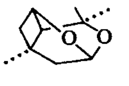
Synthesis of (±)-lineatin by the photochemical cycloaddition of allene to anhydromevalonolactone

William R. McKay, Jim Ounsworth, Phaik-Eng Sum, and Larry Weiler[1]
Department of Chemistry, University of British Columbia, Vancouver, B.C., Canada V6T 1Y6

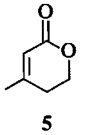
Received October 14, 1981

William R. McKay, Jim Ounsworth, Phaik-Eng Sum, and Larry Weiler. Can. J. Chem. **60**, 872 (1982).

(±)-Lineatin (**1**), the aggregation pheromone of an ambrosia beetle, was synthesized in five steps from anhydromevalonolactone (**5**) in 10% overall yield. The key step in the synthesis was a photochemical cycloaddition of **5** and allene. This photolysis produced two regioisomers (ca. 3:2) and efforts to improve the regioselectivity by varying the photolysis conditions or substituents on the allene were unsuccessful.



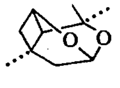
1



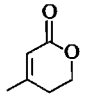
5

William R. McKay, Jim Ounsworth, Phaik-Eng Sum et Larry Weiler. Can. J. Chem. **60**, 872 (1982).

Nous avons préparé la ±-linéatine (**1**), la phéromone d'aggrégation d'une abeille de type Ambrosia, en réalisant une synthèse en 5 étapes à partir de l'anhydromévalonolactone (**5**) avec un rendement global de 10%. L'addition photochimique du composé **5** sur une allène est l'étape principale de cette synthèse. Cette photolyse conduit à deux régioisomères (environ 3:2) et nous avons vainement tenté d'améliorer la régiosélectivité en changeant les conditions d'hydrolyse ou en faisant varier les substituants sur l'allène.



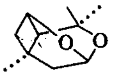
1



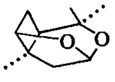
5

[Traduit par le journal]

Female ambrosia beetles, *Trypodendron lineatum*, produce an attractant aggregation pheromone while boring into fallen timber and cut lumber. The active pheromone, called lineatin, was isolated from frass and its structure was proposed to be **1** or **2** (1). Subsequently, Borden *et al.* reported three very low yielding syntheses of the pheromone which allowed them to demonstrate that lineatin in fact has structure **1** (2). Recently, Slessor *et al.* (3) and Mori and Sasaki (4) have reported more efficient syntheses of **1** and both groups have been able to resolve one of their synthetic intermediates to provide the optically active pheromone. In this paper we report a short synthetic route to lineatin (**1**) and offer some observations on the photochemical addition of allenes to α,β-unsaturated lactones.



1



2

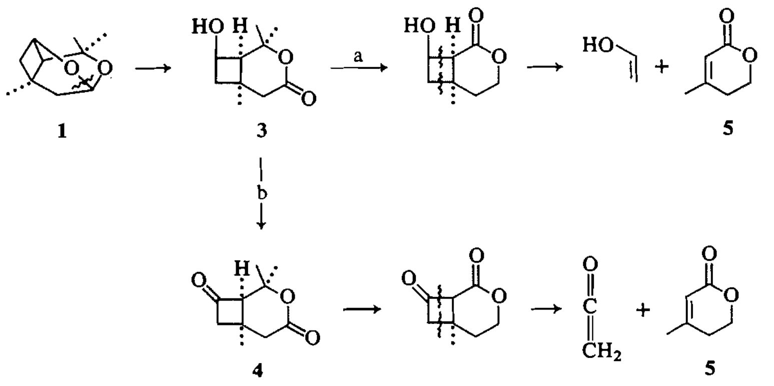
A major challenge in the synthesis of **1** is the construction of the unusual tricyclic acetal skeleton. Our retrosynthetic analysis of this problem is shown in Scheme 1. The critical point in the synthesis of an intermediate such as **3** appeared to be the construction of a cyclobutane with the correct regio- and stereochemistry. We also considered the cyclobutanone **4** derived by oxidation of **3** as a potential synthetic intermediate, since it was expected that reduction of the ketone in **4** should occur preferentially from the *exo* face to yield **3**. This route would only require a regioselective cyclobutanone formation. Finally we sought a synthetic route starting from anhydromevalonolactone (**5**) because of its ready availability (see below).

A convenient method to construct cyclobutane rings employs a [2 + 2] cycloaddition. Although ketenes can be added to trisubstituted olefins, they are not known to add to electron deficient olefins (5) such as **5**. Therefore we chose to investigate a photochemical [2 + 2] reaction of **5** and an appropriate alkene to generate the desired cyclobutane. Photolysis of lactone **5** and ethylene gave the cycloadduct **6** in 70% yield (eq. [1]) (6). Indeed a number of alkenes undergo a photochemical [2 + 2] cycloaddition to α,β-unsaturated lactones (6*b*).

---

[1] Author to whom correspondence may be addressed.

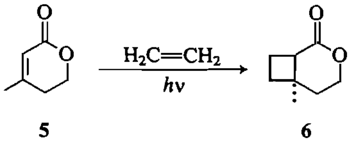
0008-4042/82/070872-09$01.00/0



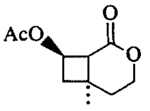
SCHEME 1. Possible retrosynthetic analyses for lineatin (1)

Unfortunately there are very few reports on the cycloaddition of heteroatom substituted alkenes to conjugated lactones. The photolysis of **5** and vinyl acetate gave only 4% of the adduct **7** (2). For these reasons, we considered the cycloaddition of allene and **5** as the key step in the synthetic plan.

[1]

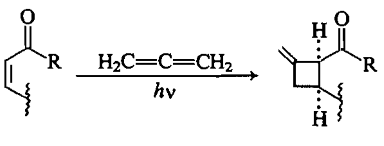


There are a number of examples of the photochemical [2 + 2] cycloaddition of allene to α,β-unsaturated ketones and aldehydes (7). In all cases the methylenecyclobutane produced has the *cis* stereochemistry for cyclic olefinic starting materials, and in almost all cases the regioselectivity is that shown in eq. [2] (7). This is precisely the stereochemistry we would require to synthesize a cyclobutanone such as **4** from lactone **5**. Before the initiation of this work we were not aware of any photochemical addition of allene or its derivatives to an α,β-unsaturated lactone. During the course of our work Baker *et al.* reported an intramolecular photolysis of a substituted allene and a lactone (8) (see below).



