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STUDIES ON THE TERPENOIDS AND RELATED ALICYCLIC COMPOUNDS—XXII[1]

STEREOCHEMICAL STUDY ON THE ANGULAR HYDROXYLATION OF POLYCYCLIC KETONES USING BENZENESELENINIC ANHYDRIDE

KOJI YAMAKAWA,* TSUYOSHI SATOH, NOBUYUKI OHBA, REIJI SAKAGUCHI, SATOSHI TAKITA and NOBUHIKO TAMURA

Faculty of Pharmaceutical Sciences, Science University of Tokyo
Ichigaya-funagawara-machi, Shinjuku-ku, Tokyo 162, Japan

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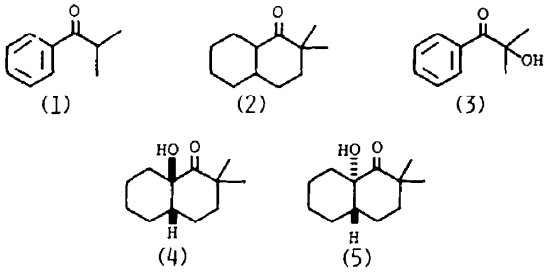
Abstract—Introduction of an OH group to the tertiary carbon of simple ketones (**1**, **2** and **6**), furanoeremophilane-type ketones (**12**–**19**), and tricyclic ketones (**20**–**22**) by the use of benzeneseleninic anhydride is described. 10β-Hydroxy compounds were obtained in the case of **12**–**14**, and **20**–**22**. 10α-Hydroxy compounds were obtained in the case of **15** and **16**. In the hydroxylation reaction of polycyclic ketones using benzeneseleninic anhydride, the results suggest that the thermodynamically more stable product was usually produced as the major product.

Benzeneseleninic anhydride, $(PhSeO)_2O$, is an effective oxidation reagent, although a number of alicyclic alcohols were oxidized to carbonyl derivatives and the corresponding enones were obtained in some cases by further oxidation. Furthermore, a number of phenols were oxidized to *o*-hydroxyketones or quinones by this reagent. These extensive studies have been reported by Barton *et al.*[2] The authors[3] have recently reported, as preliminary communication, the introduction of an OH group into the angular position of tricyclic ketones using $(PhSeO)_2O$. We describe here, in detail, the hydroxylation of polycyclic ketones and related simple compounds by this reagent and its stereochemical considerations.

Oxidation of simple ketones using $(PhSeO)_2O$

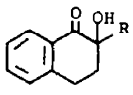
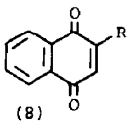
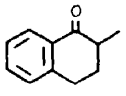
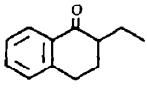
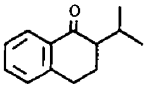
Oxidation of phenyl isopropyl ketone (**1**) and 2,2-dimethyldecalone[4] (**2**) using $(PhSeO)_2O$ gave the corresponding a hydroxy compound (**3**), oil in 44% yield and a mixture of **4**, oil, and **5**, m.p. 98–100°, in 30% yield. Structure and stereoformula of A/B ring *cis*-**4** and A/B ring *trans*-**5** was assumed from their spectral data. A signal of the Me protons of **5** shows lower shift, $\Delta\delta$ 0.11 ppm, than that of **4** due to 1,3-diaxial interaction of the OH group at 8a.



(1) (2) (3) (4) (5)

(**1**)-(**5**)

Table 1.

	BSA* eq.	NaH eq.	$AlCl_3$ eq.	time hr	 (7)	 (8)	recovered 6 (%)	total yield (%)
	2			1.5	25	75		78
	2	1.1		3.5	93	7		86
(6a)	2		2	1.5	0	100	33	51
	2			2	20	80	14	82
	2	2		10	90	10	16	81
(6b)	2		2	5	0	100	20	51
	2			3	28	72		99
	2	1.2		5.5	94	6		96
(6c)	2		2	5	0	100	21	24

* Benzeneseleninic anhydride

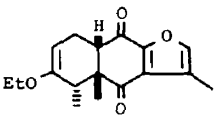
2-Methyl-, 2-ethyl, and 2-isopropyl-1-tetralones (**6a–c**) were prepared, according to the procedure reported by Couture.[5] Oxidation of **6a–c** with $(PhSeO)_2O$ gave a mixture of hydroxy compounds (**7a–c**) as minor product and naptho-1,4-quinone derivatives (**8a–c**) as major product, respectively. In the presence of sodium hydride in these reaction mixtures, respectively, the corresponding hydroxy compounds (**7a–c**) were obtained as major product, whereas in the presence of aluminium chloride instead of sodium hydride gave only the corresponding quinone derivatives (**8a–c**), respectively. These reaction results are summarized in Table 1.

Treatment of **7a–c** under the same oxidation conditions gave unchanged starting material, therefore quinones (**8a–c**) could not be formed via route (a). Hydroxy compounds (**7a–c**) presumably were formed via O-ester intermediate (A) by enolization of the 1-oxo group of **6a–c**. The formation of intermediate (A) was increased by means of sodium hydride as hard base. In the presence of aluminium chloride, enolization of the 1-oxo group was prevented due to chelation with aluminium chloride, and then C-phenylselenoxylation of **6a–c**, respectively, occured via route (b). Resulting enones were further oxidized by $(PhSeO)_2O$ to give naphtho-1,4-quinones (**8a–c**). The reaction mechanism is proposed in Scheme 1.

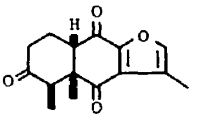
Oxidation of eremophilane-type ketones using $(PhSeO)_2O$

Eight furanoeremophilane-type ketones (**12–19**) and three tricyclic ketones (**20 22**)[6] were used as substrates in this oxidation. The ketones (**12** and **15**) were prepared starting from the diene adduct (**9**) which was previously reported.[7] The ketone **14** was synthesized according to the Bohlmann's procedure.[8] Reduction of furanoeremophilane-3,6,9-trione (**10**)[9] with tris-t-butoxy lithium aluminum hydride gave 3β-hydroxyfuranoeremophilane-6,9-dione (**13a**) and hemiacetal compound (**11**).[8] **13a** was converted into the acetate (**13b**), m.p. 164–166 . The preparation procedures of other ketones (**16–19**) are described in the Experimental s.

