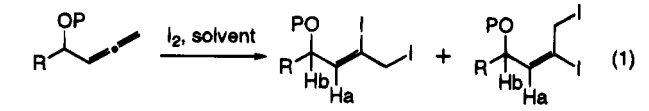
The Stereoselective Iodination of Secondary α-Allenic Alcohols and Their Derivatives

Richard W. Friesen,* Christopher I. Bayly,* and Julia A. Fogg

Department of Medicinal Chemistry, Merck Frosst Centre for Therapeutic Research, P.O. Box 1005, Pointe Claire-Dorval, Québec, Canada H9R 4P8

Received July 21, 1994

It is well established that iodine (I_2) adds regioselectively to 1,1-disubstituted allenes to afford 1,2-diiodo-3,3-dialkyl-2-alkenes, the more highly substituted and thermodynamically more stable olefin.[1] The analogous reaction with *mono*substituted allenes is much less studied, although in the course of other investigations, we[2] and others[3] have noted that I_2 does add regioselectively to the terminal double bond of these systems (eq 1). We were intrigued by the observation that the *Z*/*E*



1a-h R = n-heptyl
3a,d,g R = t-butyl

Z-2a-h
Z-4a,d,g

E-2a-h
E-4a,d,g

ratio of diiodides that was observed in the iodination of secondary α-allenic alcohols (P = H) was relatively invariant with respect to the steric size or makeup of the R substituent in these molecules.[2d] In contrast, it appeared that the P group did play a role in the iodination reaction since the *Z*/*E* ratios that were observed upon iodination of these derivatized alcohols were dramatically different from that of the analogous free alcohol.[2a-c] Since these diiodide products are potentially useful synthetic intermediates,[1] and in an effort to determine the principal factors that affect their isomeric distribution, we have studied the iodination reaction of α-allenic alcohols **1d** and **3d** and some of their derivatives.

Our initial investigations were conducted with **1a**, the TBDMS derivative of the allenic alcohol **1d**,[4] and the results are shown in Table 1, entries 1–6. All of the iodination reactions were conducted at room temperature in ambient room light, using approximately 0.1 M solutions of allene **1a** and 1.1 equiv of I_2. The reactions were monitored by ^{1}H NMR until isomerization of the diiodide products **Z-2a** and **E-2a** no longer occurred. As can be seen from these data, the equilibrium distribution and time required to reach equilibrium is relatively invariant with respect to solvent (Table 1, entries 1–4), leading to the predominance of the *Z* isomer **Z-2a** in each case (~13:1). The olefin geometry was easily assigned on the basis of the chemical shift of the vinylic protons Ha in the ^{1}H NMR spectrum of the crude diiodide reaction

Table 1. Addition of Iodine to α-Allenic Alcohols 1 and 3 and Their Derivatives[a]

entry	substrate (P)	reaction solvent[b]	*Z*:*E* ratio initial[c]	*Z*:*E* ratio equilibrium[d]	time to equilibrium (h)[e]
1	**1a**, P = TBDMS	CD_2Cl_2	0.8:1	11:1	3
2		C_6D_6	0.9:1	14:1	3
3		THF-d_8	0.8:1	12:1	3
4		$CDCl_3$	0.8:1	13:1	3
5		$CDCl_3$	0.8:1	0.8:1[f]	(24)
6		$CDCl_3$	0.8:1	0.8:1[g,h]	(15)
7	**1b**, P = TES	$CDCl_3$	0.8:1	13:1	3
8	**1c**, P = TIPS	$CDCl_3$	0.6:1	13:1	6
9	**1d**, P = H	$CDCl_3$	1.6:1	7:1	0.25
10	**1e**, P = Me	$CDCl_3$	0.8:1	7:1	3
11	**1f**, P = MOM	$CDCl_3$	0.7:1	5:1[i]	(4)
12	**1g**, P = Ac	$CDCl_3$	0.8:1	3:1	2
13	**1h**, P = CO^{t}Bu	$CDCl_3$	0.9:1	3:1	3
14	**3a**, P = TBDMS	$CDCl_3$	0.2:1	0.2:1	(24)
15	**3a**, P = TBDMS	$CDCl_3$	0.2:1	6:1[i,j]	(144)
16	**3d**, P = H	$CDCl_3$	1.3:1	8:1	8
17	**3g**, P = Ac	$CDCl_3$	0.4:1	2:1	48

