. These already reported procedures include conventional Lewis acids such as AlI_3, $TiCl_3$, and $AlCl_3$, which are neither safe nor environmentally friendly. They can not be recovered after the reactions are complete and their waste disposal is also tedious. With an increasing focus on green methodologies we report herein a safe and environmentally friendly procedure for the deoxygenation of organic *N*-oxides using $Zn(OTf)_2$ and $Cu(OTf)_2$.



Scheme 1

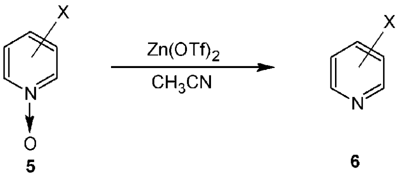
Azoxybenzene **1a** and $Zn(OTf)_2$ in equimolar amounts, after a reaction time of 70 minutes at 80 °C, furnished azobenzene **2a** in an excellent 82% yield. Similarly, other azoxybenzenes **1b**–**d** were found to furnish their corresponding azobenzenes **2b**–**d** in excellent yields.



Scheme 2

Encouraged by these results, we extended this reagent to nitrones **3** and *N*-heteroarene *N*-oxides **5** and **7**. Nitrones gave their corresponding imines **4** (Scheme 2, Table 1) and *N*-heteroarene *N*-oxides, i.e. pyridine *N*-oxides **5** and quinoline *N*-oxides **7**, afforded the deoxygenated products **6** and **8** (Schemes 3 and 4) respectively in quantitative yields (Table 2).

The selectivity of the present method is fairly wide, as several functionalities remain unaffected under these reaction conditions. Attempts to perform the deoxygenation



Scheme 3

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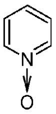
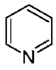
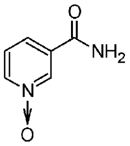
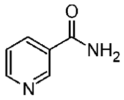
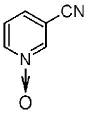
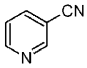
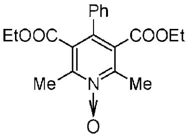
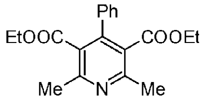
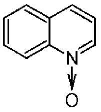
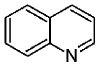
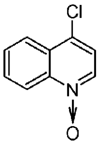
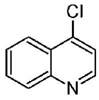
Table 1 Deoxygenation[24] of Azoxybenzenes and Nitrones Using $Zn(OTf)_2$ and $Cu(OTf)_2$

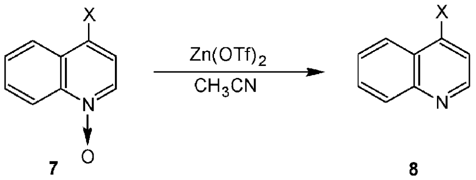
Entry	Product[a]	R^1	R^2	Time[b] (min)	Yield[b,c] (%)	Mp[d] (°C)
1	**2a**	H	H	70 (75)	82 (79)	67–68 (68)[25]
2	**2a**	H	H	200 (200)	n.r.[e]	–
3	**2b**	4-Cl	4-Cl	55 (65)	86 (78)	187–88 (188)[25]
4	**2c**	4-CH_3	4-CH_3	65 (65)	82 (87)	143–44 (144)[25]
5	**2d**	3-Cl	3-Cl	60 (55)	78 (76)	103–04 (104)[26]
6	**4a**	H	H	55 (55)	74 (77)	51–52 (52)[27]
7	**4b**	H	4-Cl	55 (60)	81 (80)	61–62 (62)[28]
8	**4c**	4-Cl	H	45 (50)	78 (72)	65–66 (66)[29]
9	**4d**	4-Cl	4-Cl	45 (45)	79 (76)	110–11(111)[30]
10	**4e**	4-CH_3	H	55 (50)	81 (83)	47–48 (48)[30]
11	**4f**	4-CH_3	4-Cl	60 (70)	80 (74)	112–14 (114)[30]

[a] Mps, IR, and ^1H NMR spectra were in accordance with those of authentic samples.
[b] Values in parentheses were obtained using $Cu(OTf)_2$.
[c] Isolated yields.
[d] Lit. mp in parentheses.
[e] No/negligible reaction at r.t.