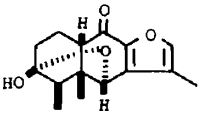
Oxidation of 3,3-ethylenedioxy-furanoeremophilane-6,9-dione (**12**)[7] with $(PhSeO)_2O$ gave an hydroxy compound (**23**), m.p. 130–132 , and (**24**), m.p. 195–199 , in 57% and 17% yields, respectively. The structures of **23** and **24** were confirmed from their



(9)

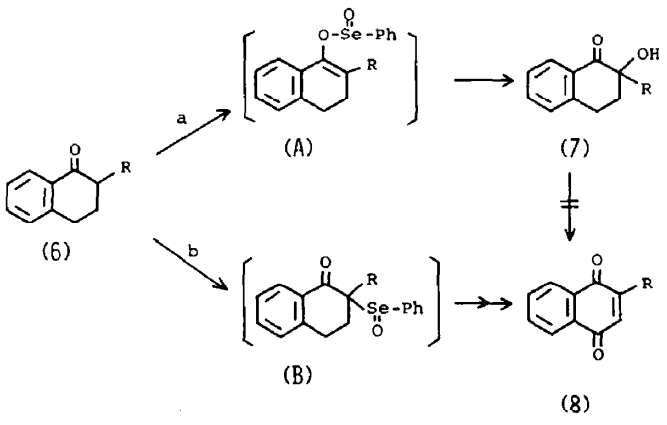


(10)



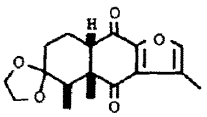
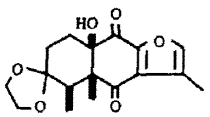
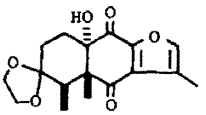
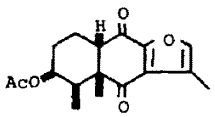
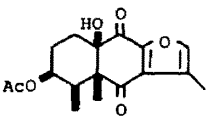
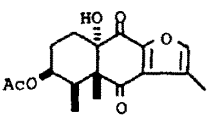
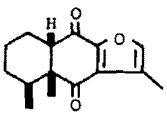
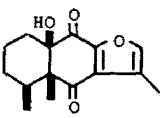
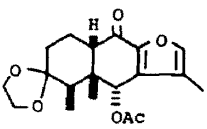
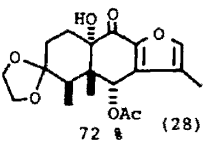
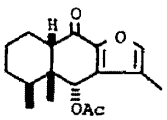
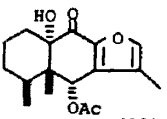
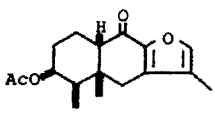
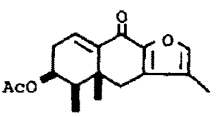
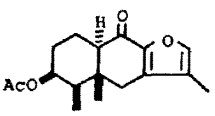
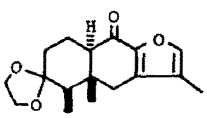
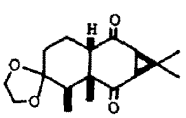
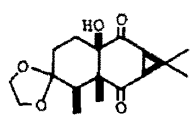
(11)

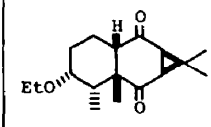
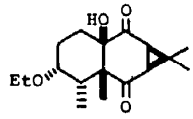
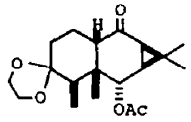
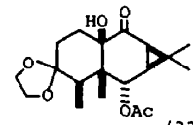
spectral data. In ^{13}C-NMR spectra of **12** and **23**, a doublet signal of 10-C at δ 53.7 in **12** changed to a singlet signal at δ 80.6 in **23** due to introduction of an OH group. In the ^1H-NMR spectrum of **23**, C-4 H appeared as a quartet signal at δ 2.81 with long-range coupling (J = 1 Hz) with C-2-H attributed to the "W" arrangement. While C-4 H of **24** did not show long-range coupling. From these spectral data, the stereoformula of major product (**23**) should be a 10β-hydroxy compound by the non-steroidal conformation, and also a minor product (**24**) showed to be a 10α-hydroxy compound. Oxidation of 3β-acetoxy-furanoeremophilane-6,9-dione (**13b**) with $(PhSeO)_2O$ under the similar conditions for **12** gave the 10β-hydroxy product (**25**), m.p. 148–150 , as major (57% yield) product and the 10α-hydroxy compound (**26**), m.p. 221–223 , as minor (12% yield) product. Oxidation of furanoeremophilane-6,9-dione (**14**)[8] with $(PhSeO)_2O$ under conditions described above gave only the 10β-hydroxy compound (**27**), m.p. 147–149 , in 42% yield. Stereoformula of the major 10β-hydroxy compounds **25** and **27** were confirmed by their ^1H-NMR spectral data as described for **23**. 10β-Hydroxy compounds (**23**, **25**, and **27**) were the major product in this oxidation of **12**, **13b**, and **14**, respectively. However, oxidation of 6α-acetoxyfuranoeremophilan-9-one derivatives (**15** and **16**) with $(PhSeO)_2O$ in chlorobenzene gave only 10α-hydroxy compounds (**28**), m.p. 224–226 , and (**29**), m.p. 158–160 , respectively. Stereoformula of 10α-hydroxy compounds (**28** and **29**) were confirmed by means of their spectral data and chemical evidence as similar to **24** and **26**.



Scheme 1

Table 2.

