A Novel Method. The Synthesis of Ketones and Azobenzenes Using Supported Permanganate[1]

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Abstract: The heterogeneous use of potassium permanganate, supported on copper(II) sulfate pentahydrate, provides a simple and effective means for oxidizing amines. Primary aliphatic amines, such as *sec*-butylamine, are oxidized to the corresponding carbonyl compounds in good to excellent yields. Primary aromatic amines, such as 4-chloroaniline, are converted quantitatively into the corresponding azo compounds. Carbon–carbon bond cleavage, which usually occurs when alkylbenzene side chains are oxidized by permanganate under homogeneous conditions, does not occur. Under appropriate reaction conditions carbon–hydrogen bond cleavage at the benzylic position, known to occur under heterogeneous permanganate conditions, is also eliminated. For example, a quantitative yield of bis(2,4,6-trimethylphenyl)diazene is obtained from the oxidation of 2,4,6-trimethylaniline using small amounts of permanganate and copper(II) sulfate pentahydrate.

Key words: heterogeneous permanganate oxidation, amines, copper(II) sulfate pentahydrate, ketones, azobenzenes

The last three decades have witnessed the development and utilization of heterogeneous reactions in synthetic organic chemistry. For example, it has been documented that permanganate can be used effectively as a selective heterogeneous oxidant in organic solvents, such as dichloromethane, if it is adsorbed onto a hydrated metal cation.[2] To obtain high yields while employing a simple, straightforward experimental procedure, one may consider the use of heterogeneous reactions. In fact, the literature contains descriptions of the products that are obtained from heterogeneous permanganate oxidations of numerous classes of compounds such as alcohols,[3–5] sulfides and selenides,[6] thiols,[7] enamines[8] and arenes.[9,10]

Previous reports have indicated that the heterogeneous use of permanganate dramatically modifies its selectivity. This is apparent, for example, from the comparative oxidations of arenes; in homogeneous solutions degradation of the side chain occurs resulting in the formation of benzoic acid derivatives.[11] However, under heterogeneous conditions permanganate is a milder reagent that oxidizes side chains at the benzylic positions without carbon–carbon bond cleavage; ketones and alcohols are obtained in good yields when the side chains are secondary or tertiary, respectively.[12]

In this paper, we would like to describe a method for the oxidation of primary aliphatic and aromatic amines while emphasizing the remarkable advantage of using heterogeneous over homogeneous oxidation reactions in particular, when potassium permanganate adsorbed onto copper(II) sulfate pentahydrate is used as the oxidizing reagent.

The products obtained from the heterogeneous oxidation of primary aliphatic and aromatic amines by permanganate are similar to those that have been reported for homogeneous permanganate oxidations. Rawalay and Shechter, for example, have reported that cyclohexylamine is converted into cyclohexanone in 75% yield when treated with permanganate in an aqueous solution of *tert*-butyl alcohol.[13] Similarly, Johnson and Hornstein undertook an investigation into the homogeneous ferrate oxidation of aniline and its para-substituted analogues.[14] Although the focal point was exclusively of a kinetic nature, the report revealed an important discovery; conversion of arylamines either nitro- or azo compounds could be achieved dependent upon the pH of the reaction medium. Therefore, it is apparent that the use of heterogeneous conditions does not result in the formation of new or unexpected products when primary aliphatic and aromatic amines are oxidized. In this respect, it is not similar to the oxidation of other substrates, such as thiols, where different products are obtained under heterogeneous[7] and homogeneous conditions.[15] The value of the heterogeneous procedure is nevertheless very obvious; better yields, milder conditions and the products are more easily isolated. In a typical procedure for the work that is represented here, a solution of the amine in dichloromethane is added to potassium permanganate, adsorbed onto hydrated copper(II) sulfate, and the reaction takes place with stirring at room temperature or under reflux. After a designated period, typically 24 h, the isolation of products in quantitative yields is easily achieved by filtration and flash evaporation of solvent.

Similarly, it has been reported that dihaloazobenzenes were obtained from the heterogeneous permanganate oxidation of haloanilines; however, no yields were reported and the oxidation of other aniline derivatives was not attempted.[16] Furthermore, in a somewhat similar reaction, haloanilines are oxidatively coupled by bis(2,2-bipyridyl)copper(II) permanganate to give the corresponding azo compounds in moderate yields.[17] Although both experimental methods are similar, the use of supported permanganate offers several practical advantages; better yields, simpler experimental procedure, and the utilization of commercially available oxidant that is safe to handle. On the other hand, the bipyridyl reagent has to be prepared and is extremely sensitive to sintered glass and

metallic objects as they cause the oxidant to burst into flames. Moreover, Hedayatullah and Dechatre have reported that some primary aromatic amines could be oxidized into the corresponding azo compounds using silver carbonate in boiling benzene.[18] In addition to the carcinogenic risk of benzene, the oxidation of few amines was attempted and the yield ranged between 30% for 1,2-bis(2,4,-dimethylphenyl)diazene to 75% for 1,2-bis (2,4,6,-trimethylphenyl)diazene. Therefore, it is expected that the heterogeneous permanganate procedure may supplant all other heterogeneous and all homogeneous methods for the oxidation of primary aliphatic and aromatic amines.

