Total Synthesis of the Marine Natural Product $\Delta^{9(12)}$-Capnellene. Reversal of Regiochemistry in the Intramolecular 1,3-Diyl Trapping Reaction

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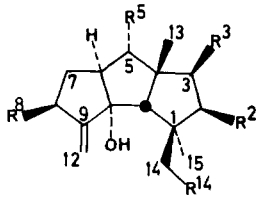
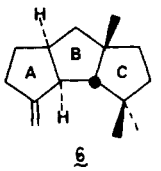
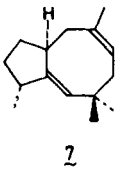
Abstract: A total synthesis of the marine natural product $\Delta^{9(12)}$-capnellene (**6**) is described. An intramolecular 1,3-diyl trapping reaction constituted the cornerstone of the strategy that was utilized to achieve this objective. Unlike all previous intramolecular diyl trapping reactions that have been conducted, the major product was *not* a linearly fused tricyclopentanoid. Rather, ketone **16**, possessing a tricyclo[5.3.1.$0^{2,6}$]undecane ring system, was unambiguously characterized by single-crystal X-ray analysis as the major product. Ketone **16** is formed via a reversal of the previously observed regiochemical mode of addition of the diylophile to the diyl. A brief mechanistic rationale is presented.

In 1974, a manuscript appeared describing the characterization of a sesquiterpene that was isolated from the methylene chloride extracts of the soft coral *Capnella imbricata* (Coelenterata, Octocorallia) collected off Sewaru, Leti Island, Indonesia.[1] The skeletal type was given the name capnellane, and the structure and absolute configuration of the compound, named $\Delta^{9(12)}$-capnellene-3β,8β,10α-triol (**1**), was secured by single-crystal X-ray







1, R^2 = R^5 = R^{14} = H; R^3 = R^8 = OH
2, R^3 = R^5 = R^{14} = H; R^2 = R^8 = OH
3, R^3 = R^{14} = H; R^2 = R^5 = R^8 = OH
4, R^2 = R^5 = H; R^3 = R^8 = R^{14} = OH
5, R^2 = R^3 = R^{14} = H; R^5 = R^8 = OH

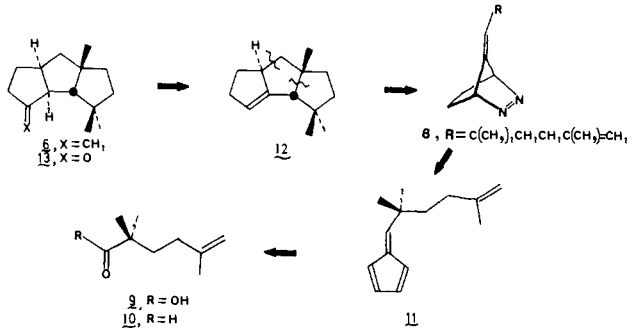
analysis.[2] Over a period of several years, other capnellols, **2–5**, were isolated from *C. imbricata*.[3] In addition to these alcohols, two hydrocarbons, $\Delta^{9(12)}$-capnellene (**6**), the presumed biogenetic precursor of alcohols **1–5**, and precapnelladiene (**7**), the presumed immediate precursor to the tricyclopentanoid skeleton found in **6**, were also isolated from *C. imbricata*.[4]

From the ecological viewpoint, it has been suggested that, like other colenterate terpenoids, compounds **1–7** may serve to deter attack by predators and also to protect the coral against invasion by microorganisms, larvae, and/or algae.[5]

In addition to our preliminary account, two other synthetic approaches to the capnellanes have been published.[6] For example, Stevens and Paquette have described a total synthesis of $\Delta^{9(12)}$-capnellene (**6**) using methodology that calls for the successive annulation of two of the three five-membered rings onto a preexisting cyclopentenylcarboxaldehyde. Birch and Pattenden have tackled the problem from a significantly different point of view, one patterned to follow the presumed biogenetic conversion of precapnelladiene (**7**) into the capnellenes. Thus, **7**, previously prepared by using a novel photocycloaddition–fragmentation sequence, was converted to Δ^8-capnellene upon treatment with boron trifluoride etherate.

Our solution to the problem utilized an intramolecular 1,3-diyl trapping reaction as the cornerstone of the strategy.[7] While we were able to complete a total synthesis of $\Delta^{9(12)}$-capnellene (**6**),

Scheme I



the level of our success proved to be less than that which was desired. Despite the rather negative tone of this remark, it must be noted that several important factors that serve to more clearly define the scope as well as to suggest potential new applications of the diyl trapping reaction were discovered during the course of our investigations (vide infra).

We report the details of our total synthesis of $\Delta^{9(12)}$-capnellene (**6**) as well as the isolation and characterization of a new product resulting from the intramolecular diyl trapping reaction, namely, tricyclic ketone **16**. Ketone **16** is the major product formed and arises via a reversal of the previously observed regiochemical mode

