followed by the calculation of a difference electron density synthesis which revealed most of the hydrogen atom positions. Full-matrix least-squares refinements in which the positional and anisotropic thermal parameters of the nonhydrogen atoms were varied and the anomalous contribution of the Br (2.6 electrons) was included have converged to a standard crystallographic residual of 0.063 for the structure and 0.071 for its enantiomer. (See supplementary material for additional crystallographic details.)

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Registry No. 3, 72853-80-6; 4, 17274-65-6; 5, 61-50-7; 6, 72853-81-7; 7, 72853-82-8; 8, 72853-83-9; 9, 72853-84-0; 10, 72853-85-1; 11, 72853-86-2; 12, 72853-87-3; 14, 69809-39-8; 15, 72866-02-5; 16, 39707-54-5; 17, 69880-60-0; 18, 69809-38-7; 19, 72903-64-1; 20, 72937-17-8; 21, 57291-88-0; 22, 72903-65-2; 23, 72853-88-4; 24, 72853-89-5; 25, 72853-90-8; 25 acetate, 72853-91-9; 27, 72853-92-0.

Supplementary Material Available: Positional and thermal parameters (Table 1), bond distances (Table 2), and bond angles (Table 3) (5 pages). Ordering information is given on any current masthead page.

Tulirinol, an Antifeedant Sesquiterpene Lactone for the Gypsy Moth Larvae from *Liriodendron tulipifera*

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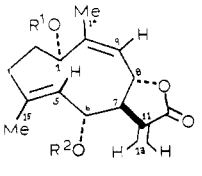
The isolation and structure determination of tulirinol (1), an antifeedant for the gypsy moth larvae from the leaves of *Liriodendron tulipifera* L., are reported. Tulirinol is the first recognized *trans*-4,*cis*-9-cyclodecadiene sesquiterpene, details of which are given for its characterization by spectral methods including X-ray crystallography. The absolute stereochemistry was determined by the Horeau partial resolution method. Tatridin A was identified as deacetyltulirinol (5).

The leaves of *Liriodendron tulipifera* L. (Magnoliaceae), commonly known as the tulip poplar, gave an ethanolic extract that inhibited the feeding of gypsy moth larvae, *Lymantria dispar* L.[2] Systematic fractionation of the extract has already yielded three feeding-deterrent sesquiterpene lactones: lipiferolide, epitulipinolide diepoxide,[3] and peroxyferolide.[4] This report is on the isolation and characterization of a fourth antifeedant, tulirinol (1), by spectral and chemical methods, including X-ray crystallography.

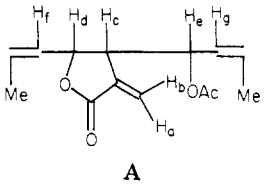
Tulirinol (1), mp 204–6 °C, was isolated by extensive



1; R^1 = H, R^2 = Ac
2; R^1 = R^2 = Ac
5; R^1 = R^2 = H
6; R^1 = PhCH(Et)CO, R^2 = Ac

chromatography of a partition fraction by monitoring biological activity at each stage of purification.[5] The molecular formula, $C_{17}H_{22}O_5$, was established by elemental analysis and mass spectrometry. The IR spectrum showed absorptions for hydroxyl, two carbonyls, a lactone (1768 cm^{-1}), and an ester (1738 cm^{-1}), while the UV spectrum had a low-wavelength peak at λ_{max} 208 nm (log ϵ 4.33) typical of an α-methylene γ-lactone. The ^1H NMR spectrum was most informative, exhibiting two weakly split olefinic methyl peaks at δ 1.81 and 1.91, and a three-proton singlet at δ 2.05 assignable to an acetate methyl. At low field, a pair of doublets with additional fine splitting (J = 0.6 Hz) were located at δ 5.72 (J = 3.1 Hz) and 6.07 (J = 3.4 Hz), which are characteristic of γ-lactone α-methylene protons.

Double-resonance experiments allowed for the ordering of all functional groups except the hydroxyl. Irradiation at either of the two exocyclic olefinic proton frequencies caused collapse of the geminal coupling (0.6 Hz) in the other and a change in a multiplet at δ 3.08 (H_c) from a triple triplet to a split triplet. These protons, H_a, H_b, and H_c, could be arranged as in A. Irradiation at δ 3.08 col-



A

(1) (a) Department of Pharmacology, Case Western Reserve University, Cleveland, OH. (b) American Cyanamid Co., Bound Brook, NJ.
(2) R. W. Doskotch, T. M. ODell, and P. A. Godwin, *Environ. Entomol.*, **6**, 563 (1977).
(3) R. W. Doskotch, S. L. Keely, Jr., C. D. Hufford, and F. S. El-Feraly, *Phytochemistry*, **14**, 769 (1975).
(4) R. W. Doskotch, F. S. El-Feraly, E. H. Fairchild, and C.-T. Huang, *J. Org. Chem.*, **42**, 3614 (1977).
(5) Tulirinol showed a significant feeding inhibitory activity.[2] At concentrations of 50 and 250 μg/mL feeding was 69 and 53%, respectively.

