Iodine Monobromide (IBr) at Low Temperature: Enhanced Diastereoselectivity in Electrophilic Cyclizations of Homoallylic Carbonates

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Iodine monobromide affords superior diastereoselectivity in low-temperature electrophilic cyclizations of homoallylic carbonates. Solvent and temperature effects and the scope and limitations of the method are discussed; optimal selectivity is obtained in toluene at −80 to −85 °C. The latter protocol generally furnishes significantly enhanced selectivity, vis-á-vis the original procedure employing I_2 in acetonitrile at −20 °C; for example, the IBr-induced cyclization of 14 affords a 25.8:1 mixture of 15 and 16, whereas I_2 gives an 8.4:1 ratio. An equilibration experiment established that the diastereoselectivity derives primarily or exclusively from kinetic control of the cyclization process.

Epoxide moieties serve as important structural elements in many natural products of interest to the chemical and biomedical communities; prominent examples include the periplanones,[1a,b] phyllanthostatins,[1c] dynemicins,[1d] and the neocarzinostatin chromophore A.[1e-g] In many cases, this functionality is essential for biological activity. Epoxides are also valuable synthetic intermediates because they react efficiently with a variety of carbon, hydrogen, and heteroatom nucleophiles.[2] As a result, the diastereoselective and asymmetric preparations of epoxides have attracted considerable attention during the last 2 decades.[2,3] In connection with our calyculin synthetic venture,[4] we became interested in the conversion of homoallylic alcohol (+)-1 to epoxide 2. Numerous published reports indicated that the direct epoxidation of simple homoallylic alcohols, either with peracids or hydroperoxide–transition metal reagents, generally proceeds with very modest selectivity.[5-9] These precedents foreshadowed the unsatisfactory results obtained in the epoxidation of our calyculin intermediate. For example, reaction of (+)-1 with *t*-BuOOH/VO(acac)$_2$[7] afforded a 3:2 mixture of (−)-2 and the unwanted diastereomeric epoxide.

(+)-1 Calyculin precursor (-)-2

Our search for a more effective approach led us to the iodocarbonate cyclization. In 1981, Cardillo[10a] first described the diastereoselective iodine-induced electrophilic cyclization of homoallylic lithium carbonates [3 (R = Li) → 4, Scheme I]. One year later, Bartlett reported that similar yields and isomer ratios could be achieved by treatment of the corresponding *tert*-butyl, benzyl, 4-methoxybenzyl, and 2,4-dimethoxybenzyl carbonates with iodine in acetonitrile at −20 °C.[11] The less reactive methyl carbonates (3, R = Me), on the other hand, proved to be inferior because higher temperatures were required.[10b] As outlined in Scheme I, the resultant six-membered iodo carbonates 4 are versatile intermediates which readily furnish: (a) epoxy alcohols 5, as required for the calyculins (3 equiv of K_2CO_3 in methanol or Amberlyst 26-A, OH^- form in methanol),[10b,11] (b) methyl carbonate derivatives 6 (1.1 equiv of K_2CO_3 in methanol and water),[11] (c) iodohydrins 7 (1 equiv of K_2CO_3 in methanol at 0 °C),[11] (d) triols 8 (Amberlyst 26-A, CO_3^{2-} form in benzene),[10b] (e) diols 9 (lithium aluminum hydride),[11] and (f) cyclic carbonates 10 (tributyltin hydride).[11]

(1) (a) Persoons, C. J.; Verwiel, P. E. J.; Ritter, F. J.; Talman, R. E.; Nooijen, P. J. F.; Nooijen, W. J. *Tetrahedron Lett.* **1976**, 2055. (b) Still, W. C. *J. Am. Chem. Soc.* **1979**, *101*, 2493. (c) Pettit, G. R.; Cragg, G. M.; Suffness, M. I.; Gust, D.; Boettner, F. E.; Williams, M.; Saenz-Renauld, J. A.; Brown, P.; Schmidt, J. M.; Ellis, P. D. *J. Org. Chem.* **1984**, *49*, 4258. (d) Konishi, M.; Ohkuma, H.; Tsuno, T.; Oki, T.; VanDuyne, G. D.; Clardy, J. *J. Am. Chem. Soc.* **1990**, *112*, 3715. (e) Napier, M. A.; Holmquist, B.; Strydom, D. J.; Goldberg, I. H. *Biochem. Biophys. Res. Commun.* **1979**, *89*, 635. (f) Koide, Y.; Ishii, F.; Hasuda, K.; Koyama, Y.; Edo, K.; Katamine, S.; Kitame, F.; Ishida, N. *J. Antibiot.* **1980**, *33*, 342. (g) Suzuki, H.; Miura, K.; Kumada, Y.; Takeuchi, T.; Tanaka, N. *Biochem. Biophys. Res. Commun.* **1980**, *94*, 255.

(2) For reviews of preparations and synthetic applications of epoxides, see: (a) Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta* **1979**, *12*, 63. Also see: Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1986; Vol. 5, pp 247-308. (b) Rao, A. S.; Paknikar, S. K.; Kirtane, J. G. *Tetrahedron* **1983**, *39*, 2323. (c) Rossiter, B. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1986; Vol. 5, pp 193-246.

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(4) (a) Smith, A. B., III; Duan, J. J.-W.; Hull, K. G.; Salvatore, B. A. *Tetrahedron Lett.* **1991**, *32*, 4855. (b) Smith, A. B., III; Salvatore, B. A.; Hull, K. G.; Duan, J. J.-W. *Tetrahedron Lett.* **1991**, *32*, 4859. (c) Smith, A. B., III; Duan, J. J.-D.; Hull, K. G.; Salvatore, B. S.; Bertounesque, E. *Abstracts of Papers*, 203rd National Meeting of the American Chemical Society, San Francisco, CA, Spring 1992; American Chemical Society: Washington DC, 1992; ORGN 216.

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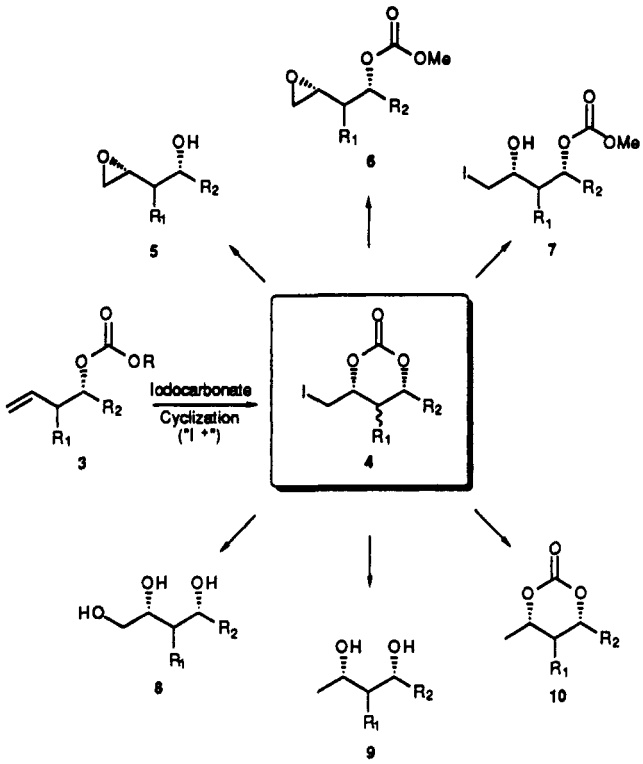
Scheme I



For our calyculin program, the iodine-induced carbonate cyclization of **11**, the *tert*-butyl carbonate derived from **1**, furnished an encouraging 5.7:1 isomer ratio (*vide infra*). In an effort to enhance the diastereoselectivity of this transformation, we next investigated the use of iodine monobromide (IBr) as electrophile.[12,13] In this full account, we describe the development of a highly effective new protocol for low-temperature, IBr-induced cyclization of diverse homoallylic carbonates.

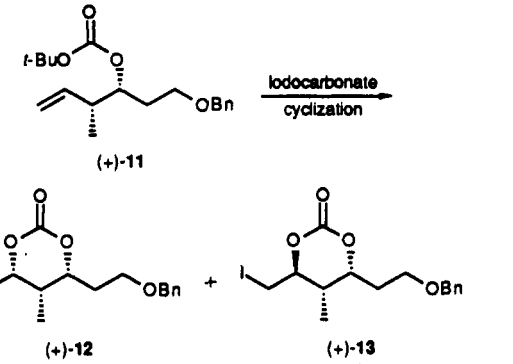
Iodine Monobromide-Induced Cyclization: An Interesting Interplay of Solvent and Temperature Effects. Because the cationic leaving groups (e.g., *tert*-butyl, benzyl) have previously exerted little effect on selectivity,[11] *tert*-butyl carbonates were employed throughout this study. As noted above, exposure of carbonate (+)-**11** to Bartlett's original conditions (iodine in acetonitrile at −20 °C) furnished a 5.7:1 mixture of the desired isomer (+)-**12**[14] and the epimer (+)-**13**[14] (Table I, entry 1). We anticipated that the selectivity could be improved by lowering the reaction temperature; however, even at −20 °C the cyclization proceeded relatively slowly, suggesting that a more reactive electrophilic reagent might be required. The relatively high melting point of acetonitrile (−48 °C) prompted us to consider alternative solvents as well, but the I_2 cyclizations reportedly proceeded smoothly only in CH_3CN; other solvents such as CH_2Cl_2 and CCl_4 afforded low yields of intractable mixtures.[11]

Iodine monobromide,[15] a potent electrophile toward olefinic bonds,[16] reacted readily with (+)-**11** at −20 °C in acetonitrile; indeed, the dramatic rate increase relative to iodine led to complete conversion within 15 min (Table I, entry 2). This result set the stage for the investigation of new solvents and lower temperatures. In contrast with molecular iodine, iodine monobromide induced efficient carbonate cyclization in methylene chloride. As the temperature was decreased from −20 to −94 °C (liquid nitrogen/hexane bath), the isomer ratio improved from 3.3:1 to 8.7:1 (entries 3–5). We also carried out the reaction at −110 °C (liquid nitrogen/carbon disulfide bath) in ether (entry 6), but this variation offered no advantage. It is noteworthy that the IBr cyclizations in both CH_3CN and CH_2Cl_2 at −20 °C were less selective than Bartlett's method (3.1–3.3:1 vs 5.7:1, entries 1–3). Thus, the enhancement achieved at −94 °C with IBr in CH_2Cl_2 derived solely from temperature effects.

Interestingly, when the IBr-induced cyclization of (+)-**11** was performed in toluene at −80 to −85 °C (dry ice/diethyl ether bath),[17] the selectivity improved significantly to 13.9:1 (Table I, entry 8). The superiority of toluene as solvent was further demonstrated by the generation of a 6.7:1 mixture of (+)-**12** and (+)-**13** at −20 °C (entry 7; cf., entries 2 and 3). At this temperature, IBr in toluene also provided better selectivity than the Bartlett iodine/acetonitrile protocol (cf., entry 1).

