adamantanediyl dications, the first examples of dipositive ions with two cationic centers in a single adamantane skeleton. Such dications are, however, stable only when the 2,6-tertiary cationic centers are substituted by stabilizing groups such as phenyl, cyclopropyl, and hydroxyl. ^{13}C NMR spectroscopic study of the obtained dications indicates that the positive charges are significantly delocalized into the substituents due to their close proximity in the adamantyl cage. Attempts to generate related dications at the 1,4-position of the adamantyl skeleton were unsuccessful.

Experimental Section

Adamantane-2,6-dione, **6**, was prepared by literature procedure[11] starting from Meerwein's ester. Reaction of the diketone with excess methyllithium, phenyllithium, or cyclopropyl-Grignard reagent in THF gave the corresponding dimethyl, diphenyl, and dicyclopropyl diols **5**. $LiAlH_4$ reduction of the diketone in THF gave the secondary diol, **5**-H. 5-Bromoadamantanone was prepared by direct bromination of adamantanone according to literature procedure.[15] Reaction of the bromo ketone with methyllithium at 0 °C in ether gave 5-bromo-2-methyl-2-adamantanol. 5-Hydroxyadamantanone was obtained by nitric acid oxidation of 2-adamantanone.[16] All the new compounds (i.e., **5**-c-C_3H_5, **5**-C_6H_5, and **15**) gave satisfactory elemental analysis and their ^{13}C NMR chemical shifts are listed in Tables I and III along with the data for other compounds.

Preparation of Carbocations and Carbodications. Freshly distilled SbF_5 and FSO_3H were used. To appropriate superacid dissolved in twofold excess amount of SO_2ClF or SO_2 at −80 °C was slowly added with vigorous stirring a cooled slurry or solution of the appropriate precursor in SO_2ClF or SO_2 resulting in an approximately 10–15% solution of the cation or dication.

^{13}C NMR spectra were obtained on Varian Models FT-80 and XL-200 NMR spectrometers equipped with low-temperature broad band probes. The ^{13}C NMR chemical shifts are referenced from external capillary tetramethylsilane.

Acknowledgment. Support of our work by the National Institutes of Health is gratefully acknowledged.

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Furans in Synthesis. 5.[1] Furan-Terminated Cationic Cyclizations in the Preparation of Fused, Spirocyclic and Bridged Ring Systems. An Application to the Synthesis of Nakafuran 9

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Received January 23, 1985

The title compounds **36–42** and nakafuran 9 (**43**) were prepared by furan-terminated cationic cyclizations. The cyclization substrates, allylic alcohols **16**, **17**, **25**, **26**, **33**, and **34**, and the derived enone **19** were prepared by CuCN moderated S_N2' addition of Grignard reagents derived from 2-(3-furyl)-1-bromoethane (**12**) and 3-(3-furyl)-1-bromopropane (**13**) to vinyl epoxides **14** and **22** and epoxy enol ether **21**. Treatment of substrate allylic alcohols with a two-phase mixture of HCO_2H and cyclohexane resulted in facile cyclization when the forming ring was six or seven membered. Enone closures proceeded only when a six-membered ring was produced or in the case of enone **48** which leads to nakafuran 9 (**43**).

The exploitation of cationic π-cyclizations in the construction of polycyclic ring systems has been the object of intense study since the early 1950s.[3] While the methodology for the preparation of fused-ring systems has been well developed and extensively utilized relatively few general srategies for the construction of spiro[4] and bridged systems[5] have been developed. Therefore, there remains a need for methodology which facilitates the preparation

(1) For the previous report in this series, see: Tanis, S. P.; Head, D. B. *Tetrahedron Lett.* **1984**, *25*, 4451.

(2) Recipient of a Camille and Henry Dreyfus Grant for Young Faculty in Chemistry, 1980–84.

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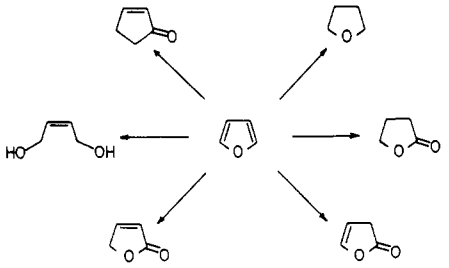
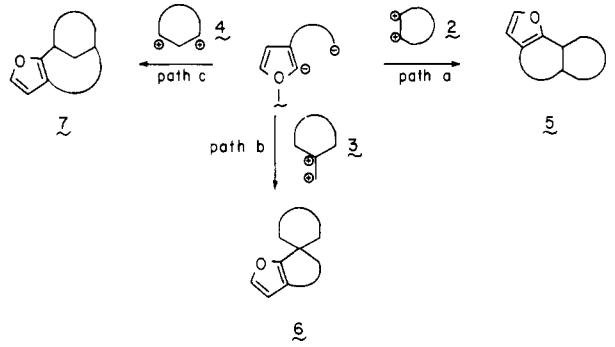
0022-3263/85/1950-3988$01.50/0

Scheme I. Furan Equivalencies



Scheme II



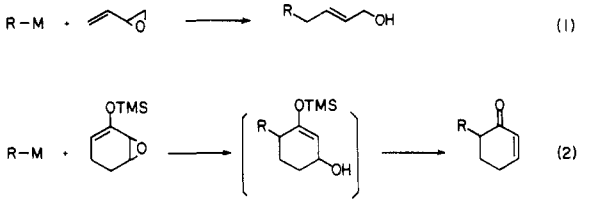
of spiro and bridged ring systems which might be couched within complex molecular environments. These methods should proceed in high chemical yield with excellent regio- and stereochemical control. Also, the fused, spirocyclic, or bridged ring systems thus prepared must provide sufficient "handles" so that the synthesis endeavor can be completed.

As part of a general program in furan chemistry, we have previously examined epoxide-initiated furan-terminated cationic cyclizations for the preparation of fused-ring systems.[6] Our interest in developing substituted furans as bis-nucleophilic synthons in annulative processes stemmed from the variety of useful functional groupings which might be realized from the relatively unreactive furyl nucleus. As is illustrated in Scheme I, a furan can serve as the operational equivalent of acyclic, carbocyclic, and heterocyclic systems, providing these subunits after standard chemical manipulations.

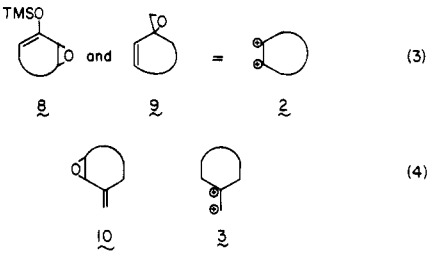
Our earlier work[6] demonstrated the utility of epoxide-initiated furan-terminated cationic cyclizations. However, these substrates provided access only to rather simple and relatively unfunctionalized fused-ring systems. In addition, the difficulties encountered in the preparation of the requisite epoxyfurans rendered this approach less than general. In an attempt to expand the usefulness of furan-terminated cationic cyclizations, we have examined the reaction of furyl dianion equivalent 1 (Scheme II) with a variety of bis-electrophilic synthons (**2–4**). The interaction of the active furan side-chain nucleophilic center with the bis-electrophile will provide a coupling product; subsequent activation of the second electrophilic center followed by aromatic substitution could provide fused (**5**), spirocyclic (**6**), and bridged (**7**) ring systems. Manipulation of the furan nucleus (see Scheme I) and other residual functional groups would provide complex intermediates for the preparation of diverse classes of bioactive natural products.

Design and Synthesis of Cyclization Substrates

Of paramount importance to this study was the selection of the bis-electrophilic moieties illustrated in Scheme II. The relative level of reactivity must be arranged so that the active furan side-chain nucleophilic center reacts at the desired electrophilic site to furnish the desired regioisomer upon cyclization. In order to minimize potential selectivity problems in the initial addition, we sought equivalents of bis-electrophiles **2** and **3** (Scheme II, paths A and B) which would reveal a second electrophilic center on the adjacent carbon as a result of the initial addition. Recent reports by Marino,[7a,c–f] Wender,[7g] and Ziegler[7b] have demonstrated the usefulness of vinyl epoxides[7a–f] and enol ethers of α,β-epoxy ketones[7f,g] in S_N2'-type addition of cuprates (eq 1 and 2). In these processes, and allylic



alcohol and enone, respectively, are created, providing a potential second electrophilic center on the carbon adjacent to the position of initial attack. These results suggest the applicability of α,β-epoxy ketone enol ethers **8** and vinyl spiro epoxides **9** (eq 3) as equivalents of the hypothetical **2** in the formation of fused ring compounds (Scheme II, path A). An *exo*-methylene vinyl epoxide (**10**, eq 4) would provide access to spirocyclic substances as the operational equivalent of **3** (Scheme II, path B). The syntheses of bridged species (Scheme II, path C) in which the distance between the electrophilic centers can be variable is best dealt with on a case-to-case basis. This analysis suggests that a variety of readily available allylic alcohols,[3a–h,4v,8] derived from **9** and **10** (eq 1), or prepared by enone reduction (eq 2) could serve as initiators in the cyclization step as might the corresponding enones and enals.[4v,9]



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(6) Tanis, S. P.; Herrinton, P. M. *J. Org. Chem.* **1983**, *48*, 4572.

(7) For recent examples of the reaction of cuprates with vinyl epoxides, see: (a) Marino, J. P.; Abe, H. *J. Am. Chem. Soc.* **1981**, *103*, 2907. (b) Ziegler, F. E.; Cady, M. A. *J. Org. Chem.* **1981**, *46*, 122. (c) Marino, J. P.; Abe, H. *Synthesis* **1980**, *11*, 872. (d) Marino, J. P.; Hatanaka, N. *J. Org. Chem.* **1979**, *44*, 4467. (e) Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1979**, 675. For reactions of cuprates with enol ethers of α,β-epoxy enones, see: (f) Marino, J. P.; Jaen, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 3165. (g) Wender, P. A.; Erhardt, J. M.; Letendre, L. J. *J. Am. Chem. Soc.* **1981**, *103*, 2114.

(8) For some other recent examples of allylic alcohol initiated cationic cyclizations, see: Brunke, E.-J.; Hammerschmidt, J.-J.; Struwe, H. *Tetrahedron* **1981**, *37*, 1033 and references cited therein.

