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Dinitrogen Tetraoxide Complexes of Iron(III) and Copper(II) as Efficient and Mild Reagents for Oxidation of Hydroxy Compounds

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$Fe(NO_3)_3 \cdot 1.5N_2O_4$ is a highly efficient reagent for the oxidation of various classes of hydroxy compounds in dichloromethane at room temperature, or in the absence of solvent. $Cu(NO_3)_2 \cdot N_2O_4$ oxidizes different hydroxy compounds in refluxing carbon tetrachloride and is a highly selective reagent for oxidation of primary benzylic alcohols in refluxing EtOAc.

The low oxidation ability of copper(II) and iron(III) nitrates has been overcomed by impregnating these on different supporting agents.[1—5] Among the supported reagents, clayfen and claycop, clay supported iron(III) and copper(II), are introduced as multi-purpose reagents.[2] Although claycop is stable at room temperature,[2b] cleyfen is unstable and may be stored for a few days under pentane[2a] In comparison with hydrated metal nitrates, the anhydrous ones show exceptional reactivity towards organic substrates. Unfortunately, they are usually unstable for isolation or are unknown.[2,6] Dinitrogen tetraoxide complexes of metal nitrates have been regarded as being a source for the in situ generation of anhydrous metal nitrates by heating.[6] The use of gaseous N_2O_4 in the oxidation of benzylic alcohols,[7] sulfides,[8] and thiols,[9] oxidative deoximation to multiple ketones,[10] cleavage of carboxamides of carboxylic acids,[11] and oxidation of ethers in the presence of silica gel[12] are reported.

During the last decade we have been interested in studying the oxidation ability of compounds consisting of strong oxidizing moieties e.g. Ce(IV) and $H_2IO_6^{3-}$, CrO_4^{2-},[13a,13d] or Cu(II) and MnO_4^-,[13e] or Ag^{2+} and $S_2O_8^{2-}$ [13f,13g] as well as the oxidizing abilities of $Fe(NO_3)_3 \cdot 1.5N_2O_4$[6b,14] and $Cu(NO_3)_2 \cdot N_2O_4$,[6b,15] which consist of two oxidizing species: N_2O_4, Fe(III) and Cu(II) nitrates.

Results and Discussion

$Fe(NO_3)_3 \cdot 1.5N_2O_4$[14] and $Cu(NO_3)_2 \cdot N_2O_4$[15] were prepared according to the reported procedures by passing N_2O_4[16] gas into a mixture of anhydrous $FeCl_3$ or copper powder in EtOAc, respectively at −10 °C. Both reagents are stable compounds up to 70 °C, and can be stored at room temperature in a capped bottle for months without any loss of activity. Having metal nitrates and N_2O_4 as two oxidizing agents together, each compound showed a synergetic effect on the oxidation of hydroxy compounds to their corresponding carbonyl analogues. This is parallel to our recent observation concerning the use of these complexes in the nitration of phenolic compounds,[17a] catalytic coupling of thiols,[17b] and the selective oxidation of thioethers.[17c] The oxidation of different classes of alcohols with $Fe(NO_3)_3 \cdot 1.5N_2O_4$ proceeds very efficiently at room temperature. Primary and secondary saturated and benzylic alcohols were converted to their corresponding aldehydes and ketones in excellent yields in CH_2Cl_2 (Table 1). Alcohols with carbon–carbon double bonds form complexes with the reagent, and the reactions do not proceed further (Entry 15, Table 1).

Primary and secondary saturated and benzylic alcohols are oxidized to their carbonyl compounds with $Cu(NO_3)_2 \cdot N_2O_4$ in refluxing carbon tetrachloride (Table 1). $Cu(NO_3)_2 \cdot N_2O_4$ is a good reagent for the oxidation of α-hydroxy ketones to their corresponding diketones in excellent yields. Carbon–carbon bond cleavage has also been observed among the substrates under our studies (Entry 6, Table 2). 1,2-Diphenylethanediol is converted very easily to benzil with a high yield (Table 2, Entry 5). In contrast with $Cu(NO_3)_2 \cdot N_2O_4$, the iron analogue $Fe(NO_3)_3 \cdot 1.5N_2O_4$ is a rather sluggish reagent for this purpose, which also forms stable complexes with some α-hydroxy ketones and 1,2-diols (Entry 2,5 Table 2). $Cu(NO_3)_2 \cdot N_2O_4$ shows high selectivity for the oxidation of primary benzylic alcohols in refluxing EtOAc in the presence of the other types of hydroxy compounds (Table 3).