[a] Iodination reactions carried out at rt in ambient room light on approximately 0.1 M solutions of substrate using 1.1 equiv I_2. [b] Deuterated solvents were shaken with Na_2CO_3 and $MgSO_4$ immediately prior to use. [c] Ratio obtained within 2–5 min of addition of I_2 to the sample. [d] When no change in ratio occurs over 1 h. [e] Values in parentheses refer to the last time point taken for those reactions that did not reach equilibrium. [f] 0.75 equiv of I_2 used in this reaction. [g] Reaction carried out in the dark. [h] When put into the light, *Z*/*E* ratio goes to 13:1 in 3 h. [i] Ratio still changing but some slight decomposition occurring as well. [j] Reaction carried out at 60 °C.

Table 2. ^{1}H NMR Data: Vinyl Proton Resonances for the Diiodides 2 and 4[a]

entry	diiodide	*Z* isomer δ Ha (ppm)	*Z* isomer J_{ab} (Hz)	*E* isomer δ Ha (ppm)	*E* isomer J_{ab} (Hz)
1	**2a**[b]	5.89	7.6	6.21	8.4
2	**2b**	5.87	7.6	6.19	8.2
3	**2c**	5.94	7.4	6.22	8.3
4	**2d**[b]	5.94	7.6	6.19	8.5
5	**2e**	5.80	8.0	6.09	8.9
6	**2f**	5.88	8.1	6.10	9.3
7	**2g**[b]	5.98	7.6	6.10	9.5
8	**2h**	5.93	7.7	6.06	9.6
9	**4a**[b]	5.84	8.5	6.19	9.5
10	**4d**	5.94	8.5	6.27	9.2
11	**4g**	5.89	8.9	6.16	10.2

[a] Spectra obtained in $CDCl_3$. [b] NOE experiments similar to those described in the text for **Z-2a** and **E-2a** were performed using these substrates.

mixture.[2a,b] The vinyl proton resonance in the major *Z* isomer **Z-2a** is 0.32 ppm upfield from the corresponding resonance in the *E* isomer **E-2a** (see Table 2). This assignment was also confirmed by appropriate NOE experiments. Irradiation at the resonance frequency of Ha in the *Z* isomer **Z-2a** (δ 5.89) resulted in an enhancement of the =CHICH_2I resonance (δ 4.28 and 4.39), while irradiation of the analogous resonance in the *E* isomer **E-2a** (δ 6.21) did not result in the enhancement of any other resonance. The isomerization of the diiodides from the initially observed ratio (*Z*/*E* ≈ 0.8:1) requires an excess of I_2 (Table 1, entry 5) and the presence of light (Table 1, entry 6). These observations suggest that, following the initial rapid addition of I_2 to the allene system (~5 min), the subsequent isomerization and equilibration of the diiodides proceeds via a radical mechanism involving excess I_2 and that the final *Z*/*E* ratio is governed by the thermodynamics of the system. Presumably the isomerization mechanism involves the

(1) (a) Coulomb, F.; Roumestant, M. L. *Bull. Soc. Chim. Fr.* **1973**, 3352. (b) Georgoulis, C.; Smadja, W.; Valery, J. M. *Synthesis* **1981**, 572.

