Diallylic Sulfides as Key Structures for Carotenoid Syntheses

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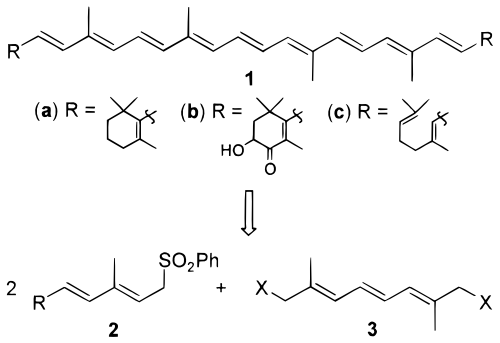
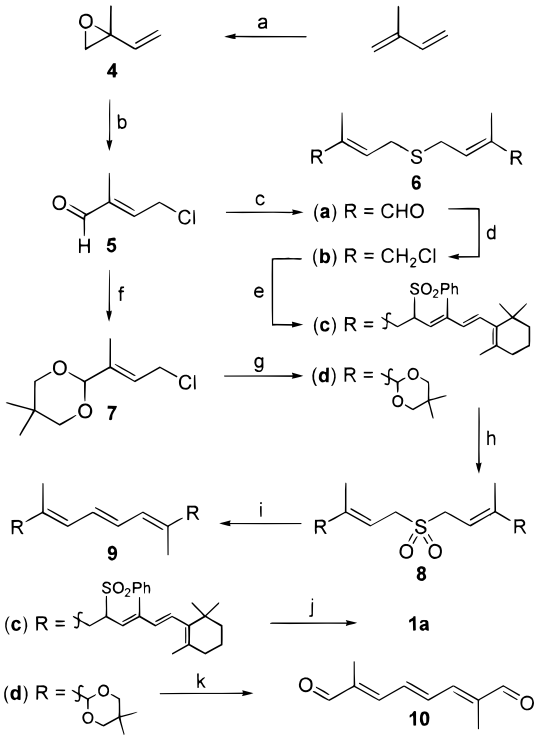
The polyene chain **1** is the basic structural feature of carotenoids[1] such as *β*-carotene (**1a**), astaxanthin (**1b**), and lycopene (**1c**), which are utilized as natural pigments for foodstuffs (Scheme 1). Recently, chemoprevention of carotenoids against certain cancers has been reported and the usage as food additives has been dramatically increased. Two representative synthetic approaches for the polyene chain of carotenoids are Wittig olefination[2] and the bismetal acetylide coupling/partial hydrogenation.[3] Even though the highly efficient Julia's sulfone olefination protocol[4] has found wide use in the preparation of simple double bonds and conjugated polyenes, there has been no report of carotenoid syntheses based on this method, as generalized in Scheme 1, because of the presumed instability of dihalotriene **3**.[5] To circumvent the instability problem of **3**, we decided to use diallylic sulfide **6b**, where the sulfur atom isolated the two allylic halide units, thus providing stability to the system. The sulfur atom can be oxidatively removed by means of a Ramberg−Bäcklund reaction[6] in the later stage. Using this strategy, we were able to synthesize *β*-carotene (**1a**), as described in Scheme 2.

The preparation of diallylic sulfide **6b**, a key intermediate for the polyene chain syntheses, requires 4-chloro-2-methyl-2-buten-1-al (**5**),[7] which is made from isoprene monoxide (**4**). Isoprene monoxide (**4**) is more efficiently prepared via isoprene bromohydrin[8] than direct epoxidation of isoprene by peroxy acids.[7] The dimeric coupling of allylic halide **5** with sulfur dianion (S^{2-}) proceeded efficiently in alcoholic solvents but produced complex mixtures using other solvents. This observation suggested the use of alcohols as protecting groups for aldehydes. An acid catalyst was added to ensure the protection of aldehydes. The diacetals of the coupling product were hydrolyzed, and the resulting formyl groups of **6a** were reduced and then halogenated to give rise to bis(allylic halide) **6b**. The Julia-type coupling reaction of

Scheme 1



Scheme 2[a]



[a] Reagents: (a) (i) NBS, H_2O, (ii) NaOH; (b) $CuCl_2$, LiCl, EtOAc, 80 °C, 65% from isoprene; (c) (i) MeOH, *p*-TsOH (cat.), (ii) Na_2S, (iii) HCl, 85%; (d) (i) LAH, THF, 0 °C, (ii) PPh_3, CCl_4, CH_3CN or $SOCl_2$, 73%; (e) (**2a**), NaH, THF, then NaI; 85%; (f) neopentyl glycol, *p*-TsOH (cat.), benzene, reflux, 75%; (g) Na_2S, MeOH; 95%; (h) urea-hydrogen peroxide, phthalic anhydride, CH_3CN, 0 °C, 72% from **6c**, 80% from **6d**; (i) KOH, *t*-BuOH, CCl_4, 69% from **8c**, 82% from **8d**; (j) Na, EtOH, reflux, 75%; (k) THF, HCl, 94%.