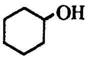
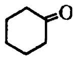
Due to recent attention on the solid phase, or solvent-free reactions,[18,19] some of the oxidations are being performed with the reagents in the absence of solvent. In has been observed that the reaction of $Cu(NO_3)_2 \cdot N_2O_4$ with alcohols under neat conditions is not clean, and that the reaction times are too long (Table 4). In contrast, the reaction of $Fe(NO_3)_3 \cdot 1.5N_2O_4$ with alcohols under the same reaction conditions is clean and fast and the yields of the products are also excellent (Table 4).

In (Table 5) we compare some of our results with some of those reported based on other methods.

Conclusions

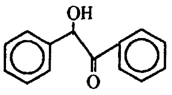
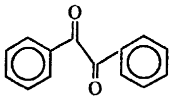
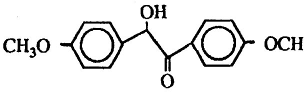
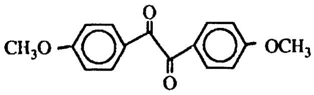
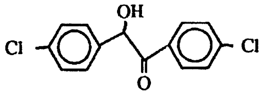
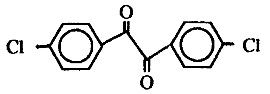
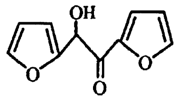
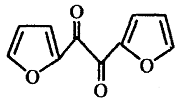
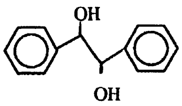
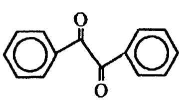
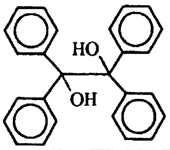
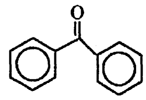
In this study two new oxidizing agents were introduced for the oxidation of hydroxy compounds. We observed that

Table 1. Oxidation of Some Hydroxy Compounds with $Fe(NO_3)_3 \cdot 1.5N_2O_4$ and $Cu(NO_3)_2 \cdot N_2O_4$

Entry	Substrate	Product	Mp or Bp/Torr	$Fe(NO_3)_3 \cdot 1.5N_2O_4$[a]			$Cu(NO_3)_2 \cdot N_2O_4$					
			°C	Time	Oxid.	Yield[b]	in CCl_4			in EtOAc		
				min	Subst.	%	Time	Oxid.	Yield	Time	Oxid.	Yield
							min	Subst.	%	min	Subst.	%
1	$PhCH_2OH$	$PhCHO$	175—178/760	a[c]	1	90	10	1.5	92	30	2	89
2	$4\text{-}CH_3C_6H_4CH_2OH$	$4\text{-}CH_3C_6H_4CHO$	82— 85	a[c]	1	100	30	1.5	90	120	2	95
3	$4\text{-}CH_3OC_6H_4CH_2OH$	$4\text{-}CH_3OC_6H_4CHO$	245—248/760	a[c]	1	95	30	1.5	93	75	1.5	93
4	$4\text{-}ClC_6H_4CH_2OH$	$4\text{-}ClC_6H_4CHO$	42— 45	45	1	93	30	2.5	95	60	6	94
5	$4\text{-}BrC_6H_4CH_2OH$	$4\text{-}BrC_6H_4CHO$	53— 56	60	1	98	45	2.5	98	135	6	93
6	$4\text{-}O_2NC_6H_4CH_2OH$	$4\text{-}O_2NC_6H_4CHO$	103—106	90	2	100	200	4	100	48(h)	10	80
7	$PhCHOHCH_3$	$PhCOCH_3$	172/760	15	1	85	30	2	82	No reaction		
8	$PhCHOHC_2H_5$	$PhCOC_2H_5$	218/760	15	1	88	30	2	88	No reaction		
9	$PhCHOHPh$	$PhCOPh$	49— 51	a[c]	1	86	30	1.5	85	90	1.5	70
10	$PhCH_2CH_2CH_2OH$	$PhCH_2CH_2CHO$	97— 98/12	10	1.5	96	30	3	86	No reaction		
11	$CH_3(CH_2)_6CH_2OH$	$CH_3(CH_2)_6CHO$	135/100	20	1.5	91	30	3	82	No reaction		
12	$CH_3(CH_2)_5CHOHCH_3$	$CH_3(CH_2)_5COCH_3$	171—172/760	10	2	89	60	3	86	No reaction		
13			154—156/760	30	2	100[d]	60	3	100[d]	No reaction		
14	Hydroquinone	Benzoquinone	113—114	a[c]	1	92	—	—	—	15	1	89
15	$PhCH{=}CH\text{-}CH_2OH$[e]	—	—	—	—	—	—	—	—			

a) Reaction occurs in CH_2Cl_2 at room temperature. b) Isolated yield after purification. c) Reaction occur immediately. G. C. yield. e) Complexation occurs with both reagents.