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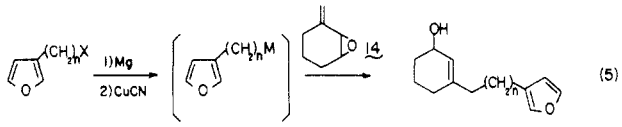
In the event, Grignard reagents prepared from 3-(chloromethyl)furan (**11**),[10a] 2-(3-furyl)-1-bromoethane (**12**),[10b] and 3-(3-furyl)-1-bromopropane[10c] (**13**) were treated with

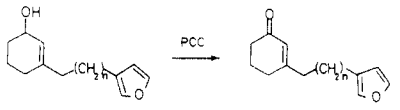


(5)

	n	X
11	1	Cl
12	2	Br
13	3	Br

	n	Yield
15	1	82%
16	2	58%
17	3	62%

CuCN[7a,c-f] and allowed to react with the readily available vinyl epoxide **14**[7] (eq 5) to provide allylic alcohols **15–17**, precursors to spiro[4.5]decane, -[5.5]undecane, and -[5.6]dodecane systems, respectively, in good to excellent yields. The corresponding enones **18–20** were readily prepared (eq 6) via oxidation (PCC)[11] of alcohols **15–17**.

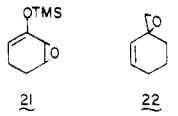


(6)

	n
15	1
16	2
17	3

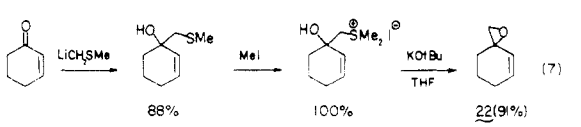
	n	Yield
18	1	87%
19	2	83%
20	3	84%

The synthesis of fused-ring compounds requires **8** and **9** as annulation partners. For this study, cyclohexenone was selected as the precursor to **8** and **9** which when treated with the Grignard reagents derived from **13** and **14** might lead to fused bicyclo[4.4.0]decane and bicyclo-[5.4.0]undecane ring systems, respectively. Enol ether **21**

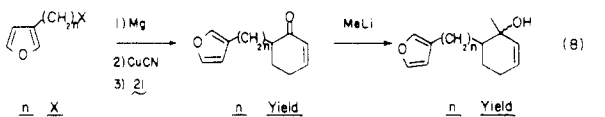


21 **22**

was easily prepared by the methods of Marino[7f] and Wender[7g] from cyclohexenone; however, to the best of our knowledge, **22** has not been reported in the literature. A direct approach to **22** using Corey's dimethylsulfonium methylide[12] provided **22** in variable (0–35%) yields. We then examined the alternative procedure outlined in eq 7. The addition of [(methylthio)methyl]lithium[13] to cyclohexenone provided the tertiary allylic alcohol in 88% yield. Methylation at sulfur (CH_3I, 100%) and treatment of the resulting sulfonium salt with KO-*t*-Bu (THF) provides **22** in 80% overall yield from cyclohexenone.[14] With **21** and **22** available, the fused-ring cyclization substrates were prepared as described in eq 8 and 9.



(7)

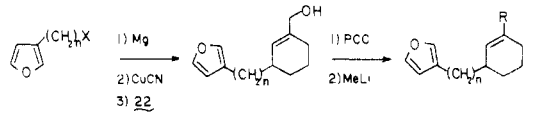


(8)

	n	X
12	2	Br
13	3	Br

	n	Yield
23	2	75%
24	3	72%

	n	Yield
25	2	90%
26	3	90%



(9)

	n	X
11	1	Cl
12	2	Br
13	3	Br

	n	Yield
27	1	78%
28	2	56%
29	3	58%

	n	R	Yield
30	1	CHO	79%
31	2	CHO	83%
32	3	CHO	78%
33	2	CH_2OH	90%
34	3	CH_2OH	85%

Treatment of the Grignard reagents derived from **12** and **13** with CuCN[7] followed by **21** provided enones **23** and **24** in 75% and 72% yields, respectively. The addition of MeLi afforded tertiary allylic alcohol cyclization substrates **25** and **26** (90%). Similarly (eq 9), S_N2' addition to spiro epoxides **22** provided allylic alcohols **27** (78%), **28** (56%), and **29** (58%). Oxidation (PCC) of **27–29** gave enals **30** (79%), **31** (83%), and **32** (78%); the addition of CH_3Li to **31** and **32** afforded secondary allylic alcohols **33** (90%) and **34** (85%).

Cyclization Studies

With the desired cyclization substrates available, the ring closing sequence was examined. Given the relatively poor nucleophilic character of the furyl residue relative to standard terminator functions[4,15] and the increased acid lability of the derived product disubstituted furans compared with the starting materials,[15] the choice of reaction conditions should have a profound effect in the partitioning of the reaction between a fruitful cyclization pathway and undesired products. During our study of epoxide-initiated cyclizations,[6] we observed that the mild Lewis acids Ti(O-*i*-Pr)$_3$Cl and ZnI_2·OEt_2 provided the best balance between Lewis and Brønsted acidity of the medium resulting in high yields of cyclized products. Such Lewis acids as well as the alkyl aluminum halides examined by Snider[9k] might cause enones **18–20** and enals **30–32** to undergo cyclization. Enones and enals have also been cyclized with acid,[9] Ac_2OH^+,[9] and $(CF_3CO)_2O$, CF_3CO_2H.[9] However, the fragility of the products and the facility of furan acylation may render these reaction conditions useless. Allylic alcohol initiators for cationic cyclizations have been extensively examined by Johnson and others[3a-h,8] and the reaction conditions which have been employed generally involve a protic acid of reasonable strength in a solvent in which it is soluble. Of the myriad of conditions reported in the literature, the two-phase mixture of cyclohexane and anhydrous formic acid[8] appeared to be the mildest method for initiating the cyclization of allylic alcohols **15–17**, **25**, **26**, **33**, and **34**.

Exposure of allylic alcohols **15**, **16** and **17** (eq 10) to anhydrous formic acid–cyclohexane for 5–15 min at room temperature resulted in the smooth closure of **16** and **17** to provide the corresponding spiro[5.5]undecane **36** (72%) and spiro[5.6]dodecane **37** (58%) ring systems. Allylic alcohol **15**, precursor to a spiro[5.4]decane, failed to provide **35**, yielding instead the formate (84%). The inability of

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(11) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

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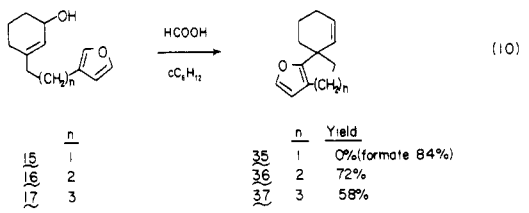
(14) Several other examples have been examined: Tanis, S. P.; McMills, M. C.; Herrinton, P. M. *J. Org. Chem.*, in press.

(15) See: (a) Dunlop, A. P.; Peters, F. N. In "The Furans"; Reinhold: New York, 1953. (b) Bosshard, P.; Eugster, C. H. *Adv. Heterocycl. Chem.* **1966**, *7*, 377–491. (c) Sargent, M. V.; Crisp, T. M. In "Comprehensive Organic Chemistry"; Sammes, P. G., Ed.; Pergamon Press: Oxford, 1979; Vol 4, pp 693–744. (d) Dean, F. M. *Adv. Heterocycl. Chem.* **1982**, *30*, 167–238.

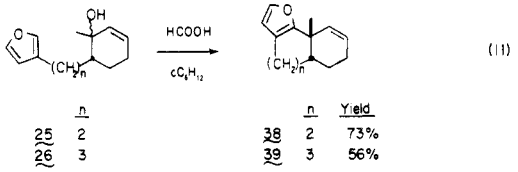


(10)

n		n	Yield
15	1	35	1 0%(formate 84%)
16	2	36	2 72%
17	3	37	3 58%

allylic alcohol **15** to form a five-membered ring was expected on the basis of upon our earlier experience with epoxyfurans.[6] As we have previously noted with cyclization substrates related to **15**, the overlap required for closure to occur is difficult to achieve as **15**, after ionization, possesses but two sp^3-hybridized carbon atoms in the forming cycle.[16]

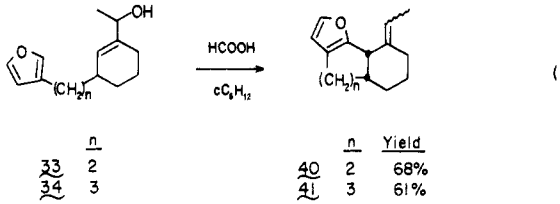
Alcohols **25** and **26**, when treated with formic acid and cyclohexane (eq 11), provide good yields of the fused fu-



(11)

n		n	Yield
25	2	38	2 73%
26	3	39	3 56%

ran-containing bicyclo[4.4.0]decane **38** (73%) and bicyclo[5.4.0]undecane **39** (56%). The assignment of the cis ring fusion in **38** and **39** is based upon precedent[3] and is expected from the method of synthesis. Similar exposure of primary allylic alcohols **27**, **28**, and **29**, also precursors to fused ring systems, led to the isolation of the corresponding formate esters in excellent (80–90%) yields. However, the related secondary allylic alcohols **33** and **34** cyclized smoothly as is illustrated in eq 12, affording **40** (68%) and **41** (61%) as a mixture of *exo*-ethylidene double bond isomers.



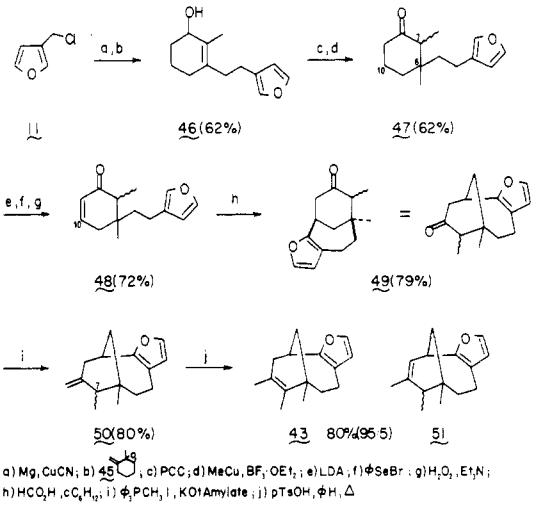
(12)

n		n	Yield
33	2	40	2 68%
34	3	41	3 61%

With allylic alcohols firmly established as initiators for furan-terminated cationic cyclization, we next examined the cyclization of enones **18–20** and enals **30–32**. Compounds **18–20** and **30–32** were exposed to various Lewis acids[17] under numerous sets of reaction conditions to no avail. However, when milder Lewis acids such as $MgBr_2$, ZnI_2, and $Ti(O\text{-}i\text{-}Pr)_3Cl$ were employed, the starting materials were recovered in nearly quantitative yields. Acylative-type enone and enal cyclizations similar to those reported by Andersen,[9c,h] Marshall,[9e] and Harding[9f,i] were then attempted. Treatment of enones **18–20** and enals **30–32** with either Ac_2O, $HClO_4$, EtOAc or $(CF_3CO)_2O$, CF_3CO_2H resulted in a facile and high yield acylation of the furyl nucleus at the 2-position. Having failed to cyclize **18–20** and **30–32** under the relatively mild Lewis acid or acylation reaction conditions, we turned to a protic acid mediated closure. Enones **18–20** were each separately placed in cyclohexene and formic acid was added to gen-

(16) Stork (a) and van Tamelen (b) have also noted similar constraints in five-membered ring formation. (a) Stork, G.; Cohen, J. F. *J. Am. Chem. Soc.* **1974**, *96*, 5270. (b) van Tamelen, E. E.; Pedlar, A. D.; Li, E.; James, D. R. *Ibid.* **1977**, *99*, 6778. van Tamelen, E. E.; Leiden, T. M. *Ibid.* **1982**, *104*, 2061.

