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Studies on New Synthetic Pathways to $\Delta^{\alpha,\beta}$-Butenolides from α-Methylbutanolides. III.[1] Regiospecific Preparation of α-Methyl-$\Delta^{\alpha,\beta}$-butenolides and α-Methylene-γ-butyrolactones by Electrolysis of α-Carboxy-α-methylbutanolides and by Oxidation of α-Dimethylamino-α-methylbutanolides in a Fused Lactone System

SEIICHI INAYAMA, TAKESHI KAWAMATA, and NOBUKO SHIMIZU (née OHIZUMI)

Pharmaceutical Institute, School of Medicine, Keio University[2]

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New methods have been developed for the preparation of α-methylene-γ-butyrolactones (*exo*-type olefin) and α-methyl-$\Delta^{\alpha,\beta}$-butenolides (*endo*-type olefin) starting from an α-carboxy-α-methyl-γ-butyrolactone in a fused lactone system, *e.g.*, (+)-11β-carboxy-(**2a**) and (+)-11α-carboxy-3α,4β,5α,6βH-hexahydrosantonin (**2c**).

The method for exocyclic ($\Delta^{\alpha,\beta'}$) butenolides, *e.g.*, $\Delta^{11(13)}$-dehydrohexahydrosantonin (**5a**), consists of the oxidative *syn* elimination of an 11β-oriented α-dimethylaminolactone (**4b**) derived smoothly with retention of the configuration of the α-substituent through several intermediates, starting from an α-carboxy-α-methylbutanolide, *e.g.*, 11β-carboxy-3α,4β,5α,6βH-hexahydrosantonin (**2a**) (11β-COOH/7α-H: *trans*).

The method for *endo*-type butenolides, *e.g.*, $\Delta^{7(11)}$-dehydrohexahydrosantonin (**8a**), consists of electrolytic oxidation of the *trans*- or *cis*-carboxylactone acid, *e.g.*, 11β-carboxy-(**2a**) and 11α-carboxy-3α,4β,5α,6βH-hexahydrosantonin (**2c**) (11α-COOH/7α-H: *cis*), irrespective of the configuration of the α-carboxyl group in the santanolide.

Keywords——regiospecific preparation; α-methyl-$\Delta^{\alpha,\beta}$-butenolide(*e.g.* $\Delta^{7(11)}$-dehydro-3α,4β,5α,6βH-hexahydrosantonin); α-methylene-γ-butyrolactone(*e.g.* $\Delta^{11(13)}$-dehydrohexahydrosantonin); α-dimethylamino-α-methylbutanolide (*e.g.* 11β-dimethylaminohexahydrosantonin); electrolytic oxidation; α-carboxy-α-methylbutanolides (*e.g.* 11α-carboxy- and 11β-carboxyhexahydrosantonins); stereocontrolled transformation

Our preceding papers[3a,3b] reported the introduction of an ester group α to the carbonyl in simple α-methyl-γ-butyrolactones. The same alkoxycarbonylation has been utilized for lactones in a fused system, such as *l*-α-santonin and its derivatives, together with an alternative carboxylation, which will be reported in a subsequent paper. We report here the regioselective introduction of *exo*- and *endo*-type double bonds into fused γ-butyrolactones, a regiospecific conversion from β-oriented 11-carboxysantanolide to the corresponding α-methylene-γ-butyrolactone by oxidation of the 11β-oriented dimethylaminolactone intermediate, and regiospecific transformation of both α- and β-oriented 11-carboxysantanolides to the corresponding α-methyl-$\Delta^{\alpha,\beta}$-butenolide by electrolytic oxidation.

In the former pathway we considered that if 11β-oriented carboxylactones could be transformed to 11β-dimethylamino analogs through fairly few intermediary derivatives, the N-oxide of the aminolactone should afford the corresponding exocyclic olefin ($\Delta^{\alpha,\beta}$-isomer), but not the endocyclic derivative ($\Delta^{\alpha,\beta}$-isomer), by *syn* elimination. This synthetic strategy seems reasonable, since the initial configuration of the carboxyl group is generally retained in the course of the Curtius reaction, N-methylation, and oxidation.

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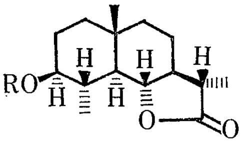
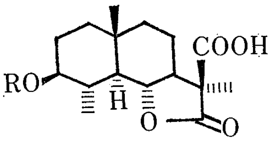
1) Presented in part at the 18th Symposium on Perfumes, Terpenes and Ethereal Oils, Symp. Papers, **1974**, p. 195.

