cyanate. A solution of sulfamide (2.26 g, 7.1 mmol) and phenyl isocyanate (1.1 g, 9.2 mmol) in 50 mL of benzene was heated to reflux and stirred for 72 h. Ethyl alcohol (11.8 g, 256 mmol) was added to react with excess isocyanate, and the solution was allowed to reflux for 1 h. The solvent was evaporated and the residue eluted through a silica gel column with a 1:1 hexane–ether mixture. Three fractions were collected: 1.04 g of unreacted starting material, 0.21 g of ethyl *N*-phenylcarbamate, and 0.64 g (68% yield based on consumed sulfamide) of urea: mp 157.5–158.5 °C (hexane) (lit.[1] mp 158.5–159.5 C); NMR ($CDCl_3$) δ 1.18 (s, 6 H), 1.56 (s, 6 H), 1.79 (s, 2 H), 3.37 (s, 2 H), 7.32–7.46 (s, 5 H).

***tert*-Octyl Azide.** A modification of the literature procedure was employed.[4] Diisobutylene (22.4 g, 0.20 mol) in a mixture of 57% H_2SO_4 (200 mL), $CHCl_3$ (200 mL), and 10 drops of Aliquat 336 was cooled in an ice–water bath. Sodium azide (19.5 g, 0.30 mol) was added over a period of 5 min, and the mixture was stirred for 12 h. The mixture was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with H_2O (200 mL), 5% $NaHCO_3$ (200 mL), and H_2O (200 mL) and dried ($MgSO_4$). The solvent was removed to give 31.1 g (100%) of *tert*-octyl azide which was distilled under reduced pressure: 90–92 °C (62 mm); IR (neat) 2100 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.02 (s, 9 H), 1.31 (s, 6 H), 1.52 (s, 2 H). Anal. Calcd for $C_8H_{17}N_3$: C, 61.90; H, 11.04; N, 27.07. Found: C, 61.94; H, 11.08; N, 27.17.

Photochemical Decomposition of *tert*-Octyl Azide. Azide (1.00 g, 6.5 mmol) dissolved in benzene (400 mL) was placed in an Hanovia reactor, degassed with N_2 for 20 min, and irradiated with a 450-W Hg lamp for 1 h. The reaction mixture was extracted with 5% HCl (3 × 100 mL). The HCl extract was made basic with NaOH and extracted with ether (3 × 75 mL). The ether extracts were dried (K_2CO_3) and the ether was removed in vacuo at 0 °C to give 0.39 g (53%) of 4,4-dimethyl-2-pentanone: IR (neat) 1720 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.02 (s, 9 H), 2.06 (s, 3 H), 2.28 (s, 2 H).

The benzene layer was dried (K_2CO_3) and the benzene was removed in vacuo to give a dark oil (0.20 g, 24% based on loss of N_2 from the azide), but no further attempts were made to identify the components of this mixture.

***tert*-Octylbenzaldimine.** Benzaldehyde (22.39 g, 0.211 mol) and *tert*-octylamine (32.25 g, 0.25 mol) were dissolved in benzene (100 mL) and heated to reflux in a flask fitted with a Dean–Stark trap. After the stoichiometric amount of H_2O was collected, the benzene and the excess amine were removed in vacuo. The imine was distilled (0.1 mm, 98–101 °C) to give a light yellow viscous liquid: 39.03 g (85%); IR (neat) 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.95 (s, 9 H), 1.31 (s, 6 H), 1.69 (s, 2 H), 7.3–7.85 (m, 5 H), 8.24 (s, 1 H).

3-Phenyl-2-*tert*-octyloxazirane. Imine (21.70 g, 0.10 mol) was dissolved in benzene (100 mL) and cooled in an ice–water bath. *m*-Chloroperbenzoic acid (22.4 g, 0.13 mol) was added over a 30-min period, and the mixture was allowed to warm to room temperature. After 6 h the reaction mixture was filtered, and the filtrate was washed with saturated K_2CO_3 solution (3 × 100 mL), 5% HCl (100 mL), saturated $NaHSO_3$ solution (100 mL), and water (100 mL) and dried ($MgSO_4$). The solvent was removed in vacuo to give oxazirane: 15.58 g, (67%); IR (neat) 1710 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.01 (s, 9 H), 1.13 (s, 3 H), 1.25 (s, 3 H), 1.69 (s, 2 H), 4.70 (s, 1 H), 7.3–7.5 (m, 5 H). Anal. Calcd for $C_{15}H_{23}NO$: C, 77117; 9.95, N, 6.03. Found: C, 77.01; H, 9.81.