Solvent effects in the IBr cyclizations were further investigated with the readily available carbonate (±)-**14**,[14] as summarized in Table II. Best results (25.8:1 ratio of diastereomeric iodocarbonates (±)-**15**[14] and (±)-**16**,[14] 95% yield) were again obtained in toluene at −80 to −85 °C (entry 5). DME proved inferior to both toluene and methylene chloride (entry 3), whereas THF not unexpectedly led to a complex product mixture (entry 2). The

Table I. Optimization of the IBr-Induced Cyclization of (+)-11

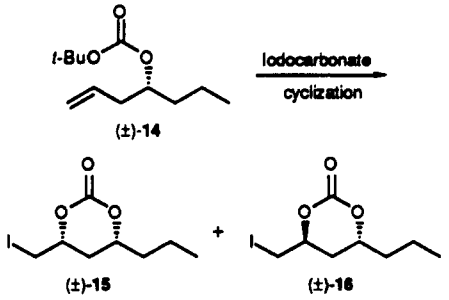


entry	"I+"	conditions	yield, % (12 + 13)[a]	ratio (12/13)
1	I_2	CH_3CN, −20 °C, 6.5 h	79	5.7:1[b]
2	IBr	CH_3CN, −20 °C, 15 min	67	3.1:1[c]
3	IBr	CH_2Cl_2, −20 °C, 15 min	75	3.3:1[b]
4	IBr	CH_2Cl_2, −85 °C, 15 min	74	7.7:1[d]
5	IBr	CH_2Cl_2, −94 °C, 15 min	83	8.7:1[d]
6	IBr	Et_2O, −110 °C, 15 min	75	7.3:1[d]
7	IBr	PhMe, −20 °C, 30 min	*e*	6.7:1[b]
8	IBr	PhMe, −80 to −85 °C, 11 h[f]	85	13.9:1[b]

[a] After flash chromatography. [b] Determined by 125-MHz ^{13}C NMR analysis of crude mixture. [c] Determined by separation via flash chromatography. [d] Determined by 500-MHz ^1H NMR analysis of crude mixture. [e] Not determined. [f] Reaction time for 52.7 mmol of (+)-**11**.

(12) For a preliminary communication, see: Duan, J. J.-W.; Sprengeler, P. A.; Smith, A. B., III. *Tetrahedron Lett.* **1992**, *33*, 6439.
(13) Taken in part from the Ph.D. dissertation of J. J.-W. Duan, University of Pennsylvania, 1992.
(14) All new compounds gave satisfactory infrared, 500-MHz ^1H NMR, and 125-MHz ^{13}C NMR spectra, as well as appropriate parent ion identification by high resolution mass spectrometry.
(15) Iodine monobromide was purchased from Aldrich Chemical Co., Inc. and used without purification.
(16) White, E. P.; Roberson, P. W. *J. Chem. Soc.* **1939**, 1059.
(17) In view of the limited solubility of iodine monobromide in toluene at low temperature, the cyclization was not attempted at temperatures below −85 °C in this solvent. At −80 to −85 °C, increases in scale necessitated longer reaction times. For example, the cyclization of 6.2 mmol of (+)-**11** was complete within 6 h whereas a 52.7-mmol reaction with this substrate required 11 h. However, the selectivity remained consistent.

Table II. Iodocarbonate Cyclizations of (±)-14



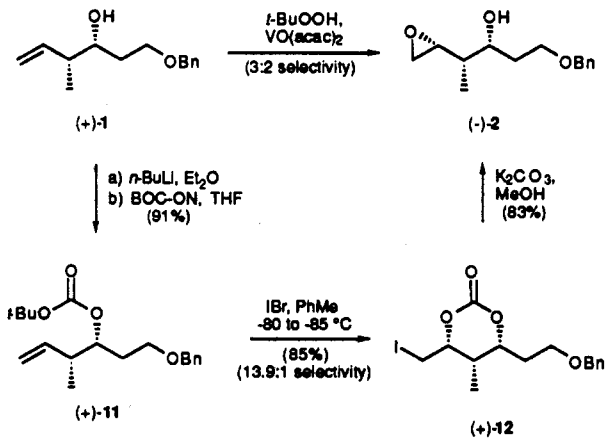
entry	"I+"	conditions	yield, % (15 + 16)[a]	ratio (15/16)[b]
1	IBr	hexane, −80 to −85 °C, 30 min, then −45 °C, 30 min[c]	73[d]	7.7:1
2	IBr	THF, −80 to −85 °C, 30 min	*e*	*e*
3	IBr	DME, −80 to −85 °C, 30 min	89	10.0:1
4	IBr	CH_2Cl_2, −80 to −85 °C, 30 min	90	12.3:1
5	IBr	toluene, −80 to −85 °C, 30 min	95	25.8:1
6	I_2	CH_3CN, −20 °C, 30 min	90	8.4:1
7	ICl	CH_2Cl_2, −80 to −85 °C, 30 min	85	5.8:1

[a] After flash chromatography. [b] Determined by 125-MHz ^{13}C NMR analysis of crude mixture. [c] IBr did not dissolve in hexane at −80 to −85 °C. [d] Some 14 also recovered. [e] Complex product mixture.

utility of hexane as solvent is limited by the extremely low solubility of IBr at low temperature (entry 1). Finally, we note that iodine monochloride in dichloromethane at −80 to −85 °C furnished significantly lower selectivity than IBr under similar conditions (5.8:1 vs. 12.3:1, entries 7 and 4).

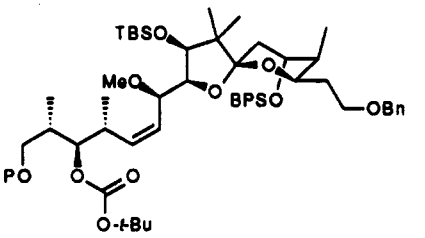
Treatment of iodocarbonate (+)-12 with K_2CO_3 (3 equiv) in dry methanol furnished the desired epoxide (−)-2[14] required for our calyculin synthesis, in 83% yield (Scheme II). In contrast with the 3:2 diastereomer mixture generated in the *t*-BuOOH/VO(acac)$_2$ epoxidation of (+)-1, the three-step sequence employing the new cyclization protocol provided the epoxide in 60% overall yield with 13.9:1 selectivity.

Scheme II



Evaluation of IBr and I_2 in the Cyclization of Diverse Homoallylic Carbonates. We next compared the published I_2/CH_3CN procedure with our IBr/CH_2Cl_2 and IBr/PhMe protocols for the cyclization of structurally diverse substrates. The results are summarized in Tables III and IV. The cyclizations outlined in Table III were effected with 3 equiv of iodine in acetonitrile at −20 °C for 5–10 h or with 1.5–2.0 equiv of iodine monobromide at −80 to −85 °C, either in methylene chloride[18] for 30 min or in toluene for 0.5–1 h. In the latter experiments, the limited solubility of IBr in toluene at −80 to −85 °C necessitated the addition of the reagent as a 1.0 M dichloromethane solution. IBr generally furnished higher diastereomer ratios in toluene than in methylene chloride, whereas iodine in acetonitrile was the least selective. The functionalized substrates (+)-**26** and (+)-**28** (entries 6 and 7) cyclized readily upon exposure to iodine monobromide; the factors responsible for diminished selectivity in these cases remain to be elucidated. In contrast, (+)-**26** failed to react with iodine, even at room temperature.

Iodine reportedly reacts smoothly with diene carbonate (±)-**30** to give the desired cyclization product (±)-**31** with 6.5:1 selectivity (Table IV, entry 1).[11] Unfortunately, the IBr protocols led to complex mixtures of products with this substrate (entries 2 and 3). Addition of IBr to the isolated olefin in (±)-**30** was competitive even when only 0.75 equiv of the electrophile was used (entry 3). Thus, IBr cannot usually be employed for the cyclizations of polyolefinic substrates. Carbonates **33** and **34** also failed to react cleanly with IBr or I_2 under various conditions, presumably because these substrates are both sterically hindered and unusually labile.



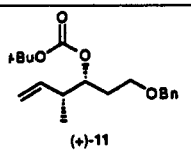
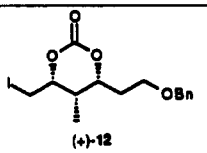
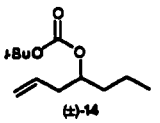
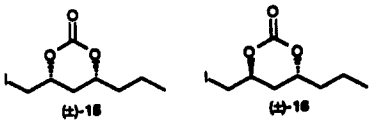
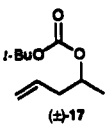
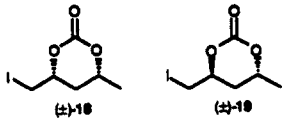
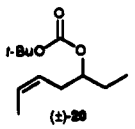
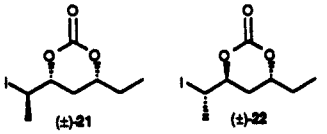
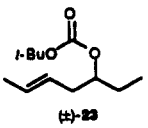
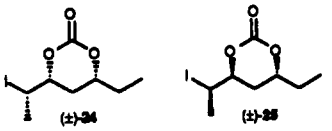
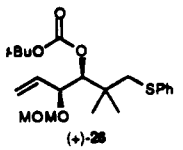
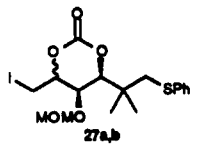
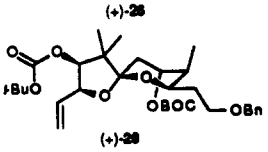
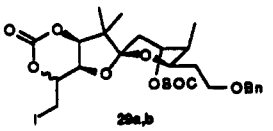
33: P = PMB
34: P = Ac
(BPS = *t*-BuPh$_2$Si)

Kinetic vs Thermodynamic Control. As noted earlier, cyclization of (±)-**14** with IBr in CH_2Cl_2 at −80 to −85 °C for 30 min furnished a 12.3:1 mixture of (±)-**15** and (±)-**16** in 90% yield. To probe for equilibration, an equimolar mixture of starting *tert*-butyl carbonate (±)-**14** and the minor product isomer (±)-**16** was resubmitted to the reaction conditions. The recovery of a 0.94:1.0 mixture of (±)-**15** and (±)-**16** indicated that the selectivity in the IBr-induced cyclization derives primarily or exclusively from kinetic control.

