Tetrahedron. Vol. 32, pp. 955 to 959. Pergamon Press 1976. Printed in Great Britain

THE PHOTOISOMERIZATION OF DIHYDROCOSTUNOLIDE[1]

RUDOLPH E. K. WINTER*
Department of Chemistry, University of Missouri, St. Louis, MO 63121, U.S.A.

and

RICHARD F. LINDAUER
Department of Chemistry, Polytechnic Institute of New York, NY 11201, U.S.A.

(*Received in USA* 5 *August* 1975; *Received in UK for publication* 20 *November* 1975)

Abstract—Photoisomerization of the germacranolide dihydrocostunolide (**2**) proceeds with a high degree of regio- and stereoselectivity to give the guaianolide photunolide (**16**) as the only major product. The conversion of photunolide to two guaianolides of known structure (**8** and **9**) and synthesis from O-acetylisophotosantonic lactone (**11**) provide unambiguous proof of both the structure and the stereochemistry of photunolide. The photoisomerization of **2** to **16** appears to involve an intramolecular hydrogen shift.

INTRODUCTION

Sesquiterpenes based on 1,5-dimethyl-8-isopropylcyclodecane (germacranes) and the corresponding γ-lactones (germacranolides) were once thought to be rare but now are known to constitute a large class of naturally-occurring compounds, within which the 1,5-diene system or related epoxides and alcohols are common structural features.[2] Transannular cyclizations involving these moities typically take place with a high degree of stereospecificity under cationic or radical conditions to afford *trans*-fused eudesmanes as the major products. Sutherland has taken this as evidence of the importance of reactive conformations in which the double bonds are crossed.[3] However, in an earlier and seminal speculation on the biogenesis of sesquiterpenes, Hendrickson had pointed out that such regioselectivity was in accord with electronic effects.[4] Concerted cyclization by *trans*-antiparallel addition to both double bonds of a 1,5-cyclodecadiene in the Markownikoff sense would afford eudesmanes, but guaiane formation would necessitate an anti-Markownikoff addition to one double bond. Costunolide (**1**) and dihydrocostunolide (**2**) are typical *trans, trans*-germacra-1,5-dienolides,[5] and in solution the double bonds of both **1** and **2** adopt the "crossed" conformation.[6] Not surprisingly, only eudesmanolides appear to be produced by electrophilic cyclization of **1**,[7] **2**,[8,9] and their 1,10-monoepoxides[10] or by thermolysis of **2**.[11]

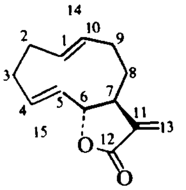
Costunolide has been isolated from sources as taxonomically and geographically diverse as the American tulip tree (*Liriodendron tulipifera* L., family Magnoliaceae)[12] and the central Asian herb, lemon wormwood (*Artemesia balchanorum*, family Compositae);[8,13] dehydrocostus lactone (**3**) and costunolide together constitute 50% of the root oil of the Indian costus plant (*Saussurea lappa* C., family Compositae).[14] Because of its ubiquitous nature and structural simplicity costunolide is thought to be very closely related to the biogenetic precursor of many sesquiterpene groups.[15]

As part of a continuing study of natural and synthetic guaianolides, we decided to investigate the photochemistry of dihydrocostunolide (**2**) under conditions thought to generate the olefin triplet state.[16] It was anticipated that this might significantly alter the electronic and conformational effects which control the ground state chemistry of diene **2** and thereby facilitate guaianolide formation. Sometime after this work was initiated photolysis of the germacra-1,5-diene dilactone dihydroisabelin (**4**) in benzene was reported to give a guaianolide as the major product.[17] The observation that diene **4** in solution also has the "crossed-olefin" conformation augured well for an analogous reaction with diene **2**.

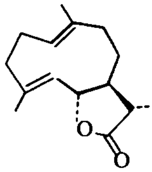
PRESENTATION AND DISCUSSION OF RESULTS

Photolysis of dihydrocostunolide (**2**) in 10% xylene–isopropanol at 254 nm resulted in smooth disappearance of starting material and formation of several products detectable by thin-layer and gas chromatography. Preparative chromatography gave homogenous samples of the major photoproduct, photunolide.

