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# Intramolecular 1,3-Diyl Trapping Reactions. Total Synthesis of (±)-Hypnophilin and (±)-Coriolin. Formation of the Trans-Fused Bicyclo[3.3.0]octane Ring System

Luc Van Hijfte,[†,‡] R. Daniel Little,*[‡] Jeffrey L. Petersen,[§] and Kevin D. Moeller[‡,⊥]

*Department of Chemistry, University of California, Santa Barbara, Santa Barbara, California 93106, and Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506*

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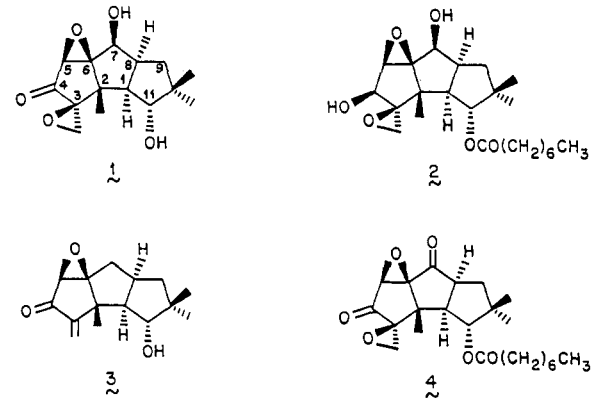
The intramolecular 1,3-diyl trapping reaction served as the key step in a total synthesis of (±)-coriolin (1) and the first total synthesis of (±)-hypnophilin (3). In the process, four of the required eight (coriolin) or six (hypnophilin) stereocenters were established. The reaction was studied as a function of temperature. The highest yield and greatest stereo-/regioselectivity was obtained when the reaction was initiated photochemically at −60 °C in methyl alcohol. From the temperature dependence, it was established that enthalpic rather than entropic factors were responsible for governing the selectivity of the process. The required cis, anti ring-fused product **10** was favored over the minor products by $\Delta\Delta H^{\ddagger} = -2.19$ kcal mol$^{-1}$. Two noteworthy steps in the conversion of tricyclopentanoid **10** to the natural products included the Lewis acid facilitated 1,4-addition of $Li_2Cu(CN)(CH_3)_2$ to the hindered $C_2$ carbon in **26** and the epoxidation of compounds **10**, **24**, and **29**. Each olefin **10** and **24** led to the formation of products containing both cis- *and* trans-fused bicyclo[3.3.0]octane ring systems. Molecular mechanics calculations (MM2) were used to calculate differences in strain energies between the two types of products. In the case of olefin **39**, *only* the trans-fused AB-ring junction stereochemistry was observed. Single-crystal X-ray analysis verified the stereochemical assignments and served to provide a rationale for the unanticipated formation of these trans-fused products.

## Introduction

Coriolin (1) and coriolin B (2) were first isolated from the mycelial cake of *Coriolus consors* by Umezawa and co-workers in 1971; both compounds have attracted widespread interest due primarily to their interesting molecular architecture as well as their antibiotic and antitumor properties.[1,2] Ten years later, Steglich, Anke, and co-workers isolated and characterized the linearly fused tricyclopentanoid hypnophilin (3).[3] It too is biologically active, displaying activity toward gram-positive and gram-negative bacteria, fungi, and yeasts, as well as antitumor activity. Diketocoriolin B (4) is not a natural product; instead, it is derived from 2 by oxidation using chromic anhydride. However, in addition to being active toward a wide spectrum of microorganisms, it possesses more potent antitumor activity than its precursor and is not immunosuppressive. In fact, daily intraperitoneal injection actually leads to an increase in the number of antibody-forming cells in mouse spleen, a result which is clearly in contrast with that observed for many antitumor agents.[4]



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[†] Senior Research Assistant of the Belgian National Fund for Scientific Research. Present address: Merrell Dow Research Institute, Strasbourg, France.
[‡] UCSB.
[§] West Virginia University.
[⊥] In part.

(1) Takeuchi, T.; Iinuma, H.; Iwanaga, J.; Takahashi, S.; Takita, T.; Umezawa, H. *J. Antibiot.* **1969**, *22*, 215.
(2) Takahashi, S.; Nagnanawa, H.; Iinuma, H.; Takita, T.; Maeda, K.; Umezawa, H. *Tetrahedron Lett.* **1971**, 1955. Nakamura, H.; Takita, T.; Umezawa, H.; Kunishita, M.; Nakayama, Y.; Iitaka, Y. *J. Antibiot.* **1974**, *27*, 301.
(3) Kupka, J.; Anke, T.; Giannetti, B. M.; Steglich, W. *Arch. Microbiol.* **1981**, *130*, 223. Giannetti, B. M.; Steffan, B.; Steglich, W.; Kupka, J.; Anke, T. *Tetrahedron* **1986**, *42*, 3587. Steglich, W. *Pure Appl. Chem.* **1981**, *53*, 1233.

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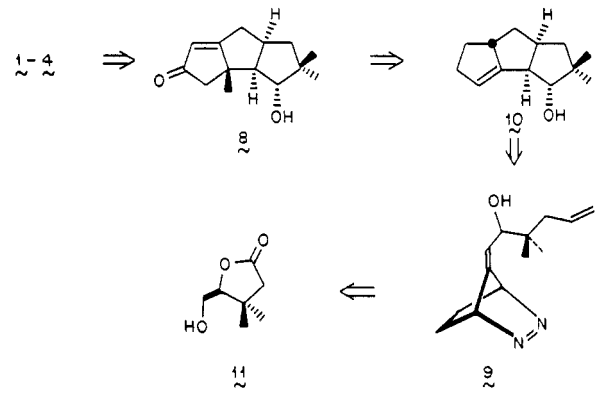
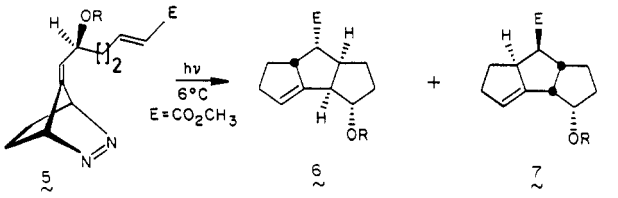
**Scheme I**



We report a stereo- and regiocontrolled formal total synthesis of coriolin (1)[5] as well as the first total synthesis of hypnophilin (3). In addition, several unanticipated results leading to the formation of trans-fused polyquinanes are presented along with a discussion of the relative importance of enthalpic and entropic factors in controlling the product distribution in intramolecular 1,3-diyl trapping reactions.

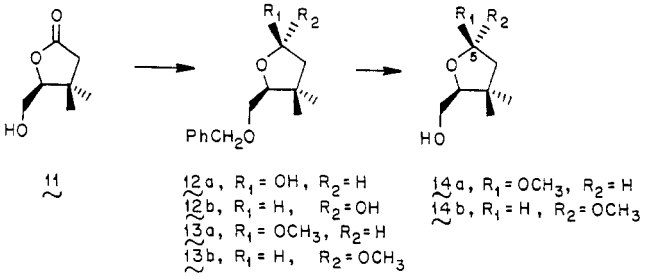
**Analysis of the Problem.** To achieve these results, we have capitalized upon our knowledge of and previous experience with the intramolecular 1,3-diyl trapping reaction.[6] Thus, the selection of diazene **9** (note Scheme 1) rather than any of several reasonable diyl precursors was guided by our knowledge of the following principles. First, the intramolecular 1,3-diyl trapping reaction is stereoselective and favors the formation of cis,anti rather than cis,syn ring-fused tricyclopentanoids. We therefore assumed that this preference would be observed once again, thereby leading to the establishment of the proper stereochemistries at $C_1$, $C_6$, and $C_8$ (coriolin numbering). In addition, we were aware of the fact that photodeazetation of optically active diazene **5** at 6 °C led to the cis,anti tricyclopentanoids **6** (CA) and **7** (ca) in a ratio of 26:1. The major product possessed the same relative and absolute stereochemistry at the relevant stereocenters as is found in compounds **1–3**, thereby suggesting that deazetation of **9** should lead to a large preference for the formation of the required relative and, if desired, absolute stereochemistry at $C_{11}$. Finally, while the use of an unactivated diylophile



has on rare occasion led to the formation of diyl dimer, we elected to use an unactivated diylophile in the present instance because we were aware that as long as the trapping reaction occurred from the singlet rather than the triplet manifold of the diyl, then either an activated or an unactivated diylophile could be utilized without fear of competing unimolecular cyclization and diyl dimerization.

Commercially available dihydro-5-(hydroxymethyl)-4,4-dimethyl-2(3*H*)-furanone (**11**) was chosen as the starting material since it incorporates all of the essential structural features which are present in the acyclic chain of diazene **9**,[7] (Scheme I). To synthesize both coriolin (1) and hypnophilin (3), enone **8** was selected as a common intermediate. While **8** had previously been converted to coriolin (1),[5e,i] its conversion to hypnophilin (3) had not been accomplished.

**Preparation of Diazene 9.** The furanone **11**, although commercially available, could also be obtained in large amounts by epoxidation of 3,3-dimethyl-4-pentenoic acid with 3-chloroperoxybenzoic acid (MCPBA) in chloroform at room temperature (84%). After protection of the primary alcohol as a benzyl ether ($C_6H_5CH_2Br$, $Ag_2O$, DMF, 76%), the carbonyl unit was reduced with diisobutylaluminum hydride in ether at −78 °C to afford the diastereomeric pair of lactols **12a,b** in 97% yield and a ratio of approximately 2:1 (by 300-MHz $^1H$ NMR). The lactols



were then methylated with *p*-toluenesulfonic acid in methanol to afford the functionalized tetrahydrofurans **13a,b** in nearly quantitative yield and a 2.8:1 ratio as discerned by capillary column GC analysis; the protected lactols were used without separation. The benzyl group was removed by hydrogenolysis over palladium hydroxide on carbon to afford the alcohols **14a,b** in 94% isolated yield; use of other catalysts, such as palladium on carbon, gave less reproducible results.

To obtain information about the relative stereochemistry in the major (**14a**) and minor (**14b**) isomers, nuclear Overhauser effect difference spectroscopy (NOEDS) experiments were carried out on the major isomer **14a**. Irradiation of the β-oriented methyl group led to an enhancement of the signal due to the methylene protons of the hydroxymethylene group. In addition, presaturation of the methoxy protons led to a measurable effect upon the β-methyl group signal. These results clearly indicate a cis relationship between the hydroxymethylene and methoxyl group. While this is so, the precise stereochemistry at $C_5$ is irrelevant with respect to the ultimate ob-

(4) Kunimota, T.; Umezawa, H. *Biochim. Biophys. Acta* **1974**, *298*, 513. Ishizaka, M.; Iinuma, H.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1972**, *25*, 320.

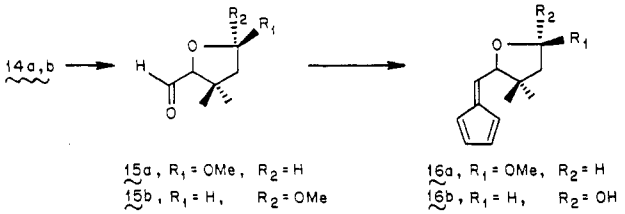
(5) For a preliminary account on a portion of this work, see: Van Hijfte, L.; Little, R. D. *J. Org. Chem.* **1985**, *50*, 3940. Previous syntheses of coriolin include: (a) Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 2097. (b) Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3460. (c) Shibasaki, M.; Iseki, K.; Ikegami, S. *Tetrahedron Lett.* **1980**, *21*, 2587. (d) Iseki, K.; Yamazaki, M.; Shibasaki, M.; Ikegami, S. *Tetrahedron* **1981**, *37*, 4411. (e) Trost, B. M.; Curran, D. P. *J. Am. Chem. Soc.* **1981**, *103*, 7380. (f) Ito, T; Tomiyoshi, N.; Nakamura, K.; Azuma, S.; Izawa, M.; Maruyama, F.; Yanagiya, M.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1982**, *23*, 1721; (g) Ito, T.; Tomiyoshi, N.; Nakamura, K.; Azuma, S.; Izawa, M.; Maruyama, F.; Yanagiya, M.; Shirahama, H.; Matsumoto, T. *Tetrahedron* **1984**, *40*, 241. (h) Schuda, P. F.; Heimann, M. R. *Tetrahedron* **1984**, *40*, 2365. (i) Koreeda, M.; Mislankar, S. G. *J. Am. Chem. Soc.* **1983**, *105*, 7203. (j) Exon, C.; Magnus, P. *J. Am. Chem. Soc.* **1983**, *105*, 2477. (k) Demuth, M.; Ritterskamp, P.; Schaffner, K. *Helv. Chim. Acta* **1984**, 1167, 2023. (l) Demuth, M.; Ritterskamp, P.; Weight, E.; Schaffner, K. *J. Am. Chem. Soc.* **1986**, *108*, 4149. (m) Funk, R. L.; Bolton, G. L.; Daggett, J. U.; Hansen, M. M.; Horcher, L. H. M. *Tetrahedron* **1985**, *41*, 3479. (n) Tatsuta, K.; Akimoto, K.; Kinoshita, M. *J. Antibiot.* **1980**, *33*, 4365 (o) Mehta, G.; Reddy, A. V.; Murthy, A. N.; Reddy, D. S. *J. Chem. Soc., Chem. Commun.* **1982**, 540. (p) Wender, P. A.; Howbert, J. J. *Tetrahedron Lett.* **1983**, *24*, 5325. (q) Mehta, G.; Murthy, A. N.; Reddy, D. S.; Reddy, A. V. *J. Am. Chem. Soc.* **1986**, *108*, 3443.

(6) For a recent review refer to: Little, R. D. *Chem. Rev.* **1986**, *86*, 875. Note also the references cited therein.

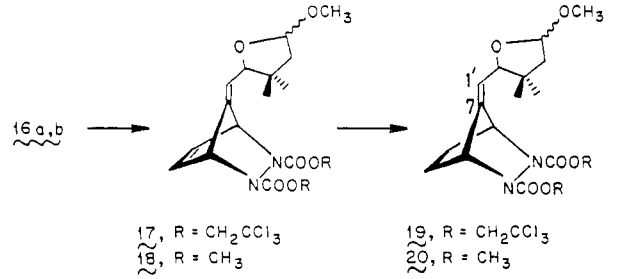
(7) Available from Dynamit Nobel Aktiengesellschaft, D-5210 Troisdorf, Federal Republic of Germany.

jectives since $C_5$ eventually becomes an $sp^2$-hybridized center.

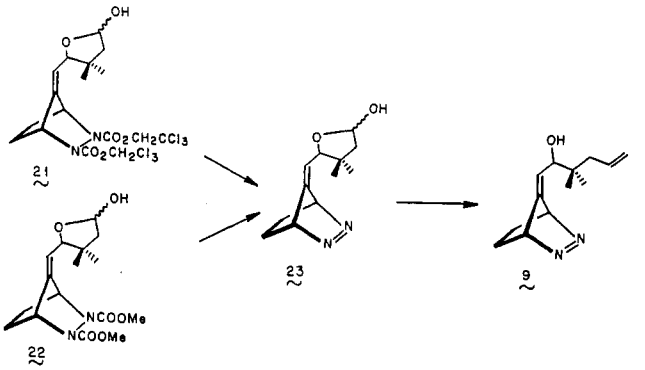
The conversion of **14a,b** to the aldehydes **15a,b** was carried out by using a Swern oxidation.[8] Thus, treatment of **14a,b** with oxalyl chloride in dimethyl sulfoxide at −60 °C followed by triethylamine, afforded aldehydes **15a,b** which were sufficiently pure to allow them to be used directly. Treatment of **15a,b** with methanol, cyclopentadiene, and pyrrolidine, under conditions developed in these laboratories,[9] led to the formation of fulvenes **16a,b**. After 24 min no starting material could be detected; an intermediate (imine?) formed and was transformed very slowly into the required fulvenes **16a,b**. Prolonged reaction times led to decomposition of the fulvene which had formed, so that it proved advantageous to workup the reaction after 24 h. Under the slightly acidic workup conditions the intermediate was converted to the starting material, which in turn was recycled. After several recyclings, the yield of fulvenes ranged from 40% to 45%. It was eventually discovered that the rate of fulvene formation increased dramatically when acetic acid was added to the reaction mixture. Thus, treatment of the aldehydes **15a,b** with 1 equiv of acetic acid, 2 equiv of pyrrolidine, and 2.5 equiv of cyclopentadiene in methanol at room temperature gave, after 12 h, the fulvenes **16a,b** in 55% isolated yield over two steps (viz., Swern plus fulvene formation); no starting material could be recovered.




With the fulvene unit destined to become the carbon framework of the diyl in hand, the next task called for preparation of the bicyclic skeleton of diazene **9**. This was accomplished by carrying out a Diels–Alder reaction between the fulvenes **16a,b** and either bis(2,2,2-trichloroethyl) azodicarboxylate in ether at 0 °C for 1 h or dimethyl azodicarboxylate in ether at 0 °C for 3 days, thereby forming products **17** and **18**, respectively. The $C_{5,6}$ $\pi$ bond of both adduct **17** and **18** was selectively hydrogenated by using diimide to afford **19** and **20** in 82% and 91% isolated yield, respectively (two steps). Both **19** and **20** consisted of a mixture of diastereomers. However, this was of no importance with respect to the remainder of the sequence since, as already mentioned, one of the centers ($C_5$ in **14a**) was destined to be converted to an $sp^2$-hybridized carbon. In addition, from previous studies, there was evidence to suggest that the diyl would exist as a time-averaged planar intermediate and that the existence of diastereoisomers about the $C_7$–$C_1$, bond would not have any bearing upon the stereochemical outcome; that is, the outcome would be expected to be the same regardless of the geometry about $C_7$–$C_{1'}$.[6,10] Thus, we were confident that any of the four diastereomers of **19** and **20** would ultimately lead to the same products.