Entry		BSA* eq.	solv.	temp.	time hr	Product
1	 (12)	2	$PhCH_3$	110°	4	 57 % (23)  17 % (24) (12) 24 %
2	 (13b)	5	$PhCH_3$	110°	9	 57 % (25)  12 % (26)
3	 (14)	3	$PhCH_3$	110°	2.5	 42 % (27)
4	 (15)	4	PhCl	131°	2	 72 % (28)
5	 (16)	4	PhCl	100°	12	 20 % (29)
6	 (17)	5	PhCl	131°	4	 9 % (30) (17) 53 %
7	 (18)	5	PhCl	131°	3	(30) 16 % (18) 20 %
8	 (19)	3	PhCl	131°	4	decomposition
9	 (20)	1.2	PhCl	131°	4.5	 47 % (31) (20) 35 %

10	 (21)	1.15	$PhCH_3$	110°	5	 43 % (32)	(21) 39 %
11	 (22)	1.2	$PhCH_3$	110°	4	 37 % (33)	(22) 54 %

* Benzeneseleninic anhydride

A chlorobenzene solution of 3β-acetoxyfurano-eremophilan-9-one derivatives (**17** and **18**) and $(PhSeO)_2O$ was heated under reflux to afford only 3β-acetoxy-$\Delta^{1(10)}$-furanoermophilan-9-one (**30**) in low yield. Treatment of 3,3-ethylenedioxy-10αH-furano-eremophilan-9-one (**19**) with $(PhSeO)_2O$ under the same condition described for **17** and **18** did not give a pure product due to decomposition. The results are summarized in Table 2.

Oxidation of tricyclic ketones (**20–22**) *using* $(PheSO)_2O$

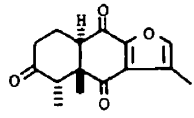
A solution of tricyclic ketones containing a cyclopropane ring (**20–22**), which were prepared starting from the major diene adduct of 3-ethoxy-1,3-pentadiene and (+)-3-carene-2,5-dione,[6] and $(PhSeO)_2O$ in toluene, except for **20** in chlorobenzene, was heated under reflux for 4–5 hr. 10β-Hydroxy compounds (**31**), m.p. 148–150°, (**32**), m.p. 155–157°, and (**33**), m.p. 170.5–172°, were the only products in 73%, 80%, and 70% yields from **20**, **21**, and **22**, respectively. These results are summarized in Table 2.

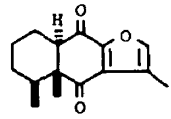
Structures of **31–33** were confirmed from their spectral data. The OH absorption band in the IR spectra of **31–33** appeared at 3450, 3380, and 3420 cm^{-1}, respectively. In the ^{13}C-NMR spectra of **31**, **32**, and **33**, the chemical shift of 10-C appeared as a singlet signal by off-resonance techniques at δ 79.7, 78.1, and 79.9, respectively. In the ^1H-NMR spectra of **31** and **33**, C-4 H appeared as a quartet signal at δ 2.58 and 2.61, respectively, with long-range coupling with C-2 H attributed to the "W" arrangement. From these spectral data, the stereoformula of **31** and **33** should be a non-steroidal conformation.

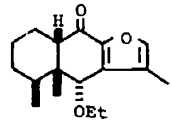
Stereochemical considerations

The oxidation of some ketones of furanoeremophilanes and tricyclic compounds using $(PhSeO)_2O$ gave two stereoisomeric A/B *cis*- and *trans* ring angular hydroxy compounds as described above. The stereochemistry of the hydroxylation via enolic O-ester intermediate (A) are considered below.

We previously reported[9] that the A/B ring *trans* compound, 10αH-furanoeremophilane-3,6,9-trione (**34**) was isomerized to A/B ring *cis* compound (**10**) by *p*-toluenesulfonic acid catalyst. Bohlmann *et al.*[8] has also reported that A/B ring *trans* 6,9-diketone (**35**) was isomerized to A/B ring *cis* diketone (**14**) by triethylamine catalyst. This evidence strongly suggests that A/B ring *cis*-6,9-diketofuranoeremophilanes are


(34)


(35)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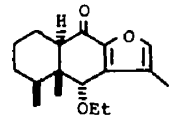
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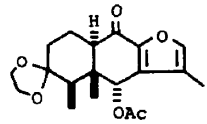
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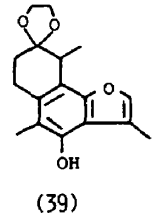
(39)

thermodynamically more stable than the corresponding A/B ring *trans*-6,9-diketones. As shown (entry 1–3 in Table 2) A/B ring *cis*-10β-hydroxy-6,9-diketones (**23**, **25**, and **27**) were formed as the major products.

On the other hand, Sorm *et al.*[10] reported that A/B ring *cis*-furanoeremophilan-6α-ethyl ether (**36**) was isomerized to A/B ring *trans*-6α-ether (**37**) by alkaline catalyst. Now, treatment of A/B ring *cis*-furanoeremophilan-6α-acetate (**15**) with sodium hydride catalyst gave A/B ring *trans*-6α-acetate (**38**), m.p. 203–205°, and benzofuran derivative (**39**), m.p. 172–174°, in 57% and 20% yields, respectively. This evidence suggests that A/B ring *trans*-furanoeremophilan-6α-acetates

are thermodynamically more stable than the corresponding A/B ring *cis*-6α-acetates. As shown (entry 4 and 5 in Table 2) A/B ring *trans*-10α-hydroxy-6α-acetates were obtained as the only products.

In tricyclic ketones including a cyclopropane ring (**20**–**22**), A/B ring *cis* compounds are considered thermodynamically more stable than the corresponding A/B ring *trans* compounds. As shown (entry 9–11 in Table 2) A/B ring *cis* hydroxy compounds (**31**–**33**) were obtained.

In the hydroxylation reactions of polycyclic ketones using $(PhSeO)_2O$, these results suggest that the thermodynamically more stable product was usually produced as the major product. In the oxidations it is considered that "product development control" is a major factor governing the reaction via O-selenyloxy ester intermediate (A) as shown in Scheme 1.

