

Intramolecular β,γ -Addition of Allylic Alkoxy Radicals. A New General Synthesis of α -Iodoepoxides by Photolysis of Allylic Alcohol Hypoiodites in the Presence of Mercury(II) Oxide, Iodine and Pyridine in Benzene¹

Hiroshi Suginome* and Jian Bo Wang

Organic Synthesis Division, Faculty of Engineering, Hokkaido University, Sapporo 060, Japan

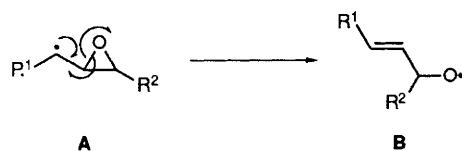
The formation of α -iodoepoxides arising from an intramolecular β,γ -addition of an allylic alkoxy radical is a major general process in the photolysis of tertiary and some secondary allylic alcohol hypoiodites in the presence of iodine and pyridine in benzene.

It has been reported that the generation of a carbon radical α to an epoxide function by various methods resulted in radical fission of the epoxide C–O bond to give an allylic alkoxy radical as outlined in Scheme 1.² The process has been applied to some synthetic problems.³

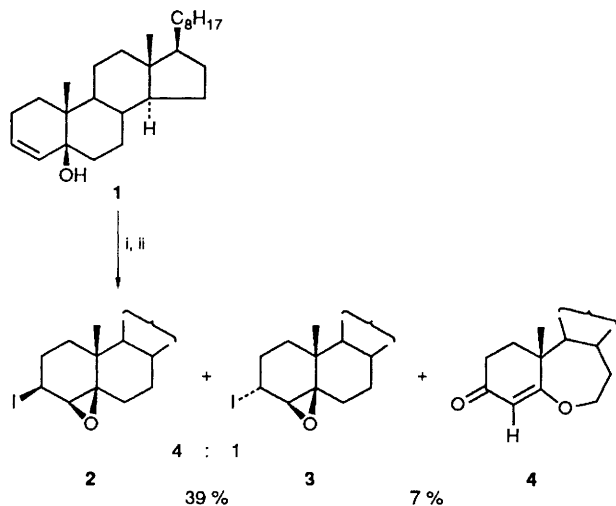
We report here the formation of α -iodoepoxides^{2b} in high yields by photolysis of tertiary and some secondary allylic alcohol hypoiodites. The formation involves a reverse process to the radical fission process cited above (**B** \rightarrow **A**, Scheme 1); an intramolecular addition of tertiary allylic alkoxy radicals to the β,γ -double bond to give epoxide rings. The process is general and is potentially useful in synthesis.

Thus, the photolysis of a solution of 5-hydroxy-5 β -cholest-3-ene **1**⁴ (200 mg, 0.52 mmol) in benzene (25 ml) containing red mercury(II) oxide (335 mg, 1.55 mmol) and iodine (395 mg, 1.55 mmol) (3 equiv. of each) in a Pyrex tube with a 100 W high pressure mercury arc while stirring at 25 °C gave products from which a mixture of two isomeric products **2** and **3** (39%) and a ketone **4** (7%) were obtained by PLC as outlined in Scheme 2. Virtually no reaction took place under 'dark' conditions. The IR, ¹H NMR and mass spectra of the mixture indicated that it was a 4 : 1 mixture of 3 β -iodo-4 β ,5-epoxy-5 β -

