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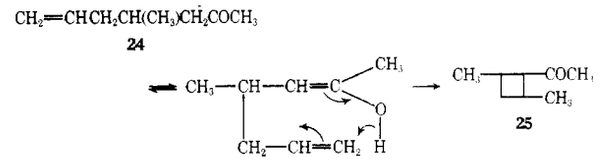
(31) Since the amount of this ketone **25** in the pyrolysis product increased at higher temperatures or when the residence time of the mixture in the pyrolysis tube increased, we presume that this ketone **25** is formed from ketone **24** by the following thermal reorganization. Reported examples of



analogous rearrangements included (a) J. Brocard, G. Moinet, and J. M. Conia, *Bull. Soc. Chim. Fr.*, 1711 (1973); (b) F. Leyendecker, J. Drouin, and J. M. Conia, *Tetrahedron Lett.*, 2931 (1974); (c) U. Schirmer and J. M. Conia, *ibid.*, 3057 (1974); (d) J. Drouin, F. Leyendecker, and J. M. Conia, *ibid.*, 4053 (1975).
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Total Synthesis of (+)-Costunolide

Paul A. Grieco* and Mugio Nishizawa

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

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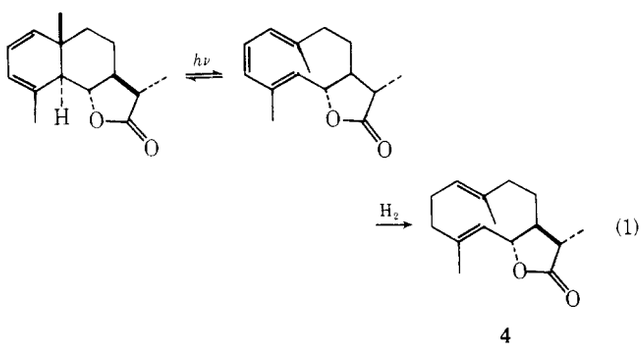
The total synthesis of the germacranolide costunolide (**2**) is described which employs the Cope rearrangement of synthetic dehydrosaussurea lactone (**1**) for generation of the ten-membered carbocyclic cyclodecadiene unit. In addition the synthesis of saussurea lactone (**3**) and its conversion to dihydrocostunolide (**4**) is recorded. The synthesis demonstrates the potential of the Shapiro olefin forming reaction in the presence of a reactive carbonyl and the usefulness of selenium in organic synthesis.

Costunolide (**2**)[1] is a member of the germacrane class of sesquiterpenes. Over the years the cyclodecane ring system of germacranolides has received little attention from synthetic chemists. This is primarily due to the primitive state of conformational analysis of ten-membered rings and the lack of methods for elaboration of the ten-membered carbocyclic framework. To date there has been no recorded total synthesis of costunolide. The only synthesis of a germacranolide is that of dihydrocostunolide (**4**) which employs a photolytic cleavage of a hexahydronaphthalene derivative for construction of the cyclodecane ring system (cf. eq 1).[2]



(1)

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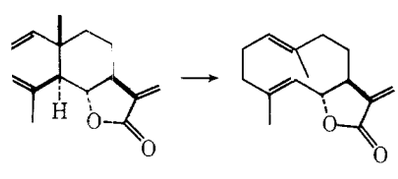
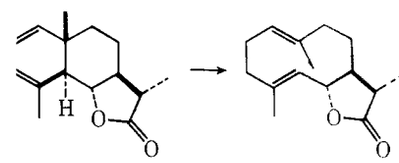
We describe herein the total synthesis of costunolide (**2**) via synthetic dehydrosaussurea lactone (**1**) utilizing the Cope



(2)

1 **2**

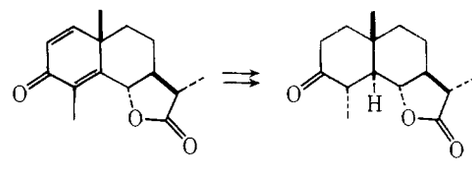


(3)