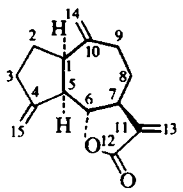
The mass spectrum of photunolide exhibited a parent ion at *m/e* 234·1617, indicating a molecular formula isomeric with that of **2** (Calc. for $C_{15}H_{22}O_2$; 234·1620). The IR spectrum suggested the presence of a γ-lactone



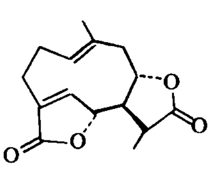
1



2

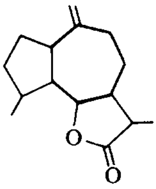


3

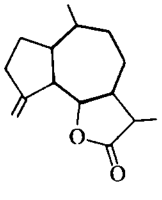


4

(1780 cm^{-1}) and a terminal methylene (1632 and 892 cm^{-1}), and the only olefinic protons evident in the PMR spectrum appeared as slightly broadened 1H singlets at $5{\cdot}12$ and $5{\cdot}15\tau$. The PMR spectrum of photunolide also showed a Me doublet at $8{\cdot}85\tau$ ($J = 9$ Hz), a doublet at $8{\cdot}79\tau$ ($J = 6{\cdot}6$ Hz) for the α-Me on the lactone ring, and a triplet at $6{\cdot}16\tau$ ($J = 9{\cdot}7$ Hz) for the methine proton at C-6.[18] These data strongly suggest a guaianolide skeketon and cannot be accomodated within a typical eudesmane structure. Two reasonable partial structures for photunolide are shown in formulas **5** and **6**.



5



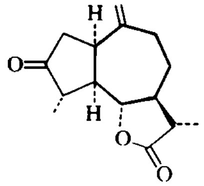
6

Two guaianolides known to be epimeric at C-10 were available to us from previous studies on the stereochemistries of achillin[19] and **3**.[20,21] The major hydrogenation product of olefin **7** had been stereospecifically deoxygenated to lactone **8** by reduction of the corresponding ethylene thioketal, and the minor hydrogenation product had been converted to lactone **9** in similar fashion. Catalytic hydrogenation of photunolide proceeded very rapidly to give two dihydro derivatives readily separable by preparative GLC. Careful comparison of the physical data showed that the major and minor dihydrophotunolides were identical to guaianolides **8** and **9**, respectively. Thus, photunolide may confidently be assigned partial structure **5** with the stereochemistry at the asymmetric centers C-4, C-5, C-6, C-7 and C-11 being identical to that of lactones **8** and **9**.

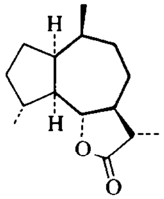
However, since allylic migration of the exocyclic double bonds to endocyclic positions including C-1(10) has been observed[22] during the hydrogenation of costus lactone (**10**), a similar and concomitant loss of C-1 stereochemistry during hydrogenation of photunolide could not be ruled out *a priori*. Clarification of this final structural ambiguity was accomplished synthetically via intermediates (**11–15**) of known stereochemistry.

Catalytic hydrogenation of O-acetylisophotosantonic lactone (**11**) followed by reduction with a mixture of pinanylboranes and quantitative dehydration with mesyl chloride afforded acetoxy olefin **14** with a yield considerably higher (58%) than that of the reported sequence (<25%).[23] Basic hydrolysis of **14** to hydroxy olefin **15**,[24] catalytic hydrogenation, and dehydration with thionyl chloride gave a mixture of three major products, one of which was purified by GLC and shown to be identical to photunolide. Since conversion of **15** to **16** should not affect the configuration at C-1, the stereostructure of photunolide must be that shown in formula **16**.

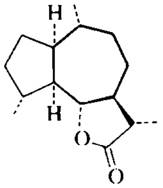
Transformation of dihydrocostunolide to photunolide must involve (in a formal sense, at least) a transfer of hydrogen from C-14 to C-4. Since it was of some interest to determine whether this was an inter- or intra-molecular process, irradiation of **2** was carried out in deuterated solvents. Mass-spectral analysis of photunolide recovered from the reaction mixture showed no evidence of deuterium incorporation. Photoisomerization of **2** thus



