THF (10 mL). The reaction mixture was allowed to warm to 20 °C and stirred for 2 h. Acetic acid (10 mmol) was added and stirring was continued for 30 min. The THF was removed in vacuo. The residue was dissolved in hexane (50 mL), washed with H_2O (2 × 50 mL), and dried ($MgSO_4$) and the hexane was evaporated. The residue was purified by filtration through a short column of silica gel (10 g) with hexane, followed by evaporative distillation (110 °C, 0.05 mm) to give (*Z*)-1-(phenylseleno)-1-hexene (85%): VPC analysis (24 ft × ⅛ in., 1.5% DEGS on 100/120 Chromosorb G, 180 °C, 30 mL He/min) indicated >95% isomeric purity; ^1H NMR, see Table II; IR (neat) 1595, 1490, 1455, 1035, 745, 700 cm^{-1}.

Synthesis of (*Z*)-1-(Phenylseleno)-2-phenylethene (4e)[10] by Dicyclohexylborane Reduction of 5e. The experimental procedure described above was utilized on **5e** to give (*Z*)-1-(phenylseleno)-2-phenylethene (90%): bp 100 °C, 0.05 mm; ^1H NMR, see Table II; IR (neat) 1610, 1585, 1485, 1450, 1080, 1030, 955, 740, 700 cm^{-1}.

Synthesis of (*E*)-1-(Phenylseleno)-1-hexene (3b) from (*E*)-1-Hexenylboronic Acid (6b). A mixture of 1-hexyne (1.10 mmol) and catecholborane (1.00 mmol) was refluxed in an atmosphere of Ar for 2 h. The mixture was cooled to 25 °C, H_2O (3 mL) was added, and the reaction was stirred for 1 h. A solution of 0.50 M NaOH (2.0 mL) was added, the reaction mixture was stirred for 1 min, and a solution of PhSeBr (1.00 mmol) in THF (5 mL) was added. The dark green reaction mixture was stirred for 5 min, the THF was removed in vacuo, and the residue was extracted with ether (2 × 25 mL). The ether extracts were dried ($MgSO_4$), the ether was evaporated, and the residue was purified by evaporative distillation (85 °C, 0.01 mm) to give (*E*)-1-(phenylseleno)-1-hexene (70%). VPC analysis indicated >95% isomeric purity. ^1H NMR was identical to sample prepared by dehydrohalogenation of **2b.**

Synthesis of (*E*)-1-(Phenylseleno)-2-phenylethene (3e)[10] from (*E*)-2-Phenyl-1-ethenylboronic Acid (6e). The experimental procedure described above was utilized on **6e** to give (*E*)-1-(phenylseleno)-2-phenylethene (90%): bp 100 °C, 0.05 mm; ^1H NMR identical to sample prepared by dehydrohalogenation of **2e;** IR (neat) 1685, 1480, 1445, 1070, 1025, 1005, 950, 735, 690 cm^{-1}.

Synthesis of (*E*)-1-(Phenylseleno)-2-phenylethene (3e)[10] from (*E*)-2-Phenyl-1-ethenylmercuric Chloride (7e). A mixture of phenylacetylene (1.00 mmol) and catecholborane (1.00 mmol) under an atmosphere of Ar was heated at 140 °C for 10 min. The reaction was cooled to 0 °C and treated with THF (5 mL), $Hg(OAc)_2$ (1.0 mmol) was added, and the mixture was stirred vigorously for 10 min and then poured into ice water (10 mL) containing NaCl (10 mmol). The THF was removed in vacuo, and the resulting alkenylmercuric chloride **7e** was dried in vacuo. A suspension of the alkenylmercuric chloride in CH_2Cl_2 (5 mL) was treated with a solution of PhSeCl (1.00 mmol) in CH_2Cl_2 (5 mL) at 0 °C. The mixture was stirred for 10 min, treated with Et_2O (50 mL), washed with H_2O (2 × 10 mL) and brine (10 mL), and dried ($MgSO_4$). Evaporation of the solvents in vacuo and purification by filtration through a column of silica gel (10 g) with hexane, followed by evaporative distillation (100 °C, 0.05 mm), gave (*E*)-1-(phenylseleno)-2-phenylethene (80%). ^1H NMR was identical to samples prepared above.

Acknowledgment. We wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Registry No.—**4e,** 60466-30-0; **5b,** 68001-64-9; **5e,** 30665-96-4; **6b,** 42599-18-8; **6e,** 6783-05-7; **7e,** 36525-03-8; 1-hexyne, 693-02-7; phenylselenenyl bromide, 34837-55-3; phenylacetylene, 536-74-3.