3 **4**

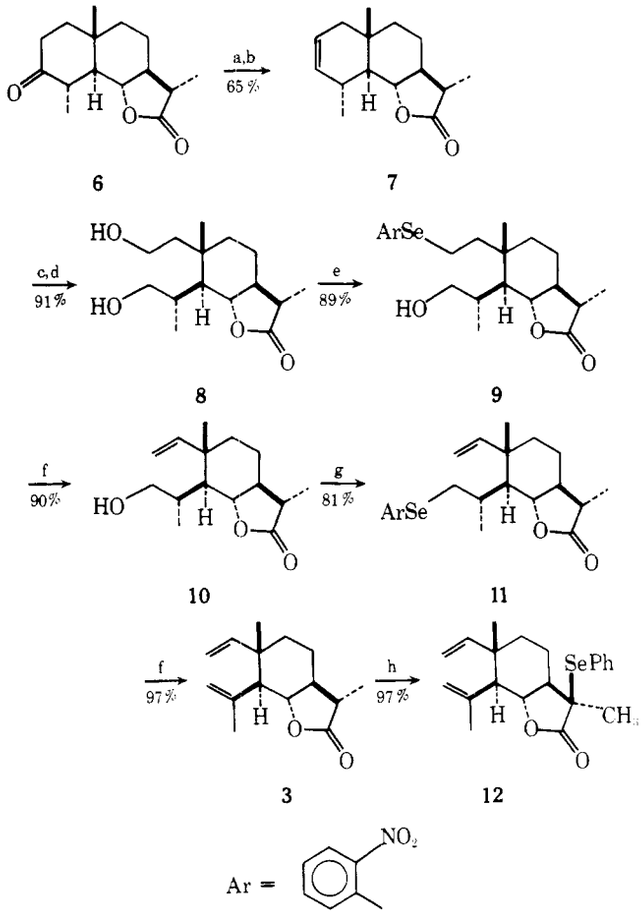
rearrangement[3,4] for construction of the ten-membered carbocyclic unit (eq 2). In addition we record the synthesis of saussurea lactone (**3**)[5] and its conversion to dihydrocostunolide (**4**) (eq 3).

The starting point of our synthesis (Chart I) was the keto lactone **6**, which was prepared from santonin (**5**) by the known two-step procedure involving hydrogenation and epimerization at C-4.[6] Treatment of the keto lactone **6** with tosylhydrazine provided the corresponding hydrazone which when treated with excess lithium diisopropylamide in dry tetrahydrofuran at 0 °C gave a 65% isolated yield (overall) of the crystalline olefin **7**, mp 142–143 °C. The use of lithium diisopropylamide in the Shapiro olefin-forming reaction[7] allows for the presence within the same molecule of a reactive carbonyl function as evidenced by the conversion of **6** → **7**. The lactone enolate undoubtedly acts as a protecting group for the lactone moiety. Lithium dialkylamides have recently been employed in the Shapiro olefin-forming reaction; however, no reactive carbonyl groups were present.[8] Sodium bis(tri-



5 **6**

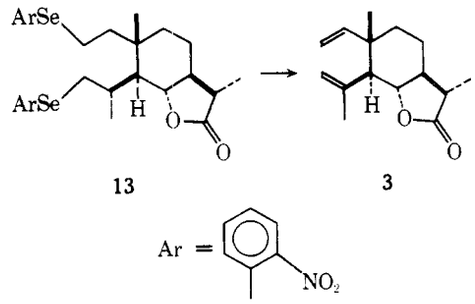
Chart I



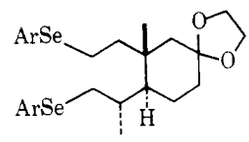
a, $TsNHNH_2$, PhH, $BF_3{\cdot}Et_2O$; b, LDA, THF, −78 → 0°C; c, O_3, CH_2Cl_2–MeOH (1:1), −78°C; d, $NaBH_4$, −78 → 25°C; e, $NO_2C_6H_4SeCN$, Bu_3P, THF–Py (1:1); f, 50% H_2O_2, THF; g, $O_2NC_6H_4SeCN$, Bu_3P, THF; h, LDA, PhSeSePh, HMPA, THF, −78 → −20°C.

methylsilyl)amide has been employed in the presence of a nonenolizable ketone.[9]

Ozonolysis of **7** followed by treatment with sodium borohydride gave the crystalline diol **8**, mp 182–183 °C. We had anticipated that the diol **8** would provide direct access to the bis-*o*-nitrophenyl selenide **13** which would upon oxidation undergo smooth elimination[10] of 2 equiv of *o*-nitrophenylselenenic acid with formation of saussurea lactone (**3**). This, however, was not to be the case since we have not been able to prepare the bisselenide **13**.



