A New and Convenient Preparation of Conjugated Dienals

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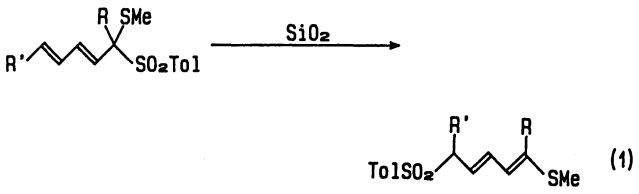
For preparation of 5-monosubstituted or 5,5-disubstituted 2,4-dienals, 1-(methylthio)-5-(*p*-tolylsulfonyl)-1,3-pentadiene (**4**) is revealed to be an important precursor. When 5-(methylthio)-5-(*p*-tolylsulfonyl)-1,3-pentadiene, that is easily obtainable from (methylthio)methyl *p*-tolyl sulfone, was treated with silica gel, 1,5-rearrangement of *p*-tolylsulfonyl group occurred to give **4**. The conditions for mono- or dialkylation of **4** followed by hydrolysis leading to the dienals are described.

For preparation of various biologically active unsaturated compounds, conjugated dienals are often utilized as synthetic intermediates.[1] Although there have been reported many synthetic methods of 2,4-dienals,[2] most of them involve either carbon-chain elongation of aldehydes and ketones[2g,h,i,m] or functionalization of vinyl compounds,[2a,b,d,k] and therefore, do not seem to be widely applicable. In this paper, we report an entirely new and versatile route to 5-monosubstituted and 5,5-disubstituted 2,4-dienals using 1-(methylthio)-5-(*p*-tolylsulfonyl)-1,3-pentadiene (**4**) as a key compound (Scheme 1).

Results and Discussion

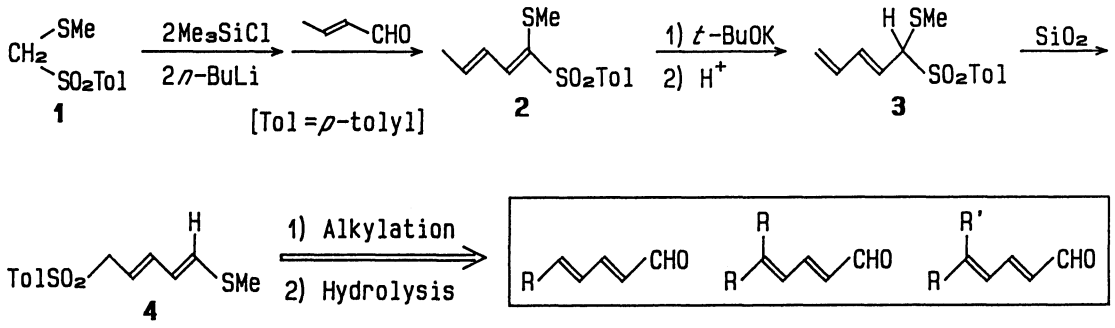
In a previous paper,[3] we disclosed a facile 1,5-rearrangement of *p*-tolylsulfonyl group in a 1-alkylated 1-methylthio-2,4-pentadienyl system (Eq. (1); R=alkyl).



During further investigation of this intriguing 1,5-rearrangement of the sulfonyl group, we found that 5-(methylthio)-5-(*p*-tolylsulfonyl)-1,3-pentadiene (**3**), which lacks an alkyl group at 5-position, undergoes 1,5-rearrangement of the sulfonyl group by the action of silica gel to give **4**. (1*E*,3*E*)-1-(Methylthio)-1-(*p*-tolylsulfonyl)-1,3-pentadiene (**2**) was obtained from (methylthio)methyl *p*-tolyl sulfone (**1**)[4] by the reaction of the anion of a trimethylsilylated **1**[3] (see Experimental) with crotonaldehyde followed by geometric isomerization with iodine in diethyl ether.[3] After **2** was treated with an excess amount (1.5 equiv) of *t*-BuOK in THF at −20 °C, the reaction was quenched with aqueous NH_4Cl to afford **3** quantitatively (by ^1H NMR analysis).[5] The crude product was placed in the column packed with silica gel, and elution with benzene gave **4** in 84% overall yield from **2**. Since the unrearranged product (**3**) was not detected in any fraction, *p*-tolylsulfonyl group was shown to completely migrate.

