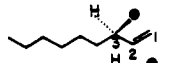
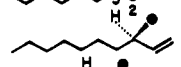
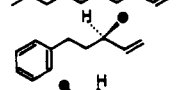
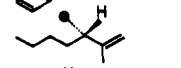
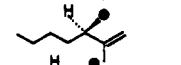
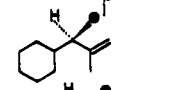
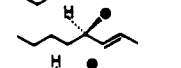
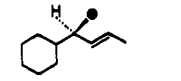
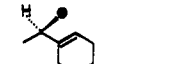
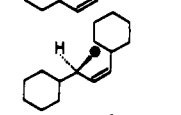
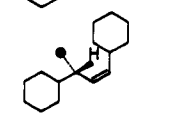
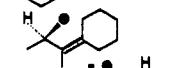
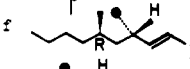
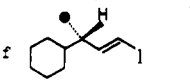
Table I. CD and NMR Coupling Constant Data of Acyclic Allylic Alcohol Benzoates[a,b]

	Compound	ee[c]	abs. config.	CD λ_{ext}, nm(Δε)	^{1}H NMR $J_{2,3}$, Hz
1.		(96%)	R	239 (-2.86)	6.3
2.		(96%)	R	237 (-2.86)	6.2
3.		(98%)	R	241 (-0.33)[d]	5.2
4.		(96%)	S	238 (+2.08)[e]	-
5.		(96%)	R	237 (-2.94)[e]	-
6.		(93%)	R	240 (-3.39)	-
7.		(96%)	R	240 (-5.08)	7.6
8.		(90%)	R	240 (-5.13)	7.6
9.		(96%)	R	240 (-2.81)	-
10.		(90%)	R	240 (-7.62)	8.5
11.		(82%)	R	238 (-8.73)	9.0
12.		(42%)	R	240 (-8.42)[e]	9.4
13.		(62%)	S	240 (+12.0)[e]	9.2
14.		(95%)	R	240 (-8.50)	-
15.[f]			S	243 (+11.24)	6.2
16.[f]			S	243 (+7.91)	6.9

[a] (•) *p*-Br-C_6H_4-COO-. [b] All CD spectra were taken in methanol with the exception of the iodo compounds, which were taken in hexane. [c] Enantiomeric excess of sample used; the CD values have been calculated for a single pure enantiomer. [d] The small Δε value is most probably due to additional interaction between the benzoate and phenyl chomophores. [e] The discrepancies between the values for *R* and *S* enantiomers are due to experimental error(s) in the enantiomeric excess percent and/or CD measurements. [f] We are grateful to Dr. Seiji Kurozumi, Teijin Ltd., Tokyo, for gift of these compounds. The *S* configurations were assigned on various grounds: Kurozumi, et al., to be submitted for publication.

inance of rotamer Ia will give rise to a negative CD. The large J_{vic} of 5.2–9.2 Hz between the olefinic and carbinyl protons (Table I) is consistent with this analysis. As expected, the magnitude of both the Cotton effects and the $J_{2,3}$ coupling constants reach a zenith for the *Z*-type allylic benzoates shown in entries 10–14 of Table I. For these benzoates conformer Ia is virtually the only stable rotamer.[16] What is less expected is the apparent general preference for conformer Ia (over conformers Ib and Ic) exhibited by the entire family of allylic benzoates represented in Table I. If exceptions are encountered to the rules set down in this work, one imagines they will arise in cases where both R_1 and R_2 (especially R_2) have large steric requirements.

Provided there is sufficient difference in the bulk of substituents, the present method is also applicable to acyclic *tert*-allylic alcohols, e.g., linalool, where in Figure 3, Ia, H is CH_3, R_1 is CH_2CH_2C-H=$C(CH_3)_2$, and R is H.[17]

We have thus shown that the current CD exciton method, which partly covers the empirical rules forwarded by Mills,[18] Brewster,[19] Yogev et al.,[15a] Scott and Wrixon,[15b] Harada et al.,[20] and Beecham et al.[21] is applicable to acyclic as well as cyclic allylic alcohols.

