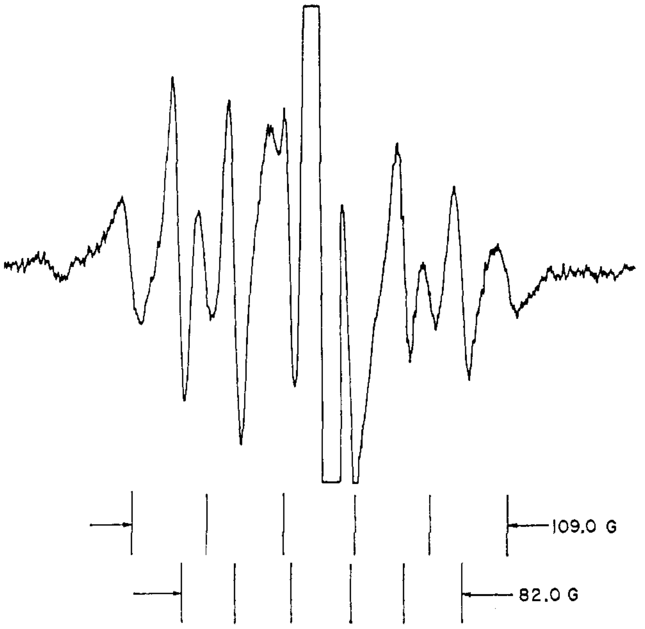

Figure 1. Esr spectrum of $C_6H_5(CH_3)_2COO$ cotaining ^{17}O enriched oxygen at −105°.

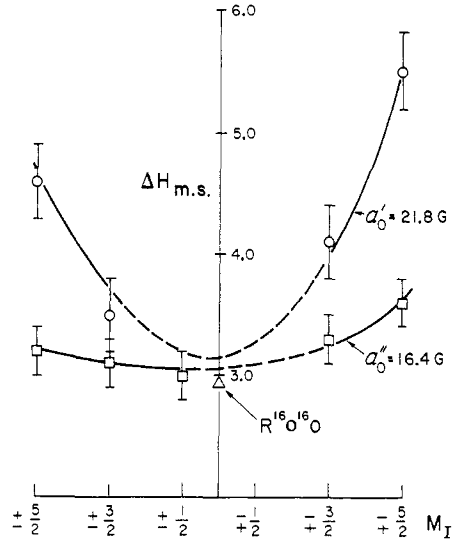

Figure 2. Variation in maximum slope line width across ^{17}O manifolds of esr spectrum of $C_6H_5(CH_3)COO$ at −105°.

$R^{17}O^{16}O$, having an ^{17}O hyperfine interaction of $|16.4|$ G. In addition, the ratio of the spin densities on the two oxygens is approximately 2:1, in favor of the terminal oxygen.

Doubly Substituted Species. Part of the spectrum due to $R^{17}O^{17}O$ could also be detected. The lowest field line and the highest field line of $R^{17}O^{17}O$ were 187 ± 1 G apart, compared to the expected separation of 191 G, calculated from the values of a_O' and a_O''. An attempt was also made to measure the relative intensities of individual lines due to the different isotopic species. The intensity in a line was assumed to be proportional to $l(\Delta H_{ms})^2$, where l is the amplitude of the derivative presentation and ΔH_{ms} the maximum slope width. The intensity ratio between lines of either singly ^{17}O substituted species and the outside lines due to $R^{17}O^{17}O$ was 6 ± 1, compared to the expected 6.8. However, the ratio between the intensity of the center line, due to $R^{16}O^{16}O$, and a line due to either singly substituted species was 11.5 ± 0.5, approximately twice the expected 6.8. The simplest explanation of this anomaly would appear to be that the $R^{16}O^{16}O$ line has a different shape from that of lines from the ^{17}O containing species, but it is difficult to understand why this should be the case.

Acknowledgment. The authors are grateful to Dr. R. W. Fessenden for helpful correspondence.