This was indeed surprising in view of the direct high-yield formation of the bis-*o*-nitrophenyl selenide **14**[11] obtained by treatment of the corresponding diol with 2.2 equiv of *o*-nitrophenyl selenocyanate in tetrahydrofuran containing 2.2 equiv of tributylphosphine.[12] Treatment of diol **8** with either 1 or 2 equiv of *o*-nitrophenyl selenocyanate[13,14] in pyridine–



14

tetrahydrofuran (1:1) containing 1 or 2 equiv, respectively, of tributylphosphine gave exclusively in excellent yield the monoselenide **9**[15] [NMR ($CDCl_3$) δ 3.08 (m, 2 H, CH_2Se), 3.60 (d, 2 H, J = 7 Hz, CH_2O), 7.65 (m, 3 H), 8.35 (d, 1 H)].

Prior to oxidation of selenide **9** to its corresponding selenoxide, we attempted to convert monoselenide **9** to the bisselenide **13** by resubmission of **9** to the reaction conditions described above. However, no bisselenide was isolated; only monoselenide **9** was recovered. Upon oxidation monoselenide **9** was smoothly transformed into the olefinic alcohol **10**, mp 71–72 °C. Fortunately, direct conversion of alcohol **10** to selenide **11** proceeded without difficulty. Elimination of the corresponding *o*-nitrophenylselenoxide gave crystalline saussurea lactone (**3**), mp 149–150 °C, $[\alpha]^{24}_D$ +65° (chloroform). Thermolysis (210 °C) of saussurea lactone (**3**) in a sealed tube under nitrogen gave in near-quantitative yield a 1:1 mixture of dihsyrocostunolide (**4**) [mp 74–75 °C, $[\alpha]^{24}_D$ +108° (chloroform)] and saussurea lactone.

Selenenylation[16] of saussurea lactone gave exclusively selenide **12** which was converted upon treatment with *2.2 equiv* of 30% hydrogen peroxide in tetrahydrofuran into dehydrosaussurea lactone (**1**), mp 82–83 °C, $[\alpha]^{24}_D$ +63° (chloroform), in 93% yield. Thermolysis of dehydrosaussurea lactone gave a 20% yield of crystalline costunolide [mp 105–106 °C, $[\alpha]^{24}_D$ +122° (chloroform)] along with a 42% yield of recovered **1**. The NMR and IR spectra of synthetic (+)-costunolide were in complete agreement with the published NMR[17] and IR[1a] spectra of natural costunolide.

Experimental Section

Melting points were determined on a Fisher-Johns hot stage melting point apparatus. All melting points and boiling points are uncorrected. Infrared (IR) spectra were determined on a Perkin-Elmer 247 grating infrared spectrometer and nuclear magnetic resonance (NMR) spectra were recorded at either 60 MHz (Varian A-60A or T-60 spectrometer) or at 250 MHz as indicated. Chemical shifts are reported in parts per million (δ) relative to Me_4Si (δ_{Me_4Si} 0.0 ppm) as an internal standard. Low-resolution spectra were recorded on an LKB-9000 spectrometer. High-resolution spectra were recorded on a Varian MAT CH-5DF instrument. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

Reactions were run under an atmosphere of nitrogen. "Dry" solvents were dried immediately before use. Tetrahydrofuran and dimethoxyethane were distilled from lithium aluminum hydride; dimethylformamide (DMF), hexamethylphosphoramide (HMPA), dimethyl sulfoxide (Me_2SO), and pyridine were distilled from calcium hydride. Diethyl ether and dioxane were distilled from sodium. Methylene chloride was passed through a column of alumina prior to use.

5α*H*,4,6,11β-Eudesm-2-en-6,13-olide (7). A solution of 510 mg (2.04 mmol) of keto lactone **6** and 455 mg (2.50 mmol) of tosylhydrazine in 5 mL of benzene containing a drop of boron trifluoride etherate was stirred at 25 °C. After 3 h the reaction mixture was diluted with 20 mL of methylene chloride and dried over anhydrous magnesium sulfate. Evaporation of the filtrate under reduced pressure gave 945 mg of a white foam [IR ($CHCl_3$) 1770, 1630, 1600 cm^{-1}] which was used directly in the next reaction.