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2 equiv of C_{15} sulfone **2a**[4b] with bis(allylic halide) **6b** did not produce **6c** unless NaI was added, by which allylic chlorides were converted in situ to the more reactive allylic iodides. Now that the required carbon skeleton was installed, it was only necessary to form the 11 double bonds in conjugation from **6c** to afford β-carotene (**1a**). We decided to apply the Ramberg−Bäcklund reaction first and then exploit the base-promoted desulfonation, since it has been reported that the Ramberg−Bäcklund reaction of retinyl sulfone did not produce β-carotene.[9] Chemoselective oxidation of sulfide **6c** to sulfone **8c** was realized by the slow addition of perphthalic acid at 0 °C, which was generated in situ by oxidation of phthalic anhydride with urea−hydrogen peroxide.[10] Ramberg−Bäcklund reaction of diallylic sulfone **8c** using Meyers' condition[11] gave unstable conjugated triene **9c**, which is best stored under Ar at low temperature. The base-promoted desulfonation of **9c** in Na/EtOH produced exclusively *trans*-β-carotene (**1a**). The overall yield of β-carotene was 13% in nine steps from isoprene.

The same sequence of the olefination strategy has been applied to allylic sulfide **6d** to synthesize 2,7-dimethyl-2,4,6-triene-1,8-dial (**10**)[12] (Scheme 2). Dial **10** is the key intermediate for the carotenoid syntheses using a Wittig-base strategy. The required allylic sulfide **6d** was prepared from 4-chloro-2-methyl-2-buten-1-al (**5**) by the protection of the formyl group with neopentyl glycol, followed by the dimeric coupling of the resulting allylic chloride **7** with sulfur dianion (S^{2-}). Oxidation of the central sulfur atom of **6d** by perphthalic acid gave allylic sulfone **8d**. Application of the Ramberg−Bäcklund reaction to sulfone **8d** followed by hydrolysis of the protected formyl groups of the resulting triene **9d** produced trienedial **10** in 29% overall yield in seven steps from isoprene.

In summary, we have demonstrated that diallylic sulfides **6** are the key intermediates for the syntheses of symmetrical polyene chains, where the sulfur moiety not only allows efficient assembly of two allylic chains but also provides the polyene systems with stability during the coupling reaction. This sulfur atom can be removed oxidatively to produce the central double bond, allowing the polyenes to be fully conjugated. More importantly, this strategy can generally be applied to the construction of various types of polyene chains.

Experimental Section

General Experimental Procedures. ^{1}H (300 MHz) and ^{13}C NMR (75.5 MHz) spectra were recorded in deuterated chloroform ($CDCl_3$). Solvents for extraction and chromatography were reagent grade and used as received. The column chromatographies were performed by the method of Still with silica gel 60, 230−400 mesh ASTM supplied by Merck. Solvents used as reaction media were dried over predried molecular sieve (5 Å) by microwave oven. All reactions were performed under a dry argon atmosphere in oven dried glassware, except for those reactions utilizing water as a solvent, which were run in air.

4-Chloro-2-methyl-2-buten-1-al (5).[7] To a stirred mixture of isoprene (27.0 g, 0.40 mol) and H_2O (150 mL) in a cold water bath was added *N*-bromosuccinamide (70.0 g, 0.39 mol). The mixture was stirred vigorously at that temperature for 10 h, and 10 M NaOH solution (32.0 g, 0.80 mol in 80 mL H_2O) was added. The mixture was then stirred at room temperature for 1 h, extracted with EtOAc (50 mL × 3), dried over anhydrous K_2CO_3, and filtered. The filtrate was treated with $CuCl_2$ (67.0 g, 0.39 mol) and LiCl (16.7 g, 0.39 mol). The resulting mixture was heated to 80 °C for 30 min and cooled by adding 150 g of ice. The mixture was filtered through a sintered glass funnel under reduced pressure. The organic phase of filtrate was separated, and the aqueous layer was extracted with hexanes. The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography over silica gel to give 4-chloro-2-methyl-2-buten-1-al (**5**) (30.1 g, 0.25 mol) in 65% yield. Data for **5**: ^{1}H NMR δ 1.84 (3H, s), 4.33 (2H, d, J = 7.5 Hz), 6.59 (1H, t, J = 7.5 Hz), 9.51 (1H, s); ^{13}C NMR 9.1, 38.6, 141.0, 145.7, 194.3 ppm; IR (CH_2Cl_2) 1690, 1645 cm^{-1}; MS (EI, 70 eV) 120 [$(M + 2)^+$], 118 (M^+).