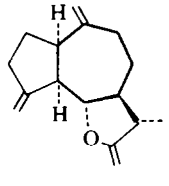
7



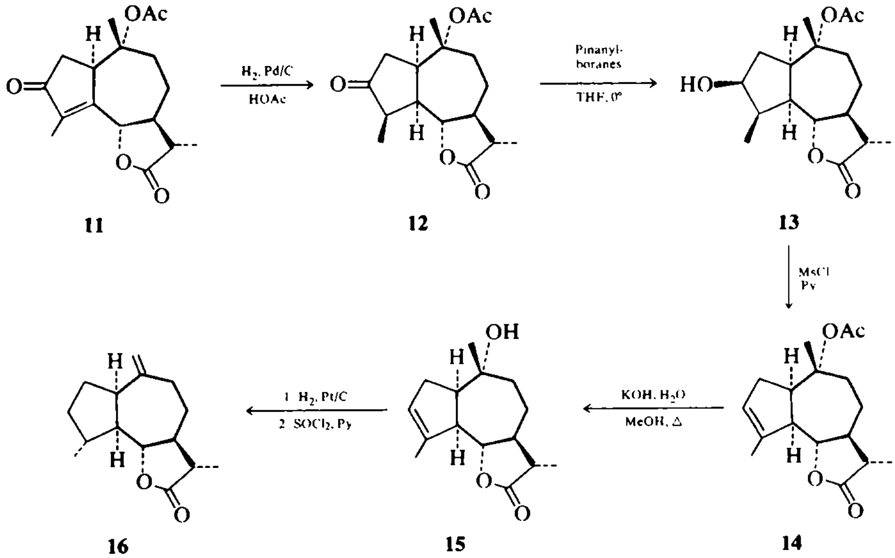
8



9



10



appears to involve an intramolecular hydrogen shift. In its simplest form, the photoisomerization could be either concerted or two-step. The concerted process would be an example of a photo-ene reaction and would require a specific "crossed-olefin" conformation in order to successfully account for the observed stereospecificity (Fig. 1). This would be in accord with previously noted findings on the ground-state conformations of **2**.[6] However, examination of molecular models suggests that a 1,4-biradical intermediate could also effect a stereospecific intramolecular hydrogen transfer (Fig. 2). The isolation of at least one other photodihydrocostunolide (cf. Experimental) is perhaps more easily accommodated by the intermediacy of a biradical. Formation of *endo,endo*-2,6-divinyl-*cis*-bicyclo[3.3.0]octane by photolysis of isomeric 1,5,9-cyclododecatrienes in benzene–acetone has been explained in terms of reversible cyclization of an initial olefin triplet, forming a biradical which reacts further.[25] Alternatively, the photochemical behavior of dihydrocostunolide might best be considered a reaction more typical of a monoene than a 1,5-diene; sensitized intramolecular hydrogen transfers by olefins are precedented.[26] We are continuing our investigation of the photochemical behavior of the costunolides in an effort to define further mechanistic details.

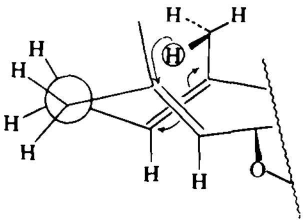


Fig. 1.

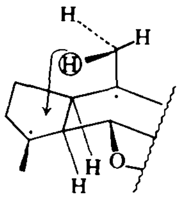


Fig. 2.

EXPERIMENTAL

Unless otherwise noted, the following general information applies.

IR spectra were recorded on Perkin-Elmer Spectrophotometers (Models 521, 21 or 137). PMR were recorded with a Varian A-60 Spectrometer; chemical shifts are reported as ppm relative to TMS internal standard at 10·00τ. Mass spectral fragmentation patterns were obtained by electron impact at 80 eV, using a Hitachi/Perkin-Elmer RMU-6E Mass Spectrometer. Rotations were measured at the sodium D line in a Rudolph Model 63 or Perkin-Elmer model 141 Polarimeter.

Gas chromatographic separations, both analytical and preparative, were performed on a Varian-Aerograph Model 1520 GC, equipped with 6′ × 1/8″ (O.D.) stainless steel columns packed with 5% Carbowax 20M on Gaschrom Q (80/100 mesh) and operated at 180–200°; glass-lined injector ports were used. TLC were carried out on plates of Brinkmann alumina (ALOX N-HR/UV-254) or silica gel (SIL N-HR/UV-254) with the solvents indicated; visualization was achieved with iodine vapor, phosphomolybdic acid soln (3% in isopropanol), alkaline potassium permanganate or alkaline *m*-dinitrobenzene. Dry column chromatographic separations were achieved with neutral alumina or silica gel (Woelm, activity grades II–III) with the indicated solvents. Characteristic GLC retention times (rrt) and TLC mobilities (R_{st}) are reported relative to the starting material for the reaction under investigation.