As illustrated by the reactions depicted in Equations 1 and 2, using copper(II) sulfate pentahydrate as the solid support, almost quantitative yields of ketones and azobenzenes could be produced from the heterogeneous permanganate oxidations of primary aliphatic and aromatic amines respectively.

As could be seen from Equation 2 and Table 1, several arylamines were converted into the corresponding azo compounds in excellent yields; results that clearly demonstrate the high selectivity of permanganate when used under *appropriate* heterogeneous conditions. The synthetic value of these results is apparent when it is noted that under homogeneous conditions carbon–carbon bond cleavage occurs readily at the benzylic position.[11] Moreover, in previous investigations it was reported that under given heterogeneous reaction conditions, permanganate could be used for the oxidation of arenes into carbonyl compounds.[9,12] In our attempt to pinpoint a practical, economical and simple method for the quantitative synthesis of
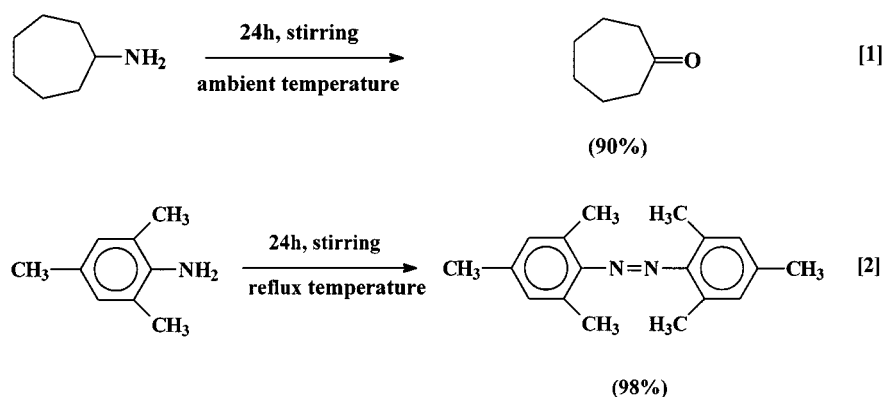
Table 1 Heterogeneous Permanganate Oxidation of Amines

Substrate[a]	Oxidant (g)	Conditions[b]	Products	Yield (%)
Cyclobutylamine	2.0	R, 24h	Cyclobutanone	87[c]
Cyclohexylamine	2.0	R, 24h	Cyclohexanone	68[c]
sec-Butylamine	1.5	R, 24h	2-butanone	100[c]
1-Methylhexylamine	1.5	R, 24h	2-heptanone	68[c]
Cycloheptylamine	2.0	R, 48h	Cycloheptanone	95[c]
Cyclooctylamine	2.5	R, 24h	Cyclooctanone	90[d]
Aniline[e]	2.0	R, 48h	Azobenzene	100[c]
				78[d]
2-Butylaniline[e]	1.5	S, 48h	1,2-Bis(2-butylphenyl)diazene	93[c]
2-Isopropylaniline[e]	1.5	S, 48h	1,2-Bis(2-isopropylphenyl)diazene	88[c]
4-sec-Butylaniline[e]	1.5	S, 48h	1,2-Bis(4-*sec*-butylphenyl)diazene	95[c]
				77[d]
2-sec-Butylaniline[e]	1.5	S, 48h	1,2-Bis(2-*sec*-butylphenyl)diazene	90[c]
4-Butylaniline[e]	1.5	S, 48h	1,2-Bis(4-butylphenyl)diazene	83[c]
4-Isopropylaniline[e]	1.5	S, 48h	1,2-Bis(4-isopropylphenyl)diazene	94[c]
4-Iodoaniline[e]	1.5	S, 48h	1,2-Bis(4-iodophenyl)diazene	100[c]
				87[d]
4-Chloroaniline[e]	1.5	S, 48h	1,2-Bis(4-chlorophenyl)diazene	100[c]

[a] 2.0 mmol were used.
[b] R: stirring under reflux; S: stirring at ambient temperature.
[c] gc.
[d] Isolated.
[e] Freshly distilled prior to use.

substituted azobenzenes, the experimental conditions were carefully selected resulting in an excellent selectivity. Under mild conditions that are described in this article (ambient temperature, shorter duration, and or utilizing smaller amounts of oxidant), oxidation of side chains could be eliminated.