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(1) Kaisin, M.; Sheikh, Y. M.; Durham, L J.; Djerassi, C.; Tursch, B.; Daloze, D.; Braekman, J. C.; Losman, D.; Karlsson, R. *Tetrahedron Lett.* **1974**, 2239–2242.
(2) Karlsson, R. *Acta. Crystallogr., Sect. B* **1977**, *B33*, 1143–1147.
(3) (a) Kaisin, M.; Tursch, B.; Declercq, J. P.; Germain, G.; Van Meerssche, M. *Bull. Soc. Chim. Belg.* **1979**, *88*, 253–258. (b) Ayanoglu, E.; Gebreyesus, T.; Beechan, C. M.; Djerassi, C.; Kaisin, M. *Ibid.* **1978**, *89*, 1671. (c) Sheikh, Y. M.; Singy, G.; Kaisin, M.; Eggert, H.; Djerassi, C.; Tursch, B.; Daloze, D.; Braekman, J. C. *Tetrahedron* **1976**, *32*, 1171. (d) Sheikh, Y. M.; Djerassi, C.; Braekman, J. C.; Daloze, D.; Kaisin, M.; Tursch, B.; Karlsson, R. *Ibid.* **1977**, *33*, 2115. (e) Karlsson, R. *Acta Crystallogr., Sect. B* **1976**, *B32*, 2609.
(4) Ayanoglu, E.; Gebreyesus, T.; Beechan, C. M.; Djerassi, C.; Kaissin, M. *Tetrahedron Lett.* **1978**, 1671–1674.
(5) Tursch, B.; Braekman, J. C.; Daloze, D.; Kaisin, M. In "Marine Natural Products, Chemical and Biological Perspectives"; Scheuer, P. J., Ed.; Academic Press: New York, 1978; Vol. II, Chapter 4. See also: Burkolder, P. R.; Burkolder, L. M. *Science (Washington, D.C.)* **1958**, *127*, 1174–1175. Ciereszko, L. S. *Trans. N.Y. Acad. Sci.* **1962**, *24*, 502–503. Ciereszko, L. S.; Karns, T. K. B. In "Biology and Geology of Coral Reefs"; Jones, O. A., Endean, R., Eds.; Academic Press: New York, 1973; Vol. II, Chapter 6.
(6) (a) Stevens, K. E.; Paquette, L. A. *Tetrahedron Lett.* **1981**, *22*, 4393–4396. (b) Birch, A. M.; Pattenden, G. *Ibid.* **1982**, *23*, 991–994 and references therein. (c) Little, R. D.; Carroll, G. L. *Ibid.* **1981**, *22*, 4389–4392.
(7) (a) Little, R. D.; Muller, G. W. *J. Am. Chem. Soc.* **1979**, *101*, 7129–7130. (b) Little, R. D.; Muller, G. W. *Ibid.* **1981**, *103*, 2744–2749. (c) Little, R. D.; Muller, G. W.; Venegas, M. G.; Carroll, G. L.; Bukhari, A.; Patton, L.; Stone, K. *Tetrahedron Symp. Print. No.* 3 **1981**, *37*, 4371–4383.

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of addition of the diylophile to the diyl.

General Synthetic Strategy

We have previously demonstrated the utility of the intramolecular 1,3-diyl trapping reaction for the construction of linearly fused tricyclopentanoids by successfully completing a total synthesis of the mold metabolite, hirsutene.[7b] From that and several other investigations, we were aware of the following points: (1) The reaction is stereoselective in that cis,anti ring-fused tricyclopentanoids are formed in preference to cis,syn. (2) The reaction is stereospecific in that the geometry about the diylophile double bond is maintained in the product. (3) While secondary orbital interactions between the diyl and the diylophile probably play some role in deterining the observed preference for the formation of the cis,anti ring-fused systems, conformational factors and nonbonded interactions involving the diyl and the acyclic chain that links the two play a much more significant role.[7c]

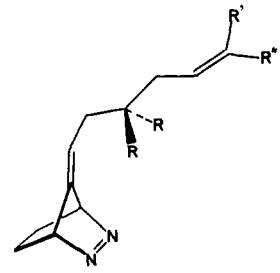
With this information in hand, it appeared as though the trapping reaction would be ideally suited for a total synthesis of $\Delta^{9(12)}$-capnellene (**6**). The synthetic plan, illustrated in Scheme I, required a synthesis of the bicyclic diazene **8**, which was to serve as the direct precursor to the required diyl. From the outset we were well aware of the potentially more stringent requirements that were to be imposed upon the present trapping reaction in comparison with those that we have conducted in the past. Our immediate attention was directed to the fact that an unactivated diylophile was to be used and therefore that the diyl trapping reaction might be slowed down sufficiently to allow other reactions such as dimerization of the diyl to compete. However, we felt assured that the intramolecular nature of the desired reaction would still allow it to overcome the rate drop that was anticipated upon removal of the activating group. While these concerns proved to be real, the problems caused by them were easily surmounted. The more notable difference between the present and past traps stems quite naturally from the requirements imposed upon the strategy by the capnellene structure itself and have to do with the location of the *gem*-methyl pair on the acyclic chain. As will become apparent from the discussion that follows, this factor provided a problem for which there was no simple solution.

Preparation of Diazene 8

Diazene **8** was prepared in short order from readily available starting materials by using a straightforward sequence. Thus, acid **9**, prepared in the standard way from isobutyric acid dianion[8] and 3-methyl-3-butenyl *p*-toluenesulfonate, was first reduced with lithium aluminum hydride and then oxidized by using PCC/Celite to afford aldehyde **10** in 88% yield.

In preparation for the Diels–Alder reaction that was to be used to assemble the bicyclic framework found in **8**, aldehyde **10** was converted to fulvene **11**. Initially, we attempted to accomplish this objective using methodology developed by Freisleben.[9] Our past experience, using aldehydes that were either mono- or disubstituted at the α-carbon atom, provided very good yields of fulvenes that were, in several cases, otherwise difficult to obtain without significant competition and aldol condensation reactions.[7] In the present instance, however, treatment of **10** with cyclopentadiene and diethylamine in methanol at room temperature for 6 h led only to the recovery of unreacted aldehyde. Presumably, the neopentyl nature of the carbonyl carbon in **10** provides sufficient steric encumbrance so that the initial iminium ion forming step of the sequence does not occur at an appreciable rate under these conditions.[10] Fortunately, since **10** is devoid of α-hydrogens and is therefore not capable of undergoing an aldol condensation, the problems alluded to above could be overcome by treating **10** with lithium cyclopentadienide in THF at room temperature. In this way, fulvene **11** could be obtained in yields ranging from 67–80% after chromatography on neutral alumina.

