10-(2-Chlorophenyl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5e): mp 265–266 °C; ^{1}H NMR (Me_2SO-d_6) δ 5.03 (s, 2 H), 5.47 (s, 1 H), 6.33–7.73 (m, 8 H), 10.35 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1725 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 329 (M^+, 75), 331 (M + 2, 26), 236 (100). Anal. Calcd for $C_{17}H_{12}ClNO_2S$: C, 61.91; H, 3.67; N, 4.25. Found: C, 61.76; H, 3.77; N, 4.15.

10-(4-Bromophenyl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5f): mp 284–285 °C; ^{1}H NMR (Me_2SO-d_6) δ 5.02 (s, 2 H), 5.37 (s, 1 H), 6.7–7.57 (m, 8 H), 10.35 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1720 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 373 (M^+, 79), 375 (M + 2, 76). Anal. Calcd for $C_{17}H_{12}BrNO_2S$: C, 54.55; H, 3.23; N, 3.74. Found: C, 54.48; H, 3.56; N, 3.50.

10-Phenyl-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5g): mp 256–256.5 °C; ^{1}H NMR (Me_2SO-d_6) δ 4.97 (s, 2 H), 5.27 (s, 1 H), 6.70–7.5 (m, 9 H), 10.17 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1730 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 295 (M^+, 81), 236 (100). Anal. Calcd for $C_{17}H_{13}NO_2S$: C, 69.14; H, 4.44; N, 4.74. Found: C, 69.15; H, 4.61; N, 4.66.

10-(2-Nitrophenyl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5h): mp 252–253 °C; ^{1}H NMR (Me_2SO-d_6) δ 5.1 (s, 2 H), 6.03 (s, 1 H), 6.67–7.63 (m, 6 H), 7.87–8.17 (m, 1 H), 10.38 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1725 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 340 (M^+, 2.4), 148 (100), 135 (99). Anal. Calcd for $C_{17}H_{12}N_2O_4S$: C, 59.99; H, 3.56; N, 8.23. Found: C, 59.52; H, 3.86; N, 8.28.

10-(5-Methyl-2-thienyl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5i): mp 235–236 °C; ^{1}H NMR (Me_2SO-d_6) δ 2.22 (s, 3 H), 4.92 (s, 2 H), 5.37 (s, 1 H), 6.3 (s, 2 H), 6.71–7.52 (m, 4 H), 10.17 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1720 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 315 (M^+, 100). Anal. Calcd for $C_{16}H_{13}NO_2S$: C, 60.93; H, 4.15; N, 4.44. Found: C, 61.04; H, 4.18; N, 4.34.

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Registry No. **2** (Ar = 3,4-(methylenedioxy)phenyl), 87191-93-3; **2** (Ar = 3,4,5-trimethoxyphenyl), 87191-94-4; **2** (Ar = 4-chlorophenyl), 87191-95-5; **2** (Ar = 2-chlorophenyl), 87191-96-6; **2** (Ar = phenyl), 30030-96-7; **2** (Ar = 2-nitrophenyl), 87191-97-7; **2** (Ar = 3,4-dimethoxyphenyl), 87191-98-8; **2** (Ar = 4-bromophenyl), 87192-09-4; **2** (Ar = 5-methyl-2-thienyl), 87192-10-7; **3a**, 87191-99-9; **3b**, 87192-00-5; **3c**, 87192-01-6; **3d**, 87192-02-7; **3e**, 87192-03-8; **3f**, 87192-04-9; **3g**, 87192-05-0; **3h**, 87192-06-1; **3i**, 87207-11-2; **3j**, 87192-07-2; **3k**, 87192-08-3; **5a**, 87192-11-8; **5b**, 87192-12-9; **5c**, 87192-13-0; **5d**, 87192-14-1; **5e**, 87192-15-2; **5f**, 87192-16-3; **5g**, 87192-17-4; **5h**, 87192-18-5; **5i**, 87192-19-6.

Intramolecular Diels–Alder Reactions of Alkenylallenes. A Model Study for the Bottom Half of Chlorothricolide

Barry B. Snider*[1] and Beverly W. Burbaum

Department of Chemistry, Brandeis University, Waltham, Massachusetts 02254

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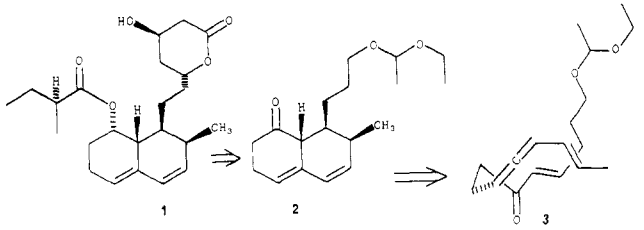
The intramolecular Diels–Alder reactions of two methyl (*E,E*)-2,7,8,10-dodecatetraenoates (**8a** and **9a**) and methyl (*E,E*)-2,6,7,9-undecatetraenoate (**8b**) have been examined. Alkenylallenes **8a** and **9a** react at 110–130 °C to give **10a** and **11a** stereospecifically. Alkenylallene **8b** undergoes an intramolecular Diels–Alder reaction to give **10b** at or below room temperature. Adduct **11a** is converted to **17**, a model for the bottom half of chlorothricolide, by epoxidation, rearrangement (BF_3), and reduction.