Photochemical Decomposition of Oxazirane. Oxazirane (1.00 g, 4.29 mmol) dissolved in ether (400 mL) was placed in an Hanovia reactor, degassed with N_2 for 20 min, and irradiated with a 450-W Hg lamp for 1 h. The ether was removed in vacuo, and the remaining oil (a mixture of two compounds by TLC) was eluted through a silica gel preparative LC column with 60:40 pentane/ether. The first fraction proved to be starting material, and the second fraction was identified as *tert*-octylbenzamide: mp 70–71 °C (lit.[5] mp 68.5 °C); IR ($CHCl_3$) 3500–3300 (br, s), 1650 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.04 (s, 9 H), 1.53 (s, 6 H), 1.87 (s, 2 H), 6.0 (s, 1 H), 7.20–7.85 (m, 5 H).

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Registry No. 4, 84499-88-7; 7, 76613-37-1; phenyl isocyanate, 103-71-9; *tert*-octyl azide, 35426-97-2; diisobutylene, 25167-70-8; 4,4-dimethyl-2-pentanone, 590-50-1; benzaldehyde, 100-52-7; *tert*-octylamine, 107-45-9; *tert*-octylbenzaldimine, 49707-52-0; 3-phenyl-2-*tert*-octyloxazirane, 61457-73-6; *tert*-octylbenzamide, 34021-55-1.

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[5] Lacey, R. N. *J. Chem. Soc.* **1960**, 1633.

Communications

Verification and Characterization of the E2C Mechanism. The Weak Base Catalyzed Elimination Reaction of β-Phenylethyl Substrates

Summary: Through application of the TDKIE criteria, a bent TS of H transfer has been characterized in the fluoride ion promoted E2C elimination reaction of β-phenylethyl substrates in aprotic solvent. The angle of H transfer of this TS is found to be a sensitive function of the nucleofugal properties of the leaving group.

Sir: The two most prominent proposals[1-5] accounting for the many rate and structural effects observed in weak base catalyzed β-elimination processes are readily distinguished by the geometries of their respective transition states. The Bunnett[5] E2 TS essentially requires linear H transfer between the substrate C_β and the base B; the Winstein–Parker[1-4] E2C-like TS provides for nonlinear H transfer in a rectangular concert of bond making and breaking. Bunnett and others[5] have advanced arguments against the viability of an E2C mechanism based on apparently sound experimental evidence. However, among the manifold criteria that have been applied in the effort (Brönsted equation considerations,[5b,c,6,7] rate–structure correla-

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[1] Winstein, S.; Darish, D.; Holness, N.J. *J. Am. Chem. Soc.* **1956**, *78*, 2915.

[2] de la Mare, P. B. D.; Vernon, C. A. *J. Chem. Soc.* **1956**, 41.

[3] Parker, A. J.; Ruane, M.; Biale, G.; Winstein, S. *Tetrahedron Lett.* **1968**, 2113.

[4] Biale, G.; Cook, D.; Lloyd, D. J.; Parker, A. J.; Stevens, I. D. R.; Takahashi, J.; Winstein, S. *J. Am. Chem. Soc.* **1971**, *93*, 4725.

[5] (a) Bunnett, J. F. *Surv. Prog. Chem.* **1969**, *5*, 53. (b) Eck, D.; Bunnett, J. F. *J. Am. Chem. Soc.* **1969**, 91, 3009. (c) Baciocchi, E.; Bunnett, J. F. *J. Org. Chem.* **1967**, *32*, 11. (d) McLennan, D. J., *J. Chem. Soc. c* **1966**, 705, 709.

[6] Parker, A. J.; Ruane, M.; Palmer, D. A.; Winstein, S. *J. Am. Chem. Soc.* **1972**, *94*, 2228.