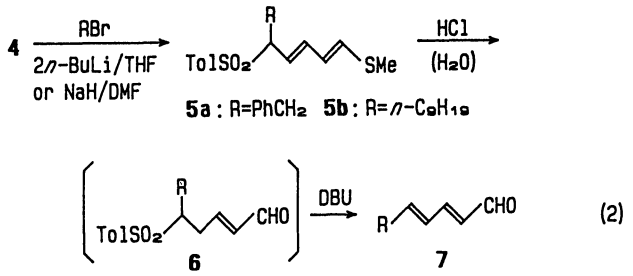
For monoalkylation of **4**, various conditions were examined, and the following conditions gave the best results for the alkylation with benzyl bromide and nonyl bromide: The dilithio derivative derived from **4** and butyllithium (2 equiv) smoothly reacted with benzyl bromide even at −78 °C and **5a** was given in 80% yield.[6] Monoalkylation of **4** with nonyl bromide was achieved under the reaction conditions using NaH (1.2 equiv) as a base and DMF as a solvent at −20 °C to afford **5b** in 56% yield[7]

Surprisingly, hydrolysis of **5** was achieved by treatment with aqueous HCl. When **5** was treated with



Scheme 1.

HCl (0.1 mol dm^{-3}) in acetonitrile-water (9:1) at 80 °C for 1 d, the corresponding 5-(*p*-tolylsulfonyl)-2-alkenal (**6**) was obtained. The structure of **6** was deduced from the ^{1}H NMR spectrum of the crude product.[8] Since usual vinyl sulfides are known to undergo hydrolysis with the aid of titanium tetrachloride[10] or mercury(II) chloride,[11] the present smooth hydrolysis may be attributable to the proton accessibility of a 1,3-dienyl sulfide to form a sulfenylated allyl cation. When crude **6** was briefly treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in acetonitrile at −20 °C, 5-monosubstituted 2,4-dienal (**7**) was given as summarized in Table 1 (Nos. 1 and 2).



In alkylation of **4** with excess alkyl halide (3 equiv) and excess NaH (3 equiv) in DMF (−20 °C to 0 °C), a dialkylated product (**8**) was obtained. Since **8** was very labile, the crude product was subjected without any purification to the acid hydrolysis. On treatment of the crude product with HCl (ca. 0.08 mol dm^{-3}) in acetonitrile-water (9:1) (50 °C/1 h and 80 °/1 h), a smooth hydrolysis occurred to directly produce a 5,5-disubstituted 2,4-dienal (**9**). In the reaction of **4** with 1,5-dibromopentane under similar conditions, a cyclization product (**8**, 2R=-$(CH_2)_5$-) was produced and the subsequent hydrolysis gave 5,5-pentamethylene-2,4-pentadienal (**9d**). In the synthesis of **9c** and **9d**, alkylation of **4** with KH and the corresponding halide in THF-HMPA (10:1) made their yields slightly higher. These results are summarized in Table 1 (Nos. 3—6).

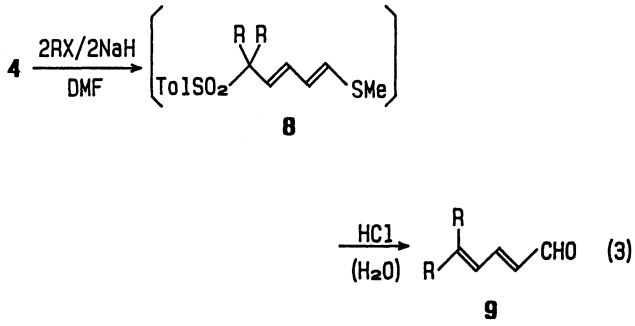
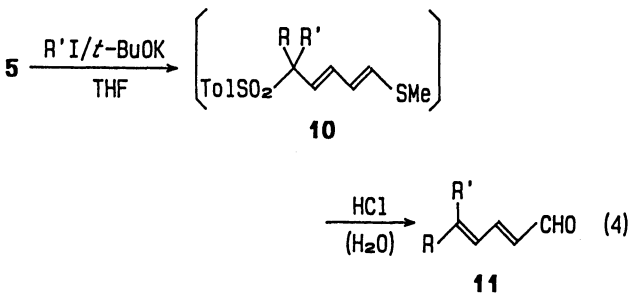


Table 1. Products and Yields in Equations (2)—(4)

No.	Equation	Starting material	Product (yield/%)
1	(2)	5a	Ph, CHO **7a** (52) [4*E*:4*Z*=95:5]
2	(2)	5b	CHO **7b** (63) [4*E*:4*Z*=91:9]
3	(3)	4	Ph, Ph, CHO **9a** (60)
4	(3)	4	CHO **9b** (63)
5	(3)	4	CHO **9c** (39, 54)[a]
6	(3)	4	CHO **9d** (33, 48)[a]
7	(4)	5a	Ph, CHO **11a** (62) [4*E*:4*Z*=66:34]
8	(4)	5b	CHO **11b** (66)[b]

a) The former is the yield obtained by alkylation of **4** using NaH/DMF system. The latter represents the yield derived from alkylation using KH/THF-HMPA (see Text) . b) The isomer ratio was not determined.[13]

5,5-Unsymmetrically-disubstituted 2,4-dienals (**11**) were also synthesized from the monoalkylated intermediate (**5**). Although the second alkylation of **5** was accomplished by treatment with an alkyl halide and NaH in DMF, the yield was relatively low. We found that *t*-BuOK is a good base for this alkylation. Alkylation of **5** with an alkyl iodide (R'I) and *t*-BuOK in THF smoothly occurred at −20 °C. The subsequent hydrolysis of the crude product with HCl afforded **11** (Nos. 7 and 8 of Table 1).