A solution of the above hydrazone in 10 mL of anhydrous tetrahydrofuran was slowly added at −78 °C over a period of 10 min to a stirred solution of lithium diisopropylamide (prepared from 2.63 g of diisopropylamine and 16.2 mL of a 1.54 M solution of *n*-butyllithium in hexane) in 20 mL of dry tetrahydrofuran. After an additional 10 min at −78 °C, the reaction mixture was warmed to 0 °C where stirring was continued for 2 h. The reaction was quenched by the addition of aqueous ammonium chloride solution and the product was isolated by extraction with ether.[18] The crude product was chromatographed on 40 g of silica gel. Elution with hexanes–ether, 5:2, gave 332 mg (65%) of crystalline 5αH,4,6,11β-eudesm-2-en-

6,13-olide (7): IR ($CHCl_3$) 2975, 2940, 2880, 1770, 1660, 1460, 1445, 1409, 1389, 1360, 1340, 1322, 1300, 1265, 1240, 1211, 1200, 1180, 1155, 1123, 1118, 1078, 1055, 1030, 1010, 988, 978, 960, 950, 912, 891, 861 cm^{-1}; NMR δ ($CDCl_3$) 0.96 (s, 3 H), 1.20 (d, 3 H, J = 7 Hz), 1.22 (d, 3 H, J = 7 Hz), 3.81 (t, 1 H, J = 10 Hz, -CHO-), 5.42 (m, 2 H, -CH=CH-).

Recrystallization from hexanes–ether gave an analytical sample of **7**, mp 142–143 °C.

Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.87; H, 9.60.

Ozonolysis of 5α*H*,4,6,11β-Eudesm-2-en-6,13-olide (7). A stirred solution of 275 mg (1.18 mmol) of 5α*H*,4,6,11β-eudesm-2-en-6,13-olide (**7**) in 35 mL of methanol cooled to −78 °C was treated with 35 mL of a precooled (−78 °C) saturated solution of ozone in methylene chloride (ca. 1.41 mmol of ozone). After 15 min 53 mg (1.3 mmol) of sodium borohydride was added at −78 °C. At 15-min intervals for ca. an additional 45 min an equal amount of sodium borohydride was added (−78 °C). The total amount of sodium borohydride was 212 mg (5.2 mmol). The reaction mixture was warmed to room temperature and the solvent was removed in vacuo. The product was isolated from the residue by ethyl acetate extraction.[18] The crude product was purified on silica gel. Elution with methylene chloride–tetrahydrofuran, 2:1, gave 288 mg (91%) of pure crystalline diol **8**: mp 180–181 °C; IR (KBr) 3260, 2975, 2940, 2880, 1767, 1509, 1462, 1385, 1370, 1338, 1272, 1245, 1225, 1205, 1191, 1169, 1149, 1131, 1040, 1020, 1010, 998, 989, 965, 915, 845 cm^{-1}; NMR δ (pyridine-d_5) 0.96 (s, 3 H), 1.07 (d, 6 H), 3.8–4.4 (m, 5 H). Recrystallization from tetrahydrofuran–hexanes gave analytically pure diol, mp 182–183 °C.

Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.42; H, 9.80.

Monoselenide Formation of Diol 8. A solution of 170 mg (0.63 mmol) of diol **8** and 286 mg (1.26 mmol) of *o*-nitrophenyl selenocyanate[14] in 1.7 mL of tetrahydrofuran and 1.7 mL of pyridine was treated with 225 mg (1.26 mmol) of tri-*n*-butylphosphine. The resulting deep red solution was stirred for 2 h. After removal of the solvent under reduced pressure, the yellow residue was dissolved in the minimum amount of benzene and directly purified on 55 g of silica gel. Elution with hexanes–ether, 2:3, gave 240 mg (89%) of pure monoselenide **9** as a yellow foam: IR ($CHCl_3$) 3600, 3500, 2975, 2938, 2875, 1770, 1595, 1570, 1518, 1460, 1390, 1339, 1309, 1275, 1258, 1220, 1190, 1145, 1135, 1105, 1072, 1055, 1040, 1025, 1012, 990, 975, 955, 905, 855 cm^{-1}; NMR δ ($CDCl_3$) 1.04 (s, 3 H), 1.06 (d, 3 H, J = 7 Hz), 2.05 (d, 3 H, J = 7 Hz), 3.08 (m, 2 H, $-CH_2Se$), 3.60 (d, 2 H, J = 7 Hz, $-CH_2OH$), 4.08 (t, 1 H, J = 10 Hz, -CHO-), 7.65 (m, 3 H), 8.35 (d, 1 H, J = 8 Hz).