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Table I. Temperature Dependence of the Kinetic Isotope Effect (TDKIE) in the Weak Base Catalyzed Elimination Reaction in the Series:

$$C_6H_5CHDCH_2X \xrightarrow[CH_3CN\ (-HX)]{Bu_4N^+F^-} [C_6H_5CH{=}CH_2 + C_6H_5CD{=}CH_2]^a$$

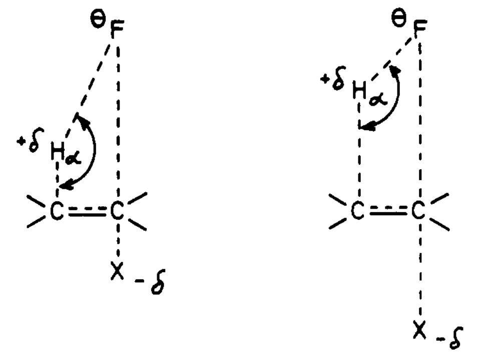
X	T, K ± 0.05°	$(k_H/k_D)_{corr}$[b]	$[\Delta E_a]_D^H$, kcal/mol	A_H/A_D	approx angle of H transfer, deg
$p\text{-}CH_3C_6H_5SO_3^-$	293.00	4.20 ± 0.02	0.09 ± 0.08	3.6 ± 0.3	110
	313.00	4.15 ± 0.04			
	333.00	4.13 ± 0.04			
	353.00	4.08 ± 0.01			
Br^-	293.00	5.06 ± 0.02	0.06 ± 0.06	4.6 ± 0.3	125
	313.00	4.99 ± 0.04			
	333.00	4.98 ± 0.03			
	353.00	4.97 ± 0.03			
$S^+(CH_3)_2$	293.00	7.367 ± 0.009	0.07 ± 0.06	6.6 ± 0.4	160
	313.00	7.325 ± 0.008			
	333.00	7.27 ± 0.01			
	353.00	7.23 ± 0.01			
$N^+(CH_3)_3$	293.00	6.177 ± 0.008	1.98 ± 0.02	0.212 ± 0.007	180
	313.00	5.139 ± 0.007			
	333.00	4.108 ± 0.002			
	353.00	3.514 ± 0.005			

[a] Analysis of the deuterium content of this mixture of styrenes was carried out by the mass spectrometric procedures previously discussed.[25] [b] Mass spectrum corrections and calculations of the isotope effect were carried out with the following data and computational procedures: $C_6H_5CH{=}CH_2$; $M_H/M_{H+1} = 9.794$, $C_6H_5CD{=}CH_2$; $M_{D\text{-}1}/M_D = 0.541$; let $M_{104}/M_{105} = R$, then $(k_H/k_D)_{corr} = (M_{105} - M_{H+1})/(M_{104} - M_{D\text{-}1}) = 0.143[(9.794 - R)/(R - 0.541)]$.

tions,[8–10] and kinetic isotope effects at a single temperature[11–13]), none are unequivocally capable of probing for the fundamental geometric distinctions between these TS proposals. Toward this objective we have applied the criterion of the temperature dependence of k_H/k_D (TDKIE), which has recently been developed[14–25] as a general approach for elucidating TS geometry in processes having a single rate-determining step.

Thus, a reaction showing a temperature-independent k_H/k_D, where $[\Delta E_a]_D^H = 0$ and the frequency factor ratio $A_H/A_D \gg 2^{1/2}$ is to be identified[20–25] with nonlinear H transfer in a bent TS. On the other hand, a reaction in which $[\Delta E_a]_D^H = 0$ and $A_H/A_D \ll 2^{1/2}$ would correspond to a single-step process involving linear H transfer in either a symmetric[14–19] or asymmetric[25] TS or via a tunneling H-transfer route.[18,22,23]

A series of β-phenylethyl derivatives, which are traditionally the substrates in β-elimination reaction studies, were chosen for application of the TDKIE criteria. The series was comprised of four different leaving groups varying widely in their nucleofugal properties (which decline from top to bottom in Table I). Fluoride ion in CH_3CN solvent, which has often been used in such eliminations,[26] was selected as the weak base reagent. The data obtained in each case over a 60 °C temperature range are listed in Table I.