Our plan for the synthesis of the hypocholesterolemic agent compactin (**1**)[2] led us to consider an intramolecular Diels–Alder reaction of **3**, in which an alkenylallene is the



diene component, to give **2**, which contains three of the four chiral centers and the diene unit of the hexahydronaphthalene moiety of **1**. Although the use of alkenylallenes as dienes in Diels–Alder reactions is well-known,[3] intramolecular Diels–Alder reactions of alkenylallenes were virtually unexplored.[4]

The successful synthesis of **3** and its conversion to **2**[5] prompted the study of the scope of the intramolecular Diels–Alder reaction of alkenylallenes reported here. Several features of this reaction make it a particularly attractive synthetic method. The required alkenylallenes can be easily synthesized by methods not applicable to normal dienes. The allene moiety is chiral and can be

(1) Fellow of the Alfred P. Sloan Foundation, 1979–1983. Dreyfus Teacher–Scholar, 1982–1987.

(2) Structure: Brown, A. G.; Smale, T. C.; King, T. J.; Hasenkamp, R.; Thompson, R. H. *J. Chem. Soc., Perkin Trans. 1*, **1976**, 1165. Activity: Mabuchi, H.; Haba, T.; Tatami, R.; Miyamoto, S.; Sakai, Y.; Wakasugi, T.; Watanabe, A.; Koizumi, J.; Takeda, R. *N. Engl. J. Med.* **1981**, *305*, 478 and references cited therein.

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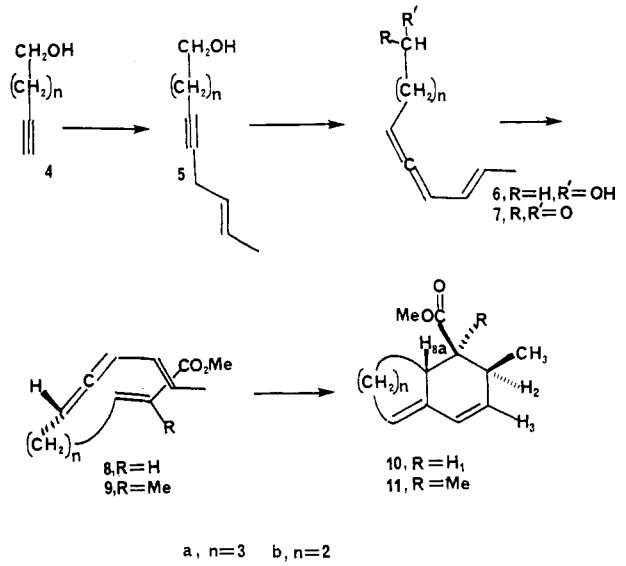
Scheme I



synthesized in optically active form which will lead to optically active adducts. Steric constraints caused by the introduction of the allene lead to different endo/exo preferences in these reactions. The products are more highly functionalized than normal Diels–Alder adducts and control of the ring fusion geometry is postponed. The model study for the bottom half of chlorothricolide illustrates the last two points.

Results

The desired alkenylallene can be efficiently constructed by base-catalyzed isomerization of a 1,4-enyne.[3] Conversion of 5-hexyn-1-ol (**4a**, Scheme I) to the dianion with MeMgBr in THF, addition of 7 mol % of CuCl and coupling with 2 equiv of crotyl bromide at 45 °C, gives an 88% yield of a 12:1 mixture of (*E*)-8-decen-5-yn-1-ol (**5a**) and the allylic isomer 7-methyl-8-nonen-5-yn-1-ol (**12a**).[6] Isomerization of this mixture with potassium *tert*-butoxide in *tert*-butyl alcohol[7] for 11 h at 40 °C gives a 91% yield of a mixture containing ≃50% of **6a**. The remainder of the mixture consists of unreacted **5a** and **12a** and conjugated enynes. Although this route to alkenylallenes is very short, the mixture of products must be carried on through the Diels–Alder reaction. We are currently exploring alternative routes to **6** and related compounds.

Oxidation of **6a** with pyridinium dichromate[8] gives a 69% yield of a mixture containing ~50% of **7a**. Reaction of this mixture with the sodium salt of trimethyl phosphonoacetate gives a 79% yield of a mixture containing ~50% of **8a**. A similar reaction with the sodium salt of trimethyl 2-phosphonopropionate gives an 85% yield of a mixture containing ~50% of **9a**.

Intramolecular Diels–Alder reaction is effected by heating crude **8a** for 3 h at 110 °C in toluene to give adduct **10a** in 11% yield, based on the mixture containing **8a** (6% overall from **4a**). Heating **8a** for 2 h at 140 °C in benzene gives a 15% yield of **10a** (8% from **4a**). Although the analysis of this mixture is complicated by the presence of byproducts from the alkylation of **4a** and the isomerization of **5a**, no isomeric Diels–Alder adducts can be detected.

The stereochemistry of **10a** is easily established by analysis of the NMR spectrum. H_1 absorbs as a doublet of doublets, $J_{1,2}$ = 5 Hz, $J_{1,8a}$ = 12 Hz. Therefore, H_1 and H_{8a} must be axial and H_2 must be equatorial. $J_{2,3}$ = 5 Hz, which confirms that H_2 is equatorial.

