Intramolecular [4 + 3] Cycloadditions. Studies of Relative Asymmetric Induction†

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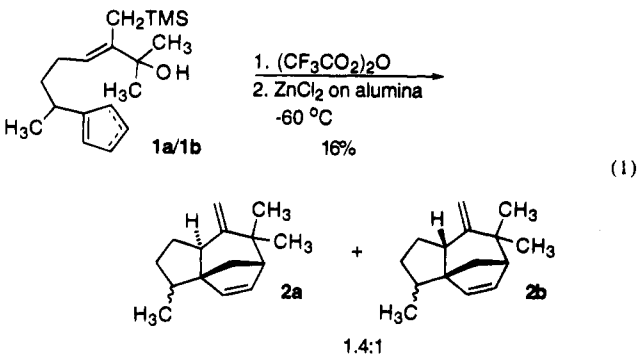
Treatment of both the *E* and *Z* isomers of alkoxyallylic sulfones **20a** and **20b** with $TiCl_4$ results in the formation of 4 + 3 cycloadducts by intramolecular cycloaddition. The distribution of diastereomers is different from each isomer of educt. This suggests that cycloaddition occurs faster than any isomerization process of the intermediate allylic cations. Both the *E* and *Z* isomers of **20c** lead to the same 4 + 3 cycloadduct with essentially complete diastereoselectivity. Inherently high simple diastereoselection and a strong conformational bias in the allylic cation intermediates for both isomers account for this selectivity. The importance of allylic cation stereochemistry in these reactions is underscored by the cyclization of **20d**. The *Z* isomer give only 4 + 3 cycloadducts with excellent relative but poor simple diastereoselection, suggestive of a concerted reaction. The *E* isomer give a [3 + 2] cycloadduct, enol ether **60**, as the major cycloadduct as well as 4 + 3 cycloadducts and chloride-trapping product **61**. This result is indicative of a stepwise reaction. The data reflect the importance of allylic cation stereochemistry in the regiochemical and stereochemical outcomes of intramolecular 4 + 3 cycloaddition reactions.

Introduction

The intramolecular 4 + 3 cycloaddition reaction of allylic cations with dienes is a promising reaction for the synthesis of fused seven-membered and other ring systems.[1,2] We have an ongoing program directed at the study of this reaction and dedicated to the development of new methodology, an understanding of stereochemical control, and the application of the process to synthesis.[3] Unlike its counterpart, the Diels–Alder reaction, the intramolecular 4 + 3 cycloaddition reaction has not received much attention, despite the potential it has for the creation of complex carbocyclic systems.[4] This is due in large part to difficulties associated with the generation and reactivity of allylic cations, a problem avoided in the Diels–Alder reaction through the use of easily accessible and stable dienophiles.

An important aspect of any intramolecular reaction which results in the formation of new stereogenic centers is the extent to which preexisting stereocenters affect the creation of new stereocenters, i.e., relative stereocontrol. This issue has been and continues to be examined in detail for the intramolecular Diels–Alder reaction and related processes. Data regarding this aspect of the intramolecular 4 + 3 cycloaddition reaction is sparse. In this report, we detail some of our work on relative stereocontrol in the formation of fused 5,7 ring systems via intramolecular 4 + 3 cycloaddition reactions.

The first example of an intramolecular 4 + 3 cycloaddition reaction in which relative stereocontrol was in principle possible came from the work of Hoffmann.[5] In the course of a synthesis of norzizaene, Hoffmann found that treatment of alcohol **1** (as a 44:56 mixture of **1a** and **1b**) with trifluoroacetic anhydride followed by zinc chloride on alumina resulted in the formation of a 16% yield



(1)

of the 4 + 3 cycloadducts **2a** and **2b** in a ratio of 1.4:1. There was no relative stereocontrol at all.

Schultz reported that photolysis of **3** gave adduct **5** in 80% yield.[6] Presumably, rearrangement to the oxyallylic species **4** is followed by intramolecular 4 + 3 cycloaddi-

† Dedicated to Professor Norman Rabjohn on the occasion of his 80th birthday.

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(1) For reviews of 4 + 3 cycloadditions, see: (a) Hosomi, A. and Tominaga, Y. [4 + 3] cycloadditions. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds., Pergamon: Oxford, 1991; Vol. 5, Chapter 5.1, pp 593–615. (b) Hoffman, H. M. R. *Angew. Chem., Intl. Ed. Engl.* **1984**, *23*, 1. (c) Mann, J. *Tetrahedron* **1986**, *42*, 4611. (d) Noyori, R.; Hayakawa, Y. *Org. React.* **1983**, *29*, 163–344.

(2) For a review of intramolecular 4 + 3 cycloadditions, see: Harmata, M. In *Advances in Cycloaddition*; Lautens, M. Ed.; JAI: Greenwich, 1995; Vol. 4 (in press).

(3) (a) Harmata, M.; Elahmad, S.; Barnes, C. L. *Tetrahedron Lett.* **1995**, *36*, 1397. (b) Harmata, M.; Elahmad, S.; Barnes, C. L. *J. Org. Chem.* **1994**, *59*, 1241. (c) Harmata, M.; Herron, B. F. *J. Org. Chem.* **1993**, *58*, 7393. (d) Harmata, M.; Herron, B. F. *Tetrahedron Lett.* **1993**, *34*, 5381. (e) Harmata, M.; Herron, B. F. *Synthesis* **1993**, 202. (f) Harmata, M.; Elahmad, S. *Tetrahedron Lett.* **1993**, *34*, 789. (g) Harmata, M.; Gamlath, C. B.; Barnes, C. L. *Tetrahedron Lett.* **1993**, *34*, 265. (h) Harmata, M.; Fletcher, V. R.; Claassen, R. J., II. *J. Am. Chem. Soc.* **1991**, *113*, 9861. (i) Harmata, M.; Gamlath, C. B.; Barnes, C. L. *Tetrahedron Lett.* **1990**, *31*, 5981. (j) Harmata, M.; Gamlath, C. B. *J. Org. Chem.* **1988**, *53*, 6154.

(4) For reviews of intramolecular Diels–Alder reactions, see: (a) Roush, W. R. In *Advances in Cycloaddition*; Curran, D. P., Ed.; JAI: Greenwich, 1990; Vol. 2, pp 91–146. (b) Roush, W. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, Chapter 4.4.

(5) Hoffmann, H. M. R.; Henning, R. *Helv. Chim. Acta* **1983**, *66*, 828.

(6) (a) Schultz, A. G.; Reilly, J. *J. Am. Chem. Soc.* **1992**, *114*, 5068. (b) Schultz, A. G.; Macielag, M.; Plummer, M. *J. Org. Chem.* **1988**, *53*, 391.

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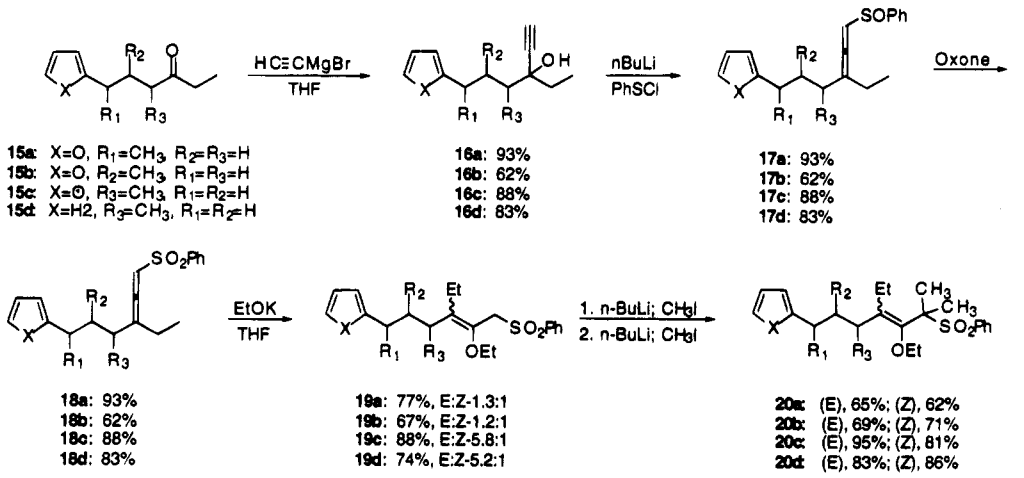
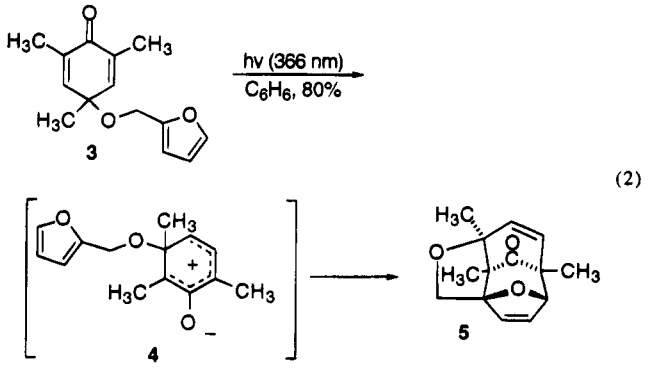
Scheme 1



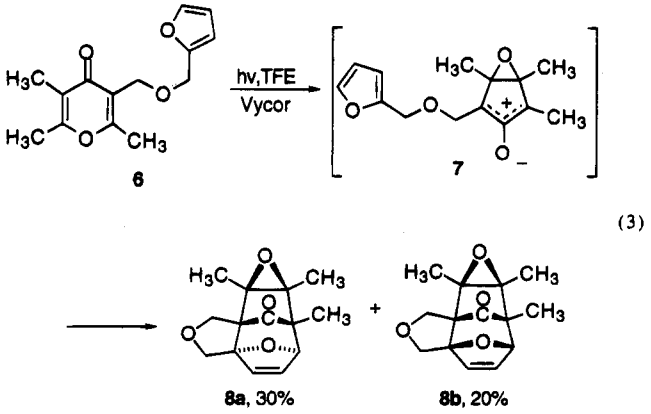
tion. The stereocenter exerts complete control over the facial selectivity of the process, as might be expected.



(2)

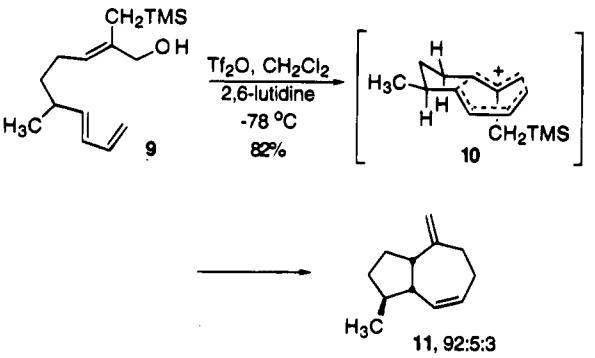
Complete endo selectivity assures the formation of a diastereomerically pure product. Other examples of this reaction are similarly stereoselective, in both intra- and intermolecular cycloadditions.

In a related reaction, West and co-workers found that photolysis of pyrone **6** resulted in the formation of two cycloadducts **8a** and **8b** in a ratio of 1.5:1.[7] Facial selectivity was complete, and relative stereocontrol provided by the resident stereocenters in intermediate **7** led to addition anti to the epoxide ring. However, steric factors lead to poor endo/exo selectivity.



(3)

As our work in this area was in progress, Giguere and co-workers reported an important result on relative stereocontrol in intramolecular 4 + 3 cycloadditions and demonstrated that allylic cation geometry has an important effect on regioselectivity in such reactions.[8] For example, treatment of **9** with triflic anhydride under conditions of high dilution resulted in the formation of cycloadduct **11** in 82% yield in a ratio of 92:5:3, possibly via transition state **10**. This was the first example of high relative stereocontrol in an intramolecular 4 + 3 cycloaddition reaction, in which such stereocontrol was mediated by a stereocenter in the tether linking cation and diene. Equally interesting and important was the finding that the isomer **9′** reacted under similar conditions to give only the 3 + 2 cycloaddition product **14** in 80% yield with high stereocontrol. This can be rationalized as having resulted from a stepwise reaction in which **12** leads to **13** which rapidly closes to give a five-membered ring.



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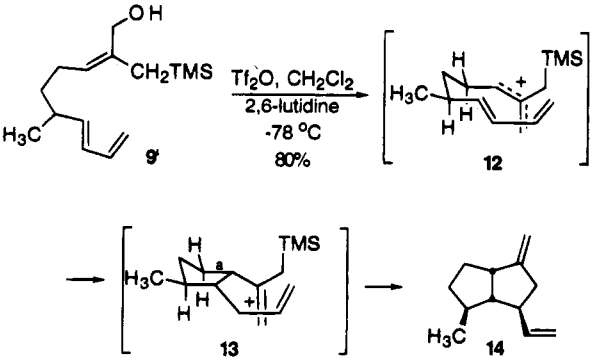


(5)

(7) West, F. G.; Hartker-Karger, C.; Koch, D. J.; Kuehn, C. E.; Arif, A. M. *J. Org. Chem.* **1993**, *58*, 6795.

(8) Giguere, R. J.; Tassely, S. M.; Rose, M. I.; Krishnamurthy, V. V. *Tetrahedron Lett.* **1990**, *31*, 4577.

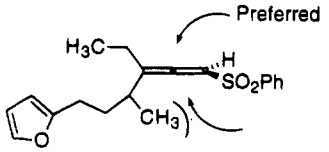
Our work serves to provide a modestly more detailed study of stereocontrol in intramolecular 4 + 3 cycloadditions and adds to the foundation necessary for further studies in this area.[9]

Results and Discussion

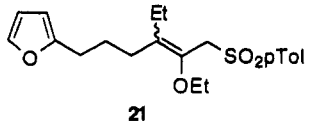
Synthesis of Cycloaddition Substrates. This study used methodology we had introduced very early in the course of our work on 4 + 3 cycloaddition reactions based on the ionization of alkoxyallylic sulfones.[3i] A relatively straightforward approach was used to prepare the eight cycloaddition substrates used in this study.

Ketones **15a–d**, prepared as described below, were treated with ethynylmagnesium bromide to afford the corresponding tertiary alcohols in good yield. Treatment of these alcohols with n-BuLi followed by phenylsulfenyl chloride[10] resulted in the formation of sulfenate esters which spontaneously rearranged to the allenic sulfoxide in overall yields from 70–91% for **17a–d** (Scheme 1).[11] Oxidation to the corresponding sulfones occurred with oxone with no apparent deleterious effect on the furan ring of **18a–d**, though the yield for this step was not particularly high.[12] Addition of potassium ethoxide to the allenic sulfones occurred as expected to give *E*/*Z* mixtures in nearly equal amounts.[13] However, addition of ethoxide to **18c** and **18d** gave products in a 75:13 and 63:12 *E*:*Z* ratio, respectively.

This expected result assists in the assignment of stereochemistry.[13] The nucleophile adds to the allene on the less hindered face, away from the methine and cis to the methylene group of the pendant alkyl groups. This mechanistic imperative leads to the stereochemical assignment.



At this stage the isomeric sulfones were separated, and their stereochemistry was assigned. In conjunction with the mechanistically based assignment discussed above, a comparison of the proton chemical shifts of the sulfonyl-bearing methylene carbons and the methylenes of the ethoxy groups of **19a–d** were made relative to **21**, whose



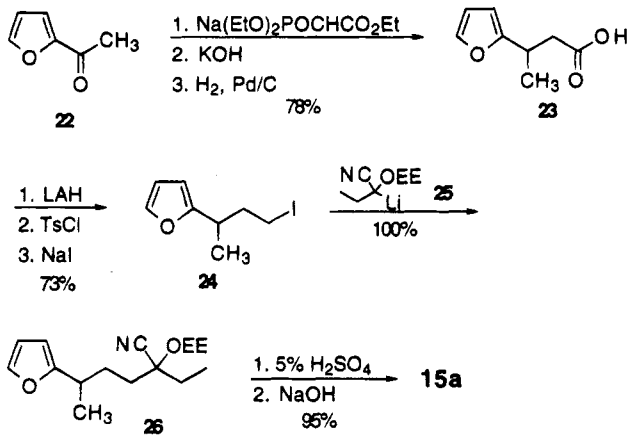
21

E and *Z* isomers were rigorously defined through a NOESY experiment in the course of another study.[3h] These data are shown in Table 1 and they are all internally consistent. Further, in all cases, including sulfone **21**, the *E* isomers were less polar than their corresponding *Z* isomers (TLC, 5% ethyl acetate in hexanes).

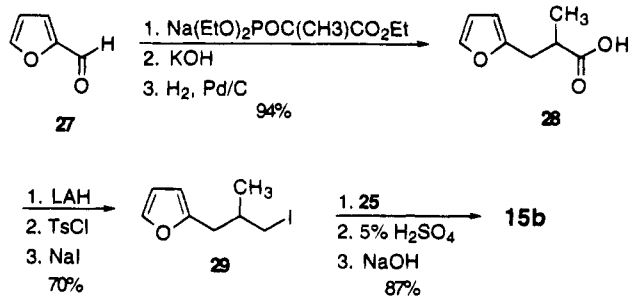
Table 1. Stereochemically Diagnostic Proton Chemical Shifts of 19a–d and 21 in $CDCl_3$

entry	compound	δ $ArSO_2CH_2$	δ OOH_2CH_3
1	(*E*)-**21**	3.92	3.59
2	(*Z*)-**21**	4.00	3.54
3	(*E*)-**19a**	3.87	3.59
4	(*Z*)-**19a**	4.00	3.50
5	(*E*)-**19b**	3.92	3.58
6	(*Z*)-**19b**	4.04	3.48
7	(*E*)-**19c**	3.94	3.58
8	(*Z*)-**19c**	4.02	3.46
9	(*E*)-**19d**	3.96	3.57
10	(*Z*)-**19d**	4.02	3.48

Scheme 2



Scheme 3



Each stereochemically pure isomer was then sequentially alkylated to give the cycloaddition substrates **20a–d**. There was no evidence for loss of stereochemical integrity and the stereochemical assignments made on **19a–d** were assumed to be maintained in **20a–d**.