1 2

	1	2
TS structure	tight	loose
angle (α) of transfer	large	small
A_H/A_D	large	small

Figure 1. Extreme types of the E2C TS*.

Clearly, the first three leaving groups show virtually temperature-independent isotope effects with A_H/A_D values much greater than $2^{1/2}$. These data provide empirical identification of a bent TS, i.e., nonlinear H transfer. By contrast, with a leaving group of the very poor nucleofugal activity of $^+N(CH_3)_3$, the isotope effect is dramatically altered. The k_H/k_D values become strongly temperature dependent, and KIE parameters identifying tunneling (linear) H transfer are observed.

The most obvious interpretation of these results in line with the TDKIE criteria of TS geometry is that above a threshold of leaving group ability an E2C mechanism of

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(7) Ford, W. T. *Acc. Chem. Res.* **1973**, *6*, 410.
(8) Ford, W. T.; Pietsek, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 2194.
(9) Lloyd, D. J.; Parker, A. J. *Tetrahedron Lett.* **1970**, 5029.
(10) Baciocchi, E. *Acc. Chem. Res.* **1979**, *12*, 430.
(11) Saunders, W. J., Jr. *Chem. Scripta* **1976**, *10*, 82; **1975**, *8*, 27.
(12) Burton, G. W.; Sims, L. B.; McLennan, D. J. *J. Chem. Soc., Perkin Trans. 2* **1977**, *2*, 1763.
(13) McLennan, D. J. *Tetrahedron* **1975**, *31*, 2999.
(14) Kwart, H.; Latimore, M. C. *J. Am. Chem. Soc.* **1971**, *93*, 3770.
(15) Kwart, H.; Nickle, J. H. *J. Am. Chem. Soc.* **1973**, *95*, 3394.
(16) Kwart, H.; Sarner, S. F.; Slutsky, J. *J. Am. Chem. Soc.* **1973**, *95*, 5242.
(17) Kwart, H.; Nickle, J. H. *J. Am. Chem. Soc.* **1976**, *98*, 2881.
(18) Kwart, H.; Stanulonis, J. J. *J. Am. Chem. Soc.* **1976**, *98*, 4009.
(19) Janssen, J. W. A. M.; Kwart, H. *J. Org. Chem.* **1977**, *42*, 1530.
(20) Kwart, H.; George, T. J.; Louw, R.; Ultee, W. *J. Am. Chem. Soc.* **1978**, *100*, 3927.
(21) Kwart, H.; Benko, D. A.; Bromberg, M. E. *J. Am. Chem. Soc.* **1978**, *100*, 7093.
(22) Kwart, H.; George, T. J. *J. Org. Chem.* **1979**, *44*, 162.
(23) Kwart, L. D.; Kwart, H.; Horgan, A. G. *J. Am. Chem. Soc.* **1981**, *103*, 1232.
(24) Kwart, H.; Brechbiel, M. *J. Am. Chem. Soc.* **1981**, *103*, 4650.
(25) Kwart, H. *Acc. Chem. Res.* **1982**, *15*, 401.
(26) Hayami, J.; Ono, N.; Kaji, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 1628.

weak base catalyzed elimination in β-phenylethyl derivatives is corroborated. Below this critical level of nucleofugal activity, the minimum energy pathway for H transfer to base is linear and consistent with the prescribed E2 geometry.[5]

These results indicate as well that the earlier proposal of Winstein[27] that all β-elimination processes proceed through a spectrum of transition states between extreme E2H and E2C cannot be correct.

The size of A_H/A_D in the E2C can be correlated with nucleofugal activity by the results of model calculations,[28] which show that at a single (constant) temperature, (i.e., $[\Delta E_a]_D^H = 0$), the angle of H transfer is a direct function of A_H/A_D. The value of $A_H/A_D = 6.6$ for $^+S(CH_3)_2$ is the largest found thus far. On the basis of such model calculations for a C–H bond, this corresponds to a ~160° angle of H transfer. Tosylate, the best leaving group tested thus far, also has the lowest value of $A_H/A_D = 3.6$, corresponding to an angle of ~110°.