Table I



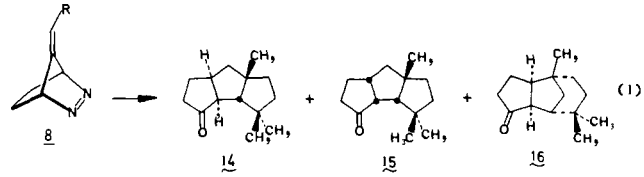
R	*R'*	*R''*	yield	anti:syn	ref
CH_3	H	$COOCH_3$	87	9:1	7c
CH_3	$COOCH_3$	H	85	3:1	7c
H	H	$COOCH_3$	85	7:1	7c
CH_3	H	$COOR^{*a}$	83	5.7:1	12

[a] R* = menthyl.

A Diels–Alder reaction between **11** and dimethyl azodicarboxylate followed by selective reduction of the Δ^5 π bond of the resulting adduct using diimide in dichloromethane provided 73–91% yields of the dimethyl dicarbamate precursor to diazene **8**, which, in turn, was obtained in 78% yield after saponification and oxidation using aqueous potassium ferricyanide.[11]

Formation of the Tricyclopentanoid Skeleton

The typical protocol for accomplishing an intramolecular diyl trapping reaction simply calls for refluxing the desired diazene in acetonitrile or THF. When the reaction is complete (TLC), the solution is cooled to room temperature and the solvent is removed in vacuo. The ^1H NMR of even the crude reaction mixture is invariably indicative of an extremely clean and efficient process leading to the production of the desired tricyclopentanoid skeleton.[7] The results obtained from a variety of different experiments that were conducted in this way are illustrated in Table I. In contrast, when diazene **8** was refluxed in acetonitrile, the initial results were abysmal! No obvious indication of the successful formation of the desired ring system was apparent. Diazene **8**, dissolved in acetonitrile, was added slowly (syringe pump or, for larger scale runs, a pressure-equalizing dropping funnel) to a refluxing solution of acetonitrile[13] to reduce the opportunity of diyl dimerization. In this way, tricyclopentanoid products could be readily detected by ^1H NMR. However, attempts to isolate the desired products were thwarted due to their higher than anticipated volatility. Even slow, careful atmospheric-pressure distillation to remove the solvent led to codistillation of the product. Fortunately, this problem was overcome by simply choosing to carry out the reaction in a minimal amount of THF (rather than acetonitrile) and then, instead of removing the solvent after diazene **8** had reacted, to immediately subject the mixture to a hydroboration–oxidation sequence, thereby producing in a ratio of 1.6:1:6.6 (56% from **8**) a mixture of three alcohols of significantly reduced volatility. The alcohols were conveniently separated by preparative HPLC, and each was independently oxidized to produce a different ketone (**14**, **15**, **16**). Since each alcohol



(1)

afforded a unique ketone, it was concluded that no alcohol was epimeric with another. Ketones **14** and **15** each display carbonyl

(8) See, for example: Creger, P. L. *Annul. Rep. Chem.* **1977**, *12*.
(9) Freisleben, W. *Angew. Chem.* **1963**, *75*, 576.
(10) Recently, Keith Stone of UCSB has demonstrated that fulvene **11** can be prepared by using a modification of the Freisleben procedure wherein diethylamine is simply replaced by pyrrolidine. Details concerning the use of this revised methodology for the facile synthesis of fulvenes will be reported on another occasion.
(11) (a) Little, R. D.; Venegas, M. G. *J. Org. Chem.* **1978**, *43*, 2921–2923. (b) Little, R. D.; Carroll, G. L. *Ibid.* **1979**, *44*, 4720–4722.
(12) Unpublished results of Kevin Moeller, UCSB.
(13) If precautions are not taken to maintain a high dilution (note the use of an unactivated diylophile), then mixtures of diyl dimers are formed.

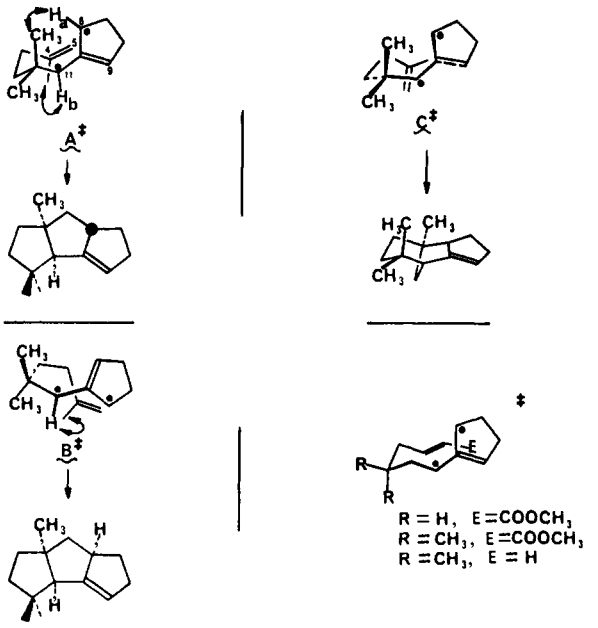


Figure 1.

absorptions at 1730 cm^{-1}, while that for **16** occurred at 1735 cm^{-1}; three different methyl proton resonances were observed for each compound. Assuming that only cis- rather than trans-fused tricyclopentanoids were formed, these results implied that one of the ketones did not possess the linearly fused tricyclopentanoid ring system.

Reverse Regiochemical Mode of Addition: Completion of the Total Synthesis

Unequivocable evidence substantiating the hypothesis that a compound whose structure was not that of a tricyclopentanoid had actually been generated as the major product was obtained from a single-crystal X-ray analysis.[14] As illustrated, ketone **16** possesses a tricyclo[5.3.1.$0^{2,6}$]undecane skeleton and corresponds, therefore, to a product that has resulted from a previously unobserved reverse regiochemical mode of addition of the diylophile to the diyl. It is of interest to note in passing that the basic tricyclic skeleton and the more abbreviated bicyclo[3.2.1]octane unit associated with **16** might serve as useful points from which to embark upon future synthetic efforts.[15]

That ketone **14** in fact corresponded to the desired cis,anti,cis ring-fused product was confirmed unambiguously by converting it to $\Delta^{9(12)}$-capnellene (**6**) with a simple Wittig reaction (80–90%, optimized). A comparison of spectral data (IR, ^1H and ^{13}C NMR, GC/MS) with those of authentic material kindly supplied to us by Professor Djerassi signaled a completion of the total synthesis.

