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INTRAMOLECULAR HYDROGEN ABSTRACTION. THE USE OF ORGANOSELENIUM REAGENTS FOR THE GENERATION OF ALKOXY RADICALS

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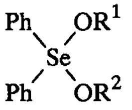
Summary: The alkoxy radical intermediates, produced by photolysis of several hydroxy compounds in the presence of diphenylselenuranes (1) and iodine, undergo intramolecular hydrogen abstraction to afford cyclic ethers in good yield.

Alkoxy radicals, that behave as very reactive species with interesting applications in organic synthesis,[1] are currently prepared mostly by photolysis of alkyl nitrites and the thermal or photochemical decomposition of hypohalites, prepared *in situ* from alcohols and a mixture of an halogen, usually iodine, and a heavy metal acetate such as Pb(IV), Hg(II), and Ag(I), or mercuric oxide.[2]

Recently we have demonstrated that hypervalent organoiodine compounds are excellent reagents not only for the preparation of alkoxy radicals but also neutral aminyl radicals. As reported radicals obtained in this way have been used to promote intramolecular hydrogen abstraction[3] and β-fragmentation reactions.[4]

Continuing with our interest in this field, we have found that diphenylselenuranes (**1**) in the presence of iodine react with alcohols to generate alkoxy radicals which are able to intramolecularly abstract hydrogen atoms from suitably positioned non-activated carbons.



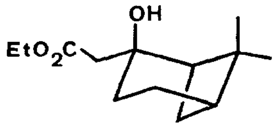
(**1a**) $R^1 = COCH_3; R^2 = OH$

(**1b**) $R^1 = R^2 = COCF_3$

These tetravalent selenium compounds have been known in the literature for some time,[5] and they have been obtained by reaction of diphenylselenoxide with the corresponding acid anhydride[5a] or by treatment of diphenylselenium dibromide with the corresponding carboxylic acid silver salt.[5b]

Despite the fact that selenoxides have recently been recognized to be mild oxidizing agents,[6] relatively little attention has been devoted to the chemistry of these selenuranes, and the use of diphenylselenium bis(trifluoroacetate) (**1b**) for the dehydrogenation of tetrahydropiperidines is the sole reference known.[7]

Diphenylselenium hydroxyacetate (**1a**) was easily prepared in good yield by reaction of diphenylselenoxide[8] with acetic anhydride in THF,[9] as a stable non-hygroscopic crystalline solid which loses acetic acid at 80 °C to give back diphenylselenoxide. Attempts to prepare (**1a**) by the procedure described by Foster[5a] (Ph_2SeO/Ac_2O, 130 °C) led, in our hands, to crystalline mixtures, with variable and irreproduceable rates of acetic acid (as determined by ^{1}HNMR spectroscopy).[10] The diphenylselenium



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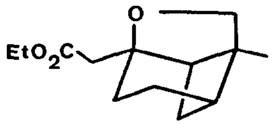

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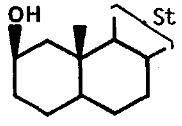

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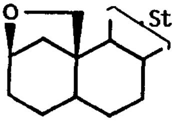

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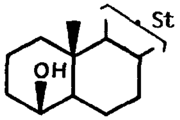

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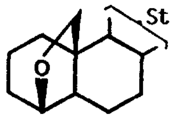

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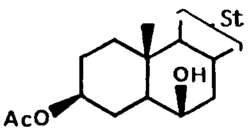

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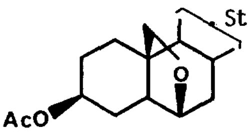

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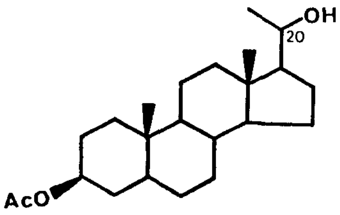

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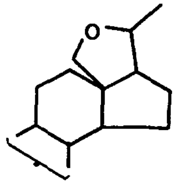

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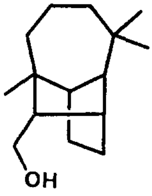

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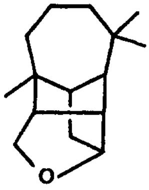

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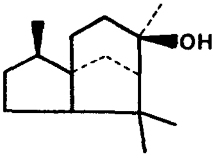

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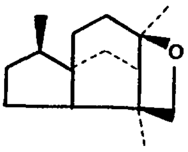

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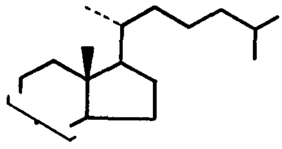

bis(trifluoroacetate) (**1b**) was prepared according to a previously reported procedure.[7]

The results of the photolysis of several alcohols with (**1a**) and (**1b**) in the presence of iodine are summarized in the Table. In general, the reactions proceeded in cyclohexane at reflux temperature with one mol-eq. of iodine and a slight excess of reagent.