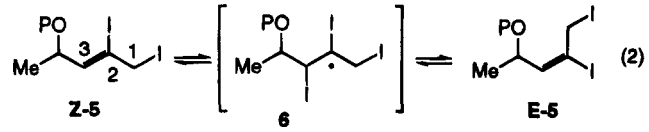
(2) (a) Friesen, R. W. *Tetrahedron Lett.* **1990**, *30*, 4249. (b) Friesen, R. W.; Kolaczewska, A. E. *J. Org. Chem.* **1991**, *56*, 4888. (c) Friesen, R. W.; Giroux, A. *Tetrahedron Lett.* **1993**, *34*, 1867. (d) Friesen, R. W.; Blouin, M. *J. Org. Chem.* **1993**, *58*, 1653.

(3) See, for example: (a) Shaw, R.; Anderson, M.; Gallagher, T. *Synlett* **1990**, 584. (b) Walkup, R. D.; Guan, L.; Kim, S. W.; Kim, Y. S. *Tetrahedron Lett.* **1992**, *33*, 3969.

(4) Cowie, J. S.; Landor, P. D.; Landor, S. R. *J. Chem. Soc., Perkin Trans. 1* **1973**, 720.

0022-3263/95/1960-0448$09.00/0

addition–elimination of I• to the olefin and the intermediacy of a radical such as **6** (eq 2).

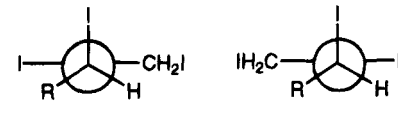


We then surveyed the iodination of derivatives of **1d** using a series of alcohol protecting groups (Table 1, entries 7–13, and Table 2) and noted several trends. Changing P in **1a** from TBDMS to different silyl protecting groups (P = TES (**1b**) or TIPS (**1c**); Table 1, entries 7 and 8) did not alter the final ratio of diiodides (*Z*/*E* 13:1) when compared with **1a** although the reaction with **1c** (P = TIPS) took twice as long to reach equilibrium. Using alkyl protecting groups (P = Me (**1e**), MOM (**1f**); Table 1, entries 10 and 11) resulted in the formation of diiodides in similar *Z*/*E* ratios (*Z*/*E* ≈ 7:1). The iodination reaction with the alcohol **1d** (Table 1, entry 9) was extremely rapid, with equilibration being complete within 15 min, resulting in a final *Z*/*E* diiodide ratio of 7:1 as well. Acyl derivatives of alcohol **1d** (P = Ac (**1g**), CO^{t}Bu (**1h**); Table 1, entries 12 and 13) provided diiodide products with identical *Z*/*E* ratios (*Z*/*E* 3:1) in approximately 3 h.

We have also explored the effect of the size of R on the iodination reaction using the α-allenic alcohol **3d** (R = *tert*-butyl), and the TBDMS and Ac derivatives **3a** and **3g**, respectively (Table 1, entries 14–17). Iodination of alcohol **3d** (P = H) provided diiodides in a ratio of *Z*/*E* 8:1, the same result as is obtained with **1d** (compare Table 1, entries 9 and 16). Similarly, the acetyl derivative of each α-allenic alcohol **1g** and **3g** (P = Ac) resulted in a *Z*/*E* diiodide ratio of 3:1 (Table 1, entries 12 and 17). For each of these examples, the time required to reach equilibrium is significantly longer for the allenes in which R = *tert*-butyl, even though the equilibrium *Z*/*E* ratios are similar to the analogous compounds in which R = *n*-heptyl. This observation suggests that the size of the R group does not play a significant role in the magnitude of the equilibrium *Z*/*E* ratio but rather the rate at which equilibrium is attained. This observation is exemplified in the case of **3a** (P = TBDMS; Table 1, entries 14 and 15) where *Z*/*E* isomerization does not occur at all at room temperature and only slowly at 60 °C. Assuming that the isomerization mechanism involves a radical reaction that proceeds via the addition of I• to the initially generated diiodides, it appears that the increased steric bulk of the R and P groups in **3a** compared to **1a** hinder the approach of I• to the olefin. As a result, there is a decrease in the rate of this addition reaction as well as the isomerization process and thermodynamic equilibrium is not achieved.