2) Location: *35 Shinanomachi, Shinjuku-ku, Tokyo 160, Japan.*

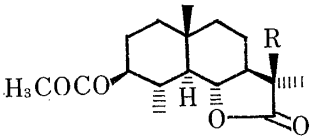
3) *a*) Part I: S. Inayama and T. Kawamata, *Chem. Pharm. Bull.*, **21**, 461 (1973); *b*) Part II: T. Kawamata, S. Inayama, and K. Sata, *ibid.*, **28**, 277 (1980); *c*) S. Inayama, T. Kawamata, and T. Hirose, *ibid.*, **28**, 288 (1980).



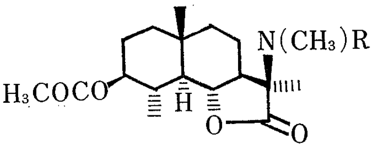
1a: R=H
1b: R=$COCH_3$



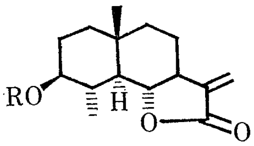
2a: R=H
2b: R=$COCH_3$
2c: 2a(11β-CH_3)



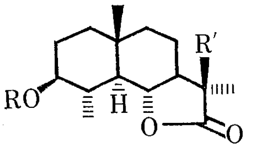
3a: R=COCl
3b: R=CON_3
3c: R=NCO
3d: R=NH_2



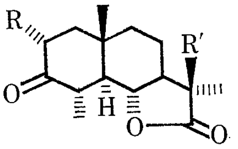
4a: R=$COCH_3$
4b: R=CH_3
4c: 4a(11β-CH_3)



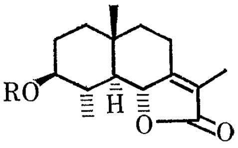
5a: R=H
5b: R=$COCH_3$



6a: R=H, R′=SPh
6b: R=$COCH_3$, R′=SPh
6c: R=H, R′=SOPh



7a: R=H, R′=COOH
7b: R=$OCOCH_3$, R′=Cl



8a: R=H
8b: R=$COCH_3$
8c: **8b** (2-keto)

Chart 1

The preparation of the starting 11β-carboxy-3α,4β,5α,6βH-hexahydrosantonin (11β-carboxy-HHS) (**2a**) by methoxycarbonylation of 3α,4β,5α,6β,11βH-hexahydrosantonin (HHS)(**1a**) and subsequent hydrolysis of the lactone ester produced will be described in a following paper.[3c] The acetate (**2b**), prepared from the carboxylactone (**2a**) in the usual manner, was converted *via* the acid chloride (**3a**) to the azidolactone (**3b**) by successive treatments with thionyl chloride and sodium azide. The azide was decomposed and rearranged to give the isocyanate (**3c**), which was finally hydrolyzed with concentrated hydrochloric acid to give the corresponding amine (**3d**). This aminolactone acetate was transformed by hydrogenation in methanol in the presence of formaldehyde, followed by acetylation with acetic anhydride–pyridine, into a mixture of N-methylacetamidolactone acetate (**4a**) and the dimethylamino derivative (**4b**) in a ratio of 1: 2. The β configurations of the amino groups at the C-11 position of the γ-butyrolactone moiety in **3d** and **4b** were supported by the proton nuclear magnetic resonance (PMR) spectra. The lower field signal attributed to the 6β-proton appeared at 4.30 and 4.39 ppm, respectively, as with the 11β-methoxycarbonyl and 11β-carboxy analogs.[3c]

Though the attempted oxidation of **4b** with hydrogen peroxide failed, the use of metachloroperbenzoic acid (MCPA) in methylene chloride effected the regioselective formation of α-methylene-γ-butyrolactone acetate (**5b**). The exocyclic double bond in the lactone was well characterized by a pair of narrowly spaced doublets at 5.39 and 6.08 ppm in the PMR spectrum. The same compound was obtained from the α-methylene-γ-butyrolactone, *i.e.*, $\Delta^{11(13)}$-dehydro-HHS (**5a**), which was prepared by the conventional method through the sulfoxide (**6c**) of 11β-phenylthio-HHS (**6a**) derived from **1a**.

