JOC*Article*

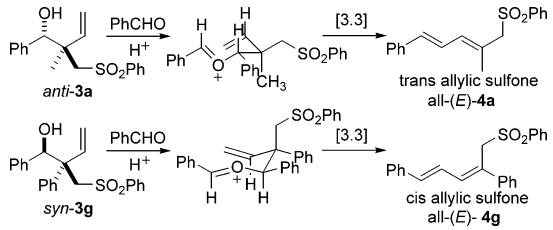
# Stereoselective Synthesis of Allylic Sulfones via the Oxonia-Cope Rearrangement of Homoallylic Alcohols Containing a Homoallylic Sulfone Moiety

Se-Young Jung, Jae-Hong Min, Jung Taek Oh, and Sangho Koo*

*Department of Chemistry, Department of Nano Science and Engineering, Myong Ji University, Yongin, Kyunggi-Do, 449-728, South Korea*

*sangkoo@mju.ac.kr*

*Received March 9, 2006*

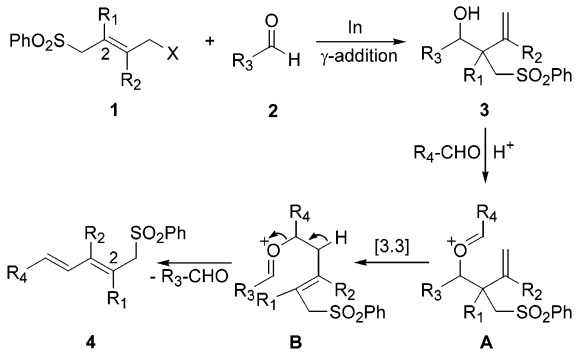



The homoallylic alcohols **3** that can be prepared by the indium-mediated addition of haloallylic sulfones **1** to aldehydes **2** undergo the oxonia-Cope rearrangement with aldehydes **2** to give rise to the allylic sulfones **4** containing a conjugated diene moiety in a highly stereoselective manner. Electron-rich aldehydes preferentially participate in this oxonia-Cope rearrangement with the homoallylic alcohols **3**. Excellent correlations of the stereochemistry (*anti*-**3** to *trans*-allylic sulfone **4** and *syn*-**3** to *cis*-allylic sulfone **4**) have been observed in the oxonia-Cope rearrangement.

## Introduction

Indium-mediated Barbier reaction of allylic halides and carbonyl compounds is an efficient synthetic method of homoallylic alcohols in that diverse functional groups are compatible under environment-friendly aqueous conditions.[1] Mildness and selectiveness of the indium-mediated reaction allows the preparation of the homoallylic alcohols **3** containing a homoallylic sulfone moiety in high yields by the $\gamma$-addition[1a,2] of haloallylic sulfones **1** to aldehydes **2** (Scheme 1).[3] This reaction is highly stereoselective, and the selectivity is originated from the nature of the substituents $R_1$ at C(2) of the haloallylic sulfone **1**: anti selectivity (OH vs $SO_2Ph$) for the $R_1$ = Me group and syn selectivity for the $R_1$ = Ph group.[3] We envisioned that the stereochemistry of the homoallylic alcohols **3** would be conveyed by the oxonia-Cope rearrangement[4−6] to the configuration

**SCHEME 1. Synthetic Plan for the Allylic Sulfones 4 by the Indium-Mediated Addition of the Haloallylic Sulfones 1 to Aldehydes 2, Followed by the Oxonia-Cope Rearrangement of the Adducts 3**




of double bonds of the allylic sulfones **4**,[7] which would be useful compounds in the synthesis of the conjugated polyene chains of carotenoids utilizing the Julia sulfone olefination method.[8] As delineated in Scheme 1, the reaction of the homoallylic alcohols **3** and aldehydes ($R_4$−CHO) under an acidic condition would generate the intermediary oxocarbenium species **A**, which would then undergo the oxonia-Cope rearrangement[4−6] to the

* To whom correspondence should be addressed. Phone: +82-31-330-6185. Fax: +82-31-335-7248.

(1) For reviews, see: (a) Li, C.-J.; Chan, T.-H. *Tetrahedron* **1999**, *55*, 11149−11176. (b) Ranu, B. C. *Eur. J. Org. Chem.* **2000**, 2347−2356. (c) Podlech, J.; Maier, T. C. *Synthesis* **2003**, 633−655.

(2) (a) Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1833−1835. (b) Isaac, M. B.; Chan, T.-H. *Tetrahedron Lett.* **1995**, *36*, 8957−8960.

(3) Min, J.-H.; Jung, S.-Y.; Wu, B.; Oh, J. T.; Lah, M. S.; Koo, S. *Org. Lett.* **2006**, *8*, 1459−1462.

10.1021/jo060517e CCC: $33.50 
Published on Web 06/02/2006

structures **B**. Elimination of aldehyde ($R_3$−CHO) from **B** would finally produce the allylic sulfones **4** containing a conjugated diene unit.

The [3.3] oxonia-Cope rearrangement proceeds in a concerted mechanism, and the stereochemical information of the starting compounds is transferred to the products through well-defined transition states.[5] Therefore, the stereochemistry (trans or cis) at C(2) of the allylic sulfones **4** should be reflected by the stereochemistry (anti or syn) of the homoallylic alcohols **3**. Considering the difficulties in stereoselective preparation of C=C bonds, we anticipated that the above strategy would constitute the most efficient stereoselective synthetic method of the allylic sulfones containing a conjugated diene unit. Details of our studies for the oxonia-Cope rearrangement of the homoallylic alcohols **3** to the allylic sulfones **4** including optimization of the reaction conditions, reaction with different aldehydes, and correlations of the stereochemistry are disclosed in this paper.