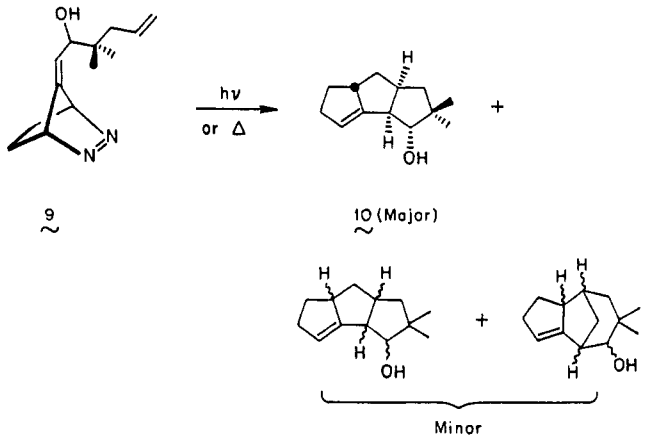



Having assembled the bicyclic framework, attention was directed toward introduction of the diylophile. Deprotection of the masked aldehyde in **19** and **20** was most efficiently accomplished by using 70% aqueous acetic acid at 50–60 °C for 5 days; the pairs of lactols **21** and **22** were obtained in 85% and 95% yield, respectively. Although these materials could be separated by liquid chromatography, they were generally carried on together in the next reaction. All attempts to introduce the methylene unit at this stage of the sequence were unsuccessful. Treatment of either **21** or **22** with triphenylphosphonium methylide led to complete destruction of the starting material. In contrast, incorporation of an activated diylophile using (carbomethoxymethylene)triphenylphosphorane presented no problem. However, we wanted to avoid assiduously the issue of removal or modification of an ester unit once the tricyclopentanoid skeleton had been assembled. Further, we were suspicious that the vicinal dicarbamate unit might in part be responsible for our difficulties and therefore elected to circumvent the problem by first converting the dicarbamate unit to a diazene linkage. For the bis(2,2,2-trichloroethyl) dicarbamate **21**, this conversion was most efficiently accomplished electrochemically (Hg, −1.7 V vs SCE, DMF, $LiClO_4$); oxidation with potassium ferricyanide afforded the diazene **23** in 73% isolated yield. More conveniently, the dimethyl dicarbamate **22** was subjected to saponification with potassium hydroxide in refluxing ethanol for 1.5 h, whereafter the in situ oxidation with potassium ferricyanide at 0 °C gave rise to the dizaene **23** in yields ranging from 76% to 86%. We were gratified to observe that treatment of **23** with triphenylphosphonium methylide in THF at room temperature led to the desired diyl precursor **9** in 56–83% yield; unexpectedly, the yield of this reaction was lower for larger scale reactions, but the reason for this behavior was not investigated.




**Intramolecular 1,3-Diyl Trapping Reaction.** When diazene **9** was heated in refluxing acetonitrile for 2.5 h, five products, one major and four minor isomers, were produced in 93% combined yield. Capillary column analysis indicated that the ratio of the major isomer (Mjr) to the *sum* of the minor isomers (Mnr) was 4:1; photodeazetation in acetonitrile at 6 °C led to a ratio of 9:1. The structure of the major product, the cis,anti ring-fused tricyclopentanoid **10**, was assigned by spectroscopic means and by analogy with the results of previous studies. Ultimately, we were assured of the correctness of our assignment based upon the conversion of compound **10** to the desired target molecules (vide infra). One of the minor

(8) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.
(9) Stone, K. J.; Little, R. D. *J. Org. Chem.* **1984**, *49*, 1849.
(10) Stone, K. J.; Little, R. D. *J. Am. Chem. Soc.* **1985**, *107*, 2495.




products was *assumed* to possess a tricyclo[5.3.1.$0^{2,6}$]undecane skeleton, although unequivocal evidence supporting the assignment was not obtained.

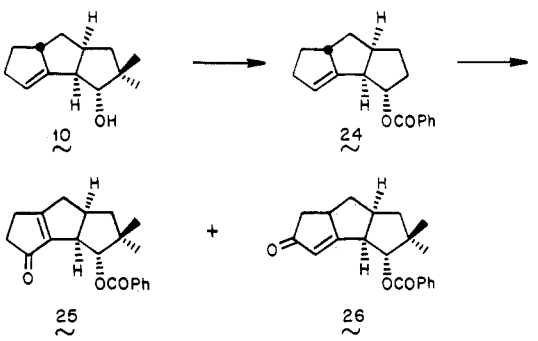
**Temperature-Dependent Diyl Trapping Reaction. Evaluation of Enthalpic and Entropic Factors.** A brief study of the diyl trapping reaction as a function of solvent (THF, $CH_3OH$, $CH_3CN$) revealed that its choice had scarcely any effect upon the ratio of major to the sum of the minor products (Mjr/Mnr) at any given temperature. However, we did discover that methanol, a solvent which had not been utilized previously in intramolecular 1,3-diyl trapping reactions, was very useful for low-temperature studies. Thus, photoinduced deazetation of **9** in methanol at −60 °C led to an increase in stereoselectivity and the ratio, Mjr/Mnr, reached a value of 30:1.

To determine whether enthalpic or entropic factors were responsible for controlling the product distribution, the diyl trapping reaction was conducted at several different temperatures. In analogy with previous results, there was reason to believe that both thermally and photochemically initiated extrusion of nitrogen would lead to the same 1,3-diyl,[10] thereby allowing one to examine a reasonably large range of temperatures. In practice, the product ratio varied from 4.7:1 in refluxing methanol to 9.1:1 when the reaction was initiated photochemically at 6 °C to 30:1 when initiated photochemically at −60 °C. As illustrated in Figure 1, a plot of ln (Mjr/Mnr) vs $1/T$ afforded a straight line from which we could conclude that the variation in product ratio had its origins in enthalpic ($\Delta\Delta H^{\ddagger} = -2.19$ kcal/mol), rather than entropic factors.

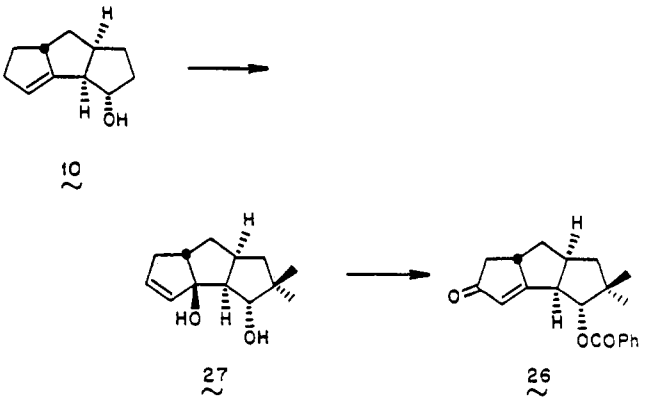
These results are in accord with a rationale which assumes that the intramolecular diyl trapping reaction is kinetically controlled and that the difference in activation enthalpies simply reflects the energy difference between the transition state representations illustrated in Figure 2. This assumes that, following the extrusion of nitrogen, the "linear" diyl $I_1$ is formed and that the activation barrier reflects the energy required to convert $I_1$ to each of the two transition states.

**Conversion of Tricyclopentanoid 10 to Coriolin (1) and Hypnophilin (3).** All attempts to convert **10** or its hydroxyl protected derivatives to enone **26** were unsuccessful. Most often (e.g., with $CrO_3{\cdot}[C_5H_5N]_2$), treatment of benzoate **24** with a variety of oxidizing agents led to complex reaction mixtures wherein, in addition to small amounts of the desired enone **26**, enone **25** was the major product.

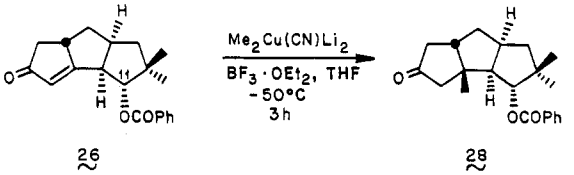
Alternative modes of enone formation were examined. A particularly promising route, based upon the independent efforts of Rickborn, Crandall, and Dauben,[11,12]




suggested that strong base-induced ring opening of the epoxide derived from **10**, followed by oxidation with pyridinium chlorochromate (PCC), would suffice. In practice, treatment of the tricyclopentanoid **10** with 3-chloroperoxybenzoic acid (MCPBA) in chloroform at 0 °C gave rise to *two* isomeric epoxides (vide infra). Heating the epoxides in THF with either $(n\text{-Bu})_2NLi$ or lithium diisopropyl amide (LDA) led to the expected diol **27** in 45% yield (two steps). All attempts to oxidize selectively the allylic alcohol met with failure; selective protection of the secondary hydroxyl group in **27** as a benzoate ester and oxidation using PCC afforded the required enone **26** in 76% yield after crystallization.




We next addressed the problems posed by the addition of a methyl group to the hindered β-carbon of enone **26**, a carbon which is emcumbered by being doubly substituted and, in a less obvious fashion, is hindered by virtue of the fact that the C-ring $C_{11}$ methine hydrogen is pointed directly toward it. Thus, we were not surprised to discover that unactivated organocopper reagents (e.g., $LiCu(CH_3)_2$ in THF) failed to produce the desired 1,4-addition product **28**. On the other hand, treatment of **26** with the higher order cuprate $Li_2CuCN(CH_3)_2$ in the presence of boron trifluoride etherate, converted it to the desired product **28** in 93% isolated yield.[13]




To introduce the $\Delta^{5,6}$ π bond, the triquinane **28** was converted into a 3:2 mixture of two regioisomeric tri-

(11) Kissel, C. L.; Rickborn, B. *J. Org. Chem.* **1972**, *37*, 2060 and references cited therein.

(12) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 682.

(13) (a) Lipshutz, B. H.; Parker, D. A.; Kozlowski, J. A.; Nguyen, S. L. *Tetrahedron Lett.* **1984**, *25*, 5959. (b) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. *Tetrahedron* **1984**, *40*, 5005.

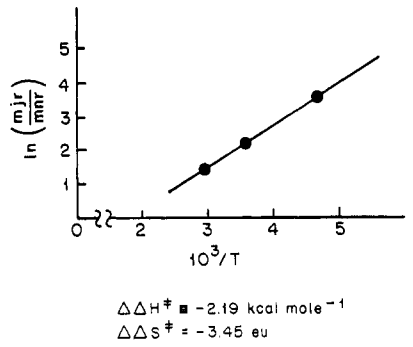



**Figure 1.** Diyl trapping reaction product ratios as a function of temperature.

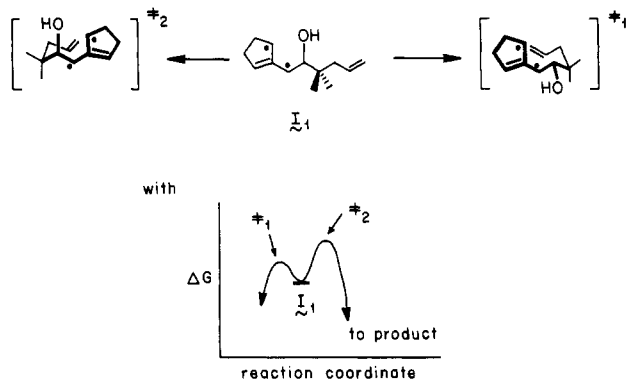
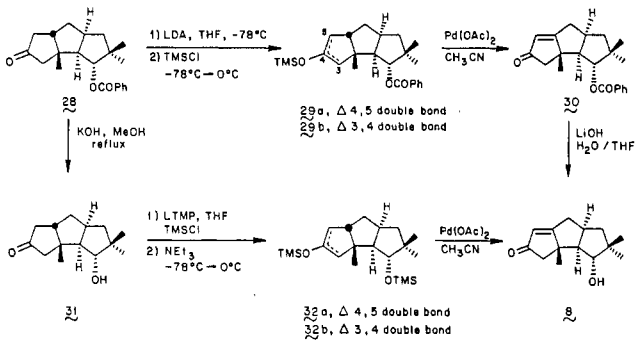


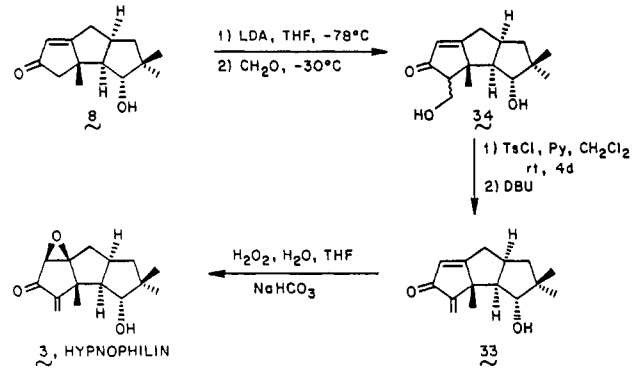

**Figure 2.** Enthalpic origin of observed product ratios: kinetic control.

methylsilyl enol ethers **29a,b** by using LDA in THF at −78 °C followed by addition of TMSCl; the major isomer, **29a**, resulted from enolate formation toward $C_5$. Treatment with palladium acetate in acetonitrile converted **29a** to the required enone **30**, while the minor product, **29b**, was reconverted to the starting ketone **28**.[14] Enone **30**, which has previously been synthesized and converted into the target molecule 8 by Koreeda and co-workers,[5i] was formed in 40% yield, along with 50% recovered starting material; intermediate **30** proved to be identical in all respects with the material synthesized by the Koreeda group.




During the course of this investigation, Funk and coworkers reported a formal total synthesis of coriolin (1).[5m] They noted that trimethylsilyl enol ether formation from **31** using lithium tetramethylpiperidide as the base, afforded the enol ethers **32a** and **32b** in a 6:1, rather than a 3:2 ratio as was observed when LDA was utilized. Hydrolysis of the benzoate **28** with potassium hydroxide in refluxing methanol gave a nearly quantitative yield of the Funk intermediate **31**. The trimethylsilyl enol ether formation proceeded as described; on the other hand, introduction of the enone C–C $\pi$ bond proved to be less reproducible, a result which we attribute to variations in the source and quality of the palladium acetate which was used.

**Hypnophilin (3).** With a formal total synthesis of coriolin (1) accomplished, we next turned our attention toward the completion of a total synthesis of hypnophilin (3). In practice, it was found that treatment of enone **8** with LDA in THF at −78 °C, followed by trapping of the resulting enolate with formaldehyde at −30 °C, led to a mixture of the diastereomeric diols **34** in 85% yield. The mixture was treated with tosyl chloride and pyridine in dichloromethane at room temperature; TLC analysis revealed that some dienone **33** was formed even under these reaction conditions. After 4 days, tosylation of the primary hydroxyl group was complete and the elimination reaction was accomplished upon addition of 1,5-diazabicyclo-[5.4.0]undec-5-ene (DBU). The dienone **33** was obtained in 80% yield and proved identical with the material synthesized previously by Schuda and Heimann.[5h]




Monoepoxidation of the $\Delta^{5,6}$ $\pi$ bond in dienones similar to **33** had already been described. Thus, under reaction conditions applied by Danishefsky and co-workers,[5a,b] dienone **33** was converted to (±)-hypnophilin (**3**) in 50% yield; some starting material (30%) was recovered. Diepoxide could also be detected, but that material decomposed during the column chromatographic purification on silica gel. Synthetic hypnophilin (**3**) displayed spectral data which were in full accord with those of natural material supplied to us by Professor Steglich.[3]

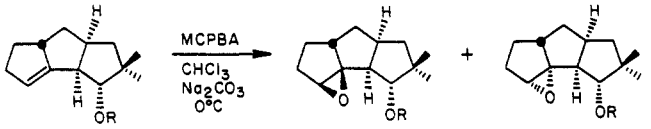
**Unexpected Formation of Trans-Fused Bicyclo-[3.3.0]octanes.** Epoxidation of hydroxyalkene **10** with MCPBA was expected to afford a single product, that resulting from delivery of oxygen to the $\alpha$-face of the olefin, thereby establishing the thermodynamically preferred cis fusion between rings A and B. This expectation was in complete accord with a basic assumption which has been used frequently by researchers engaged in efforts to construct polyquinanes.[15] That is, in a reaction wherein either a cis- or trans-fused bicyclo[3.3.0]octane can be formed, the cis-fused product will be preferred, even in a kinetically controlled process, and to an extent which is related to the difference between the strain energies of the cis- and trans-fused products. Since the difference in strain energies between cis- and trans-fused bicyclo[3.3.0]octane is ca. 7 kcal/mol,[16] it has generally been assumed that one

(14) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011.

(15) See, for example: Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 2097; Tatsuta, K.; Akimoto, K.; Kinoshita, M. *J. Am. Chem. Soc.* **1979**, *101*, 6116; Little, R. D.; Muller, G. W. *J. Am. Chem. Soc.* **1981**, *103*, 2744. See also: Winkler, J. D.; Sridar, V. *J. Am. Chem. Soc.* **1986**, *108*, 1708. Both Funk and Ikegami have independently suggested the formation of trans-fused tricyclopentanoids. See: Funk, R. L.; Bolton, G. L.; Daggett, J. U.; Hansen, M. M. M.; Horcher, L. H. M. *Tetrahedron* **1985**, *41*, 3479. Shibasaki, M. Mase, T.; Ikegami, S. *J. Am. Chem. Soc.* **1986**, *108*, 2090.

need not be concerned with the possibility of forming a trans-fused product.[17]

We were therefore surprised to discover that epoxidation of **10** furnished *two* products **35** and **36**, both of which displayed spectral characteristics consistent with a trisubstituted epoxide (90% yield; 4:1 ratio by capillary column GC). Similarly, epoxidation of the benzoate **24** afforded a mixture of two epoxides **37** and **38** in a ratio of 27:73. Interestingly, epoxidation of the silyl ether **39** lead



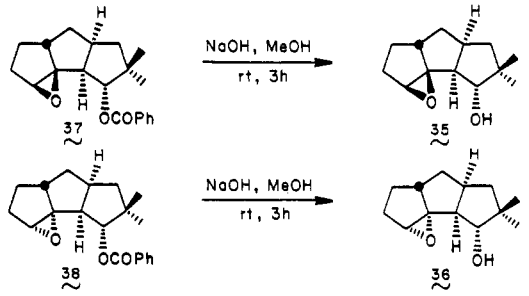

**10**, R=H
**24**, R=COPh
**39**, R = TBDMS

**35**, R=H
**37**, R=COPh

**36**, R=H
**38**, R=COPh
**40**, R = TBDMS

to the formation of epoxide **40** *only*. It is worth noting that the epoxidation reactions proceeded rapidly and were complete in less than 5 min; MM2 calculations suggest that the enhanced reactivity may be attributable to the high degree of strain which is associated with the $\pi$ bond of **10** (vide infra).