Thus, 1-(methylthio)-5-(*p*-tolylsulfonyl)-1,3-pentadiene (**4**), easily obtainable from (methylthio)methyl *p*-tolyl sulfone (**1**), has proved to be a versatile inter-

mediate for making 5-monosubstituted and 5,5-disubstituted 2,4-dienals.

Experimental

General Procedures. Melting points were determined on a hot-stage microscope apparatus (Yanagimoto) and are uncorrected. ^{1}H NMR spectra were obtained on JEOL JNM-FX 270 (270 MHz) and JEOL JNM-GSX 500 (500 MHz) spectrometers. Chemical shifts are reported in ppm down field from TMS as the internal standard (δ scale). Infrared spectra were determined with a JASCO A-200 spectrometer and data are presented in cm^{-1} for important diagnostic absorptions. Mass spectra (MS) were determined on a Hitachi RMU-7M spectrometer at 70 eV. Microanalytical data were provided by the Analysis Center of Chiba University.

(Methylthio)methyl *p*-tolyl sulfone (**1**), which was obtained from Nissan Chemical Industries Co., was recrystallized from benzene-hexane and dried over diphosphorus pentaoxide. Other materials were purchased from commercial suppliers (Aldrich Chemical Co., Tokyo Kasei Chemical Industry Co., Wako Pure Chemical Industries Co., Nakarai Chemical Co., and Kanto Chemical Co.).

Preparation of 1-(Methylthio)-1-(*p*-tolylsulfonyl)-1,3-pentadiene (2): To a solution of **1** (2.14 g, 9.87 mmol) in THF (30 ml), were successively added trimethylsilyl chloride (2.40 g, 22.1 mmol) and a 1.5 mol dm^{-3} hexane solution (15.0 ml) of butyllithium (22.5 mmol) at −78 °C under an atmosphere of N_2, and the resulting mixture was stirred at the same temperature for 2 h. After addition of crotonaldehyde (846 mg, 12.1 mmol), the reaction mixture was further stirred at −78 °C for 2 h. Then the reaction was quenched with a saturated aqueous NH_4Cl solution (60 ml) and water (60 ml), and the mixture was extracted with diisopropyl ether (IPE) (40 ml×4). The combined extracts were washed with water (50 ml×2), dried ($MgSO_4$), and evaporated in vacuo. ^{1}H NMR analysis of the residue (2.87 g) showed that this consisted of two geometric isomers (1*E* : 1*Z*=71 : 29). This residue was dissolved in diethyl ether (60 ml), and iodine (1.25 g, 4.93 mmol) was added. After being stirred at room temperature for 3 h, the solution was washed with an aqueous $Na_2S_2O_3$ solution (50 ml×3) and water (50 ml×2), dried ($MgSO_4$), and evaporated. The residual oil was subjected to column chromatography on silica gel (eluent: benzene) to give (1*E*,3*E*)-**2** (2.47 g: 93% yield) as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ=1.95 (3H, dd, *J*=1.5, 6.7 Hz), 2.24 (3H, s), 2.43 (3H, s), 6.43 (1H, qd, *J*=6.7, 15.0 Hz), 6.66 (1H, qdd, *J*=1.5, 11.0, 15.0 Hz), 7.31 (2H, d, *J*=8.0 Hz), 7.77 (1H, d, *J*=11.0 Hz), and 7.81 (2H, d, *J*=8.0 Hz); IR (neat) 1610, 1310 cm^{-1}. Found: C, 58.07; H, 5.99%. Calcd for $C_{13}H_{16}O_2S_2$: C, 58.18; H, 6.01%.

