Total Synthesis of (±)-Dactylol and Related Studies

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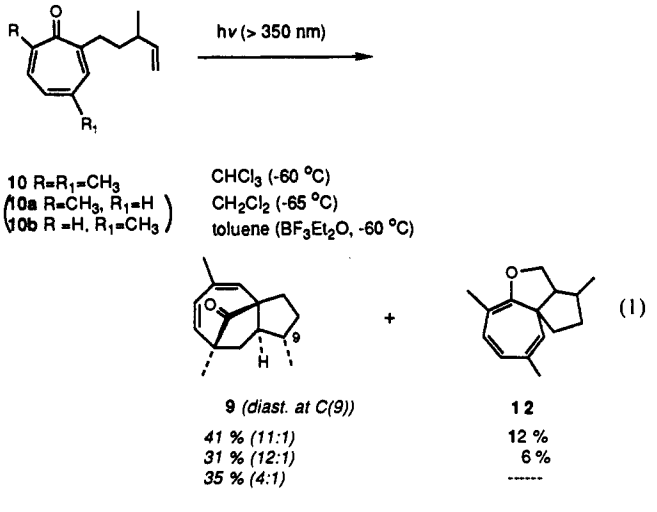
Abstract: The marine sesquiterpene (±)-dactylol was prepared from 2,5-dimethyl-7-(3-methyl-4-pentenyl)tropone in six steps. Salient features of the synthesis include: (1) a stereo- and regioselective intramolecular tropone–alkene [6π + 2π] photocyclization to furnish the dactylol carbocyclic skeleton, (2) a regioselective Baeyer–Villiger oxidation of a bisneopentyl ketone, and (3) a chemoselective 1,4-reduction of a cycloocta-1,3-diene moiety.

A concise and stereoselective synthesis of the cyclopentannelated cyclooctanoid natural product (±)-dactylol (**1**),[1] which features a novel [6π + 2π] intramolecular photocycloaddition[2] of a methylated alkenyltropone, is described herein.[2d] This irregular marine sesquiterpene has been isolated both from the sea hare *Aplysia dactylomela*[1a] and its putative food source the red seaweed *Laurencia poitei*,[1b] although a relevant biological role for dactylol in either organism has yet to be established. The unusual methylation pattern (methyl at C(3) instead of the expected C(2)) is believed to arise biogenetically through a series of alkyl shifts via carbocationic intermediates which originate from a humulene-derived africanyl (e.g., bicyclo[5.1.0]octanyl) cation.[3] This biosynthetic hypothesis was probed initially by Shirahama et al.,[3a] and later by Paquette,[4] through preparation of the africanyl cation precurser **3** followed by Lewis acid-mediated conversion into dactylol (Scheme I). An alternative nonbiogenetic strategy for the synthesis of dactylol was demonstrated by Gadwood,[5] who converted poitediol (**6**), itself available from the cyclohexenone **5**, to **1** via reductive deoxygenation at C(4). Both the Paquette and Gadwood studies featured a [3,3] sigmatropic rearrangement to construct crucial carbon–carbon bonds and establish product stereochemistry. In the Paquette route, the stereochemistry at C(9) (relative to the cyclooctane ring) was set in a Johnson orthoester-type Claisen rearrangement, while the Gadwood route featured an anionic oxy-Cope rearrangement of an alkynyl alkenylcyclobutanol to deliver the intact cyclooctadiene ring. In both approaches, difficulties in achieving stereoselective functional group transformations late in the syntheses led to production of undesired isomers.

Distinct from these approaches cited above, the cornerstone of our approach for the synthesis of (±)-dactylol (**1**) was a *cycloaddition* strategy for preparation of the core eight-membered ring. The particular cycloaddition used, the [6π + 2π] photocyclization of alkenyltropones,[2] has been demonstrated to occur through a series of discrete intermediates, including a hydroxy(or alkoxy)tropylium ion photochemical precursor (e.g., **14**), and a diradical (or zwitterionic) species in which one of the two new carbon–carbon bonds has been formed.[2c] With respect to the dactylol skeleton, this key transformation offers the potential economies of (1) construction of the cyclooctanoid ring in a single step, (2) relative asymmetric induction from C(9) to C(1) and C(8), and (3) delivery of functionality at C(1) and C(6) appropriate for completion of the synthesis. Evaluation of a retrosynthetic analysis for dactylol construction, shown in Scheme II, underscores several critical issues of reaction selectivity which must be addressed. For example, potentially problematic aspects of this synthesis include the preparation of the regioisomerically pure trisubstituted tropone **10**,[6] the sense and magnitude of relative asymmetric induction upon photocyclization of **10**, selective cleavage of bond a upon Baeyer–Villiger oxidation of the doubly neopentyl ketone in **9**, and controlled semihydrogenation of the 1,3-diene moiety in **8**. As will be described below, each of the challenges was met by judicious choice of reagents and reaction conditions, and high levels of selectivity in the desired sense were achieved.