While epoxide **35** could be converted to enone **8** and we were confident of our stereochemical assignments, indisputable direct evidence could not be garnered to establish the stereochemical assignment in the putative trans-fused epoxide **36**; consequently, indirect methods were examined first. To establish the interrelationship between the epoxides generated from **10**, **24**, and **39**, the ester unit in both **37** and **38** was first saponified by using potassium hydroxide in methanol. In this way, it was established that




**37** **35** **38** **36**

the major epoxide derived from the epoxidation of **10**, namely **35**, had the same relative stereochemistry as the minor isomer **37** derived from the epoxidation of **24**; similarly, the epoxides **36** and **38** proved to have the same carbon framework. When a 4:1 mixture of **35** and **36** was silylated with *tert*-butyldimethylsilyl chloride and imidazole in DMF, two products were obtained in nearly quantitative yield and in a 4:1 ratio; TLC and GC analysis of the mixture revealed that **40**, the sole reaction product resulting from the epoxidation of **39**, possessed the same skeleton as that found in compounds **36** and **38**.

Unequivocal evidence in support of the hypothesis that compounds **36**, **38**, and **40** correspond to materials possessing a trans-fused A,B ring junction was obtained from a single-crystal X-ray analysis of the crystalline benzoate **38**; top and side views are provided in Figures 3 and 4. Remarkably, the AB inter-ring angles ($C_5$–$C_6$–$C_7$ and

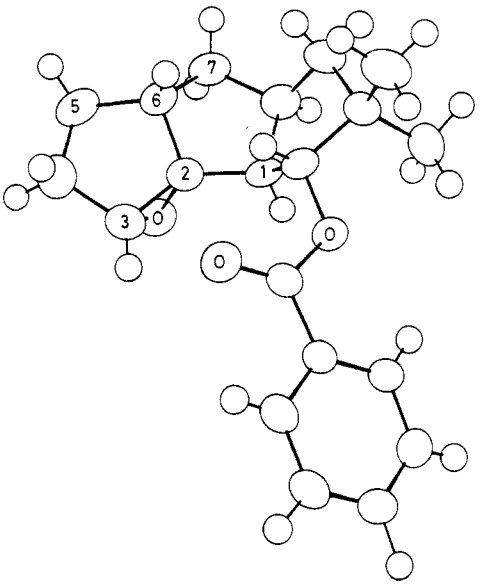



**Figure 3.** Trans-fused tricyclopentanoid epoxide **38**; top view, X-ray analysis.

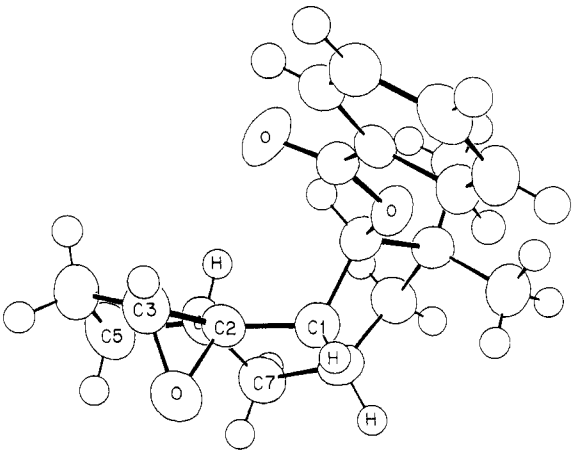



**Figure 4.** Shielded top side of trans-fused epoxide **38**.

$C_1$–$C_2$–$C_3$) are strikingly large, corresponding to 125.0° and 140.3°, respectively. MM2 calculations carried out on the alcohol **36** agree well with experiment and place the $C_5$–$C_6$–$C_7$ angle at 125.8 while the $C_1$–$C_2$–$C_3$ angle is calculated to be 134.1. For comparison, the same angles in the cis-fused alcohol **35** are calculated to be 115.6 and 119.9; the difference in calculated strain energies for **35** and **36** is 7.6 kcal/mol.

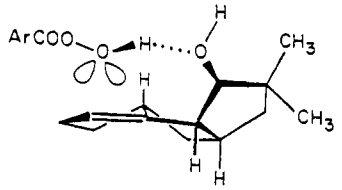
The side view of benzoate **38**, which is illustrated in Figure 4 reveals that the OCOPh group occupies space which is above the plane of the A,B ring. It is reasonable to assume that a large group could sterically shield access to the $\alpha$-face of the $\pi$ bond in alkenes **10**, **24**, and **39**. This effect was most clearly seen in the epoxidation of the silyl ether **39**, where the trans-fused epoxide **40** was formed stereospecifically.

While steric factors undoubtedly play a major role in determining the stereochemical outcome, it is possible that other factors are operable as well. For example, the conversion of alcohol **10** to a 4:1 mixture of epoxides **35** and **36** could be rationalized by simply noting that in the absence of a sterically demanding OR unit, the "natural preference" for the formation of the less strained cis-fused product is observed. In addition, however, one could suggest the operation of a Henbest-type epoxidation mechanism wherein the hydroxyl group directs the attack of the incoming epoxidizing agent.[18] From a model, it

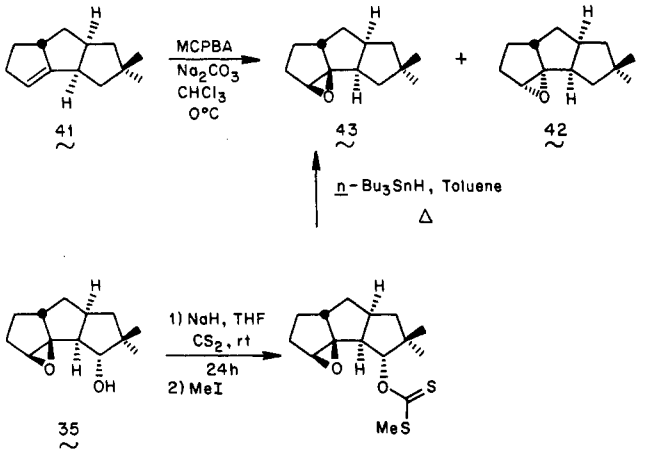
(16) Chang, S.-J.; McNally, D.; Shary-Tehrany, S.; Hickey, M. J.; Boyd, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 3109; Burkert, U.; Allinger, N. L. *Molecular Mechanics*; ACS Monograph 177; American Chemical Society: Washington, DC, 1982; and references therein.

(17) It should be noted that because useful force field parameters are known for cyclopropanes but not for epoxides, a methylene unit was substituted in place of the epoxide oxygen in both of the calculations.

appears reasonable to suggest that complexation between the C-ring hydroxyl group and the peracid could position the latter in proximity to the $\alpha$-face of the $\pi$ system, as illustrated. If this were the case, then removal of the

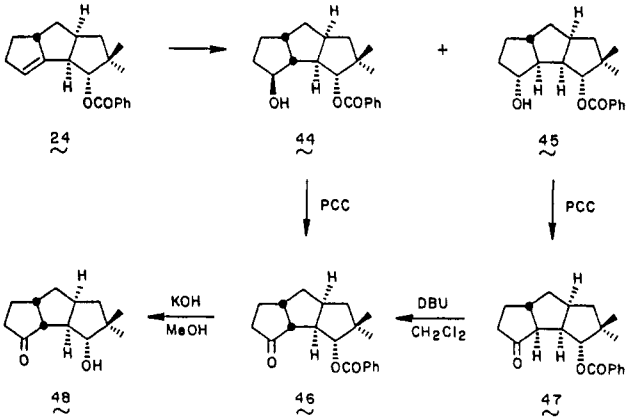


hydroxyl group should lead to a lower preference for the formation of a cis-fused product than is observed with **10**. In practice, epoxidation of **41**, a compound previously synthesized in these laboratories,[19] provided the isomers **42** and **43** in a 2:1 ratio as discerned by GC analysis. Thus,




not only was the amount of cis-fused product reduced, but in fact *the trans-fused product was formed in preference to the cis*. Evidently, the hydroxyl group in **10** *does* enhance the preference for formation of the cis fused epoxide. However, we are unable to explain why epoxidation of **41** leads to *more* trans than cis fused product. Evidence supporting the assignment of structures **42** and **43** was obtained by converting epoxide **35**, a compound whose structure had been firmly established, to the minor product resulting from the epoxidation of **41**, namely, **43**. This was achieved by treating **35** with sodium hydride and carbon disulfide in THF at room temperature (24 h), followed by the addition of methyl iodide (room temperature), to afford a xanthate; the crude product was dissolved in toluene and tri-*n*-butyltin hydride was added,[20] whereafter the mixture was refluxed for 24 h to furnish **43** in 60% yield.

A second example illustrating how easily trans-fused diquinane systems can be formed was discovered by carrying out a simple hydroboration of benzoate **24** and leading to the production of alcohols **44** and **45** in a 16:84 ratio. Neither product corresponded to a tertiary alcohol, the result of a Markovnikov addition to the $\pi$ bond, as was evidenced by the fact that each could be converted to a ketone; oxidation of **44** and **45** with PCC afforded the ketones **46** and **47**, which could not be separated because the trans-fused isomer **47** epimerized to the cis-fused derivative **46** upon chromatography over silica gel. Treatment of the mixture of isomers with 0.1 equiv of DBU in




methylene chloride at room temperature for 2 h completed the isomerization, quantitatively; the ketone **46** was obtained in 63% yield from **24**. Treatment with KOH in methanol at room temperature afforded the keto alcohol **48** in nearly quantitative yield; the same material was detected as a minor component in the reaction mixture which was formed upon refluxing the trans-fused epoxide derivative **36** and LDA in THF.

Obviously, the foregoing results clearly indicate that under the appropriate set of circumstances, trans-fused diquinanes can be formed quite easily and serve to point out the need to exercise caution in assigning ring junction stereochemistry.

## Experimental Section

Proton ($^1$H NMR) and carbon ($^{13}$C NMR) nuclear magnetic resonance spctra were recorded with a Nicolet NT 300 spectrometer at 300 and 75 MHz, respectively, with samples dissolved in $CDCl_3$ containing $Me_4Si$ as an internal standard. Carbon chemical shifts are reported in ppm relative to the central line of $CDCl_3$ (77.000 ppm). Infrared (IR) spectra were recorded on a Perkin-Elmer 283 spectrometer; absorption frequencies are reported in wavenumbers ($cm^{-1}$). Mass spectra (MS) were obtained by Dr. H. M. Webb of UCSB using a ZAB 2-F or a VG7070 mass spectrometer. Ionization was initiated by either electron impact (EI) or by chemical ionization (CI) utilizing methane. Data are reported as the mass to charge ratio of the observed ion, where M refers to the molecular ion; the relative abundance of the ion is given in parentheses. HRMS refers to high-resolution mass spectrometry. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. In several instances (e.g., with the bicyclic diazenes), analyses were not performed due to the instability of these compounds. Also, in a few instances, purified materials were taken on directly to the next step of the sequence without performing a combustion analysis in an effort to optimize material output.

Thin-layer chromatography (TLC) utilized silica gel precoated onto glass plates (E. Merck silica gel 60F-254); methods of detection included the use of a UV handlamp, as well as iodine, *p*-anisaldehyde, and/or phosphomolybdic acid strains. Gravity-flow liquid chromatography (LC) used E. Merck silica gel 60 (230–400 mesh, ASTM). Ether and Skellysolve F (SSF, 30–60 °C boiling range) were distilled prior to use; reagent grade ethyl acetate was used without further purification. Solvent mixtures were prepared by volume. Melting points are uncorrected and are reported in a format wherein the solvent used for recrystallization is listed in parentheses after the symbol mp.

Analytical gas chromatography (GC) was carried out on a Hewlett-Packard 5930A gas chromatograph equipped with a Hewlett-Packard 18850 terminal and a flame ionization detector. A Hewlett-Packard Ultra II (5% phenylmethylsilicone, 25 m × 0.200 mm) column was utilized; helium was used as the carrier gas.

**2-[(Benzyloxy)methyl]-3,3-dimethyl-5-oxotetrahydrofuran.** A mixture of commercially available[7] 2-(hydroxymethyl)-3,3-dimethyl-5-oxotetrahydrofuran (**11**, 31.1 g, 0.216 mol), benzyl bromide (59.1 mL, 0.497 mol) and silver oxide (40 g, 0.172

(18) Henbest, H. B.; McCullough, J. J. *Proc. Chem. Soc.* **1962**, 74. Henbest, H. B. *Proc. Chem. Soc.* **1963**, 159. Henbest, H. B.; Wilson, R. A. L. *J. Chem. Soc.* **1957**, 1958. Chamberlain, P.; Roberts, M. L.; Whitham, G. H. *J. Chem. Soc. B* **1970**, 1374 and references therein.

(19) Little, R. D.; Higby, R. G.; Moeller, K. D. *J. Org. Chem.* **1983**, *46*, 3139.

(20) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.

mol) in DMF (170 mL), which was protected from light, was stirred for 2 days under a nitrogen atmosphere at room temperature. The precipitate was filtered, and the residue was washed with $CHCl_3$ (1 L). The solution was placed in the refrigerator for ca. 12 h; the resulting material was filtered once again. Pyridine (100 mL) was added, and the organic layer was washed successively with water, 20% aqueous HCl, water, saturated aqueous $NaHCO_3$, and brine. Drying over $MgSO_4$ and concentration in vacuo afforded an oil, which was subjected to vacuum distillation [120–150 °C (1 mTorr)] and LC, eluting gradually with 5% EtOAc in SSF to 25% EtOAc in SSF, to afford 38.4 g (76%) of the benzylated lactone: $R_f$ (50% ether in SSF) 0.28.

The spectra data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.32 (5 H, m, Ph), 4.54 (2 H, s, $CH_2Ph$), 4.200 (1 H, t, $J$ = 4.2, $C_2H$), 3.666 (2 H, d, $J$ = 4.2, $CH_2OBzl$), 2.507 (1 H, d, $J$ = 16.9, $C_4H$), 2.278 (1 H, d, $J$ = 16.9, $C_4H$), 1.203 (3 H, s), 1.110 (3 H, s); IR (film) 3062, 3040, 2880–2960, 1785, 1455, 1160, 1140, 1115, 1055 cm$^{-1}$; MS (CI), $m/z$ 234 (M, 1.1), 128 (61), 113 (79.9), 107 (15.8), 91 (100), 85 (25.5), 69 (16), 57 (17), 43 (28.6), 41 (19.6). Anal. (HRMS (CI)) Calcd for $C_{14}H_{18}O_3$: 234.1255. Found: 234.1257.

**2-[(Benzyloxy)methyl]-5-hydroxy-3,3-dimethyltetrahydrofuran (12a,b).** To a solution of tetrahydro-2-[(benzyloxy)methyl]-3,3-dimethyl-5-oxofuran (34.2 g, 0.146 mol) in ether (480 mL), cooled in a dry ice–acetone bath to –70 °C, was added dropwise DIBAL-H (152 mL, 0.96 M in hexane, 0.146 mol) over a period of 30 min. After 20 min, methanol (85 mL) was added, and the reaction mixture was allowed to warm to room temperature. Rochelle's salt solution (350 mL of 30% aqueous sodium potassium tartrate) was added, and the mixture was stirred until two clear layers were visible (ca. 45 min). The organic layer was separated and extracted with 30% Rochelle's salt solution (2 × 100 mL). The aqueous portions were combined and extracted with $CH_2Cl_2$ (4 × 150 mL). The organic portions were combined, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude mix of diastereomeric lactols **12a,b** (33.9 g, 98%, 2:1 ratio by $^1$H NMR) was sufficiently pure according to GC and TLC analysis to be used in the next reaction without further purification: $R_f$ (50% ether in SSF) 0.21.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ [**12a** (major isomer)] 7.351 (5 H, br s, Ph), 5.572 (1 H, br dd, $J$ = 3.9, 5.5, $C_5H$), 4.643 (1 H, d, $J$ = 12.1, $PhCH_2$), 4.533 (1 H, d, $J$ = 12.1, $PhCH_2$), 4.069 (1 H, t, $J$ = 5.7, $C_2H$), 3.512 (2 H, d, $J$ = 5.7, $CH_2OBzl$), 2.83 (1 H, br s, OH), 2.052 (1 H, $J$ = 13.1, 5.9, $C_4H$), 1.740 (1 H, dd, J = 13.3, 4.0, $C_4H$), 1.141 (3 H, s), 0.893 (3 H, s), [**12b** (minor isomer)] 7.321 (5 H, m, Ph), 5.452 (1 H, br m, $C_5H$), 4.577 (2 H, s, $PhCH_2$), 3.60–3.75 (3 H, m), 1.750 (1 H, d(d), $J$ = 13.3, (second coupling not measurable because of peak overlap), $C_4H$), 1.124 (3 H, s), 1.097 (3 H, s); IR (film) 3400 (br), 3062, 3040, 2880–2960, 1452, 1070–1100 (br), 735, 692 cm$^{-1}$; MS (EI), $m/z$ 236 (M, 0.3), 218 (3.9), 115 (43.2), 97 (24.3), 92 (23.9), 91 (100), 71 (20.6), 69 (21.9), 43 (25.1). Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.12; H, 8.53.