Acknowledgment. The studies were supported by NIH grants CA-11572 and GM-28384. V.M. thanks the Fundacion Juan March of Spain for a fellowship.

Registry No. 1, 81956-40-3; **2**, 81956-41-4; **3**, 81956-42-5; **4**, 81956-43-6; **5**, 81956-44-7; **6**, 81956-45-8; **7**, 81956-46-9; **8**, 81956-47-0; **9**, 81956-48-1; **10**, 81956-49-2; **11**, 81956-50-5; **12**, 81956-51-6; **13**, 81956-52-7; **14**, 81956-53-8; **15**, 81956-54-9; **16**, 81956-55-0.

Supplementary Material Available: Preparation of the three new chiral allylic alcohols (entries 3, 6, and 14 in Table I) and the determination of their absolute configurations are described (3 pages). Ordering information is given on any current masthead page.

(16) (a) Bothner-By, A. A.; Naar-Colin, C.; Gunther, H. *J. Am. Chem. Soc.* **1962**, *84*, 2748. (b) Karabatsos, G. J.; Fenoglio, D. J. "Topics in Sterochemistry"; Allinger, N. L., Elich, E. L., Eds.; Wiley-Interscience: New York, 1970; Vol. 5, p 167. (c) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 3.

(17) For *tert*-alcohols the cinnamates rather than benzoates were employed to decrease steric hindrance of formation. The present method has been applied to determine the absolute configurations of *tert*-allylic moieties of the linalool type: R. Takeda, et al., submitted for publication.

(18) Mills, J. A. *J. Am. Chem. Soc.* **1952**, *74*, 4976.

(19) Brewster, J. H. *Tetrahedron* **1961**, *13*, 106. See also: Brewster, J. H. *J. Am. Chem. Soc.* **1959**, *81*, 5475, 5483, 5493.

(20) Harada, N.; Ohashi, M.; Nakanishi, K. *J. Am. Chem. Soc.* **1968**, *90*, 7349. Harada, N.; Nakanishi, K. *J. Am. Chem. Soc.* **1968**, *90*, 7351.

(21) Beecham, A. F.; Mathieson, A. M.; Johns, S. R.; Lamberton, J. A.; Sioumis, A. A.; Butterham, T. J.; Young, I. G. *Tetrahedron*, **1971**, *27*, 3725.

Absolute Stereochemistry of Palytoxin

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Received March 19, 1982

In a recent communication we reported the gross structure of palytoxin from Hawaiian *Palythoa toxica*.[1-3] This exceedingly poisonous substance is a mixture of anomeric isomers, since it possesses a labile hemiketal ring and, like fructose,[4] readily equilibrates to four anomeric forms, the major ones being, presumably, the α anomers. The subtle differences in the palytoxins from other *Palythoa* species[1] appear to be due to structural differences in the hemiketal ring. Detailed analyses of 360-, 500-, and 600-MHz ^{1}H NMR spectra of various degradation products from periodate oxidation and ozonolysis of *N*-(*p*-bromobenzoyl)palytoxin,[1,5] coupled with preliminary circular dichroism