Bis(3-formyl-3-methyl-2-propenyl) Sulfide (6a). To a stirred solution of 4-chloro-2-methyl-2-buten-1-al (**5**) (10.48 g, 88.2 mmol) in MeOH (80 mL) was added a catalytic amount of *p*-TsOH (48 mg, 0.25 mmol). The mixture was stirred at room temperature for 1 h to ensure that the formyl group turned to dimethyl acetal, and then $Na_2S{\cdot}9H_2O$ (10.59 g, 44.1 mmol) was added. The resulting mixture was stirred at room temperature for 10 h, and most of solvent was removed under reduced pressure. The crude product was treated with 1 M HCl (50 mL) to deprotect the formyl group. The mixture was stirred at room temperature for 1 h and extracted with CH_2Cl_2. The combined extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel to give bis(3-formyl-3-methyl-2-propenyl) sulfide (**6a**) (7.43 g, 37.5 mmol) in 85% yield. Data for **6a**: ^{1}H NMR δ 1.78 (6H, s), 3.44 (4H, d, J = 7.7 Hz), 6.53 (2H, t, J = 7.7 Hz), 9.49 (2H, s); ^{13}C NMR 9.3, 29.1, 140.9, 147.5, 194.4 ppm; IR (CH_2Cl_2) 1683, 1638 cm^{-1}; HRMS (FAB^+) calcd for $C_{10}H_{15}SO_2$ 199.0793, found 199.0800.

Bis(4-chloro-3-methyl-2-butenyl) Sulfide (6b). To a stirred solution of bis-(3-formyl-3-methyl-2-propenyl) sulfide (**6a**) (10.5 g, 53.0 mmol) in THF (80 mL) was added $LiAlH_4$ (1.33 g, 35.0 mmol). The mixture was stirred at 0 °C for 1 h and quenched with 1 M HCl (30 mL). The mixture was extracted with EtOAc. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The above residue was dissolved in CH_3CN (50 mL), and then PPh_3 (30.43 g, 0.116 mol) and CCl_4 (20 mL) were added. The resulting mixture was stirred at room temperature for 5 h, diluted with ether, and washed with 1 M HCl and H_2O. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel to produce bis(4-chloro-3-methyl-2-butenyl) sulfide (**6b**) (9.26 g, 38.7 mmol) in 73% yield. Data for **6b**: ^{1}H NMR δ 1.78 (6H, s), 3.14 (4H, d, J = 7.7 Hz), 4.03 (4H, s), 5.62 (2H, t, J = 7.7 Hz); ^{13}C NMR 14.3, 28.6, 51.5, 126.5, 134.8 ppm; IR (CH_2Cl_2) 1441, 1267 cm^{-1}; MS (EI, 70 eV) 240 [$(M+2)^+$], 239 [$(M + 1)^+$], 238 (M^+); HRMS (FAB^+) calcd for $C_{10}H_{17}SCl_2$ 239.0428, found 239.0421.

