

**INTRAMOLECULAR HYDROGEN ABSTRACTION. IODOSOBENZENE DIACETATE,  
AN EFFICIENT AND CONVENIENT REAGENT FOR ALKOXY RADICAL GENERATION**

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Summary: Photolysis of several hydroxy compounds in presence of iodosobenzene diacetate and iodine leads to alkoxy radical derivatives which undergo intramolecular hydrogen abstraction to produce cyclic ethers in good yield.

Intramolecular remote functionalization on non-activated carbon atoms promoted by alkoxy radicals has been the subject of numerous studies.<sup>1</sup> Up to now, alkoxy radicals have been generated by photolysis of nitrites or by reaction of alcohols with a variety of oxidizing reagents such as N-iodosuccinimide, mercuric oxide and acetates of Pb(IV), Hg(II), and Ag(I), usually in presence of iodine (hypoiodite reaction). Hitherto, the lead tetraacetate-iodine procedure has been the most frequently used and appears to give the best yields.

Iodosobenzene diacetate is known to be a useful oxidizing, acetoxyating, and methylating agent, behaving similarly to lead tetraacetate.<sup>2</sup>

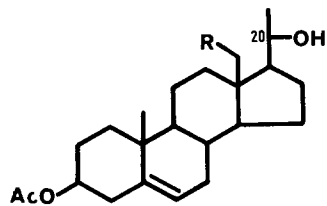
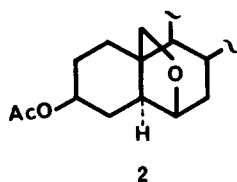
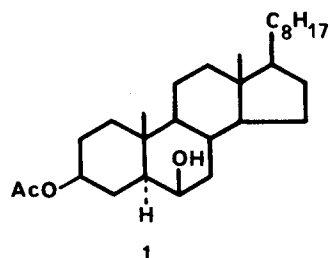
In view of these characteristics and continuing with our interest<sup>3</sup> on remote intramolecular functionalization reactions, we have found that the system iodosobenzene diacetate-iodine<sup>4</sup> is an excellent reagent for this purpose.

Results are summarized in the Table. In practice, the reaction proceeds smoothly in mild conditions and the yields are in the same order or better than those obtained with the lead tetraacetate-iodine system. It should be pointed out that only one mol-eq. of iodosobenzene diacetate and iodine is needed to complete the reaction, in contrast with the large excess of lead tetraacetate and iodine usually required.<sup>8</sup> In spite of the fact that, as shown in the Table (entry III), the presence of iodine is necessary for the reaction to take place, when only 0.3 mol-eq. of iodine has been used the reaction yield does not decrease significantly; however, longer reaction times are needed (compare entries I-II, VI-VII).

Moreover, reactions with lead tetraacetate-iodine are frequently complicated by bifunctional attack leading to lactols and/or  $\alpha$ -iodo-ethers.<sup>1b,9</sup> This drawback does not arise with iodosobenzene diacetate-iodine system in the cases examined, where only tetrahydrofuran,

tetrahydropyrene, and monoiodo-alcohol derivatives were formed.

The 18-iodo-pregnane derivatives (5) and (6) can easily be transformed into the cyclic ethers (7) and (8), respectively,<sup>10</sup> by treatment with silver acetate.<sup>11</sup>

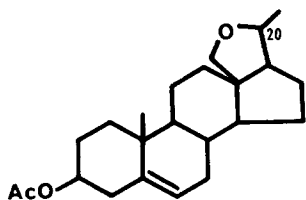


3 R = H (20R)

4 R = H (20S)

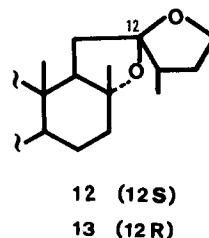
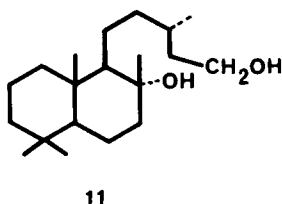
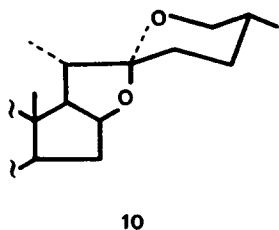
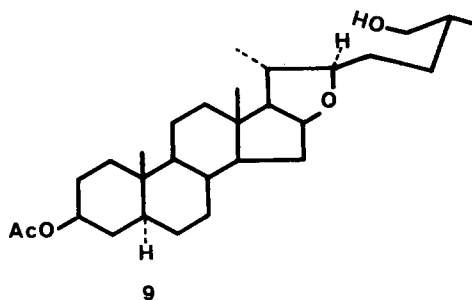
5 R = I (20R)