The Photochemistry of Isabelin

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Abstract: Irradiation of the germacranolide dilactone isabelin (**1**) at 253.7 nm in benzene afforded a single crystalline product resulting from a ($2\pi + 2\pi$) cycloaddition process. The product, photoisabelin (**3**), absorbed 1 mol of hydrogen to yield dihydrophotoisabelin (**5**), a substance also obtained as a minor product from the photolysis of dihydroisabelin (**4**). However, the major compound from the ultraviolet irradiation of dihydroisabelin was the ene photoproduct lumidihydroisabelin (**9**). Thermolysis of dihydrophotoisabelin (**5**) gave a mixture of two germacranolides, dihydroisabelin (**4**) and pyrodihydroisabelin (**7**).

Isabelin (**1**),[1] a new germacranolide dilactone from *Ambrosia psilostachya* DC. (Compositae), exists in solution at room temperature in a 10:7 ratio of two nmr-distinguishable conformers (Table I); on the basis of nmr data, the two conformers were assigned structures **1a** and **1b**: in the major conformer (**1a**) the double bonds are in a crossed orientation while in **1b** they have a parallel alignment.

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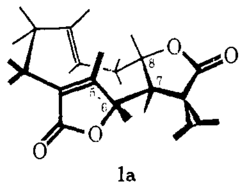
[1] (a) H. Yoshioka, T. J. Mabry, and H. E. Miller, *Chem. Commun.*, 1679 (1968); (b) H. Yoshioka and T. J. Mabry, *Tetrahedron*, **24**, 4767 (1969).

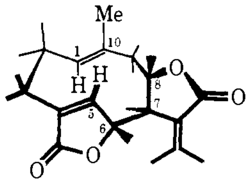
Table I. Nmr Data[a]

Compd	H_1	H_5	H_6	H_7	H_8	H_9	C_{10}-Me	C_{11}-Me	H_{12}	Other
1a	4.88 c	6.90 c	5.21 c	3.22 c	4.48 m		1.60 (d, 2)		5.88 (d, 3) 6.42	
1b	4.88 c	6.70 c	5.06 (d, 7, 2)		4.48 m		1.68 (d, 2)		6.14 (d, 3) 6.38	
3	3.02	2.78 (d, 10)	4.86 (t, 10)	2.81	3.89 (dq, 10, 10, 7)	1.82 (t, 10) 2.25 (dd, 10, 7)	1.52 s		5.89 (d, 3) 6.27	
4	4.88 c	6.92 c	5.04 c	3.08 c	4.40 m		1.61 (d, 2)	1.44 (d, 7)		
5		2.73 (d, 9)	4.74 (t, 9)		3.90 (dq, 10, 9, 7)		1.50 s	1.39 (d, 6)		
6[b]		2.83 (d, 9)	4.97 (t, 9)		4.05 (dq, 10, 9, 7)		1.54 s		3.42 s	7.35 (d, 10) 7.45 (d, 10)
7	5.28 c	6.98 c	5.06 c		4.08 m		1.80 c	1.41 (d, 6)		
8			4.72		4.72		0.87 (d, 6) 0.95 (d, 6)	1.28 (d, 6)		
9		3.16	4.63 (dd, 10, 8)	2.40	4.16 (dq, 10, 9, 5)	2.58 (dd, 12, 8) 2.98 (dd, 12, 8)		1.36 (d, 6)		5.03 c ($C_{10}{=}CH_2$)
10			4.60 (br, t, 10)		3.95 (br, t, 10)		1.12 (d, 6)	1.33 (d, 6)		
i		2.60 (d, 8)	4.65 (dd, 8, 3)				1.24 s			3.00 (piperidide) 3.50

[a] Spectra were determined in $CDCl_3$ on a Varian A-60 spectrometer unless otherwise noted. Chemical shifts are given in parts per million (δ scale). [b] Recorded in CF_3COOH.

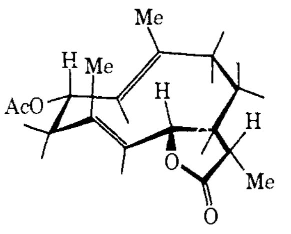


1a



1b

We previously observed that other germacranolides,[2,3] such as dihydrotamaulipin-A acetate (**2**), which is known from Nuclear Overhauser effect studies[4] to have a crossed orientation of the ring double bonds, readily equilibrate thermally at about 200° with their Cope rearrangement products. However, germacranolides of this type are recovered unchanged upon prolonged irradiation at 253.7 nm.[5]



2

The photolysis of isabelin appeared favorable since one of the double bonds in the cyclodecadiene ring of **1** is activated as a result of being conjugated to a lactone function. Both conformers have general geometrical features required for a $(2\pi + 2\pi)$ cycloaddition;[6] however, molecular models indicate that such a reaction is structurally inhibited for conformer **1a**.