**2-[(Benzyloxy)methyl]-5-methoxy-3,3-dimethyltetrahydrofuran (13a,b).** A solution of the lactols **12a,b** (30.43 g, 0.129 mol) and *p*-toluenesulfonic acid (322 mg) in methanol (645 mL) was stirred for 3 h at room temperature. Solid potassium carbonate (150 mg) was added, and the reaction mixture was stirred for 30 min. The methanol was removed in vacuo, and the crude mixture was filtered through silica gel (100 g, 20% ether in SSF). The protected lactols **13a,b** were obtained in 97% yield (31.34 g) as a mixture of diastereomers in a 2.8:1 ratio by GC analysis: $R_f$ (20% ether in SSF) 0.32.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ [**13a** (cis isomer, major)] 7.355 and 7.339 (5 H, each s, Ph), 5.034 (1 H, dd, $J$ = 3.9, 5.8, $C_5H$), 4.652 (1 H, d, $J$ = 12.1, $PhCH_2$), 4.516 (1 H, d, $J$ = 12.1, $PhCH_2$), 3.908 (1 H, t, $J$ = 5.5, $C_2H$), 3.539 (2 H, $J$ = 5.5, $CH_2OBzl$), 3.393 (3 H, s), 2.000 (1 H, dd, $J$ = 5.8, 13.4, $C_4H$), 1.704 (1 H, dd, $J$ = 3.9, 13.4, $C_4H$), 1.111 (3 H, s), 0.887 (3 H, s), [**13b** (trans isomer, minor)] 7.290 (5 H, m, Ph), 4.979 (1 H, dd, $J$ = 2.1, 6.0, $C_5H$), 4.621 (1 H, d, $J$ = 11.9, $PhCH_2$), 4.551 (1 H, d, $J$ = 11.9, $PhCH_2$), 3.813 (1 H, t, $J$ = 5.9, $CH_2$), 3.550 (2 H, d, $J$ = 5.9, $CH_2OBzl$), 3.360 (3 H, s), 1.955 (1 H, dd, $J$ = 6.0, 13.8, $C_4H$), 1.748 (1 H, dd, $J$ = 2.1, 13.8, $C_4H$), 1.085 (3 H, s), 1.053 (3 H, s); IR (film) 3065, 3040, 2880–2980, 1100 (br), 1050, 1030, 980, 695 cm$^{-1}$; GCMS (EI), [**13a**] $m/z$ 218 (M – HOMe, 15), 129 (65), 91 (100), 85 (60), 69 (40), 45 (35), [**13b**] $m/z$ 218 (M – HOMe, 15), 129 (80), 91 (100), 85 (40), 69 (50), 45 (35); MS (CI), $m/z$ 218 (M – HOMe, 4.5), 129 (85.2), 101 (24.8), 100 (21.2), 91 (100), 85 (58.7), 69 (43.3), 45 (26.2). Anal. [HRMS (CI), $m/z$ M – MeOH] Calcd for $C_{14}H_{18}O_2$: 218.1306. Found: 218.1304.

**2-(Hydroxymethyl)-3,3-dimethyl-5-methoxytetrahydrofuran (14a,b).** To a solution of the benzyl ethers **13a,b** (31 g, 0.124 mol) in methanol (250 mL) was added $Pd(OH_2)/C$ (Aldrich, 5 g), and the mixture was stirred vigorously under a hydrogen atmosphere (1 atm) for 3 h. After being flushed thoroughly with nitrogen, the reaction mixture was vacuum filtered through a 5-cm pad of Celite, which was placed in a coarse sintered-glass funnel; care was taken to ensure that the catalyst did not get dry. The filter cake was washed with methanol (100 mL), and the filtrate was concentrated in vacuo. The residue was distilled [bulb-to-bulb, 70–74 °C (1.5 Torr)] to afford 17.83 g of the diastereomeric mixture of alcohols **14a,b**. The residue was distilled (Kugelrohr, 1.5 Torr) to give an additional 833 mg of **14a,b** (combined yield: 94%): $R_f$ (70% ether in SSF) 0.32 (major, **14a**) and 0.34 (minor, **14b**).

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ [**14a** (cis isomer, major)] 5.034 (1 H, dd, $J$ = 3.7, 5.8, $C_5H$), 3.802 (1 H, t, $J$ = 5.4, $C_2H$), 3.656 (1 H, d, $J$ = 5.9, $CH_2OH$), 3.637 (1 H, d, $J$ = 5.4, $CH_2OH$), 3.386 (3 H, s), 2.007 (1 H, dd, $J$ = 5.8, 13.4, $C_4H$), 1.736 (1 H, dd, $J$ = 3.7, 13.4, $C_4H$), 1.124 (3 H, s), 0.914 (3 H, s), [**14b** (trans isomer, minor)] 5.070 (1 H, dd, $J$ = 3.7, 6.1, $C_5H$), 3.421 (3 H, s), 1.82 (2 H, m, $C_4H$), 1.180 (3 H, s), 1.097 (3 H, s). Other signals of the minor isomer overlap with signals of the major isomer. Nuclear Overhauser enhancement difference spectroscopy (NOEDS) on the major alcohol **14a** gave the following results: presaturation of the methyl protons at 3.386 ppm resulted in a NOE of $C_5H$ (7%) and of the methyl protons at 0.914 ppm (1.6%). IR (film) 3450 (br), 2880–2980, 2840, 1470, 1370, 1210, 1100 (br), 1040 (br), 975 (br) cm$^{-1}$; GCMS (EI), [**14a**] $m/z$ 129 (60), 85 (100), 69 (35), 55 (30), [*14b*] $m/z$ 129 (100), 85 (70), 69 (60), 55 (45); MS (CI), $m/z$ 129 (M – OMe, 65.4), 100 (30.2), 85 (100), 69 (37.8), 55 (29.3), 45 (30.4), 41 (35.1). Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 60.18; H, 10.28.

**6-[5-Methoxy-3,3-dimethyl-2-tetrahydrofuranyl]fulvene (16a,b).** To a solution of oxalyl chloride (11.6 mL, 0.133 mol) in $CH_2Cl_2$ (300 mL) under nitrogen and cooled in a dry ice–acetone bath was added dropwise a solution of DMSO (20.3 mL, 0.286 mol) in $CH_2Cl_2$ (20 mL). After 5 min the mixture of alcohols **14a,b** (16.3 g, 0.102 mol) dissolved in $CH_2Cl_2$ (20 mL) was added over a period of 5 min. The reaction was stirred for 15 min at –60 °C, and then triethylamine (66.8 mL, 0.479 mol) was added in one portion. After 10 min the reaction mixture was allowed to warm to room temperature. Ether (600 mL) and water (100 mL) were added and, after removal of the organic layer, the water layer was saturated with NaCl and extracted with ether (5 × 100 mL). The combined organic portions were washed with cold 1 N aqueous HCl, brine, saturated aqueous $NaHCO_3$, and brine. After drying over $MgSO_4$ the solvent was removed carefully under reduced pressure without heating and by utilizing a solvent trap cooled to –60 °C. When ca. 200 mL of solvent remained, methanol (100 mL) was added, and concentration in vacuo was continued until the vacuum dropped (a manometer was attached to the rotary evaporator). The residual solution of the aldehydes **15a,b** in MeOH was used as such in the next reaction. Concentration, as indicated above, of the solvent which was trapped at –60 °C afforded an additional 500 mg of the diastereomeric mixture of aldehydes **15a,b**: $R_f$ (20% ether in SSF) 0.20 (long tailing spot).

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ [**15a** (cis isomer, major)] 9.684 (1 H, d, $J$ = 1.9, CHO), 5.201 (1 H, dd, $J$ = 5.6, 3.8, $C_5H$), 4.032 (1 H, d, $J$ = 1.9, $C_2H$), 3.414 (3 H, s), 2.070 (1 H, dd, $J$ = 5.6, 13.4, $C_4H$), 1.788 (1 H, dd, $J$ = 3.8, 13.4, $C_4H$), 1.280 (3 H, s), 1.01 (3 H, s), [**15b** (trans isomer, minor)] 9.715 (1 H, d, $J$ = 3.2, CHO), 5.159 (1 H, dd, $J$ = 2.1, 5.7, $C_5H$), 3.853 (1 H, d, $J$ = 3.2, $C_2H$), 3.455 (3 H, s), 2.037 (1 H, dd, $J$ = 5.7, 13.2, $C_4H$), 1.843 (1 H, dd, $J$ = 2.1, 13.2, $C_4H$), 1.219 (3 H, s), 1.150 (3 H, s); IR (film) 2960, 2880, 2840, 1735, 1465, 1450, 1370, 1210, 1100, 1050 (br), 1030, 970 cm$^{-1}$.

To the crude solution of the aldehyde (ca. 0.102 mol) in MeOH (ca. 200 mL) under nitrogen was added cyclopentadiene (21 mL, 0.255 mol) and pyrrolidine (17 mL, 0.204 mol). The mixture was cooled in an ice–water bath, and acetic acid (5.84 mL, 0.201 mol) was added dropwise. The reaction mixture was allowed to warm

to room temperature and stirred for 15 h. The reaction was cooled again in an ice–water bath, and acetic acid (5.84 mL, 0.102 mol), water (500 mL), and ether (200 mL) were added. The water layer was separated and extracted with ether (4 × 200 mL). The combined organic portions were washed with brine, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated in vacuo. Although the fulvene could be purified at this stage (LC, 5% ether in SSF), it proved advantageous to use the crude fulvene **16a,b** in the next reaction without purification. Yields of the fulvenes **16a,b** after LC ranged from 50% to 55%: $R_f$ (10% ether in SSF) 0.32.

The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ [**16a** (cis isomer, major)] 6.4–6.6 (5 H, m), 5.124 (1 H, dd, $J$ = 4.2, 5.8, $C_5H$), 4.683 (1 H, d, $J$ = 8.5, $C_2H$), 3.405 (3 H, s), 2.137 (1 H, dd, $J$ = 5.8, 13.4, $C_4H$), 1.807 (1 H, dd, $J$ = 4.2, 13.4, $C_4H$), 1.095 (3 H, s), 0.953 (3 H, s), [**16b** trans isomer, minor)] 6.4–6.6 (5 H, m) 5.071 (1 H, dd, $J$ = 2.2, 6.0, $C_5H$) 4.603 (1 H, d, $J$ = 9.2, $C_2H$), 3.413 (3 H, s), 2.072 (1 H, dd, $J$ = 6.0, 13.2, $C_4H$), 1.888 (1 H, dd, $J$ = 2.2, 13.2, $C_4H$), 1.117 (3 H, s), 1.054 (3 H, s); IR (film) 3070, 2870–2960 (br), 2830, 1650, 1470, 1370, 1340, 1205, 1100, 1030, 1000, 980 $cm^{-1}$; GCMS (EI), [**16a**] $m/z$ 206 (M, 5.0), 146 (29.9), 131 (34.1), 105 (39.9), 99 (70.3), 91 (35.8), 85 (100); [**16b**] $m/z$ 206 (M, 5.1), 146 (28.3), 131 (33.2), 105 (39.4), 99 (72.3), 91 (38.7), 85 (100). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.55; H, 9.01.

***N,N'*-Bis(methoxycarbonyl)-2,3-diaza-7-[5-methoxy-3,3-dimethyl-2-tetrahydrofuranylidene]bicyclo[2.2.1]hept-5-ene (18).** The crude fulvene **16a,b** (ca. 0.06 mol) from the previous reaction was taken up in ether (200 mL). The solution was cooled in an ice–water bath, and dimethyl azodicarboxylate (11.2 mL, 0.1 mol) was added. After the mixture was stirred for 5 days at 4 °C under nitrogen atmosphere, the solvent was removed in vacuo. The Diels–Alder adduct **18** was purified by LC on silica gel with 80% ether in SSF, to afford 19.4 g (55% from **14a,b** over three steps) of **18**, which consisted of mainly three (plus *traces* of a fourth) diastereomers. When purified fulvene **16a,b** was utilized in this reaction the yield of **18** ranged from 90% to 95%: $R_f$ (80% ether in SSF) 0.23.

The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.65–6.80 (2 H, br m, $C_5$- and $C_6H$), 4.80–5.70 (2 H, br m, $C_1$- and $C_4H$), 4.90–5.10 (2 H, m, $C_7$=CH and $C_5H$), 4.1–4.2 (1 H, m, $C_2H$), 3.770, 3.760, 3.754 (6 H, each s, $COOCH_3$ of each diastereomer), 3.375, 3.377, 3.348 (3 H, each s, $OCH_3$ of each diastereomer) 1.92–2.08 and 1.66–1.80 (each 1 H, m, $C_4H$), 0.790 and 0.995, 0.916 and 0.995, 0.941 and 1.025 (6 H (2 × 3 H), each s, $CH_3$'s of each diastereomer); IR (film) 2960, 2880, 1715–1760 (br), 1445, 1320 (br), 1200, 1105, 1030 $cm^{-1}$. Anal. Calcd for $C_{17}H_{24}O_6N_2$: C, 57.94; H, 6.86; N, 7.95. Found: C, 57.83; H, 7.01; N, 7.86.

***N,N'*-Bis[(2,2,2-trichloroethoxy)carbonyl]-2,3-diaza-7-[5-methoxy-3,3-dimethyl-2-tetrahydrofuranylidene]bicyclo-[2.2.1]heptene (19).** To a solution of fulvene **16a,b** (0.93 g, 4.51 mmol) in ether (5 mL) under nitrogen atmosphere and cooled in an ice–water bath was added bis(2,2,2-trichloroethyl) azodicarboxylate (1.7 g, 4.51 mol) in ether (15 mL). After the mixture was stirred for 2 h at 0 °C the solvent was removed in vacuo to afford 2.65 g of crude Diels–Alder adduct **17**. This material was used directly in the next step of the reaction sequence. Four diastereomers (by $^1H$ NMR) were formed: $R_f$ (30% ether in SSF) 0.14, 0.13, 0.12, and 0.11.

The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.80–7.00 (2 H, br m, $C_5$- and $C_6H$), 5.30–5.80 (2 H, br m, $C_1$- and $C_4H$), 5.00–5.20 (2 H, m, $C_7$=CH and $C_5H$), 4.70–5.10 (4 H, br m, $COOCH_2$), 4.07–4.23 (1 H, m, $C_2H$), 3.367, 3.357, 3.384, 3.361 (3 H, each s, $OCH_3$ of each diastereomer), 1.55–2.10 (2 H, m, $C_4H$), 0.794 and 0.970, 0.920 and 0.997, 1.020 and probably 0.970, 0.933 and 1.038 (6 H (2 × 3 H), each s, $CH_3$'s of each diastereomer); IR (film) 2960, 2880, 1730–1770 (br), 1380, 1330, 1300 (br), 1255, 1190, 1120, 1030, 710 $cm^{-1}$.

The crude **17** was taken up in $CH_2Cl_2$ (14 mL) and dipotassium azodicarboxylate (4.17 g, 21.3 mmol) was added. The suspension was cooled to 0 °C and acetic acid (2.75 mL, 48.1 mmol) was added dropwise (gas evolution!). After the addition was complete (ca. 30 min), the reaction was stirred for an additional 3 h. The mixture was vacuum filtered through a medium glass frit, and the filter cake was rinsed with ether. The filtrate was concentrated in vacuo, and the residue was subjected to LC (40% ether in SSF) to afford 2.18 g (82%) of **19**. The four isomers I, II, III, and IV, which were formed in a ca. 5:3:2:1 ratio by $^1H$ NMR, were not separated. Detailed NMR data of the isomers were available from enriched fractions after LC: $R_f$ (30% ether in SSF) 0.14 (isomer I), 0.13 (isomer II), 0.12 (isomer III), and 0.11 (isomer IV).

The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ [isomer I] 5.384 (1 H, d, $J$ = 7.4, $C_7$=CH), 5.023 (1 H, dd, $J$ = 4.3, 5.8, $C_5H$), 4.50–5.20 (6 H, br m, $C_1H$, $C_4H$, and $COOCH_2$), 4.256 (1 H, d, $J$ = 7.4, $C_2H$), 3.366 (3 H, s), 1.80–2.20 (4 H, br m, $C_5$- and $C_6H$), 2.058 (1 H, dd, $J$ = 5.8, 13.4, $C_4H$), 1.713 (1 H, dd, $J$ = 4.3, 13.4, $C_4H$), 1.016 (3 H, s), 0.842 (3 H, s), [isomer II] 5.501 (1 H, d, $J$ = 8.0, $C_7$=CH), 4.969 (1 H, dd, $J$ = 2.1, 6.1, $C_5H$), 4.60–5.15 (6 H, br m, $C_1H$, $C_4H$, and $COOCH_2$), 4.161 (1 H, d, $J$ = 8.0, $C_2H$), 3.357 (3 H, s), 1.80–2.20 (4 H, br m, $C_5$- and $C_6H$), 1.981 (1 H, dd, $J$ = 6.1, 13.3, $C_4H$), 1.795 (1 H, dd, $J$ = 2.1, 13.3, $C_4H$), 1.039 (3 H, s), 0.979 (3 H, s), [isomer III] 5.384 (1 H, d, $J$ = 7.4, $C_7$=CH), 5.038 (1 H, dd, $J$ = 4.6, 5.6, $C_5H$), 4.50–5.00 (6 H, br m, $C_1H$, $C_4H$, and $COOCH_2$), 4.237 (1 H, d, $J$ = 7.4, $C_2H$), 3.393 (3 H, s), 1.90–2.10 (4 H, br m, $C_5$- and $C_6H$), 2.067 (1 H, dd, $J$ = 5.8, 13.4, $C_4H$), 1.717 (1 H, dd, $J$ = 4.3, 13.4, $C_4H$), 1.029 (3 H, s), 0.832 (3 H, s), [isomer IV] 5.485 (1 H, d, $J$ = 7.7, $C_7$=CH), 4.993 (1 H, dd, $J$ = 2.2, 6.1, $C_5H$), 4.50–5.20 (6 H, br m, $C_1H$, $C_4H$, and $COOCH_2$), 4.142 (1 H, d, $J$ = 7.7, $C_2H$), 3.375 (3 H, s), 1.85–2.15 (4 H, br m, $C_5$- and $C_6H$), 1.982 (1 H, dd, $J$ = 6.1, 13.3, $C_4H$), 1.784 (1 H, dd, $J$ = 2.2, 13.3, $C_4H$), 1.050 (3 H, s), 0.963 (3 H, s); IR (film) 2960, 2880, 1725–1770 (br), 1385, 1320, 1245, 1150, 1130, 1050, 1035, 715 $cm^{-1}$; MS (EI), $m/z$ 594, 592, 590, 588, 586, 206 (20.4), 147 (25.3), 129 (41.7), 105 (37.8), 100 (49.3), 99 (47.3), 85 (100), 81 (23.2). Anal. [HRMS (EI)] Calcd for $C_{19}H_{24}O_6N_2{}^{35}Cl_4$: 585.9765. Found: 585.9756.

***N,N'*-Bis(methoxycarbonyl)-2,3-diaza-7-[5-methoxy-3,3-dimethyl-2-tetrahydrofuranylidene]bicyclo[2.2.1]heptane (20).** To a suspension of **18** (19 g, 0.0539 mol) and dipotassium azodicarboxylate (52.8 g, 0.2695 mol) in $CH_2Cl_2$ (200 mL) at 0 °C under nitrogen atmosphere was added dropwise a solution of glacial acetic acid (34.8 mL, 0.609 mol) in $CH_2Cl_2$ (30 mL). After the addition was complete (45 min) the reaction was stirred at 0 °C for 3 h. The mixture was vacuum filtered through a medium glass frit, and the filter cake was rinsed with ether. After concentration in vacuo of the filtrate, the carbamate **20** was purified by LC on silica gel, eluting with 80% ether in SSF, to afford 18.2 g (96% yield) of pure **20**, as a mixture of diastereomers. The four diastereomers could not be separated and were taken on together in the next step of the sequence. The minor isomer could hardly be detected in the $^1H$ NMR spectrum of the mixture. The diastereomeric products isomer I, isomer II, and isomer III were formed in about a 6:3:1.5 ratio: $R_f$ (80% ether in SSF) 0.22–0.23.