Table 2. Oxidation of α-Hydroxy Ketones and Diols with $Fe(NO_3)_3 \cdot 1.5N_2O_4$ and $Cu(NO_3)_2 \cdot N_2O_4$ in Refluxing EtOAc

Entry	Substrate	Product	Mp or Bp/Torr	$Fe(NO_3)_3 \cdot 1.5N_2O_4$[a]			$Cu(NO_3)_2 \cdot N_2O_4$		
			°C	Time	Oxid.	Yield[a]	Time	Oxid.	Yield[a]
				h	React.	%	h	React.	%
1			94—95	2.5	3	100	1	1.5	93
2			132—135	—[b]	—	—[b]	7	1.5	100
3			198—199	3.5	3	86	2	1.5	89
4			162—164	0.5	3	72	0.25	1.5	90
5			94—95	—	—	—[b]	2.3	3	94
6			49—50	—[c]	2	100	1.5	3	94

a) Isolated yields by column chromatography. b) Complexation occurs. c) Reaction occur immediately.

$Fe(NO_3)_3 \cdot 1.5N_2O_4$ is more efficient and reacts under milder conditions than does $Cu(NO_3)_2 \cdot N_2O_4$. The latter reagent shows high selectivity for the oxidation of primary benzylic alcohols in refluxing EtOAc. In addition to the reactivity, the efficiency and mildness of the reaction conditions (in solution and under neat conditions), the stability, ease of preparation

Table 3. Competitive Oxidation of Benzyl Alcohol with $Cu(NO_3)_2 \cdot N_2O_4$ in Refluxing EtOAc

Entry No.	Substrate	Product	Oxid. / Subst.	Time / min	Yield[a] / %
1	$PhCH_2OH$	PhCHO			100
	$PhCHOHCH_3$	$PhCOCH_3$	2	30	20
2	$PhCH_2OH$	PhCHO			100
	$CH_3(CH_2)_6CH_2OH$	$CH_3(CH_2)_6CHO$	2	30	8
3	$PhCH_2OH$	PhCHO			100
	$CH_3(CH_2)_5CHOHCH_3$	$CH_3(CH_3)_5COCH_3$	2	30	0

a) G. C. yields.

Table 4. Oxidation of Some Hydroxy Compounds Without Solvent at Room Temperature

Entry	Substrate	Product	$Fe(NO_3)_3 \cdot 1.5N_2O_4$ Time / h	Oxid. / React.	Yield[a] / %	$Cu(NO_3)_2 \cdot N_2O_4$ Time / h	Oxid. / React.	Yield[a] / %
1	$4\text{-}CH_3C_6H_4CH_2OH$	$4\text{-}CH_3C_6H_4CHO$	—[b]	1	91	22	2	90
2	$4\text{-}BrC_6H_4CH_2OH$	$4\text{-}BrC_6H_4CHO$	0.08	1	100	26	2.5	100
3	$4\text{-}O_2NC_6H_4CH_2OH$	$4\text{-}O_2NC_6H_4CHO$	0.16	2	96	25	6	100
4	$PhCH(OH)CH_2CH_3$	$PhCOCH_2CH_3$	—[b]	1.5	80	26	2	85
5	$PhCH_2CH_2CH_2OH$	$PhCH_2CH_2CHO$	—[b]	1.5	85	24	3	No reaction
6	$CH_3(CH_2)_6CH_2OH$	$CH_3(CH_2)_6CHO$	—[b]	1.5	80	24	3	No reaction
7	PhCH(OH)COPh	—	24	3	No reaction	24	3	No reaction

a) Isolated yield by column chromatography. b) Reaction were occured immediately.