Stereochemical Assignments for the Cyclic Iodo Carbonates. The relative configurations of cyclic carbonates **18**, **19**, **21**, **22**, **24**, and **25** (Table III, entries 3–5) were determined spectroscopically via comparison with data reported in ref 11. For **27a,b** and **29a,b** (Table III, entries 6 and 7) the relative stereochemistry was not elucidated. Initial assignments for **12**, **13**, **15**, and **16** (Table III, entries 1 and 2), based upon literature precedents for similar reactions,[10,11] were supported by analysis of the ^1H NMR coupling constants for the carbonate rings (Table V). Specifically, carbonate (+)-**12** is likely to adopt a chair conformation with small axial–equatorial couplings for H_1–H_3 and H_2–H_3; the coupling constants both proved to be 2.7 Hz. In contrast, carbonate (+)-**13** would be expected to assume a twist-boat conformation, in accord with the observed H_1–H_3 and H_2–H_3 coupling constants of 5.4 and 6.7 Hz, respectively. Similarly, the chair conformation of

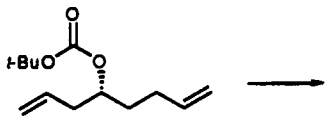
(18) Although optimal selectivity with iodine/dichloromethane was obtained at −94 °C (liquid nitrogen/hexane bath), a dry ice/ether bath afforded superior temperature regulation (−80 to −85 °C).

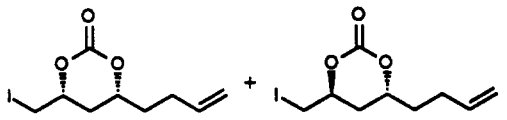
Table III. Evaluation of the I_2/CH_3CN, IBr/CH_2Cl_2, and IBr/PhMe Protocols for Cyclization of Diverse Homoallylic Carbonates

entry	starting material	products[14]	conditions	ratio[a]	yield,[b] %
1	 (+)-11	 (+)-12 (+)-13	I_2/CH_3CN	5.7:1	79
			IBr/CH_2Cl_2	8.7:1	83
			IBr/PhMe	13.9:1	85
2	 (±)-14	 (±)-15 (±)-16	I_2/CH_3CN	8.4:1	90
			IBr/CH_2Cl_2	12.3:1	90
			IBr/PhMe	25.8:1	95
3	 (±)-17	 (±)-18 (±)-19	I_2/CH_3CN	10:1[c]	77
			IBr/CH_2Cl_2	14:1	87
			IBr/PhMe	21.1:1	89
4	 (±)-20	 (±)-21 (±)-22	I_2/CH_3CN	6.5:1[c]	91
			IBr/CH_2Cl_2	12:1[d]	87
			IBr/PhMe	18.8:1	87
5	 (±)-23	 (±)-24 (±)-25	I_2/CH_3CN	4:1[c]	88
			IBr/CH_2Cl_2	6.5:1	89
			IBr/PhMe	6.4:1	86
6	 (+)-26	 27a,b	I_2/CH_3CN	–	no rxn[e]
			IBr/CH_2Cl_2	1.7:1[f]	86[g]
			IBr/PhMe	3.4:1	69[g]
7	 (+)-28	 29a,b	I_2/CH_3CN	–	*h*
			IBr/CH_2Cl_2	1.5:1[f]	61[g,i]
			IBr/PhMe	–	*h*

[a] Determined by 125-MHz ^{13}C NMR analysis of crude mixture unless otherwise stated. [b] Total yield (both diastereomers) after flash chromatography. [c] Result reported in ref 11. [d] Reaction performed at −94 °C. [e] No reaction after 8 h at −20 °C and 1 h at room temperature. [f] Ratio determined via separation by flash chromatography. [g] Relative configurations of products not determined. [h] Reaction not carried out. [i] Overall yield for two steps from corresponding diol.

Table IV. Iodocarbonate Cyclization of Diene (±)-30


(±)-30


(±)-31 (±)-32

entry	conditions	result
1	I_2 (3 equiv), CH_3CN, −20 °C	69% yield, 31/32 = 6.5:1[a]
2	IBr (2 equiv), CH_2Cl_2, −78 °C, 30 min	complex mixture
3	IBr (0.75 equiv), PhMe, −80 to −85 °C, 3 h	complex mixture containing (±)-30

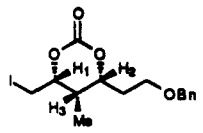
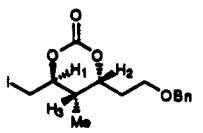
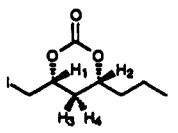
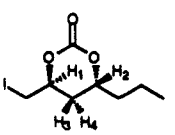
[a] Result reported in ref 11.

(±)-15 gave rise to two large axial–axial couplings (H_1–H_4 and H_2–H_4, both 11.8 Hz) and two small axial–equatorial couplings (H_1–H_3 and H_2–H_3, both 3.0 Hz). All coupling constants for (±)-16 were in the range 4.7–6.8 Hz, probably indicative of a twist-boat.

Preparation of the Homoallylic Carbonates. In general, the homoallylic *tert*-butyl carbonates employed in this study were prepared from the corresponding hydroxy compounds. Alcohols (+)-1 and (+)-35, the carbinol precursor of 28, serve as synthetic intermediates in our calyculin project.[4a] Both 1-hepten-4-ol [(±)-36] and 4-penten-2-ol [(±)-37] are commercially available. *trans*-2-Hepten-5-ol [(±)-38] was obtained in two steps from 1,2-epoxybutane [(±)-39, Scheme III]: boron trifluoride etherate-promoted epoxide opening[19] with propynyllithium furnished alcohol (±)-40[14] in 81% yield, and reduction of the latter with lithium in liquid ammonia[20] then furnished (±)-38 (84%). Sulfide (+)-42[14] was prepared in 73% yield from the known aldehyde 41[21] by sequential treatment with *Z*-[γ-(MOMO)allyl]diisopinocampheylborane[22] and trimethylamine *N*-oxide.[23] Noteworthy here is the selective oxidation of the boronate complex in the presence of a sulfide moiety.

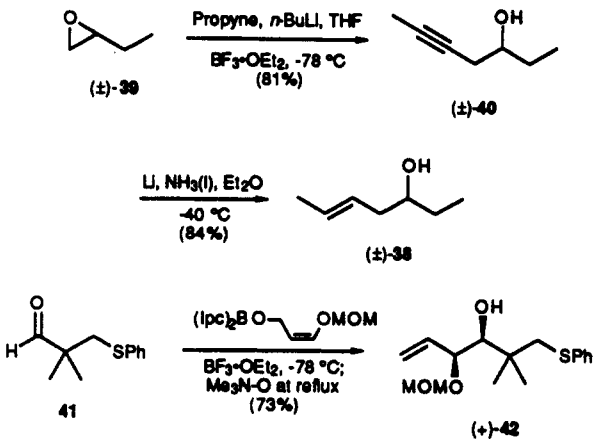
(19) Eis, M. J.; Wrobel, J. E.; Ganem, B. *J. Am. Chem. Soc.* **1984**, *106*, 3693.
(20) (a) Birch, A. J. *Quart. Rev.* **1950**, *4*, 69. (b) Harvey, R. G. *Synthesis* **1970**, 161.
(21) Chu, D. T. W. *J. Org. Chem.* **1983**, *48*, 3571.
(22) Brown, H. C.; Jadhav, P. K.; Bhat, K. S. *J. Am. Chem. Soc.* **1988**, *110*, 1535.
(23) Kabalka, G. W.; Hedgecock, H. C., Jr. *J. Org. Chem.* **1975**, *40*, 1776.

Table V. ^{1}H NMR Coupling Constants (Hz) for Cyclic Carbonates 12, 13, 15 and 16[a]

	 (+)-12	 (+)-13	 (±)-15	 (±)-16
H_1–H_3	2.7	5.4	3.0	4.9, 6.8[b]
H_1–H_4	–	–	11.8	
H_2–H_3	2.7	6.7	3.0	4.7, 6.5[b]
H_2–H_4	–	–	11.8	

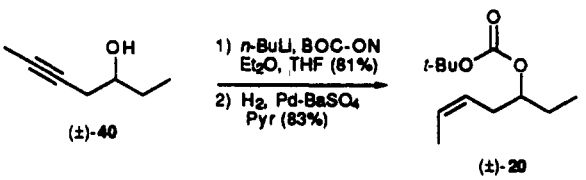
[a] Determined via 500-MHz ^{1}H homonuclear decoupling. [b] H_3 and H_4 not distinguished.

Scheme III



tert-Butyl carbonates[14] **11**, **14**, **17**, **23**, **26**, and **28** were prepared in excellent yields from the corresponding homoallylic alcohols via deprotonation with *n*-butyllithium followed by reaction with 2-[[(*tert*-butoxycarbonyl)oxy]-imino]-2-phenylacetonitrile [BOC-ON, 1.1 equiv] (Table VI). Carbonate (±)-**20**, the *cis*-isomer of (±)-**23**, was prepared from alcohol (±)-**40** via *tert*-butyl carbonate formation with *n*-butyllithium/BOC-ON followed by palladium/barium sulfate-catalyzed semihydrogenation[24] (Scheme IV).

Scheme IV

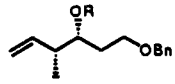
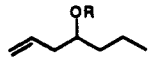
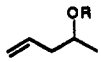
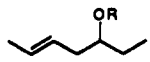
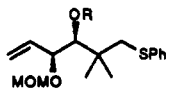
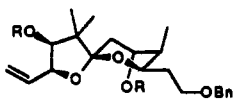


Summary. A new protocol employing iodine monobromide in toluene or methylene chloride at low temperature furnishes significantly enhanced diastereoselectivity in cyclizations of homoallylic *tert*-butyl carbonates. We anticipate that IBr may also afford increased selectivity in iodocarbonate cyclization of allylic substrates,[10] iodolactonization,[25a,b] and iodoetherification.[25b-e]

Experimental Section[26]

***tert*-Butyl Carbonate (+)-11.** *n*-Butyllithium (2.5 M in hexane, 16.3 mL, 40.7 mmol) was added dropwise to a solution of alcohol (+)-1[4a] (8.138 g, 37.0 mmol) in ether (100 mL) at −78 °C. After 30 min the cold reaction mixture was quickly transferred through a 12-gauge cannula to a solution of BOC-ON (10.01 g, 40.7 mmol) in tetrahydrofuran (40 mL) at 0 °C. The resultant mixture was stirred for 4 h at room temperature and then washed with 2 N aqueous NaOH (2 × 75 mL) and brine (75 mL). The combined aqueous phases were extracted with ether (2 × 60 mL), and the combined extracts were dried ($MgSO_4$),

Table VI. Preparation of *tert*-Butyl Carbonate Derivatives of Homoallylic Alcohols

entry	substrate	alcohol (R = H)	carbonate[a] (R = BOC)	yield,[b] %
1		(+)-1	(+)-11	91
2		(±)-36	(±)-14	96
3		(±)-37	(±)-17	94
4		(±)-38	(±)-23	96
5		(+)-42	(+)-26	95
6		(+)-35	(+)-28	94[c]

[a] Typical reaction conditions: *n*-butyllithium (1.1 equiv) was added to an ethereal solution of substrate at −78 °C. After 30 min the cold mixture was quickly added via a cannula to a THF solution of BOC-ON (1.1 equiv) at 0 °C. The resultant mixture was then stirred at room temperature for 4 h. [b] After flash chromatography. [c] Bis(carbonate) formation.