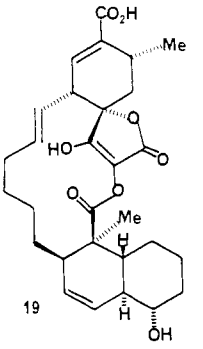
Heating crude alkenylallene **9a** for 6 h at 110 °C in toluene gives a 34% yield of adduct **11a**, based on the mixture containig **9a** (20% overall from **4a**). Alternatively, the Diels–Alder reaction occurs at 25 °C in the presence of a Lewis acid catalyst. Treatment of crude **9a** with 0.9 equiv of $EtAlCl_2$ in benzene for 18 h at 25 °C gives a 26% yield of **11a**. The stereochemical assignment of **11a** is based on the coupling constant, $J_{2,3}$ = 5 Hz, which indicates that H_2 is equatorial, and the conversion of **11a** to **15** (vide infra).

We attempted to prepare **8b** to study the suitability of this method for the preparation of tetrahydroindenes. Preparation of **7b** proceeds analogously to that of **7a**. Reaction of **7b** with sodium trimethylphosphonoacetate at 60 °C in THF surprisingly gives no **8b**. Examination of the reaction mixture indicates that **10b** has been formed under these conditions (21% from crude **7b**, 15% from **4b**). A similar Wittig reaction at 0 °C gives comparable results.

The intramolecular Diels–Alder reaction of **8b** to give **10b** thus proceeds rapidly at room temperature. This is remarkable for a simple, ester-activated dienophile.[9] A related intramolecular Diels-Alder reaction in which the alkenylallene is replaced by a diene occurs in 24 h at 150 °C.[10] Examination of models indicates that **8b** can easily adopt the conformation required for a Diels–Alder reaction. The presence of the alkenylallene decreases the rotational freedom relative to the diene. This accelerates the Diels–Alder reaction by making the entropy of activation less negative.

The stereochemistry of the Diels–Alder reaction is determined primarily by steric rather than electronic effects. Alkenylallenes **3**, **8a**, and **9a** give adducts with the same stereochemistry, although the ester is endo in the formation of **10a** and **11a** while the carbonyl is exo in the formation of **2**. Examination of models indicates that the proper orientation cannot be obtained for the formation of the isomeric Diels–Alder adduct.

Synthesis of the Chlorothricolide Model 17. Octalin **17** is a model for the bottom half of chlorothricolide (**19**).[11,12] We chose to explore the conversion of **11a** to **17**



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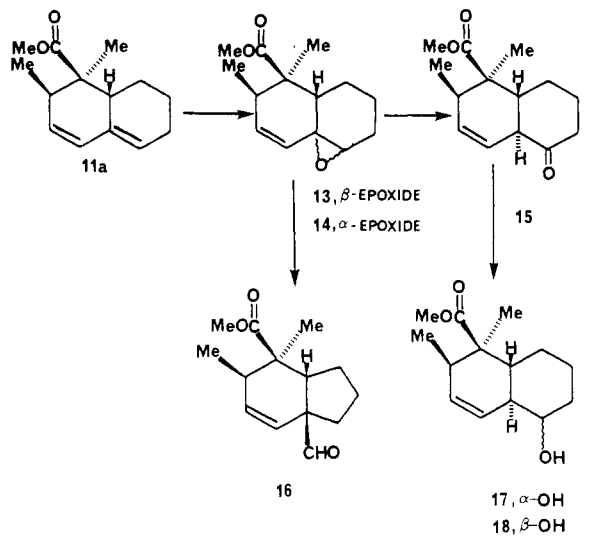
Scheme II

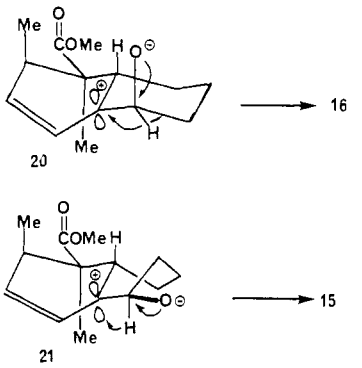


to test our hypothesis that Diels–Alder adducts such as **11a** can be converted to cis- or trans-fused decalins and to explore the reactivity of the diene moiety of **11a**. This approach is of value since Roush has observed that **17** cannot be efficiently prepared by a simple intramolecular Diels–Alder reaction.[13]

Epoxidation of **11a** with *m*-chloroperbenzoic acid in CH_2Cl_2 using aqueous $NaHCO_3$ as a proton scavenger in a two-phase system gives an 80% yield of a 5:1 mixture of the unstable epoxides **13** and **14** as determined by NMR analysis (Scheme II). The stereochemical assignment follows from further reactions. Selective hydroboration of **11a** could not be achieved.