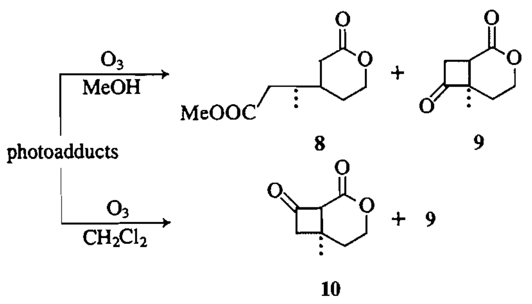
7

[2]



Anhydromevalonolactone (**5**) was conveniently synthesized from methyl vinyl ketone (6*b*, 9, 10). This procedure involves the dehydration of mevalonolactone by distillation from potassium bisulfate (6*b*). Usually the crude dehydration product was a mixture of α,β- and β,γ-unsaturated lactones. This mixture could be isomerized to the α,β-isomer **5** by redistillation from potassium bisulfate or more conveniently by a $RhCl_3$ catalyzed isomerization (11).

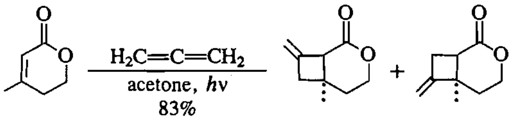
Irradiation (Vycor filter) of an acetone solution of lactone **5** and allene gave a mixture of 1:1 cycloaddition products in approximately 80% yield. The photolysis products could not be separated by thin layer or column chromatography. However, two components in the mixture were barely separable by capillary column gas chromatography. The ratio of the two products was ca. 3:2. In addition, the 270 MHz ^1H nmr spectrum of the photolysis product had two methyl singlets at δ 1.26 and 1.24 (relative intensity ca. 3:2). The photoadducts were not epimerized by base, thus each contained a *cis* fused cyclobutane. The structures of the photoadducts were determined from the following two ozonolysis experiments. First, ozonolysis of the photolysis mixture in methanol gave **8** and **9**; the ester **8** was the major product. Ozonolysis of the photolysis mixture in dichloromethane gave the cyclobutanones **9** and **10**. The



cyclobutanone **10**, although difficult to purify, was the major compound.

The results from the ozonolysis experiments and the failure of base to epimerize the adducts prove that the major photolysis product is the desired methylenecyclobutane **11** but a substantial amount of the isomeric methylenecyclobutane **12** is produced in the photolysis (eq. [3]). The low selectivity surprised us in view of the wealth of examples demonstrating the regioselective addition of allene to a variety of α,β-unsaturated ketones and aldehydes (7). It was clear that our photolysis conditions were different from those for enone additions, hence the photolysis in eq. [3] may be occurring by a different mechanism than the enone examples (eq. [2]). For example, the enone photolyses are usually carried out in ether or hydrocarbon solvents with a Pyrex filter (7). Presumably the enone is excited by direct irradiation and the reaction may proceed through the π,π* triplet (12). In the photolysis of lactone **5** (eq. [3]) the acetone is acting as a triplet sensitizer. Because the π,π* triplet of an α,β-unsaturated ester is of higher energy than the *n*,π* triplet (13) it may be that the lactone photolysis involves the *n*,π* triplet. A second possibility is that both types of photolysis reactions involve the same triplet but that the oxygen of the lactone changes the shape of the frontier orbitals involved and thus the regioselectivity of attack.

[3]

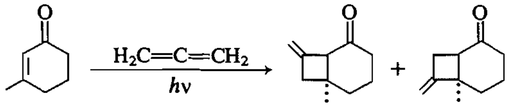


5 **11** **12**

3:2

However, before these arguments are taken too far we should note that the photochemical cycloaddition of allene to 3-methylcyclohexenone gives a 4:1 mixture of regioisomers (eq. [4]) (14). In addition, Baker *et al.* have recently reported an intramolecular photolysis of an allenic α,β-unsaturated lactone to give two regioisomeric products (eq. [5]) (8). However, photolysis of the allenic enone in eq. [6] is highly regioselective (15). Thus the factors controlling the regioselectivity in these reactions are very subtle.

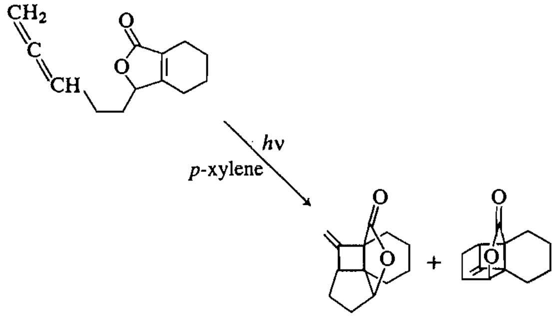
[4]



4:1

The summary of several experiments which were carried out in an effort to improve the regioselectivity in the photolysis (eq. [3]) is given in Table 1. The ratio of the regioisomers **11**:**12** was determined by 270 MHz ^1H nmr. The tertiary methyl group in these isomers has a resonance at δ 1.26 and 1.24 respectively. First we note that the ratio of **11**:**12** did not change significantly with temperature (runs 1 and 2) or using xanthone as a triplet sensitizer (run 3). Finally in runs 4–6 the polarity of the solvent was varied. In dichloromethane and dichloroethane solvents the regioselectivity was essentially the same as in pure acetone. However in methanol solvent (run 4) the regioselectivity did change but in the wrong direction. In addition the total yield of photoadducts was substantially lower in methanol (run 4). We were unable to improve the regioselectivity in eq. [3] by altering the photolysis conditions.

[5]



2.5:1

[6]

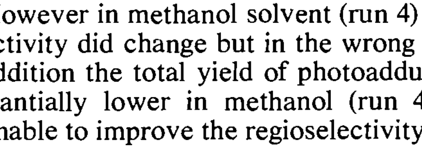
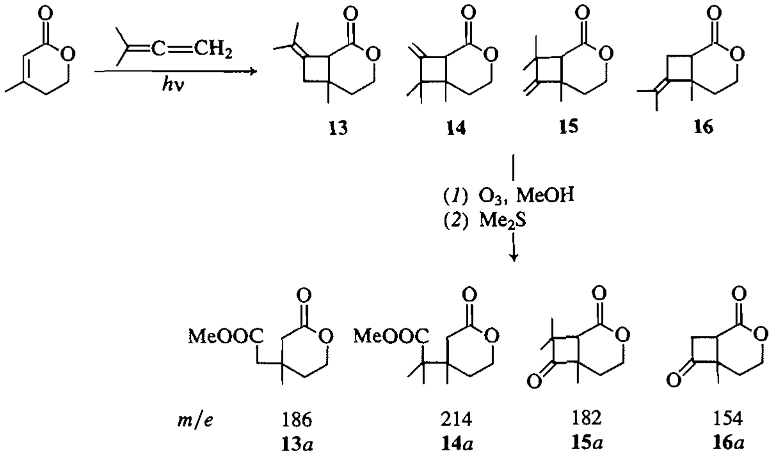


TABLE 1. Photolysis of lactone **5** and allene

Run	Solvent	Sensitizer	Temperature (°C)	Yield (%)[a]	**11**:**12**[c]
1	Acetone		25	82	5:3
2	Acetone		−78	83[b]	3:2
3	Dichloromethane	0.07% Xanthone	−78	60	4:3
4	Methanol	10% Acetone	−78	27	2:3
5	Dichloroethane	20% Acetone	−78	100[b]	3:2
6	Dichloromethane	10% Acetone	−35	74	3:2

[a] Yields are for chromatographed product except where noted.
[b] Crude yield.
[c] Ratios were determined by nmr.