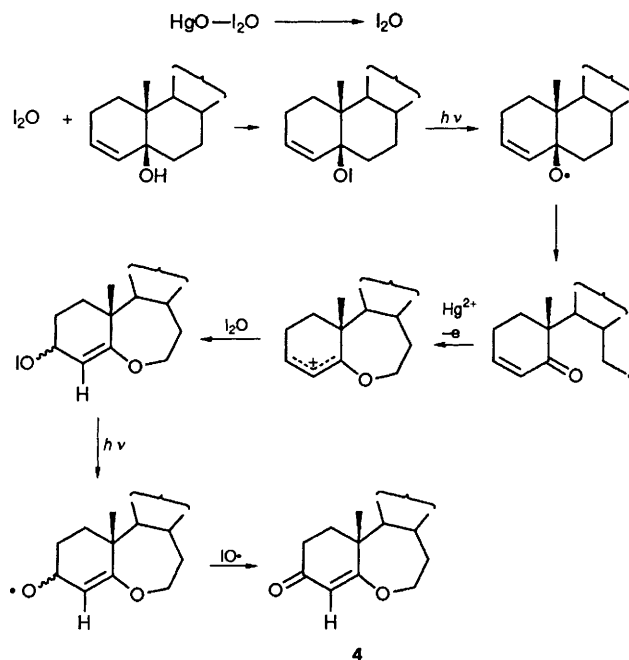
cholestane **2**,^{2d} and its 3 α -epimer **3**.^{2d†} The molecular formula of product **4** was proved to be C₂₇H₄₄O₂ by elemental analysis and mass spectrometry. The IR spectrum exhibited two bands at 1679 and 1621 cm⁻¹ attributable to the α,β -unsaturated carbonyl group. The ¹H NMR spectrum exhibited a singlet (1H) at δ 6.11 and two doublets (2H) at δ 3.34 and 3.45 (*J* 3.6 Hz) assignable to a proton attached to the trigonal carbon. These spectral results indicated that ketone **4** is 6-oxa-B-homocholest-4-en-3-one. Scheme 3 outlines a probable path for the formation of ketone **4**.



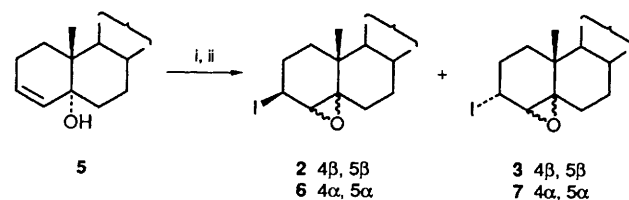
Scheme 1



Scheme 2 Reagents and conditions: i, HgO–I₂, benzene; ii, *hν*, 25 °C

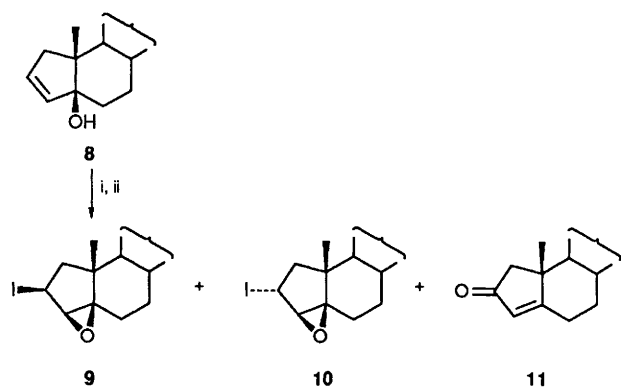


Scheme 3

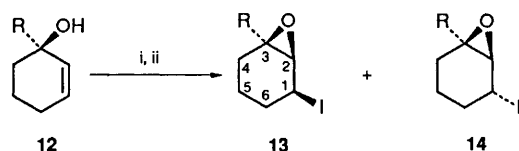


Scheme 4 Reagents and conditions: i, HgO–I₂–pyridine, benzene; ii, *hν*, 25 °C

[†] ¹H NMR (270 MHz) δ 3.08 (4/5 H, d, *J* 3.66 Hz, 4 α -H of **2**), 3.43 (1/5 H, s, 4 α -H of **3**), 4.39 (1/5 H, dd, *J* 7.32 and 6.97 Hz, 3 β -H of **3** and 4.65 (4/5 H, ddd, *J* 3.66, 4.77 and 5-13, 3 α -H of **2**).