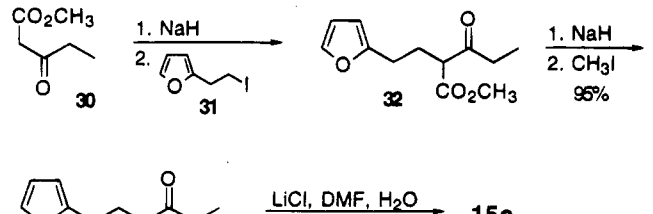
The ketones **15a–d** were easily prepared. Treatment of 2-acetylfuran with the sodium salt of triethyl phosphonoacetate gave the expected Horner–Emmons product (Scheme 2). Saponification and hydrogenation of the resulting potassium carboxylate afforded the acid **23**. Reduction with lithium aluminum hydride and straightforward functional group manipulation led to iodide **24** in 73% yield from **23**. Reaction with the lithio nitrile **25** gave **26** in essentially quantitative yield.[14] Hydrolysis afford the ketone **15a**.

In a similar fashion, Horner–Emmons reaction of furfural, saponification, and hydrogenation gave **28** in 94% yield. Ketone **15b** followed from the same sequence discussed in the preceding paragraph (Scheme 3).

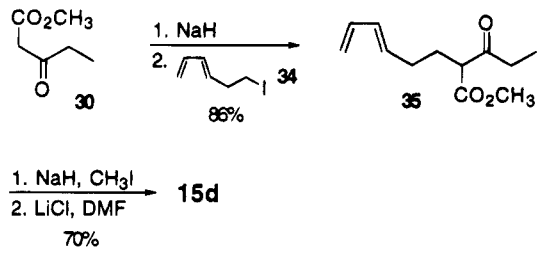
The ketone **15c** was prepared in a slightly different fashion. Alkylation of the anion of methyl 3-oxopentanoate with 2-(2-iodoethyl)furan **31** lead to the keto ester

(9) For a preliminary report of this work see ref 3f.
(10) Barrett, A. G. M.; Dhanak, D.; Graboski, G. G.; Taylor, S. J. *Org. Synth.* **1990**, *68*, 8.
(11) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147.
(12) Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, *22*, 1287.
(13) Denmark, S. E.; Harmata, M. A.; White, K. S. *J. Org. Chem.* **1987**, *52*, 4031.
(14) Young, S. D.; Buse, C. T.; Heathcock, C. H. *Org. Synth.* **1985**, *63*, 79.

Scheme 4



Scheme 5



32 in 51% yield (Scheme 4). This was further alkylated with methyl iodide to give **33** in 95% yield. Krapcho decarboalkoxylation afforded ketone **15c** in 80% yield.[15] Attempts to directly alkylate the lithium enolate of 3-pentanone were unsuccessful, and this more circuitous route to **15c** was necessary. The alkylating agent **31** was prepared by a straightforward sequence.[16] All attempts to purify **31** including chromatography and distillation resulted in decomposition to a black polymer. Traces of water contaminating the iodide were removed via azeotropic distillation with benzene, and the iodide was used without further purification.

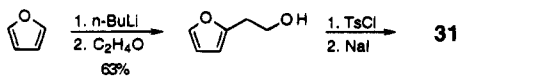
Finally, ketone **15d** was prepared in the same manner as **15c** as shown in Scheme 5.[17]

Cycloaddition Studies. One important motivation for the exploration of relative asymmetric induction in intramolecular 4 + 3 cycloadditions arose from our concern about the configurational stability of the putative allylic cation intermediate involved in the process. We had found that with a substrate such as **36**, the yield and simple diastereoselectivity of the cycloaddition reaction were unaffected by the configuration of the cycloaddition substrate (Scheme 6).[3h] We wondered if this result was circumstantial or indicative of convergence to a single intermediate. A stereogenic center in the tether joining the diene and dienophile could probably serve as an independent stereochemical marker to discern the possibilities.

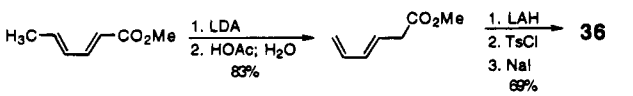
While the direct isomerization (via rotation) of one

(15) Krapcho, A. P.; Weimaster, J. F.; Eldridge, J. M.; Jahngen, Jr., E. G. E.; Lovey, A. J.; Stephens, W. P. *J. Org. Chem.* **1978**, *48*, 138.

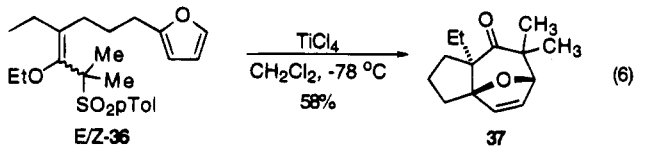
(16) Compound **31** was prepared according to the sequence shown:



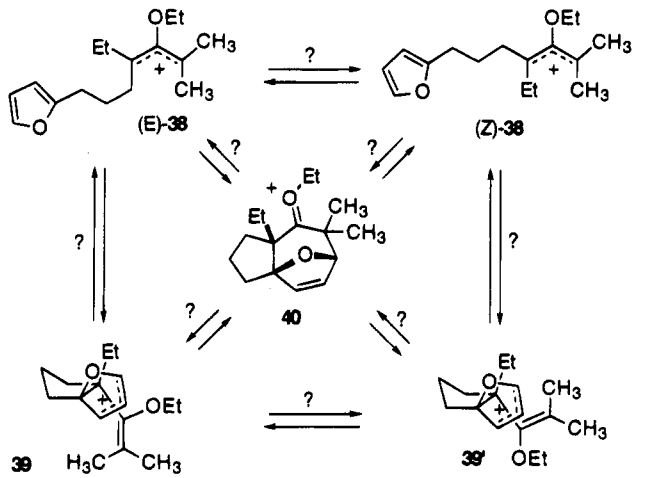
(17) Compound **36** was prepared according to the sequence shown:



Scheme 6

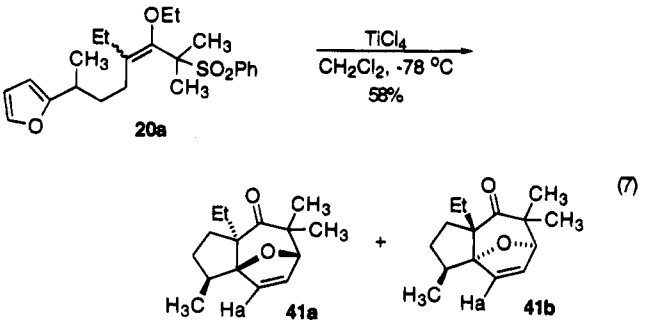


Scheme 7



allylic cation to another was considered improbable,[18] other concerns including regioisomerization and reversible cation formation would be processes that could lead to losses in stereochemical integrity in the cycloaddition substrates and the allylic cations for which they served as progenitors. Further, carbon–carbon bond-forming processes coupled with bond rotation and reversion could lead to stereochemical leakage as illustrated in Scheme 7.

In the event, treatment of (*E*)-**20a** in CH_2Cl_2 with $TiCl_4$ led to the formation of two cycloadducts in a ratio of 2.4:1. The corresponding *Z* isomer led to the same two products in a ratio of 1.5:1, respectively. Both reactions



From (Z)-**20a** : 1.5:1
From (E)-**20b** : 2.4:1

proceeded in 58% yield. This result immediately establishes that if any loss in stereochemical integrity is occurring on the path from starting material to product, it is occurring at a rate slower than cycloaddition.

The mixture of cycloadducts was separated by MPLC using gradient elution. Their relative stereochemistries were established by NOESY experiments and inspection of molecular models. The angular stereochemistry was assigned on the basis of precedent.[1-3] For example, in our earliest study of this reaction we found that both **42**

(18) Deno, N. C.; Haddon, R. C.; Nowak, E. N. *J. Am. Chem. Soc.* **1970**, *92*, 6691.

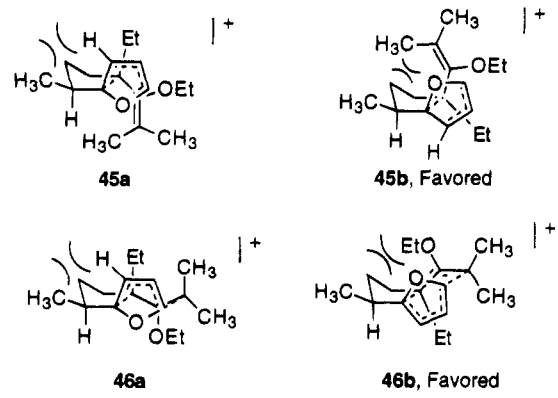
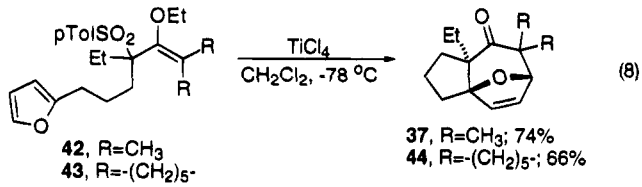
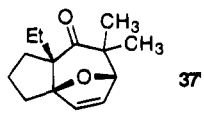


Figure 1.

and **43** reacted with $TiCl_4$ to give single cycloadducts in which this trans angular stereochemistry was manifest. Molecular mechanics calculations show that **37** is more





stable than its epimer **37′** by 3.15 kcal/mol, a result that arises from torsional strain in **37′** due principally to the presence of the oxygen bridge.[19] This effect is felt in the transition states leading to the initial products of cycloaddition, which are likely oxocarbenium ions such as **40**. If any intermediate like **40** or **39** is formed, it either reverts to allylic cation or reacts nonproductively to inisolable products.[20]

Further stereochemical analysis via NOESY showed an interaction between the methyl group on the five-membered ring and the olefinic proton in **41b** but not in **41a**. Models indicated that the methyl group in **41b** is in proximity to H_a while the methyl group of **41a** is not.

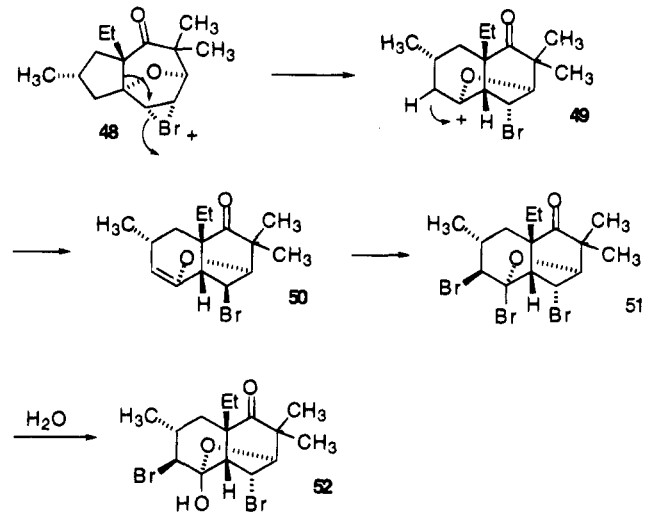
Small scale experiments using different solvents suggest minimal influence on the stereochemical outcome of the reaction. In toluene at −78 °C, (*E*)-**20a** cyclized to give **41a** and **41b** in a ratio of 1.3:1. In ethyl acetate at 25 °C the ratio was 1.5:1, but the reaction did not go to completion. Yield were not determined for these reactions. Finally, it should be noted that when cycloadducts **41a** and **41b** were separately subjected to treatment with $TiCl_4$ in CH_2Cl_2 at −78 °C, no change was observed. The cycloadducts maintain their stereochemical integrity under the reaction conditions.

Possible transition state structures for the cycloaddition process can be envisioned as shown in **45** and **46** (Figure 1). A puckered, nascent five-membered ring with the methyl group in a pseudoequatorial orientation is a reasonable conformation for the tether. The step which defines stereochemistry must orient the oxygen of the

(19) Calculations were performed using PCMODEL (version 2 or version 5).

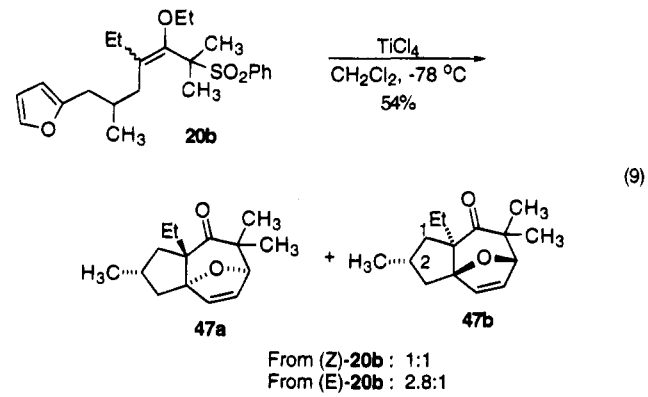
(20) We have not been able to detect any side products in these cycloadditions other than those reported.

Scheme 8



furan and the ethyl substituent on the allylic cation anti to each other. In the absence of significant electronic effects, relative stereocontrol will be determined by steric interactions. The pairs of transition state structures shown are essentially conformational isomers. Steric interactions in these pairs do not appear to be significantly different. Hence we expect and obtain low relative diastereoselection.

Similar stereochemical results were found with **20b**. Substrate (*E*)-**20b** gave cycloadducts **47a** and **47b** in 54% yield under standard conditions in a ratio of 2.8:1. No relative stereocontrol was evident at all in the reaction of (*Z*)-**20b**, which gave a 1:1 mixture of cycloadducts in 54% yield. In this case, it seems quite clear that two distinct species are generated from the isomers of **20b** and that they remain unique in the formation of cycloadducts. The stereochemistry of **47a** was determined by



X-ray crystallographic analysis of a derivative. Treatment of **47a** with excess bromine in CH_2Cl_2 at room temperature resulted in the formation of **52**, presumably via the mechanism illustrated in Scheme 8. Thus, formation of the bromonium ion **48** is followed by a 1,2-shift to give the oxocarbenium ion **49**. Elimination and addition of bromine leads to the bromo ether **51** which is hydrolyzed upon workup to give **52**. X-ray analysis of **52** made its structural assignment (and that of **47a**) unequivocal.[29] In assigning stereochemistry to **47b**, it was assumed that this isomer had a configuration at C-2 opposite to that of **47a**.

Plausible transition state structures for the cyclization of **20b** are shown in Figure 2. As in the previous case,

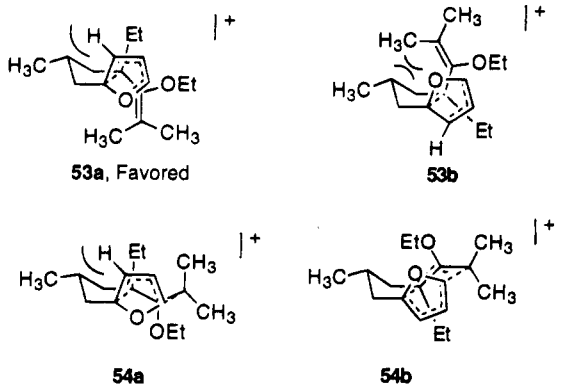


Figure 2.

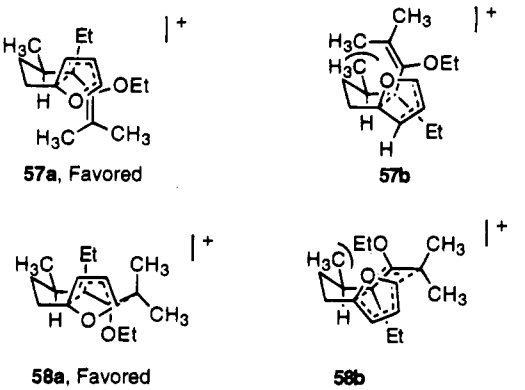
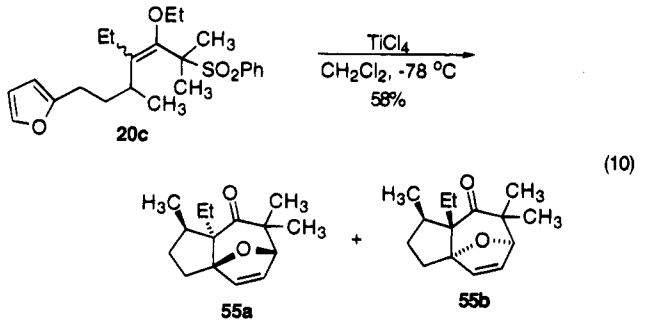


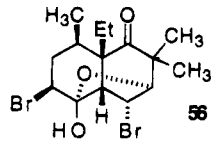
Figure 3.

steric interactions in the pairs of structures are not sufficiently different to produce good relative stereocontrol, though **53a** is favored over **53b**, which is probably a manifestation of allylic strain as shown.[21]

The situation with both (*E*)- and (*Z*)-**20c** was quite different. Both isomers underwent cycloaddition upon treatment with $TiCl_4$ with essentially complete stereocontrol. In both cases, only cycloadduct **55b** could be detected. The structure of **55b** was determined in the



(10)



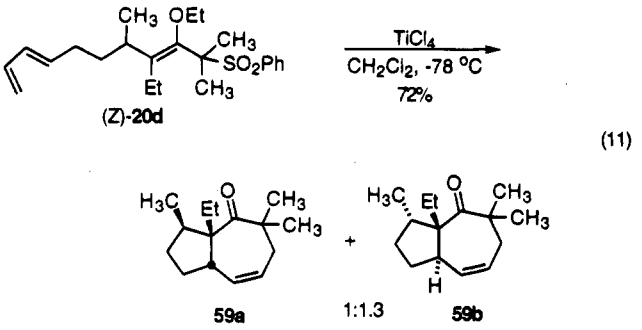
same manner as for **47a**. Thus, treatment of **55b** with excess bromine gave **56** in 73% yield. X-ray analysis of **56** established its structure and therefore that of **55b**.[29]

It is in this case that untoward steric interactions dictate a strong preference for transition state structures **57a** and **58a** over **57b** and **58b**, respectively (Figure 3). The steric problems associated with **57b** and **58b** are especially evident upon inspection of CPK models. The presence of an methyl group on the tether at a position adjacent to the allylic cation gives rise to severe 1,3-allylic interactions which are largely avoided in **57a** and **58a**. Thus, both isomers of **20c** fortuitously give rise to the same, single cycloadduct **55b**.