(24) (a) Cram, D. J.; Allinger, N. L. *J. Am. Chem. Soc.* **1956**, *78*, 2518. (b) Johnson, F.; Paul, K. G.; Farara, D. *J. Org. Chem.* **1982**, *47*, 4254.

(25) (a) For a review of halolactonization, see: Dowle, M. D.; Davies, D. I. *Chem. Soc. Rev.* **1979**, *8*, 171. (b) Bartlett, P. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, pp 411–454. (c) Semple, J. E.; Joullié, M. M. *Heterocycles* **1980**, *14*, 1825. (d) Rychnovsky, S. D.; Bartlett, P. A. *J. Am. Chem. Soc.* **1981**, *103*, 3963. (e) Marek, I.; Lefrancois, J.-M.; Normant, J.-F. *Tetrahedron Lett.* **1992**, *33*, 1747.

(26) **Materials and Methods.** Reactions were carried out in oven- or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were reagent grade. Diethyl ether and tetrahydrofuran (THF) were freshly distilled from sodium/benzophenone under argon. Dichloromethane and benzene were freshly distilled from calcium hydride. *n*-Butyllithium was standardized by titration with menthol/triphenylmethane. Unless stated otherwise, all reactions were magnetically stirred and monitored by thin-layer chromatography using E. Merck 0.25-mm precoated silica gel plates. Flash chromatography was performed with the indicated solvents using silica gel-60 (particle size 0.040–0.062 mm) supplied by E. Merck. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Melting points were determined on a Bristoline heated-stage microscope or a Thomas-Hoover apparatus and are corrected. IR and NMR spectra were measured in $CHCl_3$ and $CDCl_3$ solutions, respectively, unless otherwise noted. Infrared spectra were recorded on a Perkin-Elmer Model 283B spectrometer with polystyrene as external standard. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-500 spectrometer; chemical shifts are reported relative to internal tetramethylsilane (δ 0.00) and chloroform (δ 77.0), respectively. Optical rotations were obtained with a Perkin-Elmer Model 241 polarimeter in the indicated solvent. High resolution mass spectra were measured at the University of Pennsylvania Mass Spectrometry Service Center on either a VG Micromass 70/70H or VG ZAB-E spectrometer. Microanalyses were performed by Robertson Laboratories, Madison, NJ. High performance liquid chromatography (HPLC) was carried out with a Ranin analytical/semipreparative system.

filtered, and concentrated. Flash chromatography (hexane/ethyl acetate, 95:5) furnished (+)-11 (10.66 g, 90% yield) as a colorless oil: R_f 0.61 (hexane/ethyl acetate, 80:20); $[\alpha]^{25}_D$ +33.7° (c 1.07, $CHCl_3$); IR ($CHCl_3$) 3070 (w), 3060 (w), 3020 (w), 3000 (m), 2970 (m), 2940 (m), 2860 (m), 1740 (s), 1640 (w), 1495 (w), 1475 (w), 1450 (m), 1405 (w), 1390 (m), 1370 (s), 1280 (s), 1255 (s), 1155 (s), 1090 (s), 1020 (w), 990 (w), 915 (m), 845 (m), 685 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.04 (d, J = 6.9 Hz, 3 H), 1.47 (s, 9 H), 1.80–1.85 (m, 1 H), 1.89–1.95 (m, 1 H), 2.43–2.48 (m, 1 H), 3.46–3.54 (m, 2 H), 4.48 (ABq, J_{AB} = 11.9 Hz, $\Delta\nu_{AB}$ = 6.4 Hz, 2 H), 4.77 (ddd, J = 3.1, 6.4, 9.6 Hz, 1 H), 5.03–5.08 (m, 2 H), 5.76 (ddd, J = 7.2, 10.1, 17.5 Hz, 1 H), 7.25–7.33 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.3, 27.8, 31.8, 41.8, 66.9, 73.1, 77.4, 81.6, 115.6, 127.5, 127.7, 128.3, 128.4, 139.4, 153.5; high resolution mass spectrum (CI, NH_3) m/z 338.2364 [$(M + NH_4)^+$, calcd for $C_{19}H_{32}NO_4$ 338.2332]. Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 70.97; H, 8.64.

Iodo Carbonates (+)-12 and (+)-13. Method A: Iodine in Acetonitrile. A solution of *tert*-butyl carbonate (+)-11 (751 mg, 2.35 mmol) in acetonitrile (30 mL) at −20 °C was treated with iodine (1.97 g, 7.76 mmol) and stirred for 6.5 h. The cold bath was replaced with a room temperature water bath, and an aqueous solution containing 20% $Na_2S_2O_3$, 5% $NaHCO_3$ (25 mL), and ether (50 mL) were then added. The organic phase was washed with brine (25 mL), the combined aqueous layers were extracted with ether (2 × 10 mL), and the combined organic solutions were dried ($MgSO_4$), filtered, and concentrated. NMR analysis (125 MHz ^{13}C) showed that the crude product comprised a 5.7:1 mixture of iodo carbonates (+)-12 and (+)-13. Flash chromatography (hexane/ethyl acetate, 75:25) afforded a mixture of (+)-12 and (+)-13 (723 mg, 79% yield) as a yellow liquid.

Method B: Iodine Monobromide in Dichloromethane. A solution of (+)-11 (9.06 g, 28.3 mmol) in dichloromethane (250 mL) at −94 °C (liquid nitrogen/hexane bath) was treated with iodine monobromide (11.7 g, 56.6 mmol) and stirred for 30 min. After the cold bath was replaced with a room temperature water bath, an aqueous solution containing 20% $Na_2S_2O_3$, 5% $NaHCO_3$ (300 mL), and ether (500 mL) was added. The organic phase was washed with brine (300 mL), the combined aqueous solutions were extracted with ether (2 × 100 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. NMR analysis (125 MHz ^{13}C) indicated that the crude product comprised an 8.7:1 mixture of (+)-12 and (+)-13. Flash chromatography (hexane/ethyl acetate, 75:25) gave pure (+)-12 (8.03 g, 73% yield) as a yellow liquid.

Method C: Iodine Monobromide in Toluene. Iodine monobromide (1.0 M in dichloromethane, 94.9 mL, 94.9 mmol) was slowly added dropwise to a solution of (+)-11 (16.9 g, 52.7 mmol) in toluene (600 mL) at −80 to −85 °C (dry ice/ether bath). After 11 h the mixture was warmed to 0 °C and an aqueous solution containing 20% $Na_2S_2O_3$, and 5% $NaHCO_3$ (300 mL), and ether (500 mL) were added. The organic phase was washed with brine (300 mL), the combined aqueous layers were extracted with ether (2 × 100 mL), and the combined organic solutions were dried ($MgSO_4$), filtered, and concentrated. NMR analysis (125 MHz ^{13}C) showed that the crude product comprised a 13.9:1 mixture of (+)-12 and (+)-13. Flash chromatography (hexane/ethyl acetate, 75:25) furnished pure (+)-12 (16.3 g, 79% yield) as a yellow liquid.

Major Diastereomer (+)-12: yellow liquid; R_f 0.50 (hexane/ethyl acetate, 50:50); $[\alpha]^{25}_D$ +36.1° (c 1.00, $CHCl_3$); IR ($CHCl_3$) 3020 (w), 3000 (w), 2920 (w), 2860 (w), 1750 (s), 1450 (w), 1365 (m), 1225 (w), 1190 (m), 1165 (w), 1110 (s), 1040 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.92 (d, J = 7.2 Hz, 3 H), 1.85–1.92 (m, 1 H), 1.98–2.04 (m, 1 H), 2.39–2.45 (m, 1 H), 3.11 (dd, J = 9.9, 10.1 Hz, 1 H), 3.37 (dd, J = 5.5, 10.1 Hz, 1 H), 3.62 (td, J = 4.9, 9.6 Hz, 1 H), 3.68 (dt, J = 4.1, 9.6 Hz, 1 H), 4.51 (ABq, J_{AB} = 11.8 Hz, $\Delta\nu_{AB}$ = 21.5 Hz, 2 H), 4.67 (ddd, J = 2.9, 5.5, 9.9 Hz, 1 H), 4.72 (ddd, J = 2.5, 4.4, 8.8 Hz, 1 H), 7.28–7.38 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.7, 3.3, 31.4, 32.5, 65.3, 73.4, 79.6, 81.8, 127.7, 127.8, 128.5, 137.9, 148.0; high resolution mass spectrum (CI, NH_3) m/z 408.0638 [$(M + NH_4)^+$, calcd for $C_{15}H_{23}INO_4$ 408.0672].

Minor Diastereomer (+)-13. An analytical sample was prepared by HPLC (hexane/ethyl acetate, 67:33): yellow liquid; R_f 0.41 (hexane/ethyl acetate, 50:50); $[\alpha]^{25}_D$ + 44.0° (c 1.11, $CHCl_3$); IR ($CHCl_3$) 3020 (w), 3000 (w), 2960 (w), 2920 (w), 2860 (w), 1750 (s), 1450 (w), 1380 (m), 1300 (w), 1180 (m), 1160 (m), 1110 (m, br), 1080 (m), 1020 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (d, J = 7.1 Hz, 3 H), 1.87–1.92 (m, 2 H), 2.39–2.42 (m, 1 H), 3.40 (d, J = 5.8 Hz, 2 H), 3.62–3.70 (m, 2 H), 4.18 (td, J = 5.4, 5.8 Hz, 1 H), 4.52 (ABq, J_{AB} = 11.8 Hz, $\Delta\nu_{AB}$ = 16.8 Hz, 2 H), 4.63 (dt, J = 3.8, 6.7 Hz, 1H), 7.28–7.37 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.1, 11.8, 31.2, 32.9, 65.4, 73.4, 75.6, 81.4, 127.7, 128.5, 137.9, 148.0; high resolution mass spectrum (CI, NH_3) m/z 408.0691 [$(M + NH_4)^+$, calcd for $C_{15}H_{23}INO_4$ 408.0672].