Conversion of Monoselenide 9 to Olefin 10. To a solution of 240 mg (0.53 mmol) of monoselenide **9** in 5 mL of tetrahydrofuran at 0 °C was slowly added 290 μL of 50% aqueous hydrogen peroxide. After addition was complete, the reaction was warmed to room temperature. After 3 h, the reaction was quenched by the addition of 10 mL of water and the solvent was evaporated in vacuo. Isolation of the product by ether extraction[18] gave crude olefin **10** which was purified on 25 g of silica gel. Elution with hexanes–ether, 2:3, gave 130 mg (90%) of crystalline olefin **10**: mp 69–70 °C; IR ($CHCl_3$) 3500, 2980, 2945, 2880, 1771, 1640, 1460, 1415, 1389, 1360, 1335, 1309, 1275, 1239, 1210, 1190, 1145, 1130, 1100, 1076, 1058, 1029, 1010, 990, 969, 927, 918, 859, 838 cm^{-1}; NMR δ ($CDCl_3$) 1.00 (d, 3 H, J = 7 Hz), 1.10 (s, 3 H), 1.21 (d, 3 H, J = 7 Hz), 3.50 (d, 2 H, J = 6.5 Hz, $-CH_2OH$), 4.00 (t, 1 H, J = 11 Hz, -CHO-), 4.9–6.0 (m, 3 H, typical vinyl pattern, $-CH=CH_2$). Recrystallization from hexanes–ether gave analytically pure olefin **10**, mp 71–72 °C.

Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.28; H, 9.65.

Preparation of *o*-Nitrophenyl Selenide (11). A solution of 121 mg (0.48 mmol) of the olefinic alcohol **10** and 218 mg (0.96 mmol) of *o*-nitrophenyl selenocyanate[14] in 20 mL of tetrahydrofuran was treated at 25 °C with 194 mg of tri-*n*-butylphosphine. After 3 h the solvent was removed under reduced pressure and the yellow residue was chromatographed on silica gel. Elution with hexanes–ether, 2:1, gave 169 mg (81%) of yellow, crystalline selenide **11**. Recrystallization from hexanes–methylene chloride gave analytically pure selenide **11**: mp 162–163 °C; IR ($CHCl_3$) 3030, 2980, 2940, 2875, 1770, 1640, 1596, 1573, 1520, 1460, 1419, 1390, 1340, 1308, 1272, 1260, 1210, 1186, 1179, 1147, 1131, 1105, 1088, 1055, 1042, 1010, 990, 970, 938, 858 cm^{-1}; NMR δ ($CDCl_3$) 1.10 (d, 6 H, J = 7 Hz), 1.25 (s, 3 H), 2.98 (d, 2 H, $-CH_2Se$, J = 7 Hz), 4.05 (t, 1 H, J = 10 Hz, -CHO-), 4.8–5.9 (m, 3 H, $-CH=CH_2$), 7.50 (m, 3 H), 8.20 (d, 1 H, J = 7.5 Hz).

Anal. Calcd for $C_{21}H_{27}NO_4Se$: C, 57.80; H, 6.24; N, 3.21. Found: C, 57.88; H, 6.24; N, 3.21.

Saussurea Lactone (3). A solution of 52 mg (0.12 mmol) of selenide **11** in 1.0 mL of tetrahydrofuran was treated dropwise at 0 °C with 18 μL (0.26 mmol) of 50% aqueous hydrogen peroxide. After 3 h at 25 °C, the solvent was removed in vacuo and the product was isolated by ether extraction.[18] Purification of the crude product on silica gel (elution with hexanes–ether, 3:1) gave 27 mg (97%) of crystalline saussurea lactone (**3**), mp 147–148 °C. Recrystallization from hexanes gave analytically pure saussurea lactone: mp 149–150 °C; $[\alpha]_D$ +65° (chloroform) [lit.[5] mp 148–149 °C, $[\alpha]_D$ +66°]; IR (KBr) 3090, 2980, 2950, 2880, 1768, 1640, 1460, 1448, 1415, 1380, 1363, 1339, 1280, 1260, 1235, 1214, 1193, 1180, 1160, 1147, 1130, 1092, 1065, 1047, 1018, 1005, 978, 918, 900, 861, 843 cm^{-1}; NMR δ ($CDCl_3$) 1.09 (s, 3 H), 1.23 (d, 3 H, J = 6.5 Hz), 1.78 (s, 3 H), 2.24 (d, 1 H, J = 12 Hz), 4.16 (t, 1 H, J = 12 Hz), 4.76 (bs, 1 H), 5.10 (bs, 1 H), 4.8–6.1 (m, 3 H, $-CH=CH_2$).