Scheme 5 Reagents and conditions: i, HgO-I₂-pyridine, benzene; ii, hv, 25°C



Scheme 6 Reagents and conditions: i, HgO-I₂, pyridine, benzene; ii, hv, 5–10°C

Table 1

R	Ratio of 13:14	Yield of 13 and 14 (%)
a Me	1:0	61
b Bu	5:1 ^a	99
c Bu ^t	7:1 ^a	46
d Ph	4:1	84

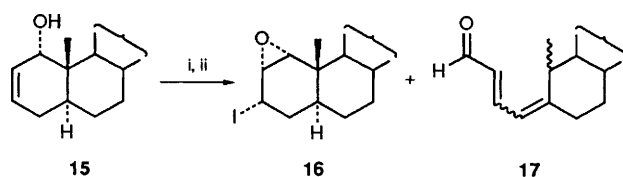
^a Isolated as a mixture. The ratio was determined by ¹H NMR.

We subsequently found that when the photolysis is carried out in the presence of pyridine (0.1 ml), the products are exclusively epoxides **2** and **3** in a ratio of 4:1 (96%) without any accompanying formation of product **4**.

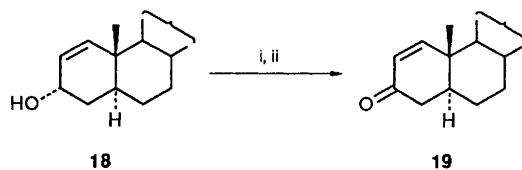
Examination of a number of substrates indicated that the formation of α-iodoepoxides is general with steroidal and nonsteroidal tertiary allylic alcohols. Thus, 5-hydroxy-5α-cholest-3-ene **5**⁵ gave epimeric α-iodoepoxides **6** (m.p. 150–153°C) and **7** (m.p. 103–105°C)‡ in a ratio of 10:1 in 86% combined yield as outlined in Scheme 4. Freshly prepared 5-hydroxy-A-nor-5β-cholest-2-ene **8** gave an epimeric mixture of α-iodoepoxides **9** and **10** in a ratio of 3:1 in a combined yield of 52% with accompanying formation of A-norcholest-3-en-2-one **11**⁶ (28%) (Scheme 5). Similar reaction of 1-alkylcyclohex-2-en-1-ols **12**§ gave mixtures of *cis* and *trans* α-iodoepoxides **13** and **14** (Scheme 6). The yields of the α-iodoepoxides obtained from the photolysis of four 1-alkylcyclohex-2-en-1-ols **12a–d** at 5–10°C and the ratios of *cis* to *trans* isomers are summarized in Table 1.

‡ All new compounds described in this paper gave satisfactory analytical and spectral (IR, ¹H NMR and mass spectrometry) results.

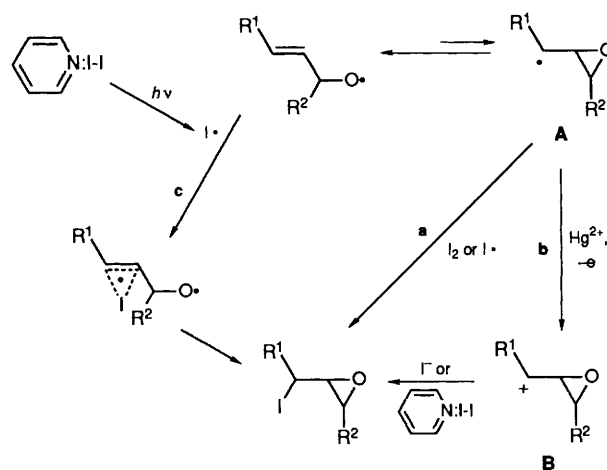
§ The reactions were carried out with the same scale and under the same conditions as described for steroidal substrate **1**.



Scheme 7 Reagents and conditions: i, HgO-I₂, pyridine, benzene; ii, hv, 25°C



Scheme 8 Reagents and conditions: i, HgO-I₂, pyridine, benzene; ii, hv, 25°C



Scheme 9

While it has been reported that secondary allylic alkoxy radicals readily lose the hydrogen atom to give α,β-unsaturated ketones,⁷ we found that photolysis of a steroidal secondary allylic alcohol, 1α-hydroxy-5α-cholest-2-ene **15**⁸ under the conditions as described above similarly gave α-iodoepoxide **16** (m.p. 154–155°C) as the major product together with a mixture of products **17** arising from a β-scission as outlined in Scheme 7. The photolysis of 3α-hydroxycholest-1-en **18**⁹ under the conditions described above, however, resulted in the formation of cholest-1-en-3-one **19** as an exclusive product in 94% yield (Scheme 8).

