Tetrahedron Letters No. 38, pp 3653 - 3656.
©Pergamon Press Ltd. 1979. Printed in Great Britain.
0040-4039/79/0915-3653$02.00/0

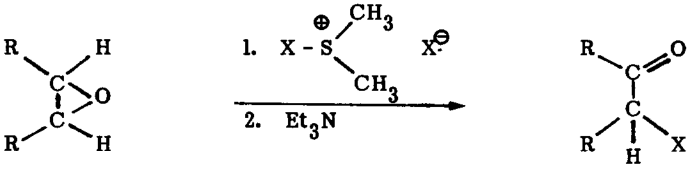
SYNTHETIC METHODS AND REACTIONS. 73[1]. CONVERSION OF EPOXIDES AND ENAMINES INTO α-HALOKETONES WITH HALODIMETHYLSULFONIUM HALIDES.

George A. Olah*, Yashwant D. Vankar, and Massoud Arvanaghi

Institute of Hydrocarbon Chemistry and Department of Chemistry
University of Southern California
University Park, Los Angeles, California 90007, USA

Summary: Epoxides, upon treatment with halodimethylsulfonium halides in the presence of triethylamine are converted in high yield into α-haloketones. Enamines similarly react with bromodimethylsulfonium bromide to give α-bromoketones.

Recently, we reported the use of bromodimethylsulfoniumbromide (BDMS) as a reagent for the dethioacetalization of thioketals[2] and oxidation of thiols to disulfides.[3] In continued study of the utility of halodimethylsulfonium ion reagents, we now report that BDMS, as well as chlorodimethylsulfonium chloride (CDMS) [generated in situ by reacting molecular chlorine with dimethylsulfide at -25° C], readily convert epoxides into α-haloketones in the presence of a tertiary amine in high yields. Results are summarized in Table 1.



X = Cl, Br

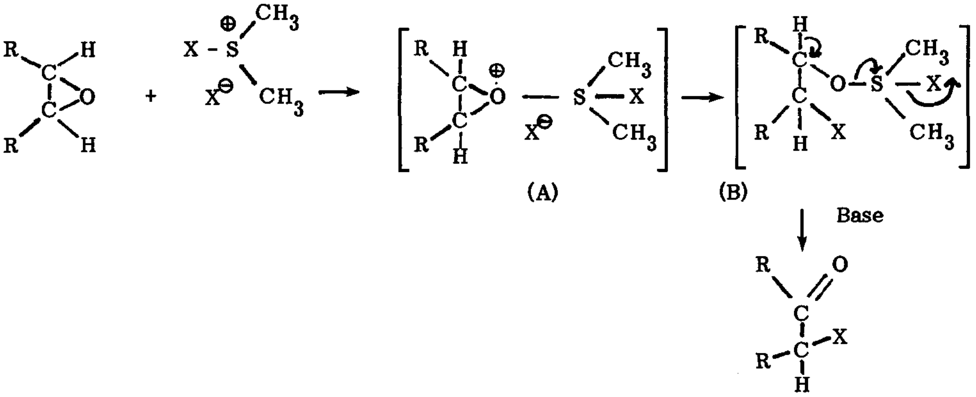
Table 1. Yields of Purified α-Chloro and α-Bromo Ketones

Epoxide	α-Haloketone	% Yield X = Cl	% Yield X = Br	Boiling Point (° C)/mm X = Cl	Boiling Point (° C)/mm X = Br
cyclopentene oxide	α-halocyclopentanone	80	80	60/6	65/6
cyclohexene oxide	α-halocyclohexanone	83	74	67-8/6	76/5.5
cycloheptene oxide	α-halocycloheptanone	82	68	85-87/7	55/5.5
octa-4-ene oxide	5-halooctane-4-one[4]	87	74	76/7	88/7
hept-2-ene oxide	2-haloheptane-3-one[a] 3-haloheptane-2-one	81	75	60-61/6.5	75/6

a) 50:50 mixture of the two compounds indicated by PMR spectroscopy.

α-Haloketones are important intermediates in organic synthesis, usually prepared by the halogenation of the parent carbonyl compounds.[5] Similarly, conversion of olefins or epoxides into α-haloketones is also of importance in natural product synthesis.[6] These conversions are, however, generally carried out in two steps: first by converting the starting material into its halohydrin, followed by the oxidation of the hydroxyl group. We consider that the present method might represent a useful alternative over the conventional methods for converting epoxides or their precursor olefins into α-haloketones under almost neutral conditions.

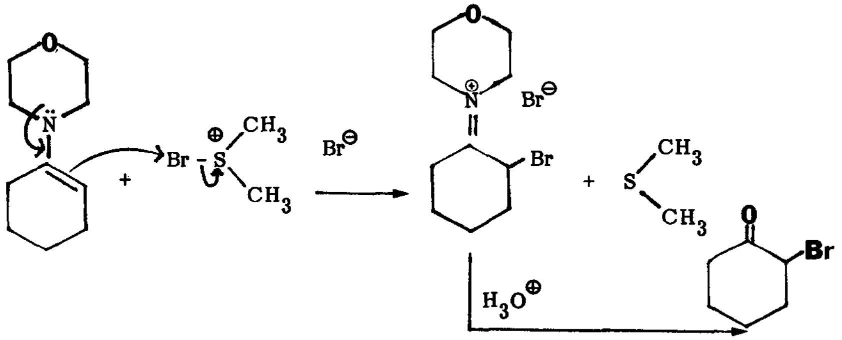
Regarding the mechanism, we suggest that the epoxide oxygen combines with the electrophilic sulfur atom of BDMS or CDMS to give an intermediate (A) (Scheme I), which undergoes ring opening by halide ion to give the second intermediate (B), which, in turn upon treatment with a base, yields the α-haloketone.



