Conformations of Iridolactones and the Stereochemistry in the Syntheses

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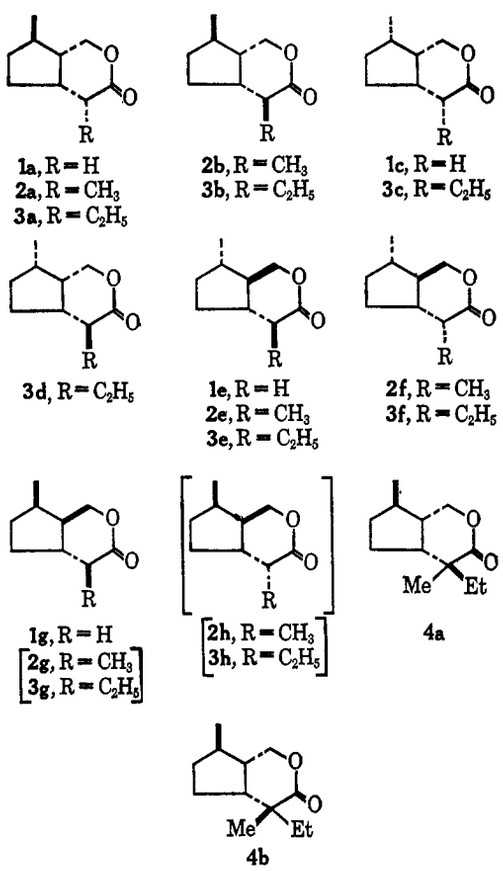
To obtain further information on stereoselective syntheses, six out of eight possible racemic stereoisomers of the lactone of 2-(2-hydroxymethyl-3-methylcyclopentyl)butyric acid (**3a–f**) were prepared from ethyl 2-(3-methyl-2-oxocyclopentyl)butyrate. The stereochemistry of the reactions was compared with the stereochemistry of the lower homologs. Configurations and conformations of these compounds and those of iridomyrmecin, boshnialactone, and their stereoisomers were studied by means of infrared spectra, spin–spin coupling constants, and solvent-induced chemical shifts.

Monoterpenoids with a cyclopentane ring including nepetalactone,[1] iridomyrmecin[2] (**2a**), isoiridomyrmecin[3] (**2b**), and boshnialactone[4] (**1c**) have recently received attention in that the 1,2,3-substituted cyclopentanes are regarded as biogenetic precursors of complex indole alkaloids.[5] The physiological activities[4,6] of these δ-lactones themselves are also interesting because of insecticidal, bactericidal, cat-attracting, and stimulating effects. The synthesis of these lactones was studied.[4,7–10] Stereoselective syntheses starting from 2-carbethoxy-5-methylcyclopentanone[11] carried out in this laboratory[12,13] furnished iridomyrmecin, boshnialactone, and the stereoisomers in racemic forms.

In continuation of these synthetic studies, the preparation of homologs of iridomyrmecin, *i.e.*, 2-(2-hydroxymethyl-3-methylcyclopentyl)butyric acid lactone (**3a–f**) was effected to obtain further information on the stereoselectivity of the syntheses. The fact that the differences in the biological activities of irido- (**2a**) and isoiridomyrmecin (**2b**) (Chart I) seemed to depend on the over-all shapes of the respective molecules but not on their epimeric relationship[14] aroused also an interest in the activities of the homologs. The conformation of iridolactones has been studied since the discovery of these compounds,[3c] but no conclusions except those based on an X-ray crystallographic analysis[14] were obtained. Conformations in solution have not been reported.

Stereoselective Syntheses.—Syntheses of the lactones of 2-(2-hydroxymethyl-3-methylcyclopentyl)butyric acid were carried out by procedures previously used for iridomyrmecin[12] and boshnialactone,[13] the stereochemistry of each process being checked (Charts II and III).

CHART I



Starting from 2-carbethoxy-5-methylcyclopentanone and ethyl 2-bromobutyrate, 2-(2-hydroxymethyl-3-methylcyclopentyl)butyric acid *cis* lactones (**3a–d**) were obtained *via* **5–10**.

Olefinic esters (**7–10**) should be a mixture of racemic *trans* olefins [(±) **7** and (±) **8**] and racemic *cis* olefins [(±) **9** and (±) **10**] in a ratio of 90:10. This ratio was determined, as described below, by the analysis of diacetates (**15–18**) derived from the olefinic esters (**7–10**) as shown in Chart IV. It was assumed that the methylene moiety of the *cis* isomers **9** and **10** would be attacked readily by the bulky dialkylborane from the side opposite the two *cis* group, while the *trans* isomers **7** and **8** were expected to resist attack because of hindrance by either one of the two substituents.[13] When the hydroboration followed by oxidation of the mixture

(1) (a) S. M. McElvain and E. J. Eisenbraun, *J. Amer. Chem. Soc.*, **77**, 1559 (1955); (b) J. Meinwald, *ibid.*, **76**, 4571 (1954).

(2) (a) M. Pavan, *Chim. Ind.* (Milan), **37**, 714 (1955); *Chem. Abstr.*, **50**, 13311c (1956); (b) R. Fusco, R. Trave, and A. Vercellone, *Chim. Ind.* (Milan), **37**, 251 (1955); *Chem. Abstr.*, **50**, 8451*f* (1956).

(3) (a) G. W. K. Cavill, D. L. Ford, and H. D. Locksley, *Chem. Ind.* (London), 465 (1956); (b) G. W. K. Cavill, D. L. Ford, and H. D. Locksley, *Aust. J. Chem.*, **9**, 288 (1956); (c) G. W. K. Cavill and H. D. Locksley, *ibid.*, **10**, 352 (1957).

(4) T. Sakan, H. Murai, Y. Hayashi, Y. Honda, T. Shono, M. Nakajima, and M. Kato, *Tetrahedron*, **23**, 4635 (1967).

(5) (a) W. I. Taylor, *Science*, **153**, 954 (1966); (b) A. R. Battersby, R. T. Brown, R. S. Kapil, A. O. Plunkett, and J. B. Taylor, *Chem. Commun.*, 46 (1966); (c) A. R. Battersby, R. T. Brown, J. A. Knight, J. A. Martin, and A. O. Plunkett, *ibid.*, 346 (1966); (d) E. S. Hall, F. McCapra, T. Money, K. Fukumoto, J. R. Hanson, B. S. Mooto, G. T. Phillips, and A. I. Scott, *ibid.*, 348 (1966).

(6) T. Sakan, A. Fujino, and F. Murai, *Nippon Kagaku Zasshi*, **81**, 1320, 1324 (1960); *Chem. Abstr.*, **56**, 11644*b*, 11644*c* (1962).

(7) K. J. Clark, G. I. Fray, R. H. Jaeger, and R. Robinson, *Tetrahedron*, **6**, 217 (1959).

(8) F. Korte, J. Falbe, and A. Zschocke, *ibid.*, **6**, 201 (1959).

(9) F. Korte, J. H. Büchel, and A. Zschocke, *Chem. Ber.*, **94**, 1952 (1961).

(10) J. Wolinsky, T. Gibson, D. Chan, and H. Wolf, *Tetrahedron*, **21**, 1248 (1965).