As is apparent from the results with the steroidal allylic alcohol **1**, the addition of pyridine dramatically enhances the yields of the α-iodoepoxides. It is well-known that pyridine forms a charge-transfer complex with iodine.^{10,11} The role of the pyridine-iodine complex in this radical addition is ambiguous at present. Probable paths (*a*, *b* and *c*) including possible roles of the complex and metal ion leading to α-iodoepoxides are outlined in Scheme 9. Some of the possible roles of pyridine or the pyridine-iodine complex would be to remove hydrogen iodide generated in the reaction, to inhibit a protonation of intermediary epoxy rings, to assist iodination of a cationic intermediate **B** (route *b*) formed by a one-electron oxidation of a radical **A** by a metal ion, or to assist route *a* or *c* by increasing the concentration of iodine atom.

Alkoxy radicals generated from 5-hydroxy-5 β -cholestane¹² and the corresponding bicyclic alcohol¹³ have been reported to result in β -scission at their C(5)–C(10) bond. In view of these results, it seems rather remarkable that the radical addition takes place in preference to β -scission of the C(5)–C(10) bond in allylic alkoxy radicals generated from allylic alcohols **1**, **5** and **8**.

Received, 11th June 1990; Com. 0/02610G

References

- 1 Previous paper in this series: K. Orito, M. Ohto, N. Sugawara and H. Suginome, *Tetrahedron Lett.*, 1990, **31**, 5921.
 - 2 (a) E. C. Sabatino and R. J. Grittev, *J. Org. Chem.*, 1963, **28**, 3437; (b) E. S. Huyser and L. R. Munson, *J. Org. Chem.*, 1965, **30**, 1436; (c) D. H. R. Barton, R. S. Hay-Motherwell and W. B. Motherwell, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2363; (d) K. Pradhan and M. Girjavallabhan, *J. Chem. Soc., Chem. Commun.*, 1975, 591; (e) W. R. Bowman, B. A. Marples and N. A. Zaidi, *Tetrahedron Lett.*, 1989, **30**, 3343.
 - 3 (a) R. C. Carlson, J. H-A. Huber and D. E. Henton, *J. Chem. Soc., Chem. Commun.*, 1973, 223; (b) A. Jones, J. A. Murphy and M. S. Sherburn, *Tetrahedron*, 1989, **24**, 7835; (c) V. H. Rawal, R. C. Newton and V. Krishnamurthy, *J. Org. Chem.*, 1990, **55**, 5181.
 - 4 P. S. Wharton and D. H. Bohlen, *J. Org. Chem.*, 1961, **26**, 3615.
 - 5 T. Nambara, S. Ikegawa, T. Ishizuka and J. Goto, *Chem. Pharm. Bull.*, 1974, **22**, 2656.
 - 6 W. G. Dauben, G. A. Boswell and W. H. Templeton, *J. Am. Chem. Soc.*, 1961, **83**, 5006.
 - 7 T. W. Campbell and G. M. Coppinger, *J. Am. Chem. Soc.*, 1951, **73**, 1788; B. C. Gilbert, R. G. G. Holmes and R. O. C. Norman, *J. Chem. Res.*, *S*, 1977, 1; *M*, 1977, 101.
 - 8 C. Djerassi, D. H. Williams and B. Berkoz, *J. Org. Chem.*, 1962, **27**, 2205.
 - 9 E. Glotter and P. Krinsky, *J. Chem. Soc., Perkin Trans. 1*, 1978, 408.
 - 10 G. Kortüm and H. Walz, *Z. Electrochem.*, 1953, **57**, 73.
 - 11 For a review see, E. M. Kosower, *Prog. Phys. Org. Chem.*, 1965, **3**, 81.
 - 12 L. Lorenc, L. Bondarenko, M. Rajkovic, A. Milovanovic and M. L. Mihailovic, *Tetrahedron*, 1983, **39**, 3609 and their earlier papers.
 - 13 M. Akhta and S. Marsh, *J. Chem. Soc. C*, 1966, 937.
-