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DINITROGEN TETROXIDE COMPLEXES OF IRON(III) AND COPPER(II) NITRATES AS NEW VERSATILE REAGENTS FOR ORGANIC SYNTHESIS. EFFICIENT AND SELECTIVE OXIDATION OF SULFIDES TO THEIR CORRESPONDING SULFOXIDES UNDER MILD CONDITIONS.

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Abstract: *$Fe(NO_3)_3 . 1.5\ N_2O_4$ and $Cu(NO_3)_2 . N_2O_4$ are new, stable, and highly efficient reagents for the quantitative transformation of sulfides to sulfoxides in dichloromethane or in the absence of solvent at room temperature. $Cu(NO_3)_2 . N_2O_4$ is highly selective for the oxidation of aryl sulfides.*

Sulfoxides are important precursors in organic synthesis. Conversion of thioethers to sulfoxides by various methods have been extensively reviewed.[1]

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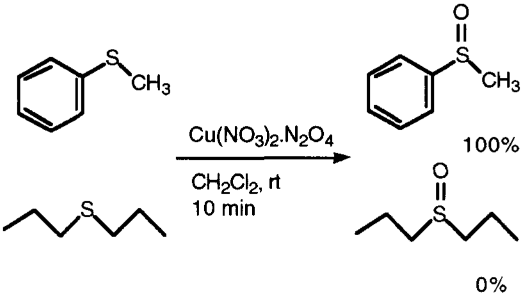
In our laboratories,we have developed and introduced reagents;$Ba(MnO_4)_2$ [2]; $Zn(BiO_3)_2$ [3],$Zn(ClCrO_3)_2 . 9H_2O$[4], and Bu_4NIO_4 [5] which are able to perform the oxidation of thioethers to their sulfoxides. Along this line we have found that stable complexes of iron(III)[6] and copper(II)[7] nitrates with dinitrogen tetroxide are efficiently able to proceed oxidation of thioethers to their corresponding sulfoxides in excellent yields. $Fe(NO_3)_3 . 1.5 N_2O_4$ is able to perform the transformations in less than 15 min. in dichloromethane at room temperature (Table 1). Thioethers with carbon-carbon double bonds form complexes with the reagents, and the reaction does not proceed further. $Cu(NO_3)_2 . N_2O_4$ behaves differently from its iron(III) analogue and attacks thioethers which in their structures an aromatic moiety is attached directly to sulfur atom. This is demonstrated by a competitive reaction between methylphenyl and dipropyl thioethers (Scheme 1).



Scheme 1

Recently, much attention has been paid to methods and reactions which are performed either in solid phase or in the absence of solvents.[8,9] These reactions are of interest from different points of views. Therefore, we have also tried oxidations of the thioethers in the absence of solvents. Surprisingly, the rate of the oxidations increases drastically and the reactions are completed immediately in

Table 1. Oxidation of Thioethers to Their Corresponding Sulfoxides with the Reagents (I) and (II).

Entry	R_1	R_2	Time (min)		Yield%[a]	
			I	II	I	II
1	C_6H_5	CH_3	-[b]	-[b]	96	98
2	C_6H_5	C_2H_5	-[b]	-[b]	97	95
3	C_6H_5	C_4H_9	-[b]	-[b]	96	100
4	C_6H_5	$C_6H_5CH_2$	-[b]	-[b]	98	99
5	C_3H_7	C_3H_7	5	-[b]	98	95
6	C_4H_9	C_4H_9	5	-[b]	99	94
7		$(CH_3)_2CH$	15	-[b]	91	95

a) Isolated yields after column chromatography.

b) Reactions were occured immediately.

I) $Fe(NO_3)_3.1.5N_2O_4/CH_2Cl_2$/rt/oxid/subst=1

II) $Fe(NO_3)_3.1.5N_2O_4$/without solvent/rt/oxid/subst=1

excellent yields (91-100%, Tables 1,2). The selectivity behaviour of $Cu(NO_3)_2.N_2O_4$ remained the same as in the presence of solvents.