References and Notes

(1) Organoselenium Chemistry. 6. For previous paper in this series, see ref 9b.
(2) S. Raucher, *J. Org. Chem.*, **40,** 2950 (1977).
(3) N. Petragnani, R. Rodrigues, and J. V. Comasseto, *J. Organomet. Chem.*, **114,** 281 (1976).
(4) H. C. Brown, "Organic Synthesis via Boranes", Wiley, New York, N.Y., 1975.
(5) H. C. Brown, T. Hamaoka, and N. Ravindran, *J. Am. Chem. Soc.*, **95,** 5786 (1973).
(6) R. C. Larock, S. K. Gupta, and H. C. Brown, *J. Am. Chem. Soc.*, **94,** 4371 (1972).
(7) (a) T. W. Campbell and J. D. McCullough, *J. Am. Chem. Soc.*, **67,** 1965 (1945); (b) G. Vicentini, E. Giesbrecht, and L. R. M. Pitombo, *Chem. Ber.*, **92,** 40 (1959).
(8) For other syntheses of vinyl phenyl selenides, see (a) E. G. Kataev, T. G. Mannafov, A. B. Remizov, and O. A. Komarvskya, *Zh. Org. Khim.*, **11,** 2322 (1975); (b) H. J. Reich and F. Chow, *Chem. Commun.*, 790 (1975); (c) ref 3, (d) N. Petragnani and R. Rodrigues, *Chem. Scr.*, **8A,** 110 (1975); (e) J. Hooz and R. Mortimer, *Tetrahedron Lett.*, 805 (1976).
(9) (a) S. Raucher and G. A. Koolpe, *J. Org. Chem.*, **43,** 3794 (1978); (b) S. Raucher and G. A. Koolpe, *ibid.*, **43,** 4252 (1978).
(10) The assignment of the stereochemistry of the PhCH=CHSePh isomers made by Petragnani, Rodrigues, and Comasseto (ref 3) is clearly incorrect. These workers assigned the compound with $J_{CH=CH}$ = 10 Hz as the trans isomer and the compound with $J_{CH=CH}$ = 16 Hz as the cis isomer. We have also carried out the addition of PhSeH to PhC≡CH as described[3] and obtained (*E*)-1-(phenylselno)-2-phenylethene (**3e**): $J_{CH=CH}$ = 16 Hz.

Stereochemistry of Woodhousin[1]

Werner Herz*

Department of Chemistry, The Florida State University, Tallahassee, Florida 32306

John F. Blount

Research Division, Hoffmann-LaRoche Inc., Nutley, New Jersey 07110

Received July 31, 1978

The results of our recent X-ray analysis of tirotundin ethyl ether (**1b**)[2] raised doubts, for reasons that have been discussed,[2] about the C-8 stereochemistry previously assigned to the heliangolides woodhousin,[3] tifruticin, and deoxytifruticin.[4] Because of this and the close relationship of woodhousin to several other hemiacetalic heliangolides,[5] we have examined single crystals of woodhousin by X-ray crystallography. The results led to structure **2a,** thus confirming our earlier conclusions about the structure and stereochemistry of woodhousin, with the exception of the configuration at C-8. Our results also establish the full stereochemistry of tagitinin B, which has been identified[5b] as desacetylwoodhousin, and tagitinin C, which has been correlated with tagitinin B, as **2b** and **3,** respectively.

Crystal data of **2a** are listed in Table I. Figure 1 is a stereoscopic drawing of the molecule which represents the absolute configuration as well since then the sign of the C=C—C=O torsion angle (ω_2 of Table II), which has been related[6] to the Cotton effect associated with the n → π^* transition of an α,β-unsaturated lactone, corresponds to the observed[3] positive sign of the Cotton effect. As usual, the sign of ω_2 is paired with the sign of the C(α)–C(β)–C(γ)–O torsion angle (ω_3). It is noteworthy that in comparison with tirotundin, introduction of the C-4, C-5 double bond has had the effect of changing the chirality of the lactone chromophore, although the overall shape of the molecule has not changed significantly.