Discussion

In all intramolecular diyl trapping reactions that have been conducted to date, the cis,anti rather than the cis,syn ring-fused tricyclopentanoid constituted the major product.[7,12] From these results, we have concluded that the extended quasi-chair transition state (note, for example, $A^‡$ of Figure 1) is of lower energy than is the alternate cis,syn ring-forming transition state $B^‡$. One might have therefore predicted a preference for the formation of the cis,anti ring-fused material in the conversion of diazene **8** to tricyclopentanoids. While this is indeed the case, the observed preference of only 1.6:1 is significantly smaller than that which has ever been obtained previously (cf. Table I). Obviously, the energy difference between the transition state leading to the cis,anti relative to that of the cis,syn product has decreased.

Consider the transition-state representations $A^‡$–$C^‡$, which are illustrated in Figure 1. Compare, for example, representation $A^‡$ with that illustrated in the lower right-hand corner of the figure. Clearly, the extended quasi-chair representation $A^‡$ suffers from two energy-raising CH_3–H interactions, one between the quasi-axial methyl group located on the acyclic chain and H_a (located on the diyl ring) and the other between the methyl group on the diylophile and H_b. The former interaction can be relieved, at least in part, by assuming a transition-state representation $B^‡$ wherein the quasi-axial methyl group has been moved out of the plane formed by H_a and C_6, C_{10}, C_{11}, and C_1 (capnellene numbering). While one CH_3–H interaction has been eased, the other remains, and in accord with previous experiments, the cis,syn ring-fused product corresponds to the minor one.

Both of the energy-rising methyl–hydrogen interactions are eliminated in representation $C^‡$. Here, the conformation of the acyclic chain has been changed from that in representation $A^‡$ by rotating about the C_1–C_{11} bond, thereby moving the quasi-axial methyl group out of the plane and reducing the CH_3–H_a interaction, and by rotation about the C_3–C_4 bond, thereby interchanging the location of the diylophile π bond and the methyl group attached to it. Bond formation between C_5 and C_{11} and between C_4 and C_6 leads to the ring system that corresponds to that of the major product.[16]

Examination of a Dreiding molecular model for $C^‡$ clearly illustrates that C_5 is closer to C_{11} than C_4 is to C_6 and therefore suggests the possibility of either a stepwise or a nonsynchronous but concerted bond-forming process. For example, if the process occurs in a stepwise fashion, with the formation of the C_5–C_{11} bond occurring prior to that between C_4 and C_6 (i.e., the formation of a six-membered ring and a tertiary radical), then rehybridization from sp^2 to sp^3 allows the methyl group attached to C_4 to move away from the diyl ring as it assumes it's ultimate location in the product. This relieved nonbonded interaction may sufficiently lower the energy of this "new" pathway to make it the preferred one. A similar argument could be applied to a situation wherein a nonsynchronous but concerted process was operative.

Concluding Remarks

We are presently focusing attention upon devising a means by which products of reverse regiochemistry can be efficiently synthesized, in a predictable fashion, as the exclusive product of a given intramolecular diyl trapping reacton. Achievement of this objective is closely related to efforts directed toward application of the methodology toward the total synthesis of several natural products, including, for example, aphidicolin.[17]

Experimental Section

^1H NMR spectra were obtained on Varian T-60, FT-80, and XL-100 spectrometers. A Varian CFT-20 was used to obtain ^{13}C NMR spectra; both fully decoupled and off-resonance decoupled spectra were recorded. Chemical shifts are given as parts per million (ppm) downfield from tetramethylsilane (Me_4Si) in δ units, and coupling constants are given in cycles per second (Hz). The data are reported as follows: chemical shift, multiplicity, number of protons, coupling constants, and assignments.

Infrared (IR) spectra were recorded on a Perkin-Elmer 283 spectrometer.

Exact mass measurements and low-resolution mass spectra were obtained on a ZAB 2-F spectrometer. The observed and calculated values for the ion of the given formula are reported. Low-resolution mass spectra are reported by giving the parent peak first (if it appeared), followed by the fragment peaks in order of decreasing mass.

Carbon–hydrogen analyses were performed by Guelph Chemical Laboratories, Ltd., of Guelph, Ontario, Canada, or by Galbraith Laboratories of Knoxville, Tennessee.

For gravity flow chromatography, E. Merck Silica Gel 60 (73–200 mesh, ASTM) was used. Florisil refers to Fischer 100–200-mesh gel,

(14) Supplementary X-ray crystallographic data are included in the microfilm version.

(15) See, for example: Büchi, G.; Chu, P.-S. *Tetrahedron* **1981**, *37*, 4509–4513. Burke, S. D.; Murtiashaw, C. W.; Saunders, J. O.; Dike, M. S. *J. Am. Chem. Soc.* **1982**, *104*, 872–874. Ireland, R. E.; Godfrey, J. D.; Thaisrivongs, S. *Ibid.* **1981**, *103*, 2246–2248.

(16) No product resulting from bonding between C_5–C_{11} and C_4–C_9 was observed.

(17) For example, see: Cargill, R. L.; Bushey, D. F.; Dalton, J. R.; Ramanujam, S. P.; Dyer, R. D.; Bordner, J. *J. Org. Chem.* **1981**, *46*, 3389–3399, and references therein dealing with biological activities, proposed biosynthesis, and previous synthetic efforts.

while the term neutral alumina refers to Sigma Co. activity 11 alumina.

Melting points were determined on a Thomas-Hoover capillary melting point apparatus, and are uncorrected.