M.p. determinations were made on a Thomas-Hoover capillary m.p. apparatus and are uncorrected. All solvents used were Reagent grade and, if required, were further purified by standard techniques prior to use.

Photolyses were carried out with a Rayonet Photochemical Reactor (Southern New England Ultraviolet Co.) equipped with RPR-2537 lamps.

Dihydrocostunolide (**2**). Selective reduction of costunolide was achieved using aluminum amalgam, prepared by dipping aluminum foil pieces (1–2 cm^2) in 3% aqueous mercuric chloride soln until the dull side of the foil was more than half-covered with mercury. Each piece was rinsed in EtOH and added without delay to a rapidly stirred soln of 1·47g costunolide in 75 ml ether containing several g of granular anhyd. Na_2SO_4. During several hr a total of 60 cm^2 of freshly amalgamated foil was added in this fashion. The mixture was maintained at 0° (ice-water) throughout the course of addition and then refrigerated overnight. The mixture was filtered, concentrated *in vacuo* and allowed to solidify; the PMR spectrum of the product was identical to that of authentic **2**, no unreacted costunolide being detected (estimated limit <1%). The white solid (1·54 g) was twice recrystallized at low temp. from ether–hexane mixtures to give pure **2**, m.p. 75–77° (lit.[5] m.p. 77–78°); IR (CCl_4) 1775, 1665, 965 and 888 cm^{-1} (lit.[5] 1779, 1667, 968 and 884 cm^{-1}); mass spectrum [*m/e* (rel. int.)] 234 (13), 152 (15) and 81 (100); PMR ($CDCl_3$) 5·0–5·5 (3H, multiplet), 8·31 (3H, s), 8·57 (3H, s) and 8·75τ (3H; d, J = 6·6 Hz).

Photolysis of dihydrocostunolide in xylene–isopropanol. A soln of 23 mg (0·1 mmol) of **2** in 1·0 ml xylene–isopropanol (1/9, v/v) was perfused with argon for 15 min in a quartz tube and then irradiated (10 lamps). The reaction was followed by GLC, starting material disappearing smoothly with time. After 2·8 hr irradiation no further changes were observed, and the composition of the product appeared to be constant during the entire reaction period. Irradiation was stopped after 3·6 hr and the soln was concentrated *in vacuo*. TLC analysis (silica gel, ether) of the resulting oil indicated two components, R_{st} 1·36 (major) and R_{st} 1·06, no unreacted **2** being detected. GLC analysis indicated one major component (rrt 0·88, area 0·5 of total) and at least seven minor components (rrt 0·68, 1·00, 1·32, 1·46, 1·64, 1·76 and 2·4).

In a typical preparative run a soln of 107 mg (0·46 mmol) of **2** in 5·0 ml 10% xylene–isopropanol was degassed in the quartz irradiation tube by four successive freeze–thaw cycles (liquid N_2, 0°, 0·1 Torr). After the last cycle argon was admitted to the tube, and the contents were allowed to equilibrate at room temp. The soln was irradiated for 2·8 hr (16 lamps), concentrated *in vacuo* and analyzed by TLC (alumina, benzene): major component, R_{st} 1·8; minor components, R_{st} 1·2 and 0–0·3. The straw-yellow oil was subjected to dry column chromatography over 84 g of alumina using benzene, and the fractions containing material were identified by TLC and concentrated *in vacuo*. The fractions containing the major component (*vide supra*) comprised 22 mg of colorless oil which was nearly homogenous by TLC and which exhibited the same TLC and GLC retention characteristics as the major component observed in the preliminary runs. A portion of this oil was purified by GLC to give homogenous **16** as a colorless oil: IR (CCl_4) 1780, 1632 and 892 cm^{-1}; mass spectrum [*m/e* (rel. int.)] 234 (8), 219 (7), 152 (100), 124 (34) and m* 101·3 (*m/e* 152→*m/e* 124); PMR ($CDCl_3$ at 220 MHz) 5·12 (1H; sbs, width at half-height ~4 Hz), 5·15 (1H; sbs, width at half-height ~4 Hz), 6·16 (1H; t, J = 9·7 Hz), 7·21 (1H; q, J ~ 9 Hz), 7·44 (1H; d–J = 12·7 Hz–of t, J = 4·0 Hz), 8·79 (3H; d, J = 6 Hz) and 8·85τ (3H; d, J = 5·9 Hz); at 60 MHz addition of benzene shifted the triplet at 6·16–6·64τ, the doublet at 8·85–8·82τ, and the doublet at 8·79–9·01τ.