## Results and Discussion

It was anticipated that the homoallylic alcohol *anti*-**3a**,[3] which has been prepared by the In-mediated reaction of (*E*)-**1a**[9] ($R_1$ = Me, $R_2$ = H, X = Cl in Scheme 1) and benzaldehyde (**2a**), would produce the *trans*-allylic sulfone, all-(*E*)-**4a**, after the oxonia-Cope rearrangement with **2a** (Scheme 2). The bulky phenyl groups of the initially formed oxocarbenium species **A-1** are presumably disposed to the equatorial positions in the six-membered cyclic transition state of the oxonia-Cope rearrangement. The anti-specific elimination of hydrogen and aldehyde from the rearranged oxocarbenium species **B-1** may produce the C=C bond of *E*-configuration at C(4) and, thus, overall provide all-(*E*)-**4a**. Various conditions for the oxonia-Cope rearrangement[4−6] utilizing Lewis acid, mineral acid, and organic acid to facilitate the formation of the oxocarbenium species **A-1** from *anti*-**3a** and **2a** have been studied (Table 1). Lewis acids were not effective to form the oxocarbenium ion **A-1**, thus producing low yields of the allylic sulfone **4a** (entries 1−4). The oxonia-Cope rearrangement of **A-1** proceeded marginally at 40 °C and required temperatures around 80 °C. The best result was obtained using a stoichiometric amount of 10-camphorsulfonic acid (CSA) at the reflux temperature of benzene for 3.5 h, in which all-(*E*)-**4a** was exclusively formed in 70% yield (entry 10).[10] The oxonia-Cope rearrangement of **3** and **2** would, thus, constitute a general stereoselective synthetic method of the allylic sulfones **4** containing a conjugated diene moiety.

**SCHEME 2. Oxonia-Cope Rearrangement of the Homoallylic Alcohol *anti*-3a with Benzaldehyde (2a) and the Origin of the Stereoselectivity for the Allylic Sulfone all-(*E*)-4a**

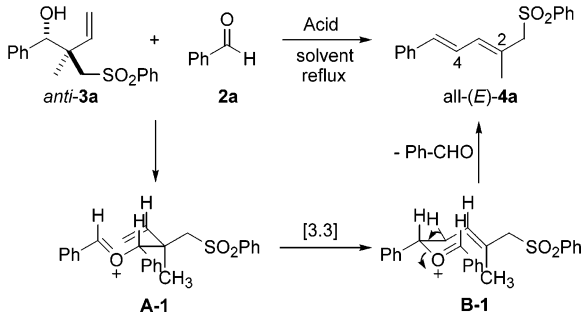



**TABLE 1. Optimization of the Condition for the Oxonia-Cope Rearrangement of the Homoallylic Alcohol *anti*-3a with Benzaldehyde (2a) at the Reflux Temperature of the Solvent**

| entry | acid (equiv) | solvent | time (h) | yield[a] (%) |
|---|---|---|---|---|
| 1 | $ZnCl_2$ (1.1) | $CH_2Cl_2$ | 8 | 8 |
| 2 | $ZnCl_2$ (1.1) | $ClCH_2CH_2Cl$ | 5 | 14 |
| 3 | $BF_3{\cdot}OEt_2$ (1.1) | $CH_2Cl_2$ | 3 | 31 |
| 4 | $ZnBr_2$ (1.1) | $CH_2Cl_2$ | 8 | 31 |
| 5 | 3 M HCl | $H_2O$ | 10 | 37 |
| 6 | *p*-TsOH (1.1) | benzene | 3 | 30 |
| 7 | CSA (0.5) | $CH_2Cl_2$ | 12 | 18 |
| 8 | CSA (0.5) | $ClCH_2CH_2Cl$ | 12 | 46 |
| 9 | CSA (1.1) | $ClCH_2CH_2Cl$ | 20 | 62 |
| 10 | CSA (1.1) | benzene | 3.5 | 70 |

[a] Isolated yield of all-(*E*)-**4a** by $SiO_2$ column chromatography.

More details about the oxonia-Cope rearrangement have been disclosed by the reactions of the homoallylic alcohols *anti*-**3** with various aldehydes **2** (Table 2). We were especially interested in two aspects of the rearrangement: (1) a catalytic use of aldehyde **2** and (2) the use of different aldehydes from the one used in the In-mediated addition reaction. Because benzaldehyde (**2a**) is regenerated in the elimination step of the rearranged oxocarbenium intermediate **B-1** (Scheme 2), the use of a catalytic amount of **2a** seems to be sufficient. However, lower yields (56∼57%) of the allylic sulfone all-(*E*)-**4a** were obtained for the reactions with less than a stoichiometric amount of **2a** (entries 2 and 3). It was also interesting to note that all-(*E*)-**4a** was obtained in 38% yield even without adding **2a** (entry 4), which manifested the fragmentation of *anti*-**3a** to give rise to **2a** under the rearrangement conditions.[6]

The second issue of using different aldehydes for the rearrangement is very important because various allylic sulfones

(4) (a) Nokami, J.; Yoshizane, K.; Matsuura, H.; Sumida, S.-i. *J. Am. Chem. Soc.* **1998**, *120*, 6609−6610. (b) Nokami, J.; Ohga, M.; Nakamoto, H.; Matsubara, T.; Hussain, I.; Kataoka, K. *J. Am. Chem. Soc.* **2001**, *123*, 9168−9169. (c) Nokami, J.; Nomiyama, K.; Matsuda, S.; Imai, N.; Kataoka, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 1273−1276. (d) Nokami, J.; Nomiyama, K.; Shafi, S. M.; Kataoka, K. *Org. Lett.* **2004**, *6*, 1261−1264. (e) Loh, T.-P.; Hu, Q.-Y.; Ma, L.-T. *J. Am. Chem. Soc.* **2001**, *123*, 2450−2451. (f) Loh, T.-P.; Hu, Q.-Y.; Chok, Y.-K.; Tan, K.-T. *Tetrahedron Lett.* **2001**, *42*, 9277−9280. (g) Loh, T.-P.; Tan, K.-T.; Hu, Q.-Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 2921−2922. (h) Loh, T.-P.; Lee, C.-L. K.; Tan, K.-T. *Org. Lett.* **2002**, *4*, 2985−2987. (i) Cheng, H.-S.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 4990−4991. (j) Lee, C.-L. K.; Lee, C.-H. A.; Tan, K.-T.; Loh, T.-P. *Org. Lett.* **2004**, *6*, 1281−1283.

(5) (a) Sumida, S.-i.; Ohga, M.; Mitani, J.; Nokami, J. *J. Am. Chem. Soc.* **2000**, *122*, 1310−1313. (b) Nokami, J.; Anthony, L.; Sumida, S.-i. *Chem.−Eur. J.* **2000**, *6*, 2909−2913.

(6) Loh, T.-P.; Hu, Q.-Y.; Ma, L.-T. *Org. Lett.* **2002**, *4*, 2389−2391.