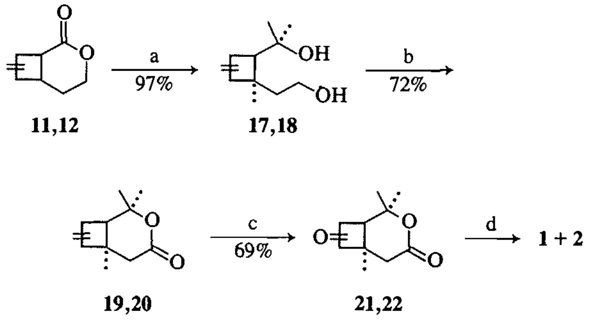


[7]

Then we turned to a study of the photochemical [2 + 2] cycloaddition of substituted allenes to lactone **5**. Since our synthetic plan involved eventual oxidative cleavage of the exocyclic double bond in the methylenecyclobutane, if the exocyclic carbon bore a substituent it would be lost in such a reaction. Phenylallene and 3,3-diphenylallene polymerized when photolyzed in acetone solutions of **5**. At −78°C, 3,3-dimethylallene did not undergo a photochemical addition to the conjugated lactone **5** in acetone. However, at 0°C a photochemical cycloaddition did occur to produce the adducts **13–15** (eq. [7]). The structures of these adducts were determined by ozonolysis of the photolysis mixture in methanol and gas chromatography – mass spectroscopic analysis of the products.

The mixture of photoadducts was ozonized as above and the mixture of products obtained was separated into three peaks by gc and these peaks had parent ions at *m/e* 186, 214, and 182. We could not detect any gc fraction with *m/e* 154 in the mixture. The ratio of the three components (by gc) in the ozonolysis mixture was **13***a*:**14***a*:**15***a* = 16:24:51. The product from the desired isomer **13** was the minor one. All of our efforts to control the regioselectivity in the photochemical cycloaddition were thwarted.

Since the adducts **11** and **12** could not be easily separated we continued the synthesis with the mixture of isomers as follows. On treatment with excess methyllithium, **11** and **12** gave the diols **17** and **18** in almost quantitative yield. These diols were oxidized (16) to the lactones **19** and **20** in 70–75% yield, which were then ozonized to give the keto lactones **21** and **22** in ca. 70% yield. Diisobutylaluminum hydride reduction of **21** and **22** followed by an acid work-up gave a mixture of (±)-lineatin (**1**) and its isomer **2** in a crude yield of 95%. The crude product could be distilled at 110°C/20 Torr. It has been shown that the isomer **2** has no biological activity (17) and the mixture of **1** and **2** is attractive to *T. lineatum* in field trapping studies.[2] In addition, these two products, **1** and **2**, were readily separated by column chromatography; however, their high volatility led to significant loss of material. Nonetheless, pure (±)-lineatin (**1**) could be isolated in 23% yield and the isomer **2** in 13.5% yield.



(a) MeLi, Et$_2$O, 0°C; (b) CrO$_3$·2py, CH$_2$Cl$_2$;
(c) O$_3$, CH$_2$Cl$_2$, −78°C, then Me$_2$S, −78°C → 25°C; (d) DIBAL, then H$^+$

SCHEME 2. Synthesis of (±)-lineatin (**1**)

It is clear from the earlier structural (1) and synthetic studies (3, 4) on lineatin that the 100 MHz ^{1}H nmr spectral data was not sufficient evidence to differentiate structures **1** and **2**. Experiments with nmr shift reagents were also inconclusive (1). The 270 MHz ^{1}H nmr spectra of **1** and **2** are sufficiently resolved (Figs. 1 and 2) that decoupling experiments can be carried out and an essentially complete assignment of the ^{1}H nmr spectra of **1** and **2** obtained (Table 2). A summary of the coupling constants obtained from the decoupling experiments is given in Table 3. The chemical shifts in lineatin (Table 2) are within the range of values

---

[2] J. A. McLean and T. Shore. Unpublished results, 1979.