The reaction conditions were determined using the bicyclic alcohol (**2**) as starting material (entries 1-5), the presence of iodine is critical for the reaction to take place and a lower yield was observed when

TABLE. Reactions of alcohols with diphenylselenuranes and iodine.[a]

Entry	Alcohol	Reagent[b]	Iodine[b]	Conditions		Products
		(mmol)	(mmol)	(h.	°C)	(yield %)
1	**2**[11]	**1a** (1.7)	1	8	55-60	**3**[11](64); **2** (28)
2	**2**	**1b** (1.7)	1	2.5	55-60	**3** (37); **2** (56)
3	**2**	**1a** (1.7)	1	5	80	**3** (95)
4	**2**	**1a** (1.7)	0.3	10	80	**3** (85)
5	**2**	**1a** (1.7)	0	10	80	**3** (trace)
6	**4**	**1a** (1.7)	1	3	80	**5**[12](89)
7	**6**[13]	**1a** (1.7)	1	4	80	**7**[14](74)
8	**8**[15]	**1a** (1.7)	1	3	80	**9**[16](97)
9	**8**	**1b** (1.6)	1	2	80	**9** (85)
10	**10**[17]	**1a** (2.8)	1	2	80	**12**[16](54)[c]
11	**11**[17]	**1a** (2.8)	1	4.5	80	**13** (68)[d]
12	**14**	**1a** (1.7)	1	8	50	**15**[18](76)[e]
13	**16**	**1a** (1.7)	1	12	50	**17**[19](67)[f]

a) All reactions were performed in cyclohexane and under irradiation with two 100 W tungsten- filament lamps; b) Per mmol of alcohol; c) The 16ξ-iodo-cholestan-3β-yl acetate (20%) was also obtained; d) By-product was 16ξ-iodo-cholestan-3β-yl acetate (4%); e) A iodohydrin (17%) was also obtained; f) A β-fragmentation product, bicyclic iodo methylketone (31%) was also obtained.

catalytic amounts were used (entries 4 and 5). The reagent (**1a**) proved to be more convenient than the less stable and highly hygroscopic bistrifluoroacetate derivative (**1b**) (compare entries 1-2 and 8-9).

The functionalization of the steroidal methyl group at C-10 was achieved from hydroxyl groups at C-2 , C-4 , and C-6 and the C-13 methyl group from the isomeric alcohols at C-20. In all cases the products obtained were the cyclic ether derivatives (entries 6-11) and no iodohydrins or products arising from a second hydrogen abstraction reaction were detected, in contrast with the results obtained with other reagents.[2]

The results of the photolysis of sequiterpenes isolongifolene (**14**) and cedrol (**16**) are shown in entries 12 and 13, an important ratio of β-fragmentation product (31%) is observed for the reaction of the tertiary hydroxyl group of cedrol (**16**).

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9. Preparation of diphenylselenium hydroxyacetate (**1a**): Diphenylselenoxide (5 g, 0.02 mmol) (dried in a vacuum oven 50°C, 24 h.) is dissolved in dry THF (25 ml) and acetic anhydride (2.04 g, 0.02 mmol) is added slowly. The solution is stirred at r.t. for 1 h., concentrated and the residue crystallized from THF/n-pentane, yield (**1a**) 4.9 g. (80%), m.p. (double) 70.5-71.5 and 109.3-111.1°C; ^{1}HNMR (200 MHz, CDCl$_3$) δ 2.05 (3H, s, OAc), 7.46-7.49 (6H, m, Ar), and 7.68-7.73 (4H, m, Ar); Anal. Calcd. for $C_{14}H_{14}O_3Se$: C, 54.38; H, 4.56; Se, 25.53 Found: C, 54.07; H, 4.54; Se, 24.9. As this reaction requires one mole of water and moisture was carefully excluded we probably used a hydrated form of the selenoxide; see C. Paulmier, "Selenium Reagents and Intermediates in Organic Synthesis", ed. J.E. Baldwin, Pergamon Press, 1986, p. 128, and references cited therein.
10. Whether these substances contain acetic acid or acetic anhydride of crystallization has not been determined.
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12. Compound (**5**): m.p. 91-92 °C (MeOH); $[\alpha]_D$ +37° (CHCl$_3$); ^{1}HNMR (200 MHz, CDCl$_3$) δ 0.61 (3H, s, 13-Me), 0.85 (6H, d, J 6.4 Hz, 25-Me$_2$), 0.89 (3H, d, J 6.7 Hz, 20-Me), and 3.64 and 3.81 (2H, AB, J 8.0 Hz, 19-H$_2$), 4.25 (1H, apparent t, 2α-H); ^{13}CNMR (50.3 MHz, CDCl$_3$) δ *inter alia* 67.62 (C-19) and 74.16 (C-2); MS m/z 386.3550 (M$^+$ 42%).
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14. Compound (**7**): m.p.202-204 °C (acetone); $[\alpha]_D$ +45° (CHCl$_3$); ^{1}HNMR (200 MHz, CDCl$_3$) δ 0.62 (3H, s, 13-Me), 0.84 (6H, d, J 6.3 Hz, 25-Me$_2$), 0.86 (3H, d, J 5.1 Hz, 20-Me), 3.64 and 3.86 (2H, AB, J 8.1 Hz, 19-H$_2$), and 3.89 (1H, m, W$_{1/2}$ 5 Hz, 4α-H); ^{13}CNMR (50.3 MHz, CDCl$_3$) δ 71.43 (C-19) and 81.47 (C-4); MS m/z 386.3542 (M$^+$, 36%).
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