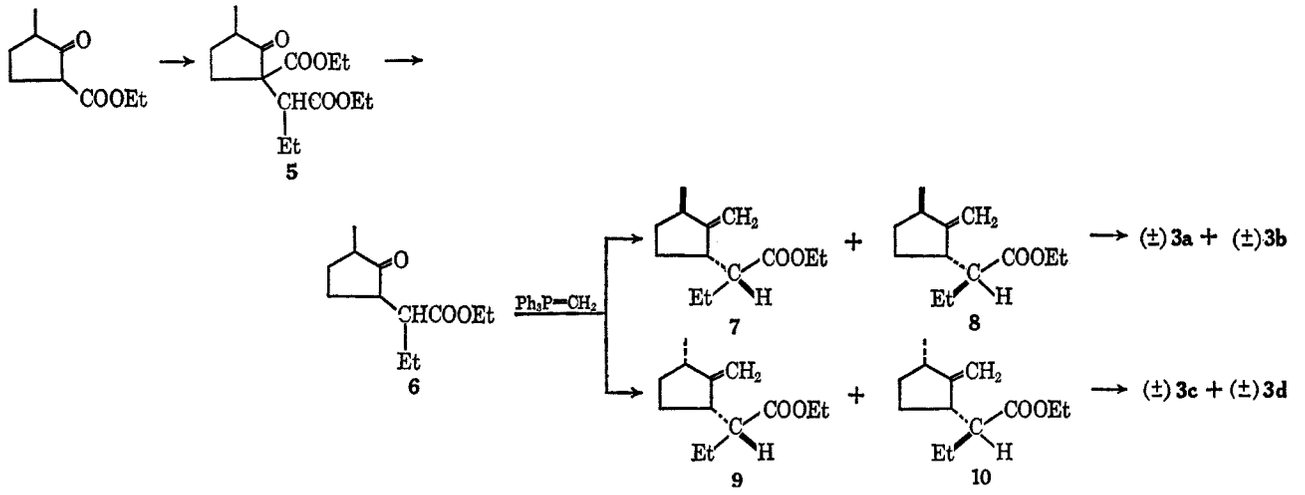
(11) K. Sisido, K. Utimoto, and T. Isida, *J. Org. Chem.*, **29**, 2781 (1964).

(12) K. Sisido, K. Utimoto, and T. Isida, *ibid.*, **29**, 3361 (1964).

(13) K. Sisido, T. Kageyama, H. Mera, and K. Utimoto, *Tetrahedron Lett.*, 1553 (1967).

(14) J. F. McConnell, A. M. Mathieson, and B. P. Schornborn, *ibid.*, 445 (1962).

CHART II



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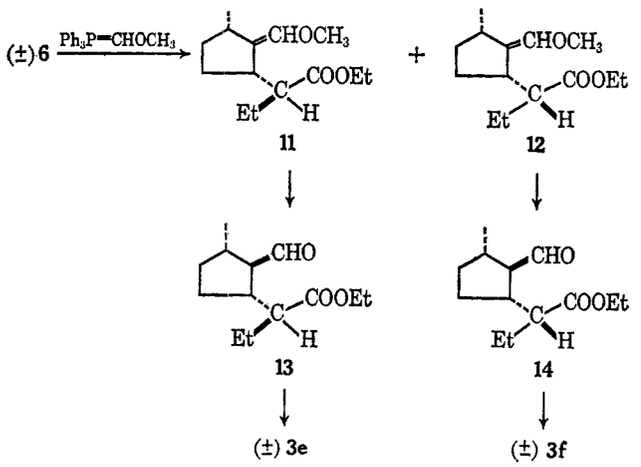
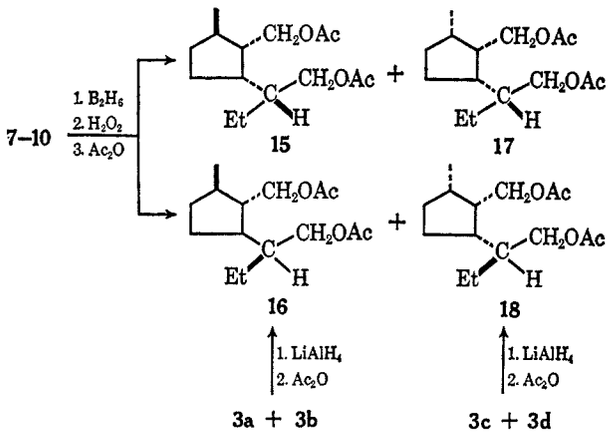


CHART IV



of *cis* and *trans* olefinic esters **7–10** was carried out with an insufficient amount of disiamylborane,[15] the *trans* isomers **7** and **8** remained unattacked. The reaction products afforded, when lactonized after removal[16] of the unchanged olefinic ester, *cis,cis* lactones [(±) **3c** and (±) **3d**]. Hydroboration of the recovered olefinic ester with unsubstituted borane, *i.e.*, diborane, gave *cis,trans* lactones [(±) **3a** and (±) **3b**] by attack from the side holding the less bulky methyl group. Since the synthetic mixture of (±) **3a** and (±) **3b** did not contain the *trans* lactones (**3g** and **3h**), it was proved that the attack of borane did not occur from the side of the butyrate group. In the case of boshnialactone [(±) **1c**], which contains the less bulky acetate group, the attack could occur also from the side of the acetate and compound (±) **1g** was produced.[13]

The lactone (±) **3a** was obtained in crystalline forms, but gas chromatography was utilized for the separation of (±) **3b**, (±) **3c**, and (±) **3d**.

Because it was difficult to carry out configurational studies on the olefinic esters **7–10**, they were converted into the corresponding diols, 2-(2-hydroxymethyl-3-methylcyclopentyl)butanol, and were compared with those prepared from **3a–d**, whose stereochemistry was determined as described below. The olefinic esters **7–10**, on hydroboration and reduction using excess diborane followed by oxidation, gave diols[12] which were acetylated to diacetates (**15–18**). The same diacetates (**15–18**) were prepared from **3a–d** *via* lithium aluminum hydride reduction followed by acetylation. Since the yield of each acetylation was nearly quantitative, it was considered that the acetylations proceeded independently of the isomeric relationships. Gas chromatographic comparison showed that the diacetates **15–18** derived directly from the olefinic esters **7–10** contained 90% *cis,trans* isomers (**15** and **16**) and 10% *cis,cis* isomers (**17** and **18**). It was deduced, therefore, that the olefinic esters obtained by the Wittig reaction was composed of 90% *trans* isomer (**7** and **8**) and 10% *cis* isomer (**9** and **10**) and that diborane attacked the methylene moiety from the direction opposite to the carboxypropyl group.

The *trans* lactones (**3e** and **3f**) were obtained from keto ester **6** *via* **11–14** in a similar way[12,13] as reported previously. Other *trans* lactone isomers [(±) **3g** and (±) **3h**] were not found among the products. This was in accord with the situation prevailing during the preparation of the *trans* isomer of boshnialactone, where the same synthetic route gave only one stereoisomer (**1e**). The methyl group of the cyclopentane ring was, therefore, *cis* to the 1-carboxypropyl group, that is, **3e** and **3f** were considered to be *trans,trans* lactones.

(15) (a) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962; (b) G. Zweifel and H. C. Brown, *Org. Reactions*, **13**, 1 (1963).

