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A METHOD FOR THE OXIDATION OF sec,tert-1,2-DIOLS TO α-HYDROXY KETONES WITHOUT CARBON-CARBON CLEAVAGE

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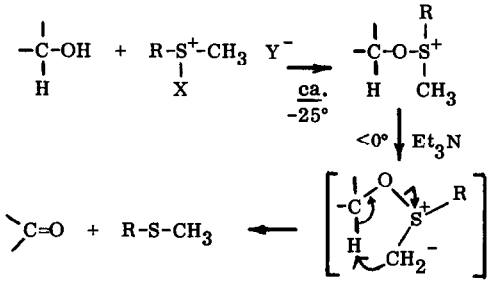
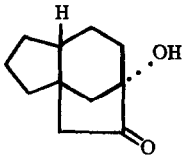
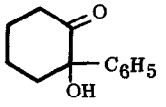
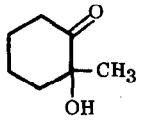
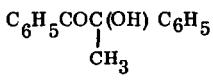
The cleavage of the carbon-carbon bond of the 1,2-diol unit, $HO-\overset{|}{C}-\overset{|}{C}-OH$, is one of the most general oxidative processes of organic chemistry and one of the most selective as well. The list of highly effective agents for this purpose includes not only the most commonly used reagents, periodate and lead tetraacetate, but also a wide variety of others, e.g., Ce (IV), Tl (III), MnO_2, and Ag CO_3. In contrast, there has been no satisfactory method for the oxidation of a secondary carbinol to a ketonic group when the hydroxyl is part of a 1,2-diol unit. Carbon-carbon cleavage predominates over carbon-hydrogen cleavage even with Cr (VI) reagents.[1] This note describes a simple and useful process for effecting such oxidations without carbon-carbon cleavage which utilizes as reagent the complex of a methyl sulfide, $RSCH_3$, with chlorine or N-chlorosuccinimide (NCS), or dimethyl sulfoxide with chlorine in a manner previously detailed for a variety of monoöls (Scheme A).[2]



Scheme A

The accompanying Table summarizes the results obtained with four different sec, tert-1, 2-diol systems.

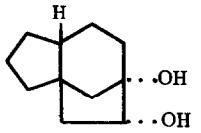
Table

Oxidation Product	Yield (%)	Reagent
 I	(80)	$Cl_2 + C_6H_5SCH_3$
	(72)	$Cl_2 + CH_3SOCH_3$
 II	(85)	$Cl_2 + C_6H_5SCH_3$
	(66)	$Cl_2 + CH_3SCH_3$
 III	(83)	$Cl_2 + C_6H_5SCH_3$
 IV	(86)	NCS + $(CH_3)_2S$

The use of NCS as a reagent for glycol → α-hydroxy ketone oxidation can be illustrated by the experimental procedure for the preparation of IV: To a solution of 294 mg (2.2 mmol) of N-chlorosuccinimide in 6 ml of toluene was added at 0°, 0.17 ml (2.3 mmol) of methyl sulfide under argon. The mixture was cooled to -25° and a solution of 228 mg (1.0 mmol) of 1,2-diphenylpropane-1,2-diol[3] in 1 ml of toluene was added with good stirring. The stirring was continued for 3 hr and then a solution of 222 mg (2.2 mmol) of triethylamine in 0.5 ml of toluene was added dropwise. The cooling bath was removed and after 5 min, 10 ml of ether was added. The organic layer was washed with 5 ml of ice-cold 1% hydrochloric acid and dried. Removal of dried solvents under reduced pressure produced a white oil which was purified by preparative tlc (silica gel) to give 168 mg (86.0%) of α-hydroxy ketone IV as white needles, mp 64.5-66.0° (lit,[4] 65-66°); ir ($CHCl_3$) 3550 (m), 1690 (s), 1450 (m), 1260 (m), 768 cm^{-1} (broad). nmr ($CDCl_3$)

δ 1.82 (S. 3H, methyl), 4.75 (broads, 1H, -OH), 7.0-7.9 (m, 10H, aromatic protons).