EXPERIMENTAL

All m.ps are uncorrected. IR spectra were recorded on a Hitachi 215 or Hitachi Perkin–Elmer 225 spectrophotometer. UV spectra were measured with a Hitachi 323 or 200 spectrophotometer. NMR spectra are for soln in $CDCl_3$ and they were measured on a JEOL JNM-FX 100 fourier transform (100 MHz), or Hitachi R-24B (60 MHz) spectrometer. Low and high-resolution mass spectra were taken on a Hitachi RMU-7 M double focusing spectrometer connected with data lyser 002 system.

Reduction of triketone (**10**) *with* $LiAlH(^tBuO)_3$. To a soln of **10**[9] (51 mg; 0.2 mmol) in THF (5 ml) was added 71 mg (0.28 mmol) of $LiAlH(^tBuO)_3$ at 0° and the soln was stirred for 25 min. Water was added to the mixture and then the soln was evaporated *in vacuo*. The residue was extracted with ether and the organic layer was washed with water and dried. After removal of the ether, the residue was separated by silica gel preparative tlc to afford 29 mg (57%) of **13a** and 16 mg (31%) of **11**. **13a**—colorless prisms, m.p. 127–129° from EtOAc hexane (reported,[8] oil). **11**—colorless prisms, m.p. 180–182° from EtOAc–hexane (reported,[8] m.p. 180°).

3β-Acetoxyfuranoeremophilane-6,9-dione (**13b**). **13a** (68 mg) was converted to the corresponding acetate (**13b**), 69 mg (88%) as colorless prisms, m.p. 164–166° from EtOAc-hexane. (Found: C, 66.75; H, 6.69. $C_{17}H_{20}O_5$ requires: C, 67.09; H, 6.62%), IR cm^{-1}: 1735, 1700, 1690 (CO), 1265 (COC); UV λ_{max}^{EtOH} 304 nm (ε 7600), 244.5 nm (ε 5400); NMR δ: 0.95 (3H, d, J = 7 Hz, 4-CH_3), 1.03 (3H, s, 5-CH_3), 2.07 (3H, s, $COCH_3$), 2.27 (3H, d, J = 1 Hz, 11-CH_3), 4.81 (1H, m, $W_{\frac{1}{2}}$ = 18 Hz, 3-H), 7.44 (1H, q, J = 1 Hz, 12-H); Mass m/z (% Rel. int.): 304 (M^+, 8), 262 ([M-C_2H_2O]$^+$, 63), 244 ([M-CH_3CO_2H]$^+$, 100).

6α-Acetoxyfuranoeremophilan-9-one (**16**). To a soln of 168 mg (0.5 mmol) of 3,3-ethylenedithio-furanoeremophilane-6,9-dione[8] in THF (20 ml) and MeOH (27 ml), $NaBH_4$ (45 mg) was added at 0° and the mixture stirred for 40 min. After work up in the usual manner, the products were dissolved in 25 ml of a mixture of Ac_2O-pyridine (1:4), and CH_2Cl_2 (13 ml) and 4-dimethylaminopyridine (27 mg) was added. The mixture was allowed to stand at room temp for 16 hr. After evaporation of the solvent, the crude acetates were separated by silica gel preparative tlc to afford 148 mg (78%) of 6α-acetate and 21 mg (11%) of 9α-acetate. 6α-Acetate colorless prisms, m.p. 159–161° from EtOAc-hexane. (Found: C, 60.16; H, 6.39. $C_{19}H_{24}O_4S_2$ requires: C, 59.97; H, 6.36%); IR cm^{-1}: 1755, 1685 (CO), 1230 (COC); UV λ_{max}^{EtOH} 284 nm (ε 14000), NMR δ: 1.28 (3H, d, J = 7 Hz, 4-CH_3), 1.29 (3H, s, 5-CH_3), 1.98 (3H, d, J = 1 Hz, 11-CH_3), 2.23 (3H, s, $COCH_3$), 3.0–3.4 (4H, m, $\begin{matrix}CH_2S\\CH_2S\end{matrix}$), 6.19 (1H, s, 6-H), 7.35 (1H, q, J = 1 Hz, 12-H); Mass m/z (% Rel. int.): 380 (M^+, 17) 320 ([M-CH_3CO_2H]$^+$, 11), 291 (10), 227 (10), 131 (100). 9α-Acetate—colorless plates, m.p. 178–180° from EtOAc-hexane. IR cm^{-1}: 1755, 1675 (CO), 1245 (COC); UV λ_{max}^{EtOH} 266 nm (ε 4600); NMR δ: 1.17 (3H, s, 5-CH_3), 1.27 (3H, d, J = 7 Hz, 4-CH_3), 2.21 (3H, s, $COCH_3$), 2.22 (3H, d, J = 1 Hz, 11-CH_3), 2.9–3.4 (4H, m, $\begin{matrix}CH_2S\\CH_2S\end{matrix}$), 6.21 (1H, d, J = 6 Hz, 9-H), 7.14 (1H, q, J = 1 Hz, 12-H); Mass m/z (% Rel. int.): 380 (M^+, 54), 320 ([M-CH_3CO_2H]$^+$, 49), 227 (37), 202 (39), 138 (76), 131 (100).

A soln of the 6α-acetate (139 mg) in dry dioxane (10 ml) was refluxed for 15 min with Raney Ni (1.4 g). After removal of Ni and evaporation of the dioxane *in vacuo*, the residue was purified by silica gel preparative tlc to afford 90 mg of desulfrized products (nearly equal amount of **16** and dehydro product). The product was dissolved in EtOAc (8 ml) and catalytically reduced with 10% Pd-charcoal (100 mg) at room temp for 24 hr. After work up, the product was purified by preparative tlc on silica gel to afford 89 mg (84%) of **16** as colorless needles, m.p. 125–126° from EtOAc–hexane (reported[8] m.p. 121°).