We were worried that the bias for trans ring fusion inherent in the 4 + 3 cycloadditions of **20a–c** resulted in an incomplete picture of the effect of allylic cation stereochemistry on the results of the 4 + 3 cycloaddition process. This analysis is certainly validated by the results of Giguere and co-workers.[8] In particular we wondered about the stepwise or concerted nature of the cycloaddition process. Furan is amenable to electrophilic addition to potentially produce, under our reaction conditions, intermediates capable of ultimately proceeding to a 4 + 3 cycloadduct (cf. Scheme 7).

On the basis of this and other concerns, we chose to examine substrate **20d** in which a tethered, but otherwise unsubstituted butadiene serves as a trap for the allylic cation. We believed that the steric effects leading to high relative stereocontrol in the reaction of **20c** would also result in high relative stereocontrol in **20d**. We anticipated that the lack of a bridge in the diene would decrease simple diastereoselection by removing the primary structural feature responsible for it in **20a–c** and that a simple diene would be much more likely to give isolable intermediates or side products associated with the cycloaddition process if indeed any were formed.

When the *Z* isomer of **20d** was added to a solution of $TiCl_4$ in CH_2Cl_2 at −78 °C, two cyclization products, **59a** and **59b**, were isolated in 72% yield in a ratio of 1:1.3. Under the same reaction conditions the *E* isomer gave a

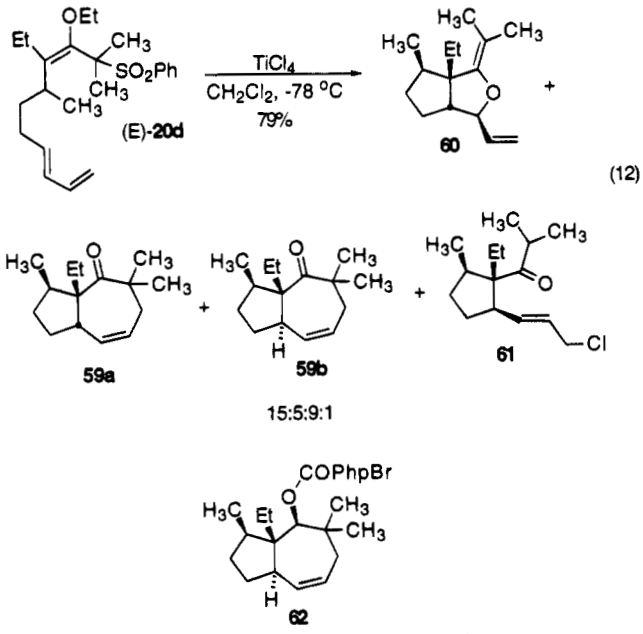


(11)

mixture of four compounds in a ratio of 15:5:9:1 by capillary gas chromatographic analysis. These products were identified as **60**, **59a**, **59b**, and **61**, respectively. The total yield after chromatographic purification of isolated material and fractions containing mixtures of these compounds was 79%.

Compounds **60**, **59a**, and **61** were isolated by repeated use of gradient MPLC. Every attempt to isolate compound **59b** failed due to contamination by **59a**. The volatility of the compounds was also a problem. A mixture of **59a** and **59b** was therefore reduced with lithium aluminum hydride and the resulting mixture treated with MeLi followed by *p*-bromobenzoyl chloride to form the corresponding esters. This mixture of esters was separated by radial chromatography. One of the bromobenzoates was crystallized from CH_2Cl_2/hexanes and the crystal structure was determined. To establish

(21) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.



the stereochemistry of the original ketone the bromobenzoate was reduced to the corresponding alcohol with LAH and the alcohol was oxidized to the ketone with PCC in CH_2Cl_2. Gas chromatographic analysis showed that the ketone was **59b** and the structure and stereochemistry of **59b** was thereby established.

Structure elucidation and the determination of relative stereochemistry for **60** and **59a** was performed by analysis of relevant spectral data. In its low resolution mass spectrum compound **60** had an M^+ peak at 220, corresponding to a molecular formula of $C_{15}H_{20}O$. The IR spectrum had strong bands at 1119 and 1154 cm^{-1} indicating the presence of an ether functionality. Two three-proton singlets at δ 1.66 and at δ 1.60 in the ^1H NMR spectrum showed the presence of two allylic methyl groups. A one-proton multiplet at δ 5.86, a one-proton doublet of triplets at δ 5.25 (J = 1.4, 17.1 Hz) and a one-proton double of triplets at δ 5.10 (J = 1.3, 10.3 Hz) indicated the presence of a vinyl group. In the ^{13}C NMR there were signals for four olefinic carbons at δ 154.9, 138.4, 115.5, and 98.8. The latter in particular suggested the presence of an enol ether. In consideration of these data structure **60** was proposed for this compound. COSY experimental data for this compound helped to elucidate the appropriate coupling relationships and allowed each proton signal to be assigned to a particular proton. NOESY experiments were performed to elucidate the relative stereochemistry of the compound. There were strong NOE interactions between the methyl group attached to the five-membered (δ 0.99) and the methylene of the angular ethyl group (δ 1.29 and δ 1.80) indicating that both groups were on the same side of the ring. The methylene of the angular ethyl group also displayed NOE interaction with the proton at the ring junction (δ 2.33) showing the the bicyclo[3.3.0]octane system was cis fused, as expected. This was also evident from the NOE interaction between the 4α-H (δ 4.00) and 6α-H (δ 1.45). Finally, the NOE interactions between the C-5 and one of the vinylic protons (δ 5.25) proved that they are cis to each other, thus confirming the relative stereochemistry of all four stereocenters of the molecule. These interactions are summarized in Figure 4. Of both structural and stereochemical interest was the fact that heating a quinoline solution of **60** in a sealed tube at 300 °C (bath)

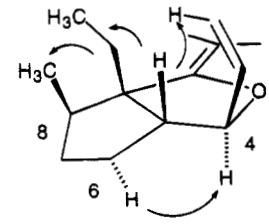


Figure 4.

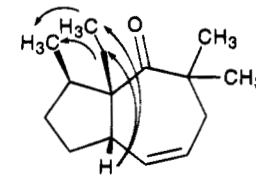


Figure 5.

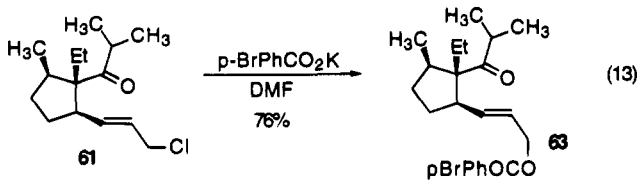
resulted in the formation of the Claisen rearrangement product **59a** in 81% yield, adding credence to the structural assignments of both **59a** and **60**.

The structural assignment of **59a** was fairly straightforward. The molecular weight was determined to be 220. The IR spectrum of **59a** had a strong band 1680 cm^{-1} indicating the presence of a carbonyl. In the ^{13}C NMR spectrum signals at δ 217.5 and at δ 135.0 and 124.4 indicated the presence of a carbonyl group and an alkene. In the proton NMR spectrum a one-proton doublet of doublets at δ 5.77 (J = 5.8, 10.9 Hz) was assigned to H-8 and a one proton doublet of doublets of triplets at δ 5.72 (J = 0.6, 6.0, 10.9 Hz) was assigned to the other olefinic proton. A NOESY experiment on this compound indicated NOE interactions between the ring junction proton (δ 2.74) with the methyl (δ 0.76) and methylene (δ 1.89, 1.35) protons of the ethyl group. The methyl group on the five-membered ring (δ 0.90) also showed NOE interaction with the same angular ethyl group suggesting they are cis to each other (Figure 5). These data strongly support the proposed structure and stereochemistry of **59a**.

Finally, in the IR spectrum of **61** there was a strong absorption at 1700 cm^{-1} and in the ^{13}C NMR a signal at δ 218.1, both indicative of a ketonic carbonyl group. A two-proton doublet at δ 4.50 (J = 7 Hz) was assigned to the protons on the carbon attached to the chlorine atom. A six-proton doublet at δ 1.06 (J = 6.5 Hz) indicated the presence of an isopropyl group. There were two olefinic carbon atoms present in the ^{13}C NMR at δ 137.3 and 126.4. In the ^1H NMR, a doublet of doublets at δ 5.80 (J = 9.0, 15.0 Hz) was assigned to the proton on the olefinic carbon attached to the five-membered ring. A one proton doublet of triplets at δ 5.63 (J = 7.1, 15.0 Hz) was assigned to the other olefinic proton. The coupling constant of 15.0 Hz between the two olefinic protons suggested that they were trans to each other.

In an effort to produce a more stable and less volatile compound, **61** was reacted with potassium *p*-bromobenzoate in DMF to give the corresponding ester **63** in 76% yield (eq 13). We were unable to obtain crystals suitable for crystallographic analysis and decided to perform COSY and NOESY experiments to establish the stereochemistry of **63** and therefore **61**.

In the NOESY spectrum of ester **63** NOE interactions between the methyl group on the five-membered ring (δ 0.99) and the methylene protons of the ethyl group (δ 1.59, 1.65) were evident. This suggested a cis relation-



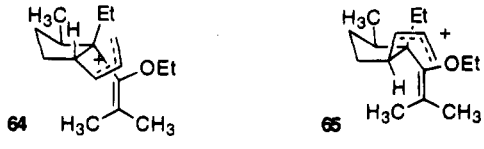
(13)

ship between these substituents. There were NOE interactions between the methine proton of the isopropyl group (δ 3.09) and the proton attached to the carbon bearing the methyl group in the five-membered ring (δ 2.49) and with the allylic methine proton (δ 3.17) (Figure 6). These data indicated that all of these protons were on the same side of the five-membered ring, and the stereochemistry of **61** was assigned accordingly.

The formation of **59a** and **59b** from (*Z*)-**20d** suggests that without control of conformation about the diene-tether bond there is little exo/endo selectivity in the cycloaddition and little likelihood of exceptional diastereoselection. The slight preference for a trans ring is noteworthy, however, and has been observed by us and Giguere and co-workers in related systems.[22] The specifics associated with this preference remain to be elucidated though they may be related to those responsible for such internal diastereoselection in the intramolecular Diels–Alder reaction.[4]

As expected, the relative stereochemical control between C-1 and C-8a was complete, implying a strong conformational bias about the allylic bond joining the allylic cation and tether. The fact that only 4 + 3 cycloaddition adducts were found suggests but does not prove that the reaction proceeds through a concerted cycloaddition. Models indicate that this is feasible.

This conclusion is supported by the fact that (*E*)-**20d** leads to an array of products, the major one of which is a [3 + 2] cycloadduct which had to have been formed via a stepwise reaction sequence based on orbital symmetry considerations.[23] The formation of **61** provides further evidence for the formation of a cationic intermediate. These results are in complete agreement with those of Giguere and co-workers.[8] However, with an allylic cation with an *E* configuration, they observed little to no 4 + 3 cycloaddition. In our case, we speculate that after initial carbon–carbon bond formation to form either **64** or **65**, a competition between various inter- and intramolecular



trapping events determines the product ratio. In **64**, the cationic center is generated in close proximity to the oxygen of the enol ether. The "hard" oxygen readily attacks the "hard" allylic cation to give **60** as the major product from **64**.[24] Slightly slower is trapping by the carbon end of the enol ether, perhaps due to steric effects. Steric factors may also help determine the regiochemistry of such an attack, with the disubstituted carbon end of the enol ether preferring the less substituted end of the

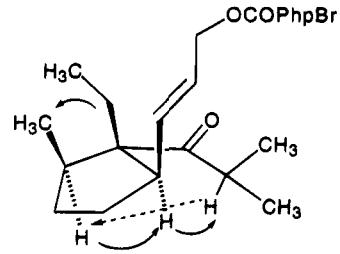


Figure 6.

allylic cation. Intermediate **64** cannot partition to a bicyclo[3.3.0]octane ring system of any type, since these would be trans fused and relatively high in energy.[25] Rather, trapping occurs in a 4 + 3 sense to give **59b** and with an external nucleophile to give **61**. The ratio of these products is 9:1, demonstrating the strong preference for intramolecular trapping.

Importantly, the ratio of **59a** and **59b** derived from (*Z*)-**20d** differs from that derived from (*E*)-**20d**. This suggests that this set of products arises from a unique intermediate from each cycloaddition precursor. It does not, however, provide any mechanistic information and conclusions about the concerted and/or stepwise nature of any of these 4 + 3 cycloaddition processes are based on reasonable assessments of the available evidence and are not beyond question.

Conclusion

In summary, we have demonstrated that stereochemically unique 4 + 3 cycloaddition precursors give rise to unique distributions of cycloadduct diastereomers. This indicates that the intermediates in the process, probably allylic cations, do not interconvert by any mechanism faster than cycloaddition. Controlling the conformation about the bonds joining the allylic cation and diene to the tether appears to be critical for obtaining high levels of relative diastereoselection unless other factors, such as torsional strain, lead to high simple diastereoselection, as in the formation of **55b**. Further studies on synthetic and mechanistic aspects of 4 + 3 cycloaddition chemistry are in progress and will be reported in due course.

Experimental Section

General Information. All air or moisture sensitive reactions were carried out in oven dried (at 120 °C) or flame dried glassware under nitrogen atmosphere. Reactive liquids were transferred by syringe or cannula and were added into the reaction flask through rubber septa. Standard workup means that the reaction mixture was added to water and extracted twice with ether. Ether layers were washed with water and brine and then dried over anhydrous $MgSO_4$. Removal of solvents was done by using a rotary evaporator attached to a water aspirator. This was usually followed by the use of a vacuum line (held at about 1 mmHg) to remove residual solvents. Ether and tetrahydrofuran were freshly distilled from sodium benzophenone ketyl, and methylene chloride was distilled from CaH_2. HMPA was distilled from CaH_2 and was stored over activated molecular sieves.

Analytical thin layer chromatography was performed on silica gel plates, (0.25 mm thickness) with F_{254} indicator. Compounds were visualized under UV lamp or by developing in iodine and/or vanillin solution followed by heating on a hot plate to about 250 °C. Flash chromatography was performed

(22) Giguere, R. J.; Duncan, S. M.; Bean, J. M.; Purvis, L. *Tetrahedron Lett.* **1988**, *29*, 6071.
(23) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag: Weinheim, 1971.
(24) Ho, T.-L. *Hard and Soft Acids and Bases Principle in Organic Chemistry*; Academic: New York, 1977.
(25) Chang, S.-J.; McNally, D.; Shary-Tehrany, S.; Hickey, M. J., Sr.; Boyd, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 3109.

as described by Still and co-workers[26] on 230–400 mesh silica gel with technical grade solvents that were distilled prior to use. ACS reagent grade ether was used without purification. Medium pressure liquid chromatography (MPLC) separations were carried out using commercially available columns. Gradient elutions were done according to Baeckström and co-workers[27] using a simple gradient mixer. Gas chromatographic analyses were done with a SPB-5 fused silica capillary column (length 15 m, i.d. 0.25 mm) and a flame ionization detector. Analytical and preparative HPLC separations were done on a silica 5 μm, 4.6 mm i.d. analytical column or a silica 12 μm, 21.4 mm i.d. preparative column. A detector set at 254 nm or at 280 nm was used for the detection of compounds.

Melting points are uncorrected. Infrared spectra were obtained as a neat liquid or as a CCl_4 solution. ^{1}H NMR spectra were recorded on a 90, 300, or 500 MHz spectrometer with tetramethylsilane as the internal standard as $CDCl_3$ solutions unless otherwise stated. ^{13}C spectra were obtained using the same instruments at 22.5, 75.5, or 125.8 MHz, respectively. The ^{1}H NMR data of mixtures of diastereomers were too complex to report the multiplicities and integrations of individual protons. Therefore, the spectrum is reported as signals which integrate for whole number of protons. High resolution mass spectra were obtained from the Midwest Center for Mass Spectroscopy, Lincoln, NE, or from the University of Missouri Mass Spectrometry Center. High resolution mass spectra of mixtures of diastereomers was done by directly introducing the mixtures to the mass spectrometer. Elemental analyses were performed by Desert Analytics, Tucson, AZ or by MHW Laboratories, Phoenix, AZ.

3-Ethynyl-6-(2-furanyl)-3-heptanol (16a). A solution of 26 mL of ethynylmagnesium bromide (0.83 M solution in THF) was added to 66 mL of THF. A solution of 3.0 g of ketone **15a** in 10 mL of THF was added while stirring at 25 °C. Stirring was continued for 14 h. The reaction mixture was poured into 20 mL of 2 N HCl and 50 mL of water. Standard workup, removal of solvents, and Kugelrohr distillation gave the alcohol **16a** as a mixture of two diastereomers in 93% yield. This was characterized as the mixture of diastereomers without separation: bp 84–86 °C/0.4 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, J = 1.5 Hz, 1H), 6.27 (dd, J = 1.9, 3.0 Hz, 1H), 6.00 (d, J = 1.8 Hz, 1H), 2.84 (m, 1H), 2.44 (s, 1H), 1.91–1.57 (m, 7H), 1.26 (d, J = 7.0 Hz, 3H), 1.01 (2t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 140.6, 109.8, 103.6, 86.4, 72.4, 71.4, 38.7, 34.6, 33.1, 30.05, 30.1, 19.18, 19.26, 8.32. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.63; H, 8.72.