Bis(11-benzenesulfonyl-11,12-dihydroretinyl) Sulfide (6c). To a stirred solution of C_{15} sulfone **2a**[4b] (14.4 g, 41.8 mmol) in THF (80 mL) was added NaH (1.20 g, 50.1 mmol). The mixture was stirred at room temperature for 15 min, and then bis(4-chloro-3-methyl-2-butenyl) sulfide (**6b**) (5.0 g, 20.9 mmol) and NaI (7.5 g, 50.1 mmol) were added consecutively. The resulting mixture was stirred at room temperature for 15 h and diluted with ether. The dilute mixture was washed with 1 M HCl and H_2O, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel to give bis(11-benzenesulfonyl-11,12-dihydroretinyl) sulfide (**6c**) (15.7 g, 17.8 mmol) in 85% yield. Data for **6c**: ^{1}H NMR δ 0.93 (6H, s), 0.96 (6H, s), 1.21 (6H, s), 1.45−1.65 (8H, m), 1.63 (12H, s), 2.00 (4H, t, J = 6.0 Hz), 2.39 (2H, dd, J = 13.2, 11.5 Hz), 2.90 (4H, d, J = 6.8 Hz), 2.90−3.10 (2H, m), 4.02 (2H, dt, J_d = 3.1, J_t = 11.0 Hz), 5.07 (2H, d, J = 10.3 Hz), 5.21 (2H, t, J = 7.0 Hz), 5.93 (4H, s), 7.45−7.53 (4H, m), 7.58−7.65 (2H, m), 7.78−7.84 (4H, m); ^{13}C NMR 12.3, 16.0, 16.0, 19.2, 21.6, 28.9, 28.9, 33.0, 34.2, 37.4, 39.5, 64.1, 122.3, 125.8, 129.2, 129.6, 130.2, 130.4, 134.0, 134.4, 136.8, 138.1, 138.5, 143.2 ppm; IR (CH_2Cl_2) 1441, 1301 cm^{-1}; HRMS (FAB^+) calcd for $C_{52}H_{71}S_3O_4 - (C_6H_6SO_2)$ 713.4426, found 713.4429.

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4-Chloro-2-methyl-2-buten-1-al, Neopentyl Acetal (7). To a stirred solution of 4-chloro-2-methyl-2-buten-1-al (**5**) (15.8 g, 0.134 mol) in benzene (100 mL) were added neopentyl glycol (16.7 g, 0.161 mol) and *p*-TsOH (190.2 mg, 6.7 mol). The mixture was heated to reflux for 3 h and cooled to room temperature. The mixture was diluted with ether and washed with H_2O. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel to give acetal **7** (20.6 g, 0.100 mol) in 75% yield. Data for **7**: ^{1}H NMR δ 0.73 (3H, s), 1.20 (3H, s), 1.79 (3H, s), 3.47 (2H, A of ABq, J = 11.0 Hz), 3.62 (2H, B of ABq, J = 11.0 Hz), 4.09 (2H, d, J = 7.9 Hz), 4.72 (1H, s), 5.85 (1H, t, J = 7.2 Hz); ^{13}C NMR 11.3, 21.7, 22.8, 30.1, 39.4, 77.1, 103.4, 124.2, 138.1 ppm; IR (neat) 1467, 1392 cm^{-1}; MS (EI, 70 eV) 205 [(M + 2)$^+$], 203 (M$^+$); HRMS (CI, H$^+$) calcd for $C_{10}H_{18}O_2Cl$ 205.0995, found 205.0989.

Bis(3-formyl-3-methyl-2-propenyl) Sulfide, Dineopentyl Diacetal (6d). The above acetal **7** (20.6 g, 0.100 mmol) was dissolved in MeOH (100 mL), and $Na_2S{\cdot}9H_2O$ (12.0 g, 50 mmol) was added. The resulting mixture was stirred at room temperature for 10 h, and most of solvent was removed under reduced pressure. The crude oil was dissolved in ether and washed with H_2O, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel to give bis(3-formyl-3-methyl-2-propenyl) sulfide, dineopentyl diacetal (**6d**) (17.6 g, 47.5 mmol) in 95% yield. Data for **6d**: ^{1}H NMR δ 0.68 (6H, s), 1.15 (6H, s), 1.68 (6H, s), 3.09 (4H, d, J = 7.5 Hz), 3.43 (4H, A of ABq, J = 11.1 Hz), 3.58 (4H, B of ABq, J = 11.1 Hz), 4.66 (2H, s), 5.63 (2H, t, J = 7.5 Hz); ^{13}C NMR 11.2, 21.8, 22.9, 28.0, 30.1, 77.1, 104.4, 125.4, 135.8 ppm; IR (neat) 1463, 1395, 1304 cm^{-1}; HRMS (CI, H$^+$) calcd for $C_{20}H_{35}SO_4$ 371.2256, found 371.2264.