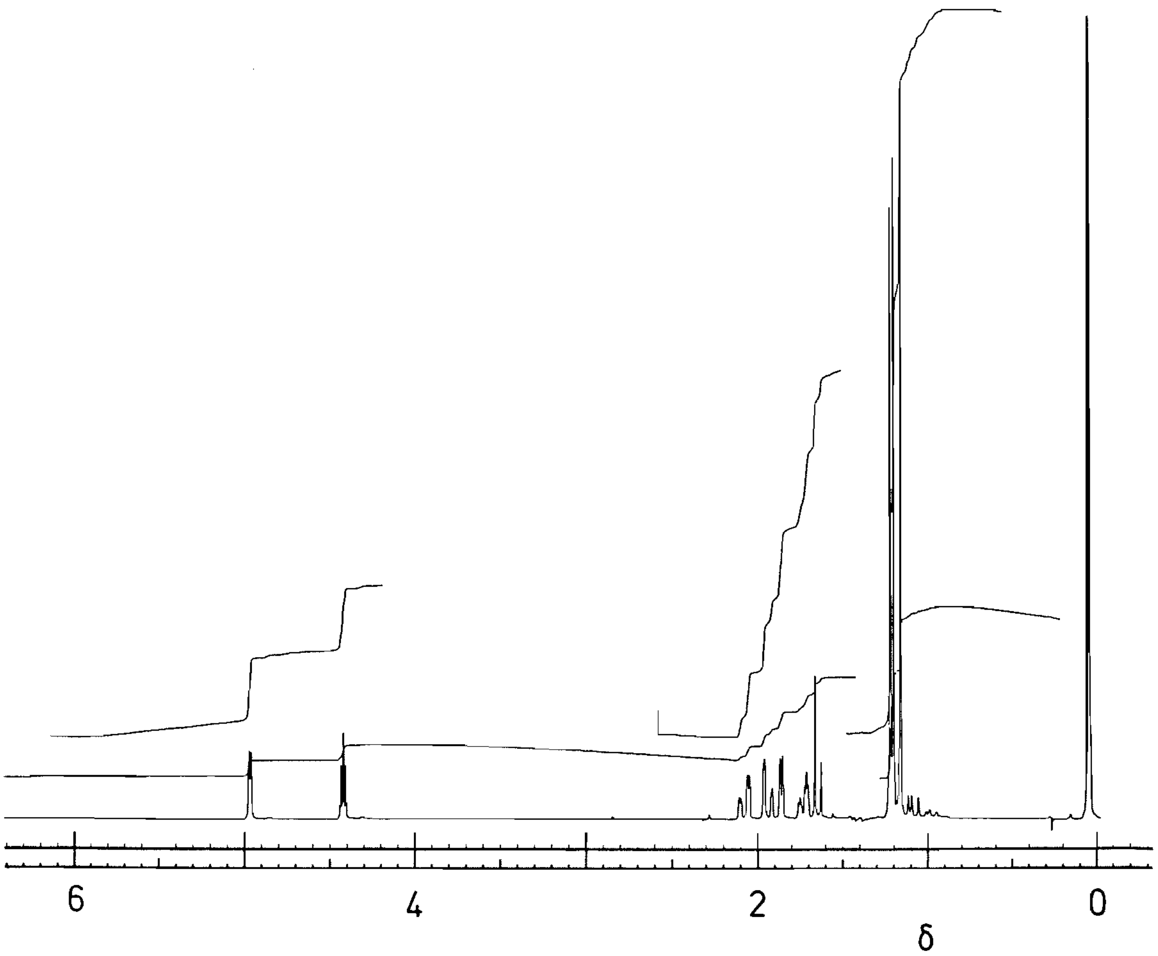
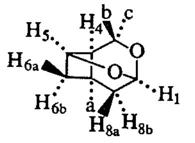
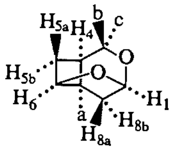


FIG. 1. 270 MHz ^{1}H nmr spectrum of lineatin (1).

found in model systems. On the other hand there are some unusual shifts in the isomer **2** (Table 2). First δ_{5a} is rather low for a cyclobutyl methylene hydrogen. Models indicate that **2** adopts a conformation in which H_{5a} and methyl(b) are forced rather close together. Thus we would suggest that the low chemical shift of H_{5a} in **2** is due to a van der Waals deshielding (18) of H_{5a} by the methyl(b). Incidentally we use this same argument to assign the lowest-field methyl singlet to b. The second unusual chemical shift in **2** is the very high field resonance of H_{8a} which may be due to a shielding effect of 0–9 (See ref. 18, p. 80).



1



2

TABLE 2. 270 MHz ^{1}H nmr chemical shift assignments of **1** and **2**[a,c]

Lineatin (1)		Isolineatin (2)	
H_1	4.93 (d, J = 4)	H_1	5.32 (d, J = 4)
H_4	1.83 (d, J = 4)	H_4	1.9 (m)
H_5	4.38 (t, J = 4)	H_{5a}	2.35 (ddd, J = 13, 9, 4)
H_{6a}	1.61 (d, J = 10.5)	H_{5b}	1.9 (m)
H_{6b}	1.69 (dt, J = 10.5, 4)	H_6	3.93 (t, J = 4)
H_{8a}	2.04 (dd, J = 12, 4)	H_{8a}	1.33 (dd, J = 12, 4)
H_{8b}	1.91 (dd, J = 12, 4)	H_{8b}	2.09 (d, J = 12)
a	1.12	a	1.08
b	1.17[b]	b	1.39
c	1.16[b]	c	1.23

[a] Chemical shifts are given in ppm (δ) from TMS in CCl_4 and coupling constants in Hz.
[b] These assignments may be reversed.
[c] All assignments were verified by decoupling experiments.

The coupling constants in **1** and **2** (Table 3) also show some differences which highlight the structural differences between **1** and **2**. In lineatin (**1**) we find a long range coupling between H_{6b} and H_{8b}, and in **2** there is a long range coupling between H_4 and H_6. In each molecule the hydrogens involved in

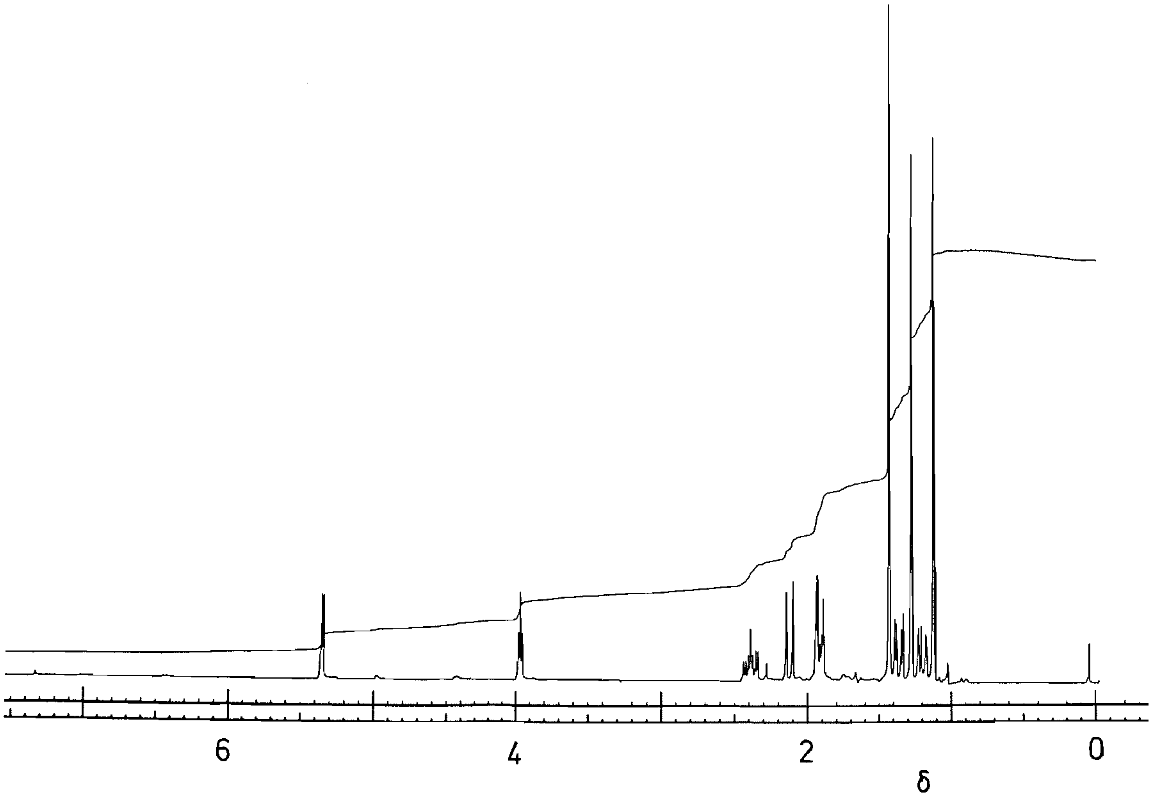


FIG. 2. 270 MHz ^{1}H nmr spectrum of isolineatin (**2**).