3-Ethynyl-6-(2-furanyl)-5-methyl-3-hexanol (16b). To a solution of 1.64 g of 6-(2-furanyl)-5-methyl-3-hexanone **15b** in 18 mL of THF, 21.8 mL of ethynylmagnesium bromide (0.625 M in THF) was added at 25 °C and the solution was stirred for 14 h. The reaction was cooled to 0 °C and quenched by adding 10 mL of 2 N HCl and 25 mL of water. Standard workup and evaporation of solvents followed by Kugelrohr distillation gave the alcohol **16b** as a mixture of two diastereomers in 62% yield: bp 95–100 °C/0.5 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (s, 1H), 6.27 (s, 1H), 6.01 (t, J = 2.6 Hz, 1H), 2.76 (m, 1H), 2.55 (m, 1H), 2.46 (s, 1H), 2.24 (m, 1H), 2.07 (s) and 2.04 (s), (1H), 1.78–1.61 (m, 3H), 1.53 (m, 1H), 1.05–1.00 (3, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1, 155.0, 140.8, 110.0, 110.0, 106.2, 106.1, 86.7, 86.6, 72.9, 72.8, 71.5, 71.3, 47.1, 47.0, 36.4, 36.2, 35.8, 35.6, 29.4, 29.2, 21.5, 21.4, 8.4, 8.3; IR (neat) 726 s, 797 w, 975 w, 1001 m, 1147 m, 1183 w, 1379 w, 1460 m, 1507 m, 2881 w, 2936 m, 2970 m, 3299 m, 3462 br m cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_2$: C, 75.69; H, 8.80. Found: C, 75.81; H, 8.62.

3-Ethynyl-6-(2-furanyl)-4-methyl-3-hexanol (16c). Prepared according to the procedure for **16b**. Purification by flash chromatography (4% EtOAc in hexane) afforded **16b** as a mixture of two diastereomers in 88% yield. This was characterized as a mixture: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, J = 1.2 Hz, 1H), 6.26 (dd, J = 3.0, 2.0 Hz, 1H), 6.00 (m), 2.78 (m, 1H), 2.61–2.55 (m, 1H), 2.41 (d, J = 5.3 Hz, 1H), 2.11 (m, 1H), 1.96 (2s, 1H), 1.77–1.69 (m, 1H), 1.69–1.60 (m, 2H), 1.50 (m, 1H), 1.06–1.01 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.1, 155.9, 140.7, 140.6, 110.0(2C), 104.7, 104.7, 85.8, 85.6, 74.7, 74.5, 73.0, 73.0, 41.4, 41.3, 31.9, 31.5, 29.8, 29.3, 26.1, 26.1, 14.2, 13.3, 8.1, 7.9; IR (neat) 729 s, 919 w, 939 w, 965 s, 1007 s, 1145 s, 1380 w, 1462 m, 1508 m, 1596 w, 2881 m, 2939 s, 2971 s, 3299 s, 3449 m, 3558 m cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.64; H, 8.77.

3-Ethynyl-4-methyl-7(*E*),9-decadien-3-ol (16d). Prepared according to the procedure for **16b**. Purification by flash chromatography (4% EtOAc in hexane) afforded the alcohol as a mixture of two diastereomers in 83% yield. This was characterized as a mixture without further separation: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.30 (dt, J = 10.2, 17.0 Hz, 1H), 6.07 (dd, J = 10.5, 15.2 Hz, 1H), 5.69 (m, 1H), 5.09 (d, J = 17.0 Hz, 1H), 4.95 (d, J = 10.1 Hz, 1H), 2.42 and 2.41 (2s, 1H), 2.24 (m, 1H), 2.02 (m, 1H), 1.97 (m, 1H), 1.90–1.60 (m, 4H), 1.25 (m, 1H), 0.98–1.05 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.21, 137.16, 135.03, 134.87, 131.15, 131.06, 114.82, 114.74, 86.04, 85.77, 74.67, 72.93, 72.92, 41.51, 41.36, 31.82, 31.54, 30.90, 30.59(2C), 30.39, 14.19, 13.30, 8.19, 7.98; IR (neat) 889 m, 967 s, 1004 s, 1039 w, 1071 w, 1114 w, 1133 m, 1266 w, 1300 m, 1348 m, 1379 m, 1415 w, 1435 w, 1461 m, 1652 w, 2881 m, 2939 s, 2971 s cm^{-1}; MS (70 eV) m/z 192 (M$^+$, 3), 159 (18), 145 (44), 133 (17), 117 (14), 105 (21), 91 (25), 83 (67), 80 (100), 67 (51), 55 (24); HRMS exact mass calcd for $C_{13}H_{20}O$: 192.1514, found 192.1499.

2-[2-(5-Ethyl-7-(phenylsufinyl)-5,6-heptadienyl)]furan (17a). To a solution of 5 g of **16a** in 97 mL of THF was added 10.35 mL of nBuLi at −78 °C. After stirring for 5 min a solution of 3.85 g of phenylsulfenyl chloride dissolved in 5 mL of THF was added at −78 °C. The reaction mixture was allowed to warm up to 25 °C. The reaction was worked up by adding a saturated solution of $NaHCO_3$ and extracting with ether (2×). The ether layers were washed with water and brine and dried over $MgSO_4$. The residue after the removal of solvents was chromatographed on silica gel (20% EtOAc in hexane) to give the sulfoxide **17a** as a mixture of three diastereoisomers in 72% yield. This was characterized as the mixture of three diastereomers without further separation. The ^{1}H NMR spectrum of this compound was too complicated to report the integration of each set of signals due to the overlap of the signals from each isomer. Therefore, the spectrum is reported as signals which integrate for a whole number of protons: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (m, 2H), 7.47 (m, 2H), 7.29 (m, J = 2.3 Hz, 1H), 6.07 (m, 1H), 5.97 (m, 1H), 2.82 (m, 1H), 2.02 (m, 4H), 1.85–1.51 (m, 3H), 1.23 (m, 3H), 1.04–0.95 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.65, 200.57, 200.54, 159.60, 159.56, 159.49, 145.10, 140.63, 140.61, 130.63, 128.98, 124.10, 115.92, 115.89, 115.83, 115.81, 109.76, 104.27, 104.08, 104.15, 104.11, 103.81, 103.76, 33.37, 33.27, 33.23, 32.58, 32.49, 32.45, 29.84, 25.63, 25.60; IR (neat) 732 s, 1009 m, 1045 s, 1084 m, 1148 w, 1443 m, 1457 w, 1506 w, 2874 w, 2932 m, 2967 m cm^{-1}.

8-Ethyl-7-methyl-10-(phenylsulfinyl)-1,3(*E*),8,9-decatetraene (17d). Prepared according to the procedure for **17a**. Purification by flash chromatography (10% EtOAc in hexane) gave the allenic sulfoxide **17d** as a mixture of four diastereomers in 70% yield. This was characterized as a mixture without further separation: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 2H), 7.45 (m, 3H), 6.31 (m, 1H), 6.11 (m, 1H), 6.04 (m, 1H), 5.09 (m, 1H), 4.95 (m, 1H), 2.08 (m, 6H), 1.66–1.32 (m, 2H), 1.08–0.98 (m, 6H). Some of the ^{13}C NMR signals were in groups of four due to presence of the four diastereomers; some signals are overlapping: ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.70, 200.66, 200.56, 200.52, 145.17, 145.07, 136.97, 136.92, 136.87, 134.32, 134.27, 134.16, 131.24, 131.22, 131.16, 130.58, 128.97, 128.95, 124.04, 120.68, 120.63, 120.58, 120.53, 114.92, 114.91, 114.83, 114.79, 104.82, 104.74, 104.70, 104.69, 36.33, 36.29, 34.54, 34.38, 34.33, 29.92, 29.88, 29.84, 29.80, 23.50, 23.46, 23.39, 23.35, 19.41, 19.23, 19.16, 12.00; IR (neat) 690 s, 740 m, 897 w, 951 w, 1004 m, 1046 m, 1084 m, 1443 m, 1457 m, 1475 w, 1652 m, 1942 w, 2853 w, 2873 w, 2931 m, 2967 m cm^{-1}; MS (70 eV) m/z 301 (M + 1, 25), 300 (M$^+$, 3), 283 (45),

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175 (100), 145 (27), 133 (67), 125 (42), 105 (67), 91 (69), 77 (39), 67 (78); HRMS exact mass calcd for $C_{19}H_{24}SO$ 300.1547, found 300.1514.

2-[2-(5-Ethyl-7-(phenylsulfonyl)-5,6-heptadienyl)]furan (18a). A solution of 4.24 g of the above sulfoxide **17a** in 55 mL of methanol was cooled to 0 °C. A solution of 8.7 g of OXONE in 55 mL of water was added to the sulfoxide solution. The reaction was complete in 2.5 h. Standard workup and the removal of solvents afforded the crude sulfone. Purification by flash chromatography (10% EtOAc in hexane) gave the allenic sulfone **18a** in 56% yield as a mixture of two diastereomers. The compound was characterized as a mixture of diastereomers without further separation: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 7.5 Hz, 2H), 7.60 (m, 1H), 7.51 (m, 2H), 7.29 (m, 1H), 6.23–6.27 (m, 2H), 5.95 (m, 1H), 2.80 (m, 1H), 2.05 (m, 2H), 2.05 (m, 4H), 1.70 (m, 1H), 1.63 (m, 1H), 1.19 (2d, 6H), 0.95 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.9, 159.5, 141.5, 140.7, 133.1, 129.0, 127.6, 127.5, 118.2, 109.8, 103.9, 02.5, 33.1, 33.0, 32.6, 32.5, 29.8, 29.7, 25.7, 25.6, 19.1, 19.0, 11.6; IR (neat) 688 s, 733 m, 796 m, 926 w, 1010 w, 1084 s, 1146 s, 1305 s, 1318 s, 1373 w, 1447 m, 1952 w, 2875 w, 2933 w, 2968 w cm^{-1}; MS (70 eV) m/z 312 (15), 295 (17), 233 (13), 218 (19), 208 (12), 207 (24), 191 (28), 189 ($M^+ - SO_2$-Ph), 188 (56), 173 (94), 155 (74), 145 (37), 128 (39), 125 (39), 77 (100), 51 (37); HRMS exact mass calcd for $C_{13}H_{17}O$ 189.1279, found 189.1275.

2-[4-Ethyl-2-methyl-6-(phenylsulfonyl)-4,5-hexadienyl]furan (18b). Prepared according to the procedure for **18a**. Purification by flash chromatography (gradient from 5% EtOAc in hexane to 8% EtOAc in hexane) gave the allenic sulfone **18b** as a mixture of two diastereomers in 62% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 7.8 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 7.29 (s, 1H), 6.28 (m, 1H), 6.22 (m, 1H), 5.99 (d, J = 2.75 Hz, 1H), 2.60 (dd, J = 6.1, 14.8 Hz, 1H), 2.49 (dd, J = 7.2, 14.8 Hz, 1H), 2.2–1.9 (m, 5H), 1.09–1.01 (m, 1H), 0.95 (t, J = 7.4 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2, 154.4, 141.0, 133.1, 129.0(2C), 127.5(2C), 116.5, 110.1, 110.0, 106.3, 101.7, 39.3, 34.9, 30.9, 25.5, 19.7, 11.6; IR (neat) 688 m, 738 m, 794 w, 884 w, 928 w, 1008 w, 1083 s, 1146 s, 1178 w, 1306 s, 1318 s, 1372 w, 1447 w, 1458 w, 1506 w, 1506 w, 1594 w, 1952 w, 2876 w, 2908 w, 2933 w, 2967 w cm^{-1}; MS (70 eV) m/z 330 (M^+, 0.1), 205 (4), 189 (100), 161 (49), 145 (10), 119 (15), 105 (17), 91 (22), 77 (21), 51 (7), 41 (12); HRMS exact mass calcd for $C_{19}H_{22}SO_3$ 330.1289, found 330.1294.

2-[4-Ethyl-3-methyl-6-(phenylsulfonyl)-4,5-hexadienyl]furan (18c). Prepared according to the procedure for **18a**. Purification by flash chromatography (10% EtOAc in hexane) afforded the sulfone **18c** as a mixture of two diastereomers in 70% yield. This was characterized as a mixture: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (m, 2H), 7.59 (m, 1H), 7.51 (m, 2H), 7.28 (d, J = 12.3 Hz, 1H), 6.26 (m, 2H), 5.96 (dd, J = 3.0, 16.0 Hz, 1H), 2.64 (t, J = 8.0 Hz, 1H), 2.58 (t, J = 7.9 Hz, 1H), 2.15 (m, 1H), 2.08 (m, 1H), 1.75 (m, 1H), 1.60 (m, 1H), 1.05 (d, J = 7.3 Hz) and 1.03 (d, J = 7.9 Hz, 3H), 0.96 (t, J = 7.0 Hz, 3H) and 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.7, 202.6, 155.5, 155.4, 141.6, 141.6, 140.8, 140.8, 133.2, 133.2, 129.0, 127.6, 127.6, 122.9, 122.8, 110.1, 110.1, 105.0, 104.9, 103.2, 103.1, 36.5, 36.4, 33.3, 33.2, 25.5, 25.4, 23.6, 19.1, 19.0, 11.8, 11.7; IR (neat) 666 m, 688 m, 740 m, 788 m, 1008 w, 1083 s, 1146 s, 1178 w, 1306 s, 1319 s, 1370 w, 1447 m, 1458 w, 1478 w, 1507 w, 1595 w, 1946 w, 2875 w, 2933 w, 2967 m cm^{-1}; MS (70 eV) m/z 189 ($M^+ - SO_2$Ph, 34), 188 (10), 161 (10), 159 (9), 155 (16), 141 (7), 128 (11), 121 (16), 105 (25), 91 (17), 81 (100), 77 (45), 57 (67), 55 (23); HRMS exact mass calcd for $C_{13}H_{17}O$ 189.12789, found 189.1280.

8-Ethyl-7-methyl-10-(phenylsulfonyl)-1,3(*E*),8,9-decatetraene (18d). Prepared according to the procedure for **18a**. Purification by flash chromatography (10% EtOAc in hexane) gave the allenic sulfone **18d** as a mixture of two diastereomers in 68% yield. This was characterized as a mixture without further separation: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (m, 2H), 7.61 (m, 1H), 7.52 (m, 2H), 6.28 (m, 1H), 6.26 (m, 1H), 6.04 (m, 1H), 5.63 (m, 1H), 5.10 (m, 1H), 4.97 (m, 1H), 2.07 (m, 5H), 1.51 (m, 1H), 1.34 (m, 1H), 1.02–0.94 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.73, 141.63, 141.60, 137.04, 136.97, 134.30, 134.19, 133.12, 131.32, 131.28, 138.98, 128.96, 127.55, 127.52, 123.09, 122.99, 115.01, 114.95, 103.02, 102.95, 36.50, 36.46, 34.42, 34.33, 29.84, 29.81, 23.57, 23.53, 19.04, 18.97, 11.69; IR (neat) 688 s, 738 m, 784 m, 907 w, 1005 m, 1083 s, 1146 s, 1319 s, 1370 w, 1445 m, 1652 w, 1947 w, 2878 w, 2933 m, 2968 m cm^{-1}; MS (70 eV) m/z 175 ($M^+ - SO_2$Ph, 64), 159 (25), 145 (35), 133 (39), 105 (48), 91 (68), 79 (66), 77 (100), 67 (71), 51 (29), 41 (28); HRMS exact mass calcd for $C_{13}H_{19}$ 175.1487, found 175.1487.

General Procedure for the Preparation of Alkoxyallylic Sulfones 19. An oven dried three-necked round bottomed flask equipped with a stirring bar, two septa, and a nitrogen inlet was weighed and was charged with a KH suspension in mineral oil. The KH was rinsed with dry THF (3×) and then dried to a powder by blowing nitrogen to get the weight of KH (0.25 equiv). Dry THF (to make 0.25 M solution) and 2 eq. of EtOH were then added. The solution was cooled to 0 °C and the allene (1.0 equiv) was added in one portion. The reaction was monitored by TLC. When the reaction was complete, usually in about 1–2 h, standard workup and removal of the solvents gave the crude product which on purification by flash chromatography or MPLC afforded the pure alkoxyallylic sulfone.

2-[5-Ethoxy-4-ethyl-1-methyl-6-(phenylsulfonyl)-4(*E*)-hexenyl]furan [(*E*)-19a] and 2-[5-Ethoxy-4-ethyl-1-methyl-6-(phenylsulfonyl)-4(*Z*)-hexenyl]furan [(*Z*)-19a]. The crude product was separated by gradient MPLC (hexane to ethyl acetate) to give 44% of the *E* isomer and 33% of the *Z* isomer. Data for (*E*)-**19a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 8.2 Hz, 2H), 7.60 (t, J = 7.5 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.31 (s, 1H), 6.30 (d, J = 1.8 Hz, 1H), 5.94 (d, J = 2.9 Hz, 1H), 3.87 (s, 2H), 3.59 (q, J = 7.0 Hz, 2H), 2.67 (m, 1H), 2.04 (m, 2H), 1.59–1.38 (m, 4H), 1.16 (d, J = 7.0 Hz, 3H), 1.11 (t, J = 7.0 Hz, 3H), 0.83 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 140.7, 138.9, 137.7, 133.9, 133.4, 128.7(2C), 128.7(2C), 109.9, 103.9, 65.0, 55.1, 34.0, 32.9, 27.0, 21.9, 19.3, 15.0, 12.5; IR (neat) 688 s, 731 m, 752 m, 1041 w, 1084 s, 1107 w, 1147 s, 1190 w, 1307 s, 1320 s, 1446 m, 1592 m, 2873 w, 2932 m, 2968 m cm^{-1}; MS (70 eV) m/z 235 ($M^+ - SO_2$Ph, 59), 189 (16), 139 (13), 122 (21), 121 (100), 109 (17), 108 (16), 95 (92), 77 (34), 41 (19); HRMS exact mass calcd for $C_{15}H_{23}O_2$ 235.1698, found 235.1701. Data for (*Z*)-**19a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 7.5 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 7.30 (s, 1H), 6.27 (t, J = 2.2 Hz, 1H), 5.97 (d, J = 3.0 Hz, 1H), 4.00 (s, 2H), 3.50 (m, 2H), 2.72 (sextet, J = 7.0 Hz, 1H), 2.01 (t, 2H), 1.74 (q, 2H), 1.56–1.61 (m, 1H), 1.46–1.38 (m, 1H), 1.22 (d, J = 7.0 Hz, 3H), 1.04 (t, J = 7.0 Hz, 3H), 0.80 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 140.5, 139.1, 137.7, 133.9, 133.5, 128.8(2C), 128.7(2C), 109.8, 103.5, 64.9, 55.2, 33.9, 33.2, 26.0, 23.2, 19.0, 15.0, 12.7; IR (neat) 688 s, 731 m, 779 w, 926 w, 1009 w, 1041 m, 1084 m, 1106 w, 1149 s, 1210 w, 1233 w, 1308 s, 1320 s, 1398 w, 1447 m, 1507 w, 2874 m, 2933 m, 2971 m cm^{-1}; MS (70 eV) m/z 235 ($M^+ - SO_2$Ph, 62), 189 (14), 139 (11), 122 (22), 121 (100), 109 (16), 108 (14), 95 (88), 77 (33), 43 (12), 41 (16); HRMS exact mass calcd for $C_{15}H_{23}O_2$ 235.1698, found 235.1698.