It is clear from these results that it is the alcohol protecting group that has the most profound effect on the *Z*/*E* diiodide ratio. Since the iodine atom is sterically smaller than the CH_2I moiety (A values:[5] I = 0.43, CH_3 = 1.73), the steric interaction between the R/OP groups and the iodine atom in the *Z* isomers would be smaller than the interaction between the R/OP groups and the CH_2I moiety in the *E* isomers. Thus, the *general* predominance of the Z olefin isomer over the *E* isomer under equilibrating conditions can be easily rationalized by arguing on steric grounds alone. What is not easily explained is the discrepancy in the magnitude of the *Z*/*E* ratios *between* the three protecting group series (P = silyl ~13:1 > alkyl/H ~7:1 > acyl ~3:1). A priori, one would expect that the P group would probably "turn away" from the I and CH_2I moieties in each of the low-energy conformations of each isomer, resulting in little interaction with these substructures. Thus, the steric size of the P group should not dramatically affect the relative thermodynamic stability and distribution of the two alkene isomers.

We have employed computational chemistry in an attempt to better understand and rationalize the basis for these *Z*/*E* ratios, in particular the ordering of the magnitude of these ratios in the series P = silyl > alkyl, H > acyl. Semiempirical calculations were carried out using the AM1, PM3, and MNDO methods to assess the relative stabilities (a) between the *E* and *Z* isomers of the model olefin **5** (**5a–c** P = H, Ac, and TMS, respectively) and (b) between the *pro-E* and *pro-Z* conformers of the radical intermediate **6** involved in the *E*/*Z* interconversion (eq 2). Preliminary calculations indicated that the iodination of the double bond to form a radical intermediate would occur on C3, generating a radical center on C2. The alternative radical intemediate that would be obtained by iodination at C2, generating a *gem*-diiodo species with the radical centered at C3, was found to be 4.5 kcal/mol (AM1) to 7.5 kcal/mol (MNDO) higher in energy (P = H). Therefore, the former structure, **6**, was used for the intermediate. Whether a *Z* or *E* olefin is formed upon departure of the iodine from the radical intermediate **6** is determined by the conformation around the bond between the sp^3-hybridized C3 and the sp^2-hybridized radical center at C2. The conformational local minima around this bond place the labile iodine approximately perpendicular (90° ± 25°) to the plane of the adjacent radical center, as electronically required to form the double bond upon iodine departure. Consequently, one substituent of the C2 radical center is approximately staggered between the large iodine and alkyl substituents at C3, while the other occupies the sterically less demanding position between the C3 iodine and hydrogen. Staggering the C2 iodo group in between the C3 iodine and alkyl substituent gives rise to the *pro-Z* conformer **Z-6**. The *pro-E* conformer **E-6** results from the other possibility, i.e. placing the larger C2 iodomethyl group in between the two largest C3 substituents, an energetically less stable arrangement.



The relative heats of formation for the olefin isomers **E-5** and **Z-5** and the intermediates **E-6** and **Z-6** are compared in Table 3. For the PM3 method, the relative energies have a magnitude consistent with the experimental data, but unfortunately they predict the equilibrium to lie in the wrong direction! The AM1 results show very small relative energy differences, which also favor the *E* isomer except in the case of **5a** (P = H). Clearly, these two semiempirical methods are not useful here in understanding the experimental results. However, the MNDO results for the radical intermediate **6** show

(5) Hirsch, J. A. In *Topics in Stereochemistry*, Volume 1; Allinger, N. L., Eliel, E. L., Eds.; John Wiley & Sons: New York, 1967; pp 199–222.