The crystal structure (Figure 1) supports our original attribution[3] of the abnormally low shift of H-7 in heliangolides of the woodhousin type to the configuration of the hemiacetal linkage (3*S*, 10*R* in woodhousin) which places H-7 in proximity to the ether oxygen. In our earlier discussion of wood-

Table I. Crystal Data for Woodhousin

formula	$C_{21}H_{28}O_8$, orthorhombic
space group	$P2_12_12_1$ (Z = 4)
a, Å	10.013 (3)
b, Å	12.974 (2)
c, Å	16.877 (4)
d_{calcd}, g cm^{-3}	1.237

Table II. Lactone Ring Torsion Angles of Woodhousin

C(6)–O(3)–C(12)–C(11)	ω_1	−7.3°
C(13)–C(11)–C(12)–O(4)	ω_2	10.0°
C(11)–C(7)–C(6)–O(3)	ω_3	11.1°
C(5)–C(6)–C(7)–C(8)	ω_4	131.4°

0022-3263/78/1943-4887$01.00/0

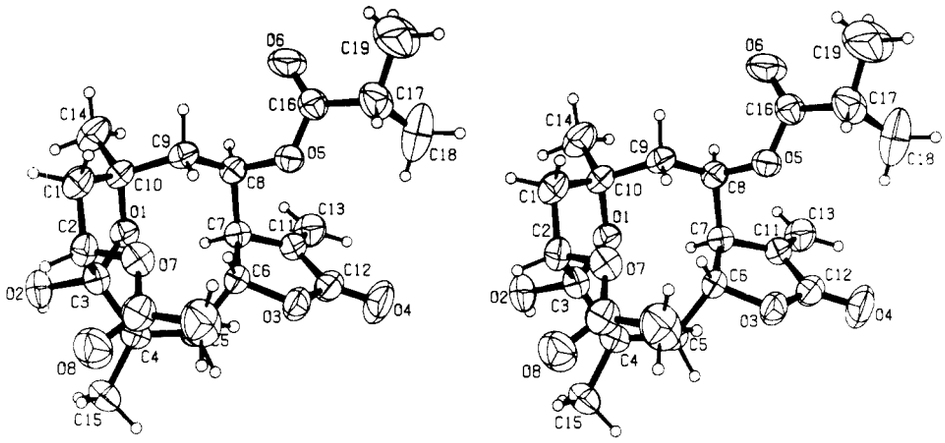
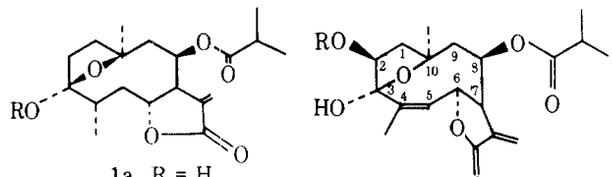
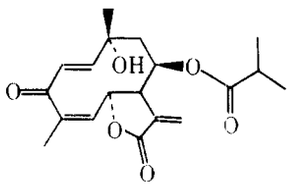


Figure 1. Stereoscopic view of woodhousin.

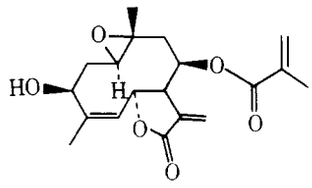


1a, R = H
b, R = Et

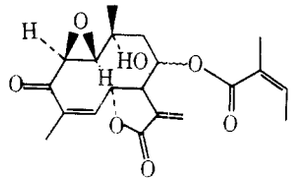
2a, R = Ac
b, R = H



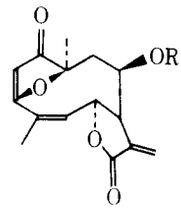
3



4

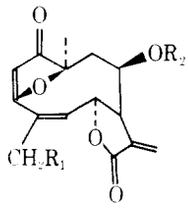


5



6a, R =

b, R =



7a, R_1 = OH; R_2 =

b, R_1 = H; R_2 =

c, R_1 = H; R_2 =

housin we also noted[3] that the observed coupling constants involving H-5, H-6, H-7, H-8, and H-9 did not permit a clear-cut decision between α and β orientation of the C-8 ester side chain.[7] Our decision in favor of α orientation was based on differences in values of $J_{7,8}$ and $J_{8,9}$ between derivatives of woodhousin and erioflorin (**4**) that were thought to be appropriate models and on NMR evidence that hydrolysis of the ester function attached to C-8 was accompanied by lactone ring reorientation toward C-8.[11] These comparisons were evidently inappropriate. Since the C-8 stereochemistry assigned to tifruticin (**5**) and deoxytifruticin was based on similar reasoning,[4] reisolation and reexamination of these compounds would also seem to be in order.

Experimental Section

Single crystals of woodhousin were prepared by slow crystallization from ethyl acetate–hexane. A small crystal measuring approximately 0.3 × 0.4 × 0.6 mm was carved out of one of the large crystals and used for data collection. Intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse height discrimination) and were not corrected for absorption. A total of 1709 reflections were measured for $\theta < 57°$, of which 1675 were chosen to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple solution procedure[12] and was refined by full-matrix least squares. In the final refinement, anisotropic thermal parameters were used for the heavier atoms and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices are $R = 0.048$ and $R_w = 0.071$ for the 1675 observed reflections. The final difference map has no peaks greater than ±0.3 e Å^{-3}.