Anal. Calcd for $C_{15}H_{22}O_2$: C, 74.88; H, 9.46. Found: C, 74.75; H, 9.70.

Dihydrocostunolide (4). Saussurea lactone (18 mg, 0.077 mmol) was heated at 210 °C for 5 min in a sealed tube. The equilibrated mixture was chromatographed on 10 g of silica gel. Elution with hexanes–ether, 3:1, gave in order of elution 10 mg (56%) of recovered saussurea lactone and 8 mg (44%) of crystalline dihydrocostunolide, mp 72–74 °C. Recrystallization from *n*-pentene gave pure dihydrocostunolide: mp 74–75 °C; $[\alpha]^{24}_D$ +108° (chloroform) [lit.[16] mp 77–78 °C, $[\alpha]^{26}_D$ +110.8° (chloroform)]; IR (CCl_4) 2975, 2945, 2880, 2870, 1780, 1674, 1460, 1443, 1395, 1388, 1358, 1309, 1270, 1240, 1230, 1205, 1090, 1060, 1050, 998, 972, 940, 896, 873, 841 cm^{-1}; NMR δ (CCl_4) 4.2–5.1 (m, 3 H), 1.70 (s, 3 H), 1.40 (s, 3 H), 1.20 (d, 3 H, J = 7 Hz).

Phenylselenenylation of Saussurea Lactone. A solution of 79 mg (0.34 mmol) of saussurea lactone in 1.2 mL of anhydrous tetrahydrofuran containing dry hexamethylphosphoramide (91 mg) was slowly added over a 10-min period to a cooled (−78 °C) solution of lithium diisopropylamide [prepared from 71 μL (0.51 mmol) of diisopropylamine and 320 μL of 1.54 M *n*-butyllithium in hexane] in 1.0 mL of dry tetrahydrofuran. After 10 min a solution of 178 mg (0.51 mmol) of diphenyl diselenide in 1.0 mL of tetrahydrofuran was added at −78 °C. After addition was complete the reaction mixture was warmed to −20 °C where stirring was continued for an additional 1 h. The reaction was quenched by the addition of aqueous ammonium chloride and the product was isolated by extraction with ether.[18] Purification of the crude product on 25 g of silica gel (hexanes–ether, 5:1) gave 127 mg (97%) of crystalline selenenylated lactone **12**. Recrystallization from hexanes gave an analytically pure sample of **12**: mp 109–110 °C; IR ($CHCl_3$) 3080, 3015, 2980, 2950, 2880, 2870, 1776, 1641, 1584, 1482, 1458, 1443, 1418, 1382, 1357, 1320, 1305, 1291, 1272, 1220, 1186, 1122, 1085, 1075, 1050, 1030, 1018, 985, 928, 905, 865, 851 cm^{-1}; NMR ($CDCl_3$) δ 7.3–7.9 (m, 5 H, aromatic protons), 4.6–6.1 (m, 5 H, $-CH=CH_2$, $CH_2=C$), 4.50 (bt, 1 H, -CHOCO), 1.70 (bs, 3 H), 1.56 (s, 3 H), 1.05 (s, 3 H).

Anal. Calcd for $C_{21}H_{26}O_2Se$: C, 64.77; H, 6.73. Found: C, 64.95; H, 6.80.