TABLE 3. Proton coupling constants in **1** and **2**[a]

Lineatin (**1**)	Isolineatin (**2**)
$J_{1,8a} = 4$	$J_{1,8a} = 4$
$J_{1,8b} = 0$	$J_{1,8b} = 0$
$J_{4,5} = 4$	$J_{4,5a} = 9$
$J_{5,6a} = 0$	$J_{5a,6} = 4$
$J_{5,6b} = 4$	$J_{5b,6} = 0$
$J_{6a,6b} = 10.5$	$J_{5a,5b} = 13$
$J_{8a,8b} = 12$	$J_{8a,8b} = 12$
$J_{6b,8b} = 4$	$J_{4,6} = 4$

[a] Coupling constants are given in Hz.

the long range coupling and the intervening carbons can adopt a *W* configuration (19). Hence we find that the high-field ^{1}H nmr data can be used to differentiate structures **1** and **2**.

Experimental

General

Unless otherwise stated the following are implied. Gas–liquid chromatography (glc) was performed on a Hewlett Packard Model 5831A gas chromatograph, using a 6 ft × 1/8 in. column of 3% OV 17 on Chromosorb W. The 60 MHz proton nuclear magnetic resonance spectra were recorded on a Varian Associates Model T-60, the 100 MHz spectra were recorded on a Varian Associates Model HA-100 or Model XL-100, and the 270 MHz spectra were recorded on a homebuilt high resolution nmr spectrometer consisting of an Oxford Instruments' 63.4 KG magnet. Chemical shifts in ppm are reported using δ scale with tetramethylsilane (TMS) as internal reference. Signal multiplicity, integrated area, and coupling constants are indicated in parentheses. Infrared spectra were recorded on either a Perkin–Elmer model 700 or 710B spectrophotometer. Solution spectra were performed using a sodium chloride solution cell of 0.2 mm thickness. Absorption positions are given in cm^{-1} and are calibrated by means of the 1601 cm^{-1} band of polystyrene. Low resolution mass spectra were determined on a Varian/Mat model CH4B mass spectrometer. High resolution mass measurements were obtained using Kratos-AEI model MS902 or model MS50 instrument. The gc–ms data were obtained with a Hewlett Packard 5700 gc interfaced with a Varian/Mat 777 mass spectrometer. Microanalyses were performed by Mr. P. Borda, Microanalytical Laboratory, University of British Columbia, Vancouver.

Analytical thin layer chromatography (tlc) plates and preparative tlc plates were prepared from silica gel GF-254 from E. Merck Co. Preparative tlc plates were of about 1 mm in thickness. Column chromatography was carried out with 100–200 mesh silica gel from Davision Chemical or with 230–400 mesh silica gel from BDH according to the procedure of Still *et al.* (20). Plates were visualized under long and short wavelength ultraviolet radiation and were developed by iodine.

Solvents and reagents used were of either Reagent grade or Certified grade. Solvents were distilled before use. The petroleum ether used was of boiling range ca. 30–60°C. Dry solvents or reagents, where indicated, were prepared as follows: ethyl ether (ether) and tetrahydrofuran (THF) by refluxing over lithium aluminum hydride followed by distillation; dichloromethane

(CH_2Cl_2) by distillation from phosphorus pentoxide; pyridine by distillation from barium oxide followed by storage over potassium hydroxide pellets; acetone by distillation from and storage over anhydrous magnesium sulfate; and methanol by refluxing over magnesium methoxide followed by distillation.

Methyllithium (in ethyl ether) was obtained from Aldrich Chemical Company, Inc., and standardized by titration against 1.0 *M* *tert*-butanol in benzene using 1,10-phenanthroline as indicator.

3-Methyl-5-hydroxy-2-pentenoic acid δ-lactone (5) (6a)

A mixture of 10.4 g (80 mmol) of mevalonolactone and 13.6 g of potassium hydrogen sulfate was heated under vacuum for 1 h and distilled at 72–78°C/0.9 Torr to give 8.0 g of colorless liquid. The nmr of the distilled liquid showed it to be a mixture of dehydrated products. The mixture of products was refluxed with 0.2 g (0.76 mmol) of rhodium(III) chloride trihydrate (11) in ethanol (50 mL) for 24 h, allowed to cool, then diluted with water and extracted with dichloromethane. The dichloromethane extract was dried over anhydrous magnesium sulfate, filtered, and the solvents removed under reduced pressure to give 8.0 g (89%) of 3-methyl-5-hydroxy-2-pentenoic acid δ-lactone (**5**). This material was shown to be 94% pure by glc. The spectral data below were the same as those reported for this compound (*6a*); ir ($CHCl_3$): 1650 and 1725 cm^{-1}; nmr ($CDCl_3$) δ: 2.01 (br s, 3H), 2.37 (t, $J = 6$ Hz, 2H), 4.33 (t, $J = 6$ Hz, 2H), and 5.73 (m, 1H); mass spectrum *m/e* (relative intensity): 41(10), 53(12), 54(44), 55(11), 82(100) and 112(59).