The following procedures provide detail relating to glycol oxidation for the specific preparation of the tricyclic α-ketol I from the glycol V.[5]



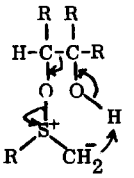
V

α-Ketol I. Procedure A: To a solution of 100 mg (1.4 mmol) of chlorine in 2 ml of methylene chloride was added at -78° a solution of 0.7 ml of dry dimethyl sulfoxide and 0.5 ml of methylene chloride via syringe with good mechanical stirring under argon. Immediately after the addition of sulfoxide, a solution of 60 mg (0.33 mmol) of cis-diol V[5] in 0.5 ml of methylene chloride was added and the reaction mixture was stirred for 2 hr. A solution of 286 mg (2.83 mmol) of triethylamine in 0.5 ml of methylene chloride was added and the mixture was warmed to 25° (10 min). After addition of 10 ml of ether, the organic layer was washed with 5 ml of ice-cold 1% hydrochloric acid and then 10 ml of water. Removal of dried solvents produced 63 mg of a slightly yellow oil (strong 1750 cm^{-1} absorption band) which was chromatographed over 4 g of Florisil using ether as eluent to afford 43 mg (72.4%) of hydroxy ketone I as colorless needles, mp 56-58°; ir ($CHCl_3$) 3500 (w), 3000 (s), 1750 (s), and 1110 (broad) cm^{-1}. nmr ($CDCl_3$) 1.4-2.2 (m, 13 H), 2.2-2.4 (m, 2H), 2.7 (1H, broad S. -OH), identical with an authentic sample.[5]

α-Ketol I. Procedure B: To a solution of 107 mg (1.5 mmol) of chlorine in 3 ml of carbon tetrachloride was added at -25° a solution of 186 mg (1.5 mmol) of thioanisole in 0.5 ml of methylene chloride under argon. A white precipitate appeared immediately after addition of sulfide. To this mixture was added a solution of 100 mg (0.55 mmol) of diol (mixture (4:1) of cis and trans) in 0.5 ml of methylene chloride. After stirring for 1.5 hr, a solution of 303 mg (3.0 mmol) of triethylamine in 0.5 ml of methylene chloride was added dropwise at -25°. After 5 min, 10 ml of ether was added and the organic layer was washed with 5 ml of cold 1% hydrochloric acid. Removal of dried solvents produced 315 mg of a mixture of thioanisole and ketol I. Separation of the mixture by preparative layer chromatography on silica gel afforded 80 mg (80%) of the α-ketol I, mp 56-58°.

It is of interest to consider possible reasons for the effectiveness of the reagents used in the experiments outlined above in promoting sec-carbinol oxidation rather than glycol C-C cleavage. There are a number of indications that the carbinol oxidation requires the intermediacy of an oxysulfonium ylide which can undergo internal elimination to a carbonyl structure as shown in Scheme A. For example, we have noted that the complex of chlorine and diphenyl sulfide does not effect the oxidation of carbinols to

carbonyl compounds as do complexes of dimethyl sulfide or methyl phenyl sulfide with chlorine. Additional evidence for Scheme A can be adduced from the studies of Johnson and Phillips[6] on oxysulfonium ylide chemistry. Such an internal or cycloelimination process for glycol cleavage would require a seven-membered cyclic transition state (VI) in contrast to the five-membered cyclic structure for carbinol



VI

oxidation (Scheme A). The operation of the internal elimination pathway coupled with an entropy advantage for the five-membered transition state can reasonably account for the success of the selective oxidation technique described herein.[7]

References

1. See, for example, J. Rocek and F. H. Westheimer, J. Amer. Chem. Soc., 84, 2241 (1962).
2. (a) E. J. Corey and C. U. Kim, J. Amer. Chem. Soc., 94, 7586 (1972); (b) idem, Tetrahedron Lett., 919 (1973); (c) idem, J. Org. Chem., 38, 1233 (1973); (d) E. J. Corey, C. U. Kim and M. Takeda, Tetrahedron Lett., 4339 (1972).
3. Prepared by the reaction of benzoin with methyllithium in hexane-tetrahydrofuran; see, R. A. Barnes and B. R. Juliano, J. Amer. Chem. Soc., 81, 6462 (1969).
4. A. McKenzie and A. Ritchie, Chem. Ber., 70, 29 (1937).
5. E. J. Corey and R. L. Carney, J. Amer. Chem. Soc., 93, 7318 (1971).
6. C. R. Johnson and W. G. Phillips, ibid., 91, 682 (1969).

7. This work was assisted financially by the National Institutes of Health and the National Science Foundation.