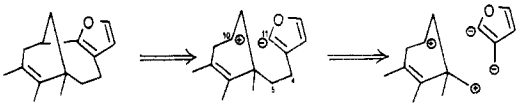
(17) $BF_3{\cdot}OEt_2$, $SnCl_4$, $TiCl_4$, $EtAlCl_2$, Et_2AlCl, $MgBr_2{\cdot}OEt_2$, ZnI_2 and $Ti(O\text{-}i\text{-}Pr)_3Cl$ were employed as Lewis Acids.



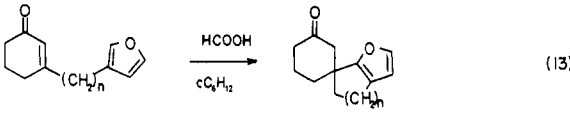
a) Mg, CuCN; b) 45, c) PCC; d) MeCu, $BF_3{\cdot}OEt_2$; e) LDA; f) ΦSeBr; g) H_2O_2, Et_3N; h) HCO_2H, cC_6H_{12}; i) Φ_3PCH_3I, KOtAmylate; j) pTsOH, ΦH, Δ

Figure 1. Synthesis of nakafuran 9 (**43**).

Scheme III. Retrosynthesis of Nakafuran 9 (**43**)



erate a red color. Quenching of the reaction after 5–15 min (eq 13) and analysis of the product mixtures demonstrated



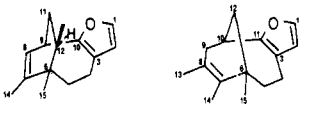
(13)

n		n	Yield
18	1		NR
19	2	42	2 66%
20	3		NR

that, of the three substrates **18–20**, only **19** had suffered cyclization, providing the furan-containing spiro[5.5]undecane **42** in 60% yield; enones **18** and **20** were recovered quantatively. More vigorous reaction conditions led to the complete destruction of **18** and **20**. Similar treatment of enals **30–32** resulted in starting material recovery, or in cases of harsher treatment, polymerization.

Synthesis of a Bridged System. Preparation of Nakafuran 9 (43)

The construction of bridged ring systems will be demonstrated within the context of a synthesis of nakafuran 9 (**43**). Nakafuran 9 (**43**) was recently isolated by



nakafuran-8 nakafuran-9

44 **43**

Scheuer[18] from the marine sponge *Dysidea fragilis* and from the nudibranchs *Hypselodoris godeffroyana* and *Chromodoris maridadilus* which graze upon *D. fragilis*. Nakafuran 9 (**43**) and the closely related nakafuran 8 (**44**) possess fish antifeedant properties, having been observed to repel predacious reef fishes which feed upon the soft bodied nudibranchs. A retrosynthesis of nakafuran 9 (**43**), presented in Scheme III, suggests that the bicyclo[4.3.1]-

(18) Schulte, G.; Scheuer, P. J.; McConnel, O. J. *Helv. Chim. Acta* **1980**, *63*, 2159. For an approach to the synthesis of nakafuran 9, see: Seto, H.; Hirokawa, S.; Fujimoto, Y.; Tatsumo, T. *Chem. Lett.* **1983**, 989.

decane skeleton of **43** would be ultimately available from the readily available 3-furylmethyl dianion[6] and a highly substituted dication.

The dication equivalent selected was the vinyl epoxide **45** (Figure 1). The coupling of the Grignard reagent prepared from 3-(chloromethyl)furan (**12**) with **45** (CuCN) provides allylic alcohol **46** (62%), thus establishing the C-4, C-5 bond of **43**. Oxidation (PCC, 89%) and treatment of the derived enone with MeCu BF_3[19] introduces the C-6-CH_3 group, giving ketone **47** (70%) as a 60:40 mixture at pro-C-7 in 62% overall yield from **46**. The second electrophilic center needed for closure at C-10 was introduced smoothly as the enone via selenylation[20] of the kinetic enolate followed by oxidation (H_2O_2, Et_3N) and elimination of the selenoxide, giving enone **48** (72%). We found it necessary to perform the oxidation–elimination in the presence of a base (Et_3N) because the phenylseleninic acid produced in the elimination promoted cyclization of **48**, providing a mixture of **48** and **49** in greatly reduced yield. Cyclization of **48** was effected with HCO_2H–c-C_6H_{12}, affording the crucial bicyclo[4.3.1]decanone **49** in excellent (79%) yield as a 60:40 mixture at C-7. All that remained to complete the synthesis of nakafuran 9 (**43**) was the introduction of a methyl at C-8 and the placement of a double bond at C-7–C-8. A methyl equivalent and double bond were simultaneously introduced via a Wittig olefination of **49** using the conditions of Conia[21] (Ph_3P–CH_3I, K-*tert*-amylate) to give **50** in 80% yield as a 60:40 mixture at C-7. Olefin migration was attempted with $(PhCN)_2PdCl_2$,[22a] $RhCl_3(H_2O)_3$,[22b] and $(Ph_3P)_3RhHCl$;[22c] in each case, starting material **50** was recovered unchanged. Acid-catalyzed olefin migration was investigated and, after extensive experimentation, we found that the exposure of **50** to a solution of *p*-TsOH in refluxing benzene for 15 min provided a 95:5 mixture of nakafuran 9 (**43**) and $\Delta^{8,9}$-iso-nakafuran 9 (**51**) in 80% yield. The identity of **43** was confirmed by a comparison of spectral data with those of authentic **43**.[23]

Conclusion

Our results clearly demonstrate the utility and potential of furan-terminated cationic cyclizations. We have found that cyclizations to form fused, spirocyclic, and bridged ring systems in which the forming cycle is six or seven membered occur in good to excellent yields, providing reasonably well functionalized products. The application of this methodology to the syntheses of a wide variety of complex biologically active natural products is currently under study. These results will be reported in due course.

Experimental Section

General Methods. Tetrahydrofuran (THF) was dried by distillation, under nitrogen from sodium benzophenone ketyl; methylene chloride was dried by distillation under nitrogen from calcium hydride; formic acid was dried by distillation under argon from phthallic anhydride; pyridine was dried by distillation, under nitrogen, from calcium hydride; diisopropylamine was dried by distillation, under nitrogen, from calcium hydride. Petroleum ether refers to 30–60 °C boiling point fraction of petroleum benzin. Diethyl ether was purchased from Mallinkrodt, Inc., St. Louis, MO, and used as received. *n*-Butyllithium in hexane and methyllithium were purchased from Aldrich Chemical Co., Milwaukee, WI, and titrated by the method of Watson and Eastham.[24] Ethyl aluminum dichloride and diethyl aluminum chloride were purchased as hexane solutions from Alfa Products, Danvers, MA, and used as received. Magnesium metal turnings were activated by successive washings with 1 N aqueous hydrochloric acid, water, acetone, and ether and dried in a dessicator over phosphorus pentoxide at reduced pressure. All other reagents were used as received unless otherwise stated; all reactions were carried out under a blanket of argon with the rigid exclusion of moisture from all reagents and glassware unless otherwise mentioned.

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Pye-Unicam SP-1000 infrared spectrophotometer with polystyrene as standard. Proton magnetic resonance spectra were recorded on a Varian T-60 at 60 MHz or a Bruker WM-250 spectrometer at 250 MHz as indicated, as solutions in deuteriochloroform unless otherwise indicated. Chemical shifts are reported in parts per million on the δ scale relative to a tetramethylsilane internal standard. Data are reported as follows: chemical shift (multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration). ^{13}C magnetic resonance spectra were recorded on a Bruker WM-250 spectrometer (68.9 MHz) and are reported in parts per million from tetramethylsilane on the δ scale. Electron impact (EI/MS) and chemical ionization (CI/MS) mass spectra were recorded on a Finnigan 4000 with an INCOS 4021 data system. High-resolution mass spectra were performed by the MSU Department of Biochemistry, Mass Spectroscopy Facility, East Lansing, MI. Elemental analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI.

All chromatography was performed by the flash technique according to the procedure of Still et al.[25] using the silica gel mentioned and eluted with the solvents mentioned. The column outer diameter (o.d.) is listed in millimeters.

Preparation of 2-(3-Furyl)-1-bromoethane (12). A solution of 2-(3-furyl)ethanol[10b] (3.35 g, 30 mmol) in pyridine (25 mL) was cooled to 0 °C (ice–water) and *p*-toluenesulfonyl chloride (6.29 g, 33 mmol) was added all in one portion. The resulting yellow mixture was stirred at 0 °C for 4 h. The suspension was cast into ice–concentrated HCl (50 g–50 mL) and ether (250 mL). The organic phase was separated, washed with 1 N aqueous HCl (200 mL), water (200 mL), and brine (200 mL), and dried ($MgSO_4$). The solvent was removed in vacuo to provide a viscous yellow liquid which was immediately taken up in dry ($CaCl_2$) acetone (150 mL), and LiBr (3.5 g, 40 mmol) was added. The mixture was heated under reflux for 12 h; after cooling to room temperature, the solvent was removed in vacuo and the residue was dissolved in water (200 mL) and ether (250 mL). The organic phase was washed with saturated aqueous sodium bicarbonate (200 mL) and brine (200 mL) and dried ($MgSO_4$) to provide 4.64 g, 88%, of a light red liquid which was used without further purification: ^1H NMR (60 MHz) δ 7.24 (m, 2 H), 6.21 (d, J = 1.7 Hz, 1 H), 3.42 (t, J = 5.1 Hz, 2 H), 2.93 (t, J = 5.1 Hz, 2 H); EI/MS (70 eV), m/e (relative intensity) 176 (22.9), 174 (25.1), 95 (49.7), 81 (base); IR (neat) 2995, 2980, 1505, 1435, 1385, 1280, 1170, 1075, 1030, 880, 790 cm^{-1}.

