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PERACID OXIDATION OF TRIMETHYLSILYL ENOL ETHERS: A FACILE α-HYDROXYLATION PROCEDURE

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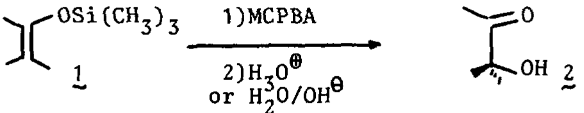
The oxidation of trimethylsilyl enol ethers, **1**, in hexane solution, with *m*-chloroperbenzoic acid (MCPBA), followed by treatment of the crude reaction mixture with acid or base, affords a general, high yield method for the specific α-hydroxylation of ketones (ie, acyloin, **2**, production) (Equation 1).[1]



(Equation 1)

Based on reported procedures for α-hydroxylation[2], the method reported here is well recommended. Perusal of Table I, which summarizes several representative oxidations, reveals that the introduction of the hydroxy group is regiospecific

Table I

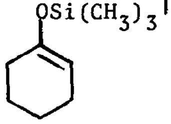
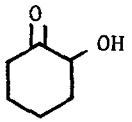
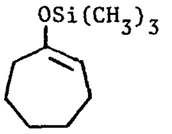
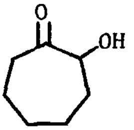
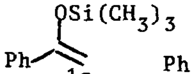
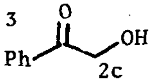
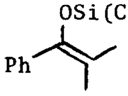
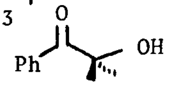
1[3,4,5]	**2**	% Yield of **2**	Hydrolysis Method	Physical Data for **2**[4]
 **1a**	 **2a**	64	a	mp 97-102° mmp 97-102° (Aldrich)
 **1b**	 **2b**	77	a	bp 92° (16mm); n_D^{22} 1.4750 lit[6] bp 97-99° (19mm); n_D^{20} 1.4753
 **1c**	 **2c**	74	b	mp 85-86° lit[7] mp 85-86°

Table I (cont.)

$1^{3,4,5}$	2	% Yield of 2	Hydrolysis Method	Physical Data for 2^4
 1d	 2d	60	c	ir, nmr, and tlc behavior match authentic sample[8]

Hydrolysis Method:

- a: The crude reaction mixture, after filtration and removal of solvent, was partitioned between ether and 10% sodium hydroxide solution (3hr) to affect hydrolysis to 2.
- b: The crude reaction mixture, after filtration and removal of solvent, was partitioned between ether and 1.5N hydrochloric acid solution (2hr) to affect hydrolysis to 2.
- c: The purified 4b was stirred for 60hr in a mixture of ether, water, and HMPA containing a ten fold excess of lithium fluoride to affect hydrolysis to 2d.

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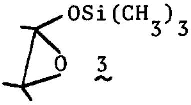
and that no exchange occurs with respect to the position of the original carbonyl group in the ketonic precursor of 1.

From the well recognized mode of reaction of olefins with MCPBA[9], the intermediacy of epoxides of type 3 would seem to be logical in the oxidation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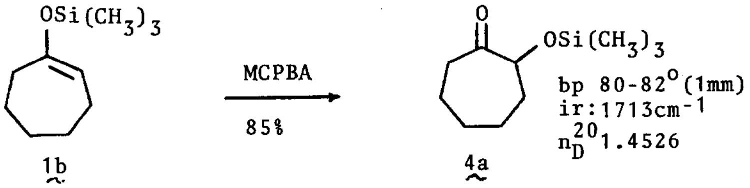
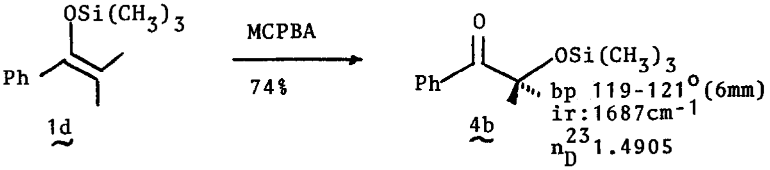
of 1. However, nonaqueous workup of the oxidation products of both 1b and 1d afforded no 3, but, rather, good yields of the α-trimethylsiloxy ketones 4a and 4b[10](Equations 2 and 3).