(16) If this separation procedure was omitted, *i.e.*, when the lactonization was carried out on the reaction mixture including unchanged acid, the resulted δ-lactone contained γ-lactone, 2-(2,3-dimethyl-2-hydroxycyclopentyl)-butyric acid lactone, separation of which caused a difficult problem.

The keto ester **6** was presumed to be an equilibrium mixture of *cis* and *trans* isomers[17] containing predominantly the *trans* isomer which, however, might readily be subjected to epimerization owing to the existence of an enolizable carbonyl group.

From the fact that the methoxymethylene derivatives gave only **3e** and **3f** and not **3g** and **3h**, the methoxymethylene derivatives were considered to contain only **11** and **12**, *i.e.*, *cis* compounds. In the reaction with **6**, methoxymethylenetriphenylphosphorane seemed to have condensed only with the sterically unhindered *cis* isomer of **6** with the *trans* isomer epimerizing to the *cis* isomer and thus yielding **11** and **12** in high purity.

A similar epimerization was observed by Marshall, Pike, and Carroll,[18] the less reactive isomer being isomerized to the more reactive epimer which then was consumed to produce the olefin. In a different situation,[19] however, when the ketone was not easily epimerized, only the less-hindered isomer reacted to form olefin and the other isomer remained.

In an earlier paper[12] the configurations of the ring methyl group of two *trans* lactones of 2-(2-hydroxymethyl-3-methylcyclopentyl)propionic acid was not established. The two compounds were assumed to be (±) **2g** and (±) **2h** (*trans,cis* lactones), but, as suggested in a later paper,[13] the correct structures should be **2e** and **2f** (*trans,trans* lactones). This matter has now been reinvestigated. The configuration of the methyl group on the lactone ring has been determined by means of solvent-induced chemical shifts.

When heated with quinoline, **3a** and **d** gave a mixture of **3a** and **b**, as well as **3c** and **d**, respectively. These facts suggested that **3a** and **b** as well as **3c** and **d** have the same configuration at the methyl group of the cyclopentane ring but opposite at the ethyl group of the lactone ring. When an equimolar mixture of **3a–d** was heated with sodium methoxide in methanol, the contents of **3b** and **d** were enriched. From the fact that iridomyrmecin [(+) **2a**] could be converted into isoiridomyrmecin [(−) **2b**] by treatment with sodium methoxide,[3c] it was assumed that **3b** and **d** had the same configuration as isoiridomyrmecin [(−) **2b**] with regard to the ethyl group at the lactone ring and that **3a** and **3c** were similar to iridomyrmecin [(+) **2a**].

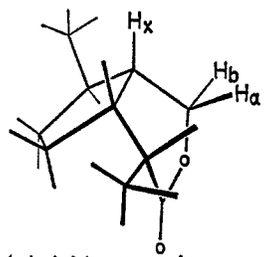
To determine the configuration of the methyl group on the cyclopentane ring, **3a** was alkylated with methyl iodide. This gave a 31:69 mixture of the two 2-methyl-2-(2-hydroxymethyl-3-methylcyclopentyl)butyric acid lactones (**4a** and **b**). Similarly (+)-isoiridomyrmecin[4] [(+)**2b**], on treatment with ethyl iodide, gave a mixture of **4a** and **b** in a 86:14 ratio. The configuration of the methyl group at the cyclopentane ring of **3a** and **2b** is, therefore, the same, which in turn determines the configurations of **3a–d**. Configurations of **3e** and **3f** were determined by physical methods as described below.

The ratios of the formations of **4a** and **4b** supported the conclusions about the configurations. Although the conformation of the iridomyrmecin (**2a**) analog **3a** is different from that of isoiridomyrmecin (**2b**)[2] as shown below, the conformation of the intermediate carbanions derived from **3a** and **2b** were considered to be similar. The alkylations by methyl iodide and ethyl iodide, respectively, would occur preferentially from the sterically less hindered side, that is, from the direction opposite to the cyclopentane ring; thus the entering alkyls should situate preferentially on opposite sides of the cyclopentane ring. Therefore, **3a** gave mainly **4b** and isoiridomyrmecin (**2b**) gave mainly **4a**.

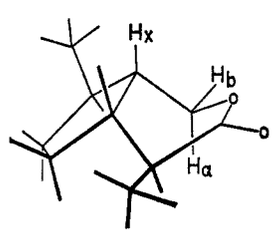
Conformational Analyses.—Configurations of the natural products, *i.e.*, **1c**,[4] **2a**,[2] and **2b**,[3] had already been determined. As to the synthetic compounds **1a**, **3a**, and **3b**, configurations had been determined by comparison with the natural products or by conversion into compounds whose stereochemistry was established as described above. For the remaining ten lactones in Chart I, configurations of the ring junctures were determined by infrared spectroscopy.[12]

According to Cheung, *et al.*,[20] δ-lactones can be assigned a boat or a half-chair form on the basis of their carbonyl absorptions. Thus, lactone rings of **1a**, **1c**, **2a**, **2b**, **3a**, **3b**, **3c**, **3d**, **4a**, and **4b**, whose carbonyl-stretching frequencies $\nu_{C=O}$ were at 1750–1765 cm^{-1}, could be classified as boat forms, while **1e**, **1g**, **2e**, **2f**, **3e**, and **3f**, showing $\nu_{C=O}$ at 1730–1740 cm^{-1}, could be classified as half-chair forms.

Inspection of Dreiding models indicated that a half-chair δ-lactone must have a rigid *trans* configuration and a boat δ-lactone must have a flexible *cis* configuration of either iridomyrmecin or isoiridomyrmecin type[14] as shown below, which shows antipodes of natural iridomyrmecin and isoiridomyrmecin. The lactone ring of these *cis* compounds are slightly folded.



(−)-Iridomyrmecin



(+)-Isoiridomyrmecin

For all lactones the same conclusion as to the stereochemistry of ring juncture was established by the respective synthetic routes.[12,13]

An attempt was also made to elucidate configurations and conformations of these lactones by nmr coupling

(17) K. Sisido, S. Kurozumi, K. Utimoto, and T. Ishida, *J. Org. Chem.*, **31**, 2795 (1966), showed that in the equilibrium mixture of 2-isopropyl-5-methylcyclopentanone 70% was the *trans* isomer and 30% was the *cis* isomer. An effort to analyze **6** was unsuccessful owing to the difficulty of the separation by gas chromatography.

(18) J. A. Marshall, M. T. Pike, and R. D. Carroll, *ibid.*, **31**, 2933 (1966).

(19) E. J. Corey, R. B. Mitra, and H. Uda, *J. Amer. Chem. Soc.*, **86**, 485 (1964).

(20) K. K. Cheung, K. H. Overton, and G. A. Sim, *Chem. Commun.*, 634 (1965).

constants and solvent-induced shifts was also made in view of previous reports.[21-26]

Application of the Karplus equation[27] to the dihedral angles of H_a and H_x as well as H_b and H_x measured from Dreiding models (Table I) gave theoretical

TABLE I
DIHEDRAL ANGLES AND COUPLING CONSTANTS OF IRIDOMYRMECIN AND ISOIRIDOMYRMECIN

	Dihedral angle, obsd,[a] deg		Coupling constant J_{ax}, Hz		Coupling constant J_{bx}, Hz	
	H_aH_x	H_bH_x	Calcd	Obsd	Calcd	Obsd
Iridomyrmecin (**2a**)	57	63	2.2	3.0	1.7	3.0
Isoiridomyrmecin (**2b**)	175	55	9.2	10.1	2.5	5.9

[a] Approximate value measured on the Dreiding models.

values for spin–spin coupling constants which were compared with the observed ones (Table I). Considering the fact that there is some dependence of coupling constant on the conformational relationship between protons and the electronegative oxygen[28,29] and that the calculated constants tend to give smaller values than the observed ones,[30] these measurements made with samples in solution are in good agreement with calculated values based on the conformations of the crystalline iridomyrmecin (**2a**) and isoiridomyrmecin (**2b**)[14] and suggest that these lactones have similar conformations both in the crystalline state and in solution.