The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ [isomer I] 5.319 (1 H, d, $J$ = 6.8, $C_7$=CH), 5.032 (1 H, dd, $J$ = 4.3, 5.8, $C_5H$), 4.40–5.20 (2 H, br m, $C_1$- and $C_4H$), 4.232 (1 H, d, $J$ = 6.8, $C_2H$), 3.776 (6 H, br s, COOMe), 3.376 (3 H, s), 1.70–2.10 (4 H, br m, $C_5$- and $C_6H$), 2.054 (1 H, dd, $J$ = 5.8, 13.4, $C_4H$), 1.715 (1 H, dd, $J$ = 4.3, 13.4, $C_4H$), 1.016 (3 H, s), 0.838 (3 H, s), [isomer II] 5.431 (1 H, d, $J$ = 8.0, $C_7$=CH) 4.978 (1 H, dd, $J$ = 6.1, 2.0, $C_5H$), 4.40–5.20 (2 H, br m, $C_1$- and $C_4H$), 4.138 (1 H, d, $J$ = 8.0, $C_2H$), 3.776 (6 H, br s, COOMe), 3.367 (3 H, s), 1.70–2.10 (4 H, br m, $C_5$- and $C_6H$), 1.982 (1 H, dd, $J$ = 6.1, 13.3, $C_4H$), 1.796 (1 H, dd, $J$ = 2.0, 13.3, $C_4H$), 1.028 (3 H, s), 0.972 (3 H, s), [isomer III] 5.440 (1 H, d, $J$ = 8.5, $C_7$=CH), 4.118, (1 H, d, $J$ = 8.5, $C_2H$), 3.387 (3 H, s), 2.059 (1 H, dd, $J$ = 5.8, 13.4, $C_4H$), 1.000 (3 H, s) [other signals were overlapping and could not be assigned]; IR (film) 2960, 2880, 1705–1760 (br), 1445, 1330 (br), 1250, 1197, 1150, 1120 $cm^{-1}$; MS (EI), $m/z$ 354 (M, 38.3), 207 (44.1), 206 (50.8), 147 (49.2), 129 (62.3), 105 (100), 99 (53.5), 91 (30.3), 85 (90.1). Anal. [HRMS (EI)] Calcd for $C_{17}H_{26}O_6N_2$: 354.1791. Found: 354.1812.

***N,N'*-Bis[(2,2,2-trichloroethoxy)carbonyl]-2,3-diaza-7-[5′-hydroxy-3′,3′-dimethyl-2′-tetrahydrofuranylidene]bicyclo[2.2.1]heptane (21a,b).** A solution of **19** (1.55 g, 2.63 mol) in 70% aqueous acetic acid (30 mL) was stirred under nitrogen atmosphere at 55 °C for 5 days. The acetic acid solution was then removed in vacuo (2 Torr) and 50% ether in SSF was added to allow crystallization of the major isomer **21a** in the refrigerator overnight. The crystals were filtered and washed twice with cold 50% ether in SSF, to afford 891 mg (59%) of pure **21a** as a white powder. The mother liquor was concentrated in vacuo, and the

oily residue was subjected to LC (70% ether in SSF) to afford an additional 127 mg of the major isomer **21a** and 264 mg of the minor isomer **21b** (85% combined yield). The lactol **21a** is mainly one isomer, while **21b** is a diastereomeric mix of two lactols in about a 5:1 ratio by $^1$H NMR.

Data for **21a**: $R_f$ (70% ether in SSF) 0.36; mp ($CHCl_3$/hexane) 151–152 °C. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.562 (1 H, m, $C_5H$), 5.376 (1 H, d, $J$ = 7.2, $C_7$=CH), 4.50–5.20 (6 H, br m, $C_1H$, $C_4H$, and $COOCH_2$), 4.405 (1 H, d, $J$ = 7.2, $C_2H$), 2.664 (1 H, br s, OH), 1.65–2.20 (4 H, br m, $C_5$- and $C_6H$), 2.110 (1 H, dd, $J$ = 5.7, 13.4, $C_4H$), 1.732 (1 H, dd, $J$ = 4.4, 13.4, $C_4H$), 1.047 (3 H, s), 0.850 (3 H, s); IR (KBr pellet) 3450 (br), 2960, 2880, 1725–1775 (br), 1450, 1390, 1320, 1243, 1188, 1125, 1050, 1005, 720 cm$^{-1}$; MS (EI), $m/z$ 580, 578, 576, 574, 572 (M), 193 (38.2), 133 (41), 131 (38.1), 113 (75), 109 (38), 95 (32.8), 80 (100), 81 (73.3), 71 (35.4). Anal. Calcd for $C_{18}H_{22}O_6N_2Cl_6$: C, 37.53; H, 3.85; N, 4.86. Found: C, 37.30; H, 3.70; N, 4.90.

For **21b**: $R_f$ (70% ether in SSF) 0.22. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ [major isomer] 5.50–5.60 (1 H, m, $C_5H$), 5.375 (1 H, d, $J$ = 7.6, $C_7$=CH), 4.50–5.20 (6 H, br m, $C_1H$, $C_4H$, and $COOCH_2$), 4.380 (1 H, s, $J$ = 7.6, $C_2H$), 2.714 (1 H, br s, OH), 1.70–2.20 (4 H, br m, $C_5$- and $C_6H$), 2.115 (1 H, dd, $J$ = 5.7, 13.4, $C_4H$), 1.733 (1 H, dd, $J$ = 4.6, 13.4, $C_4H$), 1.057 (3 H, s), 0.836 (3 H, s), [minor isomer] 5.50–5.60 (1 H, m, $C_5H$), 4.50–5.20 (6 H, br m, $C_1H$, $C_4H$, and $COOCH_2$), 4.131 (1 H, d, $J$ = 8.2, $C_2H$), 2.80 (1 H, br s, OH), 1.70–2.20 (4 H, br m, $C_5$- and $C_6H$), 2.025 (1 H, dd, $J$ = 6.1, 13.0, $C_4H$), 1.809 (1 H, dd, $J$ = 2.3, 13.0, $C_4H$), 1.025 (3 H, s) [other signals ($C_7$=CH and $CH_3$) are overlapping]; IR (film) 3430 (br), 2960, 2880, 1720–1779 (br), 1445 (br), 1388, 1320, 1245, 1199, 1130, 1055, 1010, 720 cm$^{-1}$; MS (EI), $m/z$ 580, 578, 576, 574, 572, 193 (43.7), 133 (36.7), 131 (38.7), 113 (81.6), 109 (39.5), 107 (71.4), 95 (36.8), 85 (100), 81 (73.9), 79 (31.9), 71 (33.5), 57 (36.0). Anal. [HRMS (EI)] Calcd for $C_{18}H_{22}O_6N_2{}^{35}Cl_6$: 571.9609. Found: 571.9593.

***N*,*N*′-Bis(methoxycarbonyl)-2,3-diaza-7-[5-hydroxy-3,3-dimethyl-2-tetrahydrofuranylidene]bicyclo[2.2.1]heptane (22a,b).** A solution of **20** (18.2 g, 0.0535 mol) in 70% aqueous acetic acid (300 mL) was stirred under nitrogen at 55 °C for 5 days. The acetic acid solution was then removed in vacuo (2 Torr). The residual viscous oil was subjected to LC (300 g of silica gel, gradient elution with 50% EtOAc in SSF (1 L), 60% EtOAc in SSF, and then 70% EtOAc in SSF) to affford 15.55 g (89% combined yield) of **22a** and **22b** in ratio of 2:1. Some starting material (ca. 2 g) could be recycled and afforded an additional 1.05 g of **22a,b** which gave a combined yield of 95%.

For **22a**: $R_f$ (70% EtOAc in SSF) 0.24. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$, two isomers in a ratio of about 4:1) $\delta$ [major isomer] 5.479 (1 H, t, $J$ = 5.1, $C_5H$), 5.309 (1 H, d, $J$ = 7.3, $C_7$=CH), 4.40–5.20 (2 H, br m, $C_1$- and $C_4H$), 4.226 (1 H, d, $J$ = 7.3, $C_2H$), 3.767 (6 H, br s, COOMe), 1.50–2.20 (4 H, br m, $C_5$- and $C_6H$), 2.100 (1 H, dd, $J$ = 5.6, 13.2, $C_4H$), 1.748 (1 H, dd, $J$ = 4.4, 13.2, $C_4H$), 1.019 (3 H, s), 0.838 (3 H, s), [minor isomer] 5.565 (1 H, t, $J$ = 5.1, $C_5H$), 5.399 (1 H, d, $J$ = 7.7, $C_7$=CH), 4.40–5.20 (2 H, br m, $C_1$- and $C_4H$), 4.121 (1 H, d, $J$ = 7.7, $C_2H$), 3.767 (6 H, br s, COOMe), 1.50–2.20 (4 H, br m, $C_5$- and $C_6H$) [$C_4H$ signals are overlapping and could not be assigned], 1.040 (3H, s), 0.980 (3H, s); IR (film) 3460 (br), 2960, 1880, 1700–1760 (br), 1445, 1340 (br), 1250, 1195, 1150, 1120, 1065, 1005, 770 cm$^{-1}$; MS (EI), $m/z$ 340 (M, 13.2), 113 (26.8), 107 (27.6), 85 (45), 81 (20.3), 71 (83.5), 61 (22.2), 59 (27), 45 (35.8), 43 (100). Anal. Calcd for $C_{16}H_{24}O_6N_2$: C, 56.46; H, 7.11; N, 8.23. Found, C, 56.23; H, 7.07; N, 8.09.

For **22b**: $R_f$ (70% EtOAc in SSF) 0.20. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$, two isomers in a ratio of about 4:1) $\delta$ [*major* isomer] 5.561 (1 H, dd, $J$ = 5.4, 4.9, $C_5H$), 5.314 (1 H, d, $J$ = 8.0, $C_7$=CH), 4.55–5.20 (2 H, br m, $C_1$- and $C_4H$), 4.35 (1 H, d, $J$ = 8.0, $C_2H$), 3.766 (2 H, br s, COOMe), 1.60–2.20 (4 H, br m, $C_5$- and $C_6H$), 2.103 (1 H, dd, $J$ = 5.8, 13.4, $C_4H$), 1.728 (1 H, dd, $J$ = 4.6, 13.4, $C_4H$), 1.017 (3 H, s), 0.848 (3 H, br s), [minor isomer] 5.512 (1 H, dd, $J$ = 6.2, 2.3, $C_5H$) [$C_7$=CH could not be assigned (probably under the signal at 5.314 ppm of the major isomer)], 4.55–5.20 (2 H, br m, $C_1$ and $C_4H$), 4.102 (1 H, d, $J$ = 8.8, $C_2H$), 1.60–2.20 (4 H, br m, $C_5$- and $C_6H$), 2.014 (1 H, dd, $J$ = 5.4, 13.3, $C_4H$), 1.805 (1 H, dd, $J$ = 2.5, 13.3), 1.032 (3 H, s), 1.017 (3 H, s); IR (film) 3460 (br), 2960, 2880, 1700–1760 (br), 1445, 1340 (br), 1250, 1195, 1150, 1120, 1065, 1005, 770 cm$^{-1}$; MS (EI), $m/z$ 340 (M, 28.9), 151 (57), 113 (59.7), 109 (32.3), 107 (65.8), 95 (34.4), 85 (100), 81 (39.8), 79 (31.7), 59 (46.2). Anal. [HRMS (EI)] Calcd for $C_{16}H_{24}O_6N_2$: 340.1634. Found: 340.1621.

**2,3-Diaza-7-[5-hydroxy-3,3-dimethyl-2-tetrahydrofuranylidene]bicyclo[2.2.1]hept-2-ene (23a,b). Electrolysis of 21a,b.** In the cathode compartment of a H-cell was added a degassed solution of **21a,b** (968 mg, 1.68 mmol) and lithium perchlorate (5.3 g, 50 mmol, 1 M solution) in DMF (50 mL). The anode compartment was filled with a degassed solution of lithium perchlorate in DMF (1 M, ca. 50 mL), so that the level of the solution in both compartments was equal. A mercury pool was used as cathode, and a platinum electrode was used as anode. The reduction was carried out under a positive nitrogen atmosphere at controlled potential (−1.7 V vs SCE), until 623.4 C of electricity passed (95% of theoretical). The solution was then transferred to a round-bottom flask, and the cell was rinsed with ether (2 × 50 mL). The bulk solution and the ether portions were combined and cooled to 0 °C. An aqueous solution of potassium ferricyanide (1.66 g, 5.04 mmol dissolved in 13.3 mL of water) was added, and the mixture was stirred for 1 h. Brine (50 mL) was added, and the water layer was extracted with 10% THF in ether (10 × 30 mL). The combined organic portions were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residual DMF was removed under vacuum at 0.4 Torr. The residue was subjected to LC (80% ether in SSF) to afford 273 mg (72.8% yield) of pure diazenes **23a,b**. In general, the diazenes were somewhat unstable and were therefore not submitted for analysis.

**Hydrolysis of 22a,b.** To a degassed solution of KOH in EtOH (2.5 M, 11 mL) under nitrogen atmosphere was added a solution of **22a,b** (725 mg, 2.13 mmol) in EtOH (2 mL), and the mixture was heated to reflux for 1.5 h. The reaction mixture was cooled in an ice–water bath, and an aqueous solution of potassium ferricyanide (2.1 g, 6.39 mmol, 10 mL of water) was added. After 1 h brine (20 mL) was added, and the water layer was extracted with 10% THF in ether (5 × 30 mL). The combined organic portions were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by LC (80% ether in SSF) to afford 406 mg (86% yield) of the diazenes **23a,b**. In both reactions the ratio of the two pairs of lactols **23a** and **23b** was the same as the ratio of the starting carbamates **22a** and **22b**.

For **23a**: $R_f$ (ether) 0.27. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$, two isomers in a ratio of about 5:1) $\delta$ [major isomer] 5.45–5.60 (1 H, m, $C_5H$ of both the major and minor isomer), 5.496 (1 H, d, $J$ = 2.3, $C_1$- or $C_4H$), 5.175 (1 H, d, $J$ = 2.4, $C_1$- or $C_4H$), 5.111 (1 H, d, $J$ = 8.1, $C_7$=CH), 4.273 (1 H, d, $J$ = 8.1, $C_2H$), 3.35 (1 H, br s, OH), 2.090 (1 H, dd, $J$ = 5.7, 13.4, $C_4H$), 1.719 (1 H, dd, $J$ = 4.5, 13.4, $C_4H$), 1.60–1.75 (2 H, m, $C_5H_{exo}$ and $C_6H_{exo}$ of each isomer), 1.10–1.20 (2 H, m (apparent d at 1.16, $J$ = 8.4), $C_5H_{endo}$ and $C_6H_{endo}$ of each isomer), 1.001 (3 H, s), 0.829 (3 H, s), [minor isomer] 5.470 (1 H, d, $J$ = 2.5, $C_1$- or $C_4H$), 5.280 (1 H, d, $J$ = 8.7, $C_7$=CH), 4.014 (1 H, d, $J$ = 8.7, $C_2H$), 1.997 (1 H, dd, $J$ = 6.1, 13.3, $C_4H$), 1.792 (1 H, dd, $J$ = 2.4, 13.3, $C_4H$), 1.001 (6 H, s, covered under the signal at 1.001 of the major isomer); IR (film) 3480 (br), 2965, 2880, 1005, 985, 785 cm$^{-1}$.

For **23b**: $R_f$ (ether) 0.22. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$, two isomers in a ratio of about 5:1) $\delta$ [major isomer] 5.546 (1 H, m, $C_5H$ of both major and minor isomer), 5.469 (1 H, d, $J$ = 2.8, $C_1$- or $C_4H$), 5.161 (1 H, d, $J$ = 2.7, $C_1$- or $C_4H$), 5.099 (1 H, $J$ = 8.1, $C_7$=CH), 4.276 (1 H, d, $J$ = 8.1, $C_2H$), 3.009 (1 H, br s, OH), 2.093 (1 H, dd, $J$ = 5.7, 13.4, $C_4H$), 1.65–1.81 (3 H, m, $C_4H$, $C_5H_{exo}$, and $C_6H_{exo}$ of each isomer), 1.1–1.2 (2 H, m, $C_5H_{endo}$ and $C_6H_{endo}$ of each isomer), 1.001 (3 H, s), [minor isomer] ($C_1$- and $C_4H$ are probably under the signals at 5.469 and 5.161 ppm of the major isomer) 5.261 (1 H, d, $J$ = 8.7, $C_7$=CH), 4.017 (1 H, d, $J$ = 8.7, $C_2H$), 1.994 (1 H, dd, $J$ = 6.1, 13.4, $C_4H$), 1.007 (3 H, s), 0.992 (3 H, s); IR (film) 3400 (br), 2960, 2880, 1100, 1005, 985, 790 cm$^{-1}$.

**2,3-Diaza-7-[2-hydroxy-3,3-dimethylhex-5-enylidene]bicyclo[2.2.1]hept-2-enes (9a,b).** To a suspension of methyl triphenylphosphonium bromide (3.55 g, 9.95 mmol) in THF (10 mL) at −10 °C under a nitrogen atmosphere was added dropwise a solution of *n*-BuLi in hexane (1.6 M, 5.3 mL, 8.52 mmol). After 30 min a solution of the diazenes **23a,b** (630 mg, 2.84 mmol) in

THF (3 mL) was added over a period of 5 min. The mixture was allowed to warm to room temperature, and the stirring was continued for 3 h. Saturated aqueous $NH_4Cl$ (20 mL), water (20 mL), and SSF (50 mL) were added, and the water layer was removed and extracted with 50% ether in SSF (3 × 20 mL). The organic layers were combined and washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by LC (70% ether in SSF) afforded 422 mg (67% yield) of a diastereomeric mix of two diazenes **9a,b**. The yield of this reaction was not very reproducible; the larger the scale of the reaction, the lower the yield. Yields ranged from 56% to 83%.

