Convenient Methods for Deoxygenation of Epoxides to Olefins

Kiyoyuki Yamada,* Shunsuke Goto, Hiroshi Nagase,
Yoshinori Kyotani, and Yoshimasa Hirata

*Department of Chemistry, Faculty of Science,
Nagoya University, Chikusa, Nagoya 464, Japan*

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Deoxygenation of epoxides to olefins is often required in structural and synthetic work, and various methods for this transformation have been developed.[1,2]

We have found that mono-, di-, and trisubstituted epoxides could readily be converted to olefins on treatment with methyltriphenoxyphosphonium iodide[3] (MTPI, 10 molar equivalents) in the presence of boron trifluoride etherate (1–3 molar equivalents) in acetonitrile[4] under mild conditions (room temperature, 1–2 h) (see Table I). Concerning the stereochemical aspect of this reaction, deoxygenation of trans and cis epoxides [e.g., **3** and **4** in the table] was effected to afford the corresponding trans and cis olefins, respectively, proceeding with retention of stereochemistry.[5] Since in some cases [e.g., **3**] an iodohydrin was also formed under conditions using 1 molar equivalent of boron trifluoride etherate, a derivative of the iodohydrin was deduced to be an intermediate of deoxygenation of the epoxide to the olefin; the iodohydrin could be converted to the olefin under conditions employing 3 molar equivalents of boron trifluoride etherate.

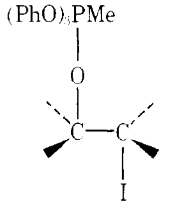
In order to investigate the effect of the reactivity of the iodide ion on the above deoxygenation reaction using MTPI, the following experiments were carried out. When sodium iodide was used instead of MTPI [NaI (10 molar equivalents)–$BF_3 \cdot OEt_2$ (1–3 molar equivalents)–acetone, room temperature, 2 h], epoxides were partly or entirely transformed into iodohydrins without formation of olefins. On the other hand, deoxygenation of epoxides could be effected by potassium iodide complexed with crown ether[6] to an extent less than in the case of MTPI [KI (10 molar equivalents)–dicyclohexyl-18-crown-6 (1 molar equivalent)–$BF_3 \cdot OEt_2$ (1–3 molar equivalents), MeCN or benzene, room temperature–50 °C, 1–5 h][7] (Table I). The above results indicate that the reactivity of the iodide ion is important for deoxygenation of epoxides to olefins. As a reagent for deoxygenation of epoxides to olefins under the present conditions, MTPI is much more effective than the "naked" iodide ion generated from potassium iodide and crown ether.

Table I. Deoxygenation of Epoxides to Olefins by MTPI–$BF_3 \cdot OEt_2$ and by KI–Crown Ether–$BF_3 \cdot OEt_2$

Epoxide	$BF_3 \cdot OEt_2$[a]	Yield[b] of olefin, % MTPI	 KI–crown ether
1-Dodecene (**1**)	3	60[c]	54[c]
5α-Androst-2-en-17-one (**2**)[d]	1	99	78
Methyl *trans*-9-octadecenoate (**3**)	3	99[e]	94[e]
Methyl *cis*-9-octadecenoate (**4**)	3	95[f]	85[f]
Methyl *trans*-13-docosenoate (**5**)	3	99[e]	71[e]
Methyl *cis*-13-docosenoate (**6**)	3	86[f]	46[f]
Citronellol methyl ether (**7**)	3	74	31
Cholest-5-ene (**8**)[g]	1	91	53
Cholest-4-en-3-one (**9**)[g]	1	99	44

[a] Molar equivalent. [b] Isolated yields except for **1**; the products were purified by preparative TLC and identified by spectral (IR, NMR, and mass) comparison with authentic samples. [c] Yields determined by GLC. [d] 2α,3α-Epoxide. [e] Trans. [f] Cis. [g] A mixture of α- and β-epoxides was employed.

