Pergamon

Tetrahedron Letters, Vol. 36, No. 17, pp. 3031-3034, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)00419-X

Efficient Desymmetrization of 1,2 and 1,3 Diols by Dimethyldioxirane

Paolo Bovicelli*, Paolo Lupattelli, Anna Sanetti

Centro C.N.R. di studio per la Chimica delle Sostanze Organiche Naturali, Dipartimento di Chimica, Università "La Sapienza", P.le A. Moro, 5 - 00185 Roma, Italy.

Enrico Mincione

D.A.B.A.C., Università della Tuscia, V. S. Camillo De Lellis, 01100 Viterbo, Italy.

Abstract: *Dimethyldioxirane was used to monooxidize 1,2 and 1,3 sec,sec-diols to the corresponding ketoalcohols, exploiting the inhibiting effect of the formed carbonyl group on the course of the process.*

The selective transformation of similar functional groups is always a challenging task for a chemist. In this field a method to select between hydroxy groups of a diol could be of particular interest.

Because of the predominating carbon-carbon cleavage,[1] when the hydroxyl is part of a 1,2-diol unit, the classic oxidants lack mainly the oxidation of a secondary carbinol to a ketonic group. Hiterto, the only procedure considered of general value for the selective oxidation of diols is the mono-oxidation of symmetric 1,2-diols with silver-carbonate on celite,[2] even if it produces modest yields from cyclic diols. On the other hand the distannoxane-bromine procedure is reported to mono-oxidize diphenylethylenglycol to benzoin in moderate yields.[3]

As we recently reported, H_2O_2/TS-1 catalytic system and Dimethyldioxirane (DMDO), efficiently performed the selective oxidation of a secondary alcoholic mojety in the presence of a primary one.

DMDO mainly captured our attention in the last years for its interesting properties. This relatively new peroxide, with a very high oxidation potential, has been used for a variety of synthetic transformations.[4] Because its acetone solution is simple to prepare,[5] DMDO should become a routine reagent. In recent studies we noted that DMDO had a very high sensitivity to stereoelectronic effects. It therefore had an exceptional

site selectivity both in the hydroxylation of steroid substrates[6] and in the epoxidation of steroid 1,4-diene-3-ones.[7] We proposed that the observed selectivities might depend on the strong dipolar interaction between DMDO and the carbonyl moiety present in the substrate. This interaction influences the approach of dioxirane to the reactive center favouring[11] or, sometimes, inhibiting[10] the attack.

The complete selectivity in oxidizing 1,2 and 1,3 diols to the corresponding 2 and 3-keto alcohols appears to confirm a deactivating effect of the generated carbonyl group lying close to the primary reaction center.

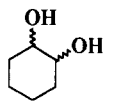
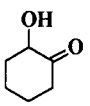
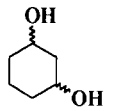
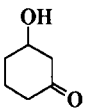
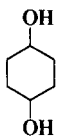
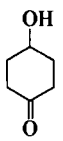
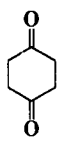
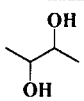
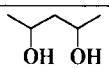
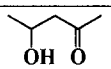
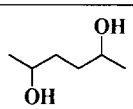
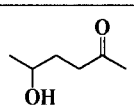
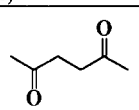
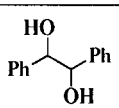
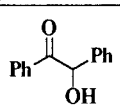
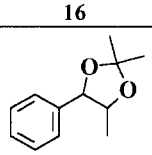
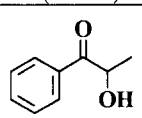
These observations encouraged us to investigate whether DMDO would mono-oxidize compounds having two hydroxyl groups of similar reactivity. Thus we found that non only the 1,2-cyclohexandiol,[8] but also the 1,3-cyclohexandiol gave the ketoalcohol in excellent yields (entries 1,2). Even with an excess of DMDO and prolonged reaction times we observed no appreciable formation of diketones. Evidently the dipole of the formed carbonyl group modifies the electronic environmental on the second reactive center, making it unreactive with DMDO. This interaction makes it possible to desymmetrize 1,2 and 1,3 symmetric diols with exceptional efficiency.

Entries 4, 5 and 7 confirm the inhibiting effect of the formed carbonyl group on the subsequent C-H oxygen insertion and the usefulness of the method reported. Obviously the proposed dipolar interaction does not affect diols with distant hydroxyl groups, for example **5** and **13** (entries 3, 6), which produce a mixture of ketoalcohols and diketones even when the conversions are kept low. In the oxidation of **16** Curci et al. reported moderate conversions to benzoin with DMDO at 0°C.[8] We observed that the reaction was complete in few hours when the temperature was kept to 30-40°C and a freshly prepared solution of DMDO was used. This reaction shows that the benzyl-alcoholic moiety is easily oxidized and that the carbonyl group exerts a strong effect, thus preventing DMDO from attacking this highly reactive benzyl position.