An exact mass determination for the apparent molecular ion from a sample of **16** obtained in a manner similar to that described above gave 234·1617 (Calc. for $C_{15}H_{22}O_2$, 234·1619).[27]

In a similar experiment one of the minor components was isolated by preparative GLC; an exact mass determination[27] for the apparent molecular ion of this substance gave 234·1631.

Hydrogenation of photunolide. A soln of GLC-purified **16** (~4 mg) in 1·5 ml MeOH was stirred under H_2 in the presence of 18 mg 5% Pt/C and the reaction was monitored by GLC. No **16** was detected in the first aliquot (t ~ 13 min), and the product composition remained constant during the next hr. After this time the mixture was filtered through Celite and the solvent was removed *in vacuo*, affording a colorless oil which crystallized on standing. GLC analysis showed only two significant components—rrt 1·04 (relative area 62%) and rrt 0·86 (relative area 35%)—which were then purified by GLC and identified by comparison to authentic samples. Guaianolide **8**, the major component, was obtained as colorless needles: m.p. 84–89° (authentic sample, m.p. 87–89°);[19] IR (KBr) 1762, 1244, 1102, 1007, 985, 977 and 676 cm^{-1}; mass spectrum [*m/e* (rel. int.)] 236 (1), 192 (14), 177 (9), 150 (27), 149 (36), 135 (38) and 81 (100). The IR and mass spectra were identical with those of authentic **8**.[19,20] An exact mass determination of the apparent molecular ion shown by **8** gave 236·1775 (Calc. for $C_{15}H_{24}O_2$, 236·1776).[27] Guaianolide **9**, the minor component, was obtained as a colorless oil: (authentic **9**, oil);[19] IR (KBr) 1774, 1220, 1115 and 985 cm^{-1} (authentic **9**, 1780, 1230, 1123 and 992 cm^{-1});[19] mass spectrum [*m/e* (rel. int.)] 236 (1), 192 (11), 177 (10), 150 (51), 149 (31), 135 (54) and 81 (100), identical with that of authentic **9**.[20] An exact mass determination of the apparent molecular ion gave 236·1769.[27]

4R-*Dihydro-O-acetylisophotosantonic lactone* (**12**). Compound **11**, prepared from α-santonin by a procedure similar to that described previously,[23] was obtained as rhombic prisms, m.p. 182·5–183·5°, $[\alpha]_D^{25}$ +46·4° (*c*, 2·1 in $CHCl_3$) (lit.[23] m.p. 180–181°; $[\alpha]_D^{25}$ +47·2°, *c*, 0·8 in $CHCl_3$); IR (KBr) 1775, 1730 and 1700 cm^{-1}; PMR ($CDCl_3$) 5·15 (1H; bd, J ~ 9 Hz), 5·83 (1H, m), 8·00 (3H, s), 8·10 (3H; t, J ~ 2 Hz), 8·72 (3H; d, J = 6·1 Hz) and 8·90τ (3H, s).

Enone **11** (6·63 g, 21·6 mmol) in 50 ml glacial AcOH was catalytically hydrogenated over 10% Pd/C (1·33 g) at room temp. and atmospheric pressure; H_2 uptake was smooth and rapid. Filtration, removal of the solvent *in vacuo*, and recrystallization from MeOH afforded a 75% yield of the crude dihydro product, m.p. 168–173° (lit.[23] 59%, m.p. 168–171°). Another recrystallization from MeOH and a final recrystallization from benzene–hexane afforded 3·91 g (59%) of colorless prisms of **12**: m.p. 174–175°; $[\alpha]_D^{25}$ −66° (*c*, 1·9 in $CHCl_3$) (lit.[23] m.p. 171–172·5°, $[\alpha]_D^{25}$ −61·7°); IR (KBr) 1770, 1730, 1210, 911 and 751 cm^{-1}; PMR ($CDCl_3$) 6·03 (1H; t, J ~ 9 Hz), 7·94 (3H, s), 8·45 (3H, s), 8·76 (3H; d, J = 6·8 Hz) and 8·78τ (3H; d, J ~ 6 Hz); mass spectrum [*m/e* (rel. int.)] 248 (84), 220 (23), 147 (48), 69 (60), 55 (86), 43 (91), 41 (100) and m* 195·4 (*m/e* 248 → *m/e* 220).