Preparation of 1-(Methylthio)-5-(*p*-tolylsulfonyl)-1,3-pentadiene (4). To a solution of **2** (2.07 g, 7.72 mmol) in THF (30 ml), was added *t*-BuOK (90% content; 1.440 g, 11.55 mmol) at −20 °C under an atmosphere of N_2. After the reaction mixture was further stirred at −20 °C for 20 min, the reaction was quenched by addition of an aqueous NH_4Cl solution (40 ml) and water (40 ml). The mixture was extracted with IPE (40 ml×4). The combined organic layers were washed with water (30 ml) and brine (30 ml), dried ($MgSO_4$), and evaporated to give a yellow oil (2.07 g), which was shown by its ^{1}H NMR spectrum to consist mainly of 5-(methylthio)-5-(*p*-tolylsulfonyl)-1,3-pentadiene (**3**): δ=2.36 (3H, s), 2.45 (3H, s), 4.38 (1H, dd, *J*=1.0, 8.9 Hz), 5.16—5.30 (2H, m), 5.60 (1H, dd, *J*=8.9, 14.8 Hz), 6.10—6.40 (2H, m), 7.33 (2H, d, *J*=7.9 Hz), and 7.76 (2H, d, *J*=8.2 Hz). This oil was subjected to column chromatography on silica gel (eluent: benzene) to give **4** (1.733 g, 84% yield) as colorless crystals: Mp 76.5—77.5 °C (from dichloromethane-hexane); ^{1}H NMR ($CDCl_3$) δ=2.28 (3H, s), 2.45 (3H, s), 3.78 (2H, d, *J*=7.7 Hz), 5.40 (1H, dt, *J*=15.0, 7.6 Hz), 5.95 (1H, dd, *J*=14.9, 10.4 Hz), 6.03 (1H, dd, *J*=10.6, 15.0 Hz), 6.28 (1H, d, *J*=14.9 Hz), 7.33 (2H, d, *J*=8.0 Hz), and 7.73 (2H, d, *J*=8.2 Hz); IR (KBr) 1290, 1144, 1126, 1087, 980, and 748 cm^{-1}. Found: C, 58.03; H, 6.00%. Calcd for $C_{13}H_{16}O_2S_2$: C, 58.20; H, 6.01%.

Preparation of 1-(Methylthio)-6-phenyl-5-(*p*-tolylsulfonyl)-1,3-hexadiene (5a). To a solution of butyllithium (1.80 mmol) in THF (1 ml) and hexane (1.2 ml), was dropwise added a solution of **4** (0.200 g, 0.754 mmol) in THF (4 ml) at −78 °C over 5 min, and the resulting solution was stirred at the same temperature for 40 min. Then, benzyl bromide (0.178 g, 1.04 mmol) was added and the reaction mixture was further stirred for 30 min at −78 °C. The reaction was quenched with an aqueous NH_4Cl solution. The usual workup (extraction with diethyl ether, being washed with water and brine, and evaporation) gave a yellow oil (0.388 g). This oil was separated by column chromatography on silica gel (eluent: an 80 : 1 mixture of benzene and ethyl acetate) to give **5a** (0.214 g, 80% yield) as colorless crystals, which were shown to consist of almost one geometric isomer. Further purification was performed by recrystallization from dichloromethane-hexane. **5a**: Mp 128.5—129.0 °C (from dichloromethane-hexane); ^{1}H NMR ($CDCl_3$) δ=2.24 (3H, s), 2.45 (3H, s), 2.85 (1H, dd, *J*=11.5, 13.5 Hz), 3.46—3.54 (1H, m), 3.67—3.75 (1H, m), 5.25 (1H, dd, *J*=14.5, 9.2 Hz), 5.70—5.90 (2H, m), 6.11 (1H, d, *J*=14.5 Hz), 7.05—7.14 (2H, diffused d, *J*=6.3 Hz), 7.14—7.30 (3H, m), 7.33 (2H, d, *J*=7.9 Hz), and 7.73 (2H, d, *J*=8.6 Hz); IR (KBr) 1288, 1130, 982, 749, 732, 593, and 532 cm^{-1}. Found: C, 67.05; H, 6.22%. Calcd for $C_{20}H_{22}O_2S_2$: C, 67.03; H, 6.19%.

Preparation of 1-(Methylthio)-5-(*p*-tolylsulfonyl)-1,3-tetradecadiene (5b). To a suspension of NaH (60% content in an oil; 48 mg, 1.2 mmol) in DMF (3 ml), were added **4** (0.268 g, 1.00 mmol) and then a DMF solution (2 ml) of nonyl bromide (0.228 g, 1.10 mmol) at −20 °C. After the resulting mixture was stirred at −20 °C for 7 h, the reaction was quenched with an aqueous NH_4Cl solution. The usual workup (extraction with IPE, being washed with brine, and evaporation) gave a brownish oil (0.407 g), which was separated by column chromatography on silica gel (eluent: a 40 : 1 mixture of benzene-ethyl acetate) to give **5b** (0.215 g, 56% yield) as a pale yellow oil. This was shown by its ^{1}H NMR spectrum to consist of mainly two geometric isomers (60 : 40): ^{1}H NMR ($CDCl_3$) δ=0.87 (3H, t, *J*=6.6 Hz), 1.02—1.46 (14H, m), 1.50—1.74 (1H, m), 1.96—2.16 (1H, m), 2.27 (3H×0.40, s), 2.29 (3H×0.60, s), 2.44 (3H, s), 3.39—3.57 (1H, m), 5.21 (1H×0.60, dd, *J*=ca. 9.4, 14.0 Hz),[12] 5.37 (1H×0.40, dd, *J*=9.6, 14.5 Hz), 5.87—6.30 (3H, m), 7.31 (2H, d, *J*=8.6 Hz), and 7.68 (2H, d, *J*=8.2 Hz); IR (neat) 2940, 1315, 1300, 1289, 1145, 1088, 979, and 666 cm^{-1} Found: C, 67.16; H, 8.68%. Calcd for $C_{22}H_{34}O_2S_2$: C, 66.96; H, 8.68%.