In order to show the oxidation ability of the reagents we have compared the results with the recently reported methods (Table 3).[10-12]

In conclusion, these oxidants which their preparation is easy, could be considered as a bench top reagents because they are stable up to 70°C and they can be stored in a capped bottle for months without loosing their activities. Fast rate of reactions, excellent yields of the products, ability to work either in solutions or in the absence of solvents, selectivity, and easy work-up are the points worthy of mention for these oxidants.

Table 2. Oxidation of Thioethers to Their Corresponding Sulfoxides with The Reagents (III) and (IV).

Entry	R_1	R_2	Time (min)		Yield%[a]	
			III	IV	III	IV
1	C_6H_5	CH_3	10	-[b]	98	97
2	C_6H_5	C_2H_5	10	-[b]	95	95
3	C_6H_5	C_4H_9	15	-[b]	91	97
4	C_6H_5	$C_6H_5CH_2$	45	10	96	100
5	C_3H_7	C_3H_7	No reaction		No reaction	
6	C_4H_9	C_4H_9	No reaction		No reaction	
7		$(CH_3)_2CH$	No reaction		No reaction	

a) Isolated yields after column chromatography.

b) Reactions were occurred immediately.

III) $Cu(NO_3)_2.N_2O_4/CH_2Cl_2$/rt/oxid/subs=2

IV) $Cu(NO_3)_2.N_2O_4$/without solvent/rt/oxid/subst=2

EXPERIMENTAL:

General: Chemicals were either prepared in our laboratories or were purchased from Fluka, Merck, B.D.H., Aldrich and Riedel Dehaen AG Chemical Companies. Products were characterized by comparison of their physical data with those of authentic samples. All yields refer to isolated products. IR and UV spectra were recorded on a Perkin Elmer 781 and Pye Unicam 8725 spectrometers. NMR spectra were recorded on a Bruker DPX 250. Mass spectra were recorded on a Shimadzu GCMS-QP 1000EX. The purity determination of the substrates and reaction monitoring were accomplished by TLC on Silica gel polygram SILG/UV 254 plates or GLC on a Shimadzu GC-14A instrument. All the solvents were

Table 3. Comparision of the Results Obtained by our Methods with Those Reported for the Other Reagents.

		Yield% (RXn Times, min)						
		Our Methods				Reported Methods		
R_1	R_2	I	II	III	IV	V^{10}	VI^{11}	VII^{12}
C_6H_5	CH_3	96(a)	98(a)	98(10)	97(a)	98(90)	89(15)	82(120)
C_6H_5	C_2H_5	97(a)	95(a)	95(10)	95(a)	99(90)	84(15)	-
C_6H_5	C_4H_9	96(a)	100(a)	91(15)	97(a)	-	84(20)	-
C_6H_5	$C_6H_5CH_2$	98(a)	99(a)	96(45)	100(10)	99(90)	-	-
C_3H_7	C_3H_7	98(5)	95(a)	no reaction	-	-	85(20)	-
C_4H_9	C_4H_9	99(5)	94(a)	no reaction	-	-	87(25)	84(30)
	$(CH_3)_2CH$	91(15)	95(a)	no reaction	-	-	-	-

I) $Fe(NO_3)_3.1.5\ N_2O_4/CH_2Cl_2/rt.$

II) $Fe(NO_3)_3.1.5\ N_2O_4$/without solvent/rt.

III) $Cu(NO_3)_2.N_2O_4/CH_2Cl_2/rt.$

IV) $Cu(NO_3)_2.N_2O_4$/without solvent/rt.

V) $(n\text{-}Bu)_2S_2O_8/CH_2Cl_2/rt.$

VI) $NaClO_2/Al_2O_3/Mn^{3+}/CH_2Cl_2/rt.$

VII) $H_2O_2/MeCN/K_2CO_3/CH_3OH.$

a) Reaction was occurred immediately.

completely dried and predistilled, particularly for preparation and using of metal nitrate-N_2O_4 adducts.