Coupling constants J_{ax} and J_{bx} might be regarded as possible mean classifying the *cis* lactones into an iridomyrmecin or an isoiridomyrmecin type. By this procedure, lactones **1a**, **1c**, **2a**, **3a**, **3c**, **4a**, and **4b** were classified as of iridomyrmecin types and lactones **2b**, **3b**, and **3d** as of isoiridomyrmecin types (Table II). Dreiding models indicated that the methyl or ethyl group on the lactone ring was in a quasi-equatorial position in these *cis* lactones.

It is reasonable to assume that, within a certain series of similar compounds, solvent induced shifts of nmr signals as well as the spin–spin coupling constants (J_{ax} and J_{bx}) have nearly equal values when the compounds in solution have the same configuration. The values of iridomyrmecin-type *cis* lactones in Table II, those of isoiridomyrmecin-type *cis* lactones in Table III, and those of *trans* lactones in Table IV were compared with each other.

It was concluded that, with respect to the methyl group at the cyclopentane ring, **1a**, **2a**, **3a**, **4a**, and **4b** (iridomyrmecin-type *cis* lactones), **2b** and **3b** (isoiridomyrmecin-type *cis* lactones), as well as **1e**, **2e**, **2f**, **3e**, and **3f** (*trans* lactones) have the same configuration, respectively, and that, because known lactones of established stereochemistry are included in this group, the methyl group was *trans* with respect to the lactonized hydroxymethyl group.

If the benzene–lactone complex formed between the carbonyl and the π electrons is assumed to be similar to that of the benzene–ketone complex described by Williams and Wilson,[26] the coordinating benzene molecule may be considered to be at the less hindered side of the lactone carbonyl group. From the observation of the Dreiding models, the solvent induced shift values of *cis*-methyl groups of the cyclopentane ring were expected to be smaller than those of *trans*-methyl groups in the case of iridomyrmecin-type lactones, and larger in the case of isoiridomyrmecin-type lactones and *trans* lactones. The exceptionally high value of **1c** was accounted for assuming repulsion due to the three groups, being situated in the *cis,cis* configuration. A somewhat modified shape of the iridomyrmecin type must be invoked for **1c**, because **1c** has no substituents. The fact

TABLE II
IR AND NMR DATA OF IRIDOMYRMECIN-TYPE *cis* LACTONES

	J_{ax}, Hz	J_{bx}, Hz	J_{ab}, Hz	Methyl group at	ΔR,[a] ppm	δ_{CDCl_3},[b] ppm	$\delta_{C_6H_6}$,[c] ppm	$\nu_{C=O}$, cm^{-1}
1a	3.0[d]	3.0	−12.0	Cyclopentane	0.34	1.04	0.70	1755
1c	5.0	1.0	−10.5	Cyclopentane	0.38	1.00	0.62	1755
2a	3.0[d]	3.0	−11.4	Cyclopentane	0.32	1.05	0.73	1755
				Lactone	0.10	1.13	1.03	
3a	3.1[d]	3.1	−11.4	Cyclopentane	0.32	1.05	0.73	1755
				Ethyl group	0.14	0.98	0.84	
3c	4.1	1.1	−12.0	Cyclopentane	0.21	1.07	0.86	1755
				Ethyl group	0.13	0.98	0.85	
4a	4.6	1.1	−11.7	Cyclopentane	0.31	1.05	0.74	1750
				Lactone	0.06	1.16	1.10	
				Ethyl group	0.13	0.93	0.80	
4b	5.6	3.4	−11.5	Cyclopentane	0.35	1.05	0.70	1750
				Lactone	0.33	1.27	0.94	
				Ethyl group	0.18	0.91	0.73	

[a] $\Delta R = \delta_{CDCl_3} - \delta_{C_6H_6}$. [b] δ_{CDCl_3} means the chemical shift in $CDCl_3$ solution. [c] $\delta_{C_6H_6}$ means the chemical shift in benzene solution. [d] Nmr spectra of these protons were very simple; *cf.* pp 363 and 364 of ref 30.

TABLE III
IR AND NMR DATA OF ISOIRIDOMYRMECIN-TYPE *cis* LACTONES

	J_{ax}, Hz	J_{bx}, Hz	J_{ab}, Hz	Methyl group at	ΔR,[a] ppm	δ_{CDCl_3},[b] ppm	$\delta_{C_6H_6}$,[c] ppm	$\nu_{C=O}$, cm^{-1}
2b	10.1	5.9	−11.0	Cyclopentane	0.42	1.07	0.65	1755
				Lactone	0.14	1.20	1.06	
3b	9.8	5.9	−10.5	Cyclopentane	0.39	1.05	0.66	1755
				Ethyl group	−0.06	0.99	1.05	
3d	10.7	5.9	−11.0	Cyclopentane	0.47	1.00	0.53	1755
				Ethyl group	−0.01	1.05	1.06	

[a] $\Delta R = \delta_{CDCl_3} - \delta_{C_6H_6}$. [b] δ_{CDCl_3} means the chemical shift in $CDCl_3$ solution. [c] $\delta_{C_6H_6}$ means the chemical shift in benzene solution.

TABLE IV
IR AND NMR DATA OF *trans* LACTONES

	J_{ax}, Hz	J_{bx}, Hz	J_{ab}, Hz	Methyl group at	ΔR,[a] ppm	δ_{CDCl_3},[b] ppm	$\delta_{C_6H_6}$,[c] ppm	$\nu_{C=O}$, cm^{-1}
1e	10.5	4.5	−10.5	Cyclopentane	0.39	1.04	0.65	1738
2e	9.8	4.7	−10.7	Cyclopentane	0.40	1.04	0.64	1740
				Lactone	0.12	1.26	1.14	
2f	9.7	4.7	−10.7	Cyclopentane	0.38	1.03	0.65	1740
				Lactone	0.21	1.21	1.00	
3e	9.7	4.7	−10.7	Cyclopentane	0.39	1.04	0.65	1740
				Ethyl group	0.04	0.94	0.90	
3f	9.7	4.4	−10.7	Cyclopentane	0.39	1.04	0.65	1740
				Ethyl group	0.02	1.04	1.02	
1g	10.5	5.0	−10.5	Cyclopentane	0.49	0.88	0.39	1740

[a] $\Delta R = \delta_{CDCl_3} - \delta_{C_6H_6}$. [b] δ_{CDCl_3} means the chemical shift in $CDCl_3$ solution. [c] $\delta_{C_6H_6}$ means the chemical shift in benzene solution.