Hydrolysis of 5a Leading to 6-Phenyl-2,4-hexadienal (7a). A Typical Procedure: To a solution of **5a** (0.359 g, 1.00 mmol) in CH_3CN (18 ml), water (2 ml) and concd hydrochloric acid (0.167 ml, 2.00 mmol) were added. After the

resulting mixture was refluxed for 24 h, water (40 ml) was added. Extraction with IPE and evaporation of the combined organic layers gave a yellow oil (0.362 g).[8] To a solution of this oil (0.122 g) in CH_3CN (10 ml) was added DBU (0.051 g, 0.3349 mmol) at −20 °C, and the resulting mixture was stirred at −20 °C for 30 min. The reaction was quenched by the addition of an aqueous NH_4Cl solution (20 ml), and water (20 ml). The mixture was extracted with IPE (20 ml×3). The organic layers were combined, washed with water (20 ml×2), dried ($MgSO_4$), and evaporated to give a yellow oil (0.095 g), which was subjected to preparative TLC on silica gel (eluent: a 3 : 1 mixture of hexane and ethyl acetate) to give **7a** (0.030 g; 52% yield) as a pale yellow oil: It was shown by ^1H NMR analysis to consist of mainly two geometric isomers (95 : 5). ^1H NMR of the major isomer ($CDCl_3$) δ=3.55 (2H, d, J=6.3 Hz), 6.10 (1H, dd, J=15.3, 7.8 Hz), 6.30—6.45 (2H, m), 7.09 (1H, dd,J=10.3, 15.3 Hz), 7.14—7.16 (5H, m), and 9.54 (1H, d, J=8.0 Hz). ^1H NMR signals of the minor isomer appeared at δ=3.67 (2H, d, J=8.0 Hz), 6.23 (1H, dd, J=15.0, 8.0 Hz), 7.56 (1H, dd, J=10.0, 15.0 Hz), and 9.65 (1H, d, J=8.0 Hz). IR (neat) 1675, 1635, 1146, 1119, 1011, 988, 750, and 701 cm^{-1}. Found: m/z 172.0883. Calcd for $C_{12}H_{12}O$: M, 172.0887.

2,4-Tetradecadienal (7b): This consists of mainly two geometric isomers (91 : 9). A pale yellow oil; ^1H NMR of the major isomer ($CDCl_3$) δ=0.88 (3H, t, J=6.6 Hz), 1.12—1.39 (12H, m), 1.39—1.56 (2H, m), 2.17—2.26 (2H, m), 6.08 (1H, dd, J=7.9, 15.2 Hz), 6.20—6.36 (2H, m), 7.05—7.13 (1H, m), and 9.54 (1H, d, J=7.9 Hz). The ^1H NMR signals of the minor isomer appeared at δ=2.26—2.40 (2H, m), 6.15 (1H, dd, J=7.9, 15.2 Hz), 7.45 (1H, dd, J=10.6, 15.2 Hz), 9.61 (1H, d, J=7.9 Hz). IR (neat) 2930, 2860, 1688, 1640, 1164, 1117, 1009, and 985 cm^{-1}. Found: m/z 208.1833. Calcd for $C_{14}H_{24}O$: M, 208.1826.