Dehydrosaussurea Lactone (1). A solution of selenenylated lactone **12** (92 mg, 0.21 mmol) in 2.0 mL of tetrahydrofuran was treated at 0 °C with 54 μL (0.46 mmol) of 30% aqueous hydrogen peroxide. After addition was complete, the temperature was raised to 25 °C and stirring was continued for 1 h. The reaction was quenched by the addition of brine. The product was isolated by extraction with ether.[18] The crude product was purified on 20 g of silica gel. Elution with hexanes–ether, 4:1, gave 55 mg (93%) of crystalline dehydrosaussurea lactone. Recrystallization from *n*-pentane gave pure **1**: mp 82–83 °C, $[\alpha]^{24}_D$ +63° (chloroform) [lit.[3b] mp 84–85 °C, $[\alpha]_D$ +65.7°]; IR ($CHCl_3$) 3098, 3030, 2980, 2950, 2880, 2870, 1770, 1680, 1645, 1460, 1450, 1415, 1385, 1355, 1305, 1266, 1215, 1193, 1175, 1148, 1135, 1095, 1068, 1008, 978, 950, 925, 908, 860, 848, 838, 820 cm^{-1}; NMR ($CDCl_3$) δ 6.11 (d, 1 H, J = 3 Hz), 5.44 (d, 1 H, J = 3 Hz), 5.62–5.99 (m, 1 H, $-CH=CH_2$), 5.10 (bs, 1 H), 5.0 (m, 2 H, $-CH=CH_2$), 4.73 (bs, 1 H), 4.13 (t, 1 H, J = 12 Hz), 2.28 (d, 1 H, J = 12 Hz), 1.80 (d, 3 H, J = 1 Hz), 1.17 (s, 3 H).

(+)-Costunolide (2). Thermal equilibration of dehydrosaussurea lactone (80 mg) was carried out on a Varian Aerograph 90P GLC unit using a 5 ft × 0.25 in. 10% OV-1 column at 200 °C with helium as the carrier gas (40 mL/min). Equilibration occurs on the column as evidenced by one broad band. There was obtained after equilibration 66 mg of a mixture of costunolide and dehydrosaussurea lactone. Preparative thin layer chromatography using hexanes–ether, 1:1, gave 34 mg of recovered **1** and 16 mg (20%) of crystalline costunolide. Recrystallization from hexanes gave colorless needles of pure (+)-costunolide: mp 105–106 °C; $[\alpha]^{24}_D$ + 122° (chloroform) [lit.[1a] mp 106 °C, $[\alpha]^{20}_D$ + 128° (chloroform)]; IR ($CHCl_3$) 2975, 2945, 2870, 1762, 1670, 1459, 1442, 1410, 1390, 1315, 1295, 1252, 1213, 1185, 1145, 1090, 1060, 971, 950, 895, 878, 840 cm^{-1}; NMR (250 MHz) δ ($CDCl_3$) 6.26

(d, 1 H, J = 3 Hz), 5.52 (d, 1 H, J = 3 Hz), 4.86 (m, 1 H), 4.72 (d, 1 H, J = 9 Hz), 4.56 (t, 1 H, J = 9 Hz), 1.71 (d, 3 H, J = 1 Hz), 1.42 (d, 3 H, J = 1 Hz).

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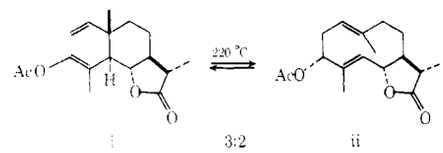
Registry No.—**1**, 28290-35-9; **2**, 553-21-9; **3**, 23527-07-3; **4**, 2225-79-8; **6**, 13902-54-0; **6** hydrazone, 61617-82-1; **7**, 60390-22-9; **8**, 61617-83-2; **9**, 61617-84-3; **10**, 61617-85-4; **11**, 61617-86-5; **12**, 61617-87-6; tosylhydrazine, 1576-35-8; *o*-nitrophenyl selenocyanate, 51694-22-5; diphenyl diselenide, 1666-13-3.

References and Notes

(1) (a) V. Herout, M. Suchý, and F. Šorm, *Collect. Czech. Chem. Commun.*, **26**, 2612 (1961); (b) A. S. Rao, G. R. Kelkar, and S. C. Bhattacharyya, *Tetrahedron*, **9**, 275 (1960).
(2) E. J. Corey and A. G. Hortmann, *J. Am. Chem. Soc.*, **87**, 5736 (1965). Recently a synthesis of dihydrocostunolide was reported [Y. Fujimoto, T. Shimizu, and T. Tarsuno, *Tetrahedron Lett.*, 2041 (1976)] which was based on the Corey use of the photolytic cleavage of a hexahydronaphthalene derivative.
(3) In 1967, N. H. Fischer and T. J. Mabry [*Chem. Commun.*, 1235 (1967)] reported the first example of the formation of a germacranolide from a