6 R = I (20S)



7 (20R)

8 (20S)



13 (12R)

Alkyl hypiodite intermediates are expected to be involved in these reactions with iodosobenzene diacetate-iodine.

Representative experimental procedure: a solution of alcohol (1) (1 mmol) in cyclohexane (100 ml) containing iodosobenzene diacetate (1.1 mmol) and iodine (1 mmol) was irradiated with two 100-W tungsten-filament lamps for 50 min. at 40°C. The reaction mixture was then poured into water and extracted with diethyl ether. The organic layer was washed with aqueous sodium thiosulphate and water. Silica gel column chromatography of the residue (eluant n-hexane:ethyl acetate 9:1) gave the tetrahydrofuran derivative (2) in 90% yield.

TABLE. Reaction of alcohols with iodosobenzene diacetate-iodine

Entry	Alcohol	Conditions <sup>a</sup>	Product (yield%)
I	1	1.1 / 1.0 ; 50 min. ; 40 °C	2 (90) <sup>5</sup>
II	1	1.1 / 0.3 ; 180 min. ; 40 °C	2 (85)
III	1	1.1 / 0 ; 120 min. ; 40 °C	no reaction
IV	3	1.1 / 1.0 ; 30 min. ; 35 °C	5 (61) <sup>6</sup>
V	4	1.1 / 1.0 ; 30 min. ; 25 °C	6 (53) <sup>7</sup>
VI	9	1.1 / 0.5 ; 40 min. ; 40 °C	10 (92) <sup>3b</sup>
VII	9	2.0 / 0.3 ; 90 min. ; 40 °C	10 (90)
VIII	9	1.1 / 0.2 ; 150 min. ; 40 °C	10 (80); 9 (10)
IX	11	2.2 / 1.0 ; 45 min. ; 40 °C	12 (60); 13 (25) <sup>3a</sup>

a) Moles of iodosobenzene diacetate / moles of iodine, per mole of hydroxy compound ; time ; temperature.

#### Acknowledgements

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#### REFERENCES AND FOOTNOTES

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2. D.F. Banks, *Chemical Reviews*, **66**, 243 (1966); A. Varvoglis, *Chem. Soc. Rev.*, **10**, 377 (1981).
3. a) A.G. González, C.G. Francisco, R. Freire, R. Hernández, J.A. Salazar, and E. Suárez, *Tetrahedron Letters*, 2725 (1976); b) C.G. Francisco, R. Freire, R. Hernández, M.C. Medina, and E. Suárez, *Tetrahedron Letters*, **24**, 4621 (1983); c) R. Hernández, A. Rivera, J.A. Salazar, and E. Suárez, *J.C.S. Chem. Commun.*, 958 (1980); C. Betancor, J.I. Concepción, R. Hernández, J.A. Salazar, and E. Suárez, *J. Org. Chem.*, **48**, 4430 (1983).