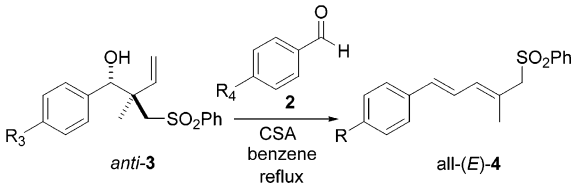
(7) (a) Kotti, S. R. S. S.; Xu, X.; Li, G.; Headley, A. D. *Tetrahedron Lett.* **2004**, *45*, 1427−1431. (b) Chandrasekhar, S.; Jagadeshwar, V.; Saritha, B.; Narsihmulu, C. *J. Org. Chem.* **2005**, *70*, 6506−6507.

(8) (a) Julia, M.; Arnould, D. *Bull. Soc. Chim. Fr.* **1973**, 746−750. (b) Manchand, P. S.; Rosenberger, M.; Saucy, G.; Wehrli, P. A.; Wong, H.; Chambers, L.; Ferro, M. P.; Jackson, W. *Helv. Chim. Acta* **1976**, *59*, 387−396. (c) Chabardes, P.; Decor, J. P.; Varagnat, J. *Tetrahedron* **1977**, *33*, 2799−2805. (d) Bernhard, K.; Mayer, H. *Pure Appl. Chem.* **1991**, *59*, 35−44. (e) Choi, H.; Ji, M.; Park, M.; Yun, I.-K.; Oh, S.-S.; Baik, W.; Koo, S. *J. Org. Chem.* **1999**, *64*, 8051−8053. (f) Ji, M.; Choi, H.; Park, M.; Kee, M.; Jeong, Y. C.; Koo, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 3627−3629. (g) Ji, M.; Choi, H.; Jeong, Y. C.; Jin, J.; Baik, W.; Lee, S.; Kim, J. S.; Park, M.; Koo, S. *Helv. Chim. Acta* **2003**, *86*, 2620−2628. (h) Lee, J. S.; Jeong, Y. C.; Ji, M.; Baik, W.; Lee, S.; Koo, S. *Synlett* **2004**, 1937−1940. (i) Jeon, H.-S.; Koo, S. *Tetrahedron Lett.* **2004**, *45*, 7023−7026. (j) Jeong, Y. C.; Ji, M.; Lee, J. S.; Yang, J.-D.; Jin, J.; Baik, W.; Koo, S. *Tetrahedron* **2004**, *60*, 10181−10185. (k) Jeon, H.-S.; Yeo, J. E.; Jeong, Y. C.; Koo, S. *Synthesis* **2004**, 2813−2820. (l) Chio, S.; Koo, S. *J. Org. Chem.* **2005**, *70*, 3328−3331. (m) Guha, S. K.; Koo, S. *J. Org. Chem.* **2005**, *70*, 9662−9665.

(9) Min, J.-H.; Lee, J.-S.; Yang, J.-D.; Koo, S. *J. Org. Chem.* **2003**, *68*, 7925−7927.

(10) The stereochemistry of the allylic sulfone **4** was determined by the $^1$H NMR NOE experiments. See Supporting Information for details.

**TABLE 2. Oxonia-Cope Rearrangement of the Homoallylic Alcohol *anti*-3 with Various Aldehydes 2**



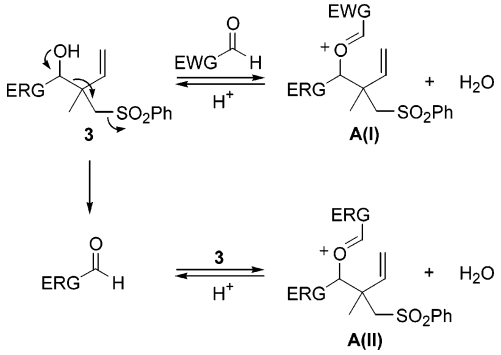

| | compd **3** | | compd **2** | | | compd **4** | | |
|---|---|---|---|---|---|---|---|---|
| entry | | $R_3$ | | $R_4$ | time (h) | | R | yield (%) |
| 1 | **3a** | H | **2a** | H | 3.5 | **4a** | H | 70 |
| 2 | **3a** | H | **2a** | H[a] | 3.5 | **4a** | H | 56 |
| 3 | **3a** | H | **2a** | H[b] | 3.5 | **4a** | H | 57 |
| 4 | **3a** | H | | | 6 | **4a** | H | 38 |
| 5 | **3a** | H | **2b** | OMe | 3 | **4b** | OMe | 68 |
| 6 | **3a** | H | **2c** | Me | 2 | **4c** | Me | 67 |
| 7 | **3a** | H | **2d** | Cl | 3 | **4a** | H | 30 |
| | | | | | | **4d** | Cl | 25 |
| 8 | **3a** | H | **2e** | CN | 3 | **4a** | H | 39 |
| 9 | **3a** | H | **2f** | $NO_2$ | 4.5 | **4a** | H | 40 |
| 10 | **3b** | OMe | **2b** | OMe | 1 | **4b** | OMe | 80[c] |
| 11 | **3b** | OMe | **2e** | CN | 1 | **4b** | OMe | 52 |
| 12 | **3c** | Me | **2c** | Me | 6 | **4c** | Me | 86 |
| 13 | **3d** | Cl | **2d** | Cl | 24 | **4d** | Cl | 52[d] |
| 14 | **3e** | CN | **2e** | CN | 9 | **4e** | CN | 0 |
| 15 | **3e** | CN | **2a** | H | 2.5 | **4a** | H | 50 |
| 16 | **3e** | CN | **2b** | OMe | 1 | **4b** | OMe | 53 |

[a] Benzaldehyde (**2a**) was used in 10 mol % of **3a**. [b] Benzaldehyde (**2a**) was used in 50 mol % of **3a**. [c] The recovered 4-methoxybenzaldehyde (**2b**) was measured to be 104% of the amount initially added. [d] The recovered 4-chlorobenzaldehyde (**2d**) was measured to be 120% of the amount initially added.