For **9a**: $R_f$ (70% ether in SSF) 0.33. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.832 (1 H, tdd, $J$ = 7.4, 17.0, 10.0, $C_5H$), 5.439 (1 H, br s, $C_1$- or $C_4H$), 5.241 (1 H, d, $J$ = 8.8, $C_7$=CH), 5.148 (1 H, d, $J$ = 2.3, $C_1$- or $C_4H$), 5.072 (1 H, d, $J$ = 10.0, $C_6H$), 5.053 (1 H, d, $J$ = 17.0, $C_6H$), 3.848 (1 H, d, $J$ = 8.8, $C_2H$), 2.100 (1 H, dd, $J$ = 13.3, 7.4, $C_4H$), 1.983 (1 H, dd, $J$ = 7.4, 13.3, $C_4H$), 1.837 (1 H, br s, OH), 1.55–1.70 (2 H, m, $C_5H_{exo}$ and $C_6H_{exo}$), 1.10–1.20 (2 H, m, $C_5H_{endo}$ and $C_6H_{endo}$), 0.855 (3 H, s), 0.796 (3 H, s); IR (film) 3400 (br), 3080, 2960, 2880, 1640, 1025, 1005, 910 cm$^{-1}$.

For **9b**: $R_f$ (70% ether in SSF) 0.18. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.827 (1 H, tdd, $J$ = 7.4, 9.3, 16.5, $C_5H$), 5.486 and 5.139 (each 1 H, each br s, $C_1$ and $C_4H$), 5.226 (1 H, d, $J$ = 8.4, $C_7$=CH), 5.075 (1 H, d, $J$ = 9.1, $C_6H$), 5.035 (1 H, d, $J$ = 16.8, $C_6H$), 3.886 (1 H, d, $J$ = 8.4, $C_2H$), 2.070 (1 H, dd, $J$ = 7.4, 13.6, $C_4H$), 1.924 (1 H, dd, $J$ = 7.4, 13.6, $C_4H$), 1.65–1.75 (2 H, m, $C_5H_{exo}$ and $C_6H_{exo}$), 1.10–1.20 (2 H, m, $C_5H_{endo}$ and $C_6H_{endo}$), 0.854 (3 H, s), 0.805 (3 H, s); IR (film) 3410 (br), 3080, 2960, 2880, 1640, 1025, 1005, 910 cm$^{-1}$.

**1,3-Diyl Trapping Reaction: Formation of (3α,3aα,6aβ,7aα)-2,3,3a,5,6,6a,7,7a-Octahydro-3-hydroxy-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (10).** The linearly fused tricyclopentanoid **10** was formed (along with four minor isomers) as the major product upon either thermally or photochemically initiated extrusion of nitrogen from the diazenes **9a,b**. The thermally initiated reactions were performed by heating a 0.01 M solution of the diazenes **9a,b** in methanol (61 °C, 4 h) or acetonitrile (81 °C, 2.5 h). For small-scale photochemically initiated reactions a setup as described by Stone and Little was utilized.[10] For larger scale (several mmoles) experiments an insulated (by a vacuum glass mantel) 450-W Hanovia lamp with cooling mantel was immersed in a stirred 0.01 M solution of **9a,b** in methanol (6 and −60 °C) or acetonitrile (6 °C); this setup was placed in a cooling bath of either ice–water (6 °C) or methanol and the temperature was controlled by utilizing a Neslab Exatrol and Cryocool immersion cooler CC-100. All reactions were conducted under oxygen-free conditions. Combined yields of the product ranged from 87% to 96%; the ratio (by GC analysis) of the major isomer **10** divided by the *sum* of the minor isomers was temperature dependent:

| solvent | temp, °C | major isomer | sum of minor isomers |
|---|---|---|---|
| $CH_3CN$ | 81 | 3.79 | 1.0 |
| | 6 | 9.06 | 1.0 |
| MeOH | 61 | 4.74 | 1.0 |
| | 6 | 9.10 | 1.0 |
| | −60 | 30.00 | 1.0 |

The crude products were taken on as such in the next reaction. For the major cis,anti-tricyclopentanoid **10**: $R_f$ (20% ether in SSF) 0.22.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.386 (1 H, br m, $C_3H$), 3.292 (1 H, dd, $J$ = 7.8, 5.7; simplifies to d upon addition of $C_2O$, $J$ = 7.8, $C_{11}H$), 3.049 (1 H, br m, $C_6H$), 2.897 (1 H, app quintuplet, $J$ = 9.0, $C_8H$), 2.641 (1 H, t, $J$ = 8.1, $C_1H$), 2.45–2.60 (2 H, m, $C_4H$), 2.144 (1 H, m), 1.724 (1 H, dd, $J$ = 8.8, 12.8, $C_9H$), 1.0–1.65 (4 H, m), 0.986 (3 H, s), 0.822 (3 H, s); IR (film) 3400 (br), 2940, 2860, 1465, 1455, 1367, 1110, 1070, 1050 cm$^{-1}$; MS (EI), $m/z$ 192 (M, 36.6), 174 (16.9), 159 (16.7), 119 (41.4), 106 (70), 105 (100), 91 (49.3). Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 80.84; H, 10.18.

**(3α,3aα,3bβ,6aβ,7aα)-2,3,3a,3b,6,6a,7,7a-Octahydro-3,3b-dihydroxy-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (27).** A solution of 3-chloroperbenzoic acid (2.02 g, 80% technical, 9.37 mmol) in $CHCl_3$ (20 mL) was added over a period of 5 min to a cooled mixture (ice–water bath, 0 °C) of the tricyclopentanoid **10** (1.5 g, 86.4% purity by GC, with the remainder of the material consisting of the other diyl trap products, GC analysis, 7.81 mmol) and solid sodium carbonate (2.48 g, 23.4 mmol) in $CHCl_3$ (30 mL). The reaction was stirred for an additional 10 min. Ether (200 mL) was added, and the solution was washed with 10% aqueous sodium bisulfite solution (10 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine, dried over $MgSO_4$, and concentrated in vacuo. The two isomeric epoxides which were formed in a 4:1 ratio by GC analysis could not be separated. The crude mixture was dissolved in dry THF (5 mL) and was added to a solution of LDA (from diisopropylamine and *n*-BuLi, each 31.2 mmol) in THF (31 mL) under an argon atmosphere. The solution was heated to reflux for 4 h. Saturated aqueous $NH_4Cl$ and ether (30 mL) were added, the organic layer was removed and the aqueous layer was extracted with ether (3 × 30 mL). The organic portions were combined, washed with brine, dried over $MgSO_4$, and concentrated in vacuo. After LC (70% ether in SSF) 756 mg (54% based on **10**) of pure allylic alcohol **27** was obtained: $R_f$ (60% ether in SSF) 0.15; mp (ether/hexane) 114–116 °C.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.830 and 5.705 (each 1 H, each dt, $J$ = 5.5, 2.2, $C_3$- and $C_4H$), 3.941 (1 H, d, $J$ = 8.4, $C_{11}H$), 2.697 (1 H, ddt, $J$ = 17.1, 6.7, 2.2, $C_5H$), 2.35–2.55 (3 H, m), 2.313 (1 H, br s, OH), 1.986 (1 H, br dt, $J$ = 17.1, 2.0, $C_5H$), 1.932 (1 H, br s, OH), 1.765 (1 H, dd, $J$ = 13.0, 10.0, $C_9H$), 1.68–1.77 (1 H, m) 1.434 (1 H, m), 1.178 (1 H, dd, $J$ = 13.0, 5.9, $C_9H$), 1.075 (3 H, s), 0.902 (3 H, s); IR (KBr pellet) 3520 (br), 3370 (br), 3050, 2930, 2860, 1390, 1125, 1075, 1047, 1018 cm$^{-1}$; MS (EI), $m/z$ 208 (M, 1.4), 190 (12.9), 109 (62.8), 108 (58), 95 (100), 82 (79.4). Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.78. Found: C, 74.86; H, 9.68.

**Benzoylation of 27.** To a solution of the diol **27** (651 mg, 3.13 mmol) and pyridine (1.26 mL, 15.65 mmol) in $CH_2Cl_2$ (6 mL) at 0 °C was added dropwise benzoyl chloride (0.76 mL, 6.26 mmol). The mixture was allowed to warm to room temperature, and stirring was continued for 11 h. Methanol (0.5 mL) was added, and after 1 h the mixture was diluted with ether (50 mL). The organic solution was washed with water (10 mL) and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was subjected to LC (20% ether in SSF) to afford 870 mg (89% yield) of the monobenzoylated derivative: $R_f$ (20% ether in SSF) 0.23.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.43–8.07 (5 H, m, Ph), 5.65–5.735 (2 H, m, $C_3$ and $C_4H$), 5.151 (1 H, d, $J$ = 6.0, $C_{11}H$), 4.474 (1 H, s, OH), 2.83 (1 H, m, $C_6H$), 2.694 (1 H, ddt, $J$ = 16.2, 6.7, 2.0, $C_5H$), 2.617 (1 H, m, $C_8H$), 2.490 (1 H, dd, $J$ = 6.0, 9.7, $C_1H$), 1.994 (1 H, dd, $J$ = 16.2, 1.4, $C_5H$), 1.777 (1 H, ddd, $J$ = 13.2, 7.9, 2.8, $C_7H$), 1.679 (1 H, dd, $J$ = 12.3, 7.1, $C_9H$), 1.32–1.41 (2 H, m, $C_7$- and $C_9H$), 1.174 (3 H, s), 1.144 (3 H, s); IR (film) 3490 (br), 3050, 2940, 2860, 1697, 1603, 1587, 1285 (br), 1125 cm$^{-1}$; MS (EI), $m/z$ 295 (M − OH, 73), 190 (M − PhCOOH, 19.0), 173 (81.4), 109 (100), 105 (69.0), 82 (51.4), 77 (42.8). Anal. [HRMS (EI)] Calcd for $C_{20}H_{23}O_2$ (M − OH): 295.1698. Found: 295.1706. Calcd for $C_{13}H_{18}O$ (M − PhCOOH): 190.1357. Found: 190.1363.

**(3α,3aα,6aβ,7aα)-2,3,3a,5,6,6a,7,7a-Octahydro-3-(benzoyloxy)-2,2-dimethyl-5-oxo-1*H*-cyclopenta[*a*]pentalene (26).** To a suspension of the benzoate **27** (800 mg, 2.56 mmol) and Celite (1.1 g) in dry $CH_2Cl_2$ (15 mL) was added pyridinium chlorochromate (1.11 g, 5.13 mmol), and the mixture was stirred for 6 h under nitrogen atmosphere at room temperature. The black slurry was diluted with ether and filtered through a short pad of silica gel (3 cm) which had been placed on a sintered-glass frit. The column was rinsed with ether until no product could be detected by TLC analysis. The solvent was removed in vacuo and the residue was crystallized from 30% ether in SSF to afford 599 mg (85%) of pure enone **26**: $R_f$ (60% ether in SSF) 0.28; mp (ether/SSF) 139–140 °C.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.44–8.10 (5 H, m, Ph), 5.683 (1 H, d, $J$ = 1.9, $C_3H$), 4.950 (1 H, d, $J$ = 7.6, $C_{11}H$), 3.299 (1 H, dd, $J$ = 8.9, 7.6, $C_1H$), 3.249 (1 H, br m, $C_6HO$), 3.088 (1 H, app qd, $J$ = 8.8, 10.3, $C_8H$), 2.674 (1 H, dd, $J$ = 18.0, 2.8, $C_5H$), 1.866–2.000 (2 H, m), 1.23–1.44 (2 H, m), 1.179 (3 H, s), 1.085 (3 H, s); IR (KBr pellet) 3065, 2960, 2865, 1728, 1698, 1625, 1455, 1280, 1270, 1120 cm$^{-1}$; MS (CI), $m/z$ 311 (M + 1, 8.0), 189 (M + 1 − PhCOOH, 100), 149 (79.1), 123

(44.3), 105 (77.1), 57 (74.6). Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.47; H, 7.21.

**(3α,3aα,3bβ,6aβ,7aα)-Decahydro-3-(benzoyloxy)-2,2,3b-trimethyl-5-oxo-1*H*-cyclopenta[*a*]pentalene (28).** In a two-neck flask with a T-valve adapter and rubber septum was added CuCN (26.5 mg, 0.3 mmol). The flask was flame-dried under vacuum and then purged three times with argon. THF (0.46 mL) was added, and, after cooling to −78 °C, boron trifluoride etherate (0.0368 mL, 0.3 mmol), followed by a solution of the enone **26** (62 mg, 0.2 mmol) in THF (0.5 mL), was added. The bath temperature was maintained between −50 and −55 °C for 3 h. The reaction was quenched at −50 °C by the addition of a solution of 10% saturated aqueous $NH_4OH$ in saturated aqueous $NH_4Cl$ (10 mL), and the aqueous layer was extracted with ether (3 × 20 mL). The combined organic portions were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was subjected to LC (60% ether in SSF) to afford 60.6 mg (93%) of the 1,4-addition product **28**. In another experiment, **26** (589 mg) was treated for 1 h at −50 °C under the same reaction conditions as above, leading to 509 mg of **28** (82.6%); 80 mg of starting material were recovered (96% yield based on recovered starting material). For **28**: $R_f$ (60% ether in SSF) 0.53; mp (ether/SSF) 100–102 °C.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) δ 7.40–8.08 (5 H, m, Ph), 5.198 (1 H, d, $J$ = 8.9, $C_{11}H$), 2.858 (1 H, apparent d quintuplet, $J$ = 1.8, 9.4, $C_8H$), 2.694 (1 H, t, $J$ = 9.4, $C_1H$), 2.39–2.54 (2 H, m, $C_5$- and $C_6H$), 2.150 (1 H, d, $J$ = 17.8, $C_5H$), 2.100 (1 H, d, $J$ = 18.5, $C_3H$), 2.021 (1 H, d, $J$ = 18.5, $C_3H$), 1.899 (1 H, dd, $J$ = 8.9, 12.9, $C_9H$), 1.743 (1 H, ddd, $J$ = 2.1, 7.6, 13.9, $C_7H$), 1.485–1.596 (1 H, br m, $C_7H$), 1.245 (1 H, dd, $J$ = 9.4, 12.7, $C_9H$), 1.072 (3 H, s), 1.037 (3 H, s), 1.026 (3 H, s); IR (KBr pellet) 2960, 2940, 2880, 1742, 1715, 1600, 1455, 1300, 1270, 1258, 1173, 1125, 710 cm$^{-1}$; MS (CI), $m/z$ 327 (M + 1, <1), 205 (M + 1 −PhCOOH, 100), 189 (47.9), 105 (80.3), 95 (37). Anal. [HRMS (CI)] Calcd for $C_{21}H_{27}O_3$ (M + 1): 327.1960. Found: 327.1941.

**(3α,3aα,3bβ,6aβ,7aα)-Decahydro-3-hydroxy-2,2,3b-trimethyl-5-oxo-1*H*-cyclopenta[*a*]pentalene (31).** A solution of the benzoate **28** (486 mg, 1.49 mmol) in a 5% potassium hydroxide in methanol solution (10 mL) was heated to reflux for 6 h under nitrogen atmosphere. The mixture was poured in brine (15 mL), water (15 mL) was added, and the aqueous layer was extracted with ether (4 × 30 mL). The combined organic layers were washed with brine (2 × 10 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified with LC (60% ether in SSF) to give 317 mg (96% yield) of the alcohol **31** as a white solid: $R_f$ (ether) 0.43; mp (ether/hexane) 118–120 °C (lit.[5i] mp 114–115 °C).

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) δ 3.512 (1 H, dd, $J$ = 8.8, 6.2, simplifies to d upon addition of $D_2O$, $J$ = 8.8, $C_{11}H$), 2.705 (1 H, app d quintuplet, $J$ = 1.2, 9.5, $C_8H$), 2.31–2.472 (2 H, m, $C_5$- and $C_6H$), 2.233 (1 H, t, $J$ = 9.2, $C_1H$), 2.134 (1 H, d, $J$ = 18.1, $C_5H$), 2.079 (2 H, s, $C_3H$), 1.813 (1 H, dd, $J$ = 9.0, 12.8, $C_9H$), 1.653 (1 H, ddd, $J$ = 1.8, 7.7, 13.6, $C_7H$), 1.41–1.53 (1 H, m, $C_7H$), 1.34 (1 H, d, $J$ = 6.2, OH), 1.216 (3 H, s), 1.014 (3 H, s), 0.98–1.1 (1 H, m, $C_9H$), 0.888 (3 H, s); IR (KBr pellet) 3450 (br), 2930 (br), 2860, 1725, 1455, 1400, 1380, 1260, 1180, 1170, 1080, 1068 cm$^{-1}$; MS (EI), $m/z$ 222. Anal. [HRMS (EI)] Calcd for $C_{14}H_{22}O_2$: 222.1620. Found: 222.1605.

**(3α,3aα,3bβ,7aα)-2,3,3a,3b,4,5,7,7a-Octahydro-3-hydroxy-2,2,3b-trimethyl-5-oxo-1*H*-cyclopenta[*a*]pentalene (8). From Alcohol 31.** To a solution of lithium tetramethylpiperidine (6.43 mmol, from tetramethylpiperidine (1.2 mL, 7.14 mmol) and *n*-BuLi (4.0 mL, 1.6 M in hexane, 6.43 mmol)) in THF (12 mL) cooled to −78 °C and under argon atmosphere was added dropwise chlorotrimethylsilane (1.8 mL, 14.3 mmol), followed by the dropwise addition of a solution of **31** (317 mg, 1.43 mmol) in THF (5 mL). After 5 min at −78 °C, triethylamine (2.98 mL, 21.4 mmol) was added, and the reaction was allowed to warm slowly to room temperature (ca. 1 h). Ether (100 mL) was added, and the organic solution was washed with water (20 mL and 15 mL) and brine, dried over $MgSO_4$, and concentrated in vacuo. The remaining tetramethylpiperidine was removed under vacuum at 0.4 Torr. The crude mix of silyl enol ethers (6:1 ratio by GC analysis) was taken up in dry acetonitrile (8 mL) and was added to a solution of palladium acetate (Aldrich, 353 mg, 1.57 mmol) in acetonitrile (10 mL). After the mixture was stirred for 12 h at room temperature under a nitrogen atmosphere the solvent was removed in vacuo. Ether was added, the mixture was filtered through a silica gel column, and the products were eluted with ether. The crude mixture, obtained upon removal of the solvent in vacuo, was taken up in 6 mL of a 5:1 THF/water mixture, and 0.05 mL of a 3 N aqueous HCl solution was added. After the mixture was stirred for 1 h, saturated $NaHCO_3$ solution (10 mL) was added, and the aqueous layer was extracted with ether (4 × 30 mL). The combined organic portions were washed with brine, dried over $MgSO_4$, and concentration in vacuo. The residue was subjected to LC (90% ether in SSF) to afford 98 mg (31%) of the enone **8** along with 210 mg of recovered starting material. The yield based on recovered **31** was 91.6%. For **8**: $R_f$ (ether) 0.22; mp (ether/SSF) 120–121 °C (lit.[2] mp 117–118 and 120–121 °C).