At last, the oxidation of **18** gave an interesting result for the mechanistic implication. **19** was obtained in good yields and no appreciable oxidation of the other alcoholic moiety was observed. At the contrary, the corresponding free diol gave low yields of **19** and considerable amounts of the other regioisomeric keto-alcohol were isolated. The rigid conformation of the substrate should play a determining role.

As a general procedure, an aliquot of standardized[9] DMDO solution (0.08-0.09M in acetone) was added rapidly to a stirred solution of diol (100 mg) in acetone (1 ml) thermostatically kept at room temperature (ca. 25°C), with a dioxirane:substrate molar ratio of 1.5:1. The reaction mixture was stirred overnight and a further dioxirane aliquot was added when necessary for the reaction to complete conversion of the substrate. The product was isolated by careful removal of the solvent by distillation on an apparatus equipped with a vigreux column, and when necessary by column flash chromatography (silica gel, n-hexane/AcOEt).

Table. Selective oxidation of diols by DMDO

entry	starting material	reaction product (yields)	
1			
	1	2 (80-90%)[a]	
2			
	3	4 (92%)[a]	
3			
	5	6 (53%)[b]	7 (37%)[b]
4			
	8	9 (85%)	10 (5%)[a]
5			
	11	12 (95%)[a]	
6			
	13	14 (50%)[b]	15 (25%)[b]
7			
	16	17 (>96%.)[a]	
8			
	18	19 (85%)[a]	

[a]isolated yields [b]ratios established by GC; products were identified as mixtures by NMR analysis

The physical and spectroscopic data agreed with published findings for compounds **4**,[10] **6**,[11] **12**[12], **14**[13] and **19**[8]. All the other compounds were commercially available. Their physical and spectroscopic data corresponded with those of authentic samples.

The method reported here showed considerable promise. Our major interest is therefore to investigate its practical applications. We therefore designed this project to study the behavior of diols and polyols having secondary hydroxy groups with different environments and to determine if it is possible to have acceptable selectivities and if it is possible to establish rules to predict them.

References and notes

1) See, for example Rouk, J.; Westheimer, F. H. *J. Am. Chem. Soc.*, **1962**, *84*, 2241. House, H. O. *Modern Synthetic Reactions*, W. A. Benjamin, Inc, 1972; pp. 353-363.
2) Fetizon, M.; Golfier, M.; Louis, J. M. *Chem. Commun.*, **1969**, 1102.
3) Veno, Y.; Okawara, M. *Tetrahedron Lett.*, **1976**, *50*, 4597.
4) For a recent review, see: Adam, W.; Hadjiarapoglon, L. P.; Curci, R.; Mello, R. in *Organic peroxides*, Ando, W., Ed.; Wiley: New York, **1992**, Chapter 4, pp. 195-219. See also refs. quoted therein.
5) Adam., W.; Bialas, J.; Hadjiarapoglon, L. *Chem. Ber.*, **1991**, *124*, 2377.
6) Bovicelli, P.; Lupattelli, P.; Fiorini V.; Mincione, E. *Tetrahedron Lett.*, **1993**, *34*, 6103.
7) Bovicelli, P.; Lupattelli, P.; Mincione, E. *J. Org. Chem.*, **1994**, *59*, 4304.
8) D'Accolti, L.; De Tomaso, A.; Fusco, C.; Rosa, A.; Curci, R. *J. Org. Chem.*, **1993**, *58*, 701.
9) Adam, W.; Bialas, J.; Hadjiarapoglou, L. P. *Chem. Ber.* **1991**, *124*, 2377. Eaton, P. E.; Wicks, G. E. *J. Org. Chem.* **1988**, *53*, 5353.
10) Molander, G. A.; Hahn, G. *J. Org. Chem.*, **1986**, *51*, 2596.
11) Haslanger, M.; Lawton, G. *Synth. Commun.*, **1974**, 155.
12) Cardillo, G.; Orena, M.; Porzi, G.; Sandri, S.; Tomasini, C. *J. Org. Chem.*, **1984**, *49*, 701.
13) Nakano, T.; Terada, T.; Ishii, Y.; Ogawa, M. *Synthesis*, **1986**, 774.

(*Received in UK* 25 *January* 1995; *revised* 24 *February* 1995; *accepted* 3 *March* 1995)