Bis(11-benzenesulfonyl-11,12-dihydroretinyl) Sulfone (8c). The mixture of UHP (urea−hydrogen peroxide)[10] (6.88 g, 73.1 mmol) and phthalic anhydride (5.41 g, 36.5 mmol) in CH_3CN (70 mL) was stirred vigorously at room temperature for 2 h to give a clear solution. This solution was added slowly for a 3 h period through a dropping funnel to a stirred solution of bis(11-benzenesulfonyl-11,12-dihydroretinyl) sulfide (**6c**) (10.8 g, 12.2 mmol) in CH_3CN (30 mL), which was placed in an ice bath. The reaction mixture was stirred at 0 °C for 1 h after addition. The mixture was then diluted with ether, washed with 1 M HCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a white solid. This crude solid was dissolved in $CHCl_3$, and the undissolved solid was filtered. The filtrate was concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel to give bis(11-benzenesulfonyl-11,12-dihydroretinyl) sulfone (**8c**) (8.06 g, 8.77 mmol) in 72% yield. At least two stereoisomers were confirmed by ^{1}H NMR spectroscopy, one of which was crystallized during chromatographic separation. The data of the pure isomer **8c**: ^{1}H NMR δ 0.91 (6H, s), 0.96 (6H, s), 1.22 (6H, s), 1.37−1.49 (4H, m), 1.55−1.67 (4H, m), 1.62 (6H, s), 1.65 (6H, s), 1.99 (4H, t, J = 5.9 Hz), 2.47 (2H, dd, J = 13.0, 11.3 Hz), 3.05 (2H, d, J = 13.0 Hz), 3.47 (4H, d, J = 4.5 Hz), 4.06 (2H, dt, J_d = 3.1, J_t = 10.8 Hz), 5.07 (2H, d, J = 10.5 Hz), 5.24 (2H, t, J = 7.4 Hz), 5.92 (2H, A of ABq, J = 16.4 Hz), 5.97 (2H, B of ABq, J = 16.4 Hz), 7.40−7.55 (4H, m), 7.55−7.70 (2H, m), 7.75−7.90 (4H, m); ^{13}C NMR 12.3, 17.0, 19.1, 21.5, 28.7, 28.8, 32.8, 34.0, 37.3, 39.3, 51.0, 63.4, 114.1, 121.0, 128.8, 129.0, 129.3, 129.7, 133.7, 135.5, 137.1, 137.2, 140.8, 142.8 ppm. IR (KBr) 1630, 1465, 1397 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{52}H_{71}S_3O_6 - (C_6H_6SO_2)$ 745.4324, found 745.4346.

Bis(3-formyl-3-methyl-2-propenyl) Sulfone, Dineopentyl Diacetal (8d). Bis(3-formyl-3-methyl-2-propenyl) sulfide, dineopentyl diacetal (**6d**) (3.39 g, 9.15 mmol) in CH_3CN (20 mL) was oxidized by perphthalic acid, which was prepared by UHP (urea−hydrogen peroxide)[10] (5.17 g, 54.9 mmol) and phthalic anhydride (4.07 g, 27.5 mmol) in CH_3CN (30 mL), to give bis-allylic sulfone **8d** (2.94 g, 7.3 mmol) in 80% yield according to the above procedure (see the preparation of **8c**). Data for **8d**: ^{1}H NMR δ 0.75 (6H, s), 1.20 (6H, s), 1.79 (6H, s), 3.50 (4H, A of ABq, J = 10.9 Hz), 3.66 (4H, B of ABq, J = 10.9 Hz), 3.72 (4H, d, J = 7.7 Hz), 4.76 (2H, s). 5.79 (2H, t, J = 7.7 Hz); ^{13}C NMR 12.3, 21.8, 22.9, 30.1, 51.3, 77.1, 103.1, 114.5, 142.3 ppm; IR (KBr) 1686, 1466, 1391 cm^{-1}; HRMS (CI, H$^+$) calcd for $C_{20}H_{35}SO_6$ 403.2154, found 403.2147.