***tert*-Butyl Carbonate (±)-14.** Via a procedure analogous to that employed in the preparation of carbonate (+)-11, alcohol (±)-36 (3.307 g, 29.0 mmol) was converted to (±)-14. Flash chromatography (hexane/ether, 97.5:2.5) gave the product (5.983 g, 96% yield) as a pale yellow liquid: R_f 0.53 (hexane/ethyl acetate, 90:10); IR ($CHCl_3$) 3020 (w), 3000 (w), 2960 (m), 2930 (w), 2870 (w), 1735 (s), 1645 (w), 1465 (w), 1455 (w), 1390 (w), 1370 (m), 1280 (s), 1250 (m), 1155 (s), 1090 (w), 910 (w), 820 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.92 (t, J = 7.3 Hz, 3 H), 1.30–1.46 (m, 2 H), 1.48 (s, 9 H), 1.49–1.62 (m, 2 H), 2.32–2.35 (m, 2 H), 4.68–4.73 (m, 1 H), 5.05–5.12 (m, 2 H), 5.74–5.82 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 18.6, 27.8, 35.8, 38.8, 76.4, 81.6, 117.6, 133.7, 153.5; high resolution mass spectrum (CI, NH_3) m/z 232.1914 [$(M + NH_4)^+$, calcd for $C_{12}H_{26}NO_3$ 232.1912].

Iodo Carbonates (±)-15 and (±)-16. Method A: Iodine in Acetonitrile. Via a procedure analogous to that employed in the preparation of (+)-12 and (+)-13, a solution of carbonate (±)-14 (276 mg, 1.29 mmol) in acetonitrile (12 mL) was treated with iodine (983 mg, 3.87 mmol) at −20 °C for 9 h. NMR analysis (125 MHz ^{13}C) showed that the crude product comprised an 8.4:1 mixture of (±)-15 and (±)-16. Flash chromatography (hexane/ether, 20:80) gave (±)-15 and (±)-16 (330 mg, 90% yield) as a partially separable mixture. An analytical sample of each isomer was obtained by collecting nonoverlapping fractions.

Method B: Iodine Monobromide in Dichloromethane. Via a procedure analogous to that employed in the preparation of (+)-12 and (+)-13, a solution of carbonate (±)-14 (1.70 g, 7.92 mmol) in dichloromethane (60 mL) was treated with iodine monobromide (3.28 g, 15.8 mmol) at −80 to −85 °C (ref 18) for 30 min. NMR analysis (125 MHz ^{13}C) indicated that the crude product comprised a 12.3:1 mixture of (±)-15 and (±)-16. Flash chromatography (hexane/ether, 20:80) afforded (±)-15 and (±)-16 (2.04 g, 91% yield) as a partially separable mixture. An analytical sample of each isomer was obtained by collecting nonoverlapping fractions.

Method C: Iodine Monobromide in Toluene. Via a procedure analogous to that employed in the preparation of (+)-12 and (+)-13, a solution of carbonate (±)-14 (107 mg, 0.500 mmol) in toluene (5 mL) was treated with iodine monobromide (1.0 M in dichloromethane, 0.75 mL, 0.75 mmol) at −80 to −85 °C for 30 min. NMR analysis (125 MHz ^{13}C) revealed that the crude product comprised a 25.8:1 mixture of (±)-15 and (±)-16. Flash chromatography (hexane/ether, 20:80) furnished (±)-15 and (±)-16 (135 mg, 95% yield) as a partially separable mixture. An analytical sample of each isomer was obtained by collecting nonoverlapping fractions.

Major diastereomer (±)-15: viscous, pale yellow oil; R_f 0.30 (hexane/ether, 20:80); IR ($CHCl_3$) 3010 (w), 3000 (w), 2950 (m), 2920 (w), 2860 (w), 1740 (s), 1390 (m), 1225 (m), 1180 (m), 1020 (m), 1000 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.97 (t, J = 7.3 Hz, 3 H), 1.41–1.80 (m, 5 H), 2.38 (td, J = 3.0, 14.1 Hz, 1 H), 3.27 (dd, J = 7.4, 10.6 Hz, 1 H), 3.40 (dd, J = 4.3, 10.6 Hz, 1 H), 4.42–4.50 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.4, 13.6, 17.7, 33.2, 37.1, 77.1, 78.2, 148.4; high resolution mass spectrum (CI, NH_3) m/z 302.0223 [$(M + NH_4)^+$, calcd for $C_8H_{17}INO_3$ 302.0252].

Minor diastereomer (±)-16: viscous, pale yellow oil; R_f 0.45 (hexane/ether, 20:80); IR ($CHCl_3$) 3020 (w), 2960 (w), 2920 (w), 2860 (w), 1750 (s), 1380 (w), 1245 (w), 1190 (w), 1170 (w), 1100 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.98 (t, J = 7.2 Hz, 3 H), 1.41–1.64 (m, 3 H), 1.78–1.85 (m, 1 H), 2.12–2.17 (m, 1 H), 2.20–2.25 (m, 1 H), 3.32 (dd, J = 8.3, 10.5 Hz, 1 H), 3.45 (dd, J = 4.7, 10.5 Hz, 1 H), 4.50–4.55 (m, 1 H), 4.58–4.63 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.7, 13.5, 18.1, 30.4, 36.5, 75.2, 76.0, 148.3; high resolution mass spectrum (CI, NH_3) m/z 302.0231 [$(M + NH_4)^+$, calcd for $C_8H_{17}INO_3$ 302.0252].

Epoxide (−)-2. A solution of iodo carbonate (+)-12 (6.87 g, 17.6 mmol) in dry methanol (50 mL) at room temperature was treated with potassium carbonate (7.48 g, 54.2 mmol) and stirred

for 6 h. The mixture was partitioned between ether (300 mL) and saturated $Na_2S_2O_3$ and $NaHCO_3$ solutions (60 mL each). The aqueous layer was then extracted with ether (3 × 60 mL), and the combined extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (hexane/ethyl acetate, 65:35) provided epoxide (−)-**2** (3.93 g, 83% yield) as a yellow liquid: R_f 0.31 (hexane/ethyl acetate, 50:50); $[\alpha]^{25}_D$ −7.8° (*c* 1.01, $CHCl_3$); IR ($CHCl_3$) 3490 (s, br), 3000 (s), 2970 (s), 2940 (s), 2920 (s), 2860 (s), 1495 (w), 1480 (m), 1455 (s), 1415 (m), 1360 (s), 1310 (w), 1255 (m), 1230 (m), 1090 (s), 1020 (m), 900 (s), 850 (w), 815 (w), 690 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.03 (d, *J* = 6.9 Hz, 3 H), 1.43–1.47 (m, 1 H), 1.70–1.75 (m, 1 H), 1.83–1.90 (m, 1 H), 2.60 (dd, *J* = 2.8, 4.9 Hz, 1 H), 2.76 (dd, *J* = 4.0, 4.9 Hz, 1 H), 2.94 (ddd, *J* = 2.8, 4.0, 6.7 Hz, 1 H), 3.08 (d, *J* = 2.5 Hz, 1 H), 3.66 (ddd, *J* = 3.8, 9.1, 9.2 Hz, 1 H), 3.75 (td, *J* = 4.7, 9.2 Hz, 1 H), 3.86–3.96 (m, 1 H), 4.53 (s, 3 H), 7.27–7.37 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.1, 33.7, 41.5, 46.5, 54.4, 69.6, 73.4, 73.5, 127.7, 127.8, 128.5, 137.7; high resolution mass spectrum (CI, NH_3) *m/z* 237.1483 [(M + H)$^+$, calcd for $C_{14}H_{21}O_3$ 237.1490]. Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 70.91; H, 8.36.

***tert*-Butyl Carbonate (±)-17.** Via a procedure analogous to that employed in the preparation of carbonate (+)-**11**, alcohol (±)-**37** (1.498 g, 17.4 mmol) was converted to (±)-**17**. Flash chromatography (hexane/ether, 98:2) furnished the product (3.053 g, 94% yield) as a pale yellow liquid: R_f 0.55 (hexane/ethyl acetate, 90:10); IR ($CHCl_3$) 3020 (w), 2980 (m), 2930 (w), 1735 (s), 1640 (w), 1450 (w), 1390 (w), 1370 (m), 1365 (m), 1280 (s), 1250 (s), 1230 (m), 1155 (s), 1120 (m), 1085 (w), 1050 (w), 990 (w), 915 (w), 860 (w), 820 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.26 (d, *J* = 6.3 Hz, 3 H), 1.48 (s, 9 H), 2.26–2.32 (m, 1 H), 2.37–2.43 (m, 1 H), 4.76 (tq, *J* = 6.3, 6.3 Hz, 1 H), 5.07–5.12 (m, 2 H), 5.74–5.82 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.4, 27.8, 40.3, 73.1, 81.7, 117.8, 133.5, 153.1; high resolution mass spectrum (CI, NH_3) *m/z* 204.1596 [(M + NH_4)$^+$, calcd for $C_{10}H_{22}NO_3$ 204.1599].

***tert*-Butyl Carbonate (±)-20.** Via a procedure analogous to that employed in the preparation of (+)-**11**, alcohol (±)-**40** (5.00 g, 44.6 mmol) was initially converted to the corresponding carbonate. Flash chromatography (hexane/ether, 97.5:2.5) furnished the product (7.72 g, 82% yield) as a yellow liquid: R_f 0.54 (hexane/ethyl acetate, 90:10); IR ($CHCl_3$) 3020 (w), 3000 (w), 2970 (m), 2930 (w), 2910 (w), 1740 (s), 1455 (w), 1390 (w), 1370 (s), 1280 (s), 1255 (s), 1160 (s), 1090 (w), 860 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.94 (t, *J* = 7.4 Hz, 3 H), 1.49 (s, 9 H), 1.67–1.81 (m, 5 H), 2.42–2.48 (m, 2 H), 4.61–4.66 (m, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 3.5, 9.5, 23.9, 26.1, 27.7, 74.2, 76.6, 77.6, 81.8, 153.2; high resolution mass spectrum (CI, NH_3) *m/z* 230.1742 [(M + NH_4)$^+$, calcd for $C_{12}H_{24}NO_3$ 230.1755].

Hydrogen was bubbled into a suspension of 5% palladium on barium sulfate (1.00 g) in pyridine (100 mL) at room temperature. After 5 min a solution of the above carbonate derivative (2.00 g, 9.43 mmol) in a small amount of pyridine was added and the hydrogenation continued for 2 h at room temperature. The catalyst was removed by filtration, and the filtrate was diluted with hexane/ether (1:1, 400 mL) and washed with water (5 × 20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (hexane/ether, 98:2) gave (±)-**20** (1.68 g, 83% yield) as a colorless liquid: R_f 0.57 (hexane/ethyl acetate, 90:10); IR ($CHCl_3$) 3010 (w), 2960 (m), 2920 (w), 2870 (w), 1730 (s), 1470 (w), 1450 (w), 1390 (w), 1370 (m), 1310 (w), 1280 (s), 1250 (m), 1160 (s), 1110 (w), 1090 (w), 950 (w), 850 (w), 830 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.4 Hz, 3 H), 1.48 (s, 9 H), 1.60–1.66 (m, 5 H), 2.33–2.36 (m, 2 H), 4.60 (quin, *J* = 6.3 Hz, 1 H), 5.37–5.42 (m, 1 H), 5.54–5.60 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.7, 12.9, 26.5, 27.8, 31.2, 78.3, 81.4, 125.0, 126.7, 153.3; high resolution mass spectrum (CI, NH_3) *m/z* 232.1878 [(M + NH_4)$^+$, calcd for $C_{12}H_{26}NO_3$ 232.1912].