1b 4a

bp 80-82° (1mm)
ir: 1713 cm^{-1}
n_D^{20} 1.4526

(Equation 2)

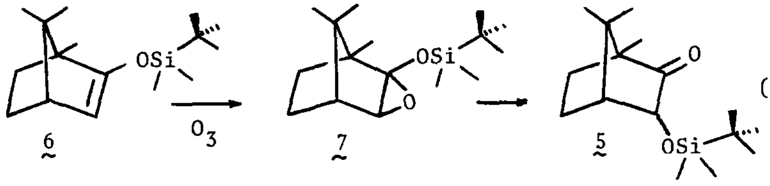


1d 4b

bp 119-121° (6mm)
ir: 1687 cm^{-1}
n_D^{23} 1.4905

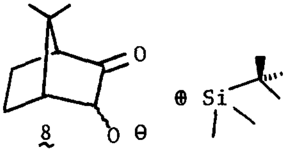
(Equation 3)

Clark and Heathcock[11] have recently shown that 5 is formed from the ozonolysis of 6, and they propose 7 as an intermediate in this reaction. Our data would seem to confirm the plausibility of Heathcock's intermediate 7 (Equation 4).



(Equation 4)

The rearrangement of 7 to 5 (or, in the present case, of 3 to 4) could involve the intermediacy of the ion pair 8, as proposed by Heathcock[11], or



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more likely, an intramolecular silicon shift involving d orbital participation[12]. This type of silicon migration has been noted before in the reaction of 1 with singlet oxygen[1,13], and we are actively studying this novel class of reactions.

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REFERENCES:

(1) Presented in part by: G.M.Rubottom, D.R.Pelegrina, M.A.Vazquez, and M.I. Lopez, Second Annual Xavier-MBS (NIH) Biomedical Symposium, April 15-16, 1974, New Orleans, La., Abstracts p 77.

(2) For a general review on the preparation of α-hydroxy ketones (acyloins) see: S.M.McElvain, Org.React.,4,256(1948). For related procedures see also: J.N.Gardner, F.E.Carlon,and O.Gnoj, J.Org.Chem.,33,1566,3294(1968); C. Ainsworth and F.Chen, ibid.,35,1272(1970), and references therein; K.L. Williamson, J.I.Colburn, and M.F.Herr, ibid.,32,3934(1967), and references therein; and T.M.Santosusso and D.Swern,Tetrahedron Lett.,4261(1968).

(3) Compounds 1a-1d were prepared by the general method outlined in: H.O.House, L.J.Czuba, M.Gall, and H.D.Olmstead, J.Org.Chem.,34,2324(1969). In this manner, 1a-1d were obtained in yields ranging from 75-80%.

(4) The ir, nmr, and mass spectral properties of the compound are in accord with the structure proposed.

(5) In a typical oxidation, a solution of 10mm of MCPBA in 35ml of dry hexane was cooled in an ice methanol bath and treated with a solution containing 10mm of 1 in 15ml of hexane. After addition was complete(ca 5min),the resulting slurry was stirred for 45min. The slurry was then filtered to remove *m*-chlorobenzoic acid and the filtrate concentrated. The residue was then hydrolyzed, as indicated in Table I, or distilled to afford compounds of type 4.

(6) J.D.Knight and D.J.Cram, *J.Amer.Chem.Soc.*,73,4136(1951).

(7) W.H.Linnell and I.M.Roushdi, *Quart.J.Pharm.Pharmacol.*,14,270(1941).

(8) Compound 2d was identical (ir,nmr, tlc retention time) to 2d prepared by the following sequence: Bromination of 1d by the method of J.Strating, S. Reiffers, and H.Wynberg, *Synth.*,1,211(1971); the α-bromoketone[4] thus obtained was converted to 2d by the method of A.Favorski and A.Umnova, *J.Russ. Phys.Chem.*,44,1380(1912).

(9) For a concise summary see: H.O.House, "Modern Synthetic Reactions",W.A. Benjamin,Inc.,Menlo Park,California,1972,p 302; and the references cited therein.

(10) Compound 4a showed the following additional properties: nmrδ-0.07(s,9H), 1.50(m,8H), 2.28(m,2H),4.18(m,1H); mass spectrum m/e200. Compound 4b showed the following additional properties: nmrδ 0.08(s,9H), 1.59(s,6H), 7.40 (m,3H), 8.26(m,2H); mass spectrum m/e236. The fact that 4a could be converted cleanly to 2b, and 4b could be cleanly converted to 2d also serves as verification for the structures proposed for 4a and 4b.

(11) R.D.Clark and C.H.Heathcock, *Tetrahedron Lett.*,2027(1974).

(12) For a recent discussion concerning silicon d-orbital participation during migration to oxygen see: T.J.Pinnavaia and J.A.McClarin, *J.Amer.Chem.Soc.*, 96,3012(1974); and the references cited therein.

(13) G.M.Rubottom and M.I.Lopez, *Tetrahedron Lett.*,2423(1972).