**4** may be synthesized from the same homoallylic alcohol **3** just by reacting with different aldehydes **2**. The oxonia-Cope rearrangement of *anti*-**3a** ($R_3$ = H) with benzaldehydes **2b**, **2c**, **2d**, **2e**, and **2f** ($R_4$ = OMe, Me, Cl, CN, and $NO_2$, respectively) has been studied (entries 5−9). We found that not all of the aldehydes **2** were incorporated in the allylic sulfones all-(*E*)-**4**. The electron-rich benzaldehydes **2b** and **2c** ($R_4$ = OMe and Me) preferentially participated in the oxonia-Cope rearrangement with *anti*-**3a** to give the corresponding allylic sulfones all-(*E*)-**4b** (68% yield) and all-(*E*)-**4c** (67% yield), respectively.[11] In the cases using electron-deficient benzaldehydes **2e** ($R_4$ = CN) and **2f** ($R_4$ = $NO_2$), the allylic sulfone all-(*E*)-**4a**, derived from the parent benzaldehyde (**2a**, $R_4$ = H), was obtained in 39 and 40% yields, respectively. Interestingly, a mixture of all-(*E*)-**4a** (R = H) and all-(*E*)-**4d** (R = Cl) was obtained when a slightly electron-deficient benzaldehyde **2d** ($R_4$ = Cl) was used for the rearrangement. This trend was confirmed again by the other examples using different aldehydes ($R_3 \neq R_4$), where the rearrangement product all-(*E*)-**4** containing the more electron-rich phenyl ring was obtained (entries 11, 15, and 16). The best yields of all-(*E*)-**4** were observed when a stoichiometric amount of the same aldehyde ($R_3 = R_4$) was used (entries 10, 12, and 13), in which the pairs of electron-rich substituents provided higher yields than the pairs of slightly electron-deficient substituents, and no rearrangement product has been observed for the pair of **3e** and **2e** with the electron-withdrawing CN substituent ($R_3$, $R_4$ = CN, entry 14).

We explain the necessity for a stoichiometric amount of benzaldehyde for the best result and the selectivity for electron-rich benzaldehydes in the oxonia-Cope rearrangement of **3** by speculating the mechanism of the reaction with an electron-deficient aldehyde (Scheme 3). The reaction of the homoallylic alcohol **3** containing an electron-releasing group (ERG) and an aldehyde with an electron-withdrawing group (EWG) may generate the oxocarbenium species **A(I)**, in which the EWG of **A(I)** destabilizes the oxocarbenium ion. Meanwhile, some of the homoallylic alcohol **3** undergoes fragmentation[6] under the reaction condition to give the aldehyde with the ERG, which can react with **3** to produce the oxocarbenium species **A(II)**. The ERG now stabilizes the oxocarbenium ion of **A(II)**, and the oxonia-Cope rearrangement of **A(II)** followed by the elimination reaction regenerates the aldehyde with the ERG. Without the added aldehyde, the fragmentation of **3** should proceed to accumulate a certain amount of aldehyde for the rearrangement, which lowered the yields of the allylic sulfone **4**. To support the above fragmentation argument, especially for the reaction with an aldehyde containing an EWG, the amount of recovered aldehyde was measured for the oxonia-Cope rearrangement of the electron-rich pair (**3b** and **2b**, entry 10 in Table 2) and that of the slightly electron-deficient pair (**3d** and **2d**, entry 13). 4-Methoxybenzaldehyde (**2b**) was recovered in 104% yield, on the other hand, 4-chlorobenzaldehyde (**2d**) was recovered in 120% yield, which was expected from the above mechanism.

**SCHEME 3. Fragmentation of 3 to Produce the Electron-Rich Aldehyde and Formation of the Oxocarbenium Species A(II) with the Electron-Rich Aldehyde**

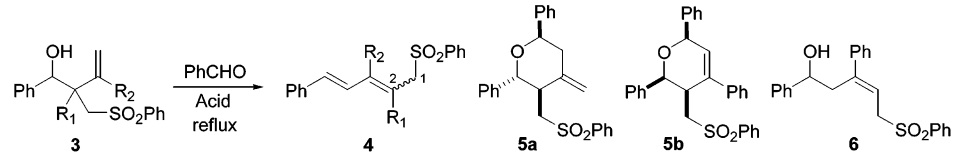


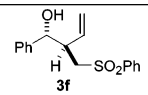
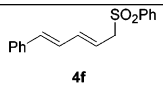
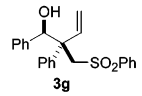
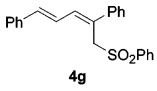
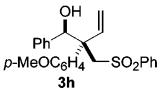
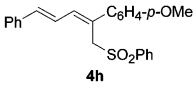
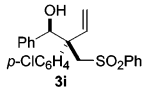
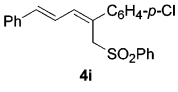
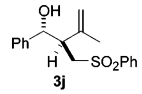
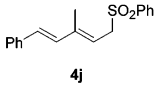
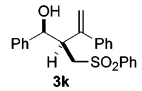
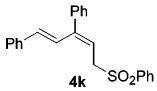

Finally, the generality for the stereoselective synthesis of the allylic sulfones **4f**−**4k** by the oxonia-Cope rearrangement of the homoallylic alcohols **3f**−**3k**, and the correlations of the stereochemistry between **3** and **4** were studied (Table 3).[10] The oxonia-Cope rearrangement of the homoallylic alcohols **3f**−**3i** with no substituent at the vinyl group ($R_2$ = H) proceeded well under the above optimized condition (CSA in benzene at reflux) to produce the allylic sulfones **4f** (68% yield), **4g** (60% yield), **4h** (78% yield), and **4i** (89% yield), respectively (entries 1−4). However, it was unavoidable to obtain the Prins rearrangement products[11,12] **5a** and **5b** under the above optimized conditions for the homoallylic alcohols **3j** and **3k** with a methyl and a phenyl substituent at $R_2$, respectively (entries 5−9). Several

(11) Crosby, S. R.; Harding, J. R.; King, C. D.; Parker, G. D.; Willis, C. L. *Org. Lett.* **2002**, *4*, 577−580.

(12) (a) Lolkema, L. D. M.; Semeyn, C.; Ashek, L.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron* **1994**, *50*, 7129−7140. (b) Rychnovsky, S. D.; Marumoto, S.; Jaber, J. J. *Org. Lett.* **2001**, *3*, 3815−3818. (c) Jaber, J. J.; Mitsui, K.; Rychnovsky, S. D. *J. Org. Chem.* **2001**, *66*, 4679−4686. (d) Loh, T.-P.; Yang, J.-Y.; Feng, L.-C.; Zhou, Y. *Tetrahedron Lett.* **2002**, *43*, 7193−7196. (e) Alder, R. W.; Harvey, J. N.; Oakley, M. T. *J. Am. Chem. Soc.* **2002**, *124*, 4960−4961. (f) Dalgard, J. E.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2004**, *126*, 15662−15663. (g) Jasti, R.; Anderson, C. D.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2005**, *127*, 9939−9945.