Preparation of 3-(3-Furyl)-1-bromopropane (13). To a solution of triphenylphosphine (7.41 g, 30 mmol) in ether (50 mL) cooled to 0 °C in an ice bath was added carbon tetrabromide (10.05 g, 30 mmol)[26] all in one portion, and the resulting suspension stirred at 0 °C for 30 min. A solution of 3-(3-furyl)propan-1-ol[10c] (1.89 g, 15 mmol) in ether (10 mL) was added all in one portion, and the mixture was heated under reflux for 4 h. The resulting suspension was cooled to room temperature, cast into hexane (150 mL), and cooled (0 °C) for 30 min. The mixture was filtered through Celite, and the solvent was removed in vacuo to provide a yellow liquid. The product was purified by chromatography on a column of silica gel (60–230 mesh, 50 g, 40 mm, o.d., petroleum ether, 25-mL fractions). Fractions 4–9 provided 2.04 g,

(19) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1978**, *100*, 2183.
(20) Sharpless, K. B.; Lauer, R. F.; Teranishi, A. Y. *J. Am. Chem. Soc.* **1973**, *95*, 6137. Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.
(21) Conia, J. M.; Limasset, J. C. *Bull. Soc. Chim. Fr.* **1967**, *6*, 1936.
(22) (a) Kaszonyi, A.; Vojtko, J.; Hrusovsky, M. *Collect. Czech. Chem. Commun.* **1982**, *47*, 2128. (b) Andrieux, J.; Barton, D. H. R.; Patin, H. *J. Chem. Soc., Perkin Trans. 1* **1977**, 359. (c) Hallman, P. S.; McGarvey, B. R.; Wilkinson, G. *J. Chem. Soc. A* **1968**, 3143.
(23) We thank Prof. P. J. Scheuer for providing spectra of authentic **43**.
(24) Watson, S. L.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.
(25) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(26) Hooz, J.; Gilani, S. S. H. *Can. J. Chem.* **1968**, *46*, 86.

72%, of the bromide **13** as a clear, colorless, sweet-smelling liquid: ^{1}H NMR (60 MHz) δ 7.18 (t, J = 1.7 Hz, 1 H), 7.07 (m, 1 H), 6.17 (m, 1 H), 3.36 (t, J = 6.2 Hz, 2 H), 2.68 (t, J = 6.6 Hz, 2 H), 2.08 (m, 2 H); EI/MS (70 eV), m/e (relative intensity) 190 (21.9), 188 (23.9), 109 (5.1), 95 (4.5), 82 (base); IR (neat) 2990, 2890, 1500, 1430, 1380, 1280, 1170, 1030, 880, 780 cm^{-1}.

Preparation of 2-Methylene-7-oxabicyclo[4.1.0]heptane (14). To a solution of methyltriphenylphosphonium bromide (35.7 g, 0.1 mol) in anhydrous THF (150 mL), cooled to −23 °C (dry ice–CCl_4), was added diisopropylamine (10.1 g, 0.1 mol) followed immediately by the addition n-butyllithium over a period of 15 min. The resulting red solution was stirred at −22 °C for 1 h and then warmed to 0 °C for 1 h. A solution of 7-oxabicyclo[4.1.0]-heptan-2-one[27] (7.8 g, 0.07 mol) in THF (50 mL) was added to the red solution over a period of 5 min, and the resulting suspension was stirred at 0 °C for 1 h and then at room temperature for 2 h. The suspension was cast into hexane (500 mL) and cooled to 0 °C for 3 h. The Ph_3PO was removed by filtration through Celite and the hexane was then distilled away. The residue was distilled under reduced pressure to provide 5.4 g, 70%, of **14** as a clear, colorless oil: $bp_{29\,mm}$ 62–63 °C; ^{1}H NMR (250 MHz) δ 5.23 (d, J = 1.4 Hz, 1 H), 5.10 (m, 1 H), 3.42 (d, J = 3.9 Hz, 1 H), 3.38 (m, 1 H), 2.26 (m, 1 H), 2.02 (m, 2 H), 1.83 (m, 1 H), 1.57 (m, 1 H), 1.42 (m, 1 H); EI/MS (70 eV), m/e (relative intensity) 110 (M^+, 12.1), 95 (17), 81 (25.4), 67 (31), 55 (55), 40 (base); IR (neat) 3050, 2900, 2895, 1645, 1440, 1400, 940, 910, 835, 755 cm^{-1}; MS M^+ calcd 110.073160, obsd 110.07323.

1-Methyl-2-methylene-7-oxabicyclo[4.1.0]heptane (45). According to the above procedure for the preparation of vinyl epoxides 1-methyl-7-oxabicyclo[4.1.0]hepan-2-one[27] (9.0 g, 70 mmol) provided 4.6 g, 53%, of **45**: $bp_{25\,mm}$ 65–70 °C; ^{1}H NMR (60 MHz) δ 5.19 (d, J = 1.3 Hz, 1 H), 5.07 (m, 1 H), 3.11 (t, J =2.1 Hz, 1 H), 1.92 (m, 6 H), 1.42 (s, 3 H); EI/MS (70 eV), m/e (relative intensity) 124 (M^+, 1.5), 97 (13.7), 81 (30.6), 67 (19.7), 57 (22.1), 43 (base); IR (neat) 3070, 2980, 2790, 1650, 1440, 940, 910, 835, 760 cm^{-1}.

General Procedure for the Preparation of Allylic Alcohols. 3-[2-(3-Furyl)ethyl]cyclohex-2-en-1-ol (15). To magnesium turnings (0.36 g, 15 mmol) covered by THF (15 mL) was added (3-furyl)chloromethane[10a] (1.74 g, 15 mmol), and the mixture was stirred at room temperature until all the magnesium had been consumed (about 2 h). The resulting golden solution was cooled to −78 °C (dry ice–isopropyl alcohol) and copper(I) cyanide (1.34 g, 15 mmol) was added all in one portion. The mixture became a yellow-green suspension which was stirred at −78 °C for 30 min. To this suspension was added a solution of vinyl epoxide **14** (1.20 g, 10 mmol) in THF (10 mL) over 5 min, and the resulting yellow suspension was allowed to slowly warm to room temperature over 4 h. The mixture was cast into saturated aqueous NH_4Cl (100 mL) and ether (150 mL). The organic phase was separated, washed with 1 N HCl (100 mL) and saturated aqueous $NaHCO_3$ (100 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified by chromatography on a column of silica gel (230–400 mesh, 50 g, 40 mm o.d., 2:5 ether–petroleum ether, 25-mL fractions). Fractions 9–15 provided 1.57 g, 82.3%, of the product as a viscous, colorless oil: ^{1}H NMR (250 MHz) δ 7.34 (dd, J = 1.6, 1.4 Hz, 1 H), 7.21 (m, 1 H), 6.26 (br s, 1 H), 5.52 (t, J = 1.5 Hz, 1 H), 4.19 (br s, 1 H), 2.55 (dd, J = 7.3, 8.3 Hz, 2 H), 2.22 (dd, J = 7.3, 8.3 Hz, 2 H), 1.95 (m, 2 H), 1.5–1.7 (m, 4 H); EI/MS (70 eV), m/e (relative intensity) 192 (M^+, 10.4), 174 (33.4), 110 (62.1), 97 (45), 91 (19), 81 (base); IR (neat) 3400, 2970, 2900, 1675, 1510, 1460, 1170, 1080, 1035, 975, 885, 790, 740 cm^{-1}.

3-[3-(3-Furyl)propyl]cyclohex-2-en-1-ol (16). According to the general procedure for the preparation of allylic alcohols, the Grignard reagent derived from 2-(3-furyl)-1-bromoethane (2.6 g, 15 mmol) was reacted (CuCN) with vinyl epoxide **14** (1.1 g, 10 mmol) to provide 1.19 g, 58%, of **16** as a colorless oil: ^{1}H NMR (250 MHz) δ 7.22 (dd, J = 1.7, 1.4 Hz, 1 H), 7.06 (m, 1 H), 6.18 (m, 1 H), 5.36 (br s, 1 H), 4.20 (br, 1 H), 4.09 (m, 1 H), 2.41 (t, J = 6.8 Hz, 2 H), 1.42 (m, 10 H); EI/MS (70 eV), m/e (relative intensity) 206 (M^+, 6.6), 123 (45.1), 110 (14.2), 97 (base); IR (neat) 3400 (br), 3050, 2970, 2900, 1675, 1500, 1460, 1170, 1055, 975, 850, 790 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.72; H, 8.73. Found: C, 75.56; H, 8.62.

3-[4-(3-Furyl)butyl]cyclohex-2-en-1-ol (17). According to the general procedure for the preparation of allylic alcohols, the Grignard reagent derived from 3-(3-furyl)-1-bromopropane (2.8 g, 15 mmol) was reacted (CuCN) with vinyl epoxide **14** (1.10 g, 10 mmol) to provide 1.36 g, 62%, of **17** as a colorless liquid: ^{1}H NMR (250 MHz) δ 7.38 (dd, J = 1.7, 1.4 Hz, 1 H), 7.22 (m, 1 H), 6.25 (m, 1 H), 5.49 (d, J = 1.4 Hz, 1 H), 4.18 (m, 1 H), 2.23 (t, J = 6.3 Hz, 2 H), 2.1–1.35 (m, 12 H); EI/MS (70 eV), me (relative intensity) 220 (M^+, 6.33), 2.18 (22.2), 202 (29.3), 136 (85), 123 (55), 110 (44), 97 (48), 81 (base); IR (neat) 3500 (br), 3010, 2980, 2900, 1670, 1500, 1430, 1170, 975, 850, 780 cm^{-1}.