Photoaddition of 3-methyl-5-hydroxy-2-pentenoic acid δ-lactone (5) to allene

A solution of 17.8 g (0.445 mol) of allene and 10.0 g (0.089 mol) of 3-methyl-5-hydroxy-2-pentenoic acid δ-lactone (**5**) in 200 mL of degassed acetone was irradiated with a 450 W Hanovia high pressure mercury arc at −78°C for 4 h through a Vycor filter. At the end of the irradiation the solvent was removed by distillation under reduced pressure to give 12.2 g (90%) of crude product. This product was purified by flash column chromatography (20) using silica gel (230–400 mesh) and a mixture of petroleum ether and ethyl acetate (3:2, v/v) as eluent to give 11.3 g (83%) of a mixture of photoadducts: 1-methyl-7-methylene-4-oxa-*cis*-bicyclo[4.2.0]octan-5-one (**11**) and 1-methyl-8-methylene-4-oxa-*cis*-bicyclo[4.2.0]octan-5-one (**12**). The material was shown to be a 3:2 mixture of **11** and **12** respectively by 270 MHz nmr and by glc (using a 23.2 m × 0.28 mm id whisker-walled column coated with Carbowax 20 M).[3] Since separation of the individual components of the photoadduct mixture was very difficult, the sequence was carried through on the mixture. The fraction isolated by the above chromatography was further distilled at 120°C/0.8 Torr (Kugelrohr) and was characterized by the following; ir ($CHCl_3$): 1725 cm^{-1}; nmr ($CDCl_3$) δ: 1.25 (s, 3H), 1.8 (m, 2H), 2.6 (m, 1H), 2.95 (m, 1H), 3.4 (m, 1H), 4.4 (m, 2H), and 4.9 (m, 2H); mass spectrum: (*a*) high resolution calcd. for $C_9H_{12}O_2$: 152.0838; found 152.0845 amu; (*b*) low resolution *m/e* (relative intensity): 41(13), 67(10), 77(27), 79(39), 91(20), 93(100), 94(24), 95(10), 107(21), 109(22), 124(15), 137(30), and 152(40). *Anal.* calcd. for $C_9H_{12}O_2$: C 71.03, H 7.95; found: C 70.77, H 8.16.

Addition of methyllithium to photoadducts 11 and 12

A solution of 8.0 g (52.60 mmol) of photoadducts **11** and **12** in ca. 20 mL of anhydrous ethyl ether was added dropwise to an ice-cooled flask containing 120 mL (210 mmol) of 1.75 *M* methyllithium in ethyl ether. The mixture was stirred at 0°C for 2 h and the excess methyllithium was decomposed with a saturated aqueous solution of ammonium chloride. The ether layer was separated and the aqueous layer extracted several times with ethyl acetate. The combined extracts were dried over anhydrous magnesium sulfate, filtered, and the solvents were removed under reduced pressure to give 9.35 g (97%) of a mixture of diols **17** and **18** which could not be separated by tlc. The crude mixture was pure enough for the next reaction. A small sample of the mixture of products was chromatographed on a 20 × 20 cm silica gel coated plate, thickness 1 mm, using a mixture of ethyl acetate and petroleum ether (7:1, v/v) as eluent. A thick colorless oil was isolated and characterized by the following data; ir ($CHCl_3$): 1680, 3420, and 3620 cm^{-1}; nmr ($CDCl_3$) δ: 1.23 (s, 3H), 1.30 + 1.33 (ss, 6H), 1.8–2.4 (m, 4H), 2.6 (m, 1H), 3.7 (br m, 2H), and 4.8 (br m, 2H); mass spectrum: (*a*) high resolution calcd. for $C_{11}H_{20}O_2$: 184.1463; found: 184.1462 amu; (*b*) low resolution *m/e* (relative intensity): 41(45), 43(100), 53(13), 55(33), 59(95), 67(24), 79(27), 83(72), 85(36), 86(32), 105(19), 107(34), 111(59), 121(49), 123(30), 135(60), 151(34), and 166(15) ($P - H_2O$).

Oxidation of mixture of diols 17 and 18

A sample of 31.2 g (312 mmol) of chromium trioxide was added to a stirred solution of 49.32 g (624 mmol) of anhydrous pyridine (16) in ca. 30 mL of anhydrous dichloromethane. The chromium trioxide – pyridine complex was stirred at room temperature for 25 min. Then a solution of 9.20 g (50 mmol) of the mixture of diols **17** and **18** in ca. 5 mL of anhydrous dichloromethane was added in one portion. A tarry, black precipitate separated immediately. After stirring for 4.5 h at room temperature, the solution was decanted from the reaction, and the dichloromethane removed under reduced pressure. The residue was diluted with ethyl ether and the reaction flask rinsed several times with ethyl ether. The combined ether layers were filtered through a bed of Celite, washed with ice-cold dilute hydrochloric acid, aqueous sodium bicarbonate solution, brine, dried over anhydrous magnesium sulfate, and filtered. The solvents were removed under reduced pressure to give 7.60 g (84%) of a mixture of 2,2,6-trimethyl-8-methylene-3-oxa-*cis*-bicyclo[4.2.0]octan-4-one (**19**) and 2,2,6-trimethyl-7-methylene-3-oxa-*cis*-bicyclo[4.2.0]octan-4-one (**20**). The crude products were purified by column chromatography using silica gel (100–200 mesh) and a mixture of petroleum ether and ethyl acetate (2:3, v/v) as eluent. The fraction isolated from this chromatography was homogeneous by tlc analysis, and was shown to be a 3:2 mixture of **19** and **20** by nmr and glc (using a 23.4 m × 0.28 mm id whisker-walled column coated with Silar 10C).[3] Since separation of the individual components from the mixture was very difficult, the next sequence of steps was carried through on the mixture. The mixture from the chromatography was further distilled at 100°C/1.0 Torr (Kugelrohr) to afford 6.5 g (72%) of a mixture of **19** and **20** which was characterized by ir ($CHCl_3$): 1680 and 1725 cm^{-1}; nmr ($CDCl_3$) δ: 1.35, 1.42 and 1.47 (ss, 9H), 2.4 (m, 5H), and 4.9 (m, 2H); mass spectrum: (*a*) high resolution calcd. for $C_{11}H_{16}O_2$: 180.1150; found: 180.1158 amu; (*b*) low resolution *m/e* (relative intensity): 41(33), 43(69), 79(77), 80(90), 93(32), 109(24), 121(20), 123(31), 125(31), 139(14), 165(10), and 180(17). *Anal.* calcd. for $C_{11}H_{16}O_2$: C 73.30, H 8.95; found: C 73.10, H 8.95.