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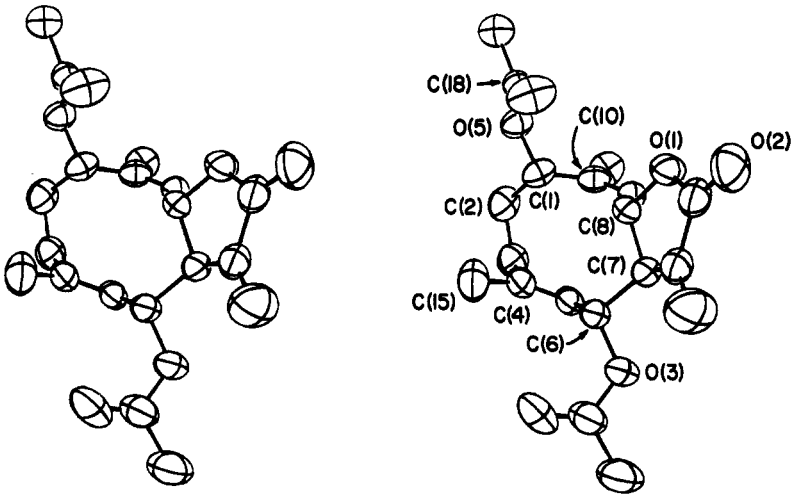
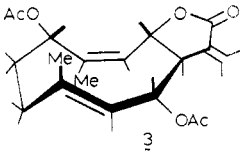


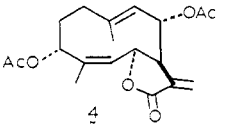
Figure 1. ORTEP stereoview of tulirinol acetate viewed on the β face. The thermal ellipsoids are drawn at the 50% level. Hydrogen atoms are omitted for clarity, and only one of the two possible conformations of the disordered acetoxy substituent at C(1) is shown.

lapsed the H_a and H_b double doublets to doublets and simplified two additional patterns. The double doublet at δ 4.78 (J = 8.7, 10.1 Hz) was reduced to a doublet (J = 10.1 Hz), as was another at δ 5.51 (J = 9.5, 10.4 Hz), with loss of the 9.5-Hz coupling. These protons, H_d and H_e, were assigned from chemical shift positions (vide infra) to carbons bearing the ether oxygens of the lactone and the ester, respectively. In turn, successive irradiation at δ 4.78 and 5.51 identified the neighboring protons H_f and H_g as broadened doublets located at 5.32 and 4.89 ppm, respectively, and changed them to broadened singlets. The signal broadening was shown to be due to allylic coupling with olefinic methyls. The methyl at δ 1.81 interacted with H_f (δ 5.32), and the one at δ 1.91 with H_g (δ 4.89). A somewhat broadened double triplet at δ 4.44 remained unaffected by the double-irradiation experiments and was considered to be the proton on a hydroxyl-bearing carbon. D_2O exchange sharpened the pattern and also eliminated a one-proton doublet at δ 3.87, which, incidently, reverted to a singlet upon irradiation at δ 4.44. In addition, acetylation of tulirinol (1) produced the acetate 2 whose ^1H NMR spectrum showed a downfield shift of the 4.44-ppm proton to 5.5 ppm, as well as a second acetate peak at δ 1.98.

Since the molecular formula of tulirinol (1) requires seven double-bond equivalents, six of which are accounted for by the unsaturated lactone, two olefins, and and acetate, the one remaining must be for a ring system. Furthermore, all of the oxygens were assigned and no aliphatic methyls were indicated, thereby requiring a ten-membered alicyclic ring. The olefins would be at positions 1 and 6, rather than 1 and 5 as in a normal germacrane ring. The alcoholic function must reside on one of the three carbons not indicated by the double-resonance experiments, but the exact location remained uncertain, although an allylic position was favored from the width of the ^1H NMR pattern for the proton on the alcoholic carbon. Some indication of relative stereochemistry or disposition of the substituents could be inferred from the ^1H coupling constants—all 9 Hz or higher, agreeing with a trans diaxial arrangement of the relevant protons (H_c through H_g); but lack of knowledge about the ring conformation precludes an established proof. Unavailability of sufficient quantities of tulirinol (1) prevented a chemical solution to the remaining structural problems (geometric and relative stereochemistry) as well as to location of the hydroxyl; thus an X-ray crystallographic study was initiated. Tulirinol (1) itself did not give suitable crystals, but the acetate derivative 2 was satisfactory, and resulted in the structure shown in Figure 1. Before the X-ray results were examined in greater detail, it was immediately evident from the derived structure that one of the double bonds of tulirinol is cis and bears an allylic hydroxyl group. Also, the ring conformation was found to be boat–chair and can be stylized as in 3 with the H(5) to H(9) protons pseudoaxially disposed—an arrangement originally indicated by the proton coupling values.



3



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The X-ray results provided only the relative stereochemistry for tulirinol acetate (2), and the molecule could accordingly also fit the heliangolide configuration 4. The absolute stereochemistry was subsequently determined by application of the Horeau procedure for establishment of the configuration at the alcoholic carbon.[6] For a closely related example, eurecurvin acetate, which bears a secondary alcohol flanked by a cis olefin and a methylene, this technique yielded conclusive results.[7] Esterification of tulirinol (1) with optically inactive α-phenylbutyric anhydride resulted in recovery of (−)-α-phenylbutyric acid in an optical yield of 56%. This requires an S configuration for the arrangement of substituents at C(1) and an absolute stereochemical structure for tulirinol as in 1. In keeping with the convention[8] of numbering the germacrane ring with reference to placing the lactone carbon [C(11)] substituent β at C(7) [H(7) is α], tulirinol (1) is, therefore, a 7,8-lactone but not of a standard subgroup.[9]

(6) (a) A. Horeau in "Stereochemistry, Fundamentals and Methods", Vol. 3, H. B. Kagan, Ed., Thieme, Stuttgart, 1977, p 51. (b) W. Herz and H. Kagan, *J. Org. Chem.*, **32**, 216 (1967).

(7) W. Herz, R. de Groote, R. Murari, and J. F. Blount, *J. Org. Chem.*, **43**, 3559 (1978).