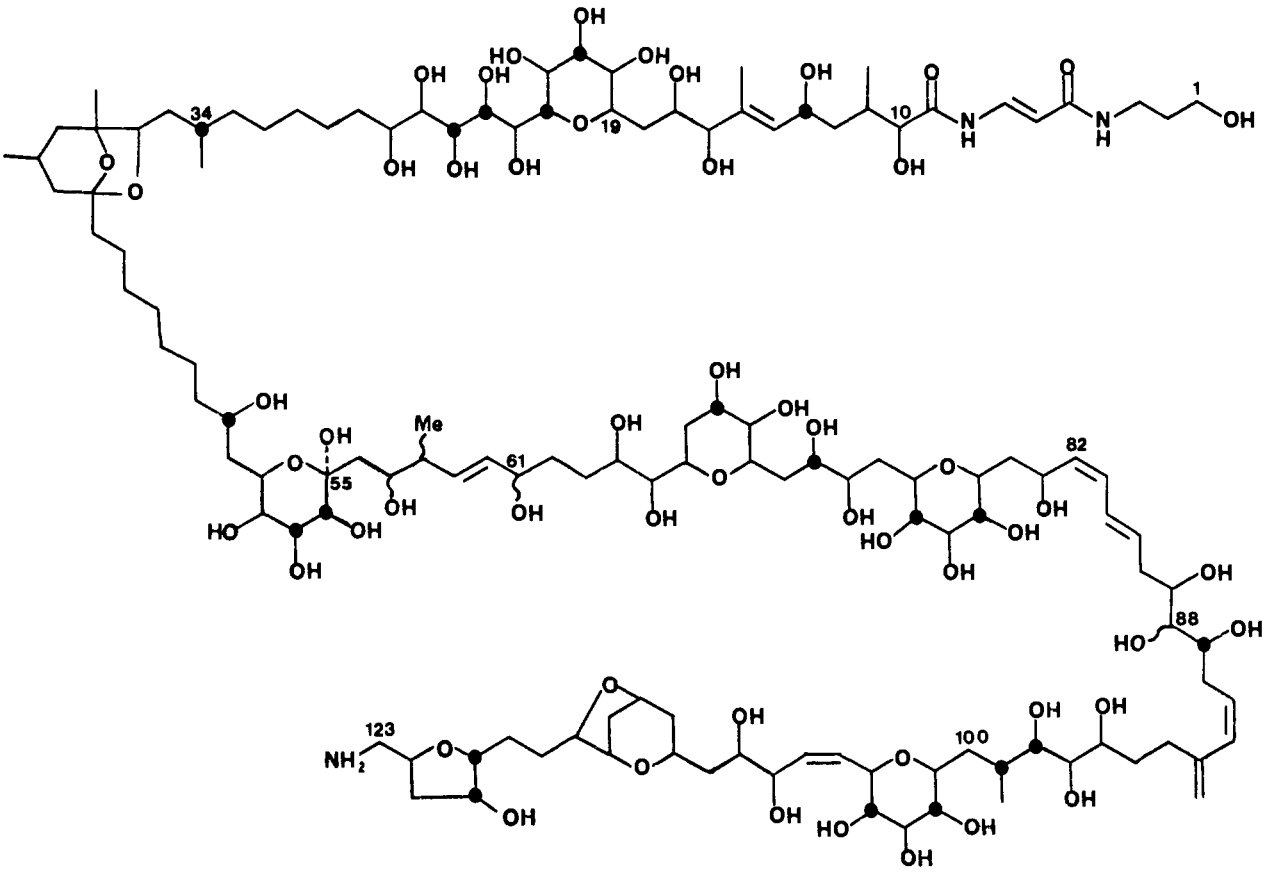
(1) Moore, R. E.; Barolini, G. *J. Am. Chem. Soc.* **1981**, *103*, 2491.

(2) Uemura, D.; Ueda, K.; Hirata, Y.; Naoki, H.; Iwashita, T. *Tetrahedron Lett.* **1981**, *22*, 2781. These authors have concluded that palytoxin from Okinawan *Palythoa tuberculosa* has the same gross structure as that of the major component (**1B** in ref 1) in palytoxin from Hawaiian *P. toxica*.

(3) We have recently found a *Vibrio* sp. (tentative identification) in Hawaiian *P. toxica* and isolated a toxin from the cultured bacterium that is chromatographically and pharmacologically identical with palytoxin: Moore, R. E.; Helfrich, P.; Patterson, G. M. L. *Oceanus*, in press.