4. Iodosobenzene diacetate is a crystalline and stable solid, and it has been used without purification (commercial grade, 98%; Aldrich).
5. M. Akhtar and D.H.R. Barton, *J. Am. Chem. Soc.*, **86**, 1528 (1964).  
Compound (2): m.p. 114-5°C (methanol);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.67 (3H, s, 13-Me), 0.83 (6H, d, J 7 Hz, 25-Me<sub>2</sub>), 0.86 (3H, d, J 7 Hz, 20-Me), 2.00 (3H, s, OAc), 3.69 (2H, s, 19-H<sub>2</sub>), 3.93 (1H, m,  $W_{1/2}$  8 Hz, 6 $\alpha$ -H), 4.6 (1H, m,  $W_{1/2}$  30 Hz, 3 $\alpha$ -H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  69.0 (19-C), 72.3 (3-C), 81.2 (6-C); MS m/z 444 ( $\text{M}^+$ , 20%), 384 ( $\text{M}^+$ -AcOH, 100%).
6. Compound (5): IR  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 3540, 1720, 1250  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.99 (3H, s, 10-Me), 1.10 (3H, d, J 6 Hz, 20-Me), 2.00 (3H, s, OAc), 3.12, 3.28 (2H, AB, J 10.6 Hz, 18-H<sub>2</sub>), 4.0 (1H, m,  $W_{1/2}$  20 Hz, 20-H), 4.6 (1H, m,  $W_{1/2}$  30 Hz, 3 $\alpha$ -H), 5.3 (1H, m,  $W_{1/2}$  13 Hz, 6-H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  10.8 (18-C), 68.4 (20-C); MS m/z 426 ( $\text{M}^+$ -AcOH, 5%), 298 ( $\text{M}^+$ -HI-AcOH, 100%).
7. Compound (6): IR  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 3600, 1720, 1250  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.99 (3H, s, 10-Me), 1.27 (3H, d, J 6 Hz, 20-Me), 2.00 (3H, s, OAc), 3.21, 3.28 (2H, AB, J 10.4 Hz, 18-H<sub>2</sub>), 4.2 (1H, m,  $W_{1/2}$  17 Hz, 20-H), 4.6 (1H, m,  $W_{1/2}$  30 Hz, 3 $\alpha$ -H), 5.3 (1H, m,  $W_{1/2}$  13 Hz, 6-H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  11.85 (18-C), 65.9 (20-C); MS m/z 426 ( $\text{M}^+$ -AcOH, 5%), 298 ( $\text{M}^+$ -HI-AcOH, 100%).
8. Although good results are obtained when molar ratios of substrate:iodine:lead tetraacetate are kept around 1:1.25:5, ratios of 1:5-20:5-30 are often reported.
9. K. Heusler, P. Wieland, and Ch. Meystre, *Org. Synth. Coll.*, vol. V, p. 692 (1973); D. N. Kirk and M.P. Hartshorn, "Steroid Reaction Mechanisms", Elsevier Publishing, Amsterdam, p. 394 (1968).
10. M. Ram, D.D. Godse, and P.K. Bhattacharyya, *Tetrahedron*, **18**, 1457 (1962).  
Compound (7): m.p. 133-5°C (methanol);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.93 (3H, s, 10-Me), 1.19 (3H, d, J 6 Hz, 20-Me), 2.00 (3H, s, OAc), 3.43, 3.70 (2H, AB, J 9.3 Hz, 18-H<sub>2</sub>), 3.7 (1H, m, 20-H), 4.6 (1H, m,  $W_{1/2}$  30 Hz, 3 $\alpha$ -H), 5.3 (1H, m,  $W_{1/2}$  13 Hz, 6-H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  71.6 (18-C), 74.0 (3-C), 84.55 (20-C); MS m/z 298 ( $\text{M}^+$ -AcOH, 100%).  
  
Compound (8): m.p. 161-3°C (methanol);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.91 (3H, s, 10-Me), 1.18 (3H, d, J 6 Hz, 20-Me), 2.00 (3H, s, OAc), 3.39, 3.67 (2H, AB, J 9.1 Hz, 18-H<sub>2</sub>), 3.9 (1H, m,  $W_{1/2}$  18 Hz, 20-H), 4.6 (1H, m,  $W_{1/2}$  30 Hz, 3 $\alpha$ -H), 5.35 (1H, m,  $W_{1/2}$  13 Hz, 6-H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  73.55 (18-C), 74.0 (3-C), 76.9 (20-C); MS m/z 298 ( $\text{M}^+$ -AcOH, 100%).
11. Typically, a solution of the iodo-derivative (6) (1 mmol) in acetone (80 ml) containing silver acetate (4 mmol) was vigorously stirred in the dark at r.t. for 24 h, to give compound (8) in 94% yield.

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