In addition to describing our photolytic studies of isabelin, this paper presents the results from the photolysis of dihydroisabelin (**4**); the latter substance, unlike isabelin, exists in solution as a single conformer which is inferred to have a crossed orientation of the carbocyclic ring double bonds. We also report the thermolysis of dihydrophotoisabelin.

Results and Discussion

Photolysis of Isabelin.[7] A benzene solution of isabelin (C, 0.07%) was irradiated at 253.7 nm for 100 min. During the course of the reaction, aliquots were periodically removed from the reaction vessel and upon evaporation of the solvent the residue was analyzed by nmr and tlc. The nmr data indicated that a product was being formed at the expense of isabelin; the ratio of **1a** and **1b** remained constant throughout the reaction due to rapid equilibrium[1] between the conformers. The reaction was followed by observing the increase in the intensity of the nmr signal for the methyl group in the photoproduct at δ 1.52 and the simultaneous decrease in the intensity of the signals for the vinyl methyl groups

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(2) N. H. Fischer, T. J. Mabry, and H. B. Kagan, *Tetrahedron*, **24**, 4091 (1968).

(3) N. H. Fischer and T. J. Mabry, *Chem. Commun.*, 1235 (1967).

(4) N. S. Bhacca and N. H. Fischer, *ibid.*, 68 (1969).

(5) T. H. Porter and T. J. Mabry, unpublished results.

(6) (a) R. Hoffmann and R. B. Woodward, *Accounts Chem. Res.*, **1**, 17 (1968); (b) R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, **87**, 2511 (1965).

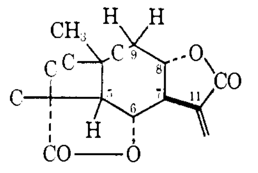
(7) No products could be obtained from the thermolysis of isabelin since it polymerizes at temperatures above 100°.

of the two conformers (δ 1.60, doublet, J = 2 Hz for **1a**; δ 1.70, doublet, J = 2 Hz for **1b**).

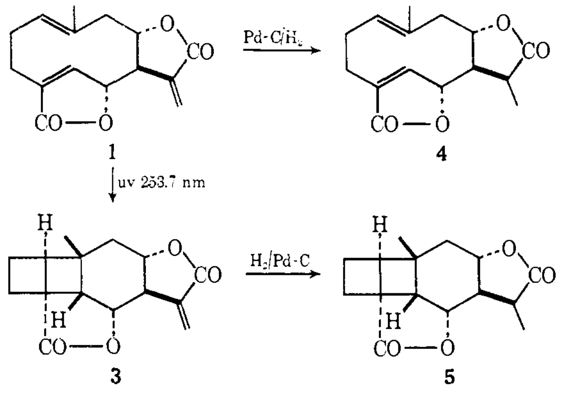
The spectral properties of photoisabelin ($C_{15}H_{16}O_4$; mp 167–167.5°) clearly indicated that the α,β-unsaturated γ-lactone ring of isabelin was still present but that the conjugated double bond of the other γ-lactone function had disappeared. The ultraviolet absorption spectrum of **3** [λ_{max} 209 nm (ϵ 10,000)] and a strong infrared band at 1750 cm^{-1} were suggestive of the presence of an α,β-unsaturated γ-lactone ring. The nmr data were even more instructive: two one-proton doublets (J = 3 Hz) at δ 5.89 and 6.27 in the nmr spectrum of **3** are typical for the two methylene protons of a C-11 exocyclic double bond. The only other downfield signals in the nmr spectrum of **3** could be assigned to the lactonic protons at C-6 [δ 4.86, triplet (dd), J = 10 Hz] and C-8 (δ 3.89, sextet); therefore, it was evident that the double bonds in the ten-membered carbocyclic ring of isabelin were not present in **3**. Moreover, **3** absorbed only 1 mol of hydrogen during exhaustive catalytic hydrogenation.

