tional flexibility in this case. Proton exchange at C-5 leading to epimerization or any other change resulting from proton loss at this center during the conversion of methyl elenolate to lactam **5** was ruled out by the use of C-5 deuterium-labeled ester, prepared by the subjection of calcium elenolate to the action of excess D_2O for 24 hr and conversion to the free acid by DCl, followed by treatment with diazomethane. Repetition with this material of the steps involving formation of lactam **5** from unlabeled ester provided deuterium-labeled **5**, mol wt (mass spectrum) 369, in which the multiplet (doublet of quartets) due to C-6 H in unlabeled **5** is cleanly decoupled to a single quartet.[7]

In a parallel observation, radioactive lactam **5** was isolated after C-5 tritium-labeled **3b** was carried through the sequence already described for preparation of unlabeled **5**.

Acknowledgment. The Stanford authors appreciate financial support from the National Science Foundation (GP 23019). The XL-100 nmr spectrometer was provided by National Science Foundation Grant No. GP 28142.

(7) A referee has suggested that the possibility of isoinversion might invalidate the condensation experiment with deuterium-labeled **3b**. However, in their paper[8] describing isoinversion, Cram, *et al.*, state "the limiting k_e/k_α value of zero has never been attained." In accord with the above statement we believe that had inversion occurred some deuterium loss should have been seen.

(8) W. T. Ford, E. W. Graham, and D. J. Cram, *J. Amer. Chem. Soc.*, **89**, 4661 (1967).

(9) National Science Foundation Fellow, 1970–1972.

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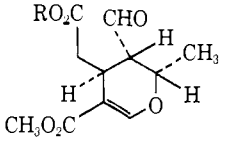
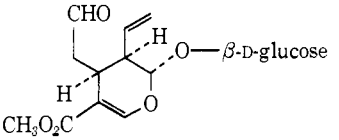
Total Synthesis of *dl*-Methyl Elenolate

Sir:

Elenolic acid derivatives, particularly the calcium salt (**1**) and methyl ester (**2**),[1] have generated considerable interest because of their potent broad range antiviral activity.[2] These compounds are structurally quite similar to *seco*-loganin (**3**), a precursor in indole alkaloid



1, R = Ca/2
2, R = CH_3



3

biosynthesis.[3] These considerations and the difficult accessibility of these compounds from olive press juices[4] led to the initiation of a program aimed at their total synthesis. This communication reports a total synthesis of *dl*-methyl elenolate and a formal total synthesis of *dl*-calcium elenolate.

Addition of a tetrahydrofuran solution of cyclopentadienylsodium to a twofold excess of methyl bromoacetate at −10° resulted in the formation of methyl 1,3-cyclopentadienyl-5-acetate[5] [nmr ($CDCl_3$) δ 2.38 (d, 1, J = 8.5 Hz), 3.67 (s, 3, OCH_3), 6.42 (s, 4, =CH)] which when treated with a two- to threefold excess of citraconic anhydride at −10° afforded **4** (see Chart I) in 50% overall yield after crystallization from ether [mp 105–108°;[6] nmr ($CDCl_3$) δ 1.66 (s, 3, CH_3), 2.41 (A_2B, 2, CH_2CO_2), 2.6 (A_2B, 1, $CHCH_2CO_2$), 3.65 (s, 3, OCH_3), 6.30 (AA′XX′, 2, =CH)]. Hydrolysis of **4** in hot water gave an 80% yield of crystalline **5**[7] on cooling [mp 151–152°;[6] nmr (D_2O) δ 1.53 (s, 3, CH_3), 2.35 (A_2B, 2, CH_2CO_2), 3.62 (s, 3, OCH_3), 6.1 (m, 2, =CH)]. Oxidation of **5** with potassium chlorate and osmium tetroxide[8] gave **6** in 35% yield [mp 122–126°;[6,9] nmr (Me_2SO-d_6) δ 1.44 (s, 3, CH_3), 1.97–2.40 (m, 4), 2.77–3.00 (m, 2), 3.60 (s, 3, OCH_3), 3.70–3.90 (m, 1, OCH), 4.33–4.55 (m, 1, OCH)]. Treatment of **6** with acetone, 2,2-dimethoxypropane, and a trace of acid resulted in a quantitative conversion to **7** [mp 154–155°;[6] nmr (Me_2SO-d_6) δ 1.20, 1.43, 1.50 (3 s, 9, CH_3), 2.75–2.98 (m, 2), 3.61 (s, 3, OCH_3)].