General Procedure for the Preparation of 2-En-1-ones and 2-En-1-als. 3-[2-(3-Furyl)ethyl]cyclohex-2-en-1-one (18). To a solution of allylic alcohol **15** (1.92 g, 10 mmol) in CH_2Cl_2 (10 mL) was added Na_2CO_3 (0.1 g, 1 mmol), and the mixture was cooled in an ice–water bath. Pyridinium chlorochromate[11] (3.23 g, 15 mmol) was added in small portions over 10 min. The resulting red-brown suspension was stirred at 0 °C for 30 min and cast into 1 N HCl (50 mL) and ether (100 mL). The organic phase was separated and washed with 1 N HCl (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and water (50 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified by chromatography on a column of silica gel (230–400 mesh, 55 g, 40 mm o.d., 1:1 ether–petroleum ether, 25-mL fractions). Fractions 8–11 provided 1.65 g, 87%, of **18** as a colorless, sweet-smelling oil: ^{1}H NMR (250 MHz) δ 7.37 (dd, J = 1.7, 1.4 Hz, 1 H), 7.21 (br s, 1 H), 6.24 (br s, 1 H), 5.88 (s, 1 H), 2.63 (t, J = 6.3 Hz, 2 H), 2.43 (t, J = 6.4 Hz, 2 H), 2.28 (m, 4 H), 2.01 (m, 2 H); EI/MS (70 eV), m/e (relative intensity) 190 (M^+, 19.6), 172 (15.1), 134 (12), 81 (base); IR (neat) 2990, 2790, 1680 (s), 1500, 1230, 1180, 1040, 880, 800 cm^{-1}.

3-[3-(3-Furyl)propyl]cyclohex-2-en-1-one (19). According to the general procedure for the preparation of 2-en-1-ones, allylic alcohol **16** (2.06 g, 10 mmol) was treated with PCC (3.23 g, 15 mmol) to provide 1.7 g, 83%, of **19** as a light yellow oil: ^{1}H NMR (250 MHz) δ 7.28 (dd, J = 1.7, 1.5 Hz, 1 H), 7.18 (m, 1 H), 6.19 (br s, 1 H), 5.76 (s, 1 H), 2.58 (t, J = 6.8 Hz, 2 H), 2.36 (m, 4 H), 2.28 (m, 2 H), 1.98 (m, 4 H); EI/MS (70 eV), m/e (relative intensity) 204 (M^+, 22.8), 188 (66), 147 (73), 123 (20.2), 110 (32.8), 94 (65.7), 82 (base); IR (neat) 2980, 2790, 1685 (br), 1500, 1245, 1170, 1030, 880, 800 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.47; H, 7.84. Found: C, 76.44; H, 7.81.

3-[4-(3-Furyl)butyl]cyclohex-2-en-1-one (20). According to the general procedure for the preparation of 2-en-1-ones, allylic alcohol **17** (2.20 g, 10 mmol) was treated with PCC (3.23 g, 15 mmol) to provide 1.83 g, 85%, of **20** as a yellow oil: ^{1}H NMR (250 MHz) δ 7.38 (dd, J = 1.5, 1.5 Hz, 1 H), 7.20 (m, 1 H), 6.23 (br s, 1 H), 5.83 (s, 1 H), 2.46 (t, J = 6.4 Hz, 2 H), 2.38 (t, J = 7.2 Hz, 2 H), 2.21 (m, 2 H), 1.98 (m, 4 H), 1.68 (m, 4 H); EI/MS (70 eV), m/e (relative intensity) 218 (M^+, 37), 175 (7.17), 126 (17.8), 94 (28.7), 82 (base); IR (neat) 2980, 2795, 1680 (br), 1630, 1260, 1195, 1030, 875, 880 cm^{-1}.

6-[2-(3-Furyl)ethyl]cyclohex-2-en-1-one (23). To magnesium metal (0.24 g, 10 mmol) covered by THF (10 mL) was added 2-(3-furyl)-1-bromoethane (**12**) (1.75 g, 10 mmol), and the mixture was stirred at room temperature until all the magnesium had been consumed (about $2^1/_2$ h). The resulting golden yellow solution was cooled to −78 °C (dry ice–isopropyl alcohol) and copper(I) cyanide (0.89 g, 10 mmol) was added in one portion. The resulting green suspension was stirred at −78 °C for 30 min and a solution of **21**[7f] (1.47 g, 8 mmol) in THF (5 mL) was added over a period of 5 min. The resulting yellow-brown suspension was stirred at −78 °C for 2 h. The mixture was cast into saturated aqueous NH_4Cl (50 mL) and ether (75 mL). The organic phase was separated, washed with 1 N HCl (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified by chromatography on a column of silica gel (230–400 mesh, 50 g, 40 mm o.d., 1:1 ether/hexane). Fractions 7–9 provided 1.14 g, 75%, of **23** as a light yellow liquid: ^{1}H NMR (250 MHz) δ 7.37 (dd, J = 1.6, 1.4 Hz, 1 H), 6.25 (m, 1 H), 6.92 (dt, J = 8.1, 3.5 Hz, 1 H), 6.32 (br s, 1 H), 6.00 (dt, J = 8.1, 2.1 Hz, 1 H), 2.49 (m, 2 H), 2.37 (m, 2 H), 1.79 (m, 2 H), 1.58 (m, 2 H); EI/MS (70 eV), m/e (relative intensity) 190 (M^+, 7.37), 167 (2.56), 96 (base),

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81 (24.6); IR (neat) 2940, 2880, 1685, 1500, 1450, 1390, 1030, 880, 800 cm^{-1}.

6-[3-(3-Furyl)propyl]cyclohex-2-en-1-one (24). To magnesium metal (0.12 g, 5 mmol) covered by THF (3 mL) was added 3-(3-furyl)-1-bromopropane[10c] (0.94 g, 5 mmol), and the mixture was stirred at room temperature until all the magnesium had been consumed (about 2 h). The resulting golden yellow solution was cooled to −78 °C (dry ice–isopropyl alcohol), and copper(I) cyanide (0.45 g, 5 mmol) was added in one portion. The resulting green suspension was stirred at −78 °C for 30 min, a solution of **21** (0.73 g, 4 mmol) in THF (3 mL) was added over a period of 5 min, and the resulting brown suspension was stirred at −78 °C for 2 h. The mixture was cast into saturated aqueous NH_4Cl (25 mL) and ether (50 mL). The organic phase was separated, washed with 1 N HCl (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified by chromatography on a column of silica gel (230–400 mesh, 50 g, 40 mm o.d., 1:1 ether/hexane). Fractions 10–14 provided 0.72 g, 72%, of **24** as a clear, colorless liquid: ^1H NMR (250 MHz) δ 7.18 (dd, J = 1.6, 1.4 Hz, 1 H), 6.99 (m, 1 H), 6.68 (dt, J = 9.8, 3.92 Hz, 1 H), 6.03 (br s, 1 H), 5.73 (dt, J = 9.8, 2.4 Hz, 1 H), 2.22 (t, J = 8.2 Hz, 2 H), 2.14 (m, 3 H), 1.90 (m, 2 H), 1.75–1.2 (m, 4 H); EI/MS (70 eV), m/e (relative intensity) 204 (M^+, 6.5), 159 (11.7), 122 (17.7), 108 (base), 96 (54), 81 (48); IR (neat) 2950, 2880, 1685, 1500, 1445, 1380, 1140, 1030, 880, 800 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.47; H, 7.84. Found: C, 76.45; H, 7.84.

1-Methyl-6-[2-(3-furyl)ethyl]cyclohex-2-en-1-ol (25). To a solution of **23** (0.38 g, 2 mmol) in THF (3 mL) cooled to −78 °C (dry ice–isopropyl alcohol) was added methyllithium (3.07 mL, 1.3 M, 4 mmol) in one portion, and the mixture was stirred at −78 °C for 30 min. The resulting solution was cast into saturated aqeous NH_4Cl (20 mL) and ether (20 mL). The organic phase was separated, washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified by chromatography on a column of silica gel (230–400 mesh, 30 g, 30 mm o.d., 1:4 ether/hexane, 10-mL fractions). Fractions 14–18 provided 0.37 g, 90%, of **25** as a clear, colorless liquid which is a 3:2 mixture of isomers by capillary GLC: ^1H NMR (250 MHz) δ 7.36 (dd, J = 1.6, 1.4 Hz, 1 H), 7.22 (m, 1 H), 6.28 (m, 1 H), 5.72–5.53 (m, 2 H), 2.47 (m, 2 H), 2.06 (m, 2 H), 1.76 (m, 2 H), 1.29 (s, 1.2 H), 1.18 (s, 1.8 H); EI/MS (70 eV), m/e (relative intensity) 206 (M^+, 4.2), 188 (3.4), 108 (10.3), 94 (20.7), 82 (base); IR (neat) 3500 (br), 3010, 2980, 2900, 1665, 1500, 1430, 1165, 975, 780 cm^{-1}.

1-Methyl-6-[3-(3-Furyl)propyl]cyclohex-2-en-1-ol (26). To a solution of enone **24** (0.15 g, 0.75 mmol) in THF (2 mL) cooled to −78 °C (dry ice–isopropyl alcohol) was added methyllithium (2.85 mL, 1.3 M, 3.7 mmol) in one portion, and the mixture was stirred at −78 °C for 30 min. The resulting yellow solution was cast into saturated aqueous NH_4Cl (10 mL) and ether (10 mL). The organic phase was separated, washed with brine (10 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified on a column of silica gel (230–400 mesh, 45 g, 40 mm o.d., 1:1 ether/hexane, 25-mL fractions). Fractions 7–10 provided 146 mg, 90%, of **26** as a 3:2 mixture of isomers: ^1H NMR (250 MHz) δ 7.35 (dd, J = 1.6, 1.4 Hz, 1 H), 7.21 (m, 1 H), 6.29 (br s, 1 H), 5.79–5.50 (m, 2 H), 2.47 (m, 2 H), 2.03 (m, 2 H), 1.81–1.38 (m, 4 H), 1.29 (s, 1.8 H), 1.17 (s, 1.2 H); EI/MS (70 eV), m/e (relative intensity) 220 (M^+, 3.16), 202 (2.75), 167 (39.2), 157 (22.9), 120 (11.2), 108 (14.8), 93 (39.0), 84 (base); IR (neat) 3500 (br), 3010, 2990, 2890, 1670, 1500, 1430, 1170, 975, 880, 780 cm^{-1}.