(21) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry. Illustrations from the Steroid Field," Holden-Day, Inc., San Francisco, Calif., 1964.
(22) M. Fetizon, J. Core, P. Laszlo, and B. Waegell, *J. Org. Chem.*, **31**, 4047 (1966).
(23) J. Ronayne and D. H. Williams, *Chem. Commun.*, 712 (1966).
(24) G. Di Maio, P. A. Tardella, and C. Iavarone, *Tetrahedron Lett.*, 2825 (1966).
(25) J. D. Connoly and R. McCrindle, *Chem. Ind.* (London), 379, 2066 (1965).
(26) D. H. Williams and D. A. Wilson, *J. Chem. Soc., B*, 144 (1966).
(27) M. Karplus, *J. Amer. Chem. Soc.*, **85**, 2870 (1963), and references cited therein.
(28) H. Boothe, *Tetrahedron Lett.*, 411 (1963), and references cited therein.
(29) Reference 21, pp 52. 53.
(30) J. W. Emsley, J. Feeney, and L. H. Sutcliff, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, Oxford, 1965, pp 166–170.

that **3c**, which has also the *cis,cis* configuration, showed a smaller value might be explained by assuming that the unfolding of the lactone ring owing to the repulsion was somewhat hindered by the interaction of the ethyl group with the cyclopentane ring.

In lactones containing ethyl groups, solvent-induced shifts of the methyl moieties of the ethyl groups were effected to be less important in helping to establish the configurations, because the methyl moiety can rotate around the carbon–carbon bond of the ethyl group. Nevertheless, although the configuration of **4a** and **b** were deduced from the synthetic routes, as described above, confirmation was provided by a comparison of the solvent-induced shift of the lactone methyl group of **4a** (ΔR = 0.06 ppm) with that of iridomyrmecin (**2a**) (ΔR = 0.10 ppm). Since **4b** showed an entirely different value of 0.33 ppm, the methyl group of **4a** apparently had the same configuration as that of iridomyrmecin (**2a**).

Since, according to the Dreiding models, the methyl group on the lactone ring of **2e** is closer to the "carbonyl plane"[31] than that of **2f**, the solvent-induced shift of the methyl group of **2e** must be smaller than that of **2f**. The observed values, ΔR = 0.12 ppm for **2e** and ΔR = 0.21 ppm for **2f**, agree with the expectation. Owing to the difficulty of determining the configuration of the ethyl groups of the lactone ring by solvent-induced shifts as described above, comparison of the coupling constants (J_{ax} and J_{bx}, shown in Table IV) and the chemical shifts [δ (H_a) and δ (H_b)] of **3e** and **3f** with those of configurationally known **2e** and **2f** was utilized. Signals of the methylene protons of hydroxymethyl group of **2e** were observed at δ 4.02 and 4.49 ppm, and these values were equal to those of **3e**. The analogous protons of **2f** had signals at δ 3.95 and 4.46 ppm, equal to those of **3f**. From this, **2e** and **3e** as well as **2f** and **3f** were considered to be of similar conformation.

Thus the configuration and conformation of boshnialactone, iridomyrmecin and homolog, and their stereoisomers in solutions were determined. The conformation of iridomyrmecin in solution was found to be the same as that established for crystalline iridomyrmecin and its stereoisomers.[14]

Experimental Section

Infrared spectra were determined on Shimadzu IR-27. Gas chromatography was carried out on Shimadzu GC-2C and Shimadzu GC-1B for packed column and Hitachi K-23 for Goley column. Nmr spectra were measured at 60 MHz with Varian Associates A-60 and Japan Electron Optics C-60-H in 5% solution. For microelemental analyses Yanagimoto Automatic Analyser CHN Corder MT-1 was used.

All identifications of the compounds were carried out by the comparison of infrared spectra and gas chromatograms.

Ethyl 2-(1-Carbethoxy-3-methyl-2-oxocyclopentyl)butyrate (5).—Analogous procedure to the synthesis of ethyl 2-(1-carboethoxy-3-methyl-2-oxocyclopentyl)propionate[12] gave the product in 70% yield: bp 123–125° (3 mm); n^{30}D 1.4545; ir (liquid film) 1765 (C=O), 1740 (ester C=O), 1200, 1025 cm^{-1}.

Anal. Calcd for $C_{15}H_{24}O_5$: C, 63.36; H, 8.51. Found: C, 63.09; H, 8.66.

2-(3-Methyl-2-oxocyclopentyl)butyric Acid.—According to the procedure of Linstead and Jones,[32] from 263 g (0.93 mol) of ethyl 2-(1-carbethoxy-3-methyl-2-oxocyclopentyl)butyrate (**5**) there was obtained 119 g (0.65 mol; yield 70%) of 2-(3-methyl-2-oxocyclopentyl)butyric acid, bp 147–148° (5 mm), which solidified to give small crystals: mp 71–87°; ir (KBr) 1740 (C=O), 1700 (acid C=O), 1240, 925 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.05; H, 8.78.

The **2,4-dinitrophenylhydrazone** had mp 205° dec.

Anal. Calcd for $C_{16}H_{20}O_6N_4$: C, 52.74; H, 5.53. Found: C, 52.53; H, 5.70.

Ethyl 2-(3-Methyl-2-oxocyclopentyl)butyrate (6).—Esterification of 71 g (0.39 mol) of the above-mentioned keto acid by the Linstead and Jones procedure[32] gave 75 g (0.36 mol; yield 92%) of ethyl 2-(3-methyl-2-oxocyclopentyl)butyrate (**6**): bp 94–95° (1 mm); n^{20}D 1.4552; ir (liquid film) 1735, 1180, 1025 cm^{-1}.

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 68.14; H, 9.23.

The **2,4-dinitrophenylhydrazone** had mp 159–160°.

Anal. Calcd for $C_{18}H_{24}O_6N_4$: C, 55.09; H, 6.19. Found: C, 55.10; H, 5.89.

Ethyl 2-(3-Methyl-2-methylenecyclopentyl)butyrate (7–10).—According to Greenwald, Chaykovsky, and Corey[33] and analogous to our previous report,[12] 17 g of **6** and 40.4 g of methyltriphenylphosphonium iodide in dimethyl sulfoxide gave 7.5 g (yield 45%) of ethyl 2-(3-methyl-2-methylenecyclopentyl)butyrates (**7–10**): bp 85–90° (5 mm); n^{25}D 1.4533; ir (liquid film) 3065, 1740, 1650, 880 cm^{-1}.

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.21; H, 10.32.

Hydroboration of Ethyl 2-(3-Methyl-2-methylenecyclopentyl)-butyrate (7–10) with Diborane. Preparation of *cis* Lactone Mixture (3a–d).—The hydroboration was carried out with 0.61 g (16 mmol) of sodium borohydride, 10.1 g (48 mmol) of ethyl 2-(3-methyl-2-methylenecyclopentyl)butyrate (**7–10**), and 2.3 g (16 mmol) of boron trifluoride etherate in 40 ml of diglyme. After oxidation with 30% hydrogen peroxide solution in an alkaline medium acidification gave *cis* lactone mixture (**3a–d**), bp 102–110° (3 mm), yield 1.9 g (10 mmol; 22%). By gas chromatographic analyses this lactone mixture was found to contain 2-(2-hydroxymethyl-3-methylcyclopentyl)butyric acid lactones (**3a–d**) (78%) and an isomeric mixture of γ-lactones (22%), 2-(2-hydroxy-2,3-dimethylcyclopentyl)butyric acid lactones, which were identified by comparison with an authentic sample synthesized as described below.