(4) Doddrell, D.; Allerhand, A. *J. Am. Chem. Soc.* **1971**, *93*, 2779

0002-7863/82/1504-3776$01.25/0

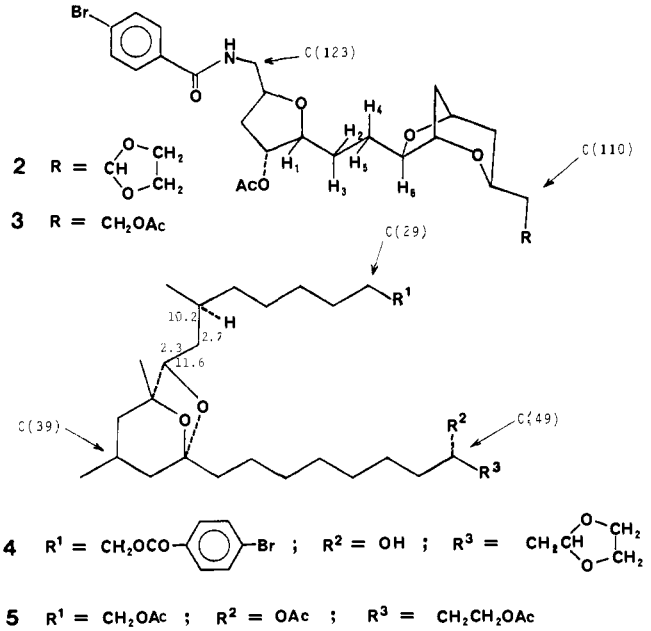


1

studies, have allowed us to propose the stereochemistry of 60 of the 64 chiral centers for the major α anomer of palytoxin from *P. toxica* (**1**).

The Hirata group has already determined the absolute stereochemistry of two portions of the *P. tuberculosa* palytoxin molecule, viz., C(110)–C(123) and C(29)–C(50), by X-ray crystallography of the periodate oxidation products **2** and **4**.[6] We find that the NMR and optical properties of the related compounds **3** and **5** from both our *P. toxica* and *P. tuberculosa* palytoxins are identical, indicating that the absolute stereochemistry of C(29)–C(50) and C(110)–C(123) in the *P. toxica* palytoxin is the same. Interestingly, in the solid state C(115)–C(116)–C(117)–C(118)–C(119)–O in **2**[6] is planar and fully extended, but our 600-MHz ^{1}H NMR studies of **3**[5] show that in the solution state C(115)–C(116)–C(117)–C(118)–C(119)–C(120) is planar and fully extended. In the solid state the C(42)–C(43)–C(44)··· side chain in **4**[6] is coplanar and fully extended with C(41)–C(40)–C(39)–CH_3 and not with either C(41)–O group; although hard evidence is presently lacking, this conformation is most likely the predominant one in solution. In the solid state C(35)–C(34)–C(33) is coplanar and fully extended with C(36)–C(37)–C(38) and not with C(36)–O; the coupling constants for the protons on C(34), C(35), and C(36) of **5**[1] and several related compounds indicate that this is also the preferred conformation in solution. Curiously in the solid state C(33)–C(32)–C(31)–C(30)··· is coplanar and fully extended with C(34)–CH_3 and not with C(34)–C(35)–C(36)–C(37)–C(38); both conformations may be prominent in solution at room temperature. The foregoing data strongly suggest that in solution an unsubstituted alkyl side chain attached to C_α of a cyclic ether orients preferentially in a coplanar and fully extended manner with C_α–C_β and not with C_α–O in the ring.