2-[5-Ethoxy-4-ethyl-2-methyl-6-(phenylsulfonyl)-4(*E*)-hexenyl]furan [(*E*)-19b] and 2-[5-Ethoxy-4-ethyl-2-methyl-6-(phenylsulfonyl)-4(*Z*)-hexenyl]furan [(*Z*)-19b]. The crude product was separated by gradient MPLC (hexane to ethyl acetate) to give 37% of the *E* isomer and 30% of the *Z* isomer. Data for (*E*)-**19b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 8.1 Hz, 2H), 7.61 (t, J = 7.3 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.29 (s, 1H), 6.28 (s, 1H), 5.95 (d, J = 2.6 Hz, 1H), 3.98 and 3.96 (ABq, J = 15.0 Hz, 2H), 3.58 (m, 2H), 2.45 (dd, J = 6.3, 14.6 Hz, 1H), 2.36 (dd, J = 7.3, 14.7 Hz, 1H), 2.07 (m, 2H), 1.86 (m, 1H), 1.67 (dd, J = 6.0, 14.5 Hz, 1H), 1.48 (dd, J = 8.8, 14.4 Hz, 1H), 1.10 (t, J = 7.0 Hz, 3H), 0.81 (t, J = 7.5 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.6, 140.9, 138.9, 138.7, 133.5, 132.9, 128.7(4C), 110.1, 106.1, 65.0, 55.3, 36.0, 35.1, 31.2, 21.9, 19.4, 15.0, 12.4; IR (neat) 688 s, 731 m, 1008 w, 1040 m, 1084 m, 1106 w, 1148 s, 1254 w, 1308 s, 1320 s, 1446 m, 2873 w, 2932 m, 2967 m cm^{-1}; MS (70 eV) m/z 235 ($M^+ - SO_2$Ph, 65), 207 (7), 189 (85), 153 (7.3), 125 (9), 122 (13), 121 (27), 109 (34), 108 (18), 91 (11), 81

(100), 77 (65), 55 (31), 53 (24), 43 (25), 41 (27); HRMS exact mass calcd for $C_{15}H_{23}O_2$ 235.1698, found 235.1706. Data for (*Z*)-**19b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 7.29 (d, J = 0.9 Hz, 1H), 6.27 (t, J = 2.4 Hz, 1H), 5.98 (d, J = 2.7 Hz, 1H), 4.04 (s, 2H), 3.48 (m, 2H), 2.54 (dd, J = 5.7, 14.9 Hz, 1H), 2.35 (dd, J = 8.0, 14.9 Hz, 1H), 2.08–1.89 (m, 3H), 1.85 (q, J = 7.5 Hz, 2H), 1.03 (t, J = 7.0 Hz, 3H), 0.82 (t, J = 7.6 Hz, 3H), 0.81 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.3, 140.7, 138.5, 133.5, 132.7, 128.8(2C), 128.6(3C), 110.0, 105.8, 64.6, 55.1, 35.4, 34.9, 31.3, 23.2, 19.7, 14.9, 12.8; IR (neat) 688 s, 737 m, 779 w, 1008 m, 1041 m, 1084 s, 1106 m, 1146 s, 1192 w, 1235 w, 1257 w, 1308 s, 1320 s, 1447 m, 2874 w, 2931 m, 2969 m cm^{-1}; MS (70 eV) m/z 235 ($M^+ - SO_2Ph$, 70), 207 (6), 189 (86), 153 (9), 125 (30), 109 (34), 91 (11), 81 (100), 77 (59), 55 (28), 43 (24), 41 (24); HRMS exact mass calcd for $C_{15}H_{23}O_2$ 235.1698, found 235.1707.

2-[5-Ethoxy-4-ethyl-3-methyl-6-(phenylsulfonyl)-4(*E*)-hexenyl]furan [(*E*)-19c] and 2-[5-Ethoxy-4-ethyl-3-methyl-6-(phenylsulfonyl)-4(*Z*)-hexenyl]furan [(*Z*)-19c]. The crude product was separated by gradient MPLC (hexane to 20% ethyl acetate in hexane) to give 75% of the *E* isomer and 13% of the *Z* isomer. Data for (*E*)-**19c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 8.1 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.2 Hz, 2H), 7.28 (s, 1H), 6.27 (s, 1H), 5.93 (d, J = 3.0 Hz, 1H), 4.00 and 3.89 (ABq, J = 14.9 Hz, 2H), 3.65 (m, 1H), 3.50 (m, 1H), 2.43 (t, J = 7.6 Hz, 2H), 2.24 (sextet, J = 6.9 Hz, 1H), 2.05–1.98 (m, 1H), 1.90–1.83 (m, 1H), 1.55 (m, 2H), 1.09 (dt, J = 6.9, 0.7 Hz, 3H), 0.93 (t, J = 7.4 Hz, 3H), 0.77 (d, J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 140.7, 139.0, 138.4, 136.6, 133.4, 128.7(2C), 128.6(2C), 110.1, 104.7, 64.2, 54.2, 34.4, 32.9, 25.7, 18.7, 18.5, 15.0, 14.1; IR (neat) 688 s, 731 m, 752 w, 1007 w, 1041 w, 1084 s, 1103 w, 1146 s, 1254 w, 1308 s, 1319 s, 1447 m, 2873 w, 2934 m, 2974 m cm^{-1}; MS (70 eV) m/z 376 (M^+, 0.8), 235 ($M^+ - SO_2Ph$, 24), 190 (9), 189 (62), 121 (16), 94 (9), 81 (100), 77 (17), 53 (11); HRMS exact mass calcd for $C_{21}H_{28}O_4S$ 376.1708, found 376.1694. Data for (*Z*)-**19c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 7.3 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.27 (d, J = 0.9 Hz, 1H), 6.25 (dd, J = 2.9, 1.9 Hz), 5.93 (d, J = 2.6 Hz, 1H), 4.05 and 4.01 (ABq, J = 14.9 Hz, 2H), 3.46 (q, J = 7.0 Hz, 2H), 2.83 (sextet, J = 7.1 Hz, 1H), 2.45 (m, 2H), 1.77 (m, 2H), 1.58 (q, J = 7.8 Hz, 2H), 1.00 (t, J = 7.0 Hz, 3H), 0.91 (d, J = 7.0 Hz, 3H), 0.88 (t, J = 7.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 140.6, 139.2, 138.8, 137.0, 133.5, 128.8(2C), 128.7(2C), 110.0, 104.5, 64.8, 55.3, 33.2, 33.1, 26.3 (19.9), 19.0, 14.9, 14.8; IR (neat) 668 s, 689 s, 728 m, 752 m, 1007 m, 1027 m, 1045 m, 1084 s, 1105 m, 1148 s, 1308 s, 1319 s, 1399 w, 1447 m, 1478 w, 1507 w, 2873 w, 2931 m, 2965 m cm^{-1}; MS (70 eV) m/z 235 ($M^+ - SO_2Ph$, 23), 190 (9), 189 (67), 122 (12), 121 (21), 95 (14), 94 (12), 81 (100), 77 (30), 55 (11), 53 (15); HRMS exact mass calcd for $C_{15}H_{23}O_2$ 235.1698, found 235.1707.

2-Ethoxy-3-ethyl-4-methyl-1-(phenylsulfonyl)-2(*E*),7-(*E*),9-decatriene [(*E*)-19d] and 2-Ethoxy-3-ethyl-4-methyl-1-(phenylsulfonyl)-2(*Z*),7(*E*),9-decatriene [(*Z*)-19d]. Separation of the product mixture by MPLC (gradient hexane to 10% EtOAc in hexane) gave the two (*E* and *Z*) isomers in 63% and 12% yield respectively. Data for (*E*)-**19d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 2H), 7.61 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 6.29 (dt, J = 10.2, 17.0 Hz, 1H), 5.97 (dd, J = 10.5, 15.2 Hz, 1H), 5.60 (dt, J = 6.8, 15.2 Hz, 1H), 5.08 (d, J = 16.8 Hz, 1H), 4.96 (d, J = 10.1 Hz, 1H), 4.11 and 3.95 (ABq, J = 14.9 Hz, 2H), 3.64 (m, 1H), 3.51 (m, 1H), 2.20 (sextet, J = 7.0 Hz, 1H), 1.99 (m, 1H), 1.87 (m, 2H), 1.32 (m, 1H), 1.26 (m, 1H), 1.10 (t, J = 7.0 Hz, 3H), 0.93 (t, J = 7.5 Hz, 3H), 0.76 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.1, 138.1, 137.0, 134.7, 133.4, 132.4, 131.1, 128.7(2C), 128.6(2C), 114.9, 64.2, 54.5, 34.8, 34.2, 30.4, 18.8, 18.6, 15.0, 14.1; IR (neat) 687 s, 731 w, 752 m, 781 m, 1005 s, 1041 m, 1083 s, 1101 s, 1148 s, 1255 m, 1320 s, 1372 w, 1409 w, 1445 s, 1650 m, 2873 m, 2932 s, 2972 s cm^{-1}; MS (70 eV) m/z 316 ($M^+ - C_2H_5OH$, 1.2), 281 (12), 253 (5), 221 ($M^+ - SO_2Ph$, 15), 175 (100), 141 (21), 107 (39), 93 (30), 79 (41), 77 (67), 67 (71), 55 (14); HRMS exact mass calcd for $C_{15}H_{25}O$ 221.1896, found 221.1905. Data for (*Z*)-**19d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 7.4 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 6.29 (dt, J = 10.2, 17.0 Hz, 1H), 6.02 (dd, J = 10.5, 15.2 Hz, 1H), 5.67 (dt, J = 6.9, 15.2 Hz, 1H), 5.07 (d, J = 17.0 Hz, 1H), 4.95 (d, J = 10.1 Hz, 1H), 4.05 and 4.01 (ABq, J = 14.8 Hz, 2H), 3.48 (m, 2H), 2.82 (m, 1H), 1.94 (m, 2H), 1.79 (m, 1H), 1.74 (m, 1H), 1.34 (m, 2H), 1.02 (t, J = 7.0 Hz, 3H), 0.88 (t, J = 7.5 Hz, 3H), 0.89 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.5, 138.6, 137.5, 137.3, 135.4, 130.9, 128.72(2C), 128.69(2C), 114.5, 64.8, 55.4, 34.5, 33.0, 30.6, 19.8, 19.0, 14.9, 14.7; IR (neat) 688 s, 752 m, 780 w, 896 m, 951 m, 1005 m, 1044 m, 1084 s, 1106 m, 1149 s, 1202 w, 1308 s, 1320 s, 1400 w, 1447 s, 1477 w, 1652 m, 2873 m, 2932 m, 2968 s cm^{-1}; MS (70 eV) m/z 316 ($M^+ - C_2H_5OH$, 1), 281 (11), 153 (5), 221 ($M^+ - SO_2Ph$, 13), 175 (100), 141 (22), 121 (23), 107 (37), 93 (26), 77 (44), 67 (47); HRMS exact mass calcd for $C_{15}H_{25}O$ 221.1896, found 221.1889.

2-[5-Ethoxy-4-ethyl-1,6-dimethyl-6-(phenylsulfonyl)-4(*E*)-heptenyl]furan [(*E*)-20a]. Compound (*E*)-**19a** (580 mg) was dissolved in 6.2 mL of THF under N_2 and the solution was cooled to −78 °C. *n*-BuLi (0.65 mL, 1.1 equiv) was added and the solution stirred for 5 min. Methyl iodide (109 μL) was added, and the reaction was allowed to warm slowly to room temperature. Standard workup afforded crude product. The product from this reaction was not characterized or purified but was immediately carried on to the next step. Thus, the crude 2-(5-ethoxy-4-ethyl-1-methyl-6-(phenylsulfonyl)-4(*E*)-heptenyl)furan (591 mg) was dissolved in 6.0 mL of THF and 0.6 mL of HMPA. This solution was cooled to −78 °C and 646 μL of n-BuLi (2.58 M) was added. After stirring for 5 min 107 μL of MeI was added and the reaction mixture was allowed to warm up to 25 °C. Standard workup and the removal of solvents under reduced pressure afforded the crude product which on purification by flash chromatography (5% EtOAc in hexane) gave pure (*E*)-**20a** as a colorless oil in 87% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 7.3 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 7.29 (s, 1H), 6.29 (dd, J = 1.9, 2.8 Hz, 1H), 5.96 (d, J = 3.0 Hz, 1H), 3.66 (m, 2H), 2.74 (sextet, J = 6.8 Hz, 1H), 2.14 (q, J = 7.5 Hz, 2H), 1.91 (m, 2H), 1.63 (m, 1H), 1.55 (m, 1H), 1.53 (s, 3H), 1.50 (s, 3H), 1.21 (d, J = 7.0 Hz, 3H), 1.15 (t, J = 7.0 Hz, 3H), 0.98 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 145.4, 140.5, 137.6, 136.9, 133.2, 130.4, 128.4, 109.8, 104.0, 69.8, 68.7, 34.1, 34.4, 26.8, 24.2, 24.2, 23.9, 18.7, 15.1, 12.5; IR (neat) 690 m, 731 s, 760 w, 925 w, 1009 w, 1026 w, 1074 s, 1127 s, 1157 s, 1237 w, 1301 w, 1386 w, 1446 m, 1507 w, 2875 w, 2932 m, 2971 m cm^{-1}; MS (70 eV) m/z 263 ($M^+ - SO_2Ph$, 24), 217 (25), 155 (58), 121 (32), 109 (10), 95 (100), 77 (15), 67 (10), 55 (14), 43 (17), 41 (21); HRMS exact mass calcd for $C_{17}H_{27}O_2$ 263.2011, found 263.2003.

2-[5-Ethoxy-4-ethyl-1,6-dimethyl-6-(phenylsulfonyl)-4(*Z*)-heptenyl]furan [(*Z*)-20a]. Prepared according to the procedure for (*E*)-**20a**. Purification by flash chromatography (5% EtOAc in hexane) gave the pure (*Z*)-**20a** as a colorless oil in 84% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 7.6 Hz, 2H), 7.61 (t, J = 7.3 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 7.30 (s, 1H), 6.28 (dd, J = 2.0, 2.8 Hz, 1H), 6.00 (d, J = 3.0 Hz, 1H), 3.56 (q, J = 7.0 Hz, 2H), 2.82 (sextet, J = 6.8 Hz, 1H), 2.20 (m, 1H), 2.08 (m, 1H), 1.78 (m, 1H), 1.66 (m, 1H), 1.58 (s, 3H), 1.57 (s, 3H), 1.25 (d, J = 7.0 Hz, 3H), 1.07 (t, J = 7.0 Hz, 3H), 0.92 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1, 145.3, 140.5, 137.8, 137.1, 133.3, 130.4(2C), 128.8, 128.4(2C), 109.8, 103.7, 69.9, 68.6, 34.1, 33.6, 28.2, 24.5, 22.9, 18.9, 15.0, 12.6; IR (neat) 690 m, 731 s, 761 w, 801 w, 926 w, 1009 w, 1074 s, 1127 s, 1156 s, 1301 s, 1387 w, 1446 m, 1507 w, 2875 w, 2932 m, 2970 m cm^{-1}; MS (70 eV) m/z 263 ($M^+ - SO_2Ph$, 25), 217 (26), 155 (27), 121 (37), 109 (11), 95 (100), 77 (17), 67 (10), 55 (13), 43 (16), 41 (22); HRMS exact mass calcd for $C_{17}H_{27}O_2$ 263.2011, found 263.2017.

2-[5-Ethoxy-4-ethyl-2,6-dimethyl-6-(phenylsulfonyl)-4(*E*)-heptenyl]furan [(*E*)-20b]. Prepared according to the procedure for (*E*)-**20a**. Purification by flash chromatography (5% EtOAc in hexane) gave the pure product as a colorless oil in 85% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 2H), 7.61 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.30 (s, 1H), 6.28 (d, J = 1.8 Hz, 1H), 6.00 (d, J = 2.3 Hz, 1H), 3.64 (m, 2H), 2.61 (dd, J = 5.4, 14.8 Hz, 1H), 2.44 (m, 1H), 2.27 (m,

3H), 2.17 (m, 1H), 2.08 (m, 1H), 1.59 (s, 3H), 1.58 (s, 3H), 1.14 (t, J = 7.0 Hz, 3H), 0.99 (t, J = 7.5 Hz, 3H), 0.89 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2, 146.5, 140.8, 137.3, 136.5, 133.3, 130.5(2C), 128.5(2C), 110.1, 106.0, 70.0, 68.8, 35.4, 35.1, 30.8, 25.4, 24.9, 23.0, 19.3, 15.1, 12.4; IR (neat) 690 s, 727 s, 760 m, 1007 m, 1027 w, 1074 s, 1106 m, 1127 s, 1156 s, 1301 s, 1387 w, 1445 m, 2876 w, 2931 m, 2970 m cm^{-1}; MS (70 eV) m/z 263 (M^+ − SO_2Ph, 63), 217 (41), 189 (9), 155 (58), 109 (26), 81 (100), 55 (29); HRMS exact mass calcd for $C_{17}H_{27}O_2$ 263.2011, found 263.2006.