Registry No.—**2a,** 33143-54-3.

Supplementary Material Available: Tables III–VII, listing final atomic parameters, final anisotropic thermal parameters, bond lengths, bond angles, and torsion angles of woodhousin (6 pages). Ordering information is given on any current masthead page.

References and Notes

(1) Work at The Florida State University was supported in part by a grant from the U. S. Public Health Service (CA-13121) through the National Cancer Institute.
(2) W. Herz and J. F. Blount, *J. Org. Chem.*, **43,** 1268 (1978).
(3) W. Herz and S. V. Bhat, *J. Org. Chem.*, **37,** 1906 (1972).
(4) W. Herz and R. P. Sharma, *J. Org. Chem.*, **40,** 3118 (1975).
(5) See, for example, (a) A. Ortega, C. Guerrero, A. Romo de Vivar, J. Romo, and A. Palafox, *Rev. Latinoam. Quim.*, **3,** 38 (1971); (b) R. Pal, D. K. Kulreshta, and R. P. Rastogi, *Indian Chem. J.*, **14B,** 77 (1976); *ibid.*, **15B,** 208 (1977); (c) F. Bohlmann and C. Zdero, *Phytochemistry*, **16,** 1065 (1977).
(6) A. F. Beecham, *Tetrahedron*, **28,** 5543 (1972).
(7) In Dreiding models of woodhousin and similar compounds, the ring portion involving C-6 through C-9 is quite flexible and permits conformations which regardless of configuration at C-8 are consonant with the observed coupling constants. It is possible that this accounts for the otherwise rather puzzling fact that calaxin (**6b**) and ciliarin (**6a**) (C-8 ester side chains presumed α by application of Horeau's rule to a hydrolysis product of hexahydrozexbrevin)[8] exhibit chemical shifts and coupling constants practically identical with those of budlein A (**7a**)[9] and the atriplicolides **7b** and **7c**,[10] which have been assigned the β C-8 configuration. In the solid state of woodhousin

the magnitudes of the relevant torsion angles C(4)–C(5)–C(6)–C(7), C(5)–C(6)–C(7)–C(8), C(6)–C(7)–C(8)–C(9), and C(7)–C(8)–C(9)–C(10) are −73, 131, −48, and −53°, respectively.

(8) A. Ortega, A. Romo de Vivar, E. Diaz, and J. Romo, *Rev. Latinoam. Quim.*, **1**, 81 (1970); A. Romo de Vivar, C. Guerrero, E. Diaz, and A. Ortega, *Tetrahedron*, **26**, 1657 (1970).
(9) A. Romo de Vivar, C. Guerrero, E. Diaz, E. Bratoeff, and L. Jiminez, *Phytochemistry*, **15**, 525 (1976).
(10) F. Bohlmann, P. K. Mahanta, A. A. Natu, R. M. King, and H. Robinson, *Phytochemistry*, **17**, 471 (1978).
(11) Germacranolides containing α-oriented lactonizable groups at C-6 and C-8 preferentially lactonize toward C-8.
(12) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, **27**, 368 (1971).

Hydrophobic Effect in Host–Guest Interactions. Hydrolysis of Nitrophenyl Carboxylates

Corwin Hansch

Department of Chemistry, Pomona College, Claremont, California 91711

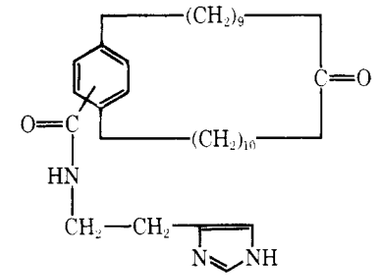
Received May 19, 1978

Widespread interest has developed in the catalytic effect of micelles on organic reactions.[1] The object of such studies has been to design simple model systems of enzymes, the parameters of which can be easily varied. Their study is expected to enhance our understanding of biochemical processes.

An elegant study along these lines, which goes a step below the micelle level, is that of Murakami et al.[2] who synthesized the [20]paracyclophane **1**. This molecule can be viewed as a "mini-enzyme" containing a hydrophobic pocket and the catalytically active imidazole moiety. This "enzyme" was used to hydrolyze esters of the type $RCOOC_6H_4$-*p*-NO_2 (Table I). In Table I, k_{rel} is the relative rate (pseudo-first-order) of hydrolysis in the presence of paracyclophane compared to hydrolysis in buffer alone. As Murakami et al. observed, it is apparent qualitatively that the more hydrophobic esters are hydrolyzed more rapidly in the presence of **1**.