1-[(Methylthio)methyl]cyclohex-2-en-1-ol. To n-butyllithium (28.6 mL, 1.75 M in hexane, 50 mmol) chilled in an ice–water bath was added TMEDA (5.8 g, 50 mmol). The mixture was warmed to room temperature and allowed to stir for 30 min. The mixture was cooled to 0 °C and dimethyl sulfide[13] (3 g, 48.4 mmol) was added. The resulting pale yellow solution was stirred for 3.5 h at room temperature and cooled to −78 °C (dry ice–isopropyl alcohol), and a solution of 2-cyclohexen-1-one (4.85 g, 50 mmol) in THF (30 mL) was added over 5 min. The mixture was warmed to room temperature and cast into ether (150 mL) and saturated aqueous NH_4Cl (150 mL). The organic phase was separated, washed with water (150 mL), dried (Na_2SO_4), and concentrated in vacuo to provide a viscous yellow liquid. The crude product was purified by distillation, $bp_{0.007\ mm}$ 65–68 °C, to provide 6.7 g, 88%, of 1-[(methylthio)methyl]cyclohex-2-en-1-ol as a colorless, viscous liquid: ^1H NMR (250 MHz) δ 5.85 (ddd, J = 10, 4, 3.15 Hz, 1 H), 5.66 (dddd, J = 9.5, 2.4, 2.0, 0.77 Hz, 1 H), 2.75 (d, J = 13.4 Hz, 1 H), 2.67 (d, J = 13.4 Hz, 1 H), 2.50 (br s, 1 H), 2.20 (s, 3 H), 1.95–2.09 (m, 2 H), 1.57–1.85 (m, 4 H); EI/MS (70 eV), m/e (relative intensity) 158 (M^+, 6.65), 141 (32.3), 97 (base); IR (neat) 3470 (br), 3050, 2950, 2855, 1645, 1435, 1220, 1185, 1055, 1000, 965 (br), 740 cm^{-1}.

1-[(Dimethylsulfonio)methyl]cyclohex-2-en-1-ol Iodide. To a solution of allylic alcohol (3.16 g, 20 mmol) in dry acetone (10 mL) was added methyl iodide (5.67 g, 40 mmol). The mixture was allowed to stir at room temperature overnight and then concentrated in vacuo to provide 6.0 g, 100%, of the sulfonium salt as a white solid, mp 155 °C dec, which was used without further purification.

8-Oxaspiro[5.2]oct-2-ene (22). To a suspension of the sulfonium salt (6.0 g, 20 mmol) in 250 mL of THF was added 2.9 g (25.9 mmol) of freshly sublimed KO-t-Bu. The mixture was allowed to stir at room temperature for 4 h, quenched with saturated aqueous $NaHCO_3$ (50 mL), and cast into ether (250 mL). The aqueous phase was separate and extracted with ether (4 × 100 mL), and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ (0.5 L) and brine (0.5 L) and dried ($MgSO_4$, K_2CO_3). The solvent was removed by distillation at atmospheric pressure, and the residue was purified by distillation, $bp_{37\ mm}$ 70–72 °C, to provide 2.0 g, 91%, of **22** as a colorless liquid: ^1H NMR (250 MHz) δ 6.12 (ddd, J = 10.07, 3.97, 3.66 Hz, 1 H), 5.25 (br d, J = 10.07 Hz, 1 H), 2.84 (d, J = 4.88 Hz, 1 H), 2.79 (d, J = 4.88 Hz, 1 H), 1.5–2.3 (m, 6 H); EI/MS (70 eV), m/e (relative intensity) 110 (M^+, 83), 93 (51), 79 (base); IR (neat) 3080, 3020, 1460, 950, 810, 760 cm^{-1}; MS, M^+ calcd for $C_7H_{10}O$ 110.073160, M^+ found 110.07320.

1-(Hydroxymethyl)-3-(3-furylmethyl)-1-cyclohexene (27). According to the general procedure for the preparation of allylic alcohols, the Grignard reagent derived from (3-furyl)chloromethane[10a] (1.7 g, 15 mmol) was reacted (CuCN) with vinyl epoxide **22** to provide 1.5 g, 78%, of **27** as a clear, colorless liquid: ^1H NMR (250 MHz) δ 7.35 (dd, J = 1.7, 1.4 Hz, 1 H), 7.22 (dd, J = 1.7, 0.77 Hz, 1 H), 6.27 (m, 1 H), 5.58 (br s, 1 H), 3.98 (br s, 2 H), 2.38 (m, 2 H), 2.30 (br s, 1 H), 1.98 (br s, 2 H), 1.77 (m, 1 H), 1.58 (m, 1 H), 1.52 (m, 1 H), 1.20 (m, 1 H); EI/MS (70 eV), m/e (relative intensity) 192 (M^+, 1.44), 174 (6.8), 161 (1.72), 128 (1.60), 111 (69), 93 (base); IR (neat) 3400 (br), 2965, 2895, 1515, 1460, 1175, 1080, 1040, 890, 800, 785, 745 cm^{-1}.

1-(Hydroxymethyl)-3-[2-(3-furyl)ethyl]-1-cyclohexene (28). According to the general procedure for the preparation of allylic alcohols, the Grignard reagent derived from 2-(3-furyl)-1-bromoethane[10b] (2.6 g, 15 mmol) was reacted (CuCN) with vinyl epoxide **22** to provide 1.15 g, 56%, of **28** as a colorless oil: ^1H NMR (250 MHz) δ 7.35 (dd, J = 1.7, 1.4 Hz, 1 H), 7.24 (m, 1 H), 6.25 (m, 1 H), 5.43 (br s, 1 H), 3.83 (br s, 2 H), 2.41 (t, J = 6.3 Hz, 2 H), 2.33 (m, 2 H), 1.98–1.23 (m, 7 H); EI/MS (70 eV), m/e (relative intensity) 206 (1.34), 175 (36), 188 (19.0), 124 (10), 95 (16), 82 (base); IR (neat) 3400 (br), 2965, 2895, 1500, 1460, 1175, 1080, 1040, 890, 800, 780 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.72; H, 8.73. Found: C, 75.66; H, 8.74.

1-(Hydroxymethyl)-3-[3-(3-furyl)propyl]-1-cyclohexene (29). According to the general procedure for the preparation of allylic alcohols, the Grignard reagent derived from 3-(3-furyl)-1-bromopropane[10c] (2.8 g, 15 mmol) was reacted (CuCN) with vinyl epoxide **22** (1.10 g, 10 mmol) to provide 1.27 g, 58%, of **29** as a light yellow oil: ^1H NMR (250 MHz) δ 7.38 (dd, J = 1.7, 1.6 Hz, 1 H), 7.21 (m, 1 H), 6.29 (br s, 1 H), 5.58 (br s, 1 H), 3.98 (s, 2 H), 2.40 (t, J = 6.1 Hz, 2 H), 2.18–2.00 (m, 4 H), 1.8–1.3 (m, 7 H); EI/MS (70 eV), m/e (relative intensity) 220 (M^+, 10.8), 202 (27.5), 189 (10.8), 120 (46.1), 111 (23.7), 95 (70.1), 81 (base); IR (neat) 3500 (br), 2980, 2895, 1500, 1450, 1190, 1060, 1045, 800, 750 cm^{-1}.

3-(3-Furylmethyl)cyclohex-1-ene-1-carboxaldehyde (30). According to the general procedure for the preparation of 2-en-1-als, allylic alcohol **27** (1.92 g, 10 mmol) was oxidized with PCC (3.23 g, 15 mmol) to provide 1.5 g, 78.9% of **30** as a clear, colorless liquid: ^1H NMR (250 MHz) δ 9.41 (s, 1 H), 7.31 (dd, J = 1.6, 1.4 Hz, 1 H), 7.22 (m, 1 H), 6.64 (br s, 1 H), 2.52 (m, 2 H), 1.8–2.18 (8 H); EI/MS (70 eV), m/e (relative intensity) 190 (M^+, 20), 172

(1.12), 161 (2.57), 108 (9), 81 (base); IR (neat) 2980, 2880, 2710, 1685, 1630, 1450, 1390, 1180, 1020, 880, 800 cm^{-1}.

3-[2-(3-Furyl)ethyl]cyclohexene-1-carboxaldehyde (31). According to the general procedure for the preparation of 2-en-1-als, allylic alcohol **28** (2.06 g, 10 mmol) was oxidized with PCC (3.23 g, 15 mmol) to provide 1.7 g, 83%, of **31** as a pale yellow oil: ^1H NMR (250 MHz) δ 9.23 (s, 1 H), 7.21 (dd, J = 1.6, 1.4 Hz, 1 H), 7.10 (m, 1 H), 6.52 (br s, 1 H), 6.18 (m, 1 H), 2.54 (t, J = 5.8 Hz, 2 H), 2.1 (t, J = 5.7 Hz, 2 H), 1.8–1.6 (m, 7 H); EI/MS (70 eV), m/e (relative intensity) 204 (M^+, 25.8), 186 (12.7), 173 (26.3), 123 (23.9), 95 (13.2), 82 (base); IR (neat) 3140 (w), 2980, 2880, 1690, 1630, 1500, 1450, 1190, 1070, 1030, 880, 780 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.47; H, 7.84. Found: C, 76.34; H, 7.88.

3-[3-(3-Furyl)propyl]-1-cyclohexene-1-carboxaldehyde (32). According to the general procedure for the preparation of 2-en-1-als, allylic alcohol **29** (2.20 g, 10 mmol) was oxidized with PCC (3.23 g, 15 mmol) to provide 1.7 g, 78%, of **32** as a yellow oil: ^1H NMR (250 MHz) δ 9.26 (s, 1 H), 7.34 (dd, J = 1.6, 1.5 Hz, 1 H), 7.21 (m, 1 H), 6.23 (br s, 1 H), 6.31 (m, 1 H), 2.43 (t, J = 7.3 Hz, 2 H), 2.38 (m, 2 H), 2.08 (m, 2 H), 1.98–1.16 (m, 7 H); EI/MS (70 eV), m/e (relative intensity) 218 (M^+, 11.2), 189 (5.8), 147 (6.9), 136 (base), 107 (12.6), 95 (19.2), 81 (33.4); IR (neat) 2980, 2880, 2720, 1690, 1630, 1500, 1450, 1380, 1185, 1020, 880, 790 cm^{-1}.

1-(1-Hydroxyethyl)-3-[2-(3-furyl)ethyl]-1-cyclohexene (33). To a solution of **31** (0.102 g, 0.5 mmol) in THF (3 mL) cooled to −78 °C (dry ice–isopropyl alcohol) was added a solution of methyllithium in hexane (1.15 mL, 1.3 M, 1.5 mmol) in one portion, and the mixture was stirred at −78 °C for 20 min. The mixture was cast into saturated aqueous NH_4Cl (10 mL) and ether (10 mL). The organic layer was separated, washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified by chromatography on a column of silica gel (230–400 mesh, 40 g, 40 mm o.d., 1:4 Et_2O/hexane, 25-mL fractions). Fractions 5–8 provided 99 mg, 90%, of **33** as a clear, colorless liquid: ^1H NMR (250 MHz) δ 7.20 (dd, J = 1.6, 1.4 Hz, 1 H), 7.10 (m, 1 H), 6.13 (m, 1 H), 5.43 (br s, 1 H), 3.98 (q, J = 7.3 Hz, 1 H), 2.42 (t, J = 6.3 Hz, 2 H), 2.0–1.3 (m, 5 H), 1.14 (d, J = 7.3 Hz, 3 H); EI/MS (70 eV), m/e (relative intensity) 220 (M^+, 0.5), 202 (19.9), 138 (5.5), 123 (6.2), 95 (49.1), 82 (base); IR (neat) 3400 (br), 2995, 2890, 1500, 1460, 1185, 1060, 1045, 800, 760 cm^{-1}.