(8) D. Rogers, G. P. Moss, and S. Neidle, *J. Chem. Soc., Chem. Commun.*, 142 (1972).

In assigning the ^1H NMR chemical shifts for the protons of tulirinol (1) and its derivatives, the designation of the proton on the carbon bearing the ether oxygen of the lactone, to which others would be related, was uncertain. Generally, the high-field position is associated with the lactonic group, while the corresponding proton on an ester-containing carbon is at lower field, with olefinic geometry playing an important role.[10] Since the double bonds of tulirinol (1) are not in the usual biogenetic positions, the unequivocal location of the lactonic and ester-related protons becomes all the more important. For example, in sesquiterpene lactones with 4 and 9 double bonds cis, the ester-related proton is located at higher field than those of the lactone.[7] To settle the case for tulirinol (1), alkaline hydrolysis and relactonization under acidic conditions afforded a diol, deacetyltulirinol (5), which on acetylation gave acetyl tulirinol (2). The lactonic proton [H(8)] in diol 5 was located at 4.65 ppm and the H(6) proton at 4.49 ppm. Double irradiation was employed as an aid in the assignments (Table I), details of which will not be presented. Thus, for trans-4,cis-9-sesquiterpene lactones, the chemical shift relationship for ester and lactonic protons follows the order observed for the cis-1-(10),trans-4 cases. The α-phenylbutyryl ester 6 of tulirinol (1) from the Horeau procedure lent support to the chemical shift designations. The olefinic methyl [H(14)] doublet of tulirinol located at 1.82 ppm (J = 1.3 Hz) is shifted upfield to 1.51 ppm in the ester 6 as a result of the magnetic shielding from the neighboring phenyl ring.

A generalization can be made concerning the preferential direction of relactonization of alkali-hydrolyzed *trans*-4,*cis*-9-cyclodecadiene terpenes with α-hydroxy groups at C(6) and C(8) to form trans γ-lactones. Since no C(6) lactone was obtained from tulirinol, the more stable lactone results from cyclization to C(8). A similar observation was made earlier[11] for the standard germacranolides, which, more recently, have been the subject of molecular mechanics calculation.[12] To our knowledge, tulirinol (1) is the first recognized *trans*-4,*cis*-9-cyclodecadiene sesquiterpene lactone. However, comparison of the physical properties of deacetyltulirinol (5) with those reported for the incompletely characterized tatridin A[13] suggested the two are very probably the same.

Table I. ^1H NMR Spectra of Tulirinol and Derivatives[a]

compd	H(1)	H(5)	H(6)	H(7)	H(8)	H(9)	H(13)	H(14)	H(15)	miscellaneous
1[b] (315 K)	4.44 dt (3, 4, 11)	4.89 br d (10.4)	5.51 dd (9.5, 10.4)	3.08 tt (3.1, 3.4, 8.7, 9.5)	4.78 dd (8.7, 10.1)	5.32 dq (1.3, 10.1)	6.07 dd (0.6, 3.4) 5.72 dd (0.6, 3.1)	1.81 d (1.3)	1.91 br s (~1.2)	2.05 s (Ac) 3.87 d (4, OH)
1[c]	4.42 br m	4.83 br d (10)	5.42 dd (10, 10)	3.03 tt (2.9, 3.2, 9.5, 10)	4.66 dd (9.5, 9.5)	5.32 br d (9.5)	6.26 d (3.2) 5.73 d (2.9)	1.82 d (1.3)	1.89 br s	2.08 s (Ac)
2[b]	5.5 m (hidden)	4.92 br d (10)	5.60 dd (8.9, 9.5)	3.16 tt (3.1, 3.2, 8.9, 8.9)	4.89 dd (8.9, 8.9)	5.5 dq (partly hidden) (1.6, 9.5)	6.08 dd (0.7, 3.2) 5.77 dd (0.7, 3.1)	1.84 d (1.6)	1.97 br s	1.98 s (Ac) 2.08 s (Ac)
5[b]	4.42 m (hidden)	4.96 br d (10)	4.49 dd (9, 10)	2.80 tt (3.2, 3.5, 9, 9)	4.65 dd (9, 10)	5.28 dq (1.4, 10)	6.18 dd (1.6, 3.2) 6.09 dd (1.6, 3.5)	1.80 d (1.4)	1.79 br s	
6[c]	5.4 m (hidden)	4.83 br d (10)	5.40 dd (10, 11)	3.00 tt (3, 3, 10, 11)	4.78 dd (10, 10)	5.30 dq (1.3, 10)	6.26 d (3) 5.72 d (3)	1.51 d (1.3)	1.92 br s	2.08 s (Ac) 0.87 t (7.3, CH_3CH_2) 1.8 m (CH_3CH_2) 3.39 t (7.6, PhCHBt) 7.25 br s (Ph)

[a] Spectra were determined in stated solvent at 90 MHz with Me_4Si as internal standard. Chemical shifts (δ) are in parts per million, coupling constants (J in Hz) are given in parentheses, and multiplicities are designated by the following symbols: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet with center given; and br, broadened signal. [b] In acetone-d_6. [c] In $CDCl_3$.