***tert*-Butyl Carbonate (±)-23.** Via a procedure analogous to that employed in the preparation of carbonate (+)-**11**, alcohol (±)-**38** (425 mg, 3.73 mmol) was converted to (±)-**23**. Flash chromatography (hexane/ether, 98:2) afforded the product (768 mg, 96% yield) as a colorless liquid: R_f 0.54 (hexane/ethyl acetate, 90:10); IR ($CHCl_3$) 2960 (m), 2920 (w), 2860 (w), 1730 (s), 1450 (w), 1390 (w), 1365 (m), 1280 (s), 1250 (m), 1155 (s), 1090 (w), 960 (m), 850 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.4 Hz, 3 H), 1.48 (s, 9 H), 1.55–1.66 (m, 5 H), 2.25–2.28 (m, 2 H), 4.57 (quin, *J* = 6.2 Hz, 1 H), 5.36–5.42 (m, 1 H), 5.47–5.54 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.6, 17.9, 26.5, 27.8, 37.0, 78.2, 81.4, 126.0, 128.1, 153.5; high resolution mass spectrum (CI, NH_3) *m/z* 215.1636 [(M + H)$^+$, calcd for $C_{12}H_{23}O_3$ 215.1647].

***tert*-Butyl Carbonate (+)-26.** Via a procedure analogous to that employed in the preparation of carbonate (+)-**11**, alcohol (+)-**42** (5.00 g, 16.9 mmol) was converted to (+)-**26**. Flash chromatography (hexane/ethyl acetate, 92:8) furnished the product (6.35 g, 95% yield) as a viscous colorless oil: R_f 0.47 (hexane/ethyl acetate, 80:20); $[\alpha]^{20}_D$ +32.4° (*c* 1.18, $CHCl_3$); IR ($CHCl_3$) 2980 (m), 2930 (w), 2890 (w), 1740 (s), 1580 (w), 1480 (m), 1440 (w), 1390 (w), 1370 (m), 1340 (w), 1280 (s), 1260 (s), 1150 (s), 1090 (m), 1020 (s), 940 (w), 910 (w), 680 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.14 (s, 3 H), 1.16 (s, 3 H), 1.46 (s, 9 H), 3.13 (ABq, J_{AB} = 12.4 Hz, $\Delta\nu_{AB}$ = 52.1 Hz, 2 H), 3.37 (s, 3 H), 4.35 (dd, *J* = 4.2, 7.6 Hz, 1 H), 4.61 (ABq, J_{AB} = 6.9 Hz, $\Delta\nu_{AB}$ = 67.2 Hz, 2 H), 4.79 (d, *J* = 4.2 Hz, 1 H), 5.27–5.32 (m, 2 H), 5.68–5.74 (m, 1 H), 7.13–7.16 (m, 1 H), 7.23–7.26 (m, 2 H), 7.35–7.37 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.9, 24.0, 27.7, 39.4, 44.1, 56.3, 76.3, 81.8, 81.9, 93.7, 119.3, 125.7, 128.8, 129.3, 134.8, 137.9, 153.7; high resolution mass spectrum (CI, methane) *m/z* 396.1983 [M$^+$, calcd for $C_{21}H_{32}O_5S$ 396.1970].

Dicarbonate (+)-28. *n*-Butyllithium (1.6 M in hexane, 0.371 mL, 0.594 mmol) was added dropwise to a solution of diol (+)-**35** (101.5 mg, 0.270 mmol) in ether (2 mL) at −78 °C. The dry ice/2-propanol bath was replaced with a dry ice/CCl_4 bath and the reaction stirred for 10 min at −20 °C, the cold bath was removed, and a solution of BOC-ON (146 mg, 0.594 mmol) in tetrahydrofuran (1 mL) was added immediately. The resultant mixture was stirred at room temperature for 4 h. Following dilution with ether (10 mL), the mixture was washed with 10% aqueous NaOH (2 × 1.5 mL) and brine (1.5 mL). The combined washings were extracted with ether (3 × 3 mL), and the combined organic solutions were dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (hexane/ethyl acetate, 88:12) provided (+)-**28** (146.2 mg, 94% yield) as a yellow oil: R_f 0.61 (hexane/ethyl acetate, 70:30); $[\alpha]^{23}_D$ +71.9° (*c* 0.91, $CHCl_3$); IR ($CHCl_3$) 3020 (w), 3000 (w), 2980 (m), 2930 (w), 2870 (w), 1730 (s), 1470 (w), 1450 (w), 1390 (w), 1370 (s), 1280 (s), 1250 (s), 1160 (s), 1100 (s), 1080 (s), 1040 (w), 1010 (m), 980 (w), 960 (w), 910 (w), 830 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.92 (d, *J* = 7.1 Hz, 3 H), 1.00 (s, 3 H), 1.06 (s, 3 H), 1.46 (s, 18 H), 1.55–1.62 (m, 1 H), 1.71–1.87 (m, 4 H), 3.68–3.72 (m, 2 H), 4.39 (td, *J* = 2.5, 10.8 Hz, 1 H), 4.54 (s, 2 H), 4.69–4.75 (m, 2 H), 4.86 (d, *J* = 5.8 Hz, 1 H), 5.00–5.04 (m, 1 H), 5.20–5.23 (m, 1 H), 5.81–5.88 (m, 1 H), 7.25–7.37 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.3, 16.4, 22.8, 27.1, 27.8, 27.9, 32.9, 34.8, 49.9, 63.5, 67.7, 72.9, 75.7, 81.4, 81.9, 81.9, 83.6, 106.5, 117.4, 127.4, 127.7, 128.2, 135.1, 138.8, 153.4, 153.8; high resolution mass spectrum (CI, NH_3) *m/z* 594.3610 [(M + NH_4)$^+$, calcd for $C_{32}H_{52}NO_9$ 594.3642].

Iodo Carbonates (±)-18 and (±)-19. Method B: Iodine Monobromide in Dichloromethane. Via a procedure analogous to that employed in the preparation of (+)-**12** and (+)-**13**, a solution of carbonate (±)-**17** (0.514 g, 2.76 mmol) in dichloromethane (20 mL) was treated with iodine monobromide (0.859 g, 4.15 mmol) at −80 to −85 °C for 30 min. NMR analysis (125 MHz ^{13}C) showed that the crude product comprised a 14:1 mixture of (±)-**18** and (±)-**19**. Flash chromatography (ether) furnished (±)-**18** and (±)-**19** (0.617 g, 87% yield) as a partially separable mixture. An analytical sample of each isomer was obtained by collecting nonoverlapping fractions.

Method C: Iodine Monobromide in Toluene. Via a procedure analogous to that employed in the preparation of (+)-**12** and (+)-**13**, a solution of carbonate (±)-**17** (93.0 mg, 0.500 mmol) in toluene (5 mL) was treated with iodine monobromide (1.0 M in dichloromethane, 0.75 mL, 0.75 mmol) at −80 to −85 °C for 30 min. NMR analysis (125 MHz ^{13}C) indicated that the crude product comprised a 21.1:1 mixture of (±)-**18** and (±)-**19**. Flash chromatography (ether) gave (±)-**18** and (±)-**19** (114 mg, 89% yield) as a partially separable mixture. An analytical sample of each isomer was obtained by collecting nonoverlapping fractions.

Major Diastereomer (±)-18: viscous colorless oil; R_f 0.26 (ether); IR ($CHCl_3$) 3010 (w), 2980 (w), 2920 (w), 1745 (s), 1390 (w), 1360 (w), 1330 (w), 1235 (m), 1180 (m), 1115 (m), 1090 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.45 (d, *J* = 6.3 Hz, 3 H), 1.69 (td, *J* = 11.6, 14.2 Hz, 1 H), 2.41 (td, *J* = 3.0, 14.2 Hz, 1 H), 3.27 (dd, *J* = 7.5, 10.6 Hz, 1 H), 3.41 (dd, *J* = 4.3, 10.6 Hz, 1 H),

4.43–4.48 (m, 1 H), 4.57–4.64 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.2, 21.0, 34.9, 74.8, 77.2, 148.3; high resolution mass spectrum (CI, NH_3) *m/z* 273.9910 [$(M + NH_4)^+$, calcd for $C_6H_{13}INO_3$ 273.9939].

Minor diastereomer (±)-19: viscous colorless oil; R_f 0.36 (ether); IR ($CHCl_3$) 3000 (w), 2970 (w), 2920 (w), 1750 (s), 1380 (m), 1350 (w), 1240 (m), 1190 (w), 1150 (m), 1130 (w), 1105 (m), 1050 (w), 1010 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (d, *J* = 6.5 Hz, 3 H), 2.09–2.14 (m, 1 H), 2.22–2.28 (m, 1 H), 3.30 (dd, *J* = 8.5, 10.5 Hz, 1 H), 3.46 (dd, *J* = 4.6, 10.5 Hz, 1 H), 4.60–4.65 (m, 1 H), 4.68–4.74 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.4, 20.6, 31.9, 72.6, 75.1, 148.2; high resolution mass spectrum (CI, NH_3) *m/z* 273.9937 [$(M + NH_4)^+$, calcd for $C_6H_{13}INO_3$ 273.9939].

Iodo Carbonates (±)-21 and (±)-22. Method B: Iodine Monobromide in Dichloromethane. Via a procedure analogous to that employed in the preparation of (+)-**12** and (+)-**13**, a solution of carbonate (±)-**20** (1.28 g, 5.99 mmol) in dichloromethane (50 mL) was treated with iodine monobromide (1.86 g, 9.00 mmol) at −94 °C for 30 min. NMR analysis (125 MHz ^{13}C) revealed that the crude product comprised a 12:1 mixture of (±)-**21** and (±)-**22**. Flash chromatography (hexane/ether, 25:75, then 20:80) provided (±)-**21** and (±)-**22** (1.48 g, 87% yield) as a partially separable mixture. An analytical sample of each isomer was obtained by collecting nonoverlapping fractions.

Method C: Iodine Monobromide in Toluene. Via a procedure analogous to that employed in the preparation of (+)-**12** and (+)-**13**, a solution of carbonate (±)-**20** (150 mg, 0.701 mmol) in toluene (7 mL) was treated with iodine monobromide (1.0 M in dichloromethane, 1.40 mL, 1.40 mmol) at −80 to −85 °C for 1 h. NMR analysis (125 MHz ^{13}C) showed that the crude product comprised an 18.8:1 mixture of (±)-**21** and (±)-**22**. Flash chromatography (hexane/ether, 25:75, then 20:80) gave (±)-**21** and (±)-**22** (174 mg, 87% yield) as a partially separable mixture. An analytical sample of each isomer was obtained by collecting nonoverlapping fractions.