Scheme I

It is found that the reaction proceeds well with alkene oxides and cycloalkene oxides of small ring size. Medium and large sized ring epoxides, however, undergo transannular rearrangements giving rise to a number of products.[7]

We have also found that enamines react with BDMS to give α-bromoketones, usually in high yields. (Table II). The reaction can be best represented as follows:



Scheme II

Table II: Yields of Purified α-Bromo Ketones

Morpholino Enamine of	α-Bromo Ketone	% Yield	B.P.° C/mm or (m.p.° C)
cyclopentanone[8]	α-bromocyclopentanone	60	65/6
cyclohexanone	α-bromocyclohexanone	80	78/6
cycloheptanone	α-bromocycloheptanone	78	62/0.8
cyclooctanone	α-bromocyclooctanone	76	80-81/1
desoxybenzoin	α-bromo-α-phenylacetophenone	80	(56-8)

A) Preparation of α-Chlorocyclohexanone

To a magnetically stirred solution of 0.71 g (10 mmol) of chlorine in 8 ml of dry dichloromethane (dried over P_2O_5) under N_2 atmosphere at -25° C (carbon tetrachloride-dry ice) was added a solution of 0.93g (15 mmol) of dimethylsulfide in 5 ml of dichloromethane. A solution of 0.98 g (10 mmol) of cyclohexene oxide in 10 ml of dichloromethane was then added to it and the stirring continued for 3 hours at -25° C. At the end of 3 hrs., a solution of 1.01 g (10 mmol) of dry triethylamine in 5 ml of dichloromethane was then added to it and stirring continued for 15 minutes. The cooling bath was removed, and after 5 minutes, the reaction mixture was diluted with 15 ml of water. The organic layer was separated and the aqueous layer extracted with dichloromethane (2 x 15 ml). Organic layers were combined and washed with water (2 x 25 ml) followed by brine (10 ml). Drying the organic layer extract over anhydrous sodium sulfate and removal of solvent gave almost pure α-chlorocyclohexanone, which was further purified by distillation. Yield 1.1 g (83%) b.p. 67-8° C/6 mm. Lit.[9] b.p. 79° C/7 mm.

B) Preparation of 5-Bromo Octane-4-one

To a magnetically stirred solution of 2.23 g (10 mmol) of BDMS in 20 ml of dry dichloromethane at 0° C was added 1.28 g (10 mmol) of oct-4-ene oxide in 10 ml of dry dichloromethane. The reaction mixture was stirred at room temperature for 2 hours and then cooled to 0° C. A solution of 1.01 g (10 mmol) of dry triethylamine in 5 ml. of dichloromethane was then added to the reaction mixture, ice-bath removed and stirring continued for 20 minutes. The reaction mixture was diluted with 20 ml of water, the organic layer separated and the aqueous layer extracted with dichloromethane (2 x 25 ml). The organic layers were combined and washed with water (2 x 25 ml) followed by brine (15 ml) and dried over anhydrous sodium sulfate. Removal of solvent gave almost pure 5-bromo octane-4-one, which was further purified by distillation. Yield 1.53 g (74%), b.p. 82° C/7 mm.

C) Preparation of α-Bromo-α-Phenylacetophenone

To a magnetically stirred solution of 1.11 g (5 mmol) of BDMS in 15 ml of dry dichloromethane was added a solution of 1.32 g (5 mmol) of morpholine enamine of desoxybenzoin in 10 ml of dichloromethane and the stirring continued for 1-1/2 hours at room temperature. A 40 ml solution of 10% aqueous hydrochloric acid was then added to it and stirring continued for additional 15 minutes. The organic layer was separated and the aqueous layer extracted with dichloromethane (2 x 25 ml). The combined organic layers were then washed with water (2 x 25 ml), followed by brine (15 ml) and then dried over anhydrous sodium sulfate. Evaporation of the solvent gave almost pure α-bromo-α-phenyl-acetophenone, which was further purified by recrystallization (ethanol). Yield: 1.77 g (80%), m.p. 56.8° C. Lit.[9] m.p. 54-5° C.

Acknowledgement:

Support of our work by the National Institutes of Health and the National Science Foundation is gratefully acknowledged.

References:

1. Synthetic Methods and Reactions Part 72, G. A. Olah, Y. D. Vankar, and A. Berrier, Synthesis (submited).

2. G. A. Olah, Y. D. Vankar, M. Arvanaghi, and G. K. S. Prakash, Synthesis (submitted).

3. G. A. Olah, M. Arvanaghi, and Y. D. Vankar, Synthesis, (submitted).

4. To our knowledge, both 5-bromo and 5-chloro-octane-4-one are not known in the literature. The structure resembles the PMR, IR data.

5. a) via silyl enol ethers, see R. H. Reuss and A. Hassner, J. Org. Chem., **39** , 1785 (1974).

   b) via enamines, see F. M. Laskovics and E. M. Schulman, Tetrahedron Letters, 759 (1977) and references cited therein for direct halogenation of ketones also.

6. P. S. Littlewood, B. Lythgoe, A. K. Saksena, J. Chem. Soc. (c), 2955 (1971).

7. A. C. Cope, J. Grisar and P. Peterson, J. Am. Chem. Soc., **81** , 1640 (1959) and references cited therein.

8. Reaction of cyclopentanone enamine with BDMS was carried out at 0° C. Otherwise, some decomposition takes place leading to the decreased yield of α-bromocyclopentanone.

9. Dictionary of Organic Compounds, Oxford University Press, New York, N. Y. (1965).

(Received in USA 8 May 1979)