Reagent-grade solvents were used for all reactions. Anhydrous diethyl ether (Mallinkrodt) from freshly opened cans was sufficiently dry to be used without further treatment. Acetonitrile and anhydrous ethyl alcohol were also purchased from Mallinkrodt and were used without further purification. Solvents referred to as "dry" were distilled from calcium hydride onto activated molecular sieves (4 Å). Tetrahydrofuran (THF) was tested for peroxides (EM test strips), collected from a calcium hydride prestill after refluxing for at least one day, and then distilled from sodium benzophenone ketyl. Pentane was distilled through a 30-cm glass column packed with glass helices.

Lithium aluminum hydride (LAH) was purchased from Ventron; pyridinium chlorochromate (PCC), 3-methyl-3-butenol, and borane–tetrahydrofuran were purchased from Aldrich. Cyclopentadiene was freshly distilled prior to use. Dipotassium azodicarboxylate was prepared from the corresponding commercially available amide according to the procedure of Berson.[18] Bis(2,2,2-trichloroethyl) azodicarboxylate was prepared according to the procedure of Venegas and Little.[19]

Brine refers to a saturated solution of sodium chloride. Except as noted, removal of the solvent in vacuo refers to the initial use of a rotary evaporator at water-aspirator pressure followed by pumping on the material at 1 mm or less to remove the last traces of solvent.

Unless otherwise indicated, all reactions were conducted under an atmosphere of nitrogen.

2,2,5-Trimethyl-5-hexenoic Acid (9). To a dry ice–acetone cooled solution of freshly distilled diisopropylamine (20.84 g, 206 mmol) dissolved in 150 mL of THF was added *n*-butyllithium (145 mL, 215 mmol). The resulting solution was stirred for 5 min and was then warmed to and maintained at 0 °C for 15 min. To the cold solution was added isobutyric acid (8.65 g, 98.1 mmol), and the solution was stirred for 0.5 h. To the resulting solution was added 3-methyl-3-butenyl *p*-toluenesulfonate (22.34 g, 93.0 mmol), and the solution was stirred at room temperature overnight. To the solution was added 450 mL of cold (0 °C) 10% HCl. The organic layer was separated, and the aqueous layer was extracted with ether (2 × 250 mL). The combined organic layers were washed with 200 mL of cold (0 °C) 10% HCl and then water (3 × 200 mL), dried ($MgSO_4$), and concentrated in vacuo. The resulting oil was purified by chromatography (3 × 100 cm column) on 200 g of silica gel. Elution with 30% ether in pentane afforded 11.40 g (79%) of acid **9**: ^{1}H NMR ($CDCl_3$) δ 8.23 (s, 1 H, CO_2H), 4.70 (br s, 2 H, C=CH_2), 1.68 (s, 3 H, C=CCH_3), 2.2–1.65 (m, 4 H, $(CH_2)_2$), 1.11 (s, 6 H, *gem*-methyls); IR (NaCl, film) 3070, 2970, 2935, 1700, 1475, 1410, 1285, 1210, 885 cm^{-1}. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.97; H, 10.19.

2,2,5-Trimethyl-5-hexenal (10). To a stirred suspension of lithium aluminum hydride (3.3 g, 87 mmol) in 120 mL of ether at room temperature was added dropwise over 1 h a solution of acid **9** (9.98 g, 63.9 mmol) dissolved in 60 mL of ether. After 45 min of stirring, the resulting suspension was cooled to 0 °C and was then quenched by the dropwise addition of 90 mL of 10% H_2SO_4. The organic layer was separated, and the aqueous layer was extracted with ether (3 × 50 mL). The combined organic layers were dired ($MgSO_4$), and the solvent was removed in vacuo to afford a quantitative yield of the desired alcohol, which was used without purification in the preparation of aldehyde **10**: ^{1}H NMR ($CDCl_3$) δ 4.66 (m, 2 H, C=CH_2), 3.28 (s, 2 H, OCH_2), 2.0 (s, 1 H, OH), 2.2–1.4 (m, 4 H, $(CH_2)_2$), 1.73 (d, 3 H, J = 2 Hz, C=CMe), 0.90 (s, 6 H, *gem*-methyls); IR (NaCl, film) 3360, 3068, 2960, 2870, 1650, 1470, 1450, 1385, 1375, 1370, 1050, 1040, 885 cm^{-1}.

The alcohol was oxidized to afford aldehyde **10** by using pyridinium chlorochromate (PCC, 6.80 g, 31.6 mmol)[20] and Celite (6.8 g) suspended in 125 mL of dichloromethane at room temperature. In this way, 3.00 g (21.1 mmol) of the alcohol, dissolved in 15 mL of dichloromethane, was converted to 2.65 g (90%) of **10** after stirring at room temperature for 2.5 h and workup. Workup consisted of diluting with 100 mL of ether, decanting, washing with ether (4 × 25 mL), and filtering the combined organic layers through a pad of Florisil. Most of the solvent was removed in vacuo. The aldehyde is volatile, and care must be exercised to avoid material loss during the latter stages of the workup. The resulting oil was pipeted away from the green precipitate to afford the aldehyde: ^{1}H NMR ($CDCl_3$) δ 9.45 (s, 1 H, CHO), 4.70 (br s, 2 H, C=CH_2), 2.3–1.4 (m, 4 H, $(CH_2)_2$), 1.73 (s, 3 H, C=CCH_3), 1.05 (s, 6 H, *gem*-methyls); IR (NaCl, film) 3080, 2975, 2940, 2880, 2700, 1730, 1650, 1470, 1380, 890 cm^{-1}. Anal. Calcd for $C_9H_{16}O$: C, 77.07; H, 11.52. Found: C, 76.52; H, 11.75.