(9) We had classified tulirinol as a melampolide from the presence of the trans-4 and a cis olefin, although the latter is not in the biogenetically expected 1,10-position [for classifications see (a) S. Neidle and D. Rogers, *J. Chem. Soc., Chem. Commun.*, 140 (1972); (b) S. F. Watkins, N. H. Fischer, and I. Bernal, *Proc. Natl. Acad. Sci. U.S.A.*, **70**, 2434 (1973)], but the referees objected. Their point is well-taken if the current adoption of subgroup names is to be strictly applied. Tulirinol does not fit into any group, nor can it be called a germacranolide, since this name is reserved for the *trans*-1(10),*trans*-4-cyclodecadienes. May we suggest that germacranolides be retained as the generic name for all cyclodecadiene sesquiterpene lactones and that costunolides be introduced for the biogenetically correct trans-1(10),trans-4 cases. With this change, the terpenes not fitting into the distinct groups would be called germacranolides prefixed with the appropriate stereochemistry and numerical designations (e.g., tulirinol is then a *trans*-4,*cis*-9-germacranolide).

(10) Germacranolides [double bonds at 1(10) and 4 both trans] follow the pattern, examples of which can be found in R. W. Doskotch and F. S. El-Feraly, *J. Org. Chem.*, **35**, 1928 (1970), and H. Tada and K. Takeda, *Chem. Pharm. Bull.*, **24**, 667 (1976), as do melampolides [cis-1(10),trans-4] given in N. H. Fischer, R. A. Wiley, D. L. Perry, and K. D. Haegele, *J. Org. Chem.*, **41**, 3956 (1976), while heliangolides [trans-1(10),cis-4] show the reverse feature: W. Herz and I. Wahlberg, *J. Org. Chem.*, **38**, 2485 (1973), and M. Holub and Z. Samek, *Collect. Czech. Chem. Commun.*, **42**, 1053 (1977).

(11) H. Yoshioka, W. Renold, and T. J. Mabry, *J. Chem. Soc. D*, 148 (1970).

(12) M. H. P. Guy, G. A. Sim, and D. N. J. White, *J. Chem. Soc., Perkin Trans. 2*, 1917 (1976).

(13) F. Shafizadeh and N. R. Bhadane, *Phytochemistry*, **12**, 857 (1973); *J. Org. Chem.*, **37**, 274 (1972).

Table II. Torsion Angles (deg) for Tulirinol Acetate (2)[a]

atoms	angle	atoms	angle
C(3)-C(2)-C(1)-C(10)	+59.8	C(8)-O(1)-C(12)-O(2)	-170.0
C(2)-C(1)-C(10)-C(9)	-123.1	C(8)-C(7)-C(11)-C(12)	-20.8
C(1)-C(10)-C(9)-C(8)	+0.3	C(8)-C(7)-C(11)-C(13)	+157.9
C(10)-C(9)-C(8)-C(7)	+122.4	C(6)-C(7)-C(11)-C(12)	-142.9
C(9)-C(8)-C(7)-C(6)	-91.2	C(6)-C(7)-C(11)-C(13)	+157.9
C(8)-C(7)-C(6)-C(5)	+49.0	C(7)-C(11)-C(12)-O(1)	+8.7
C(7)-C(6)-C(5)-C(4)	-114.4	C(7)-C(11)-C(12)-O(2)	-172.9
C(6)-C(5)-C(4)-C(3)	+161.3	C(13)-C(11)-C(12)-O(1)	-170.2
C(5)-C(4)-C(3)-C(2)	-110.7	C(8)-C(7)-C(6)-O(3)	+167.8
C(4)-C(3)-C(2)-C(1)	+42.3	C(11)-C(7)-C(6)-C(5)	+166.1
C(2)-C(3)-C(4)-C(15)	+64.2	C(11)-C(7)-C(6)-O(3)	-75.1
C(3)-C(2)-C(1)-O(5)'	+172.9	O(3)-C(6)-C(5)-C(4)	+130.5
C(3)-C(2)-C(1)-O(5)	-174.1	C(6)-C(5)-C(4)-C(15)	-13.1
C(2)-C(1)-C(10)-C(14)	+56.6	C(7)-C(6)-O(3)-C(16)	+155.6
O(5)-C(1)-C(10)-C(9)	+121.3	C(5)-C(6)-O(3)-C(16)	-86.9
O(5)'-C(1)-C(10)-C(9)	+115.2	C(6)-O(3)-C(16)-C(17)	+178.5
O(5)-C(1)-C(10)-C(14)	-59.0	C(6)-O(3)-C(16)-O(4)	-2.8
O(5) -C(1)-C(10)-C(14)	-65.1	C(2)-C(1)-O(5)'-C(18)'	+95.8
C(15)-C(10)-C(9)-C(8)	-179.4	C(2)-C(1)-O(5)-C(18)	+146.0
C(10)-C(9)-C(8)-O(1)	-120.8	C(1)-O(5)-C(18)-C(19)	+173.6
C(9)-C(8)-C(7)-C(11)	+143.5	C(1)-O(5)'-C(18)'-O(6)'	+2.7
O(1)-C(8)-C(7)-C(6)	+150.5	C(10)-C(1)-O(5)'-C(18)'	-141.0
C(9)-C(8)-O(1)-C(12)	-146.8	C(10)-C(1)-O(5)-C(18)	-89.2
C(7)-C(8)-O(1)-C(12)	-21.6	C(1)-O(5)-C(18)-O(6)	-8.5

[a] Torsion angles for the lactone ring are given in Table V.