Ozonolysis of alkenes 19 and 20

A stream of ozone and oxygen was bubbled through a solution of 6.93 g (38.5 mmol) of a mixture of compounds **19** and **20** in ca. 250 mL of anhydrous dichloromethane at −78°C until the solution turned blue. Excess dimethylsulfide was added slowly. The reaction mixture was allowed to stir at −78°C for 20 min, warmed slowly to room temperature, washed with water, dried over anhydrous magnesium sulfate, and filtered. The solvents

---

[3] We wish to thank Professor A. C. Oehlschlager and Dr. H. Pierce, Jr., Department of Chemistry, Simon Fraser University, Burnaby, B.C., Canada, for the glc analysis of this compound.

were removed under reduced pressure to give 6.27 g (89%) of crude product which was purified by column chromatography using silica gel (100–200 mesh) and a mixture of petroleum ether and ethyl acetate (1:1, v/v) as eluent. The fraction isolated from this chromatography gave 4.8 g (69%) of a mixture of 2,2,6-trimethyl-3-oxa-*cis*-bicyclo[4.2.0]octan-4,8-dione (**21**) and 2,2,6-trimethyl-3-oxa-*cis*-bicyclo[4.2.0]octan-4,7-dione (**22**). The mixture of products could not be separated by tlc and was characterized by the following spectral data; ir ($CHCl_3$): 1730 and 1785 cm^{-1}; nmr ($CDCl_3$) δ: 1.32 and 1.40 (ss, 3H), 1.53 (s, 6H), and 2.2–3.2 (m, 5H); mass spectrum: (*a*) high resolution calcd. for $C_{10}H_{14}O_3$: 182.0943; found: 182.0953 amu; (*b*) low resolution *m*/*e* (relative intensity): 40(27), 41(60), 42(20), 43(78), 44(38), 51(10), 53(32), 54(17), 55(33), 59(10), 67(35), 68(47), 69(30), 70(14), 77(14), 79(30), 81(53), 82(26), 83(28), 95(25), 96(100), 97(79), 98(42), 123(46), 125(89), 126(23), 141(19), 167(8), and 182(6).

(±)-Lineatin (1) and 3,3,7-trimethyl-2,9-dioxatricyclo-[4.2.1.0^{4,7}]nonane (isolineatin) (2)

A solution of 5.0 g (27.5 mmol) of a mixture of ketones **21** and **22** in anhydrous ether (100 mL) was cooled to −60°C and a solution of 60 mL (1.0 *M* in hexane, 60 mmol) of diisobutylaluminum hydride in hexane was added dropwise under nitrogen. The reaction mixture was stirred at −60°C for 1 h, and saturated ammonium chloride (100 mL) was added. The reaction mixture was warmed to 0°C and acidified by dilute hydrochloric acid. Stirring was continued for an additional 1 h and the mixture was extracted several times with ether. The combined extracts were washed with aqueous sodium bicarbonate solution, dried over anhydrous magnesium sulfate, filtered, and the solvents removed under reduced pressure to give 4.3 g (95%) of crude product. The material was shown to be a 1.6:1 mixture of 3,3,7-trimethyl-2,9-dioxatricyclo[3.3.1.0^{4,7}]nonane (**1**) (±-lineatin) and 3,3,7-trimethyl-2,9-dioxatricyclo[4.2.1.0^{4,7}]nonane (**2**) (isolineatin) by glc. Purification was achieved by flash column chromatography (20) using silica gel (230–400 mesh) and a mixture of petroleum ether and ethyl ether (3:2, v/v) as eluent. Two components were isolated from this chromatography, and these were, in order of elution, (±)-lineatin (**1**) (1.05 g, 23%) and 3,3,7-trimethyl-2,9-dioxatricyclo[4.2.1.0^{4,7}]nonane (**2**) (0.615 g, 13.5%). All the spectral data of compound **1** were similar to those published by MacConnell *et al.* for (±)-lineatin (**1**) and **2** (1). This synthetic (±)-lineatin (**1**) was distilled at 110°C/20 Torr (Kugelrohr) and was characterized by; ir (CCl_4): 838, 875, 905, 920, 960, 1000, 1020, 1078, 1100, 1125, 1170, 1185, 1210, 1225, 1245, 1318, 1345, 1365, 1380, 1385, 1455, 1470, 2880, 2940, and 2975 cm^{-1}; nmr (100 MHz, CCl_4) δ: 1.08 (s, 3H), 1.12 (s, 3H), 1.14 (s, 3H), 1.55–2.1 (m, 5H), 4.34 (t, J = 4 Hz, 1H), and 4.86 (d, J = 3.5 Hz, 1H); nmr (270 MHz, CCl_4) δ: 1.12 (s, 3H), 1.16 (s, 3H), 1.17 (s, 3H), 1.61 (d, J = 10.5 Hz, 1H), 1.69 (dt, J = 10.5, 4 Hz, 1H), 1.83 (d, J = 4 Hz, 1H), 1.91 (dd, J = 12, 4 Hz, 1H), 2.04 (dd, J = 12, 4 Hz, 1H), 4.38 (t, J = 4 Hz, 1H), and 4.93 (d, J = 4 Hz, 1H); mass spectrum: (*a*) high resolution calcd. for $C_{10}H_{16}O_2$: 168.1150; found: 168.1148 amu; (*b*) low resolution *m*/*e* (relative intensity): 41(44), 43(43), 55(44), 69(34), 83(58), 85(100), 96(84), 97(47), 107(68), 109(51), 111(85), 125(56), 140(12), 153(8), and 168(10). *Anal.* calcd. for $C_{10}H_{16}O_2$: C 71.39, H 9.59; found: C 71.52, H 9.76.

3,3,7-Trimethyl-2,9-dioxatricyclo[4.2.1.0^{4,7}]nonane (**2**) was distilled (Kugelrohr) at 110°C/20 Torr and was characterized by the following spectral data; ir (CCl_4): 660, 700, 850, 895, 905, 925, 938, 960, 970, 980, 990, 1000, 1018, 1040, 1050, 1080, 1100, 1115, 1140, 1160, 1178, 1195, 1205, 1220, 1238, 1255, 1295, 1300, 1325, 1345, 1360, 1365, 1382, 1435, 1455, 1470, 2875, 2950, and 2980 cm^{-1}; nmr (100 MHz, CCl_4) δ: 1.03 (s, 3H), 1.19 (s, 3H), 1.34 (s, 3H), 1.7–2.45 (m, 5H), 3.86 (t, J = 4 Hz, 1H), and 5.23 (d, J = 4 Hz, 1H); nmr (270 MHz, CCl_4) δ: 1.08 (s, 3H), 1.23 (s, 3H), 1.39 (s, 3H), 1.33 (dd, J = 12, 4 Hz, 1H), 1.9 (m, 2H), 2.09 (d, J = 12 Hz, 1H), 2.35 (ddd, J = 13, 9, 4 Hz, 1H), 3.93 (t, J = 4 Hz, 1H), and 5.32 (d, J = 4 Hz, 1H); mass spectrum: (*a*) high resolution calcd. for $C_{10}H_{16}O_2$: 168.1150; found: 168.1152 amu; (*b*) low resolution *m*/*e* (relative intensity): 41(37), 43(30), 55(23), 67(13), 69(37), 71(17), 79(14), 81(18), 83(14), 91(45), 92(29), 93(13), 95(22), 97(16), 105(16), 107(22), 109(100), 120(15), 125(15), 124(60), 125(20), 130(16), 166(6), and 168(1). *Anal.* calcd. for $C_{10}H_{16}O_2$: C 71.39, H 9.59; found: C 71.19, H 9.59.