Thus the larger angles of H transfer are to be reconciled with the smaller extents of bond making and breaking at C_α during rearward approach of the nucleophilic base and the departure of the leaving group. Consequently, large angles of H transfer denote a tighter TS with respect to the degree of double-bond development. Figure 1 summarizes the features of the extreme types 1 and 2 of transition states to be encountered with variation of nucleofugal, nucleophilic, and base properties of the reagents engaged in an E2C mechanism, as revealed by application of the TDKIE criteria.

Finally, the data in Table I indicate that in the E2C a tighter TS is associated with larger values of a temperature-independent k_H/k_D. Apparently, previous interpretations holding that increasing size of k_H/k_D generally bears a direct relationship to the looseness of the TS in β-elimination reactions can be incorrect when founded on a single temperature measurement.[5,11,13]

Moreover, the same β-phenylethyl derivatives, when subjected to HX elimination in a single-step reaction[29] with strong bases like NaOEt in EtOH, show strongly temperature-dependent isotope effects[30] with A_H/A_D values of less than $2^{1/2}$. In such cases, too, measurement of a single-temperature k_H/k_D, as is common practise, is to be recognized as an approach of dubious value in interpreting the tightness or looseness of the E2 TS.

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Registry No. $C_6H_5CHDCH_2X$ (X = p-$CH_3C_6H_4SO_3$), 84649-05-8; $C_6H_5CHDCH_2X$ (X = Br), 84649-06-9; $C_6H_5CHDCH_2X$ (X = $(CH_3)_2S^+$), 84649-07-0; $C_6H_5CHDCH_2X$ (X = $(CH_3)_3N^+$), 84649-08-1; deuterium, 7782-39-0.

---

(27) Winstein, S. "Abstracts of Papers", 144th National Meeting of the American Chemical Society, Los Angeles, CA, April 1, 1963; American Chemical Society: Washington, D.C., 1963; p 8M. *Academia Nazionale dei Lincei (Roma), VIII Corso* Estivo Di Chimica, Chimica Teoretica, **1965**, 327.

(28) More O'Ferrall, R. A. *J. Chem. Soc. B* **1970**, 785.

(29) For considerations of the isotope effect when the HX elimination involves more than one step, see: Kwart, H.; Horgan, A. G. *J. Org. Chem.* **1982**, *47*, 159.

(30) Unpublished results from these laboratories.

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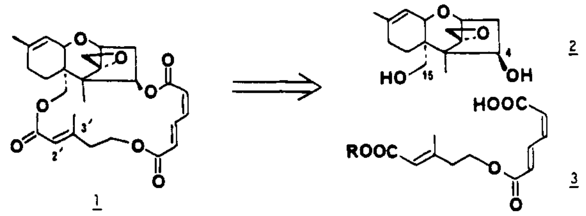
Synthesis of Verrucarin J

Summary: A synthesis of verrucarin J from verrucarol, 3-butyn-1-ol, and malealdehydic acid is described.

Sir: The trichoverroids, roridins, and verrucarins are important classes of biosynthetically related trichothecene metabolites produced by various *Myrothecium* species.[3,4] Many of these compounds possess a range of biological properties including antibacterial, antifugal, and cytostatic activity which is associated with the intact macrocycle present in the roridins and verrucarins. These factors have prompted a number of groups to initiate syntheses of some of these mycotoxins.[5] Our attention has focused recently on verrucarin J (1) which was first isolated in 1965 from the mycotoxin complex produced by *M. verrucaria*.[6] The natural product was originally assigned a *Z* configuration for the C(2′)–C(3′) double bond on the basis of chemical evidence. This assignment was later reversed to that of 1 by using spectroscopic methods;[5d,f,g] this correct structure was confirmed by the recent synthesis of verrucarin J from trichoverrin B.[5b] We report herein an alternative synthesis of 1 starting from verrucarol, 3-butyn-1-ol, and malealdehydic acid.