2-[5-Ethoxy-4-ethyl-2,6-dimethyl-6-(phenylsulfonyl)-4(*Z*)-heptenyl]furan [(*Z*)-20b]. Prepared according to the procedure for (*E*)-**20a**. Purification by flash chromatography (5% EtOAc in hexane) gave the pure product as a colorless oil in 88% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 7.3 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.6 Hz, 3H), 7.30 (d, J = 1.0 Hz, 1H), 6.28 (dd, J = 1.9, 2.8 Hz, 1H), 6.01 (d, J = 2.7 Hz, 1H), 3.61 (dd, J = 7.4, 14.0 Hz, 2H), 2.64 (dd, J = 5.3, 14.7 Hz, 1H), 2.43 (m, 2H), 2.22 (m, 2H), 2.11 (m, 2H), 1.57 (s, 3H), 1.56 (s, 3H), 1.13 (t, J = 7.0 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H), 0.91 (d, J = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.3, 146.2, 140.8, 137.5, 136.7, 133.3, 130.4(2C), 128.5(2C), 110.0, 105.9, 69.9, 68.4, 36.7, 35.6, 30.8, 25.1, 25.0, 23.1, 19.8, 15.1, 12.9; IR (neat) 691 m, 731 w, 761 w, 1008 m, 1026 w, 1075 s, 1090 w, 1108 m, 1127 s, 1156 s, 1268 w, 1301 s, 1387 w, 1446 m, 1456 w, 1506 w, 2876 w, 2930 m, 2970 m cm^{-1}; MS (70 eV) m/z 263 (M^+ − SO_2Ph, 46), 217 (37), 189 (12), 175 (4), 155 (52), 141 (11), 125 (14), 109 (26), 95 (16), 81 (100), 55 (38); HRMS exact mass calcd for $C_{17}H_{27}O_2$ 263.2011, found 263.2017.

2-[5-Ethoxy-4-ethyl-3,6-dimethyl-6-(phenylsulfonyl)-4(*E*)-heptenyl]furan [(*E*)-20c)]. Prepared according to the procedure for (*E*)-**20a**. Purification by MPLC (5% EtOAc in hexane) gave (*E*)-**20c** as a colorless oil in 95% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 7.3 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 7.28 (d, J = 0.8 Hz, 1H), 6.27 (dd, J = 0.8, 2.6 Hz, 1H), 6.00 (d, J = 2.6 Hz, 1H), 3.69 (dq, J = 1.1, 7.0 Hz, 2H), 3.37 (sextet, J = 8.0 Hz, 1H), 2.79 (m, 1H), 2.61 (m, 1H), 2.06 (m, 2H), 1.74 (m, 2H), 1.53 (s, 3H), 1.45 (s, 3H), 1.15 (t, J = 7.0 Hz, 3H), 1.10 (t, J = 7.6 Hz, 3H), 1.09 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 146.2, 142.7, 140.5, 137.6, 133.2, 130.4, 128.4, 110.0, 104.6, 69.8, 68.3, 33.8, 33.6, 26.0, 25.2, 25.1, 20.6, 18.0, 15.4, 13.9; IR (neat) 691 m, 728 s, 761 m, 969 w, 1007 m, 1026 m, 1074 s, 1103 m, 1128 s, 1156 s, 1229 w, 1301 s, 1371 w, 1389 m, 1446 m, 1507 w, 1596 w, 2874 m, 2932 m, 2971 m cm^{-1}; MS (70 eV) m/z 263 (M^+ − SO_2Ph, 21), 219 (5), 139 (12), 135 (5), 121 (7), 95 (10), 83 (7), 81 (100), 77 (14), 57 (14), 43 (20); HRMS exact mass calcd for $C_{17}H_{27}O_2$ 263.2011, found 263.2007.

2-[5-Ethoxy-4-ethyl-3,6-dimethyl-6-(phenylsulfonyl)-4(*Z*)-heptenyl]furan [(*Z*)-20c]. Prepared according to the procedure for (*E*)-**20a**. Purification by MPLC (5% EtOAc in hexane) gave (*Z*)-**20c** as a colorless oil in 81% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, J = 0.8, 8.0 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 7.29 (t, J = 1.2 Hz, 1H), 7.26 (dd, J = 1.9, 3.0 Hz, 1H), 5.99 (d, J = 3.1 Hz, 1H), 2.55 (m, 2H), 2.92 (sextet, J = 7.2 Hz, 1H), 2.63 (m, 2H), 2.30 (sextet, J = 7.5 Hz, 1H), 2.20 (sextet, J = 7.5 Hz, 1H), 1.77 (m, 1H), 1.70 (m, 1H), 1.64 (s, 3H), 1.61 (s, 3H), 1.09 (d, J = 7.0 Hz, 1H), 1.04 (t, J = 7.5 Hz, 3H), 1.03 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 146.0, 141.8, 140.6, 137.4, 133.3, 130.4(2C), 128.4(2C), 110.0, 104.7, 70.8, 68.9, 34.9, 33.9, 26.5, 24.9, 24.8, 19.4, 19.3, 15.8, 15.0; IR (neat) 691 s, 724 s, 920 w, 1007 w, 1025 w, 1073 s, 1107 m, 1127 s, 1155 s, 1195 w, 1235 w, 1301 s, 1387 w, 1446 m, 1489 w, 1507 w, 1597 w, 2875 w, 2930 m, 2973 m cm^{-1}; MS (70 eV) m/z 264 (4), 263 (M^+ − SO_2Ph, 24), 219 (6), 163 (5), 139 (13), 135 (6), 121 (8), 95 (13), 81 (100), 77 (19), 69 (11), 55 (11), 53 (10), 43 (13); HRMS exact mass calcd for $C_{17}H_{27}O_2$ 263.2011, found 263.2006.

2-Ethoxy-3-ethyl-1,1,4-trimethyl-1-(phenylsulfonyl)-2(*E*),7(*E*),9-decatriene [(*E*)-20d]. Prepared according to the procedure for (*E*)-**20a**. Purification by chromatography on silica gel using the Chromatotron (3% EtOAc in hexane) afforded pure (*E*)-**20d** in 83% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 7.6 Hz, 2H), 7.61 (t, J = 7.3, Hz, 1H), 7.51 (t, J = 7.8 Hz, 2H), 6.32 (dt, J = 10.3, 17.0 Hz, 1H), 6.08 (dd, J = 10.6, 15.2 Hz, 1H), 1.21 (dt, J = 6.9, 15.2 Hz, 1H), 5.09 (d), 17.0 (1), 4.95 (d, J = 10.1 Hz, 1H), 3.69 (m, 2H), 3.31 (m, 1H), 2.25 (m, 1H), 2.06 (m, 3H), 1.54 (s, 3H), 1.52 (s, 3H), 1.50 (m, 2H), 1.15 (t, J = 7.0 Hz, 3H), 1.09 (t, J = 7.4 Hz, 3H), 1.05 (d, J = 6.69 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.9, 143.0, 137.6, 137.3, 135.5, 133.1, 130.7, 130.3(2C), 128.4(2C), 114.4, 69.8, 68.2, 34.6, 33.9, 30.5, 25.2, 25.1, 20.6, 17.9, 15.4, 13.8; IR (neat) 643 s, 691 s, 722 s, 760 s, 895 m, 930 w, 951 m, 969 w, 1004 s, 1026 s, 1074 s, 1098 s, 1128 s, 1156 s, 1197 w, 1226 m, 1301 s, 1371 m, 1388 s, 1446 s, 1602 w, 1651 m, 2874 s, 2931 s, 2970 s, 3068 w, 3084 w cm^{-1}; MS (70 eV) m/z 249 (M^+ − SO_2Ph, 19), 203 (8), 151 (13), 149 (22), 139 (26), 135 (24), 121 (26), 109 (24), 107 (27), 95 (33), 77 (36), 69 (48), 67 (100), 55 (42), 48 (38), 41 (65); HRMS exact mass calcd for $C_{17}H_{29}O$ 249.2218, found 249.2214.

2-Ethoxy-3-ethyl-1,1,4-trimethyl-1-(phenylsulfonyl)-2(*Z*),7(*E*),9-decatriene [(*Z*)-20d]. Prepared according to the procedure for (*E*)-**20a**. Purification by silica gel chromatography using the Chromatotron (4% EtOAc in hexane) afforded pure (*E*)-**20d** in 86% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 7.4 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 6.30 (dt, J = 10.3, 17.0 Hz, 1H), 6.07 (dd, J = 10.3, 15.2 Hz, 1H), 5.72 (dt, J = 6.9, 15.2 Hz, 1H), 5.08 (d, J = 17.0 Hz, 1H), 4.95 (d, J = 10.1 Hz, 1H), 3.60 (m, 2H), 2.89 (sextet, J = 7.0 Hz, 1H), 2.28 (sextet, J = 7.5 Hz, 1H), 2.17 (m, 2H), 2.06 (m, 1H), 1.63 (s, 3H), 1.60 (s, 3H), 1.52 (m, 1H), 1.45 (m, 1H), 1.08 (t, J = 7.0 Hz, 3H), 1.06 (d, J = 7.2 Hz, 3H), 1.03 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.7, 142.1, 137.5, 137.2, 135.1, 133.1, 131.0, 130.3(2C), 128.3(2C), 114.6, 70.7, 68.9, 35.2, 34.8, 30.9, 24.9, 24.7, 19.3, 19.2, 15.7, 14.9; IR (neat) 690 s, 724 s, 759 m, 896 m, 950 m, 1004 s, 1025 m, 1073 s, 1107 s, 1127 s, 1155 s, 1196 w, 1301 s, 1387 m, 1446 s, 1489 m, 1564 w, 1602 w, 1650 w, 2878 m, 2929 s, 2972 s cm^{-1}; MS (70 eV) m/z 249 (M^+ − SO_2Ph, 69), 348 (48), 219 (48), 205 (25), 167 (26), 139 (100), 125 (42), 107 (26), 91 (28), 77 (98), 67 (58), 51 (31); HRMS exact mass calcd for $C_{17}H_{29}O$ 249.2218, found 249.2216.

Ethyl 3-(2-Furanyl)-2-butenoate. To a suspension of 4.36 g of 60% NaH in 30 mL of dry benzene was added 21.62 mL of triethyl phosphonoacetate while maintaining the temperature below 35 °C. The resulting solution was stirred at 25 °C for 30 min. 2-Acetylfuran **22** (10 g) was added to this mixture and stirred for 4 h at 25 °C. The reaction was worked up by addition to water and extraction with benzene. The benzene layers were washed with water and brine and then dried over $MgSO_4$. The residue after the removal of solvents was distilled under reduced pressure to afford the keto ester as a mixture of two isomers in 87% yield. This compound was characterized as the mixture of diastereomers without further separation, bp 99−101 °C/0.8 mmHg. ^{1}H NMR spectrum of this compound was too complicated to report the integration of each set of signals due to the overlap of the signals from each isomer. Therefore only the chemical shift and the multiplicity are reported: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (s), 7.30 (q, J = 3.4 Hz), 6.64 (d, J = 3.3 Hz), 6.45 (m), 6.37 (s), 5.73 (s), 4.15−4.27 (m), 2.45 (d, J = 1.1 Hz), 2.20 (d, J = 1.2 Hz), 1.30 (2t, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.5, 167.4, 166.4, 154.6, 151.8, 144.1, 142.5, 142.2, 138.9, 115.1, 115.0, 112.7, 112.1, 111.9, 111.4, 60.3, 60.0, 22.9, 14.9, 14.6; IR (neat) 745 m, 1022 m, 1045 m, 1094 m, 1158 s, 1176 s, 1242 m, 1281 m, 1345 m, 1366 m, 1447 w, 1482 m, 1825 s, 1709 s, 2979 w, 2955 w, 2980 w cm^{-1}. Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.64; H, 6.72. Found: C, 66.62; H, 6.65.

3-(2-Furanyl)butyric Acid (23). Fourteen grams of the above keto ester was added to a solution of 8.71 g of KOH in 50 mL of water, and the mixture was refluxed for 3 h. The resulting solution was hydrogenated in Parr apparatus using 200 mg of 5% Pd/C catalyst and at 50 psi of H_2 pressure for 8 h. After the hydrogenation was complete the solution was filtered through Celite and the filtrate was acidified with 2 N HCl. Extraction of the acid with ether and removal of solvents gave crude acid which on bulb-to-bulb distillation gave pure acid **23** in 90% yield, bp 100 °C/0.2 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (dd, J = 0.8, 1.8 Hz, 1H), 6.28 (dd, J = 1.8, 3.1 Hz, 1H), 6.03 (dt, J = 0.8, 1.6 Hz, 1H), 3.36 (sextet, J = 7.1 Hz, 1H), 2.79 (dd, J = 6.3, 15.8 Hz, 1H), 2.50 (dd, J = 8.1,

15.8 Hz, 1H), 1.32 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.7, 158.1, 141.1, 110.0 103.9, 40.1, 29.7, 18.7; IR (neat) 733 m, 918 w, 935 w, 1011 m, 1148 m, 1174 w, 1213 w, 1248 w, 1295 m, 1413 m, 1507 m, 1710 s, 2881 m, 2936 m, 2974 m, 3117 br m cm^{-1}. Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.35; H, 6.46.

3-(2-Furanyl)butan-1-ol. LAH (2.87 g) was weighed into a three-necked flask, and 100 mL of dry THF was carefully added. The suspension was cooled to 0 °C, and 10.6 g of the acid **23** dissolved in 20 mL of THF was added through a dropping funnel. The funnel was rinsed with another 20 mL of THF, and the reaction mixture was stirred for 2 h at 25 °C. When the reaction was complete it was cooled to 0 °C and 2.9 mL of water, 2.9 mL of 15% NaOH solution, and 8.7 mL of water was added. The mixture was stirred for 1 h. The precipitate was filtered, and the filtrate was evaporated under reduced pressure to remove solvents. The residue was distilled under reduced pressure to give the pure alcohol as a colorless liquid in 79% yield: bp 78–80 °C/1 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (dd, J = 0.7, 1.7 Hz, 1H), 6.28 (dd, J = 1.8, 3.0 Hz, 1H), 6.00 (d, J = 3.1 Hz, 1H), 3.64 (br, s, Hz, 1H), 3.00 (sextet, J = 7.1 Hz, 1H), 1.91–1.67 (m, 4H), 1.27 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 140.7, 109.8, 103.6, 60.5, 38.5, 29.7, 19.2; IR (neat) 731 s, 800 m, 918 m, 928 m, 1010 s, 1043 s, 1149 s, 1171 w, 1334 w, 1376 w, 1455 m, 1507 s, 1592 w, 2876 m, 2934 s, 2967 s, 3328 br s cm^{-1}. Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.46; H, 8.42.

3-(2-Furanyl)iodobutane (24). 3-(2-Furanyl)butanol was tosylated by treating with tosyl chloride and pyridine in $CHCl_3$.[28] To a solution of 14.33 g of 3-(2-furyl)butyl tosylate in 97 mL of dry acetone was added 14.62 g of NaI and stirred for 48 h at 25 °C. After the reaction was complete the reaction mixture was poured into water and extracted with pentane (2×). The pentane layers were washed with water and brine. Drying over $MgSO_4$ and removal of solvents gave the crude iodide which on Kugelrohr distillation gave pure iodide **24** as a colorless liquid in 92% yield: bp 68 °C/0.4 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (t, J = 0.9 Hz, 1H), 6.28 (t, J = 2.6 Hz, 1H), 6.30 (d, J = 3.1 Hz, 1H), 3.21–2.95 (m, 3H), 2.15 (sextet, J = 6.3 Hz, 1H), 2.03 (sextet, J = 6.2 Hz, 1H), 1.26 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 141.0, 109.0, 104.4, 39.5, 34.0, 18.6, 4.3; IR (neat) 732 s, 801 m, 884 w, 926 m, 1008 m, 1080 w, 1148 m, 1173 m, 1244 m, 1329 w, 1451 m, 1506 m, 1593 w, 2874 w, 2931 m, 2967 m cm^{-1}. Anal. Calcd for $C_8H_{11}OI$: C, 38.42; H, 4.43. Found: C, 38.64; H, 4.26.

6-(2-Furanyl)-3-heptanone (15a). A solution of 2.94 mL of diisopropylamine in 84 mL THF was cooled to 0 °C. n-BuLi (8.4 mL, 1.1 equiv) was added, and the solution was stirred for 10 min at 0 °C. Then the solution was cooled to −78 °C, and 3.0 g of 2-(1-ethoxyethoxy)butanenitrile[14] was added. The reaction mixture was stirred for 10 min at −78 °C, and 4.75 g of 3-(2-furanyl)iodobutane (**24**) was added. The mixture was allowed to come to 0 °C and stirred for 1 h. The reaction was quenched by adding water and extracting with ether (2×). Solvents were removed under reduced pressure. The residue was dissolved in 60 mL of methanol and stirred with 5 mL of 5% H_2SO_4 for 4 h at 0 °C. Brine was added, and the mixture was extracted with 150 mL of ether. The layers were separated and the ether layer was shaken with 100 mL of 1 N NaOH for 5 min. The ether layer was washed with water (2×) and brine and dried over anhydrous $MgSO_4$. The residue from the removal of the solvents was distilled (Kugelrohr) to give the pure ketone **15a** as a colorless liquid in 95% yield: bp 106–108 °C/20 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (dd, J = 0.8, 1.8 Hz, 1H), 6.27 (dd, J = 1.8, 3.1 Hz, 1H), 5.97 (dt, J = 0.7, 1.3 Hz, 1H), 2.83 (sextet, J = 7.0 Hz, 1H), 2.35 (m, 4H), 1.87 (q, J = 7.0 Hz, 2H), 1.24 (d, J = 7.0 Hz, 3H), 1.03 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.2, 159.5, 140.7, 109.8, 103.9, 39.7, 35.8, 32.5, 29.6, 19.1, 7.7; IR (neat) 732 s, 800 m, 884 w, 925 m, 1010 m, 1119 m, 1148 m, 1230 w, 1376 m, 1413 m, 1459 m, 1507 m, 1590 w, 1715 s, 2877 m, 2937 m, 2972 m cm^{-1}. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.18; H, 8.76.