Gas chromatography of **3a–d** revealed that this mixture contained 90% *cis,trans* lactones (**3a** and **b**) and 10% *cis,cis* lactones (**3c** and **d**).

2-(2-Hydroxy-2,3-dimethylcyclopentyl)butyric Acid Lactone.—An ethereal solution of methylmagnesium iodide prepared from 7.6 g (53.5 mmol) of methyl iodide and 1.3 g (53.5 mg-atoms) of magnesium was added to an ethereal solution of 8.5 g (40 mmol) of ethyl 2-(3-methyl-2-oxocyclopentyl)butyrate (**6**) in the course of 15 min, and the reaction mixture was heated under reflux for 1 hr. The reaction complex was decomposed by addition of an aqueous ammonium chloride solution and extracted with ether. After evaporation of ether, 40 ml of water and 2.5 g of sodium hydroxide were added to the residue, and the mixture was heated for 4 hr under reflux. After removal of unsaponified material, the aqueous layer was acidified to pH 3 with hydrochloric acid and heated for 30 min under reflux. The cooled reaction mixture was extracted with ether. On evaporation of ether, there was obtained 1.5 g (65%) of 2-(2-hydroxy-2,3-dimethylcyclopentyl)butyric acid lactone: bp 97–107° (4 mm); n^{24}D 1.4624; ir (liquid film) 1770 cm^{-1}.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.21; H, 9.97.

Selective Hydroboration Synthesis of (±)-*cis,cis*-2-(2-Hydroxymethyl-3-methylcyclopentyl)butyric Acid Lactones (3c and 3d).—To a solution of 1.55 g (0.022 mol) of 2-methyl-2-butene in 15 ml of tetrahydrofuran (THF), 4.1 ml of a THF solution of diborane (containing 0.010 mol of BH_3) was added at 0° under an atmosphere of nitrogen, and the mixture was stirred for 1 hr at 0° and for 2 hr at room temperature. The mixture was cooled to 0° and 4.2 g (0.020 mol) of ethyl 2-(3-methyl-2-methylenecyclopentyl)butyrate (**7–10**) was added and stirred for 2 hr at 0°. After standing overnight at room temperature, to the reaction mixture was added, at 0°, 1 ml of water, 5 ml of 3 *N* sodium hydroxide solution, and 5 ml of 30% hydrogen peroxide in a course of 15 min. After vigorous stirring for an additional 30 min

(31) "Carbonyl plane" means the plane drawn through the carbon of the carbonyl group normal to the axis of the carbonyl bond.

(32) R. P. Linstead and R. L. Jones, *J. Chem. Soc.*, 616 (1936).

(33) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).

at room temperature, the product was extracted with ether. Ether extract was washed with saturated sodium chloride solution, dried (Na_2SO_4), and concentrated. Evaporation residue afforded, on vacuum distillation, 2.5 g (60% recovery) of unchanged olefinic esters, bp 95–110° (3 mm), which were proved by vpc and ir spectroscopy to be a mixture of **7** and **8**. The residue of the vacuum distillation (1.1 g) was added to a solution of 30 ml of aqueous 3 *N* sodium hydroxide solution containing 1 ml of ethanol and heated under reflux for 5 hr with vigorous stirring. After cooling to room temperature, the solution was extracted with ether to remove unsaponified materials. The aqueous layer was acidified with hydrochloric acid and was extracted with ether. The ether extract was washed with water, dried (Na_2SO_4), concentrated, and distilled giving 0.4 g (0.0022 mol; 11%) of (±)-*cis,cis*-2-(2-hydroxymethyl-3-methylcyclopentyl)butyric acid lactones, **3c** and **d**, bp 100–115° (5 mm). Gas chromatography revealed that this *cis,cis* lactone mixture, **3c** and **d**, contained 9% *cis,trans* lactones, **3a** and **3b**.

From vpc, these *cis,cis* lactones were considered to be an about 1:2 mixture of **3c** and **d**. Pure **3c** and **d** were obtained by preparative vpc.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.62; H, 9.70.

Compound **3c** had the following spectral data: ir (liquid film), 1755, 1120, 1050, 1020 cm^{-1}; nmr ($CDCl_3$) δ 1.07 (d, 3, J = 6 Hz, CH_3–CH), 0.98 (t, 3, J = 7 Hz, CH_3–CH_2), 1.20–3.00 (m, 10), 4.31 (m, 2, –CH_2–O).

Compound **3d** had the following spectral data: ir (liquid film), 1755, 1160, 1100, 1055, 1020 cm^{-1}; nmr ($CDCl_3$) δ 1.00 (d, 3, J = 6 Hz, CH_3–CH), 1.05 (t, 3, J = 7 Hz, CH_3–CH_2), 1.20–3.00 (m, 10), 4.15 (m, 2, –CH–O).

(±)-*cis,trans*-2-(2-Hydroxymethyl-3-methylcyclopentyl)butyric Acid Lactones (3a and 3b).—To a THF (10 ml) solution of 2.4 g (11.4 mmol) of the *trans* olefinic ester (**7** and **8**), recovered as an unchanged residue in the above preparation, 3.5 ml of a THF solution of diborane containing 8.36 mmol of BH_3 was added at 0° under an atmosphere of nitrogen. After usual treatment there was obtained a mixture of *cis,trans* lactones, **3a** and **b**: bp 114–116° (5 mm); yield 1.0 g (48%). Vpc showed that this mixture contained 3% *cis,cis* lactones, **3c** and **d**, but no **3g** and **h**.

The separation of **3a** and **b** proceeded with difficulty by ordinary vpc (packed column with HVSG, PEG-6000, Apiezon-L or succinate polyester). However, from this mixture, **3a** crystallized out and recrystallization from petroleum ether (bp 60–80°) gave a pure sample, mp 55°. Pure **3b** was prepared by preparative vpc on an HVSG column.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.41; H, 10.14.

Compound **3a** had the following spectral data: ir (liquid film), 1755, 1175, 1160, 1110, 1080, 920, 755 cm^{-1}; nmr ($CDCl_3$) δ 1.05 (d, 3, J = 5 Hz, CH_3–CH), 0.98 (t, 3, J = 7 Hz, CH_3–CH_2), 1.20–2.90 (m, 10), 4.22 (m, 2, –CH_2–O).

Compound **3b** had the following spectral data: ir (liquid film) 1755, 1160, 1125, 1105, 1055, 1025 cm^{-1}; nmr ($CDCl_3$) δ 1.05 (d, 3, J = 5 Hz, CH_3–CH), 0.99 (t, 3, J = 7 Hz, CH_3–CH_2), 1.10–2.30 (m, 10), 4.10 (m, 2, –CH_2–O).

Ethyl 2-(2-Methoxymethylene-3-methylcyclopentyl)butyrates (11 and 12).—To a mixture of 70 ml of 1,2-dimethoxyethane, 1.45 g (60 mmol) of sodium hydride (2.9 g of 50% suspension in mineral oil) and 1 drop of ethanol was added 20.6 g (60 mmol) of methoxymethyltriphenylphosphonium chloride.[34,35] To the phosphorane was added 6.35 g (30 mmol) of ethyl 2-(3-methyl-2-oxocyclopentyl)butyrate (**6**). Treatment as reported previously[12] afforded 5.6 g (24 mmol; yield 78%) of ethyl 2-(2-methoxymethylene-3-methylcyclopentyl)butyrate: bp 107–109° (2 mm); $n^{20}D$ 1.4640; ir (liquid film) 1740, 1680, 1120 cm^{-1}.

Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.87; H, 9.96.

Ethyl 2-(2-Formyl-3-methylcyclopentyl)butyrates (13 and 14).—According to the procedure of Levine,[34] hydrolysis of methoxymethylene group was effected by adding 2.15 g (8.95 mmol) of ethyl 2-(2-methoxymethylene-3-methylcyclopentyl)butyrates (**11** and **12**) to 30 ml of ether saturated with 70% perchloric acid to give 1.9 g (94% yield) of ethyl 2-(2-formyl-3-methylcyclopentyl)butyrate: bp 107–109° (3 mm); $n^{24}D$ 1.4543; ir (liquid film) 2700, 1735 cm^{-1}.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.99; H, 9.80. Found: C, 68.92; H, 9.95.

The **2,4-dinitrophenylhydrazone** had mp 180–181°.

Anal. Calcd for $C_{19}H_{26}O_6N_4$: C, 56.14; H, 6.45; N, 13.79. Found: C, 56.15; H, 6.49; N, 13.65.

(±)-*trans,trans*-2-(2-Hydroxymethyl-3-methylcyclopentyl)butyric Acid Lactones (3e and 3f).—A solution of 1.0 g (4.4 mmol) of ethyl 2-(2-formyl-3-methylcyclopentyl)butyrates (**13** and **14**), 50 mg (1.3 mmol) of sodium borohydride, and 15 ml of ethanol was stirred for 1 hr. After decomposition of the residual active hydride with dilute hydrochloric acid, the reaction mixture was added to a solution of 5 g of sodium hydroxide in 20 ml of water and boiled for 4 hr under vigorous stirring. During the heating, ethanol was distilled off. After cooling, unsaponified materials were removed by extraction with ether. The aqueous solution was acidified with hydrochloric acid and refluxed for 30 min. The cooled reaction mixture was extracted with ether, and the ether extract was washed with water and dried (Na_2SO_4). When ether was evaporated, 0.5 g (2.8 mmol; yield 63%) of *trans,trans*-2-(2-hydroxymethyl-3-methylcyclopentyl)butyric acid lactones, **3e** and **f**, was obtained: bp 120–130° (5 mm); $n^{23}D$ 1.4748.

As determined by vpc peak areas, this mixture contained 79% **3e** and 21% **3f**. Using Goley column (BDS-45), this mixture was shown to be a mixture of only two components (**3e** and **f**) out of the possible four isomers (**3e–h**). Pure **3e** and **f** were obtained by preparative vpc.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.59; H, 10.08.

Compound **3e** had the following spectral properties: ir (liquid film) 1740, 1170, 1130, 1105, 1080, 1020 cm^{-1}; nmr ($CDCl_3$) δ 1.04 (d, 3, J = 5 Hz, CH_3–CH), 0.94 (t, 3, J = 7 Hz, CH_3–CH_2), 1.00–2.50 (m, 9), 3.45 (q, 1, J = 7 Hz, —CH—C=O), 4.02 (m, 1, –CH–O–), 4.49 (m, 1, –CH–O–).

Compound **3f** had the following spectral properties: ir (liquid film) 1740, 1190, 1105, 1060, 1020 cm^{-1}; nmr ($CDCl_3$) δ 1.04 (d, 3, J = 5 Hz, CH_3–CH), 1.04 (t, 3, J = 7 Hz, CH_3–CH_2), 1.10–2.40 (m 9), 2.60 (m 1, —CH—C=O), 3.95 (m, 1, –CH–O–), 4.46 (m, 1, –CH–O–).

(±)-*trans,trans*-Iridolactones (2e and f).—Pure **2e** and **f** were separated from the products reported previously[12] by preparative vpc.

Compound **2e** had the following spectral data: ir (liquid film) 1740, 1175, 1135, 1110, 1070, 1040, 1010 cm^{-1}; nmr ($CDCl_3$) δ 1.04 (d, 3, J = 5 Hz, CH_3-cyclopentane), 1.26 (d, 3, J = 7 Hz, CH_3-lactone), 1.00–2.50 (m, 8), 4.02 (m, 1, –CH–O–), 4.49 (m, 1, –CH–O–).

Compound **2f** had the following spectral data: ir (liquid film) 1740, 1220, 1195, 1105, 1040, 1010 cm^{-1}; nmr ($CDCl_3$) δ 1.04 (d, 3, J = 5 Hz, CH_3-cyclopentane), 1.23 (d, 3, J = 7 Hz, CH_3-lactone), 0.90–2.50 (m, 7), 2.87 (m, 1, –CH–C=O), 3.95 (m, 1, –CH–O–), 4.46 (m, 1, –CH–O–).

Conversion of 3a into 3b.—According to the procedure for conversion of isoiridomyrmecin into an equilibrium mixture of iridomyrmecin and isoiridomyrmecin,[36] 25 mg of **3a** in 2.5 ml of quinoline was heated at reflux temperature for 50 hr under an atmosphere of nitrogen. Vpc analysis of the reaction mixture showed that the product was about 1:1 mixture of **3a** and **3b**.

Conversion of 3d into 3c.—In the same way as described above, 10 mg of **3d** was treated with quinoline. Vpc analysis of the reaction mixture showed that it was composed of 24% **3c** and 76% **3d**.

Treatment of 3a through 3d with Sodium Methoxide.—According to Cavill and Locksley,[3c] 100 mg of an equimolar mixture of **3a** through **3d** was added to a solution of 110 mg of sodium dissolved in 15 ml of methanol. After refluxing for 2 hr, methanol was evaporated. The reaction mixture was acidified with dilute hydrochloric acid and was extracted with ether. The ether extract was washed with water and dried over anhydrous sodium sulfate. Evaporation of ether gave 85 mg of an oily substance. Vpc analysis of the substance indicated the disappearance of **3a** and **c**.

Methylation of Lactone 3a.—To 23 ml of a freshly prepared ethereal solution containing 3.45 mmol of triphenylmethylsodium, 0.50 g (2.75 mmol) of **3a** dissolved in 5 ml of ether was added under an atmosphere of nitrogen at room temperature. To this orange solution 1.0 g of methyl iodide was added and, after standing overnight at room temperature, the reaction mixture was added to a solution of 0.5 ml of acetic acid and 10 ml of water.

(34) S. G. Levine, *J. Amer. Chem. Soc.*, **80**, 6150 (1958).

(35) G. Wittig and M. Schlosser, *Chem. Ber.*, **94**, 1373 (1961).

(36) R. H. Jaeger and R. Robinson, *Tetrahedron Lett.*, No 15, 14 (1959).

The organic layer was extracted with ether, and the ethereal solution was washed with water and 10% sodium carbonate. The solution was kept over anhydrous sodium sulfate, ether was removed, and the residue was distilled to give 0.5 g of a mixture of lactones, bp 115–120° (5 mm). Vpc on HVSG showed that the mixture was composed of a mixture (89%) of **4a** and **b**, whose ratio was 31:69, and a mixture (11%) of unchanged **3a** and its epimeric lactone **3b**. Accordingly, the yield of a mixture of **4a** and **b** was found to be 80%.