The above findings suggest that a phosphorus-containing intermediate such as A would be involved in the deoxygenation of epoxides using MTPI, which would undergo more readily the β elimination effected by the iodide ion than a corresponding reaction intermediate in the case of the KI–crown ether system. The reaction intermediate similar to the above intermediate A was previously suggested in the conversion of epoxides to *cis*-1,2-dichlorides using the mechanistically related triphenylphosphine–carbon tetrachloride system.[8,9]



A

It should be noted that deoxygenation of epoxides to olefins could be made [e.g., the epoxide of methyl *trans*-13-docosenoate (**5**), 99%; the epoxide of cholest-4-en-3-one (**9**), 65%] by methyltriphenylphosphonium iodide [$Ph_3MeP \cdot I$ (10 molar equivalents)–$BF_3 \cdot OEt_2$ (1–3 molar equivalents)–MeCN, room temperature, 1–2 h] to an extent a little less than in the case of MTPI but significantly more than in the case of the KI–crown ether system, suggesting in this case again the important role of a phosphonium ion and that the reaction would proceed through a phosphorus-containing intermediate.[10]

Experimental Section[11]

Methyltriphenoxyphosphonium iodide (MTPI), which was prepared according to the procedure by Verheyden and Moffatt,[3b] was purified prior to use as follows: dry ether was added to a solution of MTPI in dry CH_2Cl_2 to afford precipitates of MTPI, and this procedure of purification was repeated three times, giving almost colorless MTPI, which was filtered and dried in vacuo. Boron trifluoride etherate was distilled from CaH_2 prior to use. Acetonitrile was refluxed over P_2O_5 for 5 h and distilled. Benzene and ether were refluxed over Na and distilled, respectively. Methylene chloride was distilled from $CaCl_2$.

Procedures for Deoxygenation. Similar procedures were used to perform deoxygenation for all the epoxides examined. Representative procedures employing MTPI–$BF_3 \cdot OEt_2$ and KI–crown ether–$BF_3 \cdot OEt_2$ follow.

Deoxygenation of the Epoxides of Cholest-5-ene (8) Using MTPI–$BF_3 \cdot OEt_2$. To a magnetically stirred solution of a mixture of α- and β-epoxides of cholest-5-ene (**8**) (20.0 mg, 0.052 mmol) and MTPI (234 mg, 0.52 mmol) in 2 mL of MeCN–benzene (v/v, 1:1) was added a solution of $BF_3 \cdot OEt_2$ in MeCN (0.066 mL containing 6.6 μL (0.052 mmol) of $BF_3 \cdot OEt_2$) at room temperature. After 1 h at room temperature the reaction mixture was diluted with saturated $NaHCO_3$ solution and extracted with $CHCl_3$ four times. The combined organic extracts were washed with saturated NaCl solution, dried, and concentrated. The crude product was purified by preparative TLC (silica gel, *n*-hexane) to afford crystals of **8**, mp 87–89 °C (17.5 mg, 91%).

Deoxygenation of 2α,3α-Epoxy-5α-androstan-17-one (2) Using KI–Crown Ether–$BF_3 \cdot OEt_2$. A solution of 2α,3α-epoxy-5α-androstan-17-one (**2**) (23.0 mg, 0.080 mmol) in 2 mL of MeCN was added with stirring to a suspension of KI (133 mg, 0.80 mmol) and dicyclohexyl-18-crown-6 (29.5 mg, 0.080 mmol) in 1 mL of MeCN at room temperature. To this mixture was added a solution of $BF_3 \cdot OEt_2$ in MeCN (0.10 mL containing 0.010 mL (0.080 mmol) of $BF_3 \cdot OEt_2$) at room temperature. After stirring was continued for 3 h at room temperature, the mixture was diluted with saturated $NaHCO_3$ solution (3 mL) and extracted with $CHCl_3$ three times. The organic extracts were washed with saturated NaCl solution, dried, and concentrated. The crude crystalline material was purified by preparative TLC (silica gel, *n*-hexane–EtOAc (v/v, 3:1)), giving crystals of **2**, mp 103–106 °C (17.0 mg, 78%).