The 11β configuration of the α-amino and dimethylamino groups in **3d** and **4b** is clearly retained in the course of derivation from the starting 11β-carboxylactone (**2a**), as expected. Hence, the transformation of **2a** to the corresponding dimethylamino derivative (**4b**) followed by oxidative *syn* elimination should constitute a general method for the regioselective preparation of α-methylene-γ-butyrolactones, *e.g.*, $\Delta^{11(13)}$-dehydro-HHS (**5a**). It is reasonable to assume that the isomeric α-methyl-$\Delta^{\alpha,\beta}$-butyrolactone, *i.e.*, $\Delta^{7(11)}$-dehydro-HHS (**8a**), might be derived from 11α-carboxylactone (**2c**) by the same method, involving *syn* elimination, since the relative stereochemistry of α-oriented dimethylamine oxide at the α-position and α-oriented hydrogen at the β-position of the lactone-carbonyl is fixed as *cis* (11α-NMe_2/7α-H) in a *trans*-fused lactone system (6β-H/7α-H) such as that of santanolides.

On the other hand, when a modified Hunsdicker reaction using lithium chloride and lead tetraacetate was applied to 11β-carboxy-4β,5α,6βH-tetrahydrosantonin[3c] (11β-carboxy-THS) (**7a**), a rather complex reaction involving decarboxylative chlorination at the C-11 position with simultaneous introduction of an acetoxy group at the C-2 position was observed. Treatment of the product, 2α-acetoxy-11β-chloro-THS (**7b**), with diazabicycloundecene (DBU) provided an α-methyl-$\Delta^{\alpha,\beta}$-butenolide, which was found to be 3-acetyl-2-keto-$\Delta^{11(13)}$-dehydro-HHS (**8c**). This seems to have been formed by acetyl migration from C-2 to C-3 through an orthoester intermediate. The structures of the chloro derivative (**7b**) and the product **8c** were determined mainly on the basis of their PMR spectra.

We found a side reaction in the above-mentioned decarboxylative chlorination with 11β-carboxylactone (**7a**) and a relatively poor availability of 11α-carboxylactone[3c] (**2c**) as a starting material for the synthesis of the α-methyl-$\Delta^{\alpha,\beta}$-butenolide (**8a**) through the corresponding 11α-dimethylamino derivative (**4c**). The method of electrolytic oxidation[3b] was therefore attempted for the preparation of **8a** from both 11β- and 11α-carboxylactone (**2a** and **2c**).

Electrolysis of the epimeric carboxylactones (**2a** and **2c**) was performed separately at room temperature using graphite plate electrodes in pyridine and water in the presence of triethylamine as a catalyst. The α-methyl-$\Delta^{\alpha,\beta}$-butenolide, $\Delta^{7(11)}$-dehydro-HHS[4] (**8a**) was found to be produced exclusively in each case. The structure of **8a** was substantiated by spectroscopic evidence for the characteristic olefinic methyl group at the C-11 position in the γ-butyrolactone moiety; no α-methylene group signal of the *exo*-isomer (**5a**) was apparent. Hence, the electrolysis of α-carboxy-α-methylbutanolide regioselectively yields α-methyl-$\Delta^{\alpha,\beta}$-butanolide, regardless of the configuration of the carboxyl group at the α-position to the lactone carbonyl. These results suggest that this electrolytic method provides an efficient synthetic route to α-methyl-$\Delta^{\alpha,\beta}$-butenolide from α-methyl-γ-butanolide, especially in a fused lactone system such as santanolide.

Thus, α-carboxy-α-methylbutanolides such as 11-carboxysantonin derivatives, which can be obtained with ease by our synthetic methods[3] from various types of α-methyl-γ-butyrolactones, seem to be useful intermediates for the preparation of α-methylene-γ-lactones and α-methyl-$\Delta^{\alpha,\beta}$-γ-lactones, and should also be applicable to syntheses of α-hydroxy- and α-acyloxy-α-methylbutanolides, for example, hydroxybalchanolide[5] and prutenin.[6]

Experimental

The melting points were determined with a Büchi melting point apparatus and are uncorrected. The infrared (IR) spectra were recorded on a Hitachi EPI-G3 instrument. PMR spectra were measured on a JEOL JNM-NH 100 or JNM-PX 60 spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard unless otherwise stated. The chemical shifts and coupling constants are given in ppm and Hz, respectively, and the following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, sext=sextet, m=multiplet, and c=complex. Optical rotations were measured with a Jasco DIP-180 automatic polarimeter. Thin–layer chromatography (TLC) was performed on silica gel G (Merck) plates with an AcOEt–benzene system. EI-, CI- and GC-mass spectra (MS) were measured on a JNS-D-300 GC-mass spectrometer.