Photoaddition of 3-methyl-5-hydroxy-2-pentenoic acid δ-lactone (5) to 3,3-dimethylallene

A solution of 0.73 g (10.7 mmol) of 3,3-dimethylallene (Aldrich) and 0.80 g (7.13 mmol) of 3-methyl-5-hydroxy-2-pentenoic acid δ-lactone (**5**) in 30 mL of degassed acetone was irradiated with a 450 W Hanovia high pressure mercury arc at 0°C for 4 h through a Vycor filter. At the end of the irradiation the solvent was removed under reduced pressure to give 1.55 g of crude product. This product was purified by flash chromatography (20) using silica gel (230–400 mesh) and a mixture of ethyl acetate and petroleum ether (1:3, v/v) as eluent to give 0.69 g (53%) of a mixture of photoadducts. This mixture was found to contain three main components by glc in the ratio 13:20:65. These were subsequently shown by the following ozonolysis experiment to correspond to compounds **13**, **14**, and **15** respectively.

Ozonolysis of alkenes 13, 14, and 15

A stream of ozone and oxygen was bubbled through a solution of 0.25 g (1.4 mmol) of a mixture of compounds **13**, **14**, and **15** in 25 mL of anhydrous methanol at −78°C until the solution turned blue. Excess dimethylsulfide was added slowly. The reaction mixture was allowed to stir at −78°C for 20 min, warmed slowly to room temperature, washed with water, dried over anhydrous magnesium sulfate, and filtered. The solvents were removed under reduced pressure to give 0.14 g (ca. 50% yield) of a mixture of compounds. This mixture was shown by gc–ms to contain compounds with *m*/*e* 186(**13***a*), 214(**14***a*), and 182(**15***a*) in the ratio 16:24:51 (glc ratios) respectively.[4]

Acknowledgements

We are grateful to the Natural Sciences and Engineering Research Council of Canada (NSERC) and the Science Council of British Columbia for financial support of this work. One of us (J.O.) is grateful to NSERC for the award of a graduate fellowship.

1. J. G. MacConnell, J. H. Borden, R. M. Silverstein, and E. Stokkink. J. Chem. Ecol. **3**, 549 (1977).
2. J. H. Borden, J. R. Handley, B. D. Johnston, J. G. MacConnell, R. M. Silverstein, K. N. Slessor, A. A. Swigar, and D. T. W. Wong. J. Chem. Ecol. **5**, 681 (1979).
3. K. N. Slessor, A. C. Oehlschlager, B. D. Johnston, H. D. Pierce, Jr., S. K. Grewal, and L. K. G. Wickremesinghe. J. Org. Chem. **45**, 2290 (1980).
4. K. Mori and M. Sasaki. Tetrahedron, **36**, 2197 (1980).
5. (*a*) R. W. Holder. J. Chem. Educ. **53**, 81 (1976); (*b*) R. Huisgen and L. A. Feiler. Chem. Ber. **102**, 3444 (1969).
6. (*a*) R. C. Gueldner, A. C. Thompson, and P. A. Hedin. J. Org. Chem. **37**, 1854 (1972); (*b*) H. Kosugi, S. Seki-

---

[4] We wish to thank Professor F. S. Abbott and Mr. R. Burton, Pharmacy, U.B.C., for this gc–ms analysis.

GUCHI, R. SEKITA, and H. UDA. Bull. Chem. Soc. Jpn. **49**, 520 (1976).

7. (*a*) P. E. EATON. Tetrahedron Lett. 3695 (1964); (*b*) E. J. COREY, J. D. BASS, R. LEMAHIEU, and R. B. MITRA. J. Am. Chem. Soc. **86**, 5570 (1964); (*c*) K. WIESNER. Tetrahedron, **31**, 1655 (1975), and references therein; (*d*) R. B. KELLY, M. L. HARLEY, and S. J. ALWARD. Can. J. Chem. **58**, 755 (1980), and references therein; (*e*) G. MARINI-BETTOLO, S. P. SAHOO, G. A. POULTON, T. Y. R. TSAI, and K. WIESNER. Tetrahedron, **36**, 719 (1980), and references therein.
8. W. R. BAKER, P. D. SENTER, and R. M. COATES. J. Chem. Soc. Chem. Commun. 1011 (1980).
9. J. W. CORNFORTH, R. H. CORNFORTH, A. PELTER, M. G. HORNING, and G. POPJAK. Tetrahedron, **5**, 311 (1959).
10. R. A. ELLISON and P. K. BHATNAGAR. Synthesis, 719 (1974).
11. (*a*) T. HUDLICKY and T. KUTCHAN. Tetrahedron Lett. **21**, 691 (1980); (*b*) J. ANDRIEUX, D. H. R. BARTON, and H. PATIN. J. Chem. Soc. Perkin Trans. I, 359 (1977).
12. (*a*) P. E. EATON. Acc. Chem. Res. **1**, 50 (1968); (*b*) P. DE MAYO. Acc. Chem. Res. **4**, 41 (1971).
13. J. R. SCHEFFER and R. A. WOSTRADOWSKI. J. Org. Chem. **37**, 4317 (1972).
14. D. K. M. DUC, M. FETIZON, I. HANNA, A. OLESKER, C. PASCARD, and T. PRANGE. J. Chem. Soc. Chem. Commun. 1209 (1980).
15. D. BECKER, Z. HAREL, and D. BIRNBAUM. J. Chem. Soc. Chem. Commun. 377 (1975).
16. R. RATCLIFFE and R. RODEHORST. J. Org. Chem. **35**, 4000 (1970).
17. J. H. BORDEN, A. C. OEHLSCHLAGER, K. N. SLESSOR, L. CHONG, and H. D. PIERCE, JR. Can. J. Entomol. **113**, 1099 (1980).
18. L. M. JACKMAN and S. STERNHILL. Applications of nuclear magnetic spectroscopy in organic chemistry. 2nd ed. Pergamon Press Ltd., Headington Hill Hall, Oxford, England. 1969. p. 70.
19. K. B. WIBERG, G. M. LAMPMAN, R. P. CIULA, D. S. CONNOR, P. SCHERTLER, and J. LAVANISH. Tetrahedron, **21**, 2749 (1965).
20. W. C. STILL, M. KAHN, and A. MITRA. J. Org. Chem. **43**, 2923 (1978).