3β-Acetoxyfuranoeremophilan-9-one (**17**). 3β-Hydroxyfuranoeremophilan-9-one[7] (24 mg) was converted to the corresponding acetate by usual manner to give 27 mg (96%) of **17** as colorless prisms, m.p. 130–132° from EtOAc hexane (Found: m/z 290.1499. $C_{17}H_{22}O_4$ requires: 290.1516); IR cm^{-1}: 1735, 1660 (CO), 1255 (COC); UV λ_{max}^{EtOH} 281.5 nm (ε 16400); NMR δ: 0.96 (3H, d, J = 7 Hz, 4-CH_3), 1.07 (3H, s, 5-CH_3), 1.99 (3H, d, J = 1 Hz, 11-CH_3), 2.08 (3H, s, $COCH_3$), 2.28 (1H, d, J = 18 Hz, 6-H), 3.10 (1H, d, J = 18 Hz, 6-H), 5.18 (1H, m, $W_{\frac{1}{2}}$ = 10 Hz, 3-H), 7.36 (1H, q, J = 1 Hz, 12-H); Mass m/z (% Rel. int.): 290 (M^+, 41), 248 ([M-C_2H_2O]$^+$, 28), 230 ([M CH_3CO_2H]$^+$, 59), 215 ([M CH_3CO_2H CH_3]$^+$, 42), 107 (100).

10αH-3β-Acetoxyfuranoeremophilan-9-one (**18**). 10αH-3β-Hydroxyfuranoeremophilan-9-one[7] (18 mg) was acetylated in a usual manner to afford 19 mg (90%) of **18** in a colorless granular form, m.p. 158–160° from EtOAc–hexane. (Found: m/z 290.1521. $C_{17}H_{22}O_4$ requires: 290.1516); IR cm^{-1}: 1735, 1680 (CO), 1260 (COC); UV λ_{max}^{EtOH} 279 nm (ε 16300); NMR δ: 0.96 (3H, s, 5-CH_3), 1.02 (3H, d, J = 7 Hz, 4-CH_3), 1.99 (3H, d, J = 1 Hz, 11-CH_3), 2.06 (3H, s, $COCH_3$), 2.43 (1H, d, J = 17 Hz, 6-H), 2.70 (1H, d, J = 17 Hz, 6-H), 5.00 (1H, m, $W_{\frac{1}{2}}$ = 6 Hz, 3-H), 7.32 (1H, q, J = 1 Hz, 12-H); Mass m/z (% Rel. int.): 290 (M^+, 44), 230 ([M-CH_3CO_2H]$^+$, 53), 215 (49), 175 (34), 162 (100).

10αH-3,3-Ethylenedioxy-furanoeremophilan-9-one (**19**). To a solution of 40 mg of 10αH-furanoeremophilane-3,9-dione[7] in 2,2-ethylenedioxybutane (16 ml) was added $TsOH \cdot H_2O$ (14 mg). The mixture was allowed to stand at room temp for 3 days. The soln was diluted with 100 ml ether, then washed with sat $NaHCO_3$aq. The ether and 2,2-ethylenedioxybutane was evaporated *in vacuo* and the residue was separated by silica gel preparative tlc to afford 26 mg (55%) of **19** as colorless needles, m.p. 135–137° from EtOAc-hexane. (Found: C, 70.16; H, 7.70. $C_{17}H_{22}O_4$ requires: C, 70.32; H, 7.64%); IR cm^{-1}: 1670 (CO); UV λ_{max}^{EtOH} 279.5 nm (ε 15200); NMR δ: 0.93 (3H, s, 5-CH_3), 0.97 (3H, d, J = 7 Hz, 4-CH_3), 1.98 (3H, d, J = 1 Hz, 11-CH_3), 2.46 (1H, d, J = 16 Hz, 6-H), 2.69 (1H, d, J = 16 Hz, 6-H), 3.7–4.1 (4H, m, $\begin{matrix}CH_2O\\CH_2O\end{matrix}$), 7.32 (1H, q, J = 1 Hz, 12-H); Mass m/z (% Rel. int.): 290 (M^+, 14), 261 ([M-C_2H_5]$^+$, 4), 99 (100).

General procedure for the oxidation of the ketones using $(PhSeO)_2O$.

(a). A soln of the ketone and $(PhSeO)_2O$ in toluene or chlorobenzene was refluxed for several hr. The mixture was cooled to room temp and the resulting ppt was filtered off. The filtrate was evaporated *in vacuo*, and the residue was purified by silica gel preparative tlc or column chromatography.

(b). A soln of the ketone, $(PhSeO)_2O$, and NaH in toluene was refluxed for several hr. The mixture was worked up exactly according to the general procedure (a).

(c). A soln of the ketone, $(PhSeO)_2O$, and $AlCl_3$ in toluene was refluxed for several hours. The mixture was worked up exactly according to the general procedure (a).

Oxidation of phenyl isopropyl keton (**1**) *using* $(PhSeO)_2O$. According to the general procedure (b), 37 mg (0.25 mmol) of **1** was treated with 180 mg (0.5 mmol) of $(PhSeO)_2O$ in the presence of NaH (50% in mineral oil, 24 mg) for 3 days to give 18 mg (44%) of **3**[11] as an oil and 10 mg (27%) of recovered **1**.

Oxidation of 2,2-dimethyl-1-decalone (**2**) *using* $(PhSeO)_2O$. According to the general procedure (b), 48 mg (0.27 mmol) of **2**[4] in chlorobenzene (2 ml) was treated with 194 mg (0.54 mmol) of $(PhSeO)_2O$ in the presence of NaH (50% in mineral oil, 26 mg) for 14 hr to give 8 mg (15%) of *cis*-**4**, oil, and 8 mg (15%) of *trans*-**5**, and 24 mg (50%) of recovered **2**. **4**—IR cm^{-1}: 3500 (OH), 1690 (CO); NMR δ: 1.13 (3 H, s, 2-CH_3), 1.23 (3 H, s, 2-CH_3); Mass *m/z* 196 (M^+). **5**—colorless needles, m.p. 98–100° from hexane. IR cm^{-1}: 3470 (OH), 1690 (CO); NMR δ: 1.05 (3 H, s, 2-CH_3), 1.34 (3 H, s, 2-CH_3); Mass *m/z* 196 (M^+).

Oxidation of 2-alkyl-1-tetralone (**6a**, **6b**, **6c**) *using* $(PhSeO)_2O$. 2-Alkyl-1-tetralones were synthesized according to the Couture's procedure.[5] 2-Ethyl-1-tetralone (**6b**), oil, IR cm^{-1}: 1680, 1690 (CO); NMR δ: 1.00 (3 H, t, J = 7.5 Hz, $-CH_2CH_3$); Mass *m/z* 174 (M^+).