Nmr spin-decoupling experiments provided a partial structure for photoisabelin. Irradiation at δ 2.81 (the region of the nmr spectrum where H-7 is expected to absorb) collapsed the doublets for the two C-11 exocyclic methylene protons into singlets and, at the same time, simplified the complex pattern for H-8 at δ 3.89 and converted the triplet (dd) at 4.86 for H-6 into a doublet. Irradiation of the latter signal transformed the H-5 doublet at δ 2.78 (J = 10 Hz) into a singlet. This latter result suggested that H-5 had no neighbor protons other than the one at C-6. Finally, the sharp three-proton singlet at δ 1.52 suggested that photoisabelin contained a tertiary methyl group.

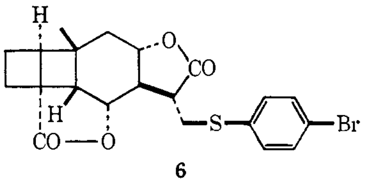
The above data suggested that photoisabelin contained a single proton at C-5, -6, and -7 as in partial structure C. Moreover, the complexity of the signal for H-8 even after spin decoupling the interaction with H-7 was in accord with the presence of two protons at C-9. Partial structure C also accounted for a tertiary methyl group and for H-5 having only one neighbor proton.



C



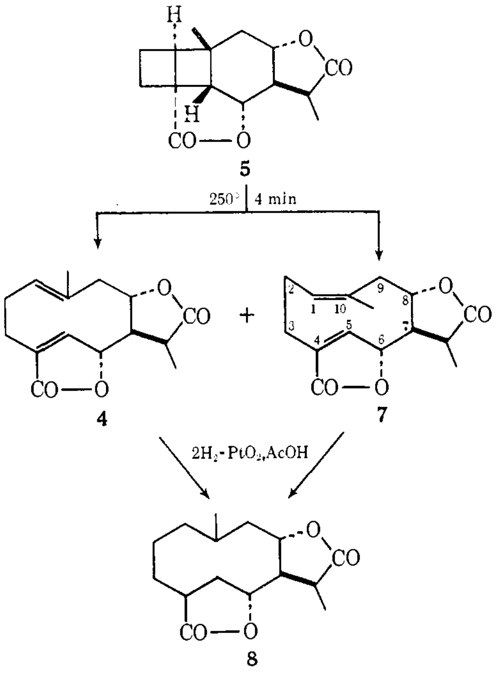
Part structure C immediately suggested structure **3** for photoisabelin, readily derived from a photolytic ($2\pi + 2\pi$) cycloaddition of conformer **1b**. Further support for this structure was obtained by extensive spin-decoupling experiments. The structure assignments for the thermally induced products from dihydrophotoisabelin[8] also were in accord with this structure assignment (see following section). Final proof that photoisabelin could be represented by **3** was provided by X-ray crystallographic analysis of a bromo derivative. The derivative, 11,12-dihydro-12-p-bromophenylthiophotoisabelin, was shown by the heavy atom method to have structure **6**.[9]



6

Thermolysis of Dihydrophotoisabelin. When dihydrophotoisabelin (**5**) was heated at 250° for 4 min, a new compound designated as pyrodihydroisabelin was isolated in 64% yield. In addition, the reaction also produced the known germacranolide dihydroisabelin (**4**) in 18% yield. Catalytic hydrogenation of both pyrodihydroisabelin, to which we ultimately assigned structure **7**, and dihydroisabelin gave hexahydroisabelin (**8**). Therefore, **7** must have not only the skeletal features of **4** but the same stereochemistry at C-6, -7, and -8 as well. These data indicated that **4** and **7** differed only in regard to the ring double bonds.

The ultraviolet spectrum (λ_{max} 218 nm, ϵ 7350) of pyrodihydroisabelin indicated the presence of an α,β-unsaturated γ-lactone ring of the type found in **4**. Fur-



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(8) It was necessary to investigate the thermolysis of dihydrophotoisabelin since the pyrolysis of photoisabelin leads to polymerized materials in accord with the known thermal instability of most germacranolides containing, in addition to the cyclodeca-1,5-diene system, an α,β'-saturated γ-lactone ring.