6-(1,1,4-Trimethyl-4-pentenyl)fulvene (11). To a stirred, cooled (0 °C) solution of freshly distilled cyclopentadiene (248 mg, 3.75 mmol) dissolved in 15 mL of THF was added dropwise *n*-butyllithium (2.50 mL, 3.70 mmol). The solution was allowed to stir for 0.5 h, warmed to room temperature for 0.25 h, and then cooled to 0 °C. To the cold solution was added dropwise 2,2,5-trimethyl-5-hexenal (**10**, 505 mg, 3.60 mmol), and the solution was stirred at 0 °C for 1.5 h. The solution was diluted with 30 mL of water and 30 mL of ether. The organic layer was separated, and the aqueous layer was extracted with ether (3 × 20 mL). The combined ether layers were washed with 25 mL of water, dried ($MgSO_4$), and concentrated in vacuo. The resulting oil was purified by chromatography (2 × 14 cm column) on 30 g of neutral alumina (activity II). Elution with pentane afforded 471 mg (70%) of the desired fulvene **11**: ^{1}H NMR ($CDCl_3$) δ 6.60–6.10 (m, 5 h, fulvene H), 4.67 (br s, 2 H, C=CH_2), 2.20–1.40 (m, 4 H, $(CH_2)_2$), 1.74 (d, 3 H, $J \sim$ 2 Hz, C=CMe), 1.30 (s, 6 H, *gem*-methyls); IR (NaCl, film) 3070, 2960, 2910, 2860, 1630, 1470, 1375, 1360, 1340, 880, 760 cm^{-1}. Anal. Calcd for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.16; H, 10.64.

***N,N'*-Bis(methoxycarbonyl)-7-(2,2,5-trimethylhex-5-enylidene)-2,3-diazabicyclo[2.2.1]heptane.** To a stirred solution of 6-(1,1,4-trimethyl-4-pentenyl)fulvene (**11**, 8.71 g, 46.2 mmol) dissolved in 90 mL of 1:1 ether/pentane at 0 °C was added dropwise over 0.5 h a solution of dimethyl azodicarboxylate (6.76 g, 46.3 mmol) dissolved in 90 mL of 1:1 ether/pentane. The resulting solution was stirred for another 3 h and was then concentrated in vacuo to afford the desired Diels–Alder adduct, which was used without further purification in the next step of the sequence: ^{1}H NMR ($CDCl_3$) δ 6.73 (apparent t, 2 H, J = 2 Hz, HC_5=C_6H), 5.65 and 5.0 (br s, 2 H, bridgeheads), 4.88 (s, 1 H, C_7=C*H*CMe_2), 4.68 (br s, 2 H, C=CH_2), 3.76 (s, 6 H, CO_2CH_3), 2.20–1.20 (m, 4 H, $(CH_2)_2$), 1.70 (d, 3 H, J = 2 Hz, C=CMe), 1.02 (s, 6 H, *gem*-methyls); IR (NaCl, film) 3070, 2950, 1755, 1710, 1650, 1490, 1320, 1100 cm^{-1}.

To a stirred solution of dipotassium azodicarboxylate (44.9 g, 231 mmol) and the Diels–Alder adduct (15.47 g, 46.2 mmol) dissolved in 200 mL of dry dichloromethane at 0 °C was added over 45 min a solution of acetic acid (26 mL, 459 mmol) dissolved in 50 mL of dry dichloromethane. The resulting suspension was stirred for an additional 3 h and filtered, and the filter cake was rinsed with ether. The solvent was removed in vacuo, and the resulting oil was purified by chromatography (3 × 80 cm column) on 170 g of silica gel. Elution with 30% ether in pentane afforded 14.10 g (91%) of the desired adduct: ^{1}H NMR ($CDCl_3$) δ 5.30 (s, 1 H, C=C*H*CMe_2), 5.05 and 4.38 (br s, 2 H, bridgeheads), 4.64 (br s, 2 H, C=CH_2), 3.75 (s, 6 H, CO_2CH_3), 2.10–1.10 (m, 4 H, $(CH_2)_2$), 1.67 (s, 3 H, C=CCH_3), 1.10 (s, 6 H, *gem*-methyls); IR (NaCl, neat) 2960, 2865, 1750, 1710, 1440, 1320, 1250, 1190, 1150, 1120 cm^{-1}. Anal. Calcd for $C_{18}H_{28}N_2O_4$: C, 64.26; H, 8.40. Found: C, 64.08; H, 8.58.

7-(2,2,5-Trimethylhex-5-enylidene)-2,3-diazabicyclo[2.2.1]hept-2-ene (8). To a stirred solution of potassium hydroxide (8.96 g, 136 mmol) dissolved in 60 mL of ethyl alcohol was added a solution of *N,N'*-bis(methoxycarbonyl)-7-(2,2,5-trimethylhex-5-enylidene)-2,3-diazabicyclo[2.2.1]heptane (3.34 g, 9.93 mmol) dissolved in 5 mL of ethyl alcohol. The solution was refluxed for 3 h and was then cooled to 0 °C. To the solution was added dropwise over 15 min a solution of potassium ferricyanide (9.92 g, 30.1 mmol) dissolved in 20 mL of water. The resulting suspension was stirred for 20 min, diluted with 250 mL of water, extracted with pentane (8 × 40 mL), and dried ($MgSO_4$), and the solvent was removed in vacuo. The resulting oil was purified by chromatography (2 × 43 cm column) on 35 g of silica gel. Elution with 10% ether in pentane afforded 1.87 g (86%) of the desired product **8**: ^{1}H NMR ($CDCl_3$) δ 5.60 and 5.0 (br s, 2 H, bridgeheads), 5.09 (s, 1 H, C=C*H*CMe_2), 4.63 (br s, 2 H, C=CH_2), 2.20–1.00 (m, 4 H, $(CH_2)_2$), 1.68 (d, 3 H, J = 2 Hz, C=CCH_3), 1.03 (s, 6 H, *gem*-methyls); IR (NaCl, film) 3065, 2950, 2860, 1645, 1450, 1360, 1110, 880 cm^{-1}. Anal. Calcd for $C_{14}H_{22}N_2$: C, 76.99; H, 10.17. Found: C, 77.23; H, 10.15.