Figure 1 shows the configuration of the molecule as found in the X-ray structure determination, with the correct absolute stereochemistry. Well-localized trans and cis double bonds are present at the 4 and 9 positions, respectively, each bearing one methyl substituent. The conformation of the cyclodecadiene ring places these methyl groups in the anti configuration with C(15) β and C(14) α. The placement of the double bonds and the trans lactone fusion at C(7)–C(8) apparently relieves some strain in the ten-membered ring and permits it to adopt the chair–boat conformation more representative of the heliangolides[7,14] than of the melampolides.[9] The reduction in ring strain is most apparent in the torsion angles of the double bonds (Table II), which at 1° (cis) and 19° (trans) are significantly less than the 8° and 24° observed in melampodin.[9] The torsion angle of the trans olefin linkage in **2** can be resolved into a 6° bend (away from ring center) and a 13° twist about the bond axis.[15] Thus, the cyclodecadiene ring in **2**, though qualitatively more open than in most germacradienes, where bends and twists in the olefin linkages of this magnitude are common,[16,17] still reflects significant strain from transannular nonbonded interactions (Table 4 in supplementary material[18]). The interior angles around the ring deviate from ideal values, another indicator of ring strain. Although the C–C and C–O distances in the molecule are in general normal when the hybridization of the involved atoms is taken into account, the average of the aliphatic C–C bonds is, at 1.496 Å, somewhat shorter than usual. This is perhaps a consequence of inductive shortening at the carbons bearing oxygen substituents.

The acetoxy substituent at C(1) is disordered, with about 53% of the molecules possessing one of the two discrete conformations. The C(19) methyl group is immobilized by crystal packing contacts. Although C(1) must certainly also possess two alternative positions, it was not possible to refine two separate sites (as was done for O(5), C(18), and O(6); vide infra) because they appear to be separated by less than 0.1 Å. Each of the acetoxy substituents, including the half-populated acetoxy groups, is planar within experimental error. There being no hydrogen bond donors in the molecule, the crystal packing is dominated entirely by van der Waals contacts.

Table III. Lactone Ring Torsion Angles (deg) in Representative Sesquiterpene Lactones

torsion angle identifier	costunolide[19]	eupaformonin[14b]	melampodin[9b]	tulirinol acetate[a]
ω_1	-8.6	+4	+8.6	+8.5
ω_2	-9.7	+9	+19.1	+8.2
ω_3	-24.9	+14	+35.0	+25.2
ω_4	+88.6	+135	-75.8	-91.2
sign of Cotton effect	(-)	(+)	(+)	(+)

[a] This work. For tulirinol, the torsion angles are identified as follows: ω_1, C(8)-O(1)-C(12)-C(11); ω_2, C(13)-C(11)-C(12)-O(2); ω_3, C(11)-C(7)-C(8)-O(1); and ω_4, C(6)-C(7)-C(8)-C(9).

The endocyclic torsion angles of the γ-lactone ring are quite different from those found in other sesquiterpene lactones (Table III). Curiously, the values for tulirinol acetate (**2**) are almost perfectly negatively correlated with those for costunolide.[19]

The CD spectrum of tulirinol (**1**) shows three Cotton effect maxima which appear at 281, 236, and 211 nm. The highest wavelength maximum with $[\theta]$ +120° was assigned the n $\rightarrow$ π^* transition of the lactone carbonyl.[20] The

(14) (a) M. Nishikawa, K. Kamiya, A. Takabataki, H. Oshio, Y. Tomiie, and I. Nitta, *Tetrahedron*, **22**, 3601 (1966); (b) A. T. McPhail and K. D. Onan, *J. Chem. Soc., Perkin Trans. 2*, 578 (1976).

(15) These values were calculated by the method of F. K. Winkler and J. D. Dunitz, *J. Mol. Biol.*, **59**, 169 (1971).

(16) H. Koyama and Y. Mizuno-Tsukuda, *J. Chem. Soc., Perkin Trans. 2*, 646 (1977); D. N. J. White, *Helv. Chim. Acta*, **56**, 1347 (1973).

(17) M. A. Beno, Ph.D. Thesis, The Ohio State University, 1979.

(18) See paragraph at end of paper regarding supplementary material.

(19) M. J. Bovill, P. J. Cox, P. D. Cradwick, M. H. P. Guy, G. A. Sim, and D. N. J. White, *Acta Crystallogr., Sect. B*, **32**, 3203 (1976).

(20) The true transition wavelength would be less than the observed 281 nm, since the intense negative maximum at 236 nm in the summation with the weaker positive peak at the higher wavelength results in the apparent maximum of the latter being shifted to a higher wavelength. The lactonic n $\rightarrow$ π^* transition is normally found between 240 and 265 nm.[21]

empirical rule of Geissman and co-workers[21] correctly predicts a trans lactone closed to C-8 for tulirinol. Also, the lactone torsion angles listed in Table III for tulirinol acetate (2) show that the chirality of both the C=C—C=O and C(11)–C(7)–C(8)–O units are positive with respective values ω_2 +8.2° and ω_3 +25.2°,[22] and that according to the empirical rule of Beecham,[23] a positive Cotton effect should be observed for the n → π* transition of the lactone. This, indeed, is the case. Tulirinol (1), therefore, conforms to both the Geissman and Beecham rules. Since the interatomic distances[18] between the 4 and 9 double bonds appear too large for effective overlapping of orbitals to show transannular conjugation, the CD maxima at 236 and 211 nm were assigned to π → π* transitions of the lactone and olefin groups, respectively.