3-Acetyl-11β-carboxy-3α,4β,5α,6βH-hexahydrosantonin (**2b**)——11β-Carboxy-HHS[3c] (**2a**) (0.5 g) was dissolved in pyridine (2 ml) and Ac_2O (0.5 ml), and the mixture was allowed to stand at room temperature overnight. The reaction mixture was diluted with H_2O (10 ml) and acidified with conc. HCl, and the precipitate formed was collected. A solution of the precipitate in satd. $NaHCO_3$ was washed with $CHCl_3$, then the aqueous layer was acidified with conc. HCl to give crystals (0.465 g, 81%). Recrystallization from AcOEt–ether gave the carboxylactone acetate (**2b**), mp 189—190°. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1790, 1712, 1694. $[\alpha]_D^{17}$ $+50.4°$ ($c=1.01$, $CHCl_3$). *Anal.* Calcd for $C_{18}H_{26}O_6$: C, 63.88; H, 7.74. Found: C, 63.56; H, 7.94. PMR δ: 0.99 (3H, s, C_{10}–$C\underline{H}_3$), 1.05 (3H, d, $J=6.5$, C_4–$C\underline{H}_3$), 1.48 (3H, s, C_{11}–$C\underline{H}_3$), 2.07 (3H, s, $OCOC\underline{H}_3$), 4.35 (1H, t, $J=10.5$, C_6–$\underline{H}$), 4.4 (1H, c, C_3–$\underline{H}$), 8.26 (1H, br s, $COO\underline{H}$).

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5) H. Krasch, V. Herout, M. Suchy, and F. Sŏrm, *Collection Czech. Chem. Commun.*, **26**, 2612 (1961).
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3-Acetyl-11β-aminohexahydrosantonin (3d)——The carboxylactone acetate (**2b**) (0.3 g) was refluxed in $SOCl_2$ (3 ml) for 1.5 hr in an oil bath. The corresponding acid chloride (**3a**) was obtained as crystals on removing excess reagent by evaporation. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1785, 1765 (sh), 1738. NaN_3 (0.08 g) in H_2O (1 ml) was added to this crystalline residue and the mixture was stirred for about 0.5 hr at room temperature. H_2O (5 ml) was added to the reaction mixture and the precipitate that separated was collected, washed with H_2O, and dried ($MgSO_4$), affording 0.272 g (84.5%) of azidolactone acetate (**3b**). A solution of **3b** (0.250 g) in benzene (15 ml) was refluxed for 2.5 hr in a water bath. Removal of the solvent under reduced pressure yielded the isocyanate (**3c**) as crystals. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 2277 (sh), 2247, 1795, 1788, 1740. A solution of **3c** in dioxane (3 ml) containing conc. HCl (3 ml) was refluxed for 3 hr in an oil bath. The reaction mixture was poured into ice-cooled Na_2CO_3 solution, saturated with NaCl, and extracted with CH_2Cl_2. The organic layer was washed with satd. NaCl and dried over $MgSO_4$. Removal of the solvent gave the aminolactone (**3d**) as crystals (0.178 g, 97%). An analytical sample of **3d** was obtained by repeated recrystallization from EtOAc as prisms, mp 178—179°, $[\alpha]_{\mathrm{D}}^{14.5}$ +71.4° (c=1.1, MeOH). *Anal.* Calcd for $C_{15}H_{25}NO_3$: C, 67.38; H, 9.43; N, 5.24. Found: C, 67.03; H, 9.73; N, 5.32. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3333, 3300 (br), 3258, 1778, 1606. PMR δ: 0.99 (3H, s, C_{10}–$C\underline{H}_3$), 1.14 (3H, d, J=5.5, C_4–$C\underline{H}_3$), 1.25 (3H, s, C_{11}–$C\underline{H}_3$), 3.03 (1H, sext, J=11, 8, 6, C_3–$\underline{H}$), 4.30 (1H, t, J=10, C_6–$\underline{H}$).