If acetoxyl substituents are present on the alkyl side chain, the carbons of the side chain prefer to fully extend with C_α and C_β of the cyclic ether as long as none of the acetate groups are gauche–gauche to other acetate groups or to the cyclic ether oxygen. In NMR studies of model compounds in which acetoxyl substituents are trans–gauche to other acetate groups or to cyclic ether oxygens in the extended conformations, e.g., as in **6**, coupling



2 R =

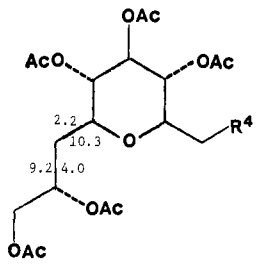
3 R = CH_2OAc

4 R^1 = CH_2OCO––Br ; R^2 = OH ; R^3 =

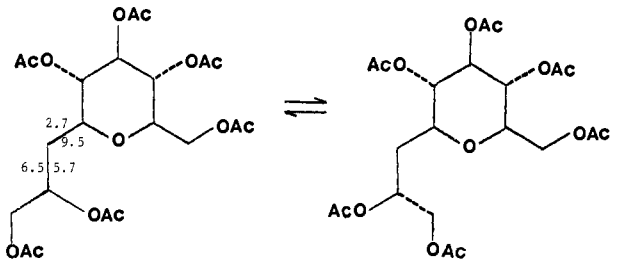
5 R^1 = CH_2OAc ; R^2 = OAc ; R^3 = CH_2CH_2OAc

(5) Moore, R. E.; Woolard, F. X.; Bartolini, G. *J. Am. Chem. Soc.* **1980**, *102*, 7370.

(6) Uemura, D.; Ueda, K.; Hirata, Y.; Katayama, C.; Tanaka, J. *Tetrahedron Lett.* **1980**, *21*, 4861.



6 R^4 = OAc
7 R^4 = CH_2OAc

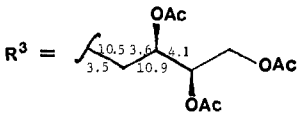


8a 8b

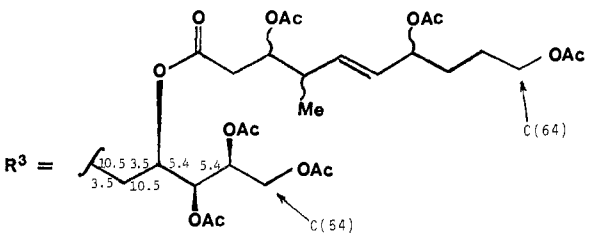
constants of 1–4.5 Hz for vicinal gauche protons and coupling constants of 6.5–10.5 Hz for trans neighbors are generally observed at 25 °C; couplings that are near 5.5 Hz at 25 °C become smaller or larger on lowering the temperature from 25 to −60 °C, depending on whether the vicinal protons are gauche or trans to each other, respectively, in the extended conformations. In NMR studies of compounds in which acetoxyl substituents are gauche–gauche to other acetate groups or to cyclic ether oxygens in the extended conformations, e.g., as in **8**, couplings of 5–6.5 Hz are seen; these couplings, however, are unaffected as the temperature is lowered from 25 to −80 °C, suggesting that in these systems extended (**8a**) and nonextended (**8b**) conformers are equally important and are rapidly interconverting.[7]

If one assumes from the evidence presented above that the carbon chains C(15)–C(16)–C(17)–C(18)–C(19)–C(20), C(21)–C(22)–C(23)–C(24)–C(25)–C(26)–C(27)–C(28)···, and ···C(49)–C(50)–C(51)–C(52)–C(53)–C(54)–C(55)–C(56)–C(57)–C(58) in **11**, ···C(49)–C(50)–C(51)–C(52)–C(53)– in **9**,[1]