11,20-Dibenzenesulfonyl-11,12,19,20-tetrahydro-β-carotene (9c). To a stirred solution of bis(11-benzenesulfonyl-11,12-dihydroretinyl) sulfone (**8c**) (1.51 g, 1.64 mmol) in *t*-BuOH (20 mL) and CCl_4 (20 mL) was added pulverized KOH (1.85 g, 32.9 mmol). The mixture was stirred vigorously at room temperature for 5 h under Ar atmosphere, and then most of solvent was removed under reduced pressure. The crude product was dissolved in CH_2Cl_2 and washed with 1 M HCl. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography over silica gel to give 11,20-dibenzenesulfonyl-11,12,19,20-tetrahydro-β-carotene (**9c**) (932 mg, 1.13 mmol) in 69% yield. Data for **9c**: ^{1}H NMR δ 0.93 (6H, s), 0.96 (6H, s), 1.20 (6H, s), 1.37−1.50 (4H, m), 1.53−1.65 (4H, m), 1.63 (6H, s), 1.68 (6H, s), 1.98 (4H, br s), 2.45 (2H, dd, J = 13.0, 11.6 Hz), 3.04 (2H, d, J = 14.2 Hz), 4.05 (2H, dt, J_d = 3.0, J_t = 10.9 Hz), 5.82−5.98 (2H, m), 5.92 (4H, s), 6.15−6.28 (2H, m), 7.40−7.54 (4H, m), 7.56−7.67 (2H, m), 7.76−7.90 (4H, m); ^{13}C NMR 12.3, 12.3, 16.7, 16.8, 19.1, 21.5, 28.8, 32.8, 34.1, 39.4, 64.2, 121.4, 127.8, 128.1, 128.7, 129.0, 129.3, 129.5, 132.9, 133.5, 136.0, 137.2, 137.6, 142.1 ppm; IR (CH_2Cl_2) 1723, 1603, 1465, 1376 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{52}H_{69}S_2O_4 - (C_6H_6SO_2)$ 679.4541, found 679.4549.

2,7-Dimethyl-2,4,6-octatriene-1,8-dial, Dineopentyl Diacetal (9d). The bis-allylic sulfone **8d** (3.00 g, 7.45 mmol) in *t*-BuOH (30 mL) and CCl_4 (30 mL) was treated with pulverized KOH (4.18 g, 74.5 mmol) to give the Ramberg−Bäcklund reaction product **9d** (2.04 g, 6.07 mmol) in 82% yield according to the above procedure (see the preparation of **9c**). Data for **9d**: ^{1}H NMR δ 0.73 (6H, s), 1.22 (6H, s), 1.85 (6H, s), 3.51 (4H, A of ABq, J = 9.8 Hz), 3.66 (4H, B of ABq, J = 9.8 Hz), 4.75 (2H, s), 6.30 (2H, d, J = 8.1 Hz), 6.50 (2H, dd, J = 7.7, 2.8 Hz); ^{13}C NMR d 11.7, 21.4, 22.6, 29.8, 76.8, 103.9, 127.6, 129.1, 134.2 ppm; IR (KBr) 1471, 1380 cm^{-1}; HRMS (CI, H$^+$) calcd for $C_{20}H_{32}O_4$ 337.2379, found 337.2383.

β-Carotene (1a). Na (674 mg, 29.3 mmol) was added to a stirred solution of 11,20-bis(benzenesulfonyl)-11,12,19,20-tetrahydro-β-carotene (**9c**) (602 mg, 0.73 mmol) in EtOH (20 mL) under Ar atmosphere. The reaction mixture was heated to reflux for 10 h and cooled to room temperature. Most of the solvent was removed under reduced pressure, and the resulting crude oil was dissolved in toluene, washed with 1 M HCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel to give exclusively *trans*-β-carotene (**1a**) (295 mg, 0.55 mmol) in 75% yield. The ^{1}H NMR spectrum of the synthetic sample was identical with that of the authentic sample.

2,7-Dimethyl-2,4,6-octatriene-1,8-dial (10). The triene **9d** (267 mg, 0.82 mmol) was dissolved in THF (12 mL), and 1 M HCl (15 mL) was added. The resulting mixture was stirred at room temperature for 2 h and extracted with ether. The combined ether extract was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel to give 2,7-dimethyl-2,4,6-octatriene-1,8-dial (**10**) (127 mg, 0.77 mmol) in 94% yield. Data for **10**: ^{1}H NMR δ 1.96 (6H, s), 7.00−7.15 (4H, m), 9.56 (2H, s); ^{13}C NMR 9.7, 134.3, 140.8, 146.1, 194.4 ppm; IR (KBr) 1662, 1614, 1414 cm^{-1}; HRMS (CI, H$^+$) calcd for $C_{10}H_{13}O_2$ 165.0916, found 165.0916.

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Supporting Information Available: ^{1}H NMR spectra of **1a**, **5**, **6a**−**d**, **7**, **8c**,**d**, **9c**,**d**, and **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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