Fremy's Salt (Potassium Nitrosodisulphonate): A Nitrosating Reagent for Amines

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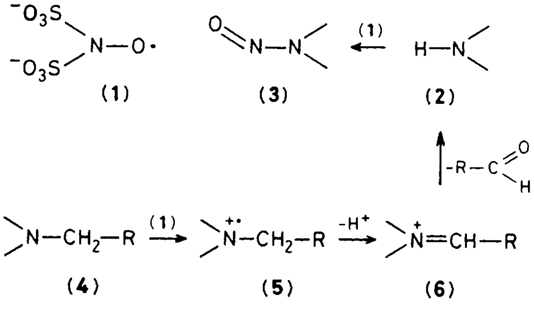
Treatment of secondary and tertiary amines with Fremy's salt in aqueous sodium carbonate or pyridine solution gives moderate yields of the corresponding *N*-nitrosoamines.

The ability of Fremy's salt (**1**) (potassium nitrosodisulphonate) to act as a one electron oxidant towards amines has recently been reported.[1] Unexpectedly, *N*-nitrosopiperidine was obtained as a secondary reaction product. This, coupled with the significance of nitrosoamines as carcinogenic pollutants, prompted us to study the scope and characteristics of this reaction. As far as we are aware no nitrosation by stable nitrosyl radicals has been reported in which they act as oxidants.[2–6]

The nitrosation of amines in aqueous solution usually requires acid media, quite rigorous conditions being necessary to nitrosate tertiary amines.[7] Secondary amines can also be nitrosated by reagents such as nitroprusside and nitrogen oxides[8] at a pH as high as 12.7; the analogous nitrosation of tertiary amines under these conditions has never, to our knowledge, been reported.[9]

We now report that (**1**) nitrosates secondary and tertiary amines at room temperature at moderately basic pH and without catalyst.

On addition of a secondary amine (**2**) to a violet solution of (**1**)† in 2% sodium carbonate (pyridine can be used as cosolvent) a slow fading of the original colour was observed.‡



G.l.c. of the reaction mixture showed the disappearance of the initial amine and the formation of the corresponding nitrosoamine (**3**), which was isolated by extraction from the acidified reaction mixture and identified by comparison (g.l.c. and n.m.r. spectroscopy) with an authentic sample. A decrease in the moderate yields for amines which are highly substituted at the α-carbon atoms was observed (Table 1). When tertiary amines§ (**4**) were treated with (**1**) nitrosamines (**3**) were also formed. This interesting reaction involves the cleavage of a nitrogen–carbon bond, the alkyl residue being lost as an aldehyde; this was proved in the case of (**4c**) and (**4d**) by a positive formaldehyde test (chromotropic acid) on the crude oxidation mixture.

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† We used either crude (**1**) or recrystallized material (95% pure by u.v. spectroscopy). The g.l.c. analyses were carried out in 0.75% KOH on a 10% Carbowax 20 m column.

‡ In a typical experiment 1.15 mmol of amine (**2d**) was allowed to react with 2 g (6 equiv.) of a 95% solution of (**1**) dissolved in 100 ml of 2% sodium carbonate. Under these conditions the reaction time was approximately 30 h.

§ The absence of any secondary amine in the starting material was verified by g.l.c.

Table 1. Isolated yields of nitrosoamines (**3**) obtained by nitrosation of secondary and tertiary amines (**2**) and (**4**) with (**1**).

	Amine	Yield of (3), %
(**2**)**a**	Diethylamine	40
b	Dibutylamine	34
c	Piperidine	33
d	Morpholine	30
e	Isopropylcyclohexylamine	7
f	2,2,6,6-Tetramethylpiperidine	0
(**4**)**a**	Triethylamine[a]	—
b	Tributylamine[b]	23
c	*N*-Methylpiperidine	20 (**3c**)
d	Trimethylamine[a]	—

[a] The nitrosoamine detected by g.l.c. [b] Pyridine was used as cosolvent.

The mechanism of nitrosation of tertiary amines with acidified nitrite has been fully investigated and it would appear that the reaction proceeds *via* an iminium cation which is formed by direct nitrosation of the amine.[10] In our case the oxidant nature of (**1**) makes a pathway in which the iminium cation is formed by electron transfer from (**1**) to the amine giving in the first place an amine cation radical[1] (**5**) more likely. This then loses an α-proton to give the iminium cation (**6**) which then undergoes hydrolysis to an aldehyde and a secondary amine which reacts further with (**1**) to give the nitrosoamine (**3**).

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