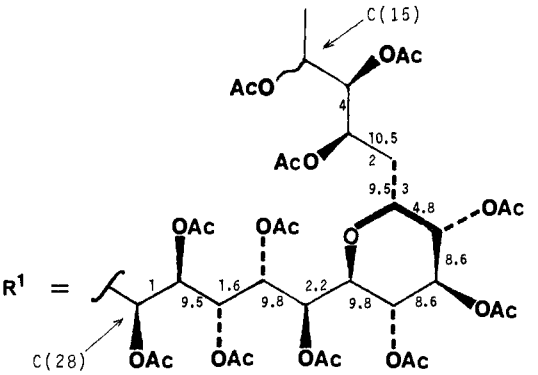
9 R^1 = CH_2OAc ; R^2 = OAc ;



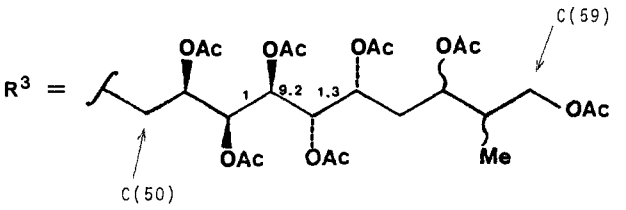
10 R^1 = CH_2OAc ; R^2 = OAc ;



···C(49)–C(50)–C(51)–C(52)–C(53)–C(54) in **10**,[1] C(107)–C(108)–C(109)–C(110)–C(111)–C(112)–C(113) in **12**,[1] C(92)–



R^2 = OAc



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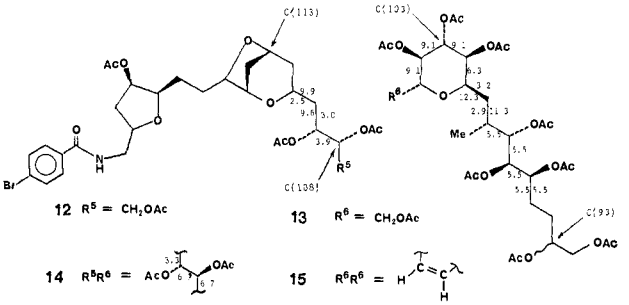
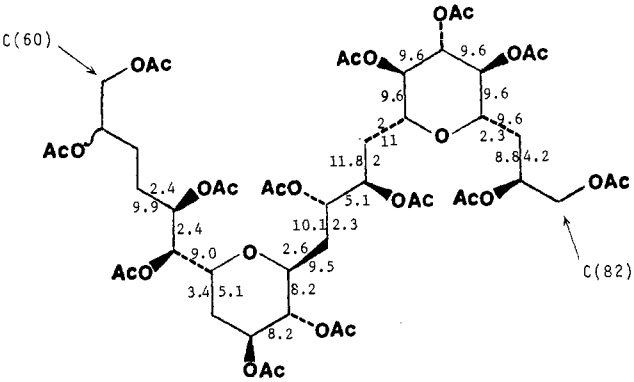


12 R^5 = CH_2OAc 13 R^6 = CH_2OAc
14 R^5R^6 = 15 R^6R^6 =

C(93)–C(94)–C(95)–C(96)–C(97)–C(98)–C(99)–C(100)–C(101)–C(102) in **13**[1] ($J_{95,96}$ = 9.3, $J_{95',96}$ = 2.9, $J_{96,97}$ = 7.8, $J_{98,99}$ = 2.9 Hz at −40 °C; for the other C(93) epimer of structure **13**, $J_{96,97}$ = 6.5, $J_{98,99}$ = 4.3 Hz at 25 °C), C(103)–C(104)–C(105)–C(106)–C(107)–C(108)–C(109)–C(110)–C(111)–C(112)–C(113) in **14** (the major product from hydroxylation of the ozonolysis product **15** with OsO_4 followed by acetylation), and C(60)–C(61)–C(62)–C(63)–C(64)–C(65)–C(66)–C(67), C(68)–C(69)–C(70)–C(71)–C(72)–C(73)–C(74)–C(75)–C(76)–C(77), and C(77)–C(78)–C(79)–C(80)–C(81)–C(82) in **16**[1] ($J_{72,73}$