Generation of NO_2-N_2O_4 gas[13]

Lead(II) nitrate (100g) was crushed into powder and was dried in an oven at 120°C for three days. The resulting powder was transfered into a one-necked round-bottomed flask (250 ml) which was equipped with an air condenser and a gas trap containing P_2O_5. The flask was heated by a Bunsen burner to generate brownish-red NO_2-N_2O_4 gas which was used immediately for the subsequent preparation of the metal nitrate complexes.

Preparation of $Fe(NO_3)_3 . 1.5\ N_2O_4$.[6]

A solution of anhydrous $FeCl_3$(16.25g, 0.1 mol) in EtOAc (100 ml) was prepared in a three-necked round-bottomed flask (250 ml) which was equipped with a magnetic stirrer, gas inlet tube, thermometer and a drying tube and was cooled to -10°C with an ice-salt bath while being stirred. Generated NO_2-N_2O_4 gas was bubbled through this solution for about 1h. The solvent was evaporated under vacuum at 50°C to give $Fe(NO_3)_3 . 1.5\ N_2O_4$ as brownish deliquescent solid compound (38 g, 100%).

Preparation of $Cu(NO_3)_2 . N_2O_4$.[7]

A solution of copper powder (16g, 0.25 mol) in EtOAc (500 ml) was prepared in a one liter three-necked round-bottomed flask which was equipped with a magnetic stirrer, gas inlet tube, thermometer and drying tube. The solution was cooled to -10°C with an ice-salt bath while being stirred. Generated NO_2-N_2O_4 gas was bubbled through this solution in three 30 min periods during 2 h. The reaction mixture was filtered after 10 h, and the solvent was evaporated under vacuum at 50°C to give $Cu(NO_3)_2 \cdot N_2O_4$ as blue deliquescent solid compound (30.5 g, 44%).

Oxidation of Benzylphenyl Thioether to its Corresponding Sulfoxide with $Cu(NO_3)_2 . N_2O_4$. A Typical Procedure.

To a solution of benzylphenyl thioether (400 mg, 2 mmol) in CH_2Cl_2(4ml), $Cu(NO_3)_2 \cdot N_2O_4$(1.12 g, 4 mmol) was added. The reaction mixture was stirred vigorously at room temperature for 0.75 h. The progress of the reaction was monitored by TLC. To the resulting reaction mixture saturated solution of NaCl (20 ml) was added. The mixture was extracted with CH_2Cl_2 (3 x 40 ml). The layers of CH_2Cl_2 were combined together and dried over anhydrous $MgSO_4$. The solvent was evaporated and the resulting crude material was presorbed on Silica gel (2 g) and was applied on a short pad of Silica gel and eluted with petroleum ether/acetone 3:2. Evaporation of the solvent afforded the pure sulfoxide in 414 mg, 96%, mp 123-124°C, (lit.[10] mp 122-125°C) (Table 2,entry 4).

Solvent Free Oxidation of Benzylphenyl Thioether to the Corresponding Sulfoxide with $Fe(NO_3)_3 . 1.5 N_2O_4$ Under Solid Phase Conditions. A Typical Procedure.

Benzylphenyl thioether (0.4 g, 2 mmol) and $Fe(NO_3)_3 \cdot 1.5\ N_2O_4$(0.76 g, 2 mmol) were mixed together in a mortar at room temperature. The reaction was completed immediately. To the resulting mixture saturated NaCl solution (20 ml) was added and extracted with CH_2Cl_2 (3 x 40 ml). The organic layers were separated, combined together, and dried over anhydrous $MgSO_4$. The solvent was evaporated and the resulting crude material was presorbed on Silica gel (2 g) and was applied on a short column of Silica gel and eluted with petroleum ether/acetone 3:1. Evaporation of the solvent afforded the pure sulfoxide in 427 mg, 99%, mp 121-122°C (lit.[10] mp 121-125°C) (Table 1, Entry 4).

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