Table 3. Relative Energies of E-5 and Z-5 and of the Corresponding Most Stable *pro-E* and *pro-Z* Conformers E-6 and Z-6

		relative energies (kcal/mol)			
		olefin		radical intermediate	
olefin **5**	semiempirical method	E-5	Z-5	E-6	Z-6
5a (P = H)	AM1	1.5	0	0	0.2
	MNDO	1.1	0	0.6	0
	PM3	0	3.2	0	2.6
5b (P = Ac)	AM1	0	0.5	0	0.6
	MNDO	0	0.2	0.5	0
	PM3	0	3.5	0	2.6
5c (P = TMS)	AM1	0	0.1	0	0.2
	MNDO	0.7	0	0.7	0
	PM3	0	4.7	0	2.9

qualitative agreement with experiment in that the *pro-Z* isomer **Z-6** is always the more stable, and the experimentally determined degree of preference for the *Z* isomer (P = TMS > H > Ac) is retained, albeit by a small amount. In contrast, the olefin energies using MNDO give rise to the ordering P = H > TMS > Ac with the *E* isomer being preferred for **5b** (P = Ac).

Thus, the MNDO calculations suggest that the experimental predominance of the *Z* isomer is rationalizable from the conformational equilibrium of the radical intermediate **6** but not from the relative energies of the corresponding olefins **E-5** and **Z-5**. Unfortunately the MNDO calculations do not offer an electronic basis for the magnitude of the *Z* isomer preference, while steric arguments alone do not explain, for example, why the P = H substitution gives a higher *Z*/*E* ratio than the P = Ac substitution. This aspect of the mechanism remains unresolved.

Nevertheless, from the experimental results it is clear that nature of the protecting group plays an important role in determining the *Z*/*E* isomer distribution, much more so than the steric size of the R group on the allenic alcohol. Although the underlying factors responsible for these observations are not apparent, the experimental results should prove to be of benefit when contemplating the preparation of diiodides such as **2** and **4** for use in subsequent synthetic operations.

Experimental Section

General Procedures. ^{1}H NMR spectra were recorded at 200, 300, or 400 MHz in $CDCl_3$, unless stated otherwise, using TMS or $CHCl_3$ as internal standard. Broad band decoupled ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$, using $CDCl_3$ as internal standard. IR spectra were recorded on neat samples. Workup procedures involving the drying of organics was done with $MgSO_4$. Column chromatography was carried out on 230–400 mesh silica gel (40–63 μm), eluting with the solvents indicated. High-resolution mass spectra determinations were performed at The Biomedical Mass Spectrometry Unit, McGill University. Compounds characterized in this manner were homogeneous by TLC analysis and gave NMR spectra indicative of their purity. α-Allenic alcohols **1d** and **3d** have been prepared previously.[2b]

4-(*tert*-Butyldimethylsiloxy)-1,2-undecadiene (1a). A mixture of α-allenic alcohol **1d** (208 mg, 1.24 mmol), TBDMSCl (224 mg, 1.2 equiv) and imidazole (212 mg, 2.5 equiv) in DMF (1.5 mL) was stirred at room temperature for 3 h. To the mixture was added 5% $NaHCO_3$, and the mixture was extracted with ether (3×). The combined organics were washed with water (3×) and brine, dried, and concentrated. Flash chromatography of the residue (200:1 hexane/ether (v/v)) provided silyl ether **1a** (290 mg, 83%) as a colorless oil: IR 2950, 2920, 2850, 1955, 1460, 1250, 835 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.04 (s, 6H), 0.86 (t, 3H, J = 7.0 Hz), 0.87 (s, 9H), 1.20–1.40 (br m, 10H), 1.45–1.60 (m, 2H), 4.12 (br q, 1H, J = 6.7 Hz), 4.65–4.76 (m, 2H), 5.07 (q, 1H, J = 6.9 Hz); ^{13}C NMR δ −4.5, 14.1, 18.2, 22.6, 25.4, 25.9, 29.3, 29.5, 31.8, 38.7, 71.6, 75.7, 95.0, 207.4; HRMS calcd for $C_{17}H_{35}OSi$ (M + H$^+$) 283.2458, found 283.2457.