Major diastereomer (±)-21: viscous yellow oil; R_f 0.25 (hexane/ether, 20:80); IR ($CHCl_3$) 3000 (w), 2960 (w), 2930 (w), 1750 (s), 1440 (w), 1390 (m), 1380 (w), 1360 (w), 1340 (w), 1230 (m), 1190 (m), 1165 (w), 1120 (m), 1100 (m), 1060 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (t, *J* = 7.5 Hz, 3 H), 1.70–1.85 (m, 3 H), 1.95 (d, *J* = 6.9 Hz, 3 H), 2.28 (td, *J* = 3.0, 14.1 Hz, 1 H), 4.22–4.28 (m, 2 H), 4.40–4.44 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.8, 22.7, 25.4, 28.0, 30.7, 79.2, 81.1, 148.7; high resolution mass spectrum (CI, NH_3) *m/z* 302.0257 [$(M + NH_4)^+$, calcd for $C_8H_{17}INO_3$ 302.0252].

Minor diastereomer (±)-22: viscous yellow oil; R_f 0.35 (hexane/ether, 20:80), IR ($CHCl_3$) 3000 (w), 2960 (w), 2920 (w), 2870 (w), 1750 (s), 1460 (w), 1440 (w), 1390 (m), 1375 (m), 1330 (w), 1270 (w), 1230 (w), 1190 (m), 1170 (w), 1140 (m), 1120 (m), 1090 (m), 1080 (m), 1060 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (t, *J* = 7.4 Hz, 3 H), 1.63–1.72 (m, 1 H), 1.86–1.95 (m, 1 H), 1.96 (d, *J* = 6.8 Hz, 3 H), 2.11–2.23 (m, 2 H), 4.25–4.32 (m, 2 H), 4.46–4.51 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.6, 22.9, 25.7, 27.6, 28.8, 78.3, 78.3, 148.8; high resolution mass spectrum (CI, NH_3) *m/z* 302.0231 [$(M + NH_4)^+$, calcd for $C_8H_{17}INO_3$ 302.0252].

Iodo Carbonates (±)-24 and (±)-25. Method B: Iodine Monobromide in Dichloromethane. Via a procedure analogous to that employed in the preparation of (+)-**12** and (+)-**13**, a solution of carbonate (±)-**23** (817 mg, 3.82 mmol) in dichloromethane (35 mL) was treated with iodine monobromide (1.42 g, 6.87 mmol) at −80 to −85 °C for 30 min. NMR analysis (125 MHz ^{13}C) showed that the crude product comprised a 6.5:1 mixture of (±)-**24** and (±)-**25**. Flash chromatography (hexane/ether, 25:75, then 15:85) afforded (±)-**24** and (±)-25 (961 mg, 87% yield) as a partially separable mixture. An analytical sample of each isomer was obtained by collecting nonoverlapping fractions.

Method C: Iodine Monobromide in Toluene. Via a procedure analogous to that employed in the preparation of (+)-**12** and (+)-**13**, a solution of carbonate (±)-**23** (150 mg, 0.701 mmol) in toluene (7 mL) was treated with iodine monobromide (1.0 M in dichloromethane, 1.40 mL, 1.40 mmol) at −80 to −85 °C for 1 h. NMR analysis (125 MHz ^{13}C) indicated that the crude product comprised a 6.4:1 mixture of (±)-**24** and (±)-**25**. Flash chromatography (hexane/ether, 25:75, then 15:85) gave (±)-**24** and (±)-**25** (172 mg, 86% yield) as a partially separable mixture. An analytical sample of each isomer was obtained by collecting nonoverlapping fractions.

Major diastereomer (±)-24: yellow liquid; R_f 0.27 (hexane/ether, 20:80); IR ($CHCl_3$) 3010 (w), 2970 (w), 2930 (w), 2880 (w), 1750 (s), 1450 (w), 1395 (w), 1385 (w), 1230 (m), 1195 (m), 1165 (w), 1105 (m), 1070 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (t, *J* = 7.5 Hz, 3 H), 1.67–1.82 (m, 3 H), 2.00 (d, *J* = 6.5 Hz, 3 H), 2.45 (td, *J* = 2.8, 14.2 Hz, 1 H), 4.15–4.21 (m, 2 H), 4.36–4.41 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.8, 23.7, 26.9, 28.0, 32.4, 79.2, 81.7, 148.5; high resolution mass spectrum (CI, NH_3) *m/z* 302.0237 [$(M + NH_4)^+$, calcd for $C_8H_{17}INO_3$ 302.0253].

Minor diastereomer (±)-25: yellow solid; mp 56.5–58.0 °C; R_f 0.44 (hexane/ether, 20:80); IR ($CHCl_3$) 3005 (w), 2970 (w), 2930 (w), 2880 (w), 1750 (s), 1450 (w), 1375 (m), 1230 (m), 1190 (m), 1160 (w), 1115 (m), 1105 (m), 1060 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (t, *J* = 7.4 Hz, 3 H), 1.64–1.73 (m, 1 H), 1.82–1.91 (m, 1 H), 2.03 (d, *J* = 6.8 Hz, 3 H), 2.23 (ddd, *J* = 4.9, 6.2, 14.5 Hz, 1 H), 2.31 (ddd, *J* = 4.9, 7.3, 14.5 Hz, 1 H), 4.23 (ddd, *J* = 6.2, 8.2, 13.7 Hz, 1 H), 4.31–4.35 (m, 1 H), 4.41–4.45 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.3, 24.0, 26.2, 27.6, 30.4, 77.8, 79.6, 148.3; high resolution mass spectrum (CI, NH_3) *m/z* 302.0261 [$(M + NH_4)^+$, calcd for $C_8H_{17}INO_3$ 302.0253].

Iodo Carbonates (−)-27a and (+)-27b. Method A: Iodine in Acetonitrile. Iodine (826 mg, 3.25 mmol) was added in one portion to a solution of carbonate (+)-**26** (429 mg, 1.08 mmol) in acetonitrile (12 mL) at −20 °C. The mixture was stirred at −20 °C for 8 h and then at room temperature for 1 h. TLC monitoring indicated that no reaction occurred. The reaction was worked up in the usual fashion and carbonate (+)-**26** was recovered.

Method B: Iodine Monobromide in Dichloromethane. Iodine monobromide (1.18 g, 5.69 mmol) was added in one portion to a solution of carbonate (+)-**26** (1.50 g, 3.79 mmol) in dichloromethane (30 mL) at −80 to −85 °C. After 30 min additional iodine monobromide (1.18 g, 5.69 mmol) was added, and the mixture was then stirred 30 min further and worked up as described for the preparation of (+)-**12** and (+)-**13**. NMR analysis (125 MHz ^{13}C) indicated that the crude product comprised a 1.7:1 mixture of diastereomers. Flash chromatography (hexane/ether, 40:60) provided iodo carbonates **27a,b** (1.53 g, 87% yield) as an inseparable mixture. An analytical sample of each isomer was obtained by HPLC (hexane/ether, 40:60).

Method C: Iodine Monobromide in Toluene. Iodine monobromide (1.0 M in dichloromethane, 0.75 mL, 0.75 mmol) was added dropwise to a solution of carbonate (+)-**26** (198 mg, 0.500 mmol) in toluene (5 mL) at −80 to −85 °C. After 30 min additional iodine monobromide (1.00 mL, 1.00 mmol) was added, and the mixture was then stirred 30 min further and worked up as described for the preparation of (+)-**12** and (+)-**13**. NMR analysis (125 MHz ^{13}C) revealed that the crude product comprised a 3.4:1 mixture of diastereomers. Flash chromatography (hexane/ether, 40:60) gave iodocarbonates **27a,b** (161 mg, 69% yield) as an inseparable mixture. An analytical sample of each isomer was obtained by HPLC (hexane/ether, 40:60).

Major diastereomer (−)-27a: viscous colorless oil; R_f 0.17 (hexane/ethyl acetate, 80:20); $[\alpha]^{23}_D$ −15.7° (*c* 1.25, $CHCl_3$); IR ($CHCl_3$) 3000 (w), 2960 (w), 2930 (w), 1760 (s), 1580 (w), 1480 (w), 1470 (w), 1440 (w), 1370 (w), 1350 (m), 1220 (w), 1190 (m), 1150 (m), 1100 (s), 1060 (w), 1030 (m), 990 (w), 910 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (s, 3 H), 1.21 (s, 3 H), 3.14 (ABq, J_{AB} = 13.1 Hz, $\Delta\nu_{AB}$ = 112.6 Hz, 2 H), 3.33–3.40 (m, 2 H), 3.42 (s, 3 H), 4.32 (t, *J* = 1.3 Hz, 1 H), 4.42 (d, *J* = 1.3 Hz, 1 H), 4.48 (ddd, *J* = 1.3, 5.6, 9.0 Hz, 1 H), 4.79 (ABq, J_{AB} = 6.4 Hz, $\Delta\nu_{AB}$ = 29.1 Hz, 2 H), 7.19–7.21 (m, 1 H), 7.26–7.30 (m, 2 H), 7.38–7.40 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.6, 22.8, 23.1, 38.8, 44.5, 56.9, 70.1, 82.2, 84.6, 99.1, 126.5, 129.1, 129.8, 136.6, 147.5; high resolution mass spectrum (CI, NH_3) *m/z* 484.0595 [$(M + NH_4)^+$, calcd for $C_{17}H_{27}INO_5S$ 484.0654].

Minor diastereomer (+)-27b: white solid; mp 81–83 °C; R_f 0.17 (hexane/ethyl acetate, 80:20); $[\alpha]^{23}_D$ +5.9° (*c* 1.67, $CHCl_3$); IR ($CHCl_3$) 2990 (w), 2950 (w), 2930 (w), 2890 (w), 1760 (s), 1580 (w), 1480 (w), 1435 (w), 1380 (w), 1360 (w), 1300 (w), 1220 (w), 1180 (m), 1150 (m), 1110 (m), 1100 (m), 1030 (m), 990 (w), 910 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.15 (s, 3 H), 1.23 (s, 3 H), 2.92–2.97 (m, 2 H), 3.31–3.34 (m, 2 H), 3.42 (s, 3 H), 4.31 (d, *J* = 1.3 Hz, 1 H), 4.33 (t, *J* = 1.3 Hz, 1 H), 4.69 (ddd, *J* = 1.3, 5.4, 9.5 Hz, 1 H), 4.75 (ABq, J_{AB} = 7.1 Hz, $\Delta\nu_{AB}$ = 18.6 Hz, 2 H), 7.17–7.21 (m, 1 H), 7.27–7.30 (m, 2 H), 7.40–7.42 (m, 2 H); ^{13}C

NMR (125 MHz, $CDCl_3$) δ 1.0, 22.9, 23.5, 38.6, 44.2, 56.7, 70.5, 79.2, 80.7, 96.1, 126.5, 129.0, 129.7, 136.4, 147.7; high resolution mass spectrum (CI, NH_3) *m/z* 484.0616 [$(M + NH_4)^+$, calcd for $C_{17}H_{27}INO_5S$ 484.0654].