We have been developing a quantitative scale of hydrophobicity of organic compounds and their substituents[3] in order to facilitate the study of structure–activity relationships of organic compounds interacting with macromolecules,[4] enzymes,[5] organelles,[6] bacteria,[6] and whole animals.[7] Our general model[3b] appears to be important in drug design.[8]

We have selected the logarithm of the octanol/water partition coefficient (P) as our model hydrophobicity scale for organic compounds. The hydrophobicity of a substituent (X) can be defined as $\pi_X = \log P_{R-X} - \log P_{RH}$. Making the extrathermodynamic assumption[9] that $\log k \propto \pi$, we have formulated eq 1 from the data in Table I. The figures in parentheses are the 95% confidence limits, n represents the number of data points used in deriving eq 1, r is the correlation coefficient, and s is the standard deviation. One data point (no. **3**) has not been used in formulating eq 1 and is seen to be poorly fit in Table I. Including this point gives essentially the same equation, but with $r = 0.950$ and $s = 0.324$. This poorer equation "explains" 90% of the variance in log P, while eq 1 "explains" 94%.



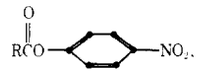
1

$$\log k = 0.45(\pm 0.09)\pi - 0.53(\pm 0.39) \quad (1)$$
$$n = 11;\ r = 0.968;\ s = 0.260$$

Equation 1 shows that hydrolysis is closely related to hydrophobicity as defined by the octanol/water system. With the exception of compounds **3**, **4**, and **7** of Table I, the relationship is sharp, showing that steric effects in general are of secondary importance. The rigid naphthyl or phenyl groups are as well fit as the more flexible alkyl groups.

The advantage of the numerical scale for hydrophobicity is that we can compare the results embodied in eq 1 with those from other systems, as the following examples illustrate. Gitler and Ochoa-Solano[10] studied the hydrolysis of esters like those in Table I in micelles of cetyltrimethylammonium bromide containing *N*-myristoyl-L-histidine. The lipophilic myristoyl group insures that the catalytic histidine moiety is held in the lipophilic micelle. An equation similar to eq 1 has been formulated[11] for the hydrolysis of five nitrophenyl carboxylates (eq 2). Log P rather than π was employed in eq 2 as the independent variable for relative hydrophobicity. This does not affect the slope of eq 2, which is close to that of eq 1, showing in quantitative terms that both processes depend almost entirely on the relative hydrophobicity of the substrates.

Table I. Hydrolysis and Hydrophobic Constants Used to Derive Equation 1

no.	 R =	Registry no.	log k_{rel} obsd[a]	log k_{rel} calcd[b]	π[c]
1	CH_3	830-03-5	0.00	−0.29	0.54
2	$(CH_2)_4CH_3$	956-75-2	0.79	0.70	2.70
3	$(CH_2)_8CH_3$	1956-09-8	2.38[d]	1.68	4.86
4	$(CH_2)_{10}CH_3$	1956-11-2	2.62	2.17	5.94
5	$(CH_2)_{14}CH_3$	1492-30-4	2.97	3.15	8.10
6	cyclohexyl	13551-17-2	0.74	0.85	3.05
7	CH_2-cyclohexyl	65426-79-1	0.66	1.10	3.59
8	$CH(CH_3)$-cyclohexyl	65426-80-4	1.30	1.23	3.87
9	CH_2-3,5-di-CH_3-cyclohexyl	65426-81-5	1.54	1.51	4.49
10	CH_2-cyclodecyl	65426-82-6	2.23	2.13	5.86
11	$CH_2C_6H_5$	1223-44-5	0.15	0.38	2.01
12	CH_2-1-naphthyl	51537-87-2	0.90	0.96	3.28

[a] k is the relative rate of hydrolysis in the presence of paracyclophane compared to hydrolysis without paracyclophane.[2] [b] Calculated using eq 1. [c] The value of 0.54 is used for each CH_2 increment. π values for **11** and **12** taken from C. Hansch et al., *J. Med. Chem.*, **16**, 1207 (1973). π values for **6–10** calculated using method of fragment constants: A. Leo et al., *J. Med. Chem.*, **18**, 865 (1975); for example, $\log P_{cyclohexane} - \log P_{H_2} = 3.51 - 0.46 = 3.05$. [d] This point was not used in deriving eq 1.

0022-3263/78/1943-4889$01.00/0