Table 5. Comparison of Oxidation of Benzoin (I) and Benzyl alcohol (II) by Different Methods

Reagent	Oxid./Subst. I	Oxid./Subst. II	Time/h I	Time/h II	Yield/% I	Yield/% II
$Cu(NO_3)_2/SiO_2$[1] [a]	2	2	6	0.5	96	90
$Cu(NO_3)_2/H\text{-}SiO_2$[5]	2.5	2	10	0.08	55	95
$Cu(NO_3)_2 \cdot N_2O_4$	1.5	1.5	0.8	0.16	93	92
$Fe(NO_3)_3/Clay$[2] [a]	0.5	0.5	5	3	95	85
$Fe(NO_3)_3 \cdot 1.5N_2O_4$	3	1	2.5	—[a]	100	90

a) Reaction was occured immediately.

of reagents, easy work-up, and high yields of the products could be considered as other advantages of the introduced methods.

Experimental

General: The chemicals were either prepared in our laboratories or were purchased from Fluka, Merck, and Aldrich Chemical Companies. The products were characterized by comparison of their physical data with those of authentic samples. IR and UV spectra were recorded on 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 of the solvents were dried and predistilled. The yields reported are the isolated yields, unless otherwise indicated.

General Procedure for Oxidation of Hydroxy Compounds with $Fe(NO_3)_3 \cdot 1.5N_2O_4$ and $Cu(NO_3)_2 \cdot N_2O_4$ as Oxidizing Agents in the Presence of Solvent. To a solution of hydroxy compound (2 mmol) in an appropriate solvent (4 ml) oxidant was added (the molar ratio of the metal nitrate dinitrogen tetraoxide complexes to the substrates were optimized, Tables 1, 2, 3, and 4. The mixture was stirred vigorously at room temperature or under reflux conditions. The progress of the reaction was monitored by TLC, or was followed by GLC. The reaction mixture was mixed with silica gel (5 g), and the resulting solid mixture was applied on a short column of silica gel. The column was eluted with petroleum ether : acetone (9 : 1). The pure product was obtained in 80—100% yields (Tables 1, 2, 3, and 4).

Oxidation of 4-Bromobenzyl Alcohol to 4-Bromobenzaldehyde with $Fe(NO_3)_3 \cdot 1.5N_2O_4$ as a Typical Procedure. To a solution of 4-bromobenzyl alcohol (0.366 g, 2 mmol) in CH_2Cl_2 (4 ml), $Fe(NO_3)_3 \cdot 1.5N_2O_4$ (0.760 g, 2 mmol) was added, the mixture was stirred magnetically at room temperature for 1 h. The progress of the reaction was followed by TLC. The reaction mixture was mixed with silica gel (5 g), and the resulting solid was applied on a short column of silica gel. The column was eluted with petroleum ether : acetone (9 : 1). The solvent was evaporated and 4-bromobenzaldehyde (0.362 g, 100%, mp 54 °C, Lit,[20] mp 56—58 °C) was obtained (Entry 5, Table 1).

Oxidation of Benzoin to Benzil with $Cu(NO_3)_2 \cdot N_2O_4$ as a Typical Procedure for Oxidation of Acyloins. To a solution of benzoin (0.424 g, 2 mmol) in EtOAc (4 ml), $Cu(NO_3)_2 \cdot N_2O_4$ (0.840 g, 3 mmol) was added and the reaction mixture was stirred vigorously under reflux conditions for 1 h. The progress of the reaction was monitored by TLC. The reaction mixture was mixed with silica gel (5 g) and the resulting mixture was applied on a short column of silica gel. The column was eluted with petroleum ether : acetone (9 : 1). After evaporation of the solvent, benzil was obtained as a pale-yellow crystalline material (0.39 g, 93%, mp 95—96 °C, Lit,[20] mp 94—95 °C) (Entry 1, Table 2).

Neat Oxidation: Oxidation of 4-Nitrobenzyl Alcohol to 4-Nitrobenzaldehyde with $Fe(NO_3)_3 \cdot 1.5N_2O_4$ as a Typical Procedure. A mixture of 4-nitrobenzyl alcohol (0.306 g, 2 mmol) and $Fe(NO_3)_3 \cdot 1.5N_2O_4$ (1.52 g, 4 mmol) was magnetically agitated at room temperature for 10 min. The progress of the reaction was followed by TLC. To the resulting mixture were added acetone (2 ml) and silica gel (5 g). The resulting powder mixture was applied on a silica-gel column and eluted with petroleum ether : acetone (9 : 1) to afford 4-nitrobenzaldehyde (0.290 g, 96%, mp 103—104 °C, Lit,[20] mp 103—105 °C) (Entry 3, Table 4).

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