1-(1-Hydroxyethyl)-3-[3-(3-furyl)propyl]-1-cyclohexene (34). To a solution of **32** (0.218 g, 1 mmol) in THF (5 mL) cooled to −78 °C (dry ice–isopropyl alcohol) was added a solution of methyllithium in hexane (2.3 mL, 1.3 M, 3 mmol) in one portion, and the mixture was stirred at −78 °C for 30 min. The mixture was cast into saturated aqueous NH_4Cl (25 mL) and ether (25 mL). The organic phase was separated, washed with water (25 mL) and brine (25 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a light yellow liquid. The crude product was purified by chromatography on a column of silica gel (230–400 mesh, 75 g, 50 mm o.d., 1:4 Et_2O/hexane, 25-mL fractions). Fractions 7–11 provided 0.20 g, 85%, of **34** as a clear, colorless liquid: ^1H NMR (250 MHz) δ 7.34 (dd, J = 1.6, 1.4 Hz, 1 H), 7.21 (m, 1 H), 6.24 (m, 1 H), 5.54 (br s, 1 H), 4.15 (q, J = 7.2 Hz, 1 H), 2.40 (t, J = 6.3 Hz, 2 H), 2.0 (m, 4 H), 1.8–1.4 (m, 8 H), 1.24 (d, J = 7.2 Hz, 3 H); EI/MS (70 eV), m/e (relative intensity) 234 (M^+, 4.2), 216 (23.9), 190 (5.1), 173 (7.9), 147 (13.5), 134 (90.4), 121 (14.9), 107 (50.5), 95 (70.9), 81 (base). IR (neat): 3400 (br), 2990, 2890, 1670, 1500, 1420, 1380, 1185, 1020, 880 cm^{-1}.

General Procedure for the Cyclization of Allylic Alcohols. Cyclization of Alcohol 16. To a solution of allylic alcohol **16** (0.1 g, 0.53 mmol) in cyclohexane (2 mL) was added anhydrous formic acid (0.5 mL), and the two-phase mixture was stirred rapidly at room temperature for 10 min. The resulting purple (lower layer) and colorless (upper layer) mixture was cast into water (10 mL) and ether (10 mL). The organic phase was separated, washed with saturated aqueous $NaHCO_3$ (10 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a pale yellow liquid. The crude product was purified by chromatography on a column of silica gel (230–400 mesh, 30 g, 30 mm o.d., 1:4 ether/hexane, 10-mL fractions). Fractions 5–7 provided 65 mg, 72%, of olefin **36** as a clear, colorless oil: ^1H NMR (250 MHz) δ 7.23 (d, J = 1.2 Hz, 1 H), 6.17 (d, J = 1.2 Hz, 1 H), 5.82 (dt, J = 10.4, 4.16 Hz, 1 H), 5.53 (br d, J = 10.4 Hz, 1 H), 2.42 (t, J = 5.2 Hz, 2 H), 2.08 (m, 2 H), 1.96 (m, 2 H), 1.8–1.6 (m, 6 H); EI/MS (70 eV), m/e (relative intensity) 188 (M^+, 36.2), 160 (base), 145 (20.9), 131 (33.7), 117 (22.3), 105 (12.4), 91 (31.6), 77 (22.4); IR (neat) 3040, 2980, 2890, 1505, 1450, 1170, 1045, 895, 730 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O$: C, 82.97; H, 8.51. Found: C, 82.90; H, 8.52.

Cyclization of Alcohol 17. According to the general procedure for the cyclization of allylic alcohols, **17** (0.1 g, 0.45 mmol) in 2 mL of cyclohexane was reacted with formic acid (0.5 mL) for 15 min to provide 53 mg, 58% yield, of olefin **37** as a clear, colorless liquid: ^1H NMR (250 MHz) δ 7.18 (d, J = 1.2 Hz, 1 H), 6.16 (d, J = 1.2 Hz, 1 H), 5.83 (dt, J = 9.89, 4.03 Hz, 1 H), 5.66 (br d, J = 9.89 Hz, 1 H), 2.50 (m, 2 H), 2.19 (m, 2 H), 2.05 (m, 2 H), 1.87 (m, 2 H), 1.8–1.5 (m, 6 H); EI/MS (70 eV), m/e (relative intensity) 202 (M^+, 74.3), 174 (base), 159 (77.0), 145 (46.3), 131 (79.9), 115 (28.8), 91 (39.9), 78 (21.3); IR (neat) 3040, 2995, 2880, 1500, 1120, 1050, 895, 730 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O$: C, 83.16; H, 8.91. Found: C, 82.91; H, 8.92.

Cyclization of Alcohol 25. According to the general procedure for the cyclization of allylic alcohols, **25** (0.1 g, 0.48 mmol) in 2 mL of cyclohexane was reacted with formic acid (0.5 mL) for 30 min to provide 68 mg, 73%, of **38** as a light yellow oil: ^1H NMR (250 MHz) δ 7.18 (d, J = 1.2 Hz, 1 H), 6.08 (d, J = 1.2 Hz, 1 H), 5.75 (d, J = 9.80 Hz, 1 H), 5.54 (dt, J = 9.81, 3.43 Hz, 1 H), 2.33 (m, 3 H), 1.92 (m, 2 H), 1.71 (m, 4 H), 1.30 (s, 3 H); EI/MS (70 eV), m/e (relative intensity) 188 (M^+, 16.3), 173 (base), 131 (13.3), 91 (21.7), 77 (13.8); IR (neat) 3040, 2990, 2885, 1500, 1440, 1165, 1030, 890, 780 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O$: C, 82.97; H, 8.51. Found: C, 82.87; H, 8.50.

Cyclization of Alcohol 26. According to the general procedure for the cyclization of allylic alcohols, **26** (0.1 g, 0.46 mmol) in 2 mL of cyclohexane was reacted with formic acid (0.5 mL) for 15 min to provide 52 mg, 56%, of olefin **39** as a clear, colorless oil: ^1H NMR (250 MHz) δ 7.18 (d, J = 1.2 Hz, 1 H), 6.08 (d, J = 1.2 Hz, 1 H), 5.82 (dt, J = 9.44, 1.3 Hz, 1 H), 5.75 (dt, J = 9.45, 4.12 Hz, 1 H), 2.50 (m, 3 H), 2.09 (m, 2 H), 1.95–1.40 (m, 6 H), 1.32 (s, 3 H); EI/MS (70 eV), m/e (relative intensity) 202 (M^+, 16.4), 187 (base), 131 (10.6), 121 (26.3), 91 (18.7), 77 (15.3); IR (neat) 3035, 2985, 2880, 1500, 1440, 1165, 1030, 890, 780 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O$: C, 83.16; H, 8.91. Found: C, 83.00; H, 8.86.

Cyclization of Alcohol 33. According to the general procedure for cyclization of allylic alcohols, **33** (0.1 g, 0.45 mmol) in 2 mL of cyclohexane was reacted with formic acid (0.5 mL) for 20 min to provide 62 mg, 68%, of the olefin **40** as a clear, colorless oil: ^1H NMR (250 MHz) δ 7.10 (d, J = 1.2 Hz, 1 H), 6.08 (d, J = 1.2 Hz, 1 H), 5.01 (m, 1 H), 3.38 (m, 2 H), 2.49 (t, J = 6.2 Hz, 2 H), 2.04 (m, 2 H), 1.8–1.4 (m, 6 H), 1.78 (s, 1.5 H), 1.63 (s, 1.5 H); EI/MS (70 eV), m/e (relative intensity) 202 (M^+, 51.6), 187 (15.2), 173 (76.7), 162 (base); IR (neat) 3035, 2990, 2880, 1500, 1450, 1165, 1040, 890, 750 cm^{-1}; MS, M^+ calcd for $C_{14}H_{18}O$ 202.13576, M^+ found 202.13569.

Cyclization of Alcohol 34. According to the general procedure for the cyclization of allylic alcohols, **34** (0.1 g, 0.43 mmol) in 2 mL of cyclohexane was reacted with formic acid (0.5 mL) for 20 min to provide 53 mg, 61%, of **41** as a clear, colorless oil: ^1H NMR (250 MHz) δ 7.20 (d, J = 1.2 Hz, 1 H), 6.13 (d, J = 1.2 Hz, 1 H), 5.23 (m, 1 H), 3.62 (m, 2 H), 2.59 (m, 2 H), 2.40 (m, 4 H), 1.90–1.23 (m, 6 H), 1.82 (s, 1.5 H), 1.73 (s, 1.5 H); EI/MS (70 eV), m/e (relative intensity) 216 (M^+, 64.5), 187 (base), 173 (33.4), 159 (21.5), 145 (20.5), 131 (34.6), 91 (30.9), 77 (16.2); IR (neat) 3035, 2990, 2880, 1510, 1450, 1165, 1040, 890, 800 cm^{-1}; MS, M^+ calcd for $C_{15}H_{20}O$ 216.15141, M^+ found 216.15139.

Cyclization of Enone 19. To a solution of enone **19** (0.1 g, 0.49 mmol) in cyclohexane (2 mL) was added anhydrous formic acid (0.5 mL), and the mixture was stirred vigorously for 20 min. The two-phase mixture was cast into water (10 mL) and ether (10 mL). The organic phase was separated, washed with saturated aqueous $NaHCO_3$ (10 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified by chromatography on a column of silica gel (15 g, 20 mm o.d., 20% ether/hexane, 10-mL fractions). Fractions 8–11 provided 66 mg, 66%, of ketone **42** as a clear, colorless liquid: ^1H NMR (250 MHz) δ 7.26 (d, J = 1.2 Hz, 1 H), 6.15 (d, J = 1.2 Hz, 1 H), 2.40 (m, 4 H), 2.18 (m, 2 H), 1.89 (m, 4 H), 1.68 (m, 4 H); EI/MS (70 eV), m/e (relative intensity) 204 (M^+, 40.8), 161 (35.7), 147 (base), 134 (32.5), 91 (20.8); IR (neat) 3010, 2990, 2980, 1715, 1500, 1380, 1260, 1180, 1040, 880, 800 cm^{-1}; MS, M^+ calcd for $C_{13}H_{16}O_2$ 204.11502, M^+ found 204.11522.