**TABLE 3. Correlations of the Stereochemistry in the Synthesis of the Allylic Sulfones 4 by the Oxonia-Cope Rearrangement of the Homoallylic Alcohols 3**




| entry | compd **3** | | acid | time (h) | compd **4** | | yield (%) |
|---|---|---|---|---|---|---|---|
| | major isomer | dr (anti:syn) | | | major isomer | *E*/*Z* ($C_2$) | |
| 1 |  **3f** | 2:1 | CSA[a] | 5 |  **4f** | 2:1 | 68 |
| 2 |  **3g** | 1:13 | CSA[a] | 4 |  **4g** | *E* | 60 |
| 3 |  **3h** | 1:25 | CSA[a] | 3 |  **4h** | *E* | 78 |
| 4 |  **3i** | 0:100 | CSA[a] | 3.5 |  **4i** | *E* | 89 |
| 5 |  **3j** | 3:2 | CSA[a] | 3.5 |  **4j** | 3:2 | 51 (49)[b] |
| 6 | **3j** | 3:2 | $In(OTf)_3$[c] | 82 | **4j** | 3:2 | 28 (31)[b] |
| 7 | **3j** | 3:2 | 3 M HCl | 5.5 | **4j** | 1.7:1 | 74 (3)[b] |
| 8 |  **3k** | 1:4 | CSA[a] | 4 |  **4k** | 2:3 | 77 (14)[d] |
| 9 | **3k** | 1:10 | CSA[a] | 3.5 | **4k** | 1:2 | 70 (18)[d] |
| 10 | **3k** | 1:10 | 5 M HCl[e] | 4 | **4k** | *Z* | 0 (78)[f] |

[a] 10-Camphorsulfonic acid (1.1 equiv) was used in benzene. [b] The Prins rearrangement product **5a** was obtained in the yield designated in parentheses. [c] $In(OTf)_3$ (1.1 equiv) was used in $CH_2Cl_2$. [d] The Prins rearrangement product **5b** was obtained in the yield designated in parentheses. [e] A 5:1 mixture of 5 M HCl solution and MeCN was used. [f] The product **6** was exclusively obtained, which has the C=C bond of *Z*-configuration.

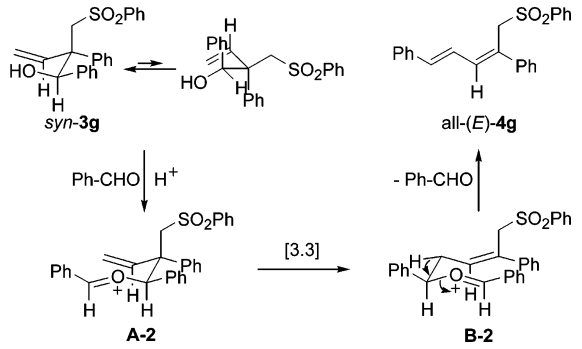
acidic conditions were tested for the rearrangement of **3j** ($R_2$ = Me) to alleviate the amount of the Prins product **5a** (entries 6 and 7). $In(OTf)_3$ was not effective, but aqueous 3 M HCl solution was very efficient to significantly reduce the Prins product **5a** (3% yield), thereby increasing the allylic sulfone **4j** (74% yield). The oxonia-Cope rearrangement of **3k** ($R_2$ = Ph) under an aqueous condition using a 5:1 mixture of 5 M HCl solution and MeCN (entry 10) exclusively generated the allylic sulfone **6** with *Z*-configuration at C(2) after hydration instead of the normal elimination (see Scheme 2), which would be consequently transformed to the allylic sulfone **4k** after dehydration.

The correlations of the stereochemistry between **3** and **4** in the rearrangement were confirmed again.[5] There were very good agreements between the ratios of *anti*-/*syn*-**3** and that of *trans*-/*cis*-allylic sulfone **4** after the rearrangement except for the case of **3k** and **4k**, where a low cis selectivity of **4k** was obtained under the condition using CSA in benzene regardless of the diastereomeric ratio of **3k** (entries 8 and 9). The stereochemical correlation in the rearrangement is exemplified for the exclusive formation of all-(*E*)-**4g** (*cis*-allylic sulfone) from *syn*-**3g** (Scheme 4).[10] The two bulky phenyl groups of *syn*-**3g** take the equatorial positions to form the oxocarbenium species **A-2** with benzaldehyde, in which the benzenesulfonyl group takes the axial position. The oxonia-Cope rearrangement to the structure **B-2**, followed by anti-specific elimination of hydrogen and aldehyde, produces the allylic sulfone all-(*E*)-**4g**.

## Conclusion

The homoallylic alcohols **3** containing a homoallylic sulfone moiety undergo oxonia-Cope rearrangement with aldehydes **2** to produce the allylic sulfones **4** containing a conjugated diene unit. Electron-rich benzaldehydes **2** preferentially participate in the oxonia-Cope rearrangement with the homoallylic alcohols **3** to give the allylic sulfones **4**. The oxonia-Cope rearrangement

**SCHEME 4. Correlation of the Stereochemistry in the Oxonia-Cope Rearrangement: *syn*-3g to *cis*-Allylic Sulfone, all-(*E*)-4g**




of **3** is highly stereoselective, and very good correlations of the stereochemistry between **3** and **4** have been observed (e.g., the exclusive formations of *trans*-allylic sulfone, all-(*E*)-**4a**, from *anti*-**3a** and *cis*-allylic sulfone, all-(*E*)-**4g**, from *syn*-**3g**). This tandem sequence of the In-mediated addition of the haloallylic sulfones **1** to aldehydes **2** and the oxonia-Cope rearrangement of the adducts **3** with aldehydes **2** thus constitutes a general stereoselective synthetic method of the allylic sulfones **4** containing a conjugated diene moiety, which may be efficiently utilized in the synthesis of unnatural carotenoid compounds with a variety of different substituent patterns. The systematic syntheses of these unnatural carotenoid compounds are currently underway in the expectations of an increased stability and new material characteristics.