3-Acetyl-11β-N-methylacetamidohexahydrosantonin (4a) and 11β-N,N-Dimethylaminohexahydrosantonin (4b)——A cold solution of **3d** (0.198 g) in MeOH (10 ml) containing a few drops of conc. HCl and 30% HCHO (0.6 ml) was added to 10 ml of MeOH containing prereduced PtO_2 (0.02 g). The mixture was hydrogenated in a hydrogen atmosphere at 45 lb/in^2 for 3 hr. After filtration to remove the catalyst, the filtrate was concentrated to a small volume. The residue was made alkaline with satd. $NaHCO_3$ and repeatedly extracted with $CHCl_3$. The combined $CHCl_3$ solution was washed with satd. NaCl and dried over $MgSO_4$. A crystalline residue (0.151 g) was obtained on removal of the solvent *in vacuo*. Ac_2O (1 ml) and pyridine (0.5 ml) were added to this residue (0.05 g), and the mixture was allowed to stand at room temperature for 2 days. The reaction mixture was poured into ice-cooled HCl solution and washed with ether, then 10% Na_2CO_3 was added, and the mixture was extracted with ether. The ether layer was washed with satd. NaCl and dried over $MgSO_4$. Removal of the solvent gave a crystalline residue (0.045 g). Recrystallization from AcOEt–petr. ether gave the N-methylacetamidolactone (**4a**) as fine needles (0.011 g, 18%), mp 237—240°. An analytical sample of **4a**, mp 242—243.5°, was obtained by recrystallization from AcOEt. $[\alpha]_{\mathrm{D}}^{24}$ +162.5° (c=0.06, MeOH). *Anal.* Calcd for $C_{20}H_{31}NO_5$: C, 65.73; H, 8.55; N, 3.83. Found: C, 65.88; H, 8.55; N, 3.12. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1780, 1739, 1642. PMR δ: 0.96 (3H, s, C_{10}–$C\underline{H}_3$), 1.09 (3H, d, J=7, C_4–$C\underline{H}_3$), 1.52 (3H, s, C_{11}–$C\underline{H}_3$), 2.07 (3H, s, $OCOC\underline{H}_3$), 2.18 (3H, s, N–$C\underline{H}_3$), 2.95 (3H, s, N–$COC\underline{H}_3$), 4.5 (2H, br. m, C_3–$\underline{H}$+C_6–$\underline{H}$).

From the mother liquor, dimethylaminolactone (**4b**) was obtained as needles, mp 105—115° (0.024 g, 40%). Recrystallization from EtOAc gave an analytical sample, mp 140—143°. $[\alpha]_{\mathrm{D}}^{24}$ +41.2° (c=1.79, MeOH). *Anal.* Calcd for $C_{19}H_{31}NO_4$: C, 67.62; H, 9.26; N, 4.15. Found: C, 67.79; H, 9.65; N, 4.00. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1781, 1736, 1251, 1241, 1022. PMR δ: 1.02 (3H, s, C_{10}–$C\underline{H}_3$), 1.03 (3H, d, J=7, C_4–$C\underline{H}_3$), 1.17 (3H, s, C_{11}–$C\underline{H}_3$), 2.05 (3H, s, $OCOC\underline{H}$), 2.25 (6H, s, $N(C\underline{H}_3)_2$), 4.39 (1H, t, J=10, C_6–$\underline{H}$), 4.31 (1H, t, J=12, C_3–$\underline{H}$).

3-Acetyl-$\Delta^{11(13)}$-dehydrohexahydrosantonin (5b)——A solution of **4b** (0.045 g) and MCPA (0.072 g, 1.4 eq) in CH_2Cl_2 (10 ml) was stirred at room temperature for 4.5 hr. The reaction mixture was diluted with CH_2Cl_2 (5 ml) and poured into 10% Na_2CO_3. The mixture was washed with satd. NaCl, and dried over $MgSO_4$. Removal of the solvent from the dried organic layer ($MgSO_4$) left a crystalline residue (0.029 g, 74.6%), which was chromatographed on silica gel (Mallinckrodt, 0.6 g) to give the α-methylenelactone acetate (**5b**). This material was identical with an authentic sample of **5b** obtained by the conventional method described below, on the basis of the IR spectra.