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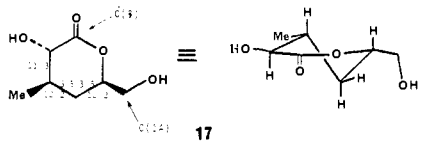
= 8.8 Hz at −60 °C) prefer to be planar and fully extended, then the coupling constants suggest the relative stereochemistries shown. Except for couplings of 5.4 Hz for $J_{51,52}$ and $J_{52,53}$ in the ^1H NMR

(7) Doskocilova, D.; Schneider, B. *Collect. Czech. Chem. Commun.* **1964**, *29*, 2290. These authors suggest that *meso*-2,4-diacetoxypentane is a rapidly interconverting mixture of two nonextended conformers, whereas the racemic diacetate exists preferentially as the extended conformer.

spectrum of **10**, only small and large vicinal couplings are observed, strongly suggesting that none of the substituents in the acyclic portions of the palytoxin molecule are gauche–gauche to other substituents or to cyclic ether oxygens in the fully extended conformations. Most the stereochemical assignments could be made from data obtained at 25 °C. Some of the couplings, however, were 5–5.5 Hz at 25 °C, and low-temperature studies were needed to make a decision. In the ^{1}H NMR spectrum of **13**, for example, couplings of 5.5 Hz for $J_{95,96}$, $J_{95',96}$, $J_{96,97}$, $J_{97,98}$, and $J_{98,99}$ suggested that the conformation in which C(93)–C(94)–C(95)–C(96)–C(97)–C(98)–C(99) is aligned with the methyl carbon on C(99) is also a prominent species in solution at 25 °C; at −40 °C, however, these coupling constants changed to larger and smaller values, indicating the predominance of a single conformer, presumably the one in which the carbon side chain is planar and fully extended with C(101)–C(102) in the tetrahydropyran ring.

The absolute configurations of 60 of the 64 chiral centers in Hawaiian *P. toxica* palytoxin have been determined as follows. 10*S*,11*R*,13*R*: The δ-lactone **17** (from HCl hydrolysis of the



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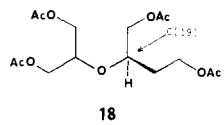
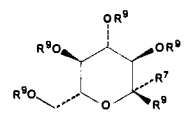