Registry No.—**1**, 2855-19-8; **1** corresponding olefin, 112-41-4; **2**,

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965-67-3; **2** corresponding olefin, 963-75-7; **3**, 6084-76-0; **3** corresponding olefin, 1937-62-8; **4**, 2566-91-8; **4** corresponding olefin, 112-62-9; **5**, 6084-74-8; **5** corresponding olefin, 7439-44-3; **6**, 6084-75-9; **6** corresponding olefin, 1120-34-9; **7**, 38595-13-0; **7** corresponding olefin, 55915-70-3; **8** α-epoxide, 20230-22-2; **8** β-epoxide, 24375-46-0; **8** corresponding olefin, 570-74-1; **9** α-epoxide, 2515-12-0; **9** β-epoxide, 1975-34-4; **9** corresponding olefin, 601-57-0.

References and Notes

(1) (a) I. T. Harrison and S. Harrison, "Compendium of Organic Synthetic Methods", Wiley-Interscience, New York, N.Y., 1971, pp 502–504; (b) *ibid.*, Vol. 2, 1974, pp 200 and 201.

(2) (a) P. Dowd and K. Kang, *J. Chem. Soc., Chem. Commun.*, 384 (1974); (b) J. M. Behan, R. A. W. Johnstone, and M. J. Wright, *J. Chem. Soc., Perkin Trans. 1*, 1216 (1975); (c) M. Rosenblum, M. R. Saidi, and M. Madhavararo, *Tetrahedron Lett.*, 4009 (1975); (d) J. E. McMurry and M. P. Flemming, *J. Org. Chem.*, **40**, 2555 (1975); (e) J. Rémion, W. Dumont, and A. Krief, *Tetrahedron Lett.*, 1385 (1976); (f) P. B. Dervan and M. A. Shippey, *J. Am. Chem. Soc.*, **98**, 1265 (1976).

(3) (a) S. R. Landauer and H. N. Rydon, *J. Chem. Soc.*, 2224 (1953); (b) J. P. H. Verheyden and J. G. Moffatt, *J. Org. Chem.*, **35**, 2319 (1970). Trivial name for this compound is triphenylphosphite methiodide.

(4) In some cases, benzene was used as a cosolvent to increase the solubilities of materials in the reaction mixture.

(5) Novel methods of converting epoxides to olefins previously reported with retention of stereochemistry: (a) J. W. Cornforth, R. H. Cornforth, and K. K. Mathew, *J. Chem. Soc.*, 112, 2539 (1959); (b) K. B. Sharpless, M. A. Umbreit, M. T. Nieh, and T. C. Flood, *J. Am. Chem. Soc.*, **94**, 6540 (1972); (c) D. L. J. Clive and C. V. Denyer, *J. Chem. Soc., Chem. Commun.*, 253 (1973); (d) W. P. Giering, M. Rosenblum, and J. Tancrede, *J. Am. Chem. Soc.*, **94**, 7170 (1972); (e) ref 2b.

(6) For generation and reactions of highly reactive anions using crown ethers, see: (a) C. J. Pedersen and H. K. Frensdorff, *Angew. Chem., Int. Ed. Engl.*, **11**, 16 (1972); (b) G. W. Gokel and H. D. Durst, *Synthesis*, 168 (1976).

(7) No deoxygenation of epoxides takes place by tetrabutylammonium iodide under the present conditions.

(8) N. S. Isaacs and D. Kirkpatrick, *Tetrahedron Lett.*, 3869 (1972).

(9) We are indebted to one of the referees for calling our attention to ref 8.

(10) No deoxygenation of epoxides could be made by methyltriphenylphosphonium bromide under the present conditions.

(11) IR spectra were recorded with a JASCO Model IRS spectrophotometer. NMR spectra were obtained using Varian HA-100D (100 MHz) and NV-21 (90 MHz) instruments. Mass spectra were determined on a Hitachi RMU-6C mass spectrometer. For TLC silica gel 60 F_{254} and 60 PF_{254} (E. Merck, A. G., Germany) were used. GLC analysis was performed on a Varian 1820-4 gas chromatograph. The organic solutions were dried over Na_2SO_4 and concentrated by vacuum rotary evaporator.