(3aβ,3bα,6aα,7aβ)-Decahydro-3,3,7a-trimethyl-1*H*-cyclopenta[*a*]pentalen-4-ol. To 2 L of stirred, refluxing THF was added dropwise over 110 h (!) a solution of 7-(2,2,5-trimethylhex-5-enylidene)-2,3-diazabicyclo[2.2.1]hept-2-ene (**8**, 4.50 g, 20.6 mmol) dissolved in 450 mL of THF.[21] After 120 h, the solution was cooled to 0 °C, at which time 42 mL (42.0 mmol) of borane–tetrahydrofuran was added over 20 min. The resulting solution was stirred for 1 h, warmed to room temperature, and

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(21) With syringe pump techniques, 7-(2,2,5-trimethylhex-5-enylidene)-2,3-diazabicyclo[2.2.1]hep-2-ene (**8**, 503 mg, 2.30 mmol) dissolved in 50 mL of THF was added to 200 mL of refluxing THF via syringe pump over a period of 72 h. The sequence, from this point on, followed that described in detail in the Experimental Section.

then stirred there for 48 h. TLC analysis (*p*-anisaldehyde) indicated incomplete reaction; so the solution was recooled to 0 °C and additional borane–tetrahydrofuran (120 mL, 120 mmol) was added. The solution was stirred at 0 °C for 1 h, warmed to room temperature, and stirred there for an additional 23 h. To the stirred solution was added dropwise over 20 min 16 mL of water. The flask was cooled (0 °C), and 55 mL of 3.0 M sodium hydroxide was added dropwise over 0.5 h. Next, 35 mL of 30% hydrogen peroxide was added dropwise over 15 min. The solution was heated to 50 °C for 1.5 h, then cooled to room temperature, and diluted with 500 mL of brine. The resulting solution was extracted with ether (3 × 350 mL), the combined organic layers were dried ($MgSO_4$), and the solvent was removed in vacuo. The oil was partially purified by chromatography (3 × 95 cm column) on 190 g of silica gel, with 15% ether in pentane as eluant. Purification using a Waters Prep 500 HPLC (2 Prep PAK silica gel columns connected in series, 150 mL/min) with 20% ether in hexane as eluant afforded 421 mg (10%) of the desired alcohol: ^{1}H NMR ($CDCl_3$) δ 3.90 (br s, 1 H, OH), 1.10 and 1.18 (both s, 9 H, methyls); IR (NaCl, film) 3310, 2940, 2860, 1570, 1560, 1460, 1110, 1100, 1030 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 66.5 (d, COH), 61.0 (d), 56.3 (s, CMe), 54.3 (d), 45.1 (d), 42.0 (t), 40.4 (t), 37.7 (t), 36.7 (t), 29.7 (q, angular methyl), 28.7 (q) and 22.3 (q, *gem*-methyls), 23.7 (t); mass spectrum, *m/e* 208 (parent), 193, 175, 121, 109, 93, 79, 55, 41 (base). Exact mass. Calcd for $C_{14}H_{24}O$: 208.1827. Found: 208.1847. Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.54; H, 11.61.

(3aα,3bα,6aα,7aα)-Decahydro-3,3,7a-trimethyl-1*H*-cyclopenta[*a*]pentalen-4-ol. This compound was also isolated from the chromatography described above (259 mg, 6%): ^{1}H NMR ($CDCl_3$) δ 1.28, 1.20, 1.14 (all s, 9 H, methyls); IR (NaCl, film) 3340, 2940, 2860, 1460, 1360, 1065, 1040 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 76.9, 67.8, 54.9, 51.3, 51.0, 47.7, 45.8, 40.2, 39.6, 35.8, 35.1, 33.8, 29.2, 24.5; mass spectrum, *m/e* 208 (parent), 193, 180, 121, 109, 107, 93, 71 (base). Anal. Calcd for $C_{14}H_{24}O$ 208.1827. Found: 208.1835.

(3aβ,4aα,8aα,8aβ)-Decahydro-4,7,7-trimethyl-4,8-methanoazulen-1(1*H*)-ol. This compound was also isolated from the chromatography described above: 1.697 g, 40% over three steps, mp 62.5–63 °C; ^{1}H NMR ($CDCl_3$) δ 0.95, 0.90, 0.87 (all s, 9 H, methyls); IR (NaCl, film) 3360, 2950, 2860, 1460, 1385, 1375, 1365, 1050 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 83.1 (d, COH), 57.3 (d), 54.3 (d), 52.0 (d), 43.9 (s), 40.6 (t), 39.8 (t), 39.0 (t), 36.6 (t), 35.2 (s), 32.5 (q), 28.9 (q), 28.7 (t), 25.2 (q); mass spectrum, *m/e* 208 (parent), 193, 137, 123, 109, 107, 93, 81, 79, 67, 55, 41 (base). Anal. Anal. Calcd for $C_{14}H_{24}O$: 208.1827. Found: 208.1838.

(3aβ,3bα,6aα,7aβ)-Decahydro-3,3,7a-trimethyl-1*H*-cyclopenta[*a*]pentalen-4-one (14). To a stirred suspension of pyridinium chlorochromate (758 mg, 3.52 mmol) and 760 mg of Celite suspended in 45 mL of dichloromethane at room temperature was added a solution of (3aβ,3bα,6aα,7aβ)-decahydro-3,3,7-trimethyl-1*H*-cyclopenta(*a*)pentalen-4-ol (410 mg, 1.97 mmol) dissolved in 2.5 mL of dichloromethane. The suspension was stirred for 1.5 h and was then diluted with 30 mL of ether. The resulting material was filtered through a pad of Florisil, which was then washed with dichloromethane (4 × 50 mL). The solvent was removed in vacuo, and the resulting oil was chromatographed on a 2 × 60 cm column packed with 60 g of silica gel. Elution with 5% ether in pentane afforded 234 mg (58%) of the desired ketone **14**: ^{1}H NMR ($CDCl_3$) δ 1.10, 1.07, and 0.95 (all s, 9 H, methyls); IR (NaCl, film) 2940, 2860, 1730, 1455, 1165; mass spectrum, *m/e* 206 (parent), 191, 137, 135 (base), 109, 107, 93; ^{13}C NMR ($CDCl_3$) δ 64.4 (d), 56.9 (d, carbon α to carbonyl), 52.9 (s, CMe), 47.8 (t), 42.2 (d), 42.0 (s, CMe_2), 41.6 (t), 40.0 (t), 34.8 (t, carbon α to carbonyl), 30.6 (q, angular methyl), 30.1 and 25.8 (q, *gem*-methyls), 24.0 (t). Anal. Calcd for $C_{14}H_{22}O$: 206.1671. Found: 206.1653. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.37; H, 10.76.