Table 2 Deoxygenation[31] of *N*-Hetroarene *N*-Oxides Using $Zn(OTf)_2$ and $Cu(OTf)_2$

Substrate	Product	Reaction time (min)[b]	Yield (%)[b,c]	Mp/bp (°C)[d]
	 **6a**	60 (65)	89 (80)	115 (115.5)[28]
	 **6b**	65 (65)	87 (79)	129–130 (129–130)[28]
	 **6c**	65 (60)	81 (78)	49–50 (50)[28]
	 **6d**	70 (65)	69 (72)	61–62 (62–63)[28]
	 **8a**	55 (60)	82 (77)	238 (238)[28]
	 **8b**	65 (65)	79 (71)	261 (261)[28]

[a] All products were identified by comparison of their IR and ^1H NMR spectra with those of authentic samples.
[b] Values in parentheses were obtained from the reaction using $Cu(OTf)_2$.
[c] Isolated yields.
[d] Lit. mp/bp in parentheses.



7 **8**

Scheme 4

with less than one equivalent of reagent afforded low yields but the selectivity remained high. Increasing the amount of reagent and reaction time did not prove to be fruitful either, decomposition products were observed. It is worth mentioning that no deoxygenated product was obtained when the reaction was carried out at room temperature (Table 1, entry 2). When $Zn(OTf)_2$ is replaced by $Cu(OTf)_2$ equivalent results were achieved. Also the use of $Sc(OTf)_3$ in place of $Zn(OTf)_2$ was equally effective but was not considered for the present study as the reagent is not water-tolerant. Also the present method is a one-pot procedure and does not involve any prior preparation of the reagent system.[20]

In conclusion, the present protocol is a mild and efficient, general method employing water tolerant $Zn(OTf)_2$ and $Cu(OTf)_2$ for the deoxygenation of *N*-oxides. Excellent yields, avoiding harsh reagents under mild reaction conditions are the main advantages of this method.

Acknowledgment

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(24) **Deoxygenation of Nitrones; Typical Procedure**

To a stirred solution of benzaldehyde *N*-phenylnitrone (**3a**, 0.39 g, 2 mmol) in CH_3CN (15 mL) was added $Zn(OTf)_2$ (2 mmol, 1 equiv) and the resulting mixture was stirred at 80 °C for 70 min. After completion of the reaction (monitored by TLC), the solvent was removed under reduced pressure, and the residue was treated with H_2O (3×30 mL). The resultant mixture was extracted with CH_2Cl_2, the organic layer was dried (Na_2SO_4), and the solvent removed by distillation to give the crude product, which was purified by column chromatography (silica, hexane–EtOAc) to afford benzylidine aniline **4a**, in 74% yield; mp 51–52 °C (Lit.[26] mp 52 °C). ^{1}H NMR (200 MHz): $\delta = 8.35$ (s, 1 H, CH=N), 7.30–7.60 (m, 10 H, Ar). ^{13}C NMR (50 MHz): $\delta = 122.0$, 12.3, 127.0, 128.4, 128.6, 129.0, 129.1, 129.6, 129.8, 130.8, 131.2, 153.2 (Ar), 163.4 (CH).

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(31) **Deoxygenation of Heteroarene *N*-Oxides: Typical Procedure**

To a stirred solution of pyridine *N*-oxide (**5a**, 0.19g, 2 mmol) in CH_3CN (15 mL) was added $Zn(OTf)_2$ (2 mmol, 1 equiv) and the resulting mixture was stirred at 80 °C for 60 min. The solvent was removed under reduced pressure and H_2O (50 mL) was added. The pH was adjusted to >7 by the addition of 25% aq NH_3 and the product extracted with Et_2O (3×50 mL). The organic layer was dried (Na_2CO_3) and evaporated to give the crude product, which after purification afforded pyridine **6a** in 89% yield; bp 113–115 °C (Lit.[27] bp 115.5 °C); picrate mp 163–164 °C (Lit.[27] mp 164–65 °C). ^{1}H NMR (200 MHz): $\delta = 7.20$ (dd, 2 H, $J = 8.2$ Hz), 7.55 (dd, 1 H, $J = 8.2$ Hz), 8.50 (d, 2 H, $J = 6.2$ Hz). ^{13}C NMR (50 MHz): $\delta = 123.2$, 123.7, 135.4, 149.6, 149.7.