## Experimental Section

**General Procedure for the Oxonia-Cope Rearrangement. 1-Benzenesulfonyl-2-methyl-5-phenyl-2,4-pentadiene (4a). Table 2, Entry 1:** To a stirred solution of *anti*-**3a** (0.36 g, 1.14 mmol) in benzene (10 mL) were added **2a** (0.13 g, 1.25 mmol) and CSA (0.29 g, 1.25 mmol). The mixture was stirred at reflux for 3.5 h and cooled to room temperature. The mixture was then diluted with $CH_2Cl_2$, washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to give all-(*E*)-**4a** (0.24 g, 0.80 mmol) in 70% yield. Data for all-(*E*)-**4a**: $^1$H NMR $\delta$ 1.96 (s, 3H), 3.84 (s, 2H), 5.82 (d, $J$ = 10.8 Hz, 1H), 6.38 (d, $J$ = 15.6 Hz, 1H), 6.88 (dd, $J$ = 15.6, 10.8 Hz, 1H), 7.21−7.39 (m, 5H), 7.52−7.67 (m, 3H), 7.85−7.88 (m, 2H) ppm; $^{13}$C NMR $\delta$ 17.7, 66.7 123.9, 125.2, 126.5, 127.9, 128.5, 128.7, 129.1, 133.7, 134.2, 134.6, 137.0, 138.5 ppm; IR (KBr) 1447, 1307, 1143 cm$^{-1}$; HRMS (FAB$^+$) calcd for $C_{18}H_{18}O_2S$, 298.1027; found, 298.1021.

**1-Benzenesulfonyl-2-methyl-5-(4-methoxyphenyl)-2,4-pentadiene (4b). Table 2, Entry 10:** The reaction of *anti*-**3b** (0.35 g, 1.00 mmol), **2b** (0.15 g, 1.10 mmol), and CSA (0.26 g, 1.10 mmol) in benzene (10 mL) at reflux for 1 h produced all-(*E*)-**4b** (0.26 g, 0.80 mmol) in 80% yield. Benzaldehyde **2b** (0.16 g, 1.15 mmol) was also recovered in 104% yield. Data for all-(*E*)-**4b**: $^1$H NMR $\delta$ 1.94 (s, 3H), 3.80 (s, 3H), 3.82 (s, 2H), 5.79 (d, $J$ = 10.8 Hz, 1H), 6.33 (d, $J$ = 15.4 Hz, 1H), 6.74 (dd, $J$ = 15.4, 11.0 Hz, 1H), 6.84 (d, $J$ = 8.8 Hz, 2H), 7.31 (d, $J$ = 8.8 Hz, 2H), 7.46−7.66 (m, 3H), 7.84−7.87 (m, 2H) ppm; $^{13}$C NMR $\delta$ 17.5, 55.2, 66.7, 114.0, 121.9, 123.7, 127.7, 128.4, 129.0, 129.7, 133.6, 133.7, 134.7, 138.4, 159.4 ppm; IR (KBr) 1509, 1446, 1305, 1249, 1142 cm$^{-1}$; HRMS (FAB$^+$) calcd for $C_{19}H_{20}O_3S$, 328.1133; found, 328.1149.

**1-Benzenesulfonyl-2-methyl-5-(4-methylphenyl)-2,4-pentadiene (4c). Table 2, Entry 12:** The reaction of *anti*-**3c** (0.35 g, 1.05 mmol), **2c** (0.14 g, 1.16 mmol), and CSA (0.269 g, 1.158 mmol) in benzene (10 mL) at reflux for 6 h produced all-(*E*)-**4c** (0.284 g, 0.909 mmol) in 86% yield. Data for all-(*E*)-**4c**: $^1$H NMR $\delta$ 1.95 (s. 3H), 2.34 (s, 3H), 3.83 (s, 2H), 5.79 (d, $J$ = 11.0 Hz, 1H), 6.35 (d, $J$ = 15.6 Hz, 1H), 6.83 (dd, $J$ = 15.6, 11.0 Hz, 1H), 7.12 (d, $J$ = 8.1 Hz, 2H), 7.27 (d, $J$ = 8.1 Hz, 2H), 7.51−7.66 (m, 3H), 7.84−7.87 (m, 2H) ppm; $^{13}$C NMR $\delta$ 17.6, 21.3, 66.7, 123.0, 123.4, 126.4, 128.5, 129.0, 129.4, 133.6, 134.2, 134.7, 137.9, 138.5 ppm; IR (KBr) 1509, 1446, 1314, 1307, 1143 cm$^{-1}$; HRMS (FAB$^+$) calcd for $C_{19}H_{20}O_2S$, 312.1184; found, 312.1194.

**1-Benzenesulfonyl-2-methyl-5-(4-chlorophenyl)-2,4-pentadiene (4d). Table 2, Entry 13:** The reaction of *anti*-**3d** (0.39 g, 1.10 mmol), **2d** (0.17 g, 1.21 mmol), and CSA (0.28 g, 1.21 mmol) in benzene (10 mL) at reflux for 24 h produced all-(*E*)-**4d** (0.19 g, 0.57 mmol) in 52% yield. Benzaldehyde **2d** (0.20 g, 1.45 mmol) was also recovered in 120% yield. Data for all-(*E*)-**4d**: $^1$H NMR $\delta$ 1.96 (s, 3H), 3.84 (s, 2H), 5.83 (d, $J$ = 10.8 Hz, 1H), 6.34 (d, $J$ = 15.6 Hz, 1H), 6.85 (dd, $J$ = 15.6, 10.8 Hz, 1H), 7.25−7.32 (m, 4H), 7.52−7.67 (m, 3H), 7.85−7.88 (m, 2H) ppm; $^{13}$C NMR $\delta$ 17.7, 66.7, 124.4, 125.9, 127.7, 128.5, 128.8, 129.1, 132.8, 133.5, 133.7, 134.3, 135.5, 138.6 ppm; IR (KBr) 1490, 1447, 1307, 1145, 1087 cm$^{-1}$; HRMS (FAB$^+$) calcd for $C_{18}H_{17}O_2ClS$, 332.0638; found, 332.0634.