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) δ 5.699 (1 H, d, $J$ = 1.9, $C_5H$), 3.794 (1 H, dd, $J$ = 8.1, 6.5, simplifies to d upon addition of $D_2O$, $J$ = 8.1, $C_{11}H$), 2.64–2.82 (2 H, m, $C_7$- and $C_8H$), 2.451 (1 H, d, $J$ = 17.6, $C_3H$), 2.340 (1 H, d, $J$ = 17.6, $C_3H$), 2.226 (1 H, ddd, $J$ = 1.9, 8.9, 14.3, $C_7H$), 2.159 (1 H, dd, $J$ = 8.5, 11.8, $C_1H$), 1.904 (1 H, dd, $J$ = 7.8, 12.7, $C_9H$), 1.496 (1 H, d, $J$ = 6.4, OH), 1.20–1.30 (1 H, m, $C_9H$), 1.220 (3 H, s), 1.072 (3 H, s), 0.940 (3 H, s); IR (KBr pellet) 3380 (br), 2930, 2860, 1675, 1622, 1360, 1258, 1227, 1117, 1060, 845, 820 cm$^{-1}$. Anal. [HRMS (EI)] Calcd for $C_{14}H_{20}O_2$: 220.1463. Found: 220.1481.

**From the Benzoate 28.** To a solution of lithium diisopropylamide (0.092 mmol, from diisopropylamine (0.014 mL, 0.092 mmol) and *n*-BuLi (0.051 mL, 1.5 M in hexane, 0.092 mmol)) in THF (0.3 mL) at −78 °C under argon atmosphere was added dropwise a solution of the benzoate **28** (5 mg, 0.0153 mmol) in THF (0.2 mL). After 15 min chlorotrimethylsilane (0.0194 mL, 0.153 mol) was added, and the reaction was allowed to warm to 0 °C. The mixture was diluted with SSF (15 mL), and the organic layer was washed with saturated aqueous $NH_4Cl$, saturated aqueous $NaHCO_3$, and brine. After drying over $MgSO_4$ for 1 min the solvent was concentrated in vacuo. By GC analysis, two isomers were formed in a 5:4 ratio. The crude silyl enol ether was taken up in acetonitrile (0.2 mL), palladium acetate (6 mg, 0.0229 mmol) was added, and the reaction was stirred for 12 h under nitrogen atmosphere. The solvent was removed in vacuo, and the residue was subjected to LC (50% ether in SSF) to afford 2 mg of **30** (40% yield) along with 2.5 mg of recovered starting material. The enone **30** was identical by GC and TLC and by $^1$H NMR with a sample kindly provided to us by Professor Koreeda: $R_f$ (50% ether in SSF) 0.28.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) δ 7.50–8.10 (5 H, m, Ph), 5.701 (1 H, d, $J$ = 1.7, $C_5H$), 5.065 (1 H, d, $J$ = 6.9, $C_{11}H$), 2.85–3.00 (1 H, m, $C_8H$), 2.814 (1 H, dd, $J$ = 8.5, 15.3, $C_7H$), 2.433 (1 H, d, $J$ = 18.2, $C_3H$), 2.27–2.40 (2 H, m, $C_1$- and $C_7H$), 2.193 (1 H, d, $J$ = 18.2, $C_3H$), 1.987 (1 H, dd, $J$ = 7.6, 12.7, $C_9H$), 1.413 (3 H, s), 1.179 (3 H, s), 1.144 (3 H, s). Hydrolysis of **30** in LiOH/THF (0.3 mL, 1/9 mixture, 1 N) at 50 °C for 48 h afforded cleanly the alcohol **8**, identical with the material synthesized from **31**.

**(3α,3aα,3bβ,4α,4β,7aα)-2,3,3a,3b,4,5,7,7a-Octahydro-3-hydroxy-4-(hydroxymethyl)-2,2,3b-trimethyl-5-oxo-1*H*-cyclopenta[*a*]pentalene (34).** A solution of the enone **8** (30 mg, 0.136 mmol) in dry THF (1 mL) was added dropwise over a period of 10 min to a solution at −78 °C under nitrogen atmosphere of lithium diisopropylamide (from diisopropylamine (0.067 mL, 0.476 mmol) and *n*-BuLi (0.281 mL, 1.45 M in hexane, 0.408 mmol) in THF (2 mL). After 15 min, the reaction was allowed to warm to −30 °C. At this temperature, formaldehyde (formed from paraformaldehyde at 150 °C) was led through the solution in a stream of dry nitrogen for about 10 min. The reaction was quenched by the addition of saturated $NH_4Cl$ (5 mL). The aqueous layer was extracted with ether (4 × 10 mL). The combined organic portions were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by LC (ether) to afford 29 mg (85%) of the diol **34**. Two isomers at $C_3$ are formed in a ratio of about 4:3 by $^1$H NMR: $R_f$ (ether) 0.23.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) δ 5.678 and 5.699 (1 H, each a d, $J$ = 1.8 and 2.1, $C_5H$ of each isomer), 3.624 and 4.135 (1 H, t, $J$ = 11.4 and dd, $J$ = 6.5, 10.8, $CH_2OH$ and $C_{11}H$), 2.70–2.90 (2 H, m), 2.45–2.65 (2 H, m), 2.20–2.40 (2 H, m), 1.866–1.949 (1 H, m), 1.282, 1.097, 0.982, and 1.167, 1.092, 0.966 (9 H, each s, 3 × $CH_3$ of each isomer); IR (KBr pellet) 3340 (br), 2846–2980, 1729, 1678, 1632, cm$^{-1}$; MS (EI), $m/z$

250 (3), 232 (14.3), 219 (21.4), 122 (33.3), 111 (100), 91 (28.6), 77 (20.7).

**Dienone 33: Prehypnophilin.** A mixture of the diol **34** (11 mg, 0.044 mmol), tosyl chloride (33.3 mg, 0.176 mmol) and pyridine (0.029 mL, 0.352 mmol) in $CH_2Cl_2$ (0.5 mL) was stirred at room temperature under a nitrogen atmosphere for 4 days. After addition of 1,8-diazabicyclo[5.4.0]undec-7-ene (0.072 mL, 0.528 mmol) the reaction was stirred for an additional 2 h, and brine (5 mL) and water (5 mL) were added. The water layer was extracted with ether (4 × 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was subjected to LC (70% ether in hexane) to afford 8.2 mg (80% yield) of the dienone **33**: $R_f$ (70% ether in hexane) 0.20.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.927 (1 H, s, $=CH_2$), 5.909 (1 H, d, $J$ = 1.8, $C_5H$), 5.352 (1 H, s, $=CH_2$), 3.873 (1 H, t, $J$ = 7.5; changes to d with $J$ = 8.4 upon addition of $D_2O$, $C_{11}H$), 2.781 (1 H, dd, $J$ = 8.1, 14.1, $C_7H$), 2.6–2.75 (1 H, m, $C_8H$), 2.245 (1 H, ddd, $J$ = 1.8, 5.7, 14.1, $C_7H$), 2.152 (1 H, dd, $J$ = 8.4, 12.0, $C_1H$), 1.910 (1 H, dd, $J$ = 7.8, 12.6, $C_9H$), 1.332 (1 H, dd, $J$ = 7.8, 12.6, $C_9H$), 1.278 (3 H, s), 1.091 (1 H, s), 0.924 (3 H, s); IR (film) 3430 (br), 2960, 2930, 2860, 1690, 1647, 1620, 1460, 1110, 1080, 750 cm$^{-1}$; MS (EI), $m/z$ 232 (9.5), 122 (39.3), 111 (100), 91 (23.8), 77 (15.5).

**(±)-Hypnophilin (3).** To a mixture of the dienone **33** (8 mg, 0.0345 mmol), sodium bicarbonate (50 mg), water (1 mL), and THF (1 mL) at 0 °C was added a 30% aqueous hydrogen peroxide solution (0.1 mL), and the reaction was stirred overnight at 4 °C. TLC analysis showed that, along with starting material and desired product **3**, some diepoxidized product formed. The reaction mixture was diluted with ether (20 mL), the solution was washed with saturated aqueous $NH_4Cl$ and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by LC (60% ether in hexane) to afford 4 mg (50% yield) of (±)-hypnophilin (**3**) along with 2.3 mg (29%) of recovered dienone **33**. For (±)-hypnophilin (**3**): $R_f$ (50% ether in hexane) 0.17.

The spectral data were in full accord with those kindly provided to us by Professor Steglich: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.135 (1 H, s, $=CH_2$), 5.459 (1 H, s, $=CH_2$), 3.869 (1 H, dd, $J$ = 6.9, 8.8; simplifies to d, $J$ = 8.8 upon addition of $D_2O$, $C_{11}H$), 3.463 (1 H, s, $C_5H$), 2.661 (1 H, m, $C_8H$), 2.139 (1 H, dd, $J$ = 8.9, 12.0, $C_1H$), 1.866–1.962 (2 H, m), 1.304 (3 H, s), 1.15–1.28 (2 H, m), 1.071 (3 H, s), 0.857 (3 H, s); IR (film) 3420, 2970, 2935, 2870, 1728, 1636, 1460, 1115, 1085, 1045 cm$^{-1}$; GCMS (EI), $m/z$ 248 (M, 3.6), 232 (10.7), 111 (100), 105 (60), 91 (49), 77 (38.6), 55 (34), 43 (45.2). Anal. [HRMS (EI)] Calcd for $C_{15}H_{20}O_3$: 248.1412. Found: 248.1377.

**Benzoylation of 10.** To a solution of the alcohol **10** (100 mg, 0.52 mmol) and pyridine (0.168 mL, 2.08 mmol) in $CH_2Cl_2$ (1 mL) at 0 °C under nitrogen atmosphere was added dropwise benzoyl chloride (0.121 mL, 1.04 mmol). The mixture was warmed to room temperature and stirred for 24 h. Water (10 mL) was added, and the aqueous layer was extracted with ether (3 × 10 mL). The combined organic portions were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was subjected to LC (4% ether in SSF) to afford 143 mg (93%) of the benzoate **24**: $R_f$ (4% ether in SSF) 0.31.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.4–8.1 (5 H, m, Ph), 5.263 (1 H, br s, $C_3H$), 4.875 (1 H, d, $J$ = 7.2, $C_{11}H$), 3.178 (1 H, br m, $C_6H$), 3.051 (1 H, apparent quintuplet, $J$ = 9.3, $C_8H$), 2.957 (1 H, t, $J$ = 7.6, $C_1H$), 2.4–2.7 (2 H, m, $C_4H$), 2.143 (1 H, m), 1.781 (1 H, dd, $J$ = 8.3, 12.5, $C_9H$), 1.669 (1 H, dd, $J$ = 7.5, 12.3, $C_9H$), 1.1–1.45 (3 H, m), 1.069 (3 H, s), 1.015 (3 H, s); IR (film) 3070, 2950, 2860, 1727, 1605, 1587, 1270, 1115, 710 cm$^{-1}$; MS (EI), $m/z$ 174 (M − PhCOOH, 56.5), 159 (67.0), 105 (100), 77 (49.9). Anal. [HRMS (CI)] Calcd for $C_{20}H_{24}O_2$: 296.1777. Found: 296.1756.

**Epoxidation of 24: Formation of (3α,3aα,3bβ,4β,6aβ,7aα)-Decahydro-3-(benzoyloxy)-3b,4-epoxy-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (37) and (3α,3aα,3bα,4α,6aβ,7aα)-Decahydro-3-(benzoyloxy)-3b,4-epoxy-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (38).** A solution of 3-chloroperbenzoic acid (63.7 mg 80% technical, 0.295 mmol) in $CHCl_3$ (2 mL) was added dropwise to a cooled mixture (water–ice bath) of the benzoate **24** (73 mg, 0.246 mmol) and solid sodium bicarbonate (50 mg) in $CHCl_3$ (2 mL). The reaction mixture was maintained at 0 °C for 10 min, and saturated aqueous $Na_2CO_3$ (5 mL) was added. The aqueous layer was extracted with ether (2 × 20 mL). The combined organic layers were washed with 10% aqueous $NaHSO_3$, saturated aqueous $NaHCO_3$, and brine (each 5 mL), dried over $MgSO_4$, and concentrated in vacuo. The two isomers were separated by using LC (10% ether in SSF until the major isomer was detected and then 20% ether in SSF) to afford 48.7 mg (63.5%) of the trans-fused derivative **38** and 18 mg (23.5%) of the cis-fused benzoate **37**.

For **37** (cis): $R_f$ (10% ether in SSF) 0.08; mp (hexane) 93–94 °C. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.39–8.07 (5 H, m, Ph), 5.372 (1 H, d, $J$ = 7.5, $C_{11}H$), 3.204 (1 H, s, $C_3H$), 2.862 (1 H apparent quintuplet, $J$ = 9.0, $C_8H$), 2.518 (1 H, dd, $J$ = 8.3, 7.7, $C_1H$), 2.476 (1 H, m, $C_6H$), 1.1–2.0 (8 H, undefined m), 1.056 (6 H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 165.388 (s, C=O), 132.524, 130.607, 129.623, and 128.099 (d, s, d, d, Ph), 82.528 (d, $C_{11}$), 77.326 (s, $C_2$), 64.415 (d, $C_3$), 43.711 (s, $C_{10}$), 45.189, 37.696, 32.257, and 24.735 (each t, $C_4$, $C_5$, $C_7$, and $C_9$), 45.189, 37.776, and 32.257 (each d, $C_1$, $C_6$, and $C_8$), 25.970 and 20.889 (each q, $CH_3$); IR (film) 3060, 3010, 2945, 2860, 1722, 1600, 1450, 1270, 1110, 707 cm$^{-1}$; MS (EI), $m/z$ 190 (80.61), 175 (100), 105 (79.6); MS (CI), $m/z$ 313 (M + 1, 26.4), 295 (15.6), 191 (68.2), 190 (100), 175 (71.2), 173 (71.1), 107 (16.4), 105 (64.6). Anal. [HRMS (CI)] Calcd for $C_{20}H_{25}O_3$ (M + 1): 313.1804. Found: 313.1784.

For **38** (trans): $R_f$ (10% ether in SSF) 0.23; mp (hexane) 103–104 °C. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.40–8.05 (5 H, m, Ph), 5.026 (1 H, d, $J$ = 8.3, $C_{11}H$), 3.584 (1 H, s, $C_3H$), 3.327 (1 H, apparent quintuplet, $J$ = 9.2, $C_8H$), 2.466 (1 H, t, $J$ = 8.9, $C_1H$), 2.33–2.44 (1 H, m, $C_6H$), 2.230 (1 H, dd, $J$ = 7.3, 13.7), 1.92–2.00 (1 H, m), 1.883 (1 H, dd, $J$ = 8.7, 13.1, $C_9H$), 1.10–1.60 (5 H, m), 1.107 (3 H, s), 1.045 (3 H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 165.960 (s, C=O), 132.787, 130.217, 129.426, and 128.230 (d, s, d, d, Ph), 82.467 (d, $C_{11}$), 79.633 (s, $C_2$), 57.445 (d, $C_3$), 43.562 (s, $C_{10}$), 46.792, 44.831, and 42.774 (each d, $C_1$, $C_6$, and $C_8$), 44.902, 33.187, 31.019, and 19.603 (each t, $C_4$, $C_5$, $C_7$, and $C_9$), 25.964 and 20.838 (each q, $CH_3$); IR (KBr pellet) 3050, 2930, 2860, 1710, 1600, 1450, 1265, 1110, 707 cm$^{-1}$; MS (EI), $m/z$ 312 (M, 0.8), 190 (85.3), 175 (100), 105 (80.9), 77 (50.4). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.61; H, 7.66. X-ray analysis: see supplementary material available.

**(3α,3aα,3bβ,4β,6aβ,7aα)-Decahydro-3b,4-epoxy-3-hydroxy-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (35) and (3α,3aα,3bα,4α,6aβ,7aα)-Decahydro-3b,4-epoxy-3-hydroxy-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (36).** The epoxides **35** and **36**, obtained from epoxidation of **10** in a 4:1 ratio as described, could be obtained in pure form upon hydrolysis of **37** and **38**. A mixture of the cis-fused isomer **37** (16 mg, 0.05 mmol) and a 3% methanolic potassium hydroxide solution (1 mL) was stirred for 4 h at room temperature. The mixture was diluted with ether (20 mL), and the solution was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was subjected to LC (50% ether in SSF) to afford 10.5 mg (100%) of **35**: $R_f$ (50% ether in SSF) 0.20; mp (ether/hexane) 104–107 °C.

The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.793 (1 H, dd, $J$ = 4.3, 7.4, simplifies to d upon addition of $D_2O$, $J$ = 7.4, $C_{11}H$), 3.325 (1 H, d, $J$ = 1.7, $C_3H$), 2.736 (1 H, apparent quintuplets, $J$ = 9.0, $C_8H$), 2.363 (1 H, dt, $J$ = 12.1, 7.2, $C_6H$), 2.221 (1 H, t, $J$ = 8.3, $C_1H$), 2.055 (1 H, br s, OH), 1.95–2.05 (1 H, m), 1.53–1.85 (4 H, m), 1.455 (1 H, dd, $J$ = 7.5, 12.7, $C_9H$), 1.277 (1 H, dt, $J$ = 12.4, 8.0), 1.140 (1 H, dd, $J$ = 10.7, 12.6, $C_9H$), 1.041 (3 H, s), 0.900 (3 H, s); IR (KBr pellet) 3420 (br), 3340 (br), 2950, 2860, 1450, 1395, 1375, 1127, 1087, 1062, 925 cm$^{-1}$; MS (EI), $m/z$ 208 (M, 54.7), 135 (48.2), 121 (49.0), 93 (84.9), 92 (100), 80 (52.7), 79 (85.8). Anal. [HRMS (EI)] Calcd for $C_{13}H_{20}O_2$: 208.1463. Found: 208.1475.