(9) We thank Dr. M. K. Wood and his research supervisor, Dr. S. H. Simonsen, for this analysis: M. K. Wood, Ph.D. dissertation, The University of Texas at Austin, 1969.

ther support for this conclusion was provided by the nmr spectrum of **7**: a conjugated olefinic proton signal at δ 6.98 could be ascribed to H-5 since spin-decoupling experiments showed that this signal was coupled to the H-6 signal at δ 5.06.

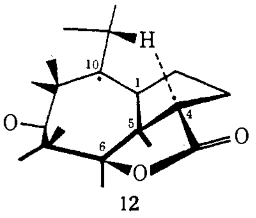
The nmr data also indicated that **7** like **4** contained a double bond between C-1 and C-10: in the nmr spectrum of **7**, H-1 appeared as a broad triplet at δ 5.2 and spin decoupling established that it was coupled to the vinyl methyl group at δ 1.8. Furthermore, the presence of two protons at C-9 in **7** was evident from the complexity of the nmr signal for the lactonic proton at C-8 even after decoupling the interaction between H-7 and H-8.

Therefore **4** and **7** differ only in the configuration about the C_1–C_{10} double bond; since **4** is known to be *trans*, **7** must be the *cis* isomer. The thermal opening of **5** to give **7** is a symmetry allowed thermal process while the formation of **4** from **5** is not symmetry allowed by a concerted thermal process. However, **4** does appear to be thermally induced product from **5** since the other product, **7**, was recovered unchanged when heated at 250°.

Photolysis of Dihydroisabelin. Dihydroisabelin (**4**) unlike isabelin exists in solution as a single conformer. Molecular models of **4** clearly indicate that the 11,12-saturated γ-lactone ring is twisted; this result requires that the cyclodecadiene ring of **4** exist in a conformation with a crossed orientation of the carbocyclic double bonds. Irradiation of **4** for 3 hr under the same conditions used for isabelin afforded two products in a 3:1 ratio. The minor substance (7% yield) was identical with dihydrophotoisabelin (**5**), while the major product appeared to be new and was designated lumidihydroisabelin.

We assign structure **9** to lumidihydroisabelin ($C_{15}H_{18}O_4$, mp 160°) on the basis of the following evidence. The guaianolide nature of **9** was established by the conversion of **9** to guaiazulene (**11**). Nmr data for **9** and its dihydro derivative (**10**) were consistent with the presence of an exocyclic double bond at C-10. A complex signal for two olefinic protons (δ 5.03) disappeared and a new secondary methyl group signal (δ 1.12 doublet, J = 6 Hz) appeared upon hydrogenation of **9** to form **10**. Moreover, nmr spin decoupling experiments for **9** located signals for two C-9 allylic protons at δ 2.58 and 2.98; the C-9 protons were shown to be coupled to both the C-8 lactonic proton (δ 4.10) and the methylene protons (δ 5.03) in the group attached at C-10. The stereochemistry in **9** at C-6, -7, and -8 is assumed to be the same as in the starting material **4**.

Formation of **9** appears to represent a rearrangement whereby a proton migrates from the C-10 methyl group of **4** to C-4. Assuming that the hydrogen atom transfer is intramolecular and proceeds through the diradical **12**, molecular models define the stereochemistry at C-1, -4, and -5 in the product, lumidihydroisabelin, to be as shown in formula **9**. The formation of **9** from **4** represents formally a photochemical ene reaction.



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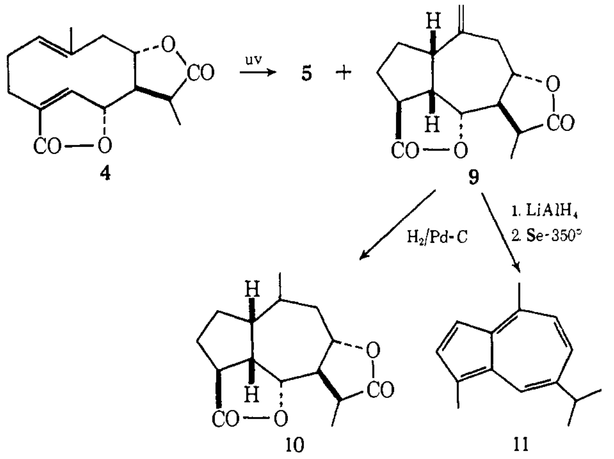
The combined photolytic results for isabelin and dihydroisabelin establish that the nature of the photoproducts for such systems is controlled in part by the conformation of the cyclodecadiene ring.