18

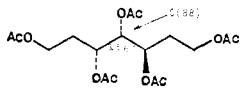


19 R^7 = H ; R^8 = Cl ; R^9 = CH_2Ph

20 R^7 = $CH_2CH{=}CH_2$; R^8 = H ; R^9 = CH_2Ph

21 R^7 = CH_2CH_2OH ; R^8 = H ; R^9 = CH_2Ph

22 R^7 = CH_2CH_2OH ; R^8 = H ; R^9 = H



23

corresponding diacetate[1]) has the absolute stereochemistry shown from NMR and CD data ($[\theta]_{224}^{EtOH}$ +2300°).[8,9] 16*R*,17*R*,19*R*,20*R*,21*R*,22*S*,23*S*,24*R*,25*R*,26*R*,27*R*,28*R*: Periodate oxidation of palytoxin leads to **18**,[1] which has a CD curve ($[\theta]_{215}^{EtOH}$ −100°) that is opposite in sign to that of *S*-**18** ($[\theta]_{215}^{MeOH}$ +100), synthesized from periodate oxidation of **22** (glucose → **19** → **20** → **21** → **22**). The absolute configuration of C(19) in **11** is therefore *R*. 34*S*,36*R*,37*R*,39*R*,41*S*,49*S*: The absolute stereochemistries of these carbons are implied from X-ray studies of **4**.[6] 49*S*,51*R*,52*R*,53*R*,54*R*,55*S*: The chiralities of the R^3 groups in **9**–**11** are as shown since all have been related to C(49) by NMR. 64*R*,65*S*,66*R*,68*S*,69*R*,70*S*,72*S*,73*R*,75*R*,76*S*,77*R*,78*R*,79*S*,81*S*:[10] Compound **7** from ozonolysis of a previously described periodate oxidation product containing the cis, trans diene system[5] has a CD spectrum ($[\theta]_{213}^{EtOH}$ −3900°) that is comparable in sign with that of **6** ($[\theta]_{215}^{EtOH}$ −1100°), synthesized from **20**. 87*R*,89*R*: The ozonolysis product **23**[1] shows a maximum peak in its CD spectrum ($[\theta]_{210}^{EtOH}$ +2000°) that is comparable in sign, position, and intensity to those of (2*R*,3*S*,4*R*)-1,2,3,4,6-pentaacetoxyhexane (from 2-deoxy-D-glucose) ($[\theta]_{212}^{MeOH}$ +2500°) and (2*R*,3*R*,4*R*)-1,2,3,4,6-pentaacetoxyhexane (from 2-deoxy-D-galactose) ($[\theta]_{212}^{MeOH}$ +2900°). 96*R*,97*S*,98*R*,99*S*,101*S*,102*S*,103*S*,104*R*,105*S*,108*S*,109*S*,111*R*,113*S*,115*R*,116*R*,119*R*,120*R*,122*S*: The absolute stereochemistry of **12** is implied from X-ray studies of **2**.[6] Detailed ^{1}H NMR analysis of **14**, which is actually a 1:1 mixture of C(93) epimers, correlates the relative stereochemistries of **12** and **13**. Interestingly, the NMR signal for one of the protons on C(123) is clearly doubled, suggesting that C(123) and the epimeric C(93) are spatially close in the preferred conformation. A Dreiding model examination of **14** shows that this is the case when the carbons of all side chains are aligned in a fully extended and planar manner with two or three carbons in each of the ether rings: C(123) and C(93) do not come in contact, however, if the absolute stereochemistry of C(92)–C(106) is opposite that shown by **13**.

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Supplementary Material Available: High-field region of the 600-MHz ^{1}H NMR spectrum of **3** and simulated spectra of H_2, H_3, H_4, and H_5 resonances (Figure 1); low-field region of the 360-MHz ^{1}H NMR spectrum of **13** at 20, 3, −20, and −40 °C (Figure 2); low-field regions of the 600-MHz ^{1}H NMR spectra of **12**, **14**, and **15** (Figure 3) (4 pages). Ordering information is given on any current masthead page.

(8) (a) Korver, O. *Tetrahedron* **1970**, *26*, 2391. (b) Cardellina, J. H., II; Moore, R. E.; Arnold, E. V.; Clardy, J. *J. Org. Chem.* **1979**, *44*, 4039.

(9) The enantiomer of **17** has been synthesized from (+)-pulegone: Thurkauf, A.; Tius, M. A., unpublished results.

(10) The same CD signs for **6** and **7** only suggest that the two compounds have the same absolute configurations. The absolute stereochemistry of the C(63)–C(82) portion of palytoxin is therefore tentative.

Ab Initio Study of Silylene Insertion into O–H Bonds. Stability of Zwitterionic Intermediates

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The current burst of activity in the study of silicon reactive intermediates[1] has brought to light increasing differences between the structural chemistry of silicon and carbon. The reluctance of silicon to form multiple bonds and its unusual preference to adopt divalent structures instead provide dramatic examples.[2] In this communication we point to another structural type, generally not adopted by carbon, that may be spectroscopically observable as a silicon compound.

We have carried out ab initio calculations with extended basis sets including significant electron correlation and zero-point energy corrections on all the stationary points of the two insertion-reaction

(1) Review: Gaspar, P. P. In "Reactive Intermediates", Jones, M., Moss, R. A., Ed.; Wiley-Interscience: New York, 1978; Vol 1, pp 229–277.

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