Allyl Ethers of Ethyl 2-Chloro-2-(2-hydroxyphenylhydrazono)acetate as Intermediates for the Synthesis of 4*H*-1,3,4-Benzoxadiazines

Luisa Garanti* and Gaetano Zecchi

Istituto di Chimica Industriale dell'Universitá,
Centro del C.N.R. per la Sintesi e Stereochimica
di Speciali Sistemi Organici, 20133 Milano, Italy

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In a study of 1,3-dipoles bearing an alkenyl substituent, we found[1] that the reaction of 1-chlorohydrazone **1c** with triethylamine gave, in addition to the expected pyrazoline derivative **3c** arising from the intermediate nitrile imine **2c**, minor quantites of the isomeric 4*H*-1,3,4-benzoxadiazines **5c** and **7c**. Since few synthetic methods are available for this ring system,[2-5] further work was done on 1-chlorohydrazones of type **1** as possible precursors of 1,3,4-benzoxadiazines. In view of the fact that 1-chlorohydrozones are well known to follow a general pattern in a basic medium, giving rise to nitrile imines,[6] thermochemical reactions of **1a–c** seemed to be worthy of investigation.

Compounds **1a–c** slowly underwent change in boiling xylene to give a mixture of several products. In all cases, the reaction mixture was worked up before the complete disappearance of the starting substrate; in fact, longer times were not advantageous since formation of tar began to occur. Products, which were isolated by column chromatography, are indicated in Table I along with the corresponding isolation yields.

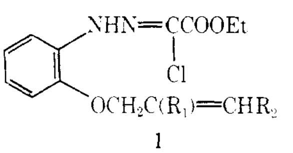
Table I. Reaction of 1-Chlorohydrazones 1 in Boiling Xylene[a]

Compd	Registry no.	Unreacted substrate, %[b]	Products	Registry no.	Mp, °C[c]	Yield, %
1a	61364-10-1	25	**4a**	65465-81-8	103	33
			6a	65465-82-9	129	11
			3a	61364-13-4	*d*	8
			5a	65465-83-0	101[e]	13
1b	65465-79-4	31	**4b**	65465-84-1	91	34
			3b	65495-44-5	132	9
			5b	65465-85-2	97[e]	17
1c	65465-80-7	29	**3c**	65465-86-3	*d*	16
			6c	61364-17-8	*d*	10
			5c	61364-19-0	*d*	20
			7c	61364-18-9	*d*	13

[a] After 42 h. [b] Recovered by column chromatography. [c] From diisopropyl ether. [d] See ref 1. [e] Yellow crystals.

Control experiments showed that compounds **4a,b** and **6a,c** are not stable in boiling xylene but slowly react to afford the corresponding 4*H*-1,3,4-benzoxadiazines **5a,b** and **7a,c**.[7] Some **6a** was detected in the product arising from **4a**.

The ring closure of **4a,b** and **6a,c** to **5a,b** and **7a,c** was greatly accelerated in the presence of basic agents. In fact, it was complete within 30 min by treating **4a,b** and **6a,c** with triethylamine (5 mol) in boiling toluene. Under these conditions, the cyclization products **5a,b** and **7a,c** were obtained in quantitative yields.



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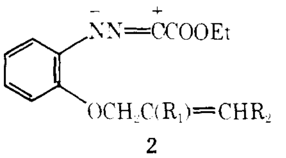

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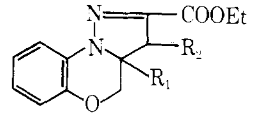

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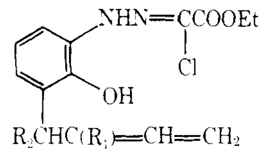

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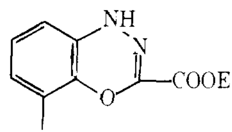

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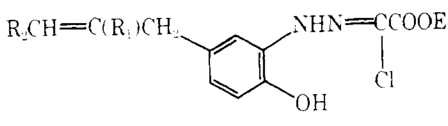

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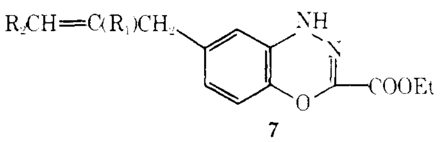

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a, $R_1 = R_2 = H$
b, $R_1 = Me$; $R_2 = H$
c, $R_1 = H$; $R_2 = Ph$

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