Ethyl 3-(2-Furanyl)-2-methylpropenoate. Ten grams of (60%) NaH and 63 mL of dry benzene were added to a 250 mL three-necked flask fitted with a condenser and a thermometer. Triethyl phosphonopropionate (53.5 mL) was added slowly using a dropping funnel while stirring vigorously. The temperature was maintained between 30–35 °C. After completion of the addition the mixture was stirred for 1 h at 25 °C and 20 g of furfural **56** was added while maintaining the temperature between 20–30 °C. The mixture was then stirred for 6 h at 25 °C. The reaction mixture was poured into water and extracted with benzene (3×). The benzene layers were washed with water and brine and dried over $MgSO_4$. After the removal of the solvents the residue was distilled under reduced pressure to give the product in 97% yield: bp 90–92°/0.3 mmHg; ^{1}H NMR (500 MHz) δ 7.51 (s, 1H), 7.44 (s, 1H), 7.59 (d, J = 3.3 Hz, 1H), 6.48 (dd, J = 1.7, 2.8 Hz, 1H), 6.24 (q, J = 7.1 Hz, 2H), 2.22 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz) δ 168.4, 151.9, 143.8, 125.5, 125.0, 114.5, 111.9, 60.7, 14.2, 13.9; IR (neat) 743 m, 1025 w, 1109 m, 1152 w, 1180 m, 1207 s, 1254 s, 1268 s, 1366 w, 1479 w, 1636 w, 1703 s, 2981 w cm^{-1}. Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.76; H, 6.58.

3-(2-Furanyl)-2-methylpropanoic Acid (28). Prepared according to the procedure for **23**. Purification by flash chromatography (15% EtOAc in hexane) afforded the acid **28** in 97% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (s, 1H), 6.28 (s, 1H), 1.06 (d, J = 2.5 Hz, 1H), 3.06 (dd, J = 6.5, 14.9 Hz, 1H), 2.85 (sextet, J = 7.0 Hz, 1H), 2.75 (dd, J = 7.5 Hz, 1H), 1.21 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.3, 152.9, 141.4, 110.2, 106.6, 38.7, 31.4, 16.5; IR (neat) 733 m, 934 w, 1009 w, 1147 w, 1332 w, 1254 w, 1296 w, 1464 w, 1708 s, 2938 w, 2979 w, 3140 br w cm^{-1}. Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.48; H, 6.53.

3-(2-Furanyl)-2-methylpropanol. Prepared from **28** according to the procedure for 3-(2-furyl)butan-1-ol. Distillation under reduced pressure using a short path distillation apparatus to obtain the alcohol as a colorless liquid in 80% yield: bp 75 °C/0.4 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, J = 0.9 Hz, 1H), 6.28 (t, J = 2.4 Hz, 1H), 6.01 (d, J = 3.0 Hz, 1H), 3.48 (m, 2H), 2.72 (dd, J = 6.2, 14.9 Hz, 1H), 2.52 (dd, J = 7.5, 14.5 Hz, 1H), 2.01 (octet, J = 6.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.6, 140.9, 110.1, 106.0, 67.3, 35.4, 31.5, 16.4; IR (neat) 724 s, 797 m, 986 w, 1008 s, 1035 s, 1147 m, 1381 w, 1432 w, 1457 m, 1507 m, 1595 w, 2874 m, 2930 m, 2958 m, 3354 br s cm^{-1}. Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.47; H, 8.52.

3-(2-Furanyl)-2-methyliodopropane (29). Prepared from the above according to the procedure for **24**. The crude iodide was dissolved in 50 mL of CH_2Cl_2 and passed through a silica gel plug. Evaporation of CH_2Cl_2 and short path distillation under reduced pressure gave pure iodide in 94% yield: bp 72–74 °C/0.45 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, J = 1.1 Hz, 1H), 6.27 (dd, J = 2.0, 2.9 Hz, 1H), 6.06 (d, J = 3.0 Hz, 1H), 3.22 (dd, J = 4.9, 9.7 Hz, 1H), 3.12 (dd, J = 9.7, 5.6 Hz, 1H), 2.68 (dd, J = 7.0, 14.9 Hz, 1H), 2.59 (dd, J = 6.6, 14.9 Hz, 1H), 1.85 (octet, J = 6.6 Hz, 1H), 1.01 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 141.2, 110.1, 106.6, 34.7, 34.1, 20.5, 16.4; IR (neat) 726 s, 738 s, 795 m, 801 m, 928 w, 1006 s, 1073 w, 1079 w, 1147 s, 1194 m, 1251 w, 1321 w, 1377 w, 1426 w, 1454 w, 1506 m, 1595 w, 2868 w, 2927 w, 2960 m cm^{-1}. Anal. Calcd for $C_8H_{11}OI$: C, 38.42; H, 4.43. Found: C, 38.57; H, 4.34.

6-(2-Furanyl)-5-methyl-3-hexanone (15b). Prepared according to the procedure for **15a**. The residue resulting from the removal of the solvents was distilled (Kugelrohr) to give the pure ketone as a colorless liquid in 79% yield: bp 110 °C/10 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (s, 1H), 6.27 (t, J = 2.4 Hz, 1H), 5.99 (d, J = 2.9 Hz, 1H), 2.56 (d, J = 6.5 Hz, 2H), 2.35–3.45 (m, 4H), 2.23 (q, J = 8.3 Hz, 1H), 1.02 (t, J = 7.4 Hz, 3H), 0.93 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz,

(28) Kabalka, G. W.; Varma, M.; Varma, M.; Varma, R. S.; Srivastava, P. C.; Knapp, F. F., Jr. *J. Org. Chem.* **1986**, *51*, 2386.

(29) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

$CDCl_3$) δ 210.8, 154.3, 141.0, 110.0, 106.3, 48.6, 36.3, 34.7, 28.9, 19.8, 7.6; IR (neat) 7.5 w, 726 m, 733 m, 738 m, 928 w, 1007 m, 1112 w, 1147 m, 1776 m, 1413 w, 1459 w, 1507 m, 1713 s, 2879 w, 2911 w, 2937 m, 2960 m, 2974 m cm^{-1}. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.26; H, 8.79.

2-(2-Furyl)-1-ethanol. A solution of 59 mL of (2.60 M) n-BuLi in 147 mL of THF was cooled to −25 °C and 10 g of furan was added. The solution was stirred at −15 °C for 4 h, and 10 mL of ethylene oxide was added. Stirring was continued for another 1 h at −15 °C and 12 h at 25 °C. The solution was poured into ice−water and extracted with ether (2×). The ether layers were washed with water followed by brine and dried over $MgSO_4$. Evaporation of the solvents and the Kugelrohr distillation of the residue gave the product in 52% yield: bp 80 °C/0.8 mmHg; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, J = 0.9 Hz, 1H), 6.28 (dd, J = 1.8, 3.1 Hz, 1H), 6.08 (dt, J = 0.8, 3.1 Hz, 1H), 3.82 (t, J = 6.2 Hz, 2H), 2.86 (t, J = 6.4 Hz, 2H), 2.53 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 141.3, 110.2, 106.3, 60.8, 31.4; IR (neat) 731 s, 803 m, 851 w, 886 m, 925 m, 1002 s, 1024 s, 1048 s, 1080 m, 1145 s, 1387 w, 1422 m, 1472 w, 1507 s, 1598 m, 2887 m, 2928 m, 2957 m, 3119 m, 3354 br s cm^{-1}. Anal. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.44; H, 6.99.

2-(2-Furyl)ethyl Iodide. Prepared according to the procedure for **24**. After the removal of pentane, dry benzene was added to it and the benzene was distilled off to remove any water contaminating the iodide. ^1H NMR (500 MHz, $CDCl_3$) δ 7.33 benzene impurity, 7.31 (dd, J = 1.9, 3.2 Hz, 1H), 6.28 (dd, J = 1.9, 3.2 Hz, 1H), 6.09 (dd, J = 0.6, 3.2 Hz, 1H), 3.32 (t, J = 7.5 Hz, 2H), 3.17 (t, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.7, 141.4, 128.2 (benzene), 110.2, 106.3, 32.5, 1.9; IR (neat) 731 s, 884 w, 921 w, 1008 s, 1106 w, 1147 m, 1170 m, 1189 w, 1209 w, 1223 w, 1264 w, 1421 w, 1505 m, 1594 w, 2963 w cm^{-1}.

6-(2-Furanyl)-4-(methoxycarbonyl)-3-hexanone (32). To a suspension of 1.62 g of (60%) NaH in 8 mL of THF, 5.27 g of methyl 3-oxopentanoate (**30**) was added dropwise at 25 °C. After the addition was complete the solution was stirred for another 1 h. (2-Furyl)ethyl iodide (9 g) was then added and the solution was refluxed for 18 h. The crude product resulting from the standard workup and the removal of solvents was purified by flash chromatography (1% EtOAc in hexane) to give 51% of the pure keto ester **32**. ^1H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, J = 0.7 Hz, 1H), 6.27 (dd, J = 1.7, 3.0 Hz, 1H), 6.00 (d, J = 3.1 Hz, 1H), 3.71 (s, 3H), 3.50 (t, J = 7.3 Hz, 1H), 2.64 (t, J = 7.4 Hz, 2H), 2.58 (q, J = 7.2 Hz, 1H), 2.49 (q, J = 7.2 Hz, 1H), 2.19 (q, J = 7.3 Hz, 2H), 1.05 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.3, 169.9, 154.1, 141.1, 110.0, 105.6, 57.2, 52.2, 35.3, 26.4, 25.4, 7.4; IR (neat) 735 m, 1008 m, 1035 w, 1077 m, 1110 m, 1152 m, 1177 m, 1212 m, 1232 m, 1262 m, 1353 m, 1436 m, 1508 m, 1597 m, 1645 w, 1716 s, 2919 m, 2954 m, 2978 m cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.15; H, 6.98.

6-(2-Furanyl)-4-(methoxycarbonyl)-4-methyl-3-hexanone (33). Keto ester **32** (448 mg) was slowly added to a suspension of 80 mg of (60%) NaH in 10 mL of THF and the solution was stirred at 25 °C for 1 h. Methyl iodide (700 mg) was then added, and stirring was continued for another 0.5 h. The residue resulting from standard workup and the removal of solvents under reduced pressure was purified by flash chromatography (2% EtOAc in hexane) to give **33** in 95% yield: ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, J = 1.8 Hz, 1H), 6.26 (dd, J = 1.9, 3.1 Hz, 1H), 5.99 (t, J = 1.8 Hz, 1H), 3.71 (s, 3H), 2.53 (m, 2H), 2.47 (dq, J = 7.3, 3.0 Hz, 2H), 2.26 (m, 1H), 2.12 (m, 1H), 1.40 (s, 3H), 1.06 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.8, 173.2, 154.7, 140.9, 110.1, 104.9, 58.8, 52.3, 33.0, 31.4, 23.1, 18.8, 8.0; IR (neat) 734 w, 1009 m, 1074 w, 1114 m, 1147 m, 1168 m, 1199 m, 1233 m, 1260 m, 1346 w, 1461 m, 1508 w, 1597 w, 1713 s, 1744 s, 2881 w, 2942 w, 2982 w cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.65; H, 7.51.

6-(2-Furyl)-4-methyl-3-hexanone (15c). To a solution of 4.7 g of **33** in 78 mL of DMF was added 1.67 g of LiCl and 0.36 mL of water. The solution was refluxed for 18 h. The reaction was worked up by addition water and extracting with pentane (2×). The pentane layers were washed with water followed by brine and dried over $MgSO_4$. The residue resulting from the removal of solvents was distilled (Kugelrohr) to give the pure ketone **15c** in 80% yield: bp 100 °C/2 mmHg; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29 (t, J = 0.9 Hz, 1H), 6.26 (t, J = 2.4 Hz, 1H), 5.97 (dd, J = 0.8, 2.3 Hz, 1H), 2.60 (t, J = 7.6 Hz, 2H), 2.55 (sextet, J = 6.9 Hz, 1H), 2.44 (dqq, J = 0.7, 7.3, 17.7 Hz, 2H), 2.03 (ddq, J = 0.7, 7.3, 13.9 Hz, 1H), 1.65 (ddq, J = 0.7, 7.3, 13.9 Hz, 1H), 1.09 (d, J = 7.0 Hz, 3H), 1.03 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.6, 155.2, 140.8, 110.0, 105.0, 44.9, 34.2, 31.0, 25.5, 16.4, 7.6; IR (neat) 730 m, 1008 m, 1104 w, 1146 w, 1377 w, 1461 m, 1508 w, 1597 w, 1712 s, 2878 m, 2937 s, 2972 s cm^{-1}. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.25; H, 8.82.

4-(Methoxycarbonyl)-7(*E*),9-decadien-3-one (35). To a suspension of 3.43 g of (60%) NaH in 170 mL of THF was added 11.16 g of methyl 3-oxopentanoate (**30**) at 25 °C. It was stirred for 0.5 h until a clear solution was obtained. Compound **34** (17.9 g) was then added and the mixture was refluxed for 18 h. Standard workup and the removal of solvents gave a crude product which on purification by flash chromatography (gradient hexane to 5% EtOAc in hexane) followed by distillation under reduced pressure gave **35** in 86% yield: ^1H NMR (500 MHz, $CDCl_3$) δ 6.28 (dt, J = 10.3, 17.0 Hz, 1H), 6.04 (dd, J = 10.5, 15.2 Hz, 1H), 5.62 (dt, J = 7.0, 15.2 Hz, 1H), 5.11 (d, J = 17.0, 15.2 Hz, 1H), 4.99 (d, J = 10.2 Hz, 1H), 3.72 (s, 3H), 3.48 (t, J = 7.2 Hz, 1H), 2.60 (dq, J = 7.2, 18.2 Hz, 1H), 2.48 (dq, J = 7.2, 18.2 Hz, 1H), 2.08 (m, 2H), 1.98 (m, 2H), 1.06 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.5, 170.1, 132.9, 132.2, 57.6, 52.2, 35.3, 30.1, 27.4, 7.5; IR (neat) 901 m, 955 w, 975 w, 1006 m, 1076 w, 1110 m, 1148 m, 1174 m, 1211 m, 1229 m, 1259 m, 1352 m, 1436 m, 1448 m, 1603 w, 1652 w, 1717 s, 1745 s, 2883 w, 2908 w, 2940 m, 2953 m, 2976 m cm^{-1}; MS (70 eV) m/z 211 (M^+ + 1, 15), 210 (M^+, 76), 179 (17), 133 (9), 101 (16), 80 (100), 67 (15), 57 (49), 41 (16); HRMS exact mass calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1239.

4-(Methoxycarbonyl)-4-methyl-7(*E*),9-decadien-3-one. Prepared according to the procedure for **33**. One gram of the crude product was purified by MPLC (gradient hexane to 20% EtOAc in hexane). Although it was homogeneous on TLC, gas chromatography revealed that it was a 90:10 mixture of the product keto ester and an unknown compound. Attempts to isolate pure product failed. Therefore it was characterized as a mixture. Signals from the 10% impurity are not listed here: ^1H NMR (500 MHz, $CDCl_3$) δ 6.28 (dt, J = 10.3, 17.0 Hz, 1H), 6.04 (dd, J = 10.4, 15.3 Hz, 1H), 5.65 (dt, J = 6.8, 15.3 Hz, 1H), 5.10 (d, J = 17.0 Hz, 1H), 4.97 (d, J = 10.2 Hz, 1H), 3.71 (s, 3H), 2.46 (m, 2H), 2.44 (m, 3H), 1.99 (m, 1H), 1.36 (s, 3H), 1.05 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.1, 173.4, 136.8, 133.5, 131.5, 115.3, 59.0, 52.2, 34.3, 31.4, 27.3, 18.9, 8.0; IR (neat) 901 w, 970 w, 1005 m, 1030 w, 1091 m, 1113 m, 1161 m, 1200 m, 1220 m, 1241 m, 1345 w, 1378 w, 1434 m, 1460 m, 1603 w, 1714 s, 1744 s, 2860 w, 2941 m, 2984 m cm^{-1}; MS (70 eV) m/z 225 (M^+, 7), 224 (5), 193 (9), 144 (100), 112 (61), 101 (18), 91 (6), 80 (44), 67 (24), 57 (67), 41 (27); HRMS exact mass calcd for $C_{13}H_{20}O_3$ 224.1412, found 224.1404.

4-Methyl-7(*E*),9-decadien-3-one (15d). Prepared according to the procedure for **15c**. Kugelrohr distillation afforded the pure ketone **15d** in 70% yield: bp 100 °C/0.6 mmHg; ^1H NMR (500 MHz, $CDCl_3$) δ 6.29 (dt, J = 10.3, 17.0 Hz, 1H), 6.04 (dd, J = 10.4, 15.2 Hz, 1H), 5.64 (dt, J = 7.0, 15.2, Hz, 1H), 5.09 (d, J = 17.0 Hz, 1H), 4.79 (d, J = 10.2 Hz, 1H), 2.55 (sextet, J = 6.9 Hz, 1H), 2.45 (m, 2H), 2.05 (m, 1H), 1.79 (m, 1H), 1.42 (m, 1H), 1.07 (d, J = 7.0 Hz, 3H), 1.04 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 215.0, 137.0, 134.2, 131.5, 115.2, 45.3, 34.3, 32.3, 30.2, 16.5, 7.7; IR (neat) 889 w, 952 w, 974 w, 1005 m, 1104 w, 1376 w, 1413 w, 1459 m, 1652 w, 1713 s, 2878 w, 2937 m, 2973 m cm^{-1}; MS (70 eV) m/z 166 (M^+, 17), 109 (5), 86 (100), 80 (32), 67 (29), 57 (61), 41 (7), 32 (5); HRMS exact mass calcd for $C_{11}H_{18}O$ 166.1358, found 166.1365.