(a). According to the general procedure (a), **6** (0.25 mmol) and $(PhSeO)_2O$ (0.5 mmol) in toluene (2 ml) was refluxed for several hr to give **7** and quinone (**8**), which were summarized in Table 1. **7a**—oil, IR cm^{-1}: 3480 (OH), 1690 (CO); NMR δ: 1.39 (3 H, s, 2-CH_3); Mass *m/z* 176 (M^+). **8a**—m.p. 108.5–109.5° (reported[12] m.p. 107°). **7b**—oil, IR cm^{-1}: 3500 (OH), 1685 (CO); NMR δ: 0.92 (3 H, t, J = 7.5 Hz, $-CH_2CH_3$); Mass *m/z* 190 (M^+). **8b**—yellow prisms, m.p. 84–86° from hexane. IR cm^{-1}: 1665 (CO); NMR δ: 1.21 (3 H, t, J = 7.5 Hz, $-CH_2CH_3$), 2.61 (2 H, dq, J = 7.5, 2 Hz, $-CH_2CH_3$), 6.74 (1 H, t, J = 2 Hz, 3-H); Mass *m/z* 186 (M^+). **7c**—m.p. 68–69° (reported[13] m.p. 66–68°). **8c**—m.p. 46.5–47° (reported[14] m.p. 45–46.5°).

(b) According to the general procedure (b), **6** and $(PhSeO)_2O$, and NaH in toluene was refluxed for several hr to give **7** and **8**, which were summarized in Table 1.

(c) According to the general procedure (c), **6** and $(PhSeO)_2O$, and $AlCl_3$ in toluene was refluxed for several hr to give only quinone (**8**) and recovered starting material, which were summarized in Table 1.

Oxidation of 3,3-ethylenedioxy-furanoeremophilane-6,9-dione (**12**) *using* $(PhSeO)_2O$. According to the general procedure (a), 122 mg (0.4 mmol) of **12**[7] in toluene (10 ml) was treated with 288 mg (0.8 mmol) of $(PhSeO)_2O$ for 4 hr to afford 74 mg (57%) of **23** and 22 mg (17%) of compound **24**, and 30 mg (24%) of recovered **12**. **23**—colorless needles, m.p. 130–132° from EtOAc–hexane. (Found: C, 63.73; H, 6.21. $C_{17}H_{20}O_6$ requires: C, 63.74; H, 6.29%); IR cm^{-1}: 3520 (OH), 1685, 1675 (CO); UV λ_{max}^{EtOH} 304 nm (ε 7900), 243 (ε 4800); NMR δ: 1.17 (3 H, d, J = 7 Hz, 4-CH_3), 1.19 (3 H, s, 5-CH_3), 2.30 (3 H, d, J = 1 Hz, 11-CH_3), 2.81 (1 H, dq, J = 7, 1 Hz 4-H), 3.7–4.2 (4 H, m, $\begin{matrix}CH_2O\\|\\CH_2O\end{matrix}$), 7.55 (1 H, q, J = 1 Hz, 12-H); Mass *m/z* (% Rel. int.): 320 (M^+, 3), 99 ([M-$C_{12}H_{13}O_4$]$^+$, 100). Compound **24**—colorless prisms, m.p. 195–199° from EtOAc–hexane. (Found: C, 63.64; H, 6.10. $C_{17}H_{20}O_6$ requires: C, 63.74; H, 6.29%); IR cm^{-1}: 3490 (OH), 1700 (CO); UV λ_{max}^{EtOH} 302 nm (ε 8400), 243 nm (ε 3900); NMR δ: 1.16 (3 H, d, J = 7 Hz, 4-CH_3), 1.27 (3 H, s, 5-CH_3), 2.25 (3 H, d, J = 1 Hz, 11-CH_3), 2.85 (1 H, q, J = 7 Hz, 4-H), 3.9–4.1 (4 H, m, $\begin{matrix}CH_2O\\|\\CH_2O\end{matrix}$), 7.47 (1 H, q, J = 1 Hz, 12-H); Mass *m/z* (% Rel. int.): 320 (M^+, 19), 99 ([M-$C_{12}H_{13}O_4$]$^+$, 100).

Oxidation of 3β-acetoxyfuranoeremophilane-6,9-dione (**13b**) *using* $(PhSeO)_2O$. According to the general procedure (a), 47 mg (0.15 mmol) of **13b** in toluene (5 ml) was treated with 273 mg (0.76 mmol) of $(PhSeO)_2O$ for 9 hr to afford 28 mg (57%) of compound **25** and 6 mg (12%) of **26**. Compound **25**—colorless crystals, m.p. 148–150° from EtOAc–hexane. Found: *m/z* 320.1231. $C_{17}H_{20}O_6$ requires: 320.1258); IR cm^{-1}: 3520 (OH), 1750, 1700, 1670 (CO), 1260, 1250 (COC); UV λ_{max}^{EtOH} 305 nm (ε 7700), 244 nm (ε 5000); NMR δ: 1.18 (3 H, d, J = 7 Hz, 4-CH_3), 1.21 (3 H, s, 5-CH_3), 2.07 (3 H, s, $COCH_3$), 2.29 (3 H, d, J = 1 Hz, 11-CH_3), 2.88 (1 H, dq, J = 7, 2.5 Hz, 4-H), 4.79 (1 H, m, $W_{\frac{1}{2}}$ = 17 Hz, 3-H), 7.52 (1 H, q, J = 1 Hz, 12-H); Mass *m/z* (% Rel. int.): 320 (M^+, 35), 260 ([M-CH_3CO_2H]$^+$, 17), 43 (100). Compound **26**—colorless prisms, m.p. 221–223°. (Found: *m/z* 320.1259. $C_{17}H_{20}O_6$ requires: 320.1258); IR cm^{-1}: 3480 (OH), 1750, 1705, 1690, 1680 (CO), 1265, 1230 (COC); UV λ_{max}^{EtOH} 302 nm (ε 8500); NMR δ: 1.21 (3 H, d, J = 7 Hz, 4-CH_3), 1.32 (3 H, s, 5-CH_3), 2.07 (3 H, s, $COCH_3$), 2.24 (3 H, d, J = 1 Hz, 11-CH_3), 2.70 (1 H, dq, J = 7, 3 Hz, 4-H), 5.06 (1 H, m, $W_{\frac{1}{2}}$ = 8 Hz, 3-H,), 7.44 (1 H, q, J = 1 Hz, 12-H); Mass *m/z* (% Rel. int.): 320 (M^+, 21), 260 ([M-CH_3CO_2H]$^+$, 56), 245 ([M-CH_3CO_2H-CH_3]$^+$, 59), 242 (41), 227 (100).