Several solid supports have been used for heterogeneous reactions, however, adsorption of permanganate onto copper(II) sulfate pentahydrate appears to be the most efficient in promoting the heterogeneous oxidation reactions. The results obtained from the oxidation of some alcohols using different solid supports are compared in Tables 2[3,19] and 3.[3] Although the same products are obtained with all solid support systems investigated, it is apparent that better yields are obtained in shorter reaction times or utilizing smaller amounts of oxidant when copper(II) sulfate pentahydrate is used.

^{1}H NMR spectra were recorded at 25 °C on a Bruker QNP spectrometer (200 MHz).IR spectra were recorded on a Perkin-Elmer FT-IR 1600 spectrophotometer. Separation of the products was performed using gas chromatograph (HP 5890) equipped with a 50-meter, cross-linked methyl silicone capillary column, and identified by use of an HP 5970A mass selective detector. CH_2Cl_2 was purified by refluxing over potassium permanganate, using a small amount of phase transfer agent (tetrabutylammonium chloride) for 24h, followed by distillation. The purity of the solvent was confirmed, by the use of gas chromatography to be 99.9% or better. The amines,

Table 2 Heterogeneous Permanganate Oxidation of 2-Decanol Using a Variety of Solid Supports[a]

Solid Support (g)	$KMnO_4$ (g)	Decan-2-one (Yield)
$CuSO_4 \cdot 5H_2O$ (0.5)	0.7	100%
K_2SO_4 (2.0)	1.0	13%
$BaCl_2 \cdot 2H_2O$ (2.0)	1.0	87%
$CaSO_4 \cdot 2H_2O$ (2.0)	0.6	11%
$CaSO_4 \cdot 2H_2O$ (2.0)	1.0	93%
$MgSO_4 \cdot 7H_2O$ (2.0)	1.0	90%
$MgSO_4 \cdot 7H_2O$ (2.0)	0.6	66%
$Al_2(SO_4)_3 \cdot 18H_2O$ (2.0)	2.0	80%
$NiSO_4 \cdot 6H_2O$ (2.0)	1.0	92%
$CoSO_4 \cdot 7H_2O$ (2.0)	1.0	84%
$MnCl_2 \cdot 4H_2O$ (2.0)	2.0	79%
MnO_2[b] (1.0)	1.0	77%

[a] Decan-2-ol (0.50 g, 3.2 mmol) was refluxed with the oxidant in (H_2Cl_2/20 ML) for 24 h.

[b] 200 μL of H_2O added.

obtained from the Aldrich Chemical Co., were purified by distillation, flash chromatography or recrystallization prior to use. Purity of the amines was confirmed by melting points, refractive indices, NMR and/or glc analysis. Identity of the products was validated by comparison of spectroscopic data with those published for the same compound. The oxidant was prepared by grinding equal amounts, by weight, of $KMnO_4$ and $CuSO_4 \cdot 5H_2O$ in a mortar until homogeneous.

Oxidation of Amines; General Procedure

The amine (2.0 mmol) in CH_2Cl_2 (20 mL) was placed in a 50 mL round bottomed flask. The oxidant (2.0g) was added and the heterogeneous mixture stirred at ambient temperature or under reflux for 48 h. The progress of the reaction was followed by tlc or glc until no starting material could be detected. After cooling to ambient temperature, the product was then filtered through Celite and the residue washed thoroughly with CH_2Cl_2 (3 x 10 mL) and Et_2O (3 x 10 mL). The product was isolated by flash evaporation and identified from spectroscopic analysis.

Following the general procedure the following compounds could be prepared:

Cycloheptanone

Oxidation of cycloheptylamine (0.226 g, 2.0 mmol) gave cycloheptanone (0.202 g, 1.80 mmol, 90%). The reaction was complete after stirring for 24 h at ambient temperature.

^{1}H NMR ($CDCl_3$): δ = 2.3–2.5, m, 8H; 1.5–1.7 m, 4H.

IR (neat): 2925, 2855, 1702, 1455, 1342, 1318 cm^{-1}.

MS: m/z (rel.int.) = 112(M$^+$,51), 97 (7.2), 84(33), 68(80), 55(100), 43(17), 42(50), 41(72).

More examples of the oxidation of aliphatic amines have been summarized in Table 1.