4-(Triethylsiloxy)-1,2-undecadiene (1b). Following the procedure described for the preparation of **1a** but substituting TESOTf for TBDMSCl, **1d** (302 mg, 1.79 mmol) was converted into **1b** (230 mg, 45%), a colorless oil: IR 2950–2850, 1960, 1455, 1235, 840 cm^{-1}; ^{1}H NMR (200 MHz) δ 0.54–0.67 (m, 6H), 0.86–1.01 (m, 12H), 1.20–1.45 (m, 10H), 1.45–1.65 (m, 2H), 4.14 (br q, 1H, J = 6.2 Hz), 4.66–4.82 (m, 2H), 5.12 (q, 1H, J = 6.7 Hz); ^{13}C NMR δ 4.9, 6.8, 14.1, 22.6, 25.5, 29.3, 29.5, 31.8, 38.7, 71.5, 75.6, 94.9, 207.4; HRMS calcd for $C_{17}H_{35}OSi$ (M + H$^+$) 283.2458; found 283.2457.

4-(Triisopropylsiloxy)-1,2-undecadiene (1c). Following the procedure described for the preparation of **1a** but substituting TIPSCl for TBDMSCl, **1d** (301 mg, 1.79 mmol) was converted into **1c** (318 mg, 55%), a colorless oil: IR 2960–2860, 1958, 1460, 1240, 880, 840 cm^{-1}; ^{1}H NMR (200 MHz) δ 0.89 (br t, 3H, J = 6.5 Hz), 1.02–1.18 (m, 21H), 1.22–45 (m, 10H), 1.50–1.70 (m, 2H), 4.27 (br q, 1H, J = 6.7 Hz), 4.65–4.80 (m, 2H), 5.12 (q, 1H, J = 7.0 Hz); ^{13}C NMR δ 12.4, 14.1, 18.0, 18.1, 22.7, 25.0, 29.3, 29.6, 31.8, 39.1, 71.8, 75.5, 95.0, 207.4; HRMS calcd for $C_{20}H_{41}OSi$ (M + H$^+$) 325.2928; found 325.2927.

4-Methoxy-1,2-undecadiene (1e). To a solution of alcohol **1d** (301 mg, 1.79 mmol) in DMF (5 mL) at 0 °C was added NaH (270 mg of 80% suspension in oil, 5 equiv) portionwise. After 30 min, MeI (0.56 mL, 5 equiv) was added and the mixture was stirred at room temperature for 24 h. Water was added, and the mixture was extracted with ether (3×). The combined extracts were washed with brine, dried, and concentrated. Flash chromatography of the residue (100:1 hexane/ether (v/v)) provided the title compound (181 mg, 56%) as an extremely volatile, colorless oil: IR 2920, 2850, 1955, 1460, 1090, 835 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.86 (t, 3H, J = 6.8 Hz), 1.02–1.70 (m, 12H), 3.29 (s, 3H), 3.62 (br q, 1H, J = 6.5 Hz), 4.64–4.80 (m, 2H), 4.95 (q, 1H, J = 7.1 Hz); ^{13}C NMR δ 14.1, 22.6, 25.4, 29.2, 29.5, 31.8, 35.8, 56.0, 75.2, 80.2, 91.3, 208.8; HRMS calcd for $C_{12}H_{23}O$ (M + H$^+$) 183.1748, found 183.1749.