Conversion of acetoxy ketone **12** *to hydroxy olefin* **15**. A soln of mixed 3-pinanylboranes was prepared under N_2 by addition of 18·1 ml of 1·1 M borane (20 mmol) in THF to 4·0 ml of (+)-α-pinene (25 mmol; $[\alpha]_D^{25}$ +46·1°, neat) and 1 ml of THF. After the exothermic reaction had subsided, the soln was added dropwise to an ice-cold stirred solution of **12** (4·62 g, 15 mmol) in 20 ml THF; stirring was continued for ~1·5 hr. Cautious addition of 20 ml of 3 M NaOH followed by addition of 20 ml 30% H_2O_2 and removal of the THF *in vacuo* afforded a soln which was then neutralized with HCl and extracted with three 60 ml portions ether. The combined extracts were washed with water, $NaHCO_3$aq and NaClaq (sat), dried over $NaSO_4$ and concentrated *in vacuo*, the final distillate boiling at 70° at 0·015 Torr. The glassy residue was identified as **13**: IR ($CHCl_3$) 3600, 3500, 1770 and 1730 cm^{-1}; PMR ($CDCl_3$) 5·4–6·1 (m), 8·03 (s), 8·53 (s) and 8·76, 8·87 and 9·00τ (overlapping d, J ~ 7 Hz) (lit.[23] IR 1770 and 1730 cm^{-1}; PMR 5·6–5·9, 8·02, 8·52, 8·75, 8·85 and 8·97τ).

The entire glassy sample of **13** was dissolved in 20 ml pyridine and treated with 1·5 ml (20 mmol) methanesulfonyl chloride. After 40 hr at room temp. the suspension was refluxed for 10 min, cooled, dissolved in water and extracted well with ether. The combined extracts were washed with water, 3 M HCl (until the wash was acidic and then twice more) and twice with water; the washes were back-extracted once with ether. The combined ether extracts were rewashed with HCl, water and $NaHCO_3$aq, dried over $MgSO_4$ and concentrated *in vacuo*, affording 4·32 g (98%) of colorless oil identified as **14**: PMR ($CDCl_3$) 4·53 (bs, width at half-height ~ 7 Hz), 5·85 (t, J = 9 Hz), 7·98 (s), 8·13 (bs, width at half-height ~ 5 Hz), 8·54 (s) and 8·79τ (d, J = 6 Hz); lit.[23] PMR 4·62 (bs, width at half-height ~ 7 Hz), 5·98 (t, J = 9·5 Hz), 8·04, 8·13 (bs, width at half-height 5 Hz), 8·57, and 8·85τ (d, J = 6 Hz).

The identification of the oil was further substantiated by hydrolysis to hydroxy olefin **15**. A soln of 0·93 g (3·2 mmol) of **14** and 0·67 g (10·1 mmol) KOH (85%, w/w) in 12 ml of water–MeOH (1/4, v/v) was refluxed for 6 hr. The soln was acidified with HCl, concentrated *in vacuo* and extracted three times with ether. The combined extracts were washed with $NaHCO_3$aq, water and NaClaq, dried over $MgSO_4$ and concentrated *in vacuo*. TLC analysis (silica gel, ether) showed complete conversion of **14** to a mixture (~1:1) of two major components, R_f, 0·47 and 0·26, respectively.