Experimental Section[4]

Isolation of Tulirinol (1). The ethanolic residue (1.5 kg) obtained from percolation of 6.7 kg of *L. tulipifera* leaves was partitioned between $CHCl_3$ and H_2O, and the $CHCl_3$ solubles were further divided between hexane and 10% aqueous MeOH as already described.[3] The residue (239 g) from the MeOH phase was taken up in 30% aqueous MeOH and extracted successively with hexane–$CHCl_3$ (4:1 and 1:1) to give 73 g of material from the last solvent, which was chromatographed in sequence through the following columns. Silicic acid (500 g, Mallinckrodt) containing 5% H_2O was eluted with $CHCl_3$ and 1%, 2%, and 5% MeOH in $CHCl_3$. The 2% and 5% MeOH in $CHCl_3$ residue (6.4 g) was separated on 120 g of silicic acid (2.5% H_2O) with C_6H_6–$CHCl_3$ (1:1 and 3:17) as eluents. The last solvent gave 4.5 g of material from which flavonoid constitutents were removed by filtration through a Sephadex LH-20 column (250 g) using MeOH as solvent. The effluent residue (3.06 g), rechromatographed on silicic acid (300 g, 2.5% H_2O) with 1.5% MeOH in $CHCl_3$, gave a fraction from which a total of 94 mg of tulirinol (1) was obtained, in a yield of 0.0014% from the dried leaves. TLC on silica gel G with hexane–EtOAc (2:3) R_f 0.33, (3:2, development ×3) R_f 0.35, or MeOH–$CHCl_3$ (3:97) R_f 0.29 was used for monitoring column fractions.

Tulirinol (1) crystallizes from Et_2O–$CHCl_3$ or absolute EtOH–hexane–*i*-Pr_2O as colorless needles: mp 204–6 °C; $[\alpha]^{23}_D$ -51° (*c* 0.3, MeOH); CD (*c* 3.3 × 10^{-3} M, MeOH) $[\theta]_{300}$ 0, $[\theta]_{281}$ +120, $[\theta]_{273}$ 0, $[\theta]_{236}$ -6900, $[\theta]_{226}$ (min) -4600, and $[\theta]_{211}$ -67 000°; UV λ_{max} 208 nm (log ε 4.33); IR ($CHCl_3$) ν_{max} 3585 (OH), 3420 (br, hydrogen-bonded OH), 1768 (lactone C=O), 1738 (ester C=O), 1660 (C=C), and 1627 cm^{-1} (weak C=C); ^1H NMR (90 MHz, Me_2CO-d_6) in Table I; ^{13}C NMR (22.63 MHz, $CDCl_3$) δ_c 15.6 and 16.8 (2 q, C(14) and C(15)), 21.0 (q, Ac), 27.2 (t, C(2)), 35.4 (t, C(3)), 49.2 (d, C(7)), 66.3 (d, C(1)), 73.2 (d, C(6)), 74.5 (d, C(8)), 122.5 (t, C(13)), 125.9 and 126.0 (2 d, C(5) and C(9)), 137.2 (s, C(11)), 138.2 and 143.2 (2 s, C(4) and C(10)), 169.7 (s, C(12)), and 170.1 (s, Ac); mass spectrum (EI), *m/e* 306 (0.1%, M^+), 288 (0.1, M – H_2O), 264 (0.6, M – CH_2CO), 246 (5, M – AcOH), 228 (4, M – H_2O – AcOH), 213 (5, M – H_2O – AcOH – Me), 191 (14), 161 (22), 121 (19), 95 (40), and 43 (100, Ac).

Anal. Calcd for $C_{17}H_{22}O_5$ (306): C, 66.65; H, 7.24. Found: C, 66.50; H, 7.20.

Tulirinol Acetate (2). A 13-mg sample of tulirinol (1) was mixed with 1 mL of pyridine and 0.5 mL of Ac_2O. After 16 h, H_2O was added, followed by absolute EtOH and C_6H_6. Evaporation of the mixture to dryness and crystallization of the residue from hexane–EtOAc gave 14 mg of acetate **2**: mp 208.5-9 °C; R_f 0.54 on TLC with hexane–EtOAc (2:3); $[\alpha]^{22}_D$ -83° (*c* 0.15, MeOH); CD (*c* 2.9 × 10^{-3} M, MeOH) $[\theta]_{300}$ 0, $[\theta]_{281}$ +96, $[\theta]_{273}$ 0, $[\theta]_{236}$ -9000, $[\theta]_{223}$ (min) -2800, and $[\theta]_{210}$ -85 000°; IR ($CHCl_3$) ν_{max} 1773 (lactone) and 1740 cm^{-1} (double intensity, ester); mass spectrum (EI), *m/e* 348.1581 (7%; $C_{19}H_{24}O_6$ requires 348.1573), 288 (3, M – AcOH), 228 (22, M – 2AcOH), and 43 (100, Ac).

A 5-mg sample of deacetyltulirinol (5) was treated with Ac_2O in pyridine to give 5.5 mg of crystalline tulirinol acetate (2) identified by direct comparison (melting point, $[\alpha]_D$, IR, and ^1H NMR) with a sample prepared from tulirinol (1).

Horeau Esterification of Tulirinol (1). A 10-mg (0.033 mmol) sample of 1 and 26.1 mg (0.084 mmol) of α-phenylbutyric anhydride were stirred in 2.5 mL of pyridine for 38 h at ambient temperature. After 1 mL of H_2O was added, stirring was continued for 6 h, and the solution was further diluted with H_2O (3 mL) and extracted with Et_2O. The Et_2O layer was extracted successively with H_2O (3 × 3 mL), 5% $NaHCO_3$ (3 × 10 mL), and H_2O (4 × 5 mL). All of the aqueous layers were combined, acidified with 1 N H_2SO_4 to pH 2, and extracted with $CHCl_3$. The H_2O-washed $CHCl_3$ phase on evaporation gave 15.4 mg of α-phenylbutyric acid as a colorless oil (one spot on TLC), $[\alpha]^{23}_D$ -12.9° (*c* 0.513, C_6H_6), corresponding to an optical yield of 56%.[6b]