Hydrolysis of the trans-fused isomer **38** under the same conditions afforded **36** quantitatively: $R_f$ (50% ether in SSF) 0.19; mp (ether/hexane) 99–101 °C. The spectral data were as follows: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.751 (1 H, s, $C_3H$), 3.535 (1 H, dd, $J$ = 7.1, 8.3, simplifies to d upon addition of $C_2O$, $J$ = 8.3, $C_{11}H$), 3.170 (1 H, apparent quintuplet, $J$ = 19.1, $C_8H$), 2.267 (1 H, dd, $J$ = 7.3, 13.8, $C_4H$), 2.197–2.302 (1 H, m, $C_6H$), 2.167 (1 H, t, $J$ = 8.9, $C_1H$), 1.776–1.881 (1 H, m), 1.796 (1 H, dd, $J$ = 9.2, 13.0,

$C_9H$), 1.402–1.587 (3 H, m), 1.376 (1 H, d, $J$ = 7.1, OH), 1.05–1.232 (2 H, m), 1.029 (3 H, s), 0.895 (3 H, s); IR (KBr pellet) 3360 (br), 3260 (br), 2950, 2865, 1453, 1120, 1092, 1055, 895, 878 $cm^{-1}$; MS (EI), $m/z$ 208 (M, 17.5), 191 (100), 173 (72.9), 119 (81.8), 107 (77.3), 95 (84.1), 93 (74.7), 57 (32.1). Anal. [HRMS (EI)] Calcd for $C_{13}H_{20}O_2$: 208.1463. Found: 208.1438.

**(3α,3aα,6aβ,7aα)-2,3,3a,5,6,6a,7,7a-Octahydro-3-[(dimethyl-*tert*-butylsilyl)oxy]-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (39).** To a solution of the alcohol **10** (10.8 mg, 0.0562 mmol) and imidazole (19 mg, 0.28 mmol) in DMF (0.1 mL) at room temperature under nitrogen atmosphere was added a solution of *tert*-butyldimethylsilyl chloride in DMF (0.28 mL, 0.5 M, 0.14 mmol). After 24 h, water (10 mL) was added, and the aqueous layer was extracted with 30% ether in SSF (3 × 10 mL). The combined organic portions were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by LC to afford 16.5 mg (96%) of **39**: $R_f$ (SSF) 0.62.

The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ 5.287 (1 H, br s, $C_3H$), 3.262 (1 H, d, $J$ = 7.1, $C_{11}H$), 3.014 (1 H, br m, $C_6H$), 2.855 (1 H, apparent quintuplet, $J$ = 9.4, $C_8H$), 2.637 (1 H, t, $J$ = 7.9, $C_1H$), 2.45–2.60 (2 H, m, $C_4H$), 2.131 (1 H, m), 1.601 (1 H, m), 1.0–1.42 (4 H, m), 0.904 (3 H, s), 0.852 (3 H, s), 0.859, 0.025, and 0.000 (9 H, 3 H, and 3 H, each s, *t*-$BuMe_2Si$); IR (film) 2960, 2940, 2900, 2860, 1465, 1257, 1120, 1100, 1070 (br), 878, 838, 775 $cm^{-1}$. Anal. [HRMS (EI)] Calcd for $C_{19}H_{34}OSi$: 306.2379. Found: 306.2388.

**Epoxidation of 39: Formation of (3α,3aα,3bα,4aα,6aβ,7aα)-Decahydro-3-[(dimethyl-*tert*-butylsilyl)oxy]-3b,4-epoxy-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (40).** The silyl ether **39** was epoxidized according to the procedure given for the benzoate **24** to afford the epoxide **40** in 90% yield after LC (5% ether in SSF). The same epoxide **40** was also obtained upon treatment of **36** with *tert*-butyldimethylsilyl chloride and imidazole in DMF (reaction conditions as described above for **10**), which established the trans fusion in **40**: $R_f$ (5% ether in SSF) 0.26.

The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ 3.719 (1 H, s, $C_3H$), 3.511 (1 H, d, $J$ = 8.0, $C_{11}H$), 3.141 (1 H, apparent quintuplet, $J$ = 9.0, $C_8H$), 2.219 (1 H, t, $J$ = 7.9, $C_1H$), 2.147–2.289 (2 H, m), 1.77–1.877 (1 H, m), 1.733 (1 H, dd, $J$ = 9.2, 13.2), 1.33–1.55 (3 H, m), 1.0–1.1 (2 H, m), 0.950 (3 H, s), 0.865 (3 H, s), 0.876, 0.037, 0.000 (9 H, 3 H, and 3 H, each s, *t*-$BuMe_2Si$); IR (film) 3040, 2960, 2940, 2860, 1465, 1255, 1128, 1110, 838, 778 $cm^{-1}$. Anal. [HRMS (EI)] Calcd for $C_{19}H_{34}O_2Si$: 322.2328. Found: 322.2323.

**(3aα,3bα,4aα,6aβ,7aα)-Decahydro-3b,4-epoxy-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (42) and (3aα,3bβ,4β,6aβ,7aα)-Decahydro-3b,4-epoxy-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (43).** Epoxidation of the tricyclopentanoid **41**, a compound previously synthesized in these laboratories,[19] according to the procedure given for the benzoate **24**, afforded the two isomers **42** and **43** in 82% yield (1.85:1 trans/cis by GC analysis) after LC (4% ether in SSF). To establish the correct relative stereochemistry in both isomers, **43** was synthesized independently as follows.[20] A suspension of sodium hydride (9.6 mg, 60% in mineral oil, 0.24 mmol, washed three times with hexane), the cis-fused alcohol **35** (5 mg, 0.024 mmol), imidazole (1 mg), and carbon disulfide (0.025 mL) in dry THF (1 mL) was stirred at room temperature under argon atmosphere for 24 h. Methyl iodide (0.025 mL) was added, and the reaction was stirred for an additional 2 h. The reaction mixture was diluted with ether (30 mL), the solution was washed with saturated aquoeus $NH_4Cl$ and brine (each 5 mL), dried over $MgSO_4$, and concentrated in vacuo. The crude xanthate was taken up in dry toluene (0.3 mL) and was added dropwise to a refluxing solution of tributyltin hydride (0.020 mL) in toluene under argon atmosphere. After 24 h the reaction was cooled, the solvent was removed in vacuo, and the residue was subjected to LC (5% ether in SSF) to afford 3 mg (60%) of **43**. This epoxide proved to be identical ($^1H$ NMR, GC and TLC behavior) with the minor isomer from the epoxidation of **41**, namely **43**.

For the cis isomer: $R_f$ (5% ether in SSF) 0.25. The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ 3.285 (1 H, d, $J$ = 1.7, $C_3H$), 2.75–2.90 (1 H, br m, $C_6H$), 2.774 (1 H, apparent quintuplet, $J$ = 9.0, $C_8H$), 2.504 (1 H, q, $J$ = 8.8, $C_1H$), 2.37–2.46 (1 H, m), 1.0–2.0 (9 H, m), 1.069 (3 H, s), 0.895 (3 H, s); IR (film) 3020, 2950, 2870, 1465, 1370, 1295, 1260, 900 $cm^{-1}$. Anal. [HRMS (EI)] Calcd for $C_{13}H_{20}O$: 192.1514. Found: 192.1505.

For the trans isomer: $R_f$ (5% ether in SSF) 0.28. The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ 3.544 (1 H, s, $C_3H$), 3.231 (1 H, apparent quintuplet, $J$ = 8.8, $C_8H$), 2.451 (1 H, dt, $J$ = 8.7, 10.1, $C_1H$), 2.25–2.36 (1 H, br m, $C_6H$), 2.224 (1 H, dd, $J$ = 7.1, 13.6), 0.9–1.9 (9 H, m), 1.057 (3 H, s), 0.897 (3 H, s); IR (film) 3030, 2950, 2870, 1465, 1455, 1368, 1292, 915, 902, 890, 815 $cm^{-1}$. Anal. [HRMS (EI)] Calcd for $C_{13}H_{20}O$: 192.1514. Found: 192.1534.

**Hydroboration of 24.** To a solution of the benzoate **24** (10.8 mg, 0.0365 mmol) in THF (0.36 mL) was added $BH_3$·THF (0.183 mL, 1 M in THF, 0.183 mmol) at 0 °C under an argon atmosphere. The reaction was allowed to warm to room temperature. After 2 h, an aliquot (ca. 0.02 mL) was removed, aqueous 2 M sodium hydroxide (0.015 mL) and 30% aqueous hydrogen peroxide (0.006 mL) were added, and the sample was kept at room temperature for 2 h. GC analysis revealed two isomeric alcohols in a ratio of 16.4:83.6. The other portion of the reaction mixture was concentrated, $CH_2Cl_2$ (1 mL), Celite (78 mg), and PCC (0.365 mmol, 78 mg) were added, and the suspension was stirred for 2 h. The mixture was filtered through a short path of silica gel and was washed with ether. Two isomeric ketones **46** and **47** were formed. All attempts to separate them failed because the major isomer **47** epimerized partly on silica gel to the minor isomer **46**. Oxidation of the two isomeric alcohols **44** and **45** with PCC for 0.5 h gave the same isomeric ketones **46** and **47** in a ratio of 20:80 by GC analysis. Treatment of the mixture of **46** and **47** with DBU (0.01 mL) in $CH_2Cl_2$ (0.5 mL) led to isomer **46**, which could be isolated in 65% yield (7 mg) after LC (30% ether in SSF). The assignment of the trans fusion in the intitially major formed ketone **47** was based on its epimerization to the thermodynamically more stable cis-fused ketone **46**.

For (3α,3aα,3bβ,6aβ,7aα)-decahydro-3-(benzoyloxy)-2,2-dimethyl-4-oxo-1*H*-cyclopenta[*a*]pentalene (**46**): $R_f$ (50% ether in SSF) 0.50. The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.40–8.07 (5 H, m, Ph), 4.787 (1 H, d, $J$ = 7.4, $C_{11}H$), 2.92–3.17 (1 H, m)8 2.83–2.89 (2 H, m), 2.719 (1 H, apparent quintuplet, $J$ = 9.0, $C_8H$), 2.22–2.40 (1 H, m), 2.251 (1 H, t, $J$ = 8.6), 2.05–2.19 (1 H, m), 1.78–1.86 (1 H, m), 1.750 (1 H, dd, $J$ = 8.6, 13.1), 1.57–1.70 (1 H, m), 1.17–1.32 (2 H, m), 1.097 (3 H, s), 1.019 (3 H, s); IR (film) 2950, 2870, 1725, 1455, 1318, 1277, 1120, 713 $cm^{-1}$; MS (EI), $m/z$ 312 (M, 7.0), 190 (35), 175 (37), 105 (100), 77 (42). Anal. [HRMS (CI)] Calcd for $C_{20}H_{25}O_3$ (M + 1): 313.1804. Found: 313.1810.

For (3α,3aα,3bα,6aβ,7aα)-decahydro-3-(benzoyloxy)-2,2-dimethyl-4-oxo-1*H*-cyclopenta[*a*]pentalene (**47**) (containing ca. 30% of **46**): $R_f$ (50% ether in SSF) 0.34. The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.40–8.10 (5 H, m, Ph), 5.030 (1 H, d, $J$ = 8.8, $C_{11}H$), 3.107 (1 H, apparent br quintuplet, $J$ = 9.0, $C_8H$), 2.726 (1 H, q, $J$ = 8.0), 2.515 (1 H, t, $J$ = 8.0), 2.295 (1 H, dd, $J$ = 6.5, 14.9), 1.861 (1 H, dd, $J$ = 9.2, 12.8), 1.011 (6 H, s); IR (film) 2950, 2875, 1745, 1728, 1455, 1318, 1302, 1275, 1120, 1070, 1030, 710 $cm^{-1}$.

**Hydrolysis of 46.** A solution of the benzoate **46** (5 mg, 0.016 mmol) in 5% methanolic potassium hydroxide (0.5 mL) was stirred for 4 h at room temperature. The reaction mixture was diluted with ether (15 mL), and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Purification by LC (80% ether in SSF) afforded 3 mg (90%) of the alcohol **48**: $R_f$ (80% ether in SSF) 0.23.

The spectral data were as follows: $^1H$ NMR (300 MHz, $CDCl_3$) δ 3.28 (1 h, d, $J$ = 7.8, $C_{11}H$), 2.891 (1 H, apparent br quintuplet, $J$ = 9.0, $C_8H$), 2.45–2.61 (3 H, m), 2.03–2.33 (2 H, m), 2.292 (1 H, t, $J$ = 8.2), 1.65–1.85 (2 H, m), 1.695 (1 H, dd, $J$ = 8.7, 12.9, $C_9H$), 1.567 (1 H, ddd, $J$ = 1.1, 7.5, 13.2), 1.3–1.4 (1 H, m), 0.996 (3 H, s), 0.880 (3 H, s); IR (film) 3440 (br), 2945, 2870, 1740, 1730, 1465, 1455, 1140, 1100, 1073 $cm^{-1}$; MS (EI), $m/z$ 208 (M, 84.7), 190 (M − $H_2O$, 25.0), 151 (42.1), 96 (100), 83 (46.5), 79 (37.7). Anal. [HRMS (EI)] Calcd for $C_{13}H_{20}O_3$: 208.1464. Found: 208.1441.

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**Supplementary Material Available:** Detailed X-ray crystal data for compound **38** (12 pages). Ordering information is given on any current masthead page.

# Intramolecular Diels–Alder Reactions of Indole-3-acrylates

Marcel K. Eberle,* Michael J. Shapiro, and Roland Stucki

*Sandoz Research Institute, Department of Chemistry, East Hanover, New Jersey 07936*

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Indole-3-carboxaldehyde was alkylated to give the N-alkylated indole-3-carboxaldehydes **1a–d** and **4**. These were extended by two carbon atoms with methyl (triphenylphosphoranylidene)acetate to the methyl indole-3-acrylates **2a–d** and **5**. When these indoles were heated to 300 °C the (tetrahydro)carbazoles **3a–d** and **6a** were obtained. Compound **3c** represents a novel ring system. Indole-3-carboxaldehyde was also acylated to give the N-acylated indole-3-carboxaldehydes **1e,f**. These were carbon extended to the N-acylated indole-3-acrylates **2e,f** which upon heating to 300 °C gave the (tetrahydro)carbazoles **3e,f** and **6b**.

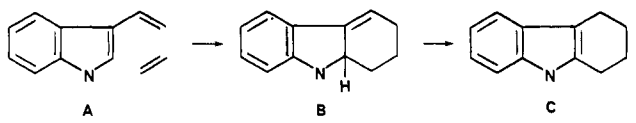
The Diels–Alder reaction as a tool for the simultaneous construction of two carbon–carbon bonds has received much attention both from synthetic[1] and theoretical[2] chemists. We have studied the intramolecular (4 + 2) cycloaddition with indole-3-acrylates substituted on the indole nitrogen with an appropriately unsaturated chain.

The classical Diels–Alder reaction with 3-vinylindoles (A) would lead to compounds of the general structure B, which then might undergo a hydrogen shift to form indoles of the general structure C (Scheme I). A direct reaction from A → C, with B serving as an intermediate, would disguise the Diels–Alder reaction and make this type of ring construction a priori less obvious. The reaction A → B has been described for the intermolecular addition of 3-vinylindoles[3] to 1,4-quinones and other dienophiles.

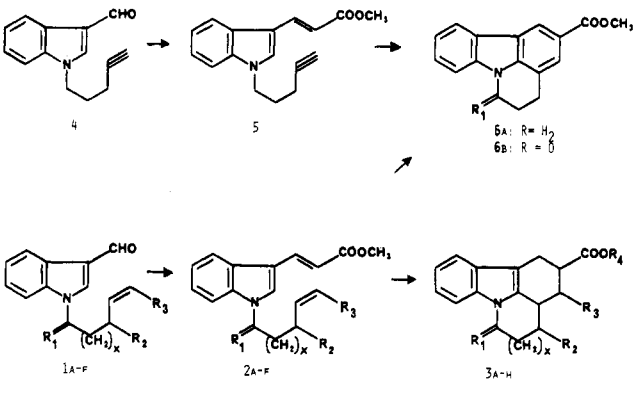
The first step in the preparation of the precursor for an intramolecular Diels–Alder reaction was the alkylation of the sodium salt of indole-3-carboxaldehyde with 5-bromopentene[4] to the aldehyde **1a** in 87% yields. From this compound the N-substituted indole-3-acrylic acid methyl ester (**2a**) was obtained via a Wittig reaction with methyl (triphenylphosphoranylidene)acetate[5] in refluxing toluene in 80% yield (Scheme II). Cyclization of **2a** was accomplished by heating the compound to 300 °C for 2 h with exclusion of air under an atmosphere of nitrogen at normal pressure. Crystallization of the cold glassy product from ether allowed the isolation of 43% of a pure isomer of mp 119–121 °C. The second isomer was secured in 13% yield from the mother liquors of the cyclization and had a melting point of 99–101 °C.

The assignment of the stereochemistry to the two isomers was based on the 500-MHz NMR spectra of the two compounds. Two-dimensional carbon–hydrogen correlated spectra on $\mathbf{3a}_2$ readily allowed the assignment of all carbon and proton resonances except for those associated with C5-H and C3a-H (see Figure 3). The key protons for the assessment of the stereochemisty of $\mathbf{3a}_1$ and $\mathbf{3a}_2$ are on carbons 4 and 5. The spectra of those protons are shown in Figures 1 and 2, respectively. In the case of the higher melting anti isomer $\mathbf{3a}_1$, the resonance at $\delta$ 1.57 can be assigned to the axial proton on C4. The coupling pattern observed is due to a combination of one geminal and one

**Scheme I**




**Scheme II**




| | x | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|---|
| **a** | 1 | $H_2$ | H | H | $CH_3$ |
| **b** | 2 | $H_2$ | H | H | $CH_3$ |
| **c** | 1 | $H_2$ | $(CH_2)_2$ | | $CH_3$ |
| **d** | 1 | $H_2$ | $(CH_2)_3$ | | $CH_3$ |
| **e** | 1 | O | H | H | $CH_3$ |
| **f** | 1 | O | $(CH_2)_3$ | | $CH_3$ |
| **g** | 1 | $H_2$ | H | H | H |
| **h** | 1 | $H_2$ | $(CH_2)_3$ | | H |

* Present address: Preclinical Research, Department of Chemistry, Sandoz Ltd., 4002 Basel, Switzerland.

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