**1-Benzenesulfonyl-5-phenyl-2,4-pentadiene (4f). Table 3, Entry 1:** The reaction of **3f** (0.51 g, 1.68 mmol, anti/syn = 2:1), **2a** (0.20 g, 1.85 mmol), and CSA (0.43 g, 1.85 mmol) in benzene (15 mL) at reflux for 5 h produced **4f** (0.33 g, 1.15 mmol, $E/Z$ = 2:1 at C-2) in 68% yield. Data for all-(*E*)-**4f**: $^1$H NMR $\delta$ 3.89 (d, $J$ = 7.7 Hz, 2H), 5.69 (dt, $J_d$ = 15.2, $J_t$ = 7.7 Hz, 1H), 6.19 (dd, $J$ = 15.2, 10.5 Hz, 1H), 6.48 (d, $J$ = 15.8 Hz, 1H), 6.72 (dd, $J$ = 15.8, 10.5 Hz, 1H), 7.25−7.34 (m, 5H), 7.48−7.68 (m, 3H), 7.87−7.89 (m, 2H) ppm; $^{13}$C NMR $\delta$ 60.4, 118.2, 126.5, 127.1, 128.1, 128.4, 128.6, 129.0, 133.7, 134.8, 136.5, 138.4, 139.4 ppm; IR (KBr) 1448, 1307, 1145 cm$^{-1}$; HRMS (FAB$^+$) calcd for $C_{17}H_{16}O_2S$, 284.0871; found, 284.0879. Data for 2-(*Z*)-**4f**: $^1$H NMR $\delta$ 4.06 (d, $J$ = 7.5 Hz, 2H), 5.42 (dt, $J_d$ = 10.3, $J_t$ = 7.5 Hz, 1H), 6.37 (dd, $J$ = 10.5, 10.3 Hz, 1H), 6.30−6.58 (m, 2H), 7.20−7.65 (m, 8H), 7.83−7.95 (m, 2H) ppm.

**1-Benzenesulfonyl-2,5-diphenyl-2,4-pentadiene (4g). Table 3, Entry 2:** The reaction of **3g** (0.13 g, 0.34 mmol, anti/syn = 1:13), **2a** (0.035 g, 0.34 mmol), and CSA (0.086 g, 0.37 mmol) in benzene (10 mL) at reflux for 4 h produced all-(*E*)-**4g** (0.073 g, 0.20 mmol) in 60% yield. Data for all-(*E*)-**4g**: $^1$H NMR $\delta$ 4.56 (s, 2H), 6.61 (d, $J$ = 14.8 Hz, 1H), 6.71 (d, $J$ = 11.0 Hz, 1H), 6.82 (dd, $J$ = 14.8, 11.0 Hz, 1H), 7.15−7.41 (m, 13H), 7.75−7.81 (m, 2H) ppm; $^{13}$C NMR $\delta$ 58.0, 124.0, 126.2, 126.8, 127.6, 127.7, 128.2, 128.4, 128.5, 128.6, 128.8, 133.6, 134.9, 136.6, 136.7, 138.5, 140.2 ppm; IR (KBr) 1541, 1507, 1457, 1320, 1150 cm$^{-1}$; HRMS (FAB$^+$) calcd for $C_{23}H_{20}O_2S$, 360.1184; found, 360.1190.

**1-Benzenesulfonyl-2-(4-methoxyphenyl)-5-phenyl-2,4-pentadiene (4h). Table 3, Entry 3:** The reaction of **3h** (0.31 g, 0.77 mmol, anti/syn = 1:25), **2a** (0.090 g, 0.84 mmol), and CSA (0.20 g, 0.84 mmol) in benzene (20 mL) at reflux for 3 h produced all-(*E*)-**4h** (0.23 g, 0.60 mmol) in 78% yield. Data for all-(*E*)-**4h**: $^1$H NMR $\delta$ 3.80 (s, 3H), 4.55 (s, 2H), 6.57 (d, $J$ = 14.7 Hz, 1H), 6.65 (d, $J$ = 11.0 Hz, 1H), 6.75 (dd, $J$ = 14.7, 11.0 Hz, 1H), 6.76−6.83 (m, 2H), 7.23−7.44 (m, 10H), 7.76−7.82 (m, 2H) ppm; $^{13}$C NMR $\delta$ 55.3, 58.1, 113.9, 124.1, 126.7, 127.2, 127.4, 128.1, 128.6, 128.6, 128.8, 132.6, 133.2, 133.6, 135.8, 136.8, 138.5, 159.2 ppm; IR (KBr) 1604, 1512, 1449, 1306, 1253, 1136, 1085 cm$^{-1}$; HRMS (EI$^+$) calcd for $C_{24}H_{22}O_3S$, 390.1290; found, 390.1289.

**1-Benzenesulfonyl-2-(4-chlorophenyl)-5-phenyl-2,4-pentadiene (4i). Table 3, Entry 4:** The reaction of *syn*-**3i** (0.31 g, 0.74 mmol), **2a** (0.086 g, 0.81 mmol), and CSA (0.19 g, 0.81 mmol) in benzene (20 mL) at reflux for 3.5 h produced all-(*E*)-**4i** (0.26 g, 0.66 mmol) in 89% yield. Data for all-(*E*)-**4i**: $^1$H NMR $\delta$ 4.53 (s, 2H), 6.64 (d, $J$ = 14.1 Hz, 1H), 6.71 (d, $J$ = 10.6 Hz, 1H), 6.77 (dd, $J$ = 14.1, 10.6 Hz, 1H), 7.20−7.47 (m, 12H), 7.78−7.83 (m, 2H) ppm; $^{13}$C NMR $\delta$ 58.0, 123.7, 126.5, 126.9, 127.5, 128.4, 128.6, 128.6, 128.7, 129.0, 133.5, 133.8, 135.3, 136.5, 137.3, 138.4, 138.7

ppm; IR (KBr) 1491, 1447, 1306, 1135, 1084 $cm^{-1}$; HRMS ($EI^+$) calcd for $C_{23}H_{19}ClO_2S$, 394.0794; found, 394.0791.