Transformation of 4 into 4-Benzyl-5-phenyl-2,4-hexadienal (9a). A Typical Procedure: To a solution of benzyl bromide (0.955 g, 5.59 mmol) and **4** (0.500 g, 1.86 mmol) in DMF (15 ml) was added NaH (60% content in an oil; 0.220 g, 5.50 mmol) at −20 °C and the resulting mixture was stirred at −20 °C for 2 h and then 0 °C for 1 h. The reaction was quenched with an aqueous NH_4Cl solution. Extractions with diethyl ether and evaporation of the combined extracts gave a yellow oil (1.158 g). This oil (0.235 g) was dissolved in a 9 : 1 mixture (10 ml) of CH_3CN and water, and concd hydrochloric acid (0.065 ml, 0.780 mmol) was added. After the resulting mixture was stirred at room temperature for 1 h and at 50 °C for 1 h, and then refluxed for 1 h, water (30 ml) was added. Extractions with diethyl ether and evaporation of the combined extracts gave a yellow oil (0.212 g), which was separated by column chromatography on silica gel (eluent: an 8 : 1 mixture of benzene and hexane) to give **9a** (0.060 g; 60% overall yield from **5a**) as a pale yellow crystals: Mp 54.0—55.0 °C; ^1H NMR ($CDCl_3$) δ=3.40 (2H, s,), 3.61 (2H, s), 6.20 (1H, dd, J=14.9, 8.0 Hz), 6.32 (1H, d, J=11.3 Hz), 7.09—7.15 (4H, m), 7.22—7.34 (6H, m), 7.53 (1H, dd, J=15.1, 11.6 Hz), and 9.59 (1H, d, J=8.0 Hz); IR (KBr) 1682, 1623, 1492, 1119, 976, 745, and 700 cm^{-1}. Found: C, 87.12; H, 6.92%. Calcd for $C_{19}H_{18}O$: C, 86.99; H, 6.92%. Found: m/z 262.1358. Calcd for $C_{19}H_{18}O$: M, 262.1357.

5-Butyl-2,4-nonadienal (9b): A pale yellow oil; ^1H NMR ($CDCl_3$) δ=0.93 (3H, t, J=7.4 Hz), 0.94 (3H, t, J=7.4 Hz), 1.25—1.56 (8H, m), 2.19 (2H, t, J=7.6 Hz), 2.32 (2H, t, J=7.6 Hz), 6.08 (1H, dd, J=8.0, 14.9 Hz), 6.13 (1H, d, J=11.6 Hz), 7.40 (1H, dd, J=11.6, 15.1 Hz), and 9.57 (1H, d, J=8.0 Hz); IR (neat) 2980, 2950, 2890, 1680, 1623, 1178, 1127, and 972 cm^{-1}. Found: m/z 194.1662. Calcd for $C_{13}H_{22}O$: M, 194.1669.

Transformation of 4 into 5-Octyl-2,4-hexadienal (9c): To a suspension of KH (35% content in an oil; 258 mg, 2.230 mmol) in THF (3 ml), were successively added octyl bromide (432 mg, 2.24 mmol), a THF solution (6 ml) of **4** (200 mg, 0.745 mmol), and HMPA (1 ml) at −78 °C. The resulting mixture was stirred at −78 °C for 1 h, at −20 °C for 3 h, and then at 0 °C for 1 h under an atmosphere of N_2. The reaction was quenched with an aqueous NH_4Cl solution. Extraction with IPE and evaporation of the combined organic layers gave a yellow oil (653 mg). This oil was dissolved in a 9 : 1 mixture (20 ml) of CH_3CN and water, and concd hydrochloric acid (0.125 ml) was added. After the resulting mixture was stirred at room temperature for 1 h and at 50 °C for 1 h, and then refluxed for 1 h. Brine (30 ml) was added, and the usual workup gave a yellow oil (631 mg), which was purified by column chromatography on silica gel (eluent: a 1 : 1 mixture of benzene and hexane) and preparative TLC on silica gel (eluent: benzene) to give **9c** (123 mg; 54%) as a pale yellow oil: ^1H NMR ($CDCl_3$) δ=0.88 (6H, t, J=6.6 Hz), 1.16—1.80 (24H, m), 2.18 (2H, t, J=7.6 Hz), 2.31 (2H, t, J=7.6 Hz), 6.08 (1H, dd, J=7.9, 15.2 Hz), 6.12 (1H, d, J=11.2 Hz), 7.40 (1H, dd, J=11.2, 15.2 Hz), and 9.57 (1H, d, J=7.9 Hz); IR (neat) 2930, 2860, 1682, 1625, 1460, 1126, and 969 cm^{-1}. Found: m/z 306.2921. Calcd for $C_{21}H_{38}O$: M, 306.2921.

In a similar manner except for the use of 1,5-dibromopentane (2 mol-equiv) instead of octyl bromide, **9d** was obtained in 48% yield.

5,5-Pentamethylene-2,4-pentadienal (9d): A pale yellow oil; ^1H NMR ($CDCl_3$) δ=1.40—1.82 (6H, m), 2.12—2.34 (2H, m), 2.34—2.56 (2H, m), 6.02—6.16 (2H, m), 7.46 (1H, dd, J=11.9, 15.2 Hz), and 9.57 (1H, d, J=7.9 Hz); IR (neat) 2950, 1674, 1628, 1445, 1158, 1125, and 981 cm^{-1}; Found: m/z 150.1035. Calcd for $C_{10}H_{14}O$: M, 150.1043.