Since recrystallization of the oily residue (ethyl acetate–hexane) failed to separate the two products completely (TLC analysis), the combined mother liquor and crystals (0·67 g, total) were chromatographed over alumina using EtOAc–hexane (1/1, v/v). Three fractions containing the less polar product were combined and concentrated *in vacuo*, affording 0·18 g of a pale yellow oil. Rechromatography over silica gel using ether afforded pure oily **15**: $[\alpha]_D^{25}$ +26° (*c*, 2·0 in $CHCl_3$); IR ($CHCl_3$) 3580, 3480 and 1760 cm^{-1}; PMR ($CDCl_3$) 4·54 (bs, width at half-height ~ 6 Hz), 5·85 (t, J = 9 Hz), 8·17 (bs, width at half-height ~ 6 Hz), 8·79 (d, J = 6 Hz) and 8·87τ (s). The data are in excellent agreement with those reported[24] for the less polar product from the hydrolysis of **14** with t-BuOK.

Hydrogenation of **15** *and dehydration to* **16**. A soln of 32 mg (0·13 mmol) of **15** in 5 ml MeOH was hydrogenated over 32 mg of 5% Pd/C and 5 mg $NaHCO_3$ at room temp. and slightly over atmospheric pressure. After 18 hr GLC analysis of the mixture showed only two major components, rrt 5·04 and 6·16 (relative areas ~ 1:1). After an additional 2·4 hr the mixture was filtered through Celite and the solvent was removed *in vacuo*. The resulting 32 mg pale yellow oil was taken up in 2 ml dry pyridine and treated with 3 drops thionyl chloride at room temp. After 15 min the brownish soln was treated with 1 ml sat $NaHCO_3$aq and extracted with ether three times. The combined extracts were concentrated *in vacuo*, and the residual brown oil was taken up in chloroform, treated with Darko K-B and reconcentrated *in vacuo*, affording 22 mg of a pale yellow oil. GLC analysis showed major components at rrt 1·30, 1·00 and 0·92 (relative to photunolide). The second of these (relative area 22%) was purified by GLC, affording ~4 mg of a colorless oil (**16**) exhibiting IR and mass spectra identical with those of photunolide prepared by photolysis of **2**. A PMR spectrum of **16**, although weak, was also in excellent agreement with that of photunolide.

Photolysis of **2** *in deuterated solvents*. A soln of 8·6 mg dihydrocostunolide (0·037 mmol) in 0·5 ml benzene-d_6–isopropanol-d_8 (1:3, v/v) was irradiated in a manner similar to that described above for undeuterated solvents. The course of the reaction was followed by GLC; irradiation was interrupted after more than 50% of **2** had been converted. The major product, **16**, and a minor component of the mixture (*vide supra*) were isolated by preparative GLC and their mass spectra were measured and compared with those of samples previously obtained. The relative intensities of M^+ (*m/e* 234) and $(M+1)^+$ (*m/e* 235) for the products isolated from deuterated and undeuterated runs were the same. Also, each product had the same fragmentation regardless of which photolysis produced it.

REFERENCES

[1a] Preliminary report of this work was presented at the 10th Annual Midwest Regional Meeting of the ACS, Iowa City, Iowa, November, 1974; [b] taken in part from the Ph.D. Thesis of RFL, submitted to the Polytechnic Institute of New York, in partial fulfillment of the degree requirements. RFL wishes to acknowledge financial support received from the National Science Foundation (Graduate Traineeship Program) and from Pfizer, Inc., during part of the work covered by this report.

[2a] F. Šorm, *J. Agr. Food Chem.* **19**, 1081 (1971); [b] F. Šorm and L. Dolejš, *Guaianolides and Germacranolides*. Hermann, Paris (1965).

[3] J. K. Sutherland, *Tetrahedron* **30**, 1651 (1974).

[4] J. B. Hendrickson, *Ibid.* **7**, 82 (1959).

[5a] A. S. Rao, G. R. Kelkar and S. C. Bhattacharyya, *Chem. Ind.* 1359 (1958); [b] A. S. Rao, G. R. Kelkar and S. C. Bhattacharyya, *Tetrahedron* **9**, 275 (1960).

[6] K. Tori, I. Horibe, Y. Tamura and H. Tada, *Chem. Comm.* 620 (1973).

[7a] T. C. Jain and J. E. McCloskey, *Tetrahedron Letters* 2917 (1969), 1415 (1971); [b] T. C. Jain, C. M. Banks and J. E. McCloskey, *Ibid.* 2387 (1970).

[8a] V. Herout and F. Šorm, *Chem. Ind.* 1067 (1959); [b]T. C. Jain, C. M. Banks and J. E. McCloskey, *Experientia* **25**, 906 (1969).