8a-Ethyl-1,2,3,6,7,8a-hexahydro-3,7,7-trimethyl-(3α,3aα,6α,8aβ)-8*H*-3a,6-epoxyazulen-8-one (41a) and 8a-Ethyl-1,2,3,6,7,8a-hexahydro-3,7,7-trimethyl-(3β,3aα,6α,8aβ)-8*H*-3a,6-epoxyazulen-8-one (41b). A solution of (*E*)-**20a** in 5 mL of CH_2Cl_2 (0.1 M) was cooled to −78 °C

and 60 μL of $TiCl_4$ (1.1 equiv) was added. TLC of the reaction mixture after 5 min did not show any starting material remaining. Standard workup gave crude product. Gas chromatographic analysis revealed that it was a 2.4:1 mixture of **41a** and **41b**. This mixture was separated by MPLC (gradient from 0% to 100% EtOAc in hexane) to give the two products **41a** and **41b** in 41% and in 16% yields, respectively. Data for **41a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.35 (dd, J = 2.0, 6.0 Hz, 1H), 6.17 (d, J = 6.0 Hz, 1H), 4.45 (d, J = 2.0 Hz, 1H), 2.37 (m, 1H), 2.08 (m, 1H), 1.94 (m, 1H), 1.73 (m, 1H), 1.44−1.69 (m, 3H), 1.33 (s, 3H), 0.99 (d, J = 6.9 Hz, 3H), 0.91 (s, 3H), 0.85 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.9, 134.9, 134.5, 97.7, 86.1, 65.3, 48.4, 36.7, 34.3, 30.5, 28.8, 28.0, 21.7, 13.3, 11.1; IR (neat) 752 w, 837 w, 909 w, 945 w, 1028 w, 1066 w, 1083 m, 1232 w, 1378 w, 1459 w, 1697 s, 2872 w, 2929 m, 2963 m cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.93; H, 9.32. Data for **41b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.36 (dd, J = 1.7, 6.1 Hz, 1H), 6.33 (d, J = 6.2 Hz, 1H), 4.41 (d, J = 1.7 Hz, 1H), 2.24 (sextet, J = 8.0 Hz, 1H), 2.05 (m, 1H), 1.90 (m, 2H), 1.30−1.45 (m, 3H), 1.30 (s, 3H), 1.19 (d, J = 7.5 Hz, 3H), 0.91 (s, 3H), 0.91 (t, J = 8.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.8, 134.3, 133.7, 98.5, 86.2, 64.8, 47.8, 41.0, 33.8, 31.6, 28.6, 25.6, 21.8, 20.0, 10.4; IR (neat) 718 m, 750 w, 905 w, 946 m, 1051 w, 1077 m, 1903 w, 1378 w, 1460 w, 1698 s, 2872 w, 2936 m, 2963 m cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 77.07; H, 9.36.

Treatment of 2-[5-Ethoxy-4-ethyl-3,6-dimethyl-6-(phenylsulfonyl)-4(*Z*)-heptenyl]furan [(*Z*)-20a] with $TiCl_4$. See preceding procedure. After the removal of solvents the residue was analyzed by GC to show that it was a 1.5:1 mixture of **41a** and **41b**. On separation by MPLC (gradient from 0% to 100% EtOAc in hexane) this gave pure **41a** and **41b** in 36% and in 22% yields, respectively.

8a-Ethyl-1,2,3,6,7,8a-hexahydro-2,7,7-trimethyl-(2α,3aα,6α,8aβ)-8*H*-3a,6-epoxyazulen-8-one (47a) and 8a-Ethyl-1,2,3,6,7,8a-hexahydro-2,7,7-trimethyl-(2β,3aα,6α,8aβ)-8*H*-3a,6-epoxyazulen-8-one (47b). See procedure for **41a/41b**. Gas chromatography of the crude product showed the ratio of **47a:47b** to be 2.8:1. The crude product mixture was chromatographed on MPLC (gradient from 0% to 100% EtOAc in hexane) to give **47a** and **47b** in 44% and in 10% yields, respectively. Data for **47a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.30 (dd, J = 1.8, 6.0 Hz, 1H), 6.23 (d, J = 6.0 Hz, 1H), 4.43 (d, J = 1.7 Hz, 1H), 2.47 (dd, J = 10.6, 14.7 Hz, 1H), 2.23 (m, 1H), 1.98 (dd, J = 7.0, 12.5 Hz, 1H), 1.72 (dd, J = 10.3, 12.4 Hz, 1H), 1.52 (dd, J = 14.8, 5.4 Hz, 1H), 1.39 (q, J = 7.4 Hz, 2H), 1.34 (s, 3H), 1.10 (d, J = 6.7 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.6, 136.2, 133.6, 96.7, 86.7, 65.7, 48.4, 43.3, 40.7, 30.7, 28.8, 26.1, 22.2, 21.6, 10.8; IR (neat) 729 w, 832 w, 877 w, 904 w, 942 w, 975 w, 1021 w, 1061 w, 1088 m, 1129 w, 1205 w, 1238 w, 1339 w, 1378 w, 1459 w, 1696 s, 2868 m, 2930 m, 2962 s cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.99; H, 9.40. Data for **47b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.35 (dd, J = 2.0, 6.0 Hz, 1H), 6.26 (d, J = 6.0 Hz, 1H), 4.43 (d, J = 2.0 Hz, 1H), 2.44 (m, 1H), 2.32 (dd, J = 9.9, 13.3 Hz, 1H), 2.01 (dd, J = 7.1, 13.4 Hz, 1H), 1.69 (dd, J = 10.3, 13.5 Hz, 1H), 1.47 (dq, J = 2.5, 7.5 Hz, 2H), 1.39 (dd, J = 6.2, 13.4 Hz, 1H), 1.31 (s, 3H), 1.06 (d, J = 6.7 Hz, 3H), 0.91 (s, 3H), 0.88 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.8, 135.4, 133.8, 97.0, 86.0, 65.1, 48.4, 42.8, 41.6, 31.4, 29.8, 28.7, 21.8, 21.8, 10.9; IR ($CDCl_3$) 729 m, 840 w, 875 w, 904 w, 939 w, 976 w, 1024 w, 1046 w, 1086 m, 1118 w, 1143 w, 1190 w, 1229 w, 1276 w, 1313 w, 1342 w, 1348 w, 1459 w, 1697 s, 2867 w, 2929 m, 2961 s cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 76.79. Found: C, 9.46; H, 9.38.

Treatment of 2-[5-Ethoxy-4-ethyl-2,6-dimethyl-6-(phenylsulfonyl)-4(*Z*)-heptenyl]furan with $TiCl_4$ [(*Z*)-20b]. See procedure for **41a/41b**. After the removal of solvents the residue was analyzed by GC to show that it was a 1:1 mixture of **47a** and **47b**. On separation by MPLC (gradient from 0% to 100% EtOAc in hexane) this gave pure **47a** and **47b** in 31% and in 23% yields, respectively.

8a-Ethyl-1,2,3,6,7,8a-hexahydro-1,7,7-trimethyl-(1β,3aα,6α,8aβ)-8*H*-3a,6-epoxyazulen-8-one (55b). From either (*E*)- or (*Z*)-**20c**. See procedure for **41a/41b**. After the removal of solvents the residue was purified by MPLC (2% EtOAc in hexane) to give the cycloadduct **55b** in 62% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.27 (d, J = 6.1 Hz, 1H), 6.25 (dd, J = 1.6, 6.1 Hz, 1H), 4.38 (d, J = 1.5 Hz, 1H), 2.59 (sextet, J = 7.1 Hz, 1H), 2.13 (m, 1H), 2.00 (m, 1H), 1.86 (m, 1H), 1.75 (sextet, J = 7.5 Hz, 1H), 1.37 (m, 1H), 1.30 (s, 3H), 1.21 (sextet, J = 7.5 Hz, 1H), 0.94 (d, J = 7.0 Hz, 3H), 0.86 (s, 3H), 0.72 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.1, 136.7, 133.3, 97.1, 86.6, 67.2, 48.3, 41.4, 31.4, 30.8, 28.8, 21.4, 20.4, 14.4, 11.8; IR (neat) 728 m, 841 w, 898 m, 912 m, 928 m, 1026 m, 1069 m, 1085 m, 1239 w, 1338 w, 1378 m, 1442 w, 1452 m, 1464 m, 1471 m, 1695 s, 2874 m, 2939 m, 2965 s cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 77.00; H, 9.68.

Treatment of 2-Ethoxy-3-ethyl-1,1,4-trimethyl-1-(phenylsulfonyl)-2-(*Z*),7(*E*),9-decatriene [(*E*)-20d] with $TiCl_4$. A solution of 338 μL of $TiCl_4$ (1.2 equiv) in 51 mL of CH_2Cl_2 (0.05 M) was cooled to −78 °C, and a solution of 1.0 g of (*E*)-**20d** in 1 mL of CH_2Cl_2 was added while stirring at −78 °C. The reaction was complete in less than 10 min. It was worked up by pouring it into 50 mL of water containing 10 mL of 2 N HCl and extracting with CH_2Cl_2. The aqueous layer was reextracted with pentane (2×). All the organic layers were washed with water followed by brine and dried over $MgSO_4$. Evaporation of solvents at 0 °C and MPLC separation (gradient from pentane to 5% ether in pentane) gave the fraction containing **59a** and **59b** in 72% yield. The ratio of **59a** and **59b** in the crude reaction mixture was found to be 1:1.3 by gas chromatographic analysis.

Treatment of 2-Ethoxy-3-ethyl-1,1,4-trimethyl-1-(phenylsulfonyl)-2(*E*),7(*E*),9-decatriene [(*E*)-20d] with $TiCl_4$. See preceding procedure. Used 5.74 g of (*E*)-**20d**. A mixture of four products was obtained. This mixture was separated by MPLC (gradient pentane to 5% ether in pentane). The fractions were analyzed by gas chromatography to identify the components. All solvent evaporations were done at 0−5 °C. Fractions which contained more than one compound were further separated by MPLC. Three compounds were isolated: **60** (1.07 g), **59a** (11.3 mg), and **61** (258 mg). The fourth compound (**59b**) was found to be difficult to isolate due to the contamination by **59a**. Total material recovery including all the other fractions which contained these four compounds was 79%. The ratio of **60:59a:59b:61** in the crude reaction mixture was found to be 15:5:9:1 by gas chromatographic analysis. Data for **60**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (ddd, J = 6.8, 17.1, 10.3 Hz, 1H), 5.25 (ddd, J = 1.4, 1.4, 17.1 Hz, 1H), 5.10 (ddd, J = 1.4, 1.4, 17.1, Hz, 1H), 4.00 (dd, J = 7.0, 7.4 Hz, 1H), 2.33 (dd, J = 7.1, 13.3 Hz, 1H), 2.23 (dt, J = 1.5, 7.6 Hz, 1H), 1.92 (m, 1H), 1.74−1.84 (m, 2H), 1.66 (s, 3H), 1.60 (s, 3H), 1.40−1.49 (m, 2H), 1.29 (m, 1H), 0.99 (d, J = 7.2 Hz, 3H), 0.85 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 138.4, 155.5, 98.8, 85.6, 59.1, 55.4, 42.8, 33.7, 26.8, 24.7, 18.6, 17.7, 15.3, 9.8; IR (neat) 921 m, 988 m, 1036 m, 1073 w, 1119 s, 1154 s, 1380 m, 1426 w, 1456 m, 1692 m, 2874 s, 2938 s, 2966 s cm^{-1}; MS (70 eV) m/z 221 (M^+ + 1, 18), 220 (M^+, 100), 192 (23), 177 (5), 165 (17), 149 (9), 135 (13), 121 (11), 107 (12), 93 (12), 79 (6); HRMS exact mass calcd for $C_{15}H_{24}O$ 220.1827, found 220.1827. Data for **59a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 (dd, J = 5.8, 10.9 Hz, 1H), 5.72 (ddt, J = 0.9, 6.1, 10.9 Hz, 1H), 2.74 (m, 1H), 2.48 (sextet, J = 7.2 Hz, 1H), 2.30 (d, J = 6.3 Hz, 2H), 1.82 (1.98, m, 3H), 1.55 (dq, J = 4.3, 8.5 Hz, 1H), 1.35 (dq, J = 7.3, 6.6 Hz, 1H), 1.25 (dq, J = 8.5, 4.2 Hz, 1H), 1.13 (s, 6H), 0.90 (d, J = 7.0 Hz, 3H), 0.76 (7.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.6, 135.0, 127.4, 65.8, 49.1, 45.7, 39.7, 36.9, 31.5, 31.2, 28.7, 27.7, 25.8, 15.1, 9.9; IR (neat) 702 w, 715 w, 741 w, 1031 w, 1052 w, 1213 w, 1356 w, 1379 m, 1458 m, 1679 s, 2875 m, 2959 s, 3023 w cm^{-1}; MS (70 eV) m/z 221 (M^+ + 1, 5), 220 (M^+, 27), 192 (10), 191 (11), 163 (17), 149 (19), 135 (29), 122 (31), 109 (53), 93 (47, 82, 100), 67 (31), 55 (34), 41 (47); HRMS exact mass calcd for $C_{15}H_{24}O$ 220.1827, found 220.1822. Data for **61**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (dd, J = 9.0, 15.0 Hz, 1H), 5.63 (dt, J = 15.0, 7.1 Hz, 1H), 4.05 (d, J = 7.0 Hz, 2H), 3.14 (q, J = 7.1 Hz, 1H), 3.08 (m, J = 6.7 Hz, 1H), 2.49 (sextet, J = 7.1 Hz, 1H), 1.78 (m, 2H), 1.65 (m, J = 7.2 Hz, 1H), 1.58 (m, 3H), 1.06 (d, J = 6.5 Hz, 6H), 1.00 (d, J = 7.2 Hz, 3H), 0.76 (t, J = 7.5 Hz, 3H); ^{13}C

NMR (125 MHz, $CDCl_3$) δ 218.1, 137.3, 126.4, 66.3, 45.9, 45.2, 37.9, 34.4, 32.2, 29.9, 21.5, 20.9, 20.7, 16.4, 10.4; IR (neat) 673 m, 970 w, 1028 w, 1089 w, 1381 m, 1458 m, 1700 s, 1727 w, 2874 m, 2939 s, 2965 s cm^{-1}; MS (70 eV) m/z 220 (M^+ − HCl, 13), 185 (51), 150 (32), 149 (81), 129 (52), 95 (64), 81 (62), 71 (82), 55 (65), 43 (100), 41 (96); HRMS exact mass calcd for $C_{15}H_{24}O$ 220.1827, found 220.1807.

Conversion of 60 to 59a via Claisen Rearrangement. To a flame dried pressure tube equipped with a stir bar, septum and N_2 source was added 4.5 mL of dry quinoline. The solvent was degassed with N_2 for 30 min. Enol ether **60** (0.112 g) was then added and the septum replaced with a screw-on Teflon cap. The tube was placed in a sand bath and heated to 300 °C (T, °C of sand in middle). After 4 h, the reaction mixture had turned from clear to dark brown. TLC (5% Et_2O/hexanes) indicated the reaction was complete. The mixture was rinsed with 20 mL of Et_2O into a separatory funnel. This was washed with 1 N HCl (3 × 10 mL), H_2O (2 × 10 mL), and brine (1 × 10 mL). Drying (Na_2SO_4) and solvent removal gave crude product which on purification by flash chromatography affored 0.0911 g (81%) of **59a** whose NMR was identical to a sample produced by 4 + 3 cycloaddition.

Bromobenzoate 62. A mixture of two cyclized products (150 mg) containing **59a** and **59b** was reduced to a mixture of alcohols by the treating with LAH in THF at 25 °C. The product mixture resulting from this reaction after workup (150 mg) was dissolved in THF (2.7 mL) and 571 μL of MeLi (1.3 M) were added at −78 °C. After stirring for 5 min at −78 °C, 163 mg of *p*-bromobenzoyl chloride were added to the solution and it was allowed to warm up to 25 °C. Standard workup and removal of solvents gave a mixture of benzoates which on separation by chromatography using a chromatotron (1% ether in pentane) afforded 72 mg of a pure benzoate. This product was recrystallized from CH_2Cl_2 and pentane. X-ray crystallography revealed the structure of the compound to be **62**.[29] LAH reduction of this compound followed by PCC oxidation gave ketone **59b** as established by gas chromatography.

***p*-Bromobenzoate 64.** Excess potassium *p*-bromobenzoate was added to a solution of 50 mg of **61** in DMF and the solution was refluxed for 14 h. Standard workup and the removal of solvents gave crude benzoate. This on purification by chromatography using a chromatotron (2% EtOAc in hexane) gave pure benzoate in 76% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.5 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H), 5.89 (dd, J = 9.0, 15.3 Hz, 1H), 5.69 (dt, J = 6.4, 15.3 Hz, 1H), 4.79 (dd, J = 6.4, 12.4 Hz, 1H), 4.75 (dd, J = 6.4, 12.4 Hz, 1H), 3.17 (br q, J = 6.6 Hz, 1H), 3.09 (septet, J = 6.6 Hz, 1H), 2.49 (sextet, J = 7.3 Hz, 1H), 1.79 (m, 2H), 1.65 (m, 1H), 1.59 (m, 2H), 1.39 (m, 1H), 1.05 (d, J = 6.6 Hz, 6H), 0.99 (d, J = 7.2 Hz, 3H), 0.76 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 218.2, 165.6, 138.2, 131.7(2C), 131.1(2C), 129.2, 128.0, 124.2, 66.2, 65.8, 46.2, 38.0, 34.5, 32.3, 30.0, 21.6, 20.9, 20.7, 16.5, 10.4.

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Supporting Information Available: Copies of ORTEP plots for **52**, **56** and **62**. Copies of ^1H and ^{13}C NMR spectra of **19a–d**, **20a–d**, **41a/b**, **47a/b**, **55b**, **59a**, **60**, **61**, and **63** (53 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.

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