Conversion of 5a into 5-Methyl-6-phenyl-2,4-hexadienal (11a). A Typical Procedure: To a solution of **5a** (0.100 g, 0.279 mmol) in THF (5 ml), were added methyl iodide (0.035 ml, 0.079 mg, 0.557 mmol) and *t*-BuOK (90% content; 41 mg, 0.365 mmol) at −20 °C, and the resulting mixture was stirred at the same temperature for 1 h. After addition of an aqueous NH_4Cl solution, the usual workup gave a yellow oil (0.115 g), which was dissolved in CH_3CN (9 ml). After water (1 ml) and concd hydrochloric acid (0.046 ml, 0.55 mmol) were added, the resulting mixture was stirred at room temperature for 1 h and at 50 °C for 1 h, and then refluxed for 1 h. After water was added, extraction with IPE and evaporation of the combined extracts gave a brownish oil (0.103 g). The residual oil was purified by preparative TLC on silica gel (eluent: benzene) to give **11a** (32 mg, 62% overall yield from **5a**). This compound was shown by ^1H NMR analysis to consist of (2*E*,4*E*)- and (2*E*,4*Z*)-isomers in a 66 : 34 ratio: A pale yellow oil; ^1H NMR ($CDCl_3$) δ=1.85 (3H×0.34, s), 1.89 (3H×0.66, d, J=0.8 Hz), 3.48 (2H×0.66, s), 3.66 (2H×0.34, s), 6.11 (1H×0.66, dd, J=15.1, 8.0 Hz), 6.17 (1H×0.34, dd, J=15.1, 8.0 Hz), 6.20 (1H×0.66, d, J=11.6 Hz), 6.31 (1H×0.34, d, J=11.6 Hz), 7.10—7.34 (5H, m), 7.39 (1H×0.66, dd, J=11.4, 15.0 Hz), 7.53 (1H×0.34, dd, J=11.6, 15.1 Hz), 9.58 (1H×0.66, d, J=8.3 Hz), and 9.60 (1H×0.34, d, J=8.0 Hz); IR (neat) 1680, 1630, 1175, 1125, 972, 745, and 702

cm^{-1}. Found: *m/z* 186.1042. Calcd for $C_{13}H_{14}O$: M, 186.1043.

5-Ethyl-2,4-tetradecadienal (11b): A pale yellow oil;[13] ^1H NMR ($CDCl_3$) δ=0.88 (3H, t, *J*=6.6 Hz), 1.09 (3H, t, *J*=7.6 Hz), 1.17—1.46 (14H, m), 2.15—2.39 (4H, m), 6.03—6.16 (2H, m), 7.41 (1H, dd, *J*=15.2, 11.2 Hz), and 9.56 (1H, d, *J*=7.9 Hz); IR (neat) 2930, 2860, 1680, 1628, 1460, 1178, 1126, and 970 cm^{-1}. Found: *m/z* 236.2141. Calcd for $C_{16}H_{28}O$: M, 236.2138.

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References

1) a) S. Takano, Y. Sekiguchi, Y. Shimazaki, and K. Ogasawara, *Tetrahedron Lett.*, **30**, 4001 (1989). b) A. A. L. Gunatilaka, N. Hirai, and D. G. I. Kingston, *Tetrahedron Lett.*, **24**, 5457 (1983). c) K. C. Nicolaou, R. Zipkin, and D. Tanner, *J. Chem. Soc., Chem. Commun.*, **1984**, 349. d) H. R. Pfaendler, F. K. Maier, and S. Klar, *J. Am. Chem. Soc.*, **108**, 1338 (1986). e) J. M. Williams and G. J. McGarvey, *Tetrahedron Lett.*, **26**, 4891 (1985). f) W. R. Roush, *J. Am. Chem. Soc.*, **102**, 1390 (1980). g) Y. Wang, J. Li, Y. Wu, Y. Huang, L. Shi, and J. Yang, *Tetrahedron Lett.*, **27**, 4583 (1986). h) J. Morris and D. G. Wishka, *Tetrahedron Lett.*,**27**, 803 (1986). g) O. Isler, H. Lindlar, M. Montavon, R. Ruegg, and P. Zeller, *Helv. Chim. Acta*, **39**, 249 (1956).