Oxidation of furanoeremophilane-6,9-dione (**14**) *using* $(PhSeO)_2O$. According to the general procedure (a), 26 mg (0.1 mmol) of **14**[8] in toluene (10 ml) was treated with 117 mg (0.33 mmol) of $(PhSeO)_2O$ for 2.5 hr to afford 12 mg (43%) of **27** as colorless needles, m.p. 147–149° from EtOAc–hexane. (Found: *m/z* 262.1228. $C_{15}H_{18}O_4$ requires: 262.1204); IR cm^{-1}: 3485 (OH), 1690, 1680 (CO); UV λ_{max}^{EtOH} 303 nm (ε 12000), 242.5 nm (ε 6700); NMR δ: 1.01 (3 H, d, J = 7 Hz, 4-CH_3), 1.20 (3 H, s, 5-CH_3), 2.28 (3 H, d, J = 1 Hz, 11-CH_3), 7.48 (1 H, q, J = 1 Hz, 12-H); Mass *m/z* (% Rel. int.): 262 (M^+, 72), 244 ([M-H_2O]$^+$, 11), 234 (41), 218 (57), 108 (100).

Oxidation of 6α-acetoxy-3,3-ethylenedioxy-furanoeremophilan-9-one (**15**) *using* $(PhSeO)_2O$. According to the general procedure (a), 40 mg (0.115 mmol) of **15**[7] in chlorobenzene (4 ml) was treated with 166 mg (0.46 mmol) of $(PhSeO)_2O$ for 2 hr to afford 30 mg (72%) of **28** as colorless prisms, m.p. 224–226° from EtOAc-hexane. (Found: C, 62.51; H, 6.63. $C_{19}H_{24}O_7$ requires: C, 62.63; H, 6.64%); IR cm^{-1}: 3550 (OH), 1740, 1680 (CO), 1235 (COC); UV λ_{max}^{EtOH} 284 nm (ε 12800), 239 nm (ε 3600); NMR δ: 0.90 (3 H, d, J = 7 Hz, 4-CH_3), 1.03 (3 H, s, 5-CH_3), 2.03 (3 H, d, J = 1 Hz, 11-CH_3), 2.15 (3 H, s, $COCH_3$), 2.58 (1 H, q, J = 7 Hz, 4-H), 3.7–4.2 (4 H, m, $\begin{matrix}CH_2O\\|\\CH_2O\end{matrix}$), 5.96 (1 H, s, 6-H), 7.43 (1 H, J = 1 Hz, 12-H); Mass *m/z* (% Rel. int.): 364 (M^+, 1.2), 304 ([M-CH_3CO_2H]$^+$, 9), 99 (100).

Oxidation of 6α-acetoxyfuranoeremophilan-9-one (**16**) *using* $(PhSeO)_2O$. According to the general procedure (a), 33 mg (0.11 mmol) of **16** in chlorobenzene (4 ml) was heated at 100° with 170 mg (0.47 mmol) of $(PhSeO)_2O$ for 12 hr to afford 7 mg (20%) of **29** as colorless needles, m.p. 158–160° from EtOAc-hexane. (Found: *m/z* 306.1451. $C_{17}H_{22}O_5$ requires: 306.1465); IR cm^{-1}: 3520 (OH), 1725, 1690 (CO), 1265 (COC); UV λ_{max}^{EtOH} 283.5 nm (ε 12000); NMR δ: 0.85 (3 H, d, J = 7 Hz, 4-CH_3), 0.85 (3 H, s, 5-CH_3), 2.03 (3 H, d, J = 1 Hz, 11-CH_3), 2.16 (3 H, s, $COCH_3$), 6.01 (1 H, s, 6-H), 7.42 (1 H, q, J = 1 Hz, 12-H); Mass *m/z* (% Rel. int.): 306 (M^+, 10), 246 ([M-CH_3CO_2H]$^+$, 83), 190 (50), 138 (60), 43 (100).

Oxidation of 3β-acetoxyfuranoeremophilan-9-one (**17**) *using* $(PhSeO)_2O$. According to the general procedure (a), 17 mg (0.58 mmol) of **17** in chlorobenzene (3 ml) was treated with 106 mg (0.29 mmol) of $(PhSeO)_2O$ for 4 hr to afford 1.5 mg (9%) of **30** and 9 mg (53%) of recovered **17**. **30**—colorless needles, m.p. 201–202° from EtOAc–hexane. (Found: *m/z* 288.1388. $C_{17}H_{20}O_4$ requires: 288.1361); IR cm^{-1}: 1740, 1670 (CO), 1625, 1605 (C=C), 1260, 1245, 1230 (COC); UV λ_{max}^{EtOH} 302 nm (ε 20700), 252 nm (ε 5400); NMR δ 1.14 (3 H, d, J = 7 Hz, 4-CH_3), 1.21 (3 H, d, J = 0.5 Hz, 5-CH_3), 2.00 (3 H, d, J = 1 Hz, 11-CH_3), 2.04 (3 H, s, $COCH_3$), 2.51 (1 H, d, J = 17 Hz, 6-H), 2.78 (1 H, d, J = 17 Hz, 6-H), 5.08 (1 H, m, $W_{\frac{1}{2}}$ = 6 Hz, 3-H), 6.78 (1 H, t, J = 4 Hz, 1-H), 7.39 (1 H, q, J = 1 Hz, 12-H); Mass *m/z* (% Rel. int.): 288 (M^+, 1), 228 ([M-CH_3CO_2H]$^+$, 80), 213 ([M-CH_3CO_2H-CH_3]$^+$, 100).