Rearrangement of the 5:1 mixture of **13** and **14** with $LiClO_4$ in refluxing benzene[14] gives a moderate yield of a 1:1 mixture of **15** and **16**. Rearrangement with 0.1 equiv of $Eu(fod)_3$ in $CDCl_3$[15] for 6 days at 25 °C gives a moderate yield of a 1:4 mixture of **15** and **16**. Fortunately, rearrangement with 0.4 equiv of $BF_3{\cdot}OEt_2$[16] in 1,2-dimethoxyethane at −50 °C for 17 h gives an 83% yield of a 10:1 mixture of **15** and **16** from which **15** can be isolated in 70% yield. The ^1H and ^{13}C NMR spectra of **15** were identical with those of an authentic sample.[13,17] As reported,[13] reduction of **15** with $BH_3{\cdot}NH_3$ gave a 2:1 mixture of **17** and **18** in 76% yield.

The formation of aldehyde **16** was not anticipated on the basis of the rearrangements of related steroid[16] and sesquiterpenoid epoxides.[18] However, examination of models indicates that it should be a major product. Epoxide **13** will open to the chair cyclohexane **20** in which the carbon–carbon bond is properly aligned for formation of **16**. If **20** flips to the boat conformer **21**, then the carbon–hydrogen bond is properly aligned for formation of **15**. The ratio of **15** to **16** may depend on the stability of the zwitterionic intermediate. $BF_3{\cdot}OEt_2$ will give rise to a stable zwitterion that will live long enough to flip from **20** to **21** and will undergo a 1,2-hydride shift. Due to 1,3-diaxial interactions, a boat conformer corresponding



to **21** is strongly favored in the epoxides that have been previously examined.[16,18]

We have shown that the intramolecular Diels–Alder reaction of alkenylallenes is a facile, stereospecific reaction and that the adducts are useful intermediates. We are currently developing a route to the bottom half of chlorothricolide based on this chemistry.

Experimental Section

NMR spectra were determined on a Perkin-Elmer R32, Varian EM 390, Bruker WH90, or homemade 270-MHz NMR spectrometer. IR spectra were recorded on a Perkin-Elmer 683 spectrometer. Analyses were performed by Galbraith Laboratories.

THF and ether were distilled from sodium benzophenone ketyl. CH_2Cl_2 was distilled from CaH_2. *tert*-Butyl alcohol was distilled from Na. $Eu(fod)_3$ was purchased from Aldrich Chemical Co. Trimethyl 2-phosphonopropionate was prepared from trimethyl phosphite and methyl 2-bromopropionate.[19]

All air-sensitive reactions were run in flame-dried glassware under nitrogen.

Synthesis of (*E*)-Dec-8-en-5-yn-1-ol (5a). 5-Hexyn-1-ol (**4a** 20.0 g, 0.2 mol) and 40 mL of THF were placed in a three-necked, 1-L flask equipped with condenser, magnetic stirrer, and nitrogen inlet. The solution was cooled to 0 °C and treated with 148 mL of 2.9 M MeMgCl in THF (0.43 mol) over 1 h. The solution was heated at 60 °C for 45 min and cooled to 25 °C. Cuprous chloride (1.5 g, 0.015 mol), crotyl bromide (62 g, 0.46 mol, 80%, remainder 3-bromo-1-butene), and THF (20 mL) were added to the semisolidified mass. The mixture was heated for 45 min at 60 °C, giving a homogeneous solution. The mixture was cooled to 25 °C and quenched with enough 10% NH_4Cl solution to give a blue solution. Sodium cyanide was added until the solution became slightly yellow. The layers were separated. The aqueous layer was extracted twice with ether. The combined organic layers were washed with brine, dried ($MgSO_4$), and evaporated to give 34.16 g of a red liquid, which was used for further experiments. Distillation of 3.232 g (74–75 °C, 0.15 torr) gave 2.586 g (88%) of an 89:8:3 mixture of **5a**, **12a**, and **4a**: NMR ($CDCl_3$) δ 4.95–5.80 (m, 2), 3.52 (t, 2, J = 8.5 Hz), 3.0 (m, 1, OH), 2.70–2.90 (m, 2), 2.05–2.35 (m, 2), 1.45–2.00 (m, 7), 1.20 (d, 3, J = 7.5 Hz, **12a**); IR (neat) 3600–3100, 3020 cm^{-1}; GC (10 ft, 10% Carbowax 20M, 160 °C) t_R 8.0 min (**4a**), 28.7 min (**12a**), and 54.5 min (**5a**). An analytical sample was prepared by preparative GC.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.70; H, 10.69.

Synthesis of (*E*)-Non-7-en-4-yn-1-ol (5b). 4-Pentyn-1-ol (**4b**; 10.71 g, 0.127 mmol) and crotyl bromide (37.71 g, 0.28 mol, 80%, remainder 3-bromo-1-butene) were reacted as described above to give 17.52 g (100%) of crude **5b** (91% of **5b**, 8% 6-methyl-7-octen-4-yn-1-ol (**12b**), and 1% **4b**, which was used without purification. A pure sample was prepared by distillation (73–75 °C, 0.2 torr): NMR ($CDCl_3$) δ 4.9–5.8 (m, 2), 3.52 (t, 2, J = 8.5 Hz), 2.95–3.15 (m, 1, OH), 2.7–2.9 (m, 2), 2.05–2.35 (m, 2), 1.45–1.8 (m, 5); 1.20 (d, 3, J = 7 Hz, **12b**); IR (neat) 3600–3100, 3020 cm^{-1}; GC (10 ft, 10% Carbowax 20M, 170 °C) t_R 4.4 min (**4b**), 12 min (12b), and 22 min (**5b**). An analytical sample was prepared by preparative GC.