A neutral Et_2O fraction contained 16.4 mg of one-spot material [TLC R_f 0.63 with hexane–EtOAc (4:6)] crystallized from *i*-Pr_2O–hexane as rosettes of **6**: mp 149–150 °C after softening at 147 °C; $[\alpha]^{24}_D$ +58° (*c* 0.45, MeOH); IR ($CHCl_3$) ν_{max} 3030 (Ar), 1770 (lactone), 1740 (double intensity, ester), 1665 (olefin), 1605 and 1495 cm^{-1} (Ar); UV λ_{max} 206 nm (log ε 4.39) and aromatic fine structure at 251 (shoulder, 254), 258 (2.47), and 264 (2.35); mass spectrum (EI), *m/e* 452.2207 (25%; $C_{27}H_{32}O_6$ requires 452.2199), 393 (13, M – AcO), 306 (5), 289 (9), 246 (12), 229 (25), 201 (7), 164 (8), 146 (12), 119 (97, PhCHEt), 91 (100), 77 (11, Ph), and 43 (47, Ac).

Deacetyltulirinol (5). Tulirinol (16 mg) and 5.3 mg of NaOH in 3 mL of H_2O were stirred under N_2 for 2 h. After acidification with 0.1 N HCl and stirring for 30 min, the solution was saturated with NaCl and extracted with EtOAc. The EtOAc phase was washed with 5% $NaHCO_3$ and H_2O. Evaporation of solvent left 13.3 mg of a white solid [R_f 0.23 on TLC with hexane–EtOAc (4:6)] that was chromatographed on 1 g of silica gel with the TLC solvent system to give 6.5 mg of diol **5** which crystallized from hexane–EtOAc to give 4.9 mg of fine needles: mp 165.5–6.5 °C; $[\alpha]^{24}_D$ -46° (*c* 0.36, MeOH); CD (*c* 7.7 × 10^{-3} M, MeOH) $[\theta]_{282}$ 0, $[\theta]_{239}$ -4400, $[\theta]_{230}$ (min) -2800, and $[\theta]_{209}$ -43 500°; IR (CH_2Cl_2) ν_{max} 3680, 3600, 2910, 2860, 1768, 1660, 1610, 1135, 998, and 963 cm^{-1}; UV λ_{max} 207 nm (log ε 4.16); mass spectrum (EI), *m/e* 264.1364 (0.9%; $C_{15}H_{20}O_4$ requires 264.1361), 246 (2, M – H_2O), 220 (1), 205 (3), 191 (2), 180 (6), 149 (6), 43 (100).

X-ray Diffraction Analysis. Tulirinol (1). Preliminary precession photography on the small, colorless, prismatic crystals of 1 indicated the monoclinic space group $P2_1$ (C_2^2, No. 4). All crystals were very small and all appeared to be twinned. Cell constants, determined by least-squares fitting of optimized diffractometer setting angles, were as follows: a = 6.937 (2) Å, b = 24.368 (8) Å, c = 19.436 (9) Å, and β = 91.96 (3)°, requiring six molecules per unit cell (three molecules per asymmetric unit) if a density of 0.92 is assumed.[24] Because of the twinning problem and the limited amount of data we were able to collect, attempts to solve the structure of the parent compound were abandoned, and efforts were directed at preparation of suitable crystals of the acetate derivative (2).

Tulirinol Acetate (2). Precession photographs suggested space group $P2_1$ (C_2^2, No. 4) as $0k0$ with k odd were absent. A suitable platelike crystal of approximate dimensions 0.31 mm × 0.43 mm × 0.15 mm was mounted approximately along c for determination of cell constants and for the X-ray data collection. The setting angles of 50 high 2θ reflections were used in the cell constant calculations, the results of which are presented in Table IV, along with other pertinent crystallographic data. All unique intensities with 4.0° ≤ 2θ ≤ 50.0° were measured with an automated four-circle diffractometer using the ω–2θ scan method with variable scan rates. Monochromatized Mo $K\bar{\alpha}$ radiation (λ = 0.71069 Å) was used throughout. No radiation damage was evident in the periodic measurements of seven check reflections. Absorption corrections were applied to the 2003 measured intensities using the Gaussian integration method with an 8 × 8 × 8 grid.[25]

After application of Lp and absorption corrections, the $R(F)$

(21) W. Stocklin, T. G. Waddell, and T. A. Geissman, *Tetrahedron*, **26**, 2397 (1970).
(22) A. T. McPhail and G. A. Sim, *Tetrahedron*, **29**, 1751 (1973).
(23) A. F. Beecham, *Tetrahedron*, **28**, 5543 (1972).
(24) The density of tulirinol is intermediate between that of 2-propanol (0.725 g cm^{-3}) and water (1.0 g cm^{-3}); there were insufficient crystals to carry out a precise density measurement.
(25) W. R. Busing and H. A. Levy, *Acta Crystallogr.*, **10**, 180 (1957).