4-(Methoxymethoxy)-1,2-undecadiene (1f). To a solution of alcohol **1d** (301 mg, 1.79 mmol) and diisopropylethylamine (1.56 mL, 5 equiv) in CH_2Cl_2 (3 mL) at 0 °C was added MOMCl (0.54 mL, 4 equiv). The mixture was stirred at room temperature for 48 h, and then water was added. The mixture was extracted with ether (3×), and the combined organics were washed with brine, dried, and concentrated. Flash chromatography of the residue (60:1 hexane/ether (v/v)) provided the title compound (276 mg, 73%) as a colorless oil: IR 3000–2800, 1955, 1460, 1210, 1150, 1095, 1030, 920, 840 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.89 (t, 3H, J = 6.8 Hz), 1.02–1.50 (m, 10H), 1.50–1.70 (m, 2H), 3.39 (s, 3H), 4.10 (br q, 1H, J = 6.6 Hz), 4.56 (d, 1H, J = 6.7 Hz), 4.76–4.85 (m, 3H), 5.03 (m, 1H); ^{13}C NMR δ 14.0. 22.6, 25.4, 29.2, 29.4, 31.7, 35.9, 55.3, 74.5, 75.6, 91.4, 93.8, 208.6; HRMS calcd for $C_{13}H_{25}O_2$ (M + H$^+$) 213.1854, found 213.1855.

4-Acetoxy-1,2-undecadiene (1g). To a solution of alcohol **1d** (302 mg, 1.79 mmol), DMAP (20 mg, 0.1 equiv), and pyridine (0.29 mL, 2 equiv) in CH_2Cl_2 (8 mL) at 0 °C was added Ac_2O (0.68 mL, 4 equiv). After 2 h at room temperature, 25% NH_4OAc buffer was added and the mixture was extracted with ether (3×). The combined organics were washed with brine, dried, and concentrated. Flash chromatography of the residue (70:1 hexane/ether (v/v)) provided the title compound (254 mg, 67%) as a colorless oil: IR 2920, 2850, 1960, 1735, 1365, 1230, 1015, 840 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.89 (t, 3H, J = 6.8 Hz), 1.20–1.50 (m, 10H), 1.50–1.75 (m, 2H), 2.06 (s, 3H), 4.84–4.92 (m, 2H), 5.15–5.30 (m, 2H); ^{13}C NMR δ 14.1, 21.2, 22.6, 25.2, 29.15, 29.24, 31.7, 34.1, 71.8, 77.1, 90.9, 170.4, 208.4; HRMS calcd for $C_{13}H_{23}O_2$ (M + H$^+$) 211.1698, found 211.1698.

4-Pivaloxy-1,2-undecadiene (1h). To a solution of alcohol **1d** (202 mg, 1.20 mmol), pyridine (0.3 mL, 3 equiv), and DMAP (14 mg, 0.1 equiv) in CH_2Cl_2 (5 mL) at room temperature was added pivaloyl chloride (0.6 mL, 4 equiv), and the mixture was refluxed for 5 h. Water and CH_2Cl_2 (10 mL) were added, and the organic phase was removed. The organic phase was washed with 10% HCl and brine, dried, and concentrated. Flash chromatography of the residue (70:1 hexane/ether (v/v)) provided the title compound (278 mg, 92%) as a colorless oil: IR 2920, 2850, 1960, 1810, 1725, 1275, 1150, 840 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.89 (t, 3H, J = 6.8 Hz), 1.20 (s, 9H), 1.20–1.45 (m, 10H),

1.45–1.75 (m, 2H), 4.75–4.91 (m, 2H), 5.17–5.30 (m, 2H); ^{13}C NMR δ 13.9, 22.5, 25.1, 26.3, 27.0, 29.0, 31.6, 34.1, 38.6, 70.9, 77.0, 91.0, 177.6, 208.0; HRMS calcd for $C_{16}H_{29}O_2$ (M + H^+) 253.2167, found 253.2168.

4-(*tert*-Butyldimethylsiloxy)-5,5-dimethyl-1,2-hexadiene (3a). Following the procedure described for the preparation of **1a**, **3d** (502 mg, 3.98 mmol) was converted into **3a** (802 mg, 84%), a colorless oil: IR 2950, 2850, 1960, 1250, 1070, 860, 835, 770 cm^{-1}; ^1H NMR (400 MHz) δ 0.02 (s, 6H), 0.85 (s, 9H), 0.88 (s, 9H), 3.73 (td, 1H, J = 1.2, 8.6 Hz), 4.56–4.71 (m, 2H), 5.03 (td, 1H, J = 6.7, 8.6 Hz); ^{13}C NMR δ 18.2, 25.69, 25.71, 25.9, 36.4, 74.6, 79.9, 91.8, 208.4; HRMS calcd for $C_{14}H_{29}OSi$ (M + H^+) 241.1988, found 241.1988.