trans-1,2-divinylcyclohexane derivative (cf. i → ii). More recently T. C. Jain, C. M. Banks, and J. E. McCloskey [*Tetrahedron Lett.*, 841 (1970)] demonstrated the reversibility of the Cope rearrangement on dihydrocostunolide and costunolide.
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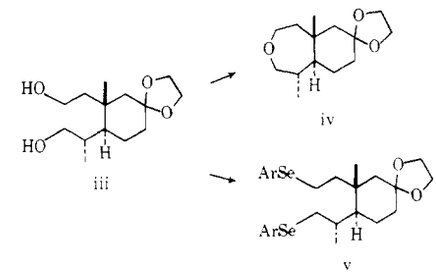
(11) Unpublished results of George Majetich, University of Pittsburgh.
(12) For the direct conversion of alcohols to alkyl aryl selenides, see P. A. Grieco, S. Gilman, and M. Nishizawa, *J. Org. Chem.*, **41**, 1485 (1976).
(13) H. Bauer, *Ber.*, **46**, 92 (1913).
(14) Previous reports[10a,13] have reported *o*-nitrophenyl selenocyanate as light brown crystals, mp 139–141[10a] and 142 °C.[13] We have found that the brown, crystalline material obtained from the procedure of Bauer[13] can be sublimed [100 °C (0.2 mmHg)] providing yellow crystals of *o*-nitrophenyl selencyanate, mp 144 °C.
(15) The fact that treatment of diol **8** with only 1 equiv of *o*-nitrophenyl selenocyanate in the presence of 1 equiv of tri-*n*-butylphosphine gave monoselenide **9** was unexpected. We had previously observed[11] that treatment of diol iii under identical conditions gave the seven-membered ring ether



iv with no evidence of monoselenide formation. In addition treatment of iii with excess reagent gave the bisselenide v. At present, we do not have any reasonable explanation to account for these observations.
(16) K. B. Sharpless, K. M. Gordon, R. F. Lauer, D. W. Patrick, S. P. Singer, and M. W. Young, *Chem. Scr.*, **8A**, 9 (1975); see also P. A. Grieco and M. Miyashita, *J. Org. Chem.*, **39**, 120 (1974).
(17) R. W. Doskotch and F. S. El-Feraly, *J. Org. Chem.*, **35**, 1928 (1970).
(18) The products were isolated by extraction of the aqueous layer with several portions of the indicated solvent. The combined organic extracts were washed with water followed by saturated brine. The organic layer was usually dried with either anhydrous sodium sulfate or anhydrous magnesium sulfate. Filtration followed by removal of the solvent in vacuo (water aspirator) employing a rotary evaporator provided the products.

Micordilin, a Complex Elemanolide from *Mikania cordifolia*[1a]

Werner Herz,*[1b] P. S. Subramaniam,[1b] Ramaswamy Murari,[1b] Nicholas Dennis,[1b] and John F. Blount[1c]

Department of Chemistry, The Florida State University, Tallahassee, Florida 32306, and Research Division, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

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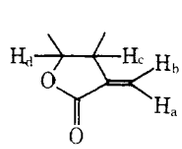
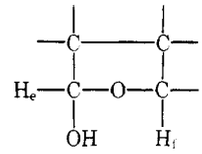
Micordilin, an intramolecular hemiacetal of a C-14-acetylated dialdehydic elemanolide, was isolated from the medicinal plant *Mikania cordifolia* (L. F.) Willd. Chemical transformations and NMR techniques eliminated all but two possible hemiacetal structures; a decision in favor of **5a** which also represents the absolute configuration was reached by x-ray analysis.

A group of interesting antitumor dilactones derived from germacranolides and elemanolides has been isolated from various *Mikania* (Eupatorieae, Compositae) species.[2-9] In the present communication we report isolation from the West Indian medicinal plant *Mikania cordifolia* (L. F.) Willd. of micordilin, a hemiacetal of the C-14-hydroxylated dialdehydic elemanolide **1**, and its structure determination as **5a**.

Micordilin, $C_{17}H_{20}O_7$ (high-resolution mass spectrum), mp 176–178 °C, was a conjugated γ-lactone (IR bands at 1770 and 1660 cm^{-1}, UV λ_{max} 212 nm). The NMR spectrum (Table I) exhibited the typical but very narrowly split H_a and H_b doublets of partial structure A at 6.13 and 5.62 ppm. The location



A



B

of the H_c multiplet at 3.12 ppm and the H_d triplet of doublets at 4.61 ppm was established by spin-decoupling experiments.

Partial hydrogenation (Pd/C, ethyl acetate) resulted in