Electrolytic decarboxylation[10] of **7** gave up to a 50% yield of **8** (oil) after silica gel chromatography: nmr ($CDCl_3$) δ 1.35, 1.53 (2 s, 6, CH_3), 1.72 (d, J = 2 Hz, 3, $=CCH_3$), 3.65 (s, 3, OCH_3). Oxidation of **8** with potassium permanganate–potassium periodate afforded **9** in 45% yield: mp 91–93°[6]; ir (mull) 1745, 1730, 1710 cm^{-1}; nmr ($CDCl_3$) δ 1.33, 1.57 (2 s, 6, CH_3), 2.29 (s, 3, $COCH_3$), 2.5–3.2 (m, 5), 3.67 (s, 3, OCH_3), 4.47–4.72 (m, 1, OCH), 4.75–4.99 (m, 1, OCH). Treatment of **9** with diazomethane gave a quantitative yield of the dimethyl ester **10** (oil): nmr ($CDCl_3$) δ 1.33, 1.57 (2 s, 6, CCH_3), 2.28 (s, 3, $COCH_3$), 3.66 (s, 3, OCH_3). Reduction of **10** with excess sodium borohydride at 0° in methanol gave an essentially quantitative yield of an oily mixture of the diastereomeric alcohols **11**, which when treated with mesyl chloride in

(1) For further information regarding the newly proposed structure for elenolic acid see the accompanying paper: F. A. MacKellar, R. C. Kelly, E. E. van Tamelen, and C. Dorschel, *J. Amer. Chem. Soc.*, **95**, 7155 (1973).

(2) (a) H. E. Renis, *Antimicrob. Agents Chemother., 1969*, 167 (1970); (b) M. G. Soret, *ibid.*, 160 (1970); (c) G. A. Elliot and E. N. DeYoung, *ibid.*, 173 (1970).

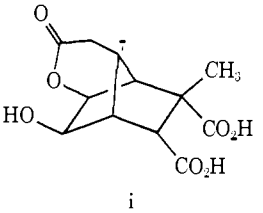
(3) (a) A. R. Battersby, A. R. Burnett, and P. G. Parsons, *J. Chem. Soc. C*, 1187 (1969), and references therein; (b) R. Guarnaccia and C. J. Coscia, *J. Amer. Chem. Soc.*, **93**, 6320 (1971).

(4) J. H. Ford, F. A. MacKellar, P. A. Meulman, R. J. Wnuk, and G. C. Prescott, *Org. Prep. Proced.*, **4**, 97 (1972).

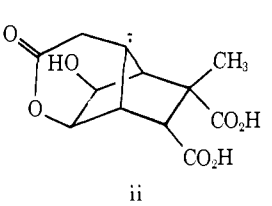
(5) This product rapidly rearranges to methyl 1,3-cyclopentadienyl-1-acetate at 25° ($t_{1/2} \simeq 1$ hr at 25°).

(6) Satisfactory elemental analyses were obtained.