Experimental Section[10]

General. All photolytic reactions were carried out using a Rayonet reactor, Model PRP-100, equipped with ultraviolet lamps (35 W; wavelength 253.7 nm) and a quartz reactor vessel (50.8 mm internal diameter, 33 cm length).

Photoisabelin (3). A solution of 300 mg of isabelin (**1**) in 450 ml of benzene was preflushed by bubbling a stream of nitrogen through the solution for 2 hr. The solution was then irradiated at 35° under nitrogen for 100 min. The residue (0.3 g) obtained upon evaporation of the solvent was chromatographed over a column of silica gel (30 g, packed in benzene). Elution of the column with benzene–ethyl acetate (4:1) afforded 0.25 g of crude crystalline material. Trituration of the material with ether–ethanol (1:1) afforded 125 mg (41.5% yield) of **3**. Recrystallization of this sample from ethyl acetate gave **3**: mp 167–167.5°; mol wt 260 (mass spectrum); $\lambda_{\max}^{\mathrm{EtOH}}$ 207 nm (ϵ 10,000); $\nu_{\max}^{\mathrm{CHCl_3}}$ 1750 cm^{-1} (lactones).

Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20; O, 24.59. Found: C, 69.27; H, 6.26; O, 24.78.

Dihydrophotoisabelin (5) from 3. A solution of 62 mg of **3** in 20 ml of ethyl acetate–ethanol (1:1) was hydrogenated in the presence of 12 mg of 5% Pd–C. After uptake of 5 ml of hydrogen in 5 min no further reaction occurred. After the catalysts were removed by filtration, the solvent was evaporated leaving colorless crystals (60 mg). Recrystallization from 95% ethanol gave **5** as needles: mp 187–188°; mol wt 262 (mass spectrum); $\lambda_{\max}^{\mathrm{EtOH}}$ 205 nm (ϵ 550); $\nu_{\max}^{\mathrm{Nujol}}$ 1770 and 1747 cm^{-1} (lactones).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.65; H, 6.87; O, 24.40. Found: C, 68.63; H, 6.88; O, 24.57;

Dihydroisabelin (4) and Pyrodihydroisabelin (7) from 5. A 100-mg sample of **5** was placed in a Pyrex glass tube (8 mm diameter) and heated at 250° in a nitrogen atmosphere for 4 min. The product was preparatively chromatographed on silica gel G plates [chloroform–ether (1:1)]. A band (R_f 0.33) yielded crystals (20 mg, 18% yield) that were identical with **4** in all respects.

Another band (R_f 0.43) gave **7** (70 mg, 64% yield). Recrystallization from ethyl acetate afforded **7**: mp 183.5–184°; mol wt 262 (mass spectrum); $\lambda_{\max}^{\mathrm{EtOH}}$ 218 nm (ϵ 7350); $\nu_{\max}^{\mathrm{CHCl_3}}$ 1748 (lactones) and 858 cm^{-1} (>C=CH–).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.65; H, 6.87; O, 24.40. Found: C, 68.60; H, 6.74; O, 24.27.

Hexahydroisabelin (8) from 7 and 4. A solution of 60 mg of **7** in 10 ml of glacial acetic acid was exhaustively hydrogenated in the presence of PtO_2 (25 mg). After filtration of the catalyst and evaporation of the solvent, colorless crystals were obtained. Recrystallization from ethanol (1 ml) afforded **8** (22 mg), mp 173–175°. The material was identical by melting point, mixture melting point,

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[10] Melting points are uncorrected. Analyses were determined by Dr. Alfred Bernhardt. Mikroanalytisches Laboratorium, Elbach über Engelskirchen, West Germany.

and nmr with the hexahydroisabelin sample obtained by hydrogenation of **4**.