(3aα,3bα,6aα,7aα)-Decahydro-3,3,7a-trimethyl-1*H*-cyclopenta[*a*]pentalen-4-one (15). The cis,syn,cis alcohol (174 mg, 0.833 mmol) was oxidized to afford ketone **15** in a manner analogous to that described above; 91 mg (53%) of ketone **15** was obtained: ^{1}H NMR ($CDCl_3$) δ 1.25, 1.12, 0.97 (all s, 9 H, methyls); IR (NaCl, film) 2940, 2860, 1730, 1460, 1380, 1120 cm^{-1}; mass spectrum, *m/e* 206 (parent), 191, 178, 177 (base), 163, 135, 122, 109, 107, 93, 41; ^{13}C NMR ($CDCl_3$) δ 70.2, 52.2, 48.3, 46.4, 45.6, 39.0, 36.9, 34.6, 33.6, 28.9, 28.1, 22.9. Anal. Calcd for $C_{14}H_{22}O$: 206.1670. Found: 206.1649.

(3aβ,4aα,8aα,8aβ)-Octahydro-4,7,7-trimethyl-4,8-methanoazulen-1(1*H*)-one (16). (3aβ,4aα,8aα,8aβ)-Decahydro-4,7,7-trimethyl-4,8-methanoazulen-1(1*H*)-ol (250 mg, 1.20 mmol) was oxidized to afford 195 mg (79%) of ketone **16** by utilizing the procedure described above: mp 53–53.5 °C; ^{1}H NMR ($CDCl_3$) δ 0.99, 0.95, 0.91 (all s, 9 H, methyls); IR (NaCl, film) 2960, 2920, 2860, 1735, 1460, 1390, 1380, 1370, 1255, 1160 cm^{-1}; mass spectrum, *m/e* 178, 149, 119, 91, 59 (base), 43; ^{13}C NMR ($CDCl_3$) δ 53.3 (d), 50.18 (d), 45.3 (d), 42.1 (s), 38.7 (t), 37.2 (t), 33.4 (t), 31.9 (t), 29.0 (q), 24.8 (q), 22.2 (t), 21.5 (q). Anal. Calcd for $C_{14}H_{22}O$: 206.1671. Found: 206.1667. X-Ray data are provided with the supplementary material.

(3aβ,3bα,6aα,7aβ)-Decahydro-4-methylene-3,3,7a-trimethyl-1*H*-cyclopenta[*a*]pentalene ($\Delta^{9(12)}$-Capnellene, 6). To a stirred solution of methyltriphenylphosphonium bromide (3.68 g, 10.3 mmol) dissolved in 35 mL of THF was added *n*-butyllithium (5.25 mL, 8.1 mmol). To the resulting mixture was added a solution of ketone **14** (208 mg, 1.01 mmol) dissolved in 10 mL of THF. After stirring for 136 h, 25 mL of water was added and the organic layer was separated. The resulting oil was purified by chromatography (2 × 25 cm column) on 30 g of silica gel. Elution with pentane afforded 165 mg of $\Delta^{9(12)}$-capnellene (**6**, 80%) and 33 mg of the starting ketone **14** (corrected yield, 95%): ^{1}H NMR ($CDCl_3$) δ 1.15, 1.06, and 0.98 (all s, 9 H, methyls); IR (NaCl, film) 3060, 2940, 2860, 1650, 1460, 1385, 1373, 1365, 870 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 158.7 (s, *C*=CH_2), 104.9 (t, C=*C*H_2), 69.4 (d), 53.5 (s, CMe), 52.4 (d), 48.3 (t), 46.1 (d), 42.4 (s, CMe_2), 41.9 (t), 40.7 (t), 31.7 (q, angular methyl), 30.8 and 26.1 (q, *gem*-methyls), 29.4 (t); mass spectrum, *m/e* 204 (parent), 189, 163, 148, 135, 133, 109, 91, 80 (base), 79, 67, 55, 41. Anal. Calcd for $C_{15}H_{24}$: 204.1833. Found: 204.1854. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.98; H, 11.79.

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Registry No. 6, 68349-51-9; **8**, 81331-93-3; **9**, 81331-90-0; **10**, 81331-91-1; **11**, 81331-92-2; **14**, 84173-37-5; **15**, 84173-38-6; **16**, 84132-88-7; cyclopentadiene, 542-92-7; dimethyl azodicarboxylate, 2446-84-6; *N,N'*-bis(methoxycarbonyl)-7-(2,2,5-trimethylhex-5-enylidene)-2,3-diazabicyclo[2.2.1]heptane, 82266-93-1; decahydro-3,3,7a-trimethyl-1*H*-cyclopenta[*a*]pentalen-4-ol, 84132-89-8; decahydro-4,7,7-trimethyl-4,8-methanoazolen-1(1*H*)-ol, 84132-90-1.

Supplementary Material Available: Method of data collection, atom labeling scheme for **16**, and tables of the crystal data, positional parameters, and the observed and calculated structure factors for **16** (18 pages). Ordering information is given on any current masthead page.