[9] Reaction of **2** with mercuric acetate in aqueous THF afforded intermediate chloromercurial eudesmanolides, borohydride reduction of which gave 4α-hydroxy-, α-, β- and γ-cyclodihydrocostunolides; cf. Ref. 1*b*.

[10a] S. P. Pathak, B. V. Bapat and G. H. Kulkarni, *Ind. J. Chem.* **8**, 471 (1970); [b]M. Suchý, V. Herout and F. Šorm, *Colln. Czech. Chem. Comm.* **31**, 2899 (1966).

[11] T. C. Jain and J. E. McCloskey, *Tetrahedron Letters* 4525 (1969).

[12] R. W. Doskotch and F. S. El-Feraly, *J. Pharm. Sci.* **58**, 877 (1969).

[13] The closest connection which can be drawn between the *Magnoliaceae* and the *Compositae* is that both belong to the same subclass (Dicotyledoneae); L. Benson, *Plant Classification*. Heath, Boston (1957).

[14] A. Paul, A. S. Bawdekar, R. S. Joshi, G. H. Kulkarni, A. S. Rao, G. R. Kelkar and S. C. Bhattacharyya, *Perf. Ess. Oil Rec.* 115 (1960).

[15] T. Geissman, *Rec. Adv. Phytochem.* **6**, 65 (1973).

[16a] P. J. Kropp, *J. Am. Chem. Soc.* **88**, 4091 (1966); [b]J. A. Marshall and R. D. Carroll, *Ibid.* **88**, 4092 (1966); [c]J. A. Marshall, *Accts. Chem. Res.* **2**, 33 (1969).

[17] H. Yoshioka, T. J. Mabry and A. Higo, *J. Am. Chem. Soc.* **92**, 923 (1970). The stereochemistry of the guaianolide, lumidihydroisabelin, was assumed from examination of molecular models and assumption of intramolecular hydrogen transfer in a diradical intermediate. No proof was offered for these assumptions.

[18] The Me assignments are based in part on the changes in chemical shift as the solvent is changed from $CDCl_3$ (8·85 and 8·79τ) to benzene (8·82 and 9·01τ, respectively); C. R. Narayanan and N. K. Venkatasubramanian, *J. Org. Chem.* **33**, 3156 (1968). The triplet is slightly upfield from its position in lactones **8** and **11** (6·03 and 5·85τ, respectively) but is very close to that reported for **3**; S. B. Hiremath, G. H. Kularni, G. R. Kelkar and S. C. Bhattacharyya, *Tetrahedron* **21**, 3575 (1965).

[19] J. S. C. Liang, M. S. (Chem) Thesis, Polytechnic Institute of Brooklyn (June 1967).

[20] Hydrogenation of costus lactone or 3 over Pd/C afforded **8** as a minor product and **9** as the major product; V. J. Mancini, B. S. (Chem) Thesis, Polytechnic Institute of Brooklyn (June 1968).

[21] R. E. K. Winter, J. S. C. Liang, V. Mancini and R. Lindauer, 158th *ACS National Meeting*, New York, New York (Sept. 1969), AGFD, 050.

[22a] N. S. Bankar and G. H. Kulkarni, *Ind. J. Chem.* **10**, 952 (1972); [b]N. S. Bankar and G. H. Kulkarni, *Chem. Ind.* 481 (1973). It appears likely that the original structural assignment—M. Suchý, V. Herout and F. Šorm, *Colln. Czech. Chem. Comm.* **29**, 1829 (1964)—of the guai-1(10)-enolide resulting from hydrogenation of costus lactone was incorrect at C-4. The only dihydroisophotosantonic lactone acetate known at the time of the Czech work was the 4*S* epimer; cf. D. H. R. Barton, J. E. D. Levisalles and J. T. Pinhey, *J. Chem. Soc.* 3472 (1962).

[23] E. H. White, S. Eguchi and J. N. Marx, *Tetrahedron* **25**, 2099 (1969).

[24] J. N. Marx and E. H. White, *Ibid.*, **25**, 2117 (1969).

[25] J. K. Crandall and C. F. Mayer, *J. Am. Chem. Soc.* **89**, 4374 (1967).

[26] See for example references cited by H.-D. Scharf in *Fort. Chem. Forschung* **11**, 216 (1969).

[27] We thank Dr. E. Block and Mr. J. Upeslacis (Harvard University) for exact mass determinations.