3-[2-(3-Furyl)ethyl]-2-methylcyclohex-2-en-1-ol (46). According to the general procedure for the preparation of allylic alcohols, the Grignard derived (3-furyl)chloromethane (2.5 g, 20 mmol) was reacted (CuCN) with vinyl epoxide **45** (2.5 g, 20 mmol) to provide 2.5 g, 62%, of **46** as a clear, colorless oil: ^{1}H NMR (250 MHz) δ 7.22 (dd, J = 1.6, 1.4 Hz, 1 H), 7.18 (m, 1 H), 6.21 (m, 1 H), 3.98 (br, 1 H), 2.46 (m, 3 H), 2.05 (m, 4 H), 1.87 (m, 4 H), 1.78 (s, 3 H); EI/MS (70 eV), m/e (relative intensity) 204 (M^+, 2.15), 128 (14.7), 110 (23.8), 95 (38.6), 81 (base); IR (neat) 3400 (br), 3045, 2970, 2880, 1670, 1500, 1465, 1170, 1060, 880, 800 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.72; H, 8.73. Found: C, 75.54; H, 8.61.

3-[2-(3-Furyl)ethyl]-2-methylcyclohex-2-en-1-one. According to the general procedure for the preparation of 2-en-1-ones, allylic alcohol **46** (3.09 g, 15 mmol) was oxidized with PCC (4.85 g, 22.5 mmol) to provide 2.72 g, 89%, of the desired enone as a clear, colorless liquid: ^{1}H NMR (250 MHz) δ 7.28 (dd, J = 1.4, 1.2 Hz, 1 H), 7.16 (m, 1 H), 6.22 (m, 1 H), 2.59 (br s, 2 H), 2.36 (m, 4 H), 2.05 (m, 4 H), 1.79 (s, 3 H); EI/MS (70 eV), m/e (relative intensity) 204 (M^+, 12.9), 186 (9.32), 133 (5.91), 108 (11.5), 91 (5.02), 81 (base); IR (neat) 2995, 2875, 1685 (s), 1500, 1460, 1230, 1180, 1030, 880, 800 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.47; H, 7.84. Found: C, 76.51; H, 7.73.

2,3-Dimethyl-3-[2-(3-furyl)ethyl]cyclohexanone (47). To a slurry of copper(I) iodide (3.8 g, 20 mmol) in anhydrous ether (20 mL) cooled to 0 °C in an ice–water bath was added a solution of methyllithium in hexane (15.4 mL, 1.3 M, 20 mmol) over a period of 10 min, and the suspension was stirred at 0 °C for 20 min. The resulting yellow suspension was cooled to −78 °C in a dry ice–isopropyl alcohol bath, and boron trifluoride etherate (2.8 g, 20 mmol) was added dropwise.[19] The mixture lightened in color and was stirred at −78 °C for 20 min. A solution of enone (2.04 g, 10 mmol) in ether (15 mL) was added over a period of 10 min, and the suspension was allowed to warm to room temperature over 5 h. The mixture was cast into 1 N HCl (100 mL) and ether (100 mL). The organic phase was separated, washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified by chromatography on a column of silica gel (230–400 mesh, 50 g, 40 mm o.d., 1:1 ether/hexane, 25-mL fractions). Fractions 10–14 provided 1.54 g, 70%, of ketone **47** as a 60:40 mixture of epimers: ^{1}H NMR (250 MHz) δ 7.36 (dd, J = 1.4, 1.5 Hz, 0.6 H), 7.33 (m, 0.4 H), 7.20 (m, 0.6 H), 7.18 (m, 0.4 H), 6.28 (m, 0.6 H), 6.23 (m, 0.4 H), 2.38 (m, 3 H), 1.90 (m, 4 H), 1.86 (m, 4 H), 1.09 (s, 1.2 H), 1.00 (d, J = 6.89 Hz, 1.2 H), 0.97 (d, J = 7.6 Hz, 1.8 H), 0.80 (s, 1.8 H); EI/MS (70 eV), m/e (relative intensity) 220 (M^+, 8.36), 148 (4.70), 125 (49.0), 111 (17.2), 95 (70.2), 81 (base); IR (neat) 2995, 2980, 1720, 1500, 1380, 1260, 1175, 1030, 880 cm^{-1}; MS, M^+ calcd for $C_{14}H_{20}O_2$ 220.14632, M^+ found 220.14627.

5,6-Dimethyl-5-[2-(3-furyl)ethyl]cyclohex-2-en-1-one (48). To a solution of diisopropylamine (0.60 g, 6 mmol) in THF (6 mL) cooled to −78 °C in a dry ice–isopropyl alcohol bath was added n-butyllithium (2.4 mL, 2.5 M in hexane, 6 mmol) over 5 min, and the solution was stirred at −78 °C for 30 min. Ketone **47** (1.12, 5 mmol) in THF (5 mL) was added over 15 min, and the resulting yellow solution was stirred at −78 °C for 30 min. To the solution was added phenylselenium bromide[20] (1.4 g, 6 mmol) in THF (3 mL). The resulting yellow solution was stirred at −78 °C for 2 h and cast into saturated aqueous NH_4Cl (50 mL) and ether (50 mL). The organic phase was separated, washed with brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The yellow residue was taken up in methylene chloride (10 mL), and triethylamine (2 mL) was added followed immediately by aqueous hydrogen peroxide (6 mL, 30%). The mixture was vigorously stirred at room temperature for 30 min and cast into 1 N HCl (50 mL) and ether (50 mL). The organic phase was separated, washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo to provide a yellow liquid. The crude product was purified by chromatography on a column of silica gel (230–400 mesh, 50 g, 40 mm o.d., 1:1 ether/hexane, 25-mL fractions). Fractions 11–15 provided 0.78 g, 72%, of enone **48** as a 60:40 mixture of epimers: ^{1}H NMR (250 MHz) δ 7.38 (dd, J = 1.6, 1.4 Hz, 1 H), 7.19 (m, 1 H), 5.89 (m, 1 H), 6.25 (m, 1 H), 5.99 (br d, J = 11.4 Hz, 1 H), 2.39 (m, 3 H), 2.20 (m, 2 H), 1.62 (m, 2 H), 1.08 (m, 4.2 H), 0.95 (s, 1.8 H); EI/MS (70 eV), m/e (relative intensity) 218 (M^+, 8.39), 135 (10.4), 123 (base), 109 (10.5), 95 (30.0), 81 (49.7); IR (neat) 3010, 2900, 1680, 1500, 1460, 1180, 1060, 990, 780 cm^{-1}.

Cyclization of Enone 48. To a solution of **48** (0.5 g, 2.3 mmol) in cyclohexane (5 mL) was added anhydrous formic acid (1.5 mL), and the mixture was stirred vigorously for 15 min at room temperature. The biphasic mixture was cast into water (25 mL) and ether (25 mL). The organic phase was separated, washed with saturated aqueous $NaHCO_3$ (25 mL) and brine (25 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified on a column of silica gel (230–400 mesh, 40 g, 33 mm o.d., 1:1 ether/hexane, 25-mL fractions). Fractions 8–10 provided 0.40 g, 79%, of **49** (60:40) as a white solid: mp 58–60 °C; ^{1}H NMR (250 MHz) δ 7.08 (m, 1 H), 6.08 (m, 1 H), 3.77 (m, 1 H), 2.75 (m, 1 H), 2.59 (m, 1 H), 2.39 (m, 3 H), 2.09 (m, 2 H), 1.76 (m, 2 H), 1.17 (m, 4 H), 1.02 (s, 2 H); EI/MS (70 eV), m/e (relative intensity) 218 (M^+, 64.3), 203 (17.9), 147 (base), 131 (14.1), 109 (46.1), 91 (32.3), 77 (31.8).

$\Delta^{8,13}$-Isonakafuran 9 (50). To a suspension of methyltriphenylphosphonium iodide (1.41 g, 3.5 mmol) in benzene (5 mL) was added a solution of potassium *tert*-amylate (2.8 mL, 1.25 M, 3.5 mmol) in benzene,[21] and the mixture was stirred at room temperature until the phosphonium salt had dissolved (about 1.5 h). Ketone **49** (0.218 g, 1 mmol) in benzene (2 mL) was added, and the resulting solution was stirred at room temperature for 3 h. The mixture was cast into saturated aqueous NH_4Cl (25 mL) and pentane (25 mL). The organic phase was separated, washed with saturated aqueous $NaHCO_3$ (25 mL) and brine (25 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a yellow liquid. The crude product was purified by rapid chromatography on a column of silica gel (230–400 mesh, 8 g, 20 mm o.d., hexane, 8-mL fractions). Fractions 6–8 provided 0.173 g, 80%, of olefin **50** as a clear, colorless, sweet-smelling liquid. The material was shown by capillary GLC to be a 80:20 mixture of epimers: ^{1}H NMR (250 MHz) δ 7.10 (d, J = 1.2 Hz, 1 H), 6.01 (m, 1 H), 4.62 (t, J = 2.1 Hz, 0.8 H), 4.59 (t, J = 2.2 Hz, 1 H), 4.56 (t, J = 2.1 Hz, 0.2 H), 2.43 (m, 4 H), 2.78 (m, 2 H), 2.25 (m, 2 H), 1.06 (d, J = 6.07, 0.6 H), 1.01 (d, J = 6.09 Hz, 2.4 H), 0.98 (s, 2.4 H), 0.86 (s, 0.6 H); EI/MS (70 eV), m/e (relative intensity) 216 (M^+, 59.3), 201 (21.3), 147 (base); IR (neat) 3050, 2990, 2890, 1500, 1430, 1050, 890, 800 cm^{-1}; MS, M^+ calcd for $C_{15}H_{20}O$ 216.15141, M^+ found 216.15147.

Preparation of Nakafuran 9 (43). To a refluxing solution of olefin **50** (0.1 g, 0.46 mmol) in benzene (3 mL) was added p-toluenesulfonic acid decahydrate (2 mg), and the mixture was heated under reflux for 20 min. The mixture was cooled and cast into saturated aqueous $NaHCO_3$ (10 mL) and ether (10 mL). The organic phase was separated, dried ($MgSO_4$), and concentrated in vacuo to provide 80 mg, 80%, of a 95:5 (capillary GLC) mixture of nakafuran 9 (**43**) and $\Delta^{8,9}$-isonakafuran 9 (**51**). Compound **43** was identical in all respects (^{1}H NMR, IR, EI/MS) when compared with spectral data provided by Professor Scheuer.[18,23]

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