(7) (a) The assignment of the relative stereochemistry at the 7 position as shown in **4** and **5** is based on the resistance of **4** to epoxidation and the formation of i and ii when **5** is oxidized with potassium chlorate



i



ii

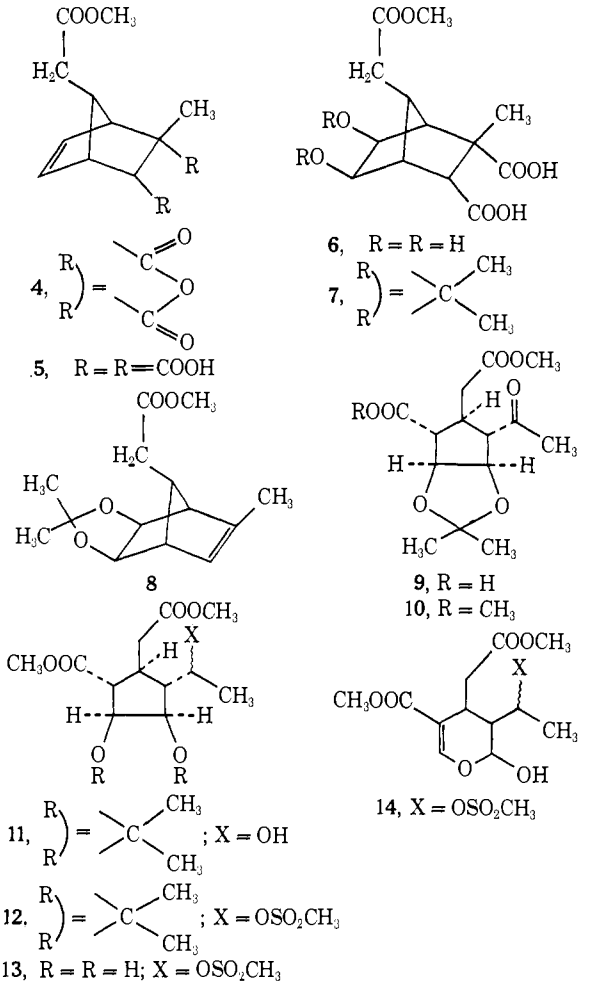
and osmium tetroxide in basic medium.[7b] (b) For a similar stereochemical outcome in the preparation of a 7-substituted norbornene see E. J. Corey, N. M. Weinshenker, T. K. Schaaf, and W. Huber, *J. Amer. Chem. Soc.*, **91**, 5675 (1969).

(8) N. A. Milas and E. M. Terry, *J. Amer. Chem. Soc.*, **47**, 1412 (1925).

(9) The melting point of **6** varied greatly depending on the crystallization solvent and the degree of solvation.

(10) (a) P. Radlick, R. Klem, S. Spurlock, J. J. Sims, E. E. van Tamelen, and T. Whitesides, *Tetrahedron Lett.*, 5117 (1968); (b) H. H. Westberg and H. J. Dauben, Jr., *ibid.*, 5123 (1968).

Chart I



pyridine gave, again in nearly quantitative yield, the mesylates **12**: nmr ($CDCl_3$) δ 1.33, 1.50 (2 s, 6, CCH_3), 1.50 and 1.55 (d, J = 6 Hz, 3, SO_3CHCH_3), 3.00 and 3.03 (s, 3, CH_3SO_3). The mixture of mesylates crystallized on standing; recrystallization afforded one of the diastereomers in pure form, mp 102–103°.[6] Hydrolysis of the latter with 60% formic acid followed by oxidation of the resultant glycol **13** with periodate (pH 6–7) afforded an isomerically pure mesylate **14** in 20% yield: mp 107–111°;[6] nmr ($CDCl_3$) δ 1.58 (d, J = 6.5 Hz, 3, $CHCH_3$), 3.02 (s, 3, O_3SCH_3), 3.70, 3.74 (2 s, 6, OCH_3), 5.62–5.82 (m, 1, OCHO), 7.55 (s, 1, OCH=). Heating **14** in an aqueous pyridine solution resulted in the formation of *dl*-methyl elenolate as an oil, identical by ir, uv, and nmr spectroscopy with the oily, chromatographically highly purified material obtained from natural elenolic acid on treatment with diazomethane. The synthetic material crystallized on standing to give isomerically pure racemic material, mp 93–98°. The natural material has not yet been obtained in crystalline form. The transformation of the mixture of mesylates **12** to methyl elenolate of the same purity as that from the single isomer of **12** could be carried out without isolation of intermediates in an overall yield of 30%.