11β-Phenylthiohexahydrosantonin (6a) and Its Acetate (6b)——BuLi (15% hexane solution) and a solution of 3-acetyl-HHS (**1b**) (2 g) in tetrahydrofuran (THF) (30 ml) were added successively very slowly at −76 to −78° to a solution of diisopropylamine (0.086 g) in THF (30 ml). The lactone enolate was treated at −78° with a solution (30 ml) of diphenyl-disulfide (1.85 g) in THF (30 ml) containing HMPA (1.52 g). After completion of the addition, the reaction mixture was stirred for 1 hr at −78°, then warmed to −20° (40 min), and finally to room temperature. The reaction mixture was acidified with 10% HCl, and saturated with NaCl, and the separated organic layer was dried over $MgSO_4$. Removal of the solvent gave an oily residue, which was chromatographed on silica gel. 3-Acetyl-11β-phenylthio-HHS (**6b**) was obtained, by elution with 5% EtOAc–benzene, as crystals of mp 168—172°. Recrystallization from EtOAc afforded 0.388 g (14.2%) of a pure sample of **6b** as prisms, mp 171—172°, $[\alpha]_{\mathrm{D}}^{23}$ +89.4° (c=0.10, MeOH), $[\alpha]_{\mathrm{D}}^{22}$ +106.4° (c=0.10, $CHCl_3$). *Anal.* Calcd for $C_{23}H_{30}O_4S$: C, 68.66; H, 7.46; S 7.96. Found: C, 68.22; H, 7.35; S, 8.07. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1777, 1741, 769, 747, 713, 695. PMR δ: 1.05 (3H, s, C_{10}–$C\underline{H}_3$), 1.10 (3H, d, J=6.5, C_4–$C\underline{H}_3$), 1.4 (3H, s, C_{11}–$C\underline{H}_3$), 1.1—2.0 (11H), 2.18 (3H, s, $OCOC\underline{H}_3$), 4.43 (2H, m, C_3–$\underline{H}$+C_6–$\underline{H}$), 7.33—7.67 (5H, m, $C_6\underline{H}_5$). Further elution of the column with 20% EtOAc–benzene gave 0.119 g (4.8%) of 11β-phenylthio-HHS (**6a**) as needles, mp 202—203°. $[\alpha]_{\mathrm{D}}^{23}$ +113.9° (c=0.10, MeOH), $[\alpha]_{\mathrm{D}}^{22}$ +113.7° (c=0.10, $CHCl_3$). *Anal.* Calcd for $C_{21}H_{28}O_3S$: C, 70.00; H, 7.78; S, 8.89. Found: C, 69.64; H, 7.92; S, 8.89. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3505, 1763, 1754, 742, 703, 690. PMR δ: 1.04 (3H, s, C_{10}–$C\underline{H}_3$), 1.26 (3H, d, J=6, C_4–$C\underline{H}_3$), 1.42 (3H, s, C_{11}–$C\underline{H}_3$), 3.14 (1H, m, C_3–$\underline{H}$), 4.50 (1H, t, J=9.5, C_6–$\underline{H}$), 7.34—7.68 (5H, m, $C_6\underline{H}_5$).

From the more polar fractions, 0.670 g (33.5%) of the starting material (**1b**) was recovered. The acetate (**6b**) (0.707 g) was dissolved in 7% KOH–MeOH (20 ml), and the solution was allowed to stand at room temperature overnight. After removal of the solvent, the residue was acidified with 10% HCl and extracted with CH_2Cl_2, then the CH_2Cl_2 solution was washed with satd. NaCl and dried over $MgSO_4$. Removal of the solvent gave a crystalline residue (0.613 g, 96.8%), which was recrystallized from EtOAc and benzene to afford a pure sample of 11β-phenylthio-HHS (**6a**) identical with that described above.

11β-Phenylsulfinilhexahydrosantonin (6c)——A solution of **6a** (0.409 g) in CH_2Cl_2 (20 ml) containing a catalytic amount of 4,4-thio-bis(6-*tert*-butyl-*m*-cresol) was treated with MCPA (0.198 g), and the mixture was refluxed in a water bath for 1 hr. The reaction mixture was then washed successively with 10% Na_2CO_3, 10% $NaHSO_3$, and satd. NaCl, and dried over $MgSO_4$. Removal of the solvent left a semisolid in nearly quantitative yield. The product was purified by chromatography on silica gel to give 25 mg (59.8%) of the sulfinyllactone (**6c**) as needles; this material was recrystallized from EtOAc to give a pure sample of **6c**, mp 174—175°. $[\alpha]_D^{23}$ +317.7° (c=0.10, $CHCl_3$). *Anal.* Calcd for $C_{21}H_{28}O_4S$: C, 66.99; H, 7.50; S, 8.52. Found: C, 66.84; H, 7.36; S, 8.61. IR ν_{max}^{KBr} cm^{-1}: 3584, 1776, 1052, 1043, 1033, 765, 752, 718, 700. PMR δ: 1.04 (3H, s, C_{10}–$C\underline{H}_3$), 1.17 (3H, d, J=8, C_4–$C\underline{H}_3$), 1.4 (3H, s, C_{11}–$C\underline{H}_3$), 3.06 (1H, m, C_3–$\underline{H}$), 4.82 (1H, t, J=10, C_6–$\underline{H}$), 7.48—7.76 (5H, br m, $C_6\underline{H}_5$).