2) a) E. L. Pippen and M. Nonaka, *J. Org. Chem.*, **23**, 1580 (1958). b) A. T. Nielsen and W. J. Honliham, *Org. React.*, **16**, 1 (1961). c) B. M. Mikhailov and G. S. Ter-Sarkisyan, *Zh. Obshch. Khim.*, **29**, 1642 and 2560 (1959). Cf. *Chem. Abstr.*, **54**, 10952f and 10988d (1960). d) T. M. Cresp, M. V. Sargent, and P. Vogel, *J. Chem. Soc., Perkin. Trans. 1*, **1974**, 37. e) R. C. Cookson and R. Gopalan, *J. Chem. Soc., Chem. Commun.*, **1978**, 924. f) R. H. Wollenberg, *Tetrahedron Lett.*, **1978**, 717. g) K. Yamamoto, M. Ohta, and J. Tsuji, *Chem. Lett.*, **1979**, 713. h) B. A. Patel, J. I. Kim, D. D. Bender, L. -C. Kao, and R. F. Heck, *J. Org. Chem.*, **46**, 1061 (1981). i) T. Jeffery, *Tetrahedron Lett.*, **26**, 2667 (1985). j) M. Furber and R. J. K. Taylor, *J. Chem. Soc., Chem. Commun.*, **1985**, 782. k) T. Rein, B. Åkermark, and P. Helquist, *Acta Chem. Scand., Ser. B.*, **42**, 569 (1988). l) P. Chabert and C. Mioskowski, *Tetrahedron Lett.*, **30**, 6031 (1989). m) L. Duhamel, J. Guillemont, Y. L. Gallic, G. Plé, J. -M. Poirier, Y. Ramondenc, and P. Chaabardes, *Tetrahedron Lett.*, **31**, 3129 (1990).

3) K. Ogura, N. Yahata, T. Fujimori, and M. Fujita, *Tetrahedron Lett.*, **31**, 4621 (1990).

4) This reagent (**1**) is easily prepared from dimethyl sulfoxide and sodium *p*-toluenesulfinate: K. Ogura, N. Yahata, J. Watanabe, and H. Iida, *Bull. Chem. Soc. Jpn.*, **56**, 3543 (1983). Now, **1** is commercially available. For organic synthetic methods using **1**, see a) K. Ogura, *Pure Appl. Chem.*, **59**, 1033 (1987); b) K. Ogura, *Studies in Natural Products Chemistry* (ed by Atta-ur-Rahman, Elsevier), **6**, 307 (1989).

5) The C-C double bond isomerization of **2** to produce **3** was not caused with triethylamine. After treatment of **2** with a catalytic amount (0.1 equiv) of *t*-BuOK in *t*-BuOH under ice-cooling, acidic workup gave a small amount of the expected **3** implying that the pentadienyl anion of **2** is not in equilibrium with **2** itself under these conditions.

6) Treatment of **4** with benzyl bromide (1.1 equiv) and NaH (1.2 equiv) in DMF (from −20 °C to 0 °C) gave the expected **5a** in 47% yield along with a dibenzylated product (9% yield) and the unreacted **4** (18% yield). When the lithio derivative, derived from **4** and butyllithium (1 equiv), was allowed to react with benzyl bromide in THF, the reaction was so slow that the lithiated **4** decomposed.

7) At −78 °C, the dilithio derivative of **4** was inactive toward nonactivated alkyl halides such as ethyl iodide and ethyl bromide. At an elevated temperature, decomposition of the dilithio derivative was observed.

8) In another run using **5a**, the crude product was purified by column chromatography (silica gel) and preparative TLC (silica gel) to afford an intermediary product (**6a**) as an oil contaminated with a small amount of **7a** and other by-products. Its ^1H NMR (60 MHz; in $CDCl_3$) exhibited the signals corresponding to a =CH-CHO group [δ=9.22 (1H, d, *J*=7.7 Hz) and 5.84 (1H, dd, *J*=15.2 and 7.7 Hz)][9] and *p*-tolylsulfonyl group [δ=2.45 (3H, s), 7.37 (2H, d, *J*=8.0 Hz), 7.78 (2H, d, *J*=8.0 Hz). Other signals could not be assigned completely. Since treatment of this oil with DBU gave **7a** as a major product, the structure of the intermediate was deduced to be **6a**.

9) R. M. Silverstein, G. C. Bassler, and T. C. Morrill, "Spectrometric Identification of Organic Compounds," 4th ed, John Wiley & Sons, New York (1981), p. 235.

10) a) T. Mukaiyama, K. Kamio, S. Kobayashi, and H. Takei, *Bull. Chem. Soc. Jpn.*, **45**, 3723 (1972). b) T. Mukaiyama, M. Shiono, and T. Sato, *Chem. Lett.*, **1974**, 37.

11) A. J. Mura, Jr., G. Majetich, P. A. Grieco, and T. Cohen, *Tetrahedron Lett.*, **1975**, 4437.

12) Olefinic protons of other minor isomers exhibited their signals at this region to disturb accurate assignment of the coupling constants.

13) Since assignment of the ^1H NMR signals of **11b** to its possible geometric isomers was impossible, its isomeric ratio was not determined.