11,12-Dihydro-12-*p*-bromophenylthiophotoisabelin (6). To a solution of 140 mg of **3** and 350 mg of *p*-bromobenzenthiol in 3.5 ml of benzene was added 2 drops[11] of piperidine. After heat evolution, fine needles precipitated. The crystals were filtered and washed with benzene. Recrystallization from acetonitrile afforded **6** as small plates:[12] mp 182–183°; $\nu_{\max}^{\text{Nujol}}$ 1775, 1735 (lactones) and 812 cm^{-1} (two vicinal protons on the benzene ring).

Anal. Calcd for $C_{21}H_{21}O_4BrS$: C, 56.15; H, 4.68; O, 14.25; Br, 17.80; S, 7.15. Found: C, 56.10; H, 4.82; O, 14.28; Br, 17.77; S, 7.05.

Lumidihydroisabelin (9) and Dihydrophotoisabelin (5) from 4. A solution of 300 mg of **4** in 500 ml of benzene was irradiated at 35° for 3 hr. Evaporation of the solvent gave a yellow syrup which was chromatographed over silica gel (30 g. packed with benzene). The column, when eluted with benzene-acetone (9:1), afforded 150 mg of partially crystalline material. The material separated into two bands when preparatively chromatographed on thick layer silica gel G plates which were developed three times with chloroform-ether (2:1). The band of larger R_f value yielded **5** (20 mg). The other band gave **9** (65 mg) (mp 159–160° from ethanol-diisopropyl ether): mol wt 262 (mass spectrum): $\lambda_{\max}^{\text{EtOH}}$ 204 nm (ϵ 740); $\nu_{\max}^{\text{CHCl}_3}$ 1750 (lactones) and 1610 cm^{-1} (C=C).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.65; H, 6.87; O, 24.40. Found: C, 68.56; H, 6.75; O, 24.28.

Dihydrolumidihydroisabelin (10). A solution of 18 mg of **9** in 10 ml of glacial acetic acid was hydrogenated in the presence of 3 mg of PtO_2 as catalyst. Hydrogenation was complete in 20 min after uptake of 2.5 ml of hydrogen. The catalyst was removed by filtration and the filtrate was concentrated to dryness *in vacuo*. Recrystallization from benzene gave **10** (10 mg), mp 154–156°, mol wt 264 (mass spectrum).

Guaiazulene (11) from 9. A solution of 30 mg of **9** in 1 ml of anhydrous tetrahydrofuran was mixed with a solution of lithium aluminum hydride (30 mg) in anhydrous ether (10 ml). After 30 min 1 ml of water and then 2 ml of 5% sulfuric acid were added. The ether layer afforded a glass, $\nu_{\max}^{\text{neat}}$ 3330 cm^{-1} (no carbonyl bands). A solution of the glassy material in 2 ml of chloroform was mixed with selenium powder (600 mg) in a test tube. The mixture was shaken until the solvent had been removed with a stream of nitrogen, then the residue was covered with additional selenium powder (500 mg). The upper and middle walls of the test tube were packed with glass wool. Then, the tube was placed in a bath preheated to 350° and the temperature was raised to 390° within 4 min. The tube was removed and rapidly cooled. The deep blue liquid in the tube was extracted with ether and upon chromatography (R_f 0.67; silica gel G; petroleum ether) yielded a bright blue compound which corresponded by R_f value and uv spectrum (in EtOH between 780 and 210 nm) with authentic guaiazulene (**11**).

Acknowledgment. We thank the Robert A. Welch Foundation (Grant F-130) and the National Science Foundation (Grant GB 5548X) for financial support. The authors thank Drs. Michael Thomas, N. H. Fischer, and Stephen Monti; Professors Hans Schmid and André Dreiding, and Mr. Mike Kobal for helpful discussions.

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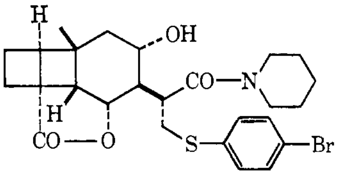
(11) If 20 to 40 drops of piperidine were added, a piperidide (i) was formed. The piperidide was converted to **6** when boiled in acetic anhydride for 1 hr.



i

(12) Seeding of the small plates into a hot solution of 100 mg of **7** in 2 ml of acetonitrile gave large plates. which were submitted for X-ray crystallographic analysis.[9]