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Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 77.95; H, 10.29.

Synthesis of (*E*)-Deca-5,6,8-trien-1-ol (6a). (*E*)-Deca-8-en-5-yn-1-ol (**5a**, 10.25 g, 0.067 mol) was added to 170 mL of 1 M potassium *tert*-butoxide in *tert*-butyl alcohol. The resulting solution was heated for 1 hr at 40 °C. The solution was cooled to 25 °C and quenched by the addition of 400 mL of 10% NH_4Cl solution. The layers were separated. The aqueous layer was extracted twice with ether. The combined organic extracts were washed exhaustively with water and brine, dried ($MgSO_4$), and evaporated to give 9.33 g (91%) of a clear red oil, which was ca. 50% **6a** as determined by NMR analysis: NMR ($CDCl_3$) δ 5.5–5.9 (m, 3), 5.05–5.37 (m, 1), 3.62 (t, 2, J = 8.5 Hz), 1.45–2.45 (m, 7), 1.80 (d, 3, J = 7 Hz), 1.00 (t, 3, J = 7.5 Hz, 7-decen-5-yn-1-ol); IR (neat) 3700–3100, 3050, 1935 cm^{-1}. The alkenylallene decomposed during GC (10 ft, 10% Carbowax 20M, 180 °C).

Synthesis of (*E*)-Nona-4,5,7-trien-1-ol (6b). Isomerization of **5b** (12.42 g, 0.09 mol) in 225 mL of 1 M potassium *tert*-butoxide at 40 °C as described above gave 10.80 g (87%) of a red oil, which was shown to be ca. 50% **6b** by NMR analysis: NMR ($CDCl_3$) δ 5.5–5.9 (m, 3), 5.05–5.37 (m, 1), 3.62 (t, 2, J = 8.5 Hz), 1.45–2.45 (m, 5), 1.80 (d, 3, J = 6 Hz), 1.00 (t, 3, J = 7 Hz, 6-nonen-4-yn-1-ol); IR (neat) 3700–3100, 3050, 1935 cm^{-1}.

Synthesis of (*E*)-5,6,8-Decatrienal (7a). Alcohol **6a** (3.498 g, 0.023 mol, ~50% **6a**) was added to a stirred suspension of pyridinium dichromate (13.4 g, 0.035 mol) in 35 mL of CH_2Cl_2. The solution was stirred for 25 h, diluted with 40 mL of ether, and filtered through Florisil with ether as eluent. Evaporation of the solvent gave 2.377 g (69%) of a mixture containing ca. 50% **7a**: NMR ($CDCl_3$) δ 9.72 (t, 1, J = 1.5 Hz), 5.72 (m, 2), 5.3–6.05 (m, 1), 5.15–5.37 (m, 1), 1.4–2.7 (m, 6), 1.71 (d, 3, J = 6 Hz); IR (neat) 3010, 2710, 1930, 1715 cm^{-1}.

Synthesis of (*E*)-4,5,7-Nonatrienal (7b). Oxidation of 0.694 g (0.005 mol, ~50% 6b) of **6b** with 2.892 g (0.0075 mol) of pyridinium dichromate as described above gave 0.458 g (67%) of a mixture containing ca. 50% **7b**: NMR ($CDCl_3$) δ 9.72 (t, 1, J = 1.5 Hz), 5.8 (m, 2), 5.5–6.2 (m, 1), 5.2–5.5 (m, 1), 2.1–2.6 (m, 4), 1.72 (d, 3, J = 6 Hz); IR (neat) 3010, 2720, 1930, 1715 cm^{-1}.

Methyl (*E*,*E*)-2,7,8,10-Dodecatetraenoate (8a). Sodium hydride (0.456 g, 10 mmol) in a flame-dried flask was washed twice with hexane. A solution of trimethyl phosphonoacetate (1.44 g, 7 mmol) in 15 mL of THF was added. The solution was allowed to stir for 1 h at 25 °C. Aldehyde **7a** (1.050 g, 7 mmol, ~50% **7a**) was slowly added by syringe. THF (2 mL) was used to add the last of the aldehyde. The reaction mixture was stirred for 30 min and quenched carefully with water (hydrogen evolution!). The layers were separated and the aqueous layer was extracted twice with pentane. The combined organic layers were washed with brine, dried ($MgSO_4$), and evaporated to give 1.142 g (79%) of **8a** as a light brown oil, which was used without further purification (the sample is a mixture of **8a** (~50%) and double-bond isomers): NMR ($CDCl_3$) δ 6.95 (dt, 1, J = 15, 7 Hz), 5.75 (br s, 2), 5.20–5.95 (m, 3), 3.72 (s, 3), 1.75–2.65 (m, 4), 1.75 (d, 3, J = 7 Hz), 1.75–1.5 (m, 2); IR (neat) 3015, 1945, 1715, 1655, 975 cm^{-1}. Attempted purification by medium-pressure liquid chromatography on silica gel was unsuccessful.