Oxidation of 10αH-3β-acetoxyfuranoeremophilan-9-one (**18**) *using* $(PhSeO)_2O$. According to the general procedure

(a), 24 mg (0.082 mmol) of **18** in chlorobenzene (4 ml) was treated with 150 mg (0.42 mmol) of $(PhSeO)_2O$ for 3 hr to give 4 mg (16%) of **30** and 5 mg (20%) of recovered **18**.

Oxidation of diketone (**20**) *using* $(PhSeO)_2O$. According to the general procedure (a), 99 mg (0.34 mmol) of **20**[6] in chlorobenzene (5 ml) was treated with 145 mg (0.4 mmol) of $(PhSeO)_2O$ for 4.5 hr to give 49 mg (47%) of **31** and 35 mg (35%) of recovered **20**. **31**—colorless needles, m.p. 148–150°. (Found: C, 66.42; H, 8.10. $C_{17}H_{24}O_5$ requires: C, 66.21; H, 7.84%); IR cm^{-1}: 3450 (OH), 1700, 1675 (CO); NMR δ: 0.96, 1.14, 1.26 (each 3 H, s, 12, 13, 15-H), 1.04 (3 H, d, J = 7 Hz, 4-CH_3), 2.58 (1 H, dq, J = 7.1 Hz, 4-H), 3.7–4.1 (4 H, m, $\begin{matrix}CH_2O\\CH_2O\end{matrix}$); Mass m/z 308 (M^+).

Oxidation of diketone (**21**) *using* $(PhSeO)_2O$. According to the general procedure (a), 180 mg (0.65 mmol) of **21**[6] in toluene (10 ml) was treated with 270 mg (0.75 mmol) of $(PhSeO)_2O$ for 5 hr to give 82 mg (43%) of **32** and 70 mg (39%) of recovered **21**. **32**—colorless plates, m.p. 155–157°. (Found: C, 69.41; H, 8.78. $C_{17}H_{24}O_4$ requires: C, 69.36; H, 8.09%); IR cm^{-1}: 3380 (OH), 1700, 1675 (CO); NMR δ: 1.00 (3 H, d, J = 7 Hz, 4-CH_3), 1.09, 1.23, 1.27 (each 3 H, s, 12, 13, 15-H), 1.18 (3 H, t, J = 7 Hz, $OCH_2C\underline{H}_3$), 2.01 (2 H, s, 7, 8-H), 3.04 (2 H, q, J = 7 Hz, $OC\underline{H}_2CH_3$); Mass m/z 294 (M^+).

Oxidation of acetate (**22**) *using* $(PhSeO)_2O$. According to the general procedure (a), 67 mg (0.2 mmol) of **22**[6] in toluene (5 ml) was treated with 86 mg (0.24 mmol) of $(PhSeO)_2O$ for 4 hr to give 26 mg (37%) of **33** and 36 mg (54%) of recovered **22**. **33**—colorless needles, m.p. 170.5–172°. IR cm^{-1}: 3420 (OH), 1745, 1700 (CO), 1255 (COC); NMR δ: 1.09, 1.19, 1.29 (each 3 H, s, 12, 13, 15-H), 1.15 (3 H, d, J = Hz 4-CH_3), 2.12 (3 H, s, $COCH_3$), 2.61 (1 H, dq, J = 7, 0.5 Hz, 4-H), 3.7–4.2 (4 H, m, $\begin{matrix}CH_2O\\CH_2O\end{matrix}$), 5.02 (1 H, d, J = 6 Hz, 6-H); Mass m/z 352 (M^+).

Isomerization of acetate (**15**). To a soln of 60 mg of **15** in THF (10 ml) was added NaH (50% in mineral oil, 5 mg) and trace amount of water. The mixture was refluxed for 1 hr and diluted with 100 ml benzene, washed with sat NH_4Claq. The benzene was evaporated *in vacuo* and the residue was separated by silica gel preparative tlc to afford 34 mg (57%) of **38** and 10 mg (20%) of **39**. **38**—colorless needles, m.p. 203–205 from EtOAc–hexane. (Found: C, 65.53; H, 6.93. $C_{19}H_{24}O_6$ requires: C, 65.50; H, 6.94%); IR cm^{-1}: 1745, 1690 (CO), 1235 (COC); UV λ_{max}^{EtOH} 283 nm (ε 12000), 237 nm (ε 3400); NMR δ: 0.89 (3 H, d, J = 7 Hz, 4-CH_3), 0.96 (3 H, s, 5-CH_3), 2.06 (3 H, d, J = 1 Hz, 11-CH_3), 2.09 (3 H, s, $COCH_3$), 3.7–4.1 (4 H, m, $\begin{matrix}CH_2O\\CH_2O\end{matrix}$), 5.82 (1 H, s, 6-H), 7.33 (1 H, q, J = 1 Hz, 12-H); Mass m/z (% Rel. int.): 348 (M^+, 8), 305 ($[M-CH_3CO]^+$, 6), 289 ($[M-CH_3CO_2]^+$, 14), 259 ($[M-C_4H_9O_2]^+$, 7), 99 (100). **39** colorless granular form, m.p. 172–174° from EtOAc–hexane. (Found: m/z 288.1371. $C_{17}H_{20}O_4$ requires: 288.1360); IR cm^{-1}: 3470 (OH); UV λ_{max}^{EtOH} 296, 285, 263.5, 256 nm; NMR δ: 1.23 (3 H, d, J = 7 Hz, 4-CH_3), 2.35 (3 H, d, J = 1 Hz, 11-CH_3), 2.49 (3 H, s, 5-CH_3), 3.8–4.2 (4 H, m, $\begin{matrix}CH_2O\\CH_2O\end{matrix}$), 7.17 (1 H, q, J = 1 Hz, 12-H); Mass m/z (% Rel. int.): 288 (M^+, 56), 202 ($[M-C_4H_6O_2]^+$, 100).

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