$\Delta^{11(13)}$-Dehydrohexahydrosantonin (5a) and Its Acetate (5b): Pyrolysis of 11β-Phenylsulfinylhexahydrosantonin (6c)——Pyrolysis of **6c** (0.190 g) was performed under reduced pressure (2 Torr) at 170—180° for 20 min. Chromatography on silica gel, eluting with benzene–AcOEt (8: 2), gave 0.07 g (55%) of $\Delta^{11(13)}$-dehydro-HHS (**5a**), which gave, on repeated recrystallization, an analytical sample of **5a**, mp 131—133°, 0.051 g (40%). $[\alpha]_D^{22}$ +104.0° (c=0.10, $CHCl_3$). *Anal.* Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.92; H, 8.74. IR ν_{max}^{KBr} cm^{-1}: 3500, 3483 (sh), 1765 (sh), 1754, 1671, 1640. PMR δ: 0.96 (3H, s, C_{10}–$C\underline{H}_3$), 1.23 (3H, d, J=5, C_4–$C\underline{H}_3$), 2.46 (1H, m, C_7–$\underline{H}$), 3.13 (1H, m, C_3–$\underline{H}$), 3.81 (1H, t, J=11, C_6–$\underline{H}$), 5.39 (1H, d, J=3, C_{13}–$\underline{H}$), 6.08 (1H, d, J=3, C_{13}–$\underline{H}$).

A sample of **5a** (0.05 g) was acetylated as usual with Ac_2O/pyridine to give the corresponding acetate (**5b**), mp 230° (blackened). $[\alpha]_D^{24}$ +48.8° (c=0.41, $CHCl_3$). MS m/e: 292 (M^+); CI-MS m/e: 293 (MH^+). IR ν_{max}^{KBr} cm^{-1}: 1768, 1727, 1250. PMR δ: 1.0 (3H, s, C_{10}–$C\underline{H}_3$), 1.12 (3H, d, J=8, C_4–$C\underline{H}_3$), 2.06 (3H, s, $OCOC\underline{H}_3$), 3.85 (1H, d, J=10.5, C_6–$\underline{H}$), 5.46 (1H, t, J=6, C_3–$\underline{H}$), 5.36 (1H, d, J=3.5, C_{13}–$\underline{H}$), 6.03 (1H, d, J=3.5, C_{13}–$\underline{H}$).

$\Delta^{7(11)}$-Dehydrohexahydrosantonin (8a) and Its Acetate (8b): Electrolyses of 11β-Carboxy- (2a) and 11α-Carboxy-hexahydrosantonin (2c)——A stirred solution of **2a** (0.251 g) [Na salt (0.296 g)] in CH_3CN (40 ml) containing Et_3N (0.5 ml) was subjected to electrolysis using graphite plates as electrodes at a current of 0.04—0.23 A (13.5—28.5 V) at room temperature for 2.25 hr. The reaction mixture was acidified with dil. HCl and concentrated *in vacuo* to give an oil. After extraction of the oil with $CHCl_3$, the $CHCl_3$ solution was washed with 10% Na_2CO_3 then satd. NaCl, and dried over $MgSO_4$. Removal of the solvent gave $\Delta^{7(11)}$-dehydro-HHS (**8a**) as a semisolid (0.097 g, 46%) [IR ν_{max}^{KBr} cm^{-1}: 3425 (br.), 1745 (br.), 1680]. This material (0.072 g) was acetylated with Ac_2O (0.4 ml) and pyridine (0.2 ml) at room temperature. The usual work-up of the reaction product, followed by recrystallization from ether-petr. ether afforded the corresponding acetate[7] (**8b**), 0.055 g (67%), mp 139—142°, $[\alpha]_D^{15}$ +46.0° (c=0.635, $CHCl_3$). λ_{max}^{EtOH} 218.5 nm (log ε 3.64). IR ν_{max}^{KBr} cm^{-1}: 1756, 1730, 1681. PMR δ: 1.09 (3H, s, C_{10}–$C\underline{H}_3$), 1.12 (3H, d, J=6, C_4–$C\underline{H}_3$), 1.80 (3H, t, J=1.5, C_{11}–$C\underline{H}_3$), 2.06 (3H, s, $OCOC\underline{H}_3$), 4.60 (1H, d, J=10, C_6–$\underline{H}$). MS m/e: 292.1679 (M^+) (Calcd for $C_{17}H_{24}O_4$ 292.1674).