The formal synthesis of calcium elenolate (**1**) was completed by the hydrolysis of natural methyl elenolate with 0.1 N sulfuric acid at 80–90° followed by treatment of the free acid with calcium carbonate.

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Dynamic Stereochemistry of Triarylsilanes[1]

Sir:

In connection with our recent studies of isomerism and isomerization in propeller-like molecules,[2] we noted with interest a report that the mesityl groups of trimesitylfluorosilane (**1**) are "... nicht mehr frei drehbar,"[3] as indicated by the doubling of the ortho methyl group resonance in the ambient temperature ^{1}H nmr spectrum. Additionally, Gilman and coworkers had previously reported the isolation of four crystalline stereoisomers of tetra-*o*-tolylsilane.[4] These two reports led to the expectation that the isolation of torsional isomers of triarylsilanes, such as trimesitylsilane (**2**), might be possible at ambient temperatures.

By analogy with acetyltriphenylsilane[5] and related compounds,[2] **2** is presumed to have a propeller (C_3) conformation in the ground state. Such a conformation is chiral and therefore capable of existing in two enantiomeric forms. In addition, each ring carries two diastereotopic ortho methyl groups: one proximal to the hydrogen on silicon and the other distal. In the absence of rotation about the carbon–silicon bonds, the two diastereotopic methyl groups would be expected to give rise to two separate signals in the ^{1}H nmr spectrum.

Trimesitylsilane was prepared by the action of excess mesityllithium on trichlorosilane in refluxing benzene for 45 hr. At ambient temperatures, the para and ortho methyl groups each appeared as a singlet in the ^{1}H nmr spectrum (Table I); upon cooling, however, the ortho methyl signal broadened and ultimately split

Table I. Properties[a] of Triarylsilane Derivatives

Compd no.	Mp, °C	$\Delta G^{\pm}_T$ (T, °C),[b] kcal/mol	$\Delta\nu$, Hz[c]	Chemical shifts[d] (δ, ppm from TMS) *p*-Me	*o*-Me
1	192–193[e]			2.23	2.04[f]
2	197–198	10.9 (−47)	23.0	2.19	2.06
3	150.5–151.5	12.1 (−24)	24.5		2.12[f]
4	143–145	12.5 (−13)	25.3		2.18
5	151.5–153.5	11.1 (−43)	22.3		2.12

[a] All compounds were recrystallized to constant melting point and gave satisfactory elemental analyses. Mass spectra were consistent with the assigned structures. Nmr spectra were recorded on a Varian A-60A spectrometer. [b] Free energy of activation for enantiomerization by a two-ring flip pathway. [c] Separation, at the slow exchange limit, of the ortho methyl signals. [d] Data refer to *ca.* 10% solutions in CS_2 with *ca.* 1% TMS as internal standard, at ambient probe temperature (*ca.* 37°). [e] Lit.[3] 193–193.5°. [f] Center of a doublet, $^5J_{HF}$ = 2.7 Hz.

(1) This work was supported by the National Science Foundation (GP-30257).
(2) D. Gust and K. Mislow, *J. Amer. Chem. Soc.*, **95**, 1535 (1973).
(3) N. Wiberg and B. Neruda, *Chem. Ber.*, **99**, 740 (1966).
(4) G. N. R. Smart, H. Gilman, and H. W. Otto, *J. Amer. Chem. Soc.*, 77, 5193 (1955).
(5) For X-ray structure see P. C. Chieh and J. Trotter, *J. Chem. Soc.*, 1778 (1969).