Pure **4a** and **b** were separated by preparative vpc.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.21; H, 9.99.

Ethylation of Isoiridomyrmecin (2b).—From 0.93 g (5.5 mmol) of (+)-isoiridomyrmecin [(+) **2b**], $[\alpha]_D$ +58°, prepared from citronellal according to Robinson, *et al.*,[7] 45 ml of an ethereal solution containing 6.7 mmol of triphenylmethylsodium and 2.0 g of ethyl iodide, there was obtained 1.0 g of a mixture of lactones, bp 122–125° (6 mm). Vpc analysis showed the presence of a mixture of **4a** and **4b** (88%), whose ratio was 86:14, and 12% unchanged isoiridomyrmecin and epimeric iridomyrmecin. The yield of **4a** and **4b** was therefore 81%.

Pure **4a** and **b** were separated by preparative vpc and their ir spectra were identical with those of samples obtained by methylation of **3a**, respectively.

Compound **4a** had the following spectral properties: ir (liquid film) 1750, 1120 cm^{-1}; nmr ($CDCl_3$) δ 1.05 (d, 3, J = 5 Hz, CH_3–CH), 0.93 (t, 3, J = 7 Hz, CH_3–CH_2), 1.16 (s, 3, CH_3–C), 1.00–2.50 (m, 9), 4.33 (m, 2, –CH_2–O).

Compound **4b** had the following spectral properties: ir (liquid film) 1750, 1120 cm^{-1}; nmr ($CDCl_3$) δ 1.05 (d, 3, J = 5 Hz, CH_3–CH), 0.91 (t, 3, J = 7 Hz, CH_3–CH_2), 1.27 (s, 3, CH_3–C), 1.10–2.50 (m, 9), 4.33 (m, 2, –CH_2–O).

2-(2-Hydroxymethyl-3-methylcyclopentyl)butanol from Olefinic Esters, 7–10.—To a solution of 1.80 g (8.6 mmol) of ethyl 2-(3-methyl-2-methylenecyclopentyl)butyrate (**7–10**) in 15 ml of anhydrous THF was added 5 ml of a THF solution containing 5 mmol of diborane at 0°. After stirring for 3 hr at 0° and standing overnight at room temperature, 10 ml of a THF solution containing 10 mmol of diborane was added once again. After keeping at room temperature for 2 days, 1 ml of water was added to the reaction mixture to decompose excess active hydride. Oxidative cleavage of carbon–boron bond was operated by addition of 15 ml of 3 N sodium hydroxide and 5 ml of 30% hydrogen peroxide with vigorous stirring over a 10-min period. About 20 ml of THF was distilled off; the reaction mixture was heated at reflux for 5 hr. After cooling, the organic layer was extracted three times with ether, and the ether extract was washed with saturated sodium chloride solution and dried (Na_2SO_4). Distillation gave 1.5 g (94% yield) of the isomeric mixture of the diols: bp 143–146° (2 mm); $n^{23}D$ 1.4875; ir (liquid film) 3340, 1030 cm^{-1}.

Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 71.03; H, 11.78.

2-(2-Acetoxymethyl-3-methylcyclopentyl)butyl Acetates (15–18).—To 1.1 g (5.9 mmol) of the diol mixture was added 15 ml of pyridine together with 15 ml of acetic anhydride and the solution was kept at room temperature overnight. The reaction mixture was treated as usual to give 1.3 g (4.8 mmol; yield 82%) of the diacetates (**15–18**): bp 141–142° (3 mm); $n^{20}D$ 1.4573; ir (liquid film) 1745, 1240, 1035 cm^{-1}.

Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.63; H, 9.69. Found: C, 66.85; H, 9.64.

Diacetate 15 and 16 from Lactones 3a and 3b.—To a stirred slurry of 50 mg of lithium aluminum hydride in 10 ml of dry ether was added 80 mg (0.44 mmol) of *cis,trans* lactones **3a** and **b**, and 30 mg of triphenylmethane which was used as an internal standard for the gas chromatographic yield calculation. After refluxing for 3 hr the complex was decomposed with 5 ml of saturated sodium chloride solution and 10 ml of 10% sulfuric acid. The reaction mixture was extracted three times with ether, washed once with saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Evaporation of ether gave an oily substance whose ir spectrum indicated no carbonyl absorption. To this oil was added 2 ml of pyridine together with 2 ml of acetic anhydride. The reaction mixture was kept at room temperature overnight and worked up as described above. Vpc analysis of the oily product indicated the presence of 109 mg (0.40 mmol; yield 92%) of the *cis,trans* diacetates **15** and **16**. Pure mixture of **15** and **16** was obtained by preparative vpc. Ir spectrum of this mixture was identical with that of diacetates obtained directly from the olefinic esters **7–10**.

Diacetates 17 and 18 from Lactones 3c and 3d.—In the same way, from 71 mg (0.39 mmol) of *cis,cis* lactones **3c** and **d**, there was obtained 93 mg (0.34 mmol; yield 88%) of the isomeric mixture of *cis,cis* diacetates **17** and **18**, whose pure sample was obtained by preparative vpc. Ir spectrum of this mixture was almost identical with that of the mixture of **15** and **16**, but the retention times of vpc on HVSG or PEG-6000 column was different from each other.

Comparison of the Vapor Phase Chromatograms of the Diacetates 15–18.—Vpc analysis of the diacetates **15–18** derived directly from the olefinic esters **7–10** showed that the diacetates were composed of 90% *cis,trans* isomers **15** and **16** and 10% *cis,cis* isomers **17** and **18**.

Registry No.—**1a**, 16802-11-2; **1c**, 16802-12-3; **1e**, 16802-13-4; **1g**, 16802-14-5; (−) **2a**, 16802-15-6; (+) **2b**, 16802-16-7; **2e**, 16802-17-8; **2f**, 16802-18-9; **3a**, 16802-19-0; **3b**, 16802-20-3; **3c**, 16802-21-4; **3d**, 16802-22-5; **3e**, 16802-23-6; **3f**, 16802-24-7; **4a**, 16802-25-8; **4b**, 16802-26-9; **5**, 16802-27-0; *cis* **6**, 16802-30-5; 2,4-dinitrophenylhydrazone of *cis* **6**, 16802-31-6; free acid of *cis* **6**, 16802-28-1; 2,4-dinitrophenylhydrazone of free acid of *cis* **6**, 16802-29-2; *trans* **6**, 16802-07-6; 2,4-dinitrophenylhydrazone of *trans* **6**, 16802-08-7; free acid of *trans* **6**, 16802-09-8; 2,4-dinitrophenylhydrazone of free acid of *trans* **6**, 16802-10-1; 2-(2-hydroxy-2,3-dimethylcyclopentyl)butyric acid lactone, 16802-32-7; **7**, 16802-33-8; **8**, 16802-34-9; **9**, 16802-35-0; **10**, 16802-36-1; **11**, 16802-37-2; **12**, 16802-38-3; **13**, 16802-39-4; 2,4-dinitrophenylhydrazone of **13**, 16802-40-7; **14**, 16802-41-8; 2,4-dinitrophenylhydrazone of **14**, 16802-42-9; **15**, 16802-43-0; **16**, 16802-44-1; **17**, 16802-45-2; **18**, 16802-46-3.

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