Methyl (*E*,*E*)-2-Methyl-2,7,8,10-dodecatetraenoate (9a). Aldehyde **7a** (1.950 g, 12 mmol, ~50% **7a**) in 10 mL of THF was added to a mixture of hexane-washed sodium hydride (0.8 g, 20 mmol) and trimethyl 2-phosphonopropionate (2.8 g, 14 mmol) in 20 mL of THF. The solution was stirred for 30 min and worked up as described for the preparation of **8a** to give 2.145 g (85%) of **9a** (~50%) as a clear red oil, which was used without purification: NMR ($CDCl_3$) δ 6.78 (tq, 1, J = 7, 1.5 Hz), 5.72 (m, 2), 5.1–5.9 (m, 2), 3.73 (s, 3), 1.35–2.9 (m, 12); IR (neat) 3015, 1940, 1715, 1650, 970 cm^{-1}.

Methyl 2,6,7,7aβ-Tetrahydro-6β-methyl-1*H*-indene-7β-carboxylate (10b). Aldehyde **7b** (0.369 g, 27 mmol, ~50% **7b**) in 8 mL of THF was added to a mixture of hexane-washed sodium hydride (0.57 g, 14 mmol) and trimethyl phosphonoacetate (0.685 g, 3.6 mmol) in 22 mL of THF. The resulting solution was heated to 65 °C for 10 min, cooled to 25 °C, and worked up as described above for the preparation of **8a** to give 0.355 g (68%) of a clear red oil. NMR analysis indicated that **10b** rather than **8b** was the major product. Medium-pressure chromatography of 0.351 g on silica gel (95:5 hexane–ethyl acetate) gave 0.106 g (21%; 15% based on **4b**) of pure **10b**: NMR ($CDCl_3$) δ 6.21 (d, 1, J = 10 Hz), 5.68 (dd, 1, J = 10, 5 Hz), 5.52 (m, 1), 3.62 (s, 3), 1.2–2.9 (m, 7), 0.91 (d, 3, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 141.0, 133.8, 125.3, 122.3, 51.3, 50.7, 39.5, 33.2, 31.5 (2 carbons?), 16.7; IR (neat) 3010, 1730, 1650 cm^{-1}.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.21; H, 8.60.

An identical reaction that was run at 0 °C for 30 min rather than 65 °C for 10 min gave virtually identical results as determined by NMR analysis.

Methyl 1,2,6,7,8,8aβ-Hexahydro-2β-methylnaphthalene-1β-carboxylate (10a). Crude **9a** (0.63 g) was dissolved in 5 mL of toluene and heated at 110 °C for 3 h. Removal of the solvent gave 0.63 g of crude product. Medium-pressure chromatography of 0.349 g on siica gel (99:1 hexane–ethyl acetate) gave 0.039 g (11%, 6% from **4a**) of pure **10a** as a colorless oil: NMR ($CDCl_3$) δ 5.91 (d, 1, J = 10 Hz), 5.58 (dd, 1, J = 10, 5 Hz), 5.52 (br s, 1), 3.68 (s, 3), 1.2–2.7 (m, 8), 2.47 (dd, 1, J = 12, 5 Hz), 0.92 (d, 3, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 174.3, 135.6, 130.4, 128.2, 126.1, 51.0, 49.9, 32.7, 31.4, 27.7, 25.8, 22.6, 16.7; IR (neat) 3010, 1735, 1650 cm^{-1}. An analytical sample was prepared by evaporative distillation (80 °C, 2.5 torr).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.34; H, 8.65.

Methyl 1,2,6,7,8,8aβ-Hexahydro-1α,2β-dimethylnaphthalene-1β-carboxylate (11a). Crude **9a** (2.0906 g, 9.5 mmol) in 20 mL of toluene containing 2 mg of BHT was heated at 110 °C for 6 h. Removal of the solvent gave 1.974 g of crude product. Medium-pressure chromatography on silica gel (9:1 hexane–ether) gave 0.685 g (34%, 20% from **4a**) of pure **11a**: NMR ($CDCl_3$) δ 5.88 (d, 1, J = 9.5 Hz), 5.59 (br s, 1, $W_{1/2}$ = 10 Hz), 5.44 (dd, 1, J = 5.5, 9.5 Hz), 3.73 (s, 3), 2.82 (br d, 1, J = 9 Hz), 2.4–1.52 (m, 7), 1.12 (s, 3), 0.93 (d, 3, J = 6.5 Hz).

Similar reaction of the ethyl ester corresponding to **9a** (1.00 g, 4 mmol) gave 1.00 g of crude product. Medium-pressure chromatography of 0.816 g on silica gel (95:5 hexane–ethyl acetate) gave 0.245 g (30%) of the ethyl ester corresponding to **11a**: NMR ($CDCl_3$) δ 5.88 (d, 1, J = 9.5 Hz), 5.59 (br s, 1, $W_{1/2}$ = 10 Hz), 5.44 (dd, 1, J = 5.5, 9.5 Hz), 4.17 (q, 2, J = 7.5 Hz), 2.82 (br d, 1, J = 10 Hz), 1.55–2.40 (m, 7), 1.27 (t, 3, J = 7.5 Hz), 1.12 (s, 3), 0.93 (d, 3, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 175.6, 134.4, 128.0, 127.3, 127.1, 59.4, 40.5, 34.8, 25.4, 23.8, 22.3, 18.0, 17.3, 13.7 (the quaternary carbon was not observed; it may be under the peak at 59.4); IR (neat) 3010, 1730, 1640 cm^{-1}.

Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 77.05; H, 9.61.

Epoxidation of 11a. Diene **11a** (0.281 g, 1.3 mmol) was dissolved in 12 mL of CH_2Cl_2; and 8 mL of 5% $NaHCO_3$ solution was added. The mixture was cooled to 0 °C and treated with *m*-chloroperbenzoic acid (0.312 g, 85%, 1.5 mmol). The reaction mixture was stirred for 3 h at 0 °C, quenched by the addition of sodium thiosulfate solution, and extracted three times with pentane. The combined organic layers were washed with 5% $NaHCO_3$ solution, dried ($MgSO_4$), and evaporated to give 0.240 g (80%) of a 5:1 mixture of **13** and **14**: NMR ($CDCl_3$) δ 5.97 (dd, 1, J = 10, 6 Hz), 5.19 (d, 1, J = 10 Hz, **14**), 5.05 (d, 1, J = 10 Hz, **13**), 3.68 (s, 3), 3.11 (br s, 1, **13**), 3.02 (br s, 1, **14**), 1.3–2.8 (m, 8), 1.34 (s, 3), 1.00 (d, 3, J = 7 Hz); IR (neat) 3010, 1730 cm^{-1}. The epoxides decomposed during attempted chromatographic purification.

Methyl 1,2,4aα,5,6,7,8,8aβ-Octahydro-1α,2β-dimethyl-5-oxonaphthalene-1β-carboxylate (15). Boron trifluoride etherate (0.046 g, 0.04 mL, 0.3 mmol) was added to the 5:1 mixture of epoxides **13** and **14** (0.179 g, 0.76 mmol) in 20 mL of 1,2-dimethoxyethane at −50 °C. The reaction mixture was stirred for 17 h at −50 °C, warmed to 25 °C, and quenched with sodium bicarbonate solution. The mixture was extracted three times wiith CH_2Cl_2. The organic layers were dried ($MgSO_4$) and evaporated to give 0.212 g of ≃10:1 mixture of **15** and **16** as determined by NMR analysis. Medium-pressure chromatography of 0.170 g on silica gel (hexane) gave 0.019 g (13%) of a 9:1 mixture of **16** and **15** followed by 0.100 g (70%) of pure **15**.

15: mp 76.5–77.0 °C; the ^1H NMR and IR data are identical with those previously reported;[13] ^{13}C NMR ($CDCl_3$) δ 209.3, 175.5, 131.1, 120.8, 51.1, 50.5, 48.3, 41.1, 40.2, 39.6, 27.1, 25.8, 18.1, 16.8.

16: NMR ($CDCl_3$) δ 9.42 (s, 1), 5.67 (br s, 2), 3.67 (s, 3), 1.5–2.7 (m, 8), 1.23 (s, 3), 1.14 (d, 3, J = 7 Hz); MS (EI), m/e (relative intensity) ethyl ester corresponding to **16** 250 (M^+, 1.3), 222 (3), 221 (8), 205 (2), 192 (6), 177 (7), 175 (7.4), 165 (14), 164 (12), 163 (53), 150 (13), 149 (73), 148 (23), 147 (100), 135 (26), 133 (17), 131 (11), 129 (15), 123 (18), 121 (15), 119 (32), 109 (11), 108 (24), 107 (26), 105 (30).

Rearrangement of 13 and 14 with $LiClO_4$. A solution of a 5:1 mixture of **13** and **14** (0.057 g, 0.24 mmol) in 8 mL of benzene containing (0.212 g, 9.0 equiv) of solid $LiClO_4$ was heated at 78 °C for 1 h under nitrogen. The solution was cooled to 25 °C, diluted with ether, washed with water, dried ($MgSO_4$), and evaporated to give 0.047 g (83%) of a ~1:1 mixture of **15** and **16** as determined by NMR analysis. Chromatography of 0.041 g as described above gave 0.008 g (16%) of **16** and 0.010 g (20%) of **15**.

Rearrangement of 13 and 14 with $Eu(fod)_3$. A solution of 0.048 g (0.20 mmol) of a 5:1 mixture of **13** and **14** in 0.5 mL of $CDCl_3$ in an NMR tube was treated with 0.0241 g (0.20 mmol) of $Eu(fod)_3$. The solution was monitored for by NMR. After 6 days, the mixture was diluted with pentane and washed with water. The aqueous layer was extracted twice with pentane. The combined organic layers were dried ($MgSO_4$) and evaporated to give 0.053 g (110%) containing fod and a 4:1 mixture of **16** and **15** as determined by NMR analysis. Chromatography of 0.039 g as described above gave 0.006 g (16%) of **16** and 0.003 g (8%) of **15**.