Electrolysis of **2a** in the same manner, except that the solvent system consisted of a mixture of pyridine (40 ml) and H_2O (4 ml) containing Et_3N (0.4 ml) or pyridine (40 ml) containing Et_3N (0.5 ml), afforded **8a** in yields of 57% and 46%, respectively.

Electrolytic oxidation of the epimeric carboxylactone (**2c**) was carried out under the latter conditions to afford **8a**, but not **5a**, in 63% yield.

2α-Acetoxy-11β-chloro-4β,5α,6βH-tetrahydrosantonin (7b)——A solution of **7a**[3c] (0.20 g) in dry benzene (20 ml) containing a catalytic amount of dimethylformamide (DMF) (0.5 ml) was treated with lead tetraacetate (1.8 g) and LiCl (0.20 g) under an argon atmosphere. The mixture was stirred for 1.5 hr at room temperature and then refluxed for 4 hr. The reaction mixture was poured into ice-water and extracted with benzene. The benzene extract was washed with 5% $NaHCO_3$, and satd. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a viscous oil, which was recrystallized from $CHCl_3$–ether to give the chlorolactone (**7b**) (0.047 g, 20%), mp 202—204° (decomp.). $[\alpha]_D^{22}$ +158.1° (c=0.253, $CHCl_3$). *Anal.* Calcd for $C_{17}H_{23}ClO_5 \cdot 1/4H_2O$: C, 58.78; H, 6.77. Found: C, 58.94; H, 6.83. IR ν_{max}^{KBr} cm^{-1}: 1790, 1743, 1725 (sh.). PMR δ: 1.25 (3H, d, J=6, C_4–$C\underline{H}_3$), 1.34 (3H, s, C_{10}–$C\underline{H}_3$), 1.72 (3H, s, C_{11}–$C\underline{H}_3$), 2.13 (3H, s, $OCOC\underline{H}_3$), 2.75 (3H, q, J=7, C_7–$\underline{H}$), 4.33 (1H, d, d, J=9.5, 10.5, C_2–H), 5.37 (1H, d, d, J=7, 13, C_6–$\underline{H}$).

3-Acetyl-2-keto-$\Delta^{7(11)}$-dehydrohexahydrosantonin (8c)——A solution of **7b** (30 mg) in toluene (10 ml) containing a small amount of DBU was refluxed for 3 hr. The reaction mixture was washed with 10% HCl,

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7) T.B.H. McMurry and D.F. Rane[4] gave the following physical data for **8b**: mp 139—140°, λ_{max}^{EtOH} 231 nm (log ε 3.68), and $[\alpha]_D$ +54.7° (c=0.08, $CHCl_3$).

and satd. NaCl, then dried over $MgSO_4$. Removal of the solvent gave 23 mg (86%) of crude crystals of the butenolide acetate (**8c**), which was recrystallized from AcOEt–ether to give an analytical sample of **8c** as prisms, mp 191—193°, $[\alpha]_D^{22}$ +261.9° (c=0.084, $CHCl_3$). MS m/e: 306.1469 (M^+) (Calcd for $C_{17}H_{22}O_5$: 306.1468). IR ν_{max}^{KBr} cm^{-1}: 1753 (sh.), 1746, 1723, 1686. PMR δ: 1.01 (3H, s, C_{10}–$C\underline{H}_3$), 1.31 (3H, d, J=6, C_4–$C\underline{H}_3$), 1.83 (3H, d, J=2, C_{11}–$C\underline{H}_3$), 2.17 (3H, s, $OCOC\underline{H}_3$), 4.67 (1H, d, J=10, C_3–$\underline{H}$), 4.80 (1H, d, J=10.5, C_6–$\underline{H}$).

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