**1-Benzenesulfonyl-3-methyl-5-phenyl-2,4-pentadiene (4j) and 3-benzenesulfonylmethyl-4-methylene-2,6-diphenyl-tetrahydropyran (5a). Table 3, Entry 5:** The reaction of **3j** (0.21 g, 0.65 mmol, anti/syn = 3:2), **2a** (0.08 g, 0.72 mmol), and CSA (0.17 g, 0.72 mmol) in benzene (10 mL) at reflux for 3.5 h produced **4j** (0.10 g, 0.33 mmol, *E*/*Z* = 3:2 at C-2) and **5a** (0.13 g, 0.32 mmol) in 51 and 49% yields, respectively. The Prins rearrangement product **5a** consisted of a 4:1:1 mixture of three stereoisomers. Data for all-(*E*)-**4j**: $^1$H NMR $\delta$ 1.53 (s, 3H), 3.99 (d, $J$ = 8.3 Hz, 2H), 5.57 (t, $J$ = 8.3 Hz, 1H), 6.51 (d, $J$ = 16.0 Hz, 1H), 6.77 (d, $J$ = 16.0 Hz, 1H), 7.20−7.71 (m, 8H), 7.83−7.92 (m, 2H) ppm; $^{13}$C NMR $\delta$ 12.3, 56.6, 116.8, 126.5, 127.8, 128.4, 128.7, 129.1, 129.6, 131.7, 133.7, 136.8, 138.5, 142.4 ppm; IR (KBr) 1447, 1306, 1151, 1090 $cm^{-1}$; HRMS ($FAB^+$) calcd for $C_{18}H_{18}O_2S$, 298.1027; found, 298.1021. Data for 2-(*Z*)-**4j**: $^1$H NMR $\delta$ 1.95 (s, 3H), 4.04 (d, $J$ = 8.3 Hz, 2H), 5.41 (t, $J$ = 8.3 Hz, 1H), 6.51 (A of ABq, $J$ = 16.0 Hz, 1H), 6.58 (B of ABq, $J$ = 16.0 Hz, 1H), 7.20−7.73 (m, 8H), 7.83−7.91 (m, 2H) ppm; $^{13}$C NMR $\delta$ 20.6, 55.5, 114.7, 126.7, 128.0, 128.3, 128.5, 128.9, 129.6, 131.7, 133.5, 136.7, 139.2, 142.3 ppm. Data for **5a** (major stereoisomer): $^1$H NMR $\delta$ 2.33 (d of A of ABq, $J_{AB}$ = 14.0, $J_d$ = 11.5 Hz, 1H), 2.43 (d of B of ABq, $J_{AB}$ = 14.0, $J_d$ = 3.2 Hz, 1H), 2.93 (dd, $J$ = 14.7, 2.4 Hz, 1H), 3.12 (ddd, $J$ = 11.0, 2.6, 2.4 Hz, 1H), 3.43 (dd, $J$ = 14.7, 11.0 Hz, 1H), 4.52 (dd, $J$ = 11.2, 3.1 Hz, 1H), 4.79 (d, $J$ = 2.6 Hz, 1H), 5.02 (s, 1H), 5.14 (s, 1H), 7.20−7.72 (m, 15H) ppm; HRMS ($CI^+$) calcd for $C_{25}H_{25}O_3S$, 405.1524; found, 405.1522.

**Table 3, Entry 7:** The reaction of **3j** (0.24 g, 0.77 mmol, anti/syn = 3:2) and **2a** (0.09 g, 0.844 mmol) in 3 M HCl (20 mL) at reflux for 5.5 h produced **4j** (0.17 g, 0.57 mmol, *E*/*Z* = 1.7:1 at C-2) and **5a** (0.008 g, 0.02 mmol) in 74 and 3% yields, respectively.

**1-Benzenesulfonyl-3,5-diphenyl-2,4-pentadiene (4k) and 3-benzenesulfonylmethyl-2,4,6-triphenyl-3,6-dihydro-2*H*-pyran (5b). Table 3, Entry 8:** The reaction of **3k** (0.61 g, 1.62 mmol, anti/syn = 1:4), **2a** (0.19 g, 1.79 mmol), and CSA (0.42 g, 1.79 mmol) in benzene (20 mL) at reflux for 4 h produced **4k** (0.44 g, 1.26 mmol, *E*/*Z* = 2:3 at C-2) and **5b** (0.11 g, 0.23 mmol) in 77 and 14% yields, respectively. Data for 2-(*Z*)-**4k**: $^1$H NMR $\delta$ 4.19 (d, $J$ = 8.4 Hz, 2H), 5.53 (t, $J$ = 8.4 Hz, 1H), 6.23 (d, $J$ = 16.0 Hz, 1H), 6.67 (d, $J$ = 16.0 Hz, 1H), 7.15−7.67 (m, 13H), 7.88−7.95 (m, 2H) ppm; IR (KBr) 1558, 1507, 1447, 1325, 1151 $cm^{-1}$; HRMS ($FAB^+$) calcd for $C_{23}H_{21}O_3S$, 361.1262; found, 361.1272. Data for all-(*E*)-**4k**: $^1$H NMR $\delta$ 3.76 (d, $J$ = 8.1 Hz, 2H), 5.87 (t, $J$ = 8.1 Hz, 1H), 5.99 (d, $J$ = 15.9 Hz, 1H), 6.97 (d, $J$ = 15.9 Hz, 1H), 7.15−7.67 (m, 13H), 7.73−7.78 (m, 2H) ppm. Data for **5b**: $^1$H NMR $\delta$ 3.14 (dd, $J$ = 15.0, 5.7 Hz, 1H), 3.50 (dd, $J$ = 15.0, 3.7 Hz, 1H), 3.77−3.83 (m, 1H), 5.20 (d, $J$ = 2.2 Hz, 1H), 6.08 (d, $J$ = 2.0 Hz, 1H), 6.62 (d, $J$ = 2.0 Hz, 1H), 7.15−7.67 (m, 20H) ppm; IR (KBr) 1684, 1653, 1558, 1507, 1457, 1325, 1144 $cm^{-1}$; HRMS ($CI^+$) calcd for $C_{30}H_{27}O_3S$, 467.1681; found, 467.1688.

**Acknowledgment.** This work was supported by the Regional Research Center program of MOCIE (Ministry of Commerce, Industry and Energy) and Kyunggi-Do.

**Supporting Information Available:** General experimental, $^1$H NMR spectra for **4a**−**4d** and **4f**−**4k**, $^{13}$C NMR spectra for **4a**−**4d** and **4f**−**4j**, and $^1$H NMR one-dimensional NOE difference spectra for all-(*E*)-**4a**, all-(*E*)-**4g**, all-(E)-**4j**, and a mixture of 2-(*Z*)-**4k** and all-(*E*)-**4k**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO060517E