1,2-Bis(2,4,6-trimethylphenyl)diazene

Oxidation of 2,4,6-trimethylaniline (0.270g, 2.0 mmol) gave 0.261 g (0.98 mmol, 98%) of 1,2-bis(2,4,6-trimethylphenyl)diazene. The reaction was complete after stirring under reflux for 24h. The product was identified from its melting point, 75–77 °C (lit. 74 °C),[18] and spectroscopic analysis.

^{1}H NMR ($CDCl_3$): δ = 6.88 (s, 4H); 2.30 (s, 12H); 2.25 (s, 6H).

IR(KBr): ν = 3016, 2953, 2915, 2843, 1601, 1569, 1458, 1432, 1407, 1376 cm^{-1}.

MS: m/z (%rel.int.) = 266 (M$^+$,17), 223 (10), 119 (100), 91 (21), 77(11).

1,2-Bis(2,4,-dimethylphenyl)diazene

After 48h stirring at reflux temperature, oxidation of 2,4-dimethylaniline (0.242g, 2.0 mmol), gave 1,2-bis(2,4-dimethylphenyl)diazene (0.224 g, 0.94 mmol, 94%); melting point 126–128 °C (lit. 128°).[18]

^{1}H NMR ($CDCl_3$): δ = 7.55 (d, 2H); 7.13 (s, 2H); 7.05 (d, 2H); 2.7 (s, 6H); 2.4 (s, 6H).

IR (KBr): ν = 2922, 1678, 1600, 1445, 1384, 1230 cm^{-1}.

MS: m/z (% rel. int.) = 238(M$^+$, 41), 223(8), 165(4), 105(100), 77(24).

1,2-Bis(4-butylphenyl)diazene

Oxidation of 4-butylaniline (0.298 g, 2.0 mmol) using 1.5g oxidant, gave after 48h stirring at ambient temperature, 1,2-bis(4-butylphenyl)diazene (0.215 g, 0.73 mmol, 73%) melting point 33–35° (lit. 36°).[20]

^{1}H NMR ($CDCl_3$): δ = 8.87 (d, 4H); 7.3 (d, 4H); 2.7 (t, 4H); 1.65 (m, 4H); 1.35 (m, 4H); 0.97 (t, 6H).

Table 3 Comparison of the Yields Obtained from the Oxidation of Unsaturated Alcohols using two Different Solid Supports[a]

Alcohol (g)	KMnO$_4$ (g)	Solid Support (g)	Time[b] (h)	Product (%)
Oct-1-en-3-ol (0.4)	5.5	Bentonite (4.0)	24	Oct-1-en-3-one (44)
Oct-1-en-3-ol (0.4)	3.0	CuSO$_4$.5H$_2$O (1.7)	24	Oct-1-en-3-one (61)
Oct-1-en-3-ol (0.4)	5.5	Bentonite (4.5)	46	Oct-1-en-3-one (61)
Non-1-en-3-ol (0.45)	3.0	CuSO$_4$.5H$_2$O (2.0)	48	Non-1-en-3-one (90)
Non-1-en-3-ol (0.45)	5.5	Bentonite (4.5)	48	Non-1-en-3-one (60)
1-Phenylbut-1-en-3-ol (0.42)	2.7	CuSO$_4$.5H$_2$O (1.6)	20	1-Phenylbut-1-en-3-one (90)
1-Phenylbut-1-en-3-ol (0.42)	4.9	Bentonite (3.6)	20	1-Phenylbut-1-en-3-one (91)

[a] CH$_2$Cl$_2$ (20 mL) was used as the solvent in each experiment.
[b] Reflux time.

IR (KBr): ν = 2958, 1665, 1458, 1381 cm^{-1}.

MS: m/z(% rel. int.): 294(M$^+$,24), 251(4), 161(17), 133(100), 105(4), 91(45).

1,2-Bis(4-bromophenyl)diazene
Oxidation of 4-bromoaniline (0.334g, 2.0 mmol) using 1.50 g oxidant, gave 1,2-bis(4-bromophenyl)diazene, mp 203–204 °C(lit 205 °C)[21] (0.279g, 0.82 mmol, 82%) after 48h stirring under reflux.

^{1}H NMR (CDCl$_3$): δ = 7.9 (d, 4H), 7.62 (d, 4H).

IR(KBr): ν = 1904, 1570, 1472, 1397, 1065, 1006 cm^{-1}.

MS: m/z(% rel. int.)] = 340(M$^+$,44), 183(59), 155(100), 157(98), 75(39).

More examples of the oxidation of aromatic amines have been summarized in Table 1.

Acknowledgement

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