Reduction of 15. Reduction of **15** (50 mg) with $BH_3{\cdot}NH_3$ in CH_3OH at 0 °C as reported by Roush and Hall[13] gave 38 mg (76%) of a 2:1 mixture of **17** and **18** which was separated by reverse-phase HPLC (Beckman Ultrasphere-ODS, 5 μm, 10 mm × 25 cm) with 60:40 H_2O–CH_3CN: **17**, t_R 33 min; **18**, t_R 44 min. The spectral data are identical with those previously reported.

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Registry No. **4a**, 928-90-5; **4b**, 5390-04-5; **5a**, 87282-60-8; **5b**, 79532-18-6; **6a**, 87282-61-9; **6b**, 87282-62-0; **7a**, 87282-63-1; **7b**, 87282-64-2; **8a**, 87282-65-3; **9a**, 87282-66-4; **9a** ethyl ester, 87282-67-5; **10a**, 87282-68-6; **10b**, 87282-69-7; **11a**, 87282-70-0; **11a** ethyl ester, 87282-71-1; **12a**, 87282-72-2; **12b**, 87282-73-3; **13**, 87282-74-4; **14**, 87333-76-4; **15**, 78685-39-9; **16**, 87282-75-5; **17**, 78669-02-0; **18**, 78669-03-1; **19**, 41093-63-4; (*E*)-crotyl bromide, 29576-14-5; trimethyl phosphonoacetate, 5927-18-4; trimethyl 2-phosphonopropionate, 26530-60-9.

Diels–Alder Reaction of 6,6-Dimethylfulvene with 2-Acetoxyacrylonitrile. Preparation of 5-(2-Hydroxyethyl)-2-cyclopenten-1-one[1]

Akira Oku,* Yohko Nozaki, Hiroshi Hasegawa, Jun Nishimura, and Toshiro Harada

Department of Chemistry, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606, Japan

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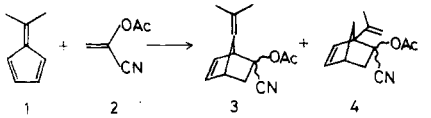
The Diels–Alder reaction of 6,6-dimethylfulvene with 1-acetoxyacrylonitrile gave two different adducts, 2-acetoxy-2-cyano-7,7-isopropylidenebicyclo[2.2.1]hept-5-ene (**3**, 70%) and 2-acetoxy-2-cyano-1-isopropenylbicyclo[2.2.1]hept-5-ene (**4**, 18%). The formation of **4**, which has not been reported before, can be suppressed by adding pyridine to the reaction mixture. Hydrolysis of **3** by sodium methoxide, followed by successive treatment with unsolvated hydroxide ion, peroxyformic acid, lithium aluminum hydride, and lead tetraacetate, gave 5-(2-hydroxyethyl)-2-cyclopenten-1-one (**15**, 35% from **3**).

The Diels–Alder reaction of 6,6-dimethylfulvene (**1**) with 1-acetoxyacrylonitrile (**2**) was reported by DePuy and coworkers,[2] where only a normal adduct, **3**, was obtained as a mixture of endo and exo isomers. Adduct **3** was then converted to (2-oxocyclopentyl)acetic acid through several-step transformations. We have found that this addition reaction often produces another adduct, **4**, as a byproduct which has not been reported before, and its yield sometimes exceeded 20%. The formation of **4**, however, can be suppressed by adding pyridine to the reaction mixture. Thus, this addition reaction, being endowed with a high chemoselectivity, can be adopted for the construction not only of bicyclo[2.2.1]heptenes but also of 5-(two-carbon chain)-substituted cyclopentenones.[3]

We have adopted adduct **3** as the starting material of a four-step synthesis of the title compound 5-(2-hydroxyethyl)-2-cyclopenten-1-one (**15**) which, as a family of 5-substituted cyclopentenones,[4] can be used in organic synthesis, but studies with regard to its preparation have been limited.[5]

Results and Discussion

The reaction of **1** with **2**, one of the ketene equivalents,[6] yielded a normal adduct **3** and an abnormal adduct **4**, each



1 2 3 4

as a mixture of endo and exo isomers, under usual reaction conditions. Results of some experiments which were carried out to optimize the reaction conditions and to suppress the formation of byproduct **4** are shown in Table I.

(1) Ketene Equivalents. 8. For part 7 see ref 6c.

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(3) A preparative method of 4-(two-carbon)-substituted cyclopentenone was recently reported by: Drian, C. L.; Greene, A. E. *J. Am. Chem. Soc.* **1982**, *104*, 5473.

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(5) The preparation of **15** has not been reported. The corresponding acid **16** was reported by: Cassar, L.; Chiusoli, G. P.; Foa, M. *Chim. Ind. (Milan)* **1968**, *50*, 515; *Chem. Abstr.* **1969**, *70*, 114671; **1969**, *71*, P3047. A number of 5-(carbon chain)-substituted 2-cyclopenten-1-ones have been reported by, for example: (a) Paulsen, H.; Maass, U. *Chem. Ber.* **1981**, *114*, 346. (b) Brady, W. T.; Lloyd, R. M. *J. Org. Chem.* **1981**, *46*, 1322. (c) Toder, B. H.; Branca, S. J.; Dieter, R. K.; Smith, A. B., III. *Synth. Commun.* **1975**, *5*, 435.

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