Iodo Carbonates 29a,b. Method B: Iodine Monobromide in Dichloromethane. Via a procedure analogous to that employed in the preparation of (+)-**12** and (+)-**13**, carbonate (+)-**28** [from 0.0816 mmol of diol (+)-**35**] in dichloromethane (2.5 mL) was treated with iodine monobromide (83.6 mg, 0.404 mmol) at −85 °C for 30 min. Flash chromatography (hexane/ether, 30:70) gave the minor diastereomer **29b** (12.6 mg, 24% yield for two steps) followed by the major diastereomer **29a** (19.8 mg, 38% yield for two steps).

Major diastereomer of 29a: colorless oil; R_f 0.18 (hexane/ethyl acetate, 70:30); IR ($CHCl_3$) 3020 (w), 3000 (w), 2980 (w), 2930 (w), 2870 (w), 1765 (s), 1730 (s), 1470 (w), 1450 (w), 1390 (m), 1370 (m), 1280 (s), 1250 (w), 1230 (w), 1170 (m), 1100 (s), 1070 (w), 1020 (m), 990 (w), 970 (w), 920 (w), 900 (w), 880 (w), 850 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (d, *J* = 7.2 Hz, 3 H), 0.98 (s, 3 H), 1.19 (s, 3 H), 1.49 (s, 9 H), 1.63–1.70 (m, 1 H), 1.78 (dd, *J* = 3.7, 15.0 Hz, 1 H), 1.91–1.97 (m, 2 H), 2.01–2.07 (m, 1 H), 3.21 (dd, *J* = 5.1, 9.9 Hz, 1 H), 3.46–3.53 (m, 3 H), 4.29–4.32 (m, 1 H), 4.34–4.37 (m, 1 H), 4.46–4.52 (m, 3 H), 4.66 (dd, *J* = 2.9, 6.0 Hz, 1 H), 4.83 (dd, *J* = 1.3, 6.3 Hz, 1 H), 7.24–7.36 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −0.8, 9.9, 16.4, 22.4, 26.6, 27.9, 30.0, 33.0, 51.4, 66.8, 66.9, 71.3, 72.3, 74.5, 81.7, 87.6, 107.8, 127.3, 127.3, 128.3, 138.8, 147.8, 153.2; high resolution mass spectrum (CI, NH_3) *m/z* 647.1753 [$(M + H)^+$, calcd for $C_{28}H_{40}IO_9$ 647.1717].

Minor diastereomer of 29b: white solid; mp 81–83 °C; R_f 0.27 (hexane/ethyl acetate, 70:30); IR ($CHCl_3$) 3000 (w), 2980 (w), 2930 (w), 2870 (w), 1775 (s), 1740 (s), 1455 (w), 1390 (w), 1370 (m), 1285 (s), 1240 (m), 1170 (m), 1160 (m), 1115 (m), 1075 (m), 1030 (m), 990 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (d, *J* = 7.1 Hz, 3 H), 0.97 (s, 3 H), 1.21 (s, 3 H), 1.48 (s, 9 H), 1.61–1.69 (m, 1 H), 1.78–1.88 (m, 4 H), 3.10 (dd, *J* = 6.9, 11.0 Hz, 1 H), 3.25 (dd, *J* = 4.3, 11.0 Hz, 1 H), 3.44–3.48 (m, 1 H), 3.52–3.56 (m, 1 H), 4.30–4.38 (m, 3 H), 4.47 (s, 2 H), 4.60 (dd, *J* = 5.1, 6.1 Hz, 1 H), 4.69–4.71 (m, 1 H), 7.27–7.35 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 2.3, 10.1, 16.3, 22.5, 26.8, 27.9, 31.3, 33.7, 51.0, 64.8, 66.3, 72.5, 74.8, 75.2, 77.7, 82.1, 86.1, 108.2, 127.5, 127.6, 128.3, 138.5, 149.0, 153.2; high resolution mass spectrum (CI, NH_3) *m/z* 647.1747 [$(M + H)^+$, calcd for $C_{28}H_{40}IO_9$ 647.1717].

***trans*-Alkene (±)-38.** A 100-mL two-necked flask equipped with a dry ice-acetone condenser was cooled to −40 °C and charged with liquid ammonia (20 mL) and ether (5 mL). Lithium wire (194 mg, 27.7 mmol) was added and the resultant mixture stirred for 15 min. A solution of alkyne (±)-**40** (620 mg, 554 mmol) in ether (2 mL) was then added dropwise. After 3 h at −40 °C, the reaction mixture was quenched with saturated NH_4Cl solution (15 mL), gradually warmed to room temperature, and extracted with ether (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (hexane/ethyl acetate, 90:10) afforded *trans*-alkene (±)-**38** (530 mg, 84% yield) as a colorless liquid: R_f 0.38 (hexane/ethyl acetate, 20:80); IR ($CHCl_3$) 3670 (w), 3460 (w, br), 3010 (w), 2970 (m), 2940 (m), 2880 (w), 1460 (w), 1450 (w), 1440 (w), 1380 (w), 1220 (w), 1005 (w), 970 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.95 (t, *J* = 7.5 Hz, 3 H), 1.45–1.53 (m, 2 H), 1.56 (br s, 1 H), 1.69 (d, *J* = 6.3 Hz, 3 H), 2.02–2.08 (m, 1 H), 2.21–2.26 (m, 1 H), 3.49–3.53 (m, 1 H), 5.41–5.47 (m, 1 H), 5.53–5.58 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.9, 18.1, 29.5, 40.2, 72.3, 127.1, 128.9; high resolution mass spectrum (CI, NH_3) *m/z* 132.1382 [$(M + NH_4)^+$, calcd for $C_7H_{18}NO$ 132.1388].

Alcohol (±)-40. A solution of propyne (47 mL, 0.830 mol) in tetrahydrofuran (200 mL) at −78 °C was treated with *n*-butyllithium (2.5 M in hexane, 167 mL, 0.417 mol) and the resultant mixture was stirred for 30 min. 1,2-Epoxybutane (**39**, 17.9 mL, 0.208 mol) and boron trifluoride etherate (28.2 mL, 0.223 mol) were successively added dropwise. After an additional 1 h at −78 °C, the cold bath was removed. Saturated aqueous $NaHCO_3$ (250 mL) was then added, the aqueous layer was extracted with ether (3 × 100 mL), and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (hexane/ethyl acetate, 85:15) furnished alcohol (±)-**40** (18.9 g, 81% yield) as a colorless liquid: R_f 0.31 (hexane/ethyl acetate, 80:20); IR ($CHCl_3$) 3660 (w), 3450 (w, br), 3000 (m), 2960 (s), 2920 (s), 2880 (m), 1460 (w), 1430 (w), 1390 (w), 1230 (w), 1090 (w), 1050 (w), 1015 (w), 970 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.95 (t, *J* = 7.4 Hz, 3 H), 1.51–1.60 (m, 2 H), 1.81 (t, *J* = 3.6 Hz, 3 H), 1.93 (d, *J* = 4.7 Hz, 1 H), 2.22–2.28 (m, 1 H), 2.35–2.41 (m, 1 H), 3.59–3.65 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.4, 9.9, 21.2, 29.0, 71.5, 75.3, 78.2; high resolution mass spectrum (CI, NH_3) *m/z* 113.0955 [$(M + H)^+$, calcd for $C_7H_{13}O$ 113.0966].

Alcohol (+)-42. *s*-Butyllithium (1.19 M in cyclohexane, 148.7 mL, 177 mmol) was added over 50 min to a solution of methoxymethyl allyl ether (23.55 g, 231 mmol) in tetrahydrofuran (100 mL) at −78 °C. After 1 h the resultant bright yellow solution was treated with a solution of (+)-*B*-methoxydiisopinocampheylborane [$(Ipc)_2BOMe$, 56.09 g, 177 mmol] in tetrahydrofuran (150 mL), added dropwise over 70 min. The mixture was stirred 2 h further, and freshly distilled boron trifluoride etherate (29.04 mL, 236 mmol) and 2,2-dimethyl-3-(phenylthio)propionaldehyde (**41**, 34.34 g, 177 mmol) were then successively introduced. The reaction was stirred for an additional 3 h at −78 °C and gradually warmed to room temperature. Following addition of trimethylamine *N*-oxide dihydrate (58.94 g, 531 mmol), the mixture was stirred at room temperature for 12 h, heated to reflux for 1 h, and cooled. Saturated NH_4Cl solution (400 mL) was added, volatile materials were removed under reduced pressure, and the aqueous residue was extracted with ether (3 × 400 mL). The combined extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Most of the isopinocampheol was carefully removed by vacuum distillation (ca. 2 mmHg) using a 6-inch column with the head temperature below 100 °C. Flash chromatography (hexane/ether/dichloromethane, 70:15:15) then gave (+)-**42** (38.16 g, 73% yield) as a pale yellow oil: R_f 0.30 (hexane/ethyl acetate, 80:20); $[\alpha]^{24}_D$ +69.8° (*c* 0.97, $CHCl_3$); IR ($CHCl_3$) 3560 (m), 3065 (w), 2990 (s), 2960 (s), 2930 (s), 2895 (s), 2820 (w), 1580 (m), 1470 (m), 1435 (m), 1385 (m), 1230 (m), 1145 (s), 1085 (s), 1020 (s), 930 (m), 900 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.08 (s, 3 H), 1.11 (s, 3 H), 2.73 (d, *J* = 6.3 Hz, 1 H), 3.10 (ABq, J_{AB} = 12.2 Hz, $\Delta\nu_{AB}$ = 75.3 Hz, 2 H), 3.38 (s, 3 H), 3.53 (dd, *J* = 3.9, 6.3 Hz, 1 H), 4.19 (dd, *J* = 3.6, 8.4 Hz, 1 H), 4.65 (ABq, J_{AB} = 6.7 Hz, $\Delta\nu_{AB}$ = 98.2 Hz, 2 H), 5.25–5.31 (m, 2 H), 5.84 (ddd, *J* = 8.4, 10.3, 17.2 Hz, 1 H), 7.12–7.15 (m, 1 H), 7.23–7.26 (m, 2 H), 7.36–7.38 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.1, 24.0, 39.2, 45.0, 56.3, 76.7, 78.2, 93.5, 119.3, 125.6, 128.7, 129.2, 136.2, 138.2; high resolution mass spectrum (CI, NH_3) *m/z* 297.1495 [$(M + H)^+$, calcd for $C_{16}H_{25}O_3S$ 297.1524].

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Supplementary Material Available: ^{13}C NMR spectral data at 125 MHz for **2**, **11–26**, **27a,b**, **28**, **29a,b**, **38**, **40**, and **42** (25 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.