Table IV. Tulirinol Acetate Crystal Data

formula $C_{19}H_{24}O_5$
mol wt 348.40 g/mol
space group $P2_1$ (C_2^2, No. 4)
ρ_{calcd} = 1.225 g/cm^3
a = 14.470 (2) Å $\alpha = \gamma = 90°$
b = 7.9661 (8) Å β = 86.637 (7)°
c = 6.7987 (5) Å V = 944.5 (2) Å^3
T = 20 (1) °C
μ(Mo K$\bar{\alpha}$) = 0.71069 Å
λ(Mo K$\bar{\alpha}$) = 0.9789 cm^{-1}
e($-\mu r_{min}$) = 0.985
e($-\mu r_{max}$) = 0.954
data collected for $4.0° \leq 2\theta \leq 50.0°$
1634 independent reflctns obsd
1048 data greater than 3σ
data to parameter ratio 6.43
final $R(F)$ = 0.064
final $R(F^2)$ = 0.069
final GOF = 1.30
1634 data used in least squares

Table V. Final Atomic Coordinates for Tulirinol Acetate[a]

atom	x	y	z
C(1)	8391 (2)	7210 (6)	2172 (5)
C(2)	8024 (2)	8112 (6)	0498 (5)
C(3)	7351 (2)	7108 (6)	−0316 (5)
C(4)	6840 (2)	6327 (6)	1282 (6)
C(5)	6840 (2)	4676 (6)	1482 (5)
C(6)	6562 (2)	3695 (5)	3253 (5)
C(7)	7245 (2)	2795 (5)	4104 (4)
C(8)	7925 (2)	4000 (5)	4346 (4)
C(9)	8508 (2)	4143 (5)	2665 (4)
C(10)	8722 (2)	5529 (6)	1684 (4)
C(11)	7116 (2)	2083 (5)	6129 (5)
C(12)	7838 (2)	2333 (5)	7147 (5)
C(13)	6513 (3)	1387 (7)	7002 (6)
C(14)	9321 (2)	5442 (7)	−0011 (5)
C(15)	6412 (2)	7508 (6)	2663 (6)
C(16)	5310 (2)	2739 (6)	2632 (6)
C(17)	4849 (2)	1278 (7)	2011 (6)
C(18)	9009 (6)	8592 (12)	4681 (14)
C(18)′	8953 (6)	9088 (10)	4386 (14)
C(19)	9639 (2)	9933 (6)	4998 (6)
O(1)	8318 (1)	3313 (0)[b]	6022 (3)
O(2)	8006 (2)	1822 (4)	8730 (4)
O(3)	6046 (1)	2353 (4)	2710 (3)
O(4)	5063 (2)	4095 (5)	3052 (5)
O(5)	8897 (3)	8526 (8)	2687 (9)
O(5)′	9115 (2)	8086 (6)	2833 (8)
O(6)	8677 (4)	7825 (9)	5844 (7)
O(6)′	8324 (3)	9235 (9)	5209 (8)

[a] All values have been multiplied by 10^4. The numbers in parentheses here and in other tables in this paper represent the esd's in the last digits of the entry. [b] To define the unit cell origin in the y direction, the y coordinate of O(1) was fixed at this arbitrary value.

and $R(wF^2)$ factors (internal disagreement indices) for the multiply measured reflections were 0.022 and 0.033. Of the 1634 independent reflections in the final data set, 1048 possessed intensities greater than $3\sigma(I)$ above background. The structure was solved by direct methods[26] and refined by standard least-squares and Fourier techniques[27] to final disagreement indices: $R(F)$ = 0.064, $R(wF^2)$ = 0.069, and GOF = 1.30[28] for all 1634 unique intensities. Hydrogen atoms were all located and their contributions included in the calculations, but their parameters were not refined. The thermal parameters for all the nonhydrogen atoms were allowed to refine anisotropically. A secondary extinction correction was included.[29] The acetate group was found to be disordered; however, the affected atoms were sufficiently removed from each other (ca. 0.5 Å to 1.0 Å) that the two conformations refined successfully with approximately equal refined populations (53%/47%). The final difference map contained a few peaks of ca. 0.30 e/Å^3 with a general noise level of ±0.20 e/Å^3. The final coordinates for the nonhydrogen atoms comprise Table V, with the final values for the anisotropic thermal parameters and the hydrogen atom coordinates deposited with the tables of structure factor amplitudes as supplementary material.[18]

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Registry No. 1, 72811-84-8; 2, 72843-65-3; 5, 41653-75-2; 6, 72796-32-8.

Supplementary Material Available: A table of structure factor amplitudes and tables of atomic thermal parameters, hydrogen atom parameters, and bond distances and bond angles between the nonhydrogen atoms (12 pages). Consult ordering information on any current masthead page.

(26) MULTAN: G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. B*, **26**, 274 (1970); L. Lessinger and T. N. Margulis, *ibid.*, **34**, 578 (1978).

(27) The computer programs used included the CRYM crystallographic computing package (D. DuChamp, Paper B-14, "Program and Abstracts", American Crystallographic Association Meeting, Bozeman, MT, 1965, and ORTEP (C. K. Johnson, Oak Ridge National Laboratory Report ORNL-3794, 1965).

(28) The function minimized in the least-squares refinement was $S = \sum w(K^2F_o^2 - F_c^2)^2$. The definitions of $R(F)$, $R(wF^2)$, and GOF are $\sum||kF_o| - |F_c||/\sum kF_o|$, $[S/\sum wK^2F_o^4]^{1/2}$ and $[S/(n_o - n_p)]^{1/2}$, respectively. The atomic form factors for C and O were taken from the "International Tables for X-ray Crystallography", Vol. 3, Kynoch Press, Birmingham, England, 1962, and that for hydrogen was taken from R. F. Stewart, E. Davidson, and W. T. Simpson, *J. Chem. Phys.*, **42**, 3175 (1965). Observational weights ($1/\sigma^2(F_o^2)$) were derived from $\sigma^2(F_o^2) = (r/Lp)(S + G^2(B_1 + B_2) + (0.02I)^2)$, where r is the scan rate, S, B_1, and B_2 are, respectively, the scan and background counts, G is the ratio of scan to background counting time, Lp is the Lorentz–polarization correction factor, and I is the net intensity ($S - G(B_1 + B_2)$).

(29) A. C. Larson, *Acta Crystallogr.*, **23**, 664 (1967).