4-Acetoxy-5,5-dimethyl-1,2-hexadiene (3g). Following the procedure described for the preparation of **1g**, **3d** (100 mg, 0.79 mmol) was converted into **3g** (105 mg, 79%), an extremely volatile colorless oil: IR 2940, 2860, 1958, 1740, 1240, 1020, 840 cm^{-1}; ^1H NMR (400 MHz) δ 0.90 (s, 9H), 2.02 (s, 3H), 4.72–4.82 (m, 2H), 4.98 (td, 1H, J = 1.9, 6.8 Hz), 5.09 (q, 1H, J = 6.8 Hz); ^{13}C NMR δ 21.0, 25.6, 34.8, 76.2, 78.8, 87.9, 170.3, 208.9; HRMS calcd for $C_{10}H_{17}O_2$ (M + H^+) 169.1229, found 169.1228.

General Procedure for ^1H NMR Iodination Experiments. To a solution of allene (0.05 mmol) in the desired solvent (0.5 mL; the deuterated solvents were shaken with solid $Na_2CO_3/MgSO_4$ and then filtered through alumina immediately prior to use) in a NMR tube was added solid iodine (0.06 mmol), and the mixture was shaken until the iodine dissolved (approximately 2–5 min). The progress of the reaction was monitored by ^1H NMR until no more equilibration took place. Pertinent ^1H NMR data are summarized in Table 2. The NMR tube was kept at the desired temperature in the light between acquisition of spectra. In some cases, the reaction mixtures were treated with 10% $Na_2S_2O_3$, extracted with EtOAc, dried, and concentrated. Inspection of the ^1H NMR spectra of these crude mixtures indicated that the Z/E ratios were identical to those observed in the NMR tubes prior to workup.

Computational Methods. All semiempirical calculations were carried out using version 6 of MOPAC for SGI hardware.[6] The approach taken was to compare the heats of formation of the global minima for (a) the E and Z isomers of the olefin and (b) the *pro-E* and *pro-Z* conformers of the radical intermediate involved in the E/Z interconversion. To establish the global minimum for the olefin species, grid searches were carried out by driving the O–C–C=C and torsion angle through 360° by 30° increments, placing the P substituent *anti* to the olefin and testing the C=C–C–I angle in both the + and – gauche positions. For the intermediate, preliminary calculations showed that the + and – gauche positions for the C–C–CH_2–I angle gave rise to virtually identical energies so this angle was set to the – gauche position. Two-dimensional grid searches were carried out by driving both the O–C–C–C and C–C–C–C torsion angles through 360° by 30° increments, placing the P substituent *anti* to the O–C–C–C bond. The most stable isomer from the grid searches was then fully optimized to give the global minimum. For comparison purposes, this approach was carried out using the AM1, PM3, and MNDO methods with the PRECISE keywords demanding higher precision in the SCF convergence. For the radical intermediates, the UHF and DOUBLET keywords were also specified.

Acknowledgment. Financial support in the form of a NSERC summer student scholarship (to J.A.F.) is acknowledged. We would like to thank Dr. Laird Trimble for carrying out the NOE difference experiments.

Supplementary Material Available: ^1H NMR spectra of the allenes **1a–1h** and **3a**, **3d**, and **3g** as well as ^1H NMR spectra of the corresponding diiodides at equilibrium (22 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9412490

(6) QCPE 455/SGRW, Quantum Chemistry Program Exchange, Creative Arts Building 181, Indiana University, Bloomington, IN 47405.