Our initial approach to 1 concentrated on a convergent strategy by which a differentiated version of diacid 3 would be coupled in a regiochemically controlled fashion to verrucarol (2).[5g,7] This approach has not yet proven successful, however, in large measure as a consequence of our inability to esterify appropriately functionalized (*Z*,*E*)-muconate half esters to C(4)–OH of the verrucarol nucleus without substantial (up to 50% even with DCC[5a]) isomerization to (*E*,*E*)-muconate diesters.[8] The successful synthesis described herein features an alternative strategy



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(1) Roger and Georges Firmenich Assistant Professor of Natural Products Chemistry; Fellow of the Alfred P. Sloan Foundation, 1982–1984.

(2) National Science Foundation Predoctoral Fellow, 1979–1982. Fellow of the Whitaker Health Sciences Fund, 1982–83.

(3) (a) Jarvis, B. B.; Stahly, G. P.; Pavanasasivam, G.; Midiwo, J. O.; De Silva, T.; Holmlund, C. E.; Mazzola, E. P.; Geoghegan, R. F., Jr. *J. Org. Chem.* **1982**, *47*, 1117. (b) Härri, E.; Loeffler, W.; Sigg, H. P.; Stähelin, H.; Stoll, C.; Tamm, C.; Wiesinger, D. *Helv. Chim. Acta* **1962**, *45*, 839. (c) Böhner, B.; Fetz, E.; Härri, E.; Sigg, H. P.; Stoll, C.; Tamm, C. *Ibid.* **1965**, *48*, 1079.

(4) (a) Doyle, T. W.; Braner, W. T. In "Anticancer Agents Based on Natural Product Models"; Cassidy, J. M., Douros, J., Eds.; Academic Press: New York, 1980; Chapter 2. (b) Tamm, C. *Fortschr. Chem. Org. Naturst.* **1974**, *31*, 63. (c) Bamburg, J. R.; Strong, F. M. In "Microbial Toxins"; Kadis, S., Ciegler, A., Ajl, S. J., Eds.; Academic Press: New York, 1971; Vol. 7, p 207.

(5) (a) Still, W. C.; Ohmizu, H. *J. Org. Chem.* **1981**, *46*, 5242. (b) Esmond, R.; Fraser-Reid, B.; Jarvis, B. B. *Ibid.* **1982**, *47*, 3358. (c) Notegen, E.-A.; Tori, M.; Tamm, C. *Helv. Chim. Acta* **1981**, *64*, 316. (d) Breitenstein, W.; Tamm, C. *Ibid.* **1978**, *61*, 1975. (e) Mohr, P.; Tori, M.; Grossen, P.; Herold, P.; Tamm, C. *Ibid.* **1982**, *65*, 1412. (f) White, J. D.; Carter, J. P.; Kezar, H. S., III *J. Org. Chem.* **1982**, *47*, 929. (g) Roush, W. R.; Blizzard, T. A.; Basha, F. Z. *Tetrahedron Lett.* **1982**, *23*, 2331. (h) Roush, W. R.; Spada, A. P. *Ibid.* **1982**, *23*, 3773. (i) Tomioka, K.; Sato, F.; Koga, K. *Heterocycles* **1982**, *17*, 311. (j) Trost, B. M. In "Asymmetric Reactions and Processes in Chemistry"; Eliel, E. L., Otsuka, S., Ed.; American Chemical Society: Washington, DC, 1982; ACS Symp. Ser. No. 185, p 3.

(6) Fetz, E.; Böhner, B.; Tamm, C. *Helv. Chim. Acta* **1965**, *48*, 1669.

(7) (a) Verrucarol was prepared from anguidine by a method developed by Fraser-Reid (described in detail in footnote 8 of ref 5b). We thank Professor Fraser-Reid for providing us with this procedure prior to publication. (b) Three total syntheses of racemic verrucarol have now been recorded: Schlessinger, R. H.; Nugent, R. A. *J. Am. Chem. Soc.* **1982**, *104*, 1116. Trost, B. M.; McDougal, P. G. *Ibid.* **1982**, *104*, 6110. Roush, W. R.; D'Ambra, T. E. *Ibid.*, in press.

0022-3263/83/1948-0758$01.50/0