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OXIDATION OF ACTIVATED HALIDES TO ALDEHYDES AND KETONES BY N-METHYLMORPHOLINE-N-OXIDE

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ABSTRACT: *N-methylmorpholine-N-oxide* (NMO) in acetonitrile solution will oxidise activated primary halides to aldehydes and secondary halides to ketones in good yields at room temperature.

The oxidation of organic halides to carbonyl derivatives is an important synthetic transformation.[1] Several reagents are known to effect this oxidation but often require high temperatures and/or produce noxious by-products. The best known of these methods is the Kornblum oxidation[2] while others such as the Kröhnke reaction[3] and the Hass-Bender oxidation[4] are still commonly used. Other procedures include the use of metal nitrates[5] and nitrites[6], chromium based reagents[7] or the Sommelet oxidation[8] and its various modifications.[9] More recently

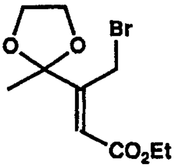
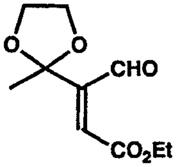
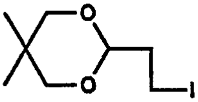
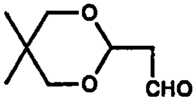
Table. Oxidation of activated halides by NMO.

Substrate	Yield Carbonyl (%)		Time (h.)
Benzylbromide	PhCHO	73	2
Benzylchoride	PhCHO	50	3
p-Methoxybenzylchoride	*p*MeO-PhCHO	59	1
Cinnamylbromide	PhCHO	72	3
Bromodiphenylmethane	PhCOPh	66	5
(1-Bromoethyl)benzene	$PhCOCH_3$	55	3

the use of amine oxides,[10] and particularly pyridine N-oxide[11] has been recommended which has become popular.[12]

In connection with other work[13] we find that N-methylmorpholine N-oxide (NMO) in acetonitrile is an efficient and inexpensive reagent for these oxidations and with activated halides, reactions take place at room temperature. We had earlier reported[13] that NMO functions as a co-oxidant with the ruthenium (VI) complex $(PPh_4)[RuO_2(O_2CCH_3)Cl_2]$ (1) for this oxidation reaction but have since found on further study that while alcohols, sulphides and phosphines are indeed catalysed by (1) with NMO as co-oxidant, the latter alone effects the halide oxidation.

The yields from some typical oxidations, all carried out at room temperature, are shown in the Table. Aldehydes and ketones can be isolated or more usually were characterized as the corresponding 2,4-dinitrophenylhydrazone derivatives. It can be seen that in the examples given there is no competing oxidation of other functional groups, such as C=C double bonds.

		86	2
		45	1

We believe that the reagent is effective because the formation of N-methylmorpholine, a strong base, assists the removal of the halide group but does not cause elimination. The incorporation of 4 Å molecular sieves in the reaction is also beneficial in that these appear to sequester by products of the reaction and improve the work-up procedures considerably.

Although NMO has been used before[14] there are no reports previously of ketone formation by this reagent. Moreover these new conditions are mild and experimentally easy to carry out, and we believe that they could be adapted to a wider range of substrates.

Experimental Section

General procedures. The oxidation of benzyl bromide is typical. Benzyl bromide (0.1g, 5.8 x 10^{-4} mol) was added to a solution of NMO (0.14g, 1.2 x 10^{-3} mol) in acetonitrile (10 cm^3) containing activated powdered 4Å molecular sieves (3 cm^3). The solution was stirred the reaction being followed by tlc. When no further changes were apparantly occuring the reaction was worked up by filtration through a pad of silica gel. The filtrate was concentrated *in vacuo* and the 2,4-dinitrophenylhydrazine derivative of the carbonyl product prepared by the addition of a methanolic solution (10 cm^3) of the 2,4-DNPH (4g in 150 cm^3 methanol containing conc. H_2SO_4 added dropwise to effect dissolution). The yield of the carbonyl was assessed by recording the weight of the derivative produced. NMO and acetonitrile were used as supplied by Aldrich.

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References:

1. Kilenyi, S.N. "Oxidation of Carbon-Halogen Bonds" in "Comprehensive Organic Synthesis", Pergamon Press, 1991, Vol 7 Chp.4 ed. S.V. Ley in press.
2. a) Epstein W.W. and F.W. Sweat, Chem. Rev., 1967, 67, 247; b)Durst T. Adv. Org. Chem., 1969, 6, 285.
3. Kröhnke F., Angew. Chem. Int. Ed., Engl., 1963, 2, 380.
4. Hass H.B. and Bender M.L. , J. Am. Chem. Soc., 1949, 71, 1767.
5. a)McKillop A. and Ford M.E. , Synth. Commun., 1974, 45; b) Kornblum N.and Frazier H.W. J. Am. Chem. Soc., 1966, 88, 685. c) Profft E. and Woft H. , Am. Chem., 1959, 96, 628; d)Baker J.W. , Nathan W.S. and Shoppe C.W., J. Chem. Soc., 1935, 1847.
6. Kornblum N. , Org. Reactions, 1962, 12, 101; Kornblum N. and Wade P.A., J. Org. Chem., 1973, 38, 1418.
7. a) Aldar K. and Flock F.H. , Chem. Ber., 1956, 89, 1732; b) Cardillo G. Orena M. and Sandri S. , J. Chem.Soc., Chem. Commun., 1976, 190; c) Cardillo G. , Orena M. , and Sandri S. , Tetrahedron Lett., 1978, 3985; d) Thuy V.M. , Bull. Soc. Chem. Belg., 1989, 98, 221.

8. Angyal S.J. , Org. Reactions, 1954, 8, 197.

9. a)Hendrickson J.B. , Bergeron R. , Giga A. , and Sternbach D. , J. Am. Chem. Soc., 1973, 95, 3412. b)Bergeron R.J.J. and Hoffman P.G. , J. Org. Chem., 1979, 44, 1835.

10. a) Franzen V. , Org. Synth., 1967, 47, 96; b)Frechet J.M.J. , Darling G. , and Farrell M.H. Polym. Prep. Am. Chem. Soc., Div. Polym. Chem., 1980, 21, 270; c)Gunn V.E. and Anselne J.-P. , J. Org. Chem., 1977, 42, 754.

11. e.g. see a) R.E. Manning and F.M. Schaefer, Tetrahedron Lett., 1975, 213, b) V.J. Traynelis and J.P. Kimball, J. Org. Chem., 1975, 40, 2365; c) J.C. Stowell, J. Org. Chem., 1970, 35, 244; d) C.A. Henrick, Tetrahedron, 1977, 33, 1845; e) W. Feely, W.L. Lehn, and V. Boekelheide, J. Org. Chem., 1957, 22, 1135.

12. For one of the most useful modifications see A.G. Godfrey, and B. Ganem, Tetrahedron Lett., 1990, 31, 4825.

13. W.P. Griffith, J.M. Jolliffe, S.V. Ley and D.J. Williams, J. Chem. Soc. Chem. Commun., 1990. 1219.

14. a) S. Suzuki, T. Onishi, Y. Fujita, H. Misawa, and J. Otera, Bull. Chem. Soc. Jpn., 1986, 59, 3287.; b) T. Hayashi, Tetrahedron Lett., 1990, 31, 4155.

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