1. Photocyclization of 10

The photocyclization of trisubstituted tropone **10**[6] proceeded in a qualitatively similar manner to that observed with the simpler 2,7- and 2,4-disubstituted analogues **10a** and **10b**.[2c] Thus, under most experimental conditions, mixtures of diastereoisomeric (at C(9)), [6π + 2π] adducts **9** and the formal [8π + 2π] adduct **12** were obtained. Unlike the disubstituted systems, however, where an acid catalyst was required for efficient photocyclization and yields of [6π + 2π] adduct as high as 70% were observed, yields no higher than 41% could be coaxed out of the trisubstituted species **10** under a variety of experimental conditions (eq 1). Furthermore, the best yields and stereoselectivity resulted from irradiation in *neutral* solution. A range of additives (BF_3·Et_2O, CF_3CO_2H, TMSOTf, CBr_3H, acetone, xanthone (E_T = 74 kcal/mol), thioxanthone (E_T = 66 kcal/mol), tocopherol,[7] and 3,4-dihydroxy-*tert*-butylbenzene) had no beneficial effect on either yield or selectivity in this process.



(1) (a) Schmitz, F. J.; Hollenbeak, K. H.; Vanderah, D. J. *Tetrahedron* **1978**, *34*, 2719. (b) Fenical, W.; Schulte, G. R.; Finer, J.; Clardy, J. *J. Org. Chem.* **1978**, *43*, 3630.

(2) (a) Feldman, K. S.; Come, J. H.; Freyer, A. J.; Kosmider, B. J.; Smith, C. M. *J. Am. Chem. Soc.* **1986**, *108*, 1327. (b) Feldman, K. S.; Come, J. H.; Fegley, G. J.; Smith, B. D.; Parvez, M. *Tetrahedron Lett.* **1987**, *28*, 607. (c) Feldman, K. S.; Come, J. H.; Kosmider, B. J.; Smith, P. M.; Rotella, D. P.; Wu, M.-J. *J. Org. Chem.* **1989**, *54*, 592. (d) Feldman, K. S.; Wu, M.-J.; Rotella, D. P. *J. Am. Chem. Soc.* **1989**, *111*, 6457.

(3) (a) Shirahama, H.; Hayano, K.; Kanemoto, Y.; Misumi, S.; Ohtsuka, T.; Hashiba, N.; Furusaki, A.; Murata, S.; Noyori, R.; Matsumoto, T. *Tetrahedron Lett.* **1980**, *21*, 4835. (b) Hayasaka, K.; Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1985**, *26*, 873.

(4) (a) Paquette, L. A.; Ham, W. H.; Dime, D. S. *Tetrahedron Lett.* **1985**, *26*, 4983. (b) Paquette, L. A.; Ham, W. H. *J. Am. Chem. Soc.* **1987**, *104*, 3025.

(5) (a) Gadwood, R. C. *J. Chem. Soc., Chem. Commun.* **1985**, 123. (b) Gadwood, R. C.; Lett, R. M.; Wissinger, J. E. *J. Am. Chem. Soc.* **1986**, *108*, 6343. (c) Gadwood, R. C.; Lett, R. M.; Wissinger, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 3869.

(6) A complete description of the synthesis of tropone **10**, along with the related species **10a/b** will be forthcoming: Funk, R. L.; Bolton, G. L.; Feldman, K. S.; Rotella, D. R.; Smith, P. S.; Wu, M.-J., manuscript in preparation.

(7) Jacobi, P. A.; Armacost, L. M.; Kravitz, J. I.; Martinelli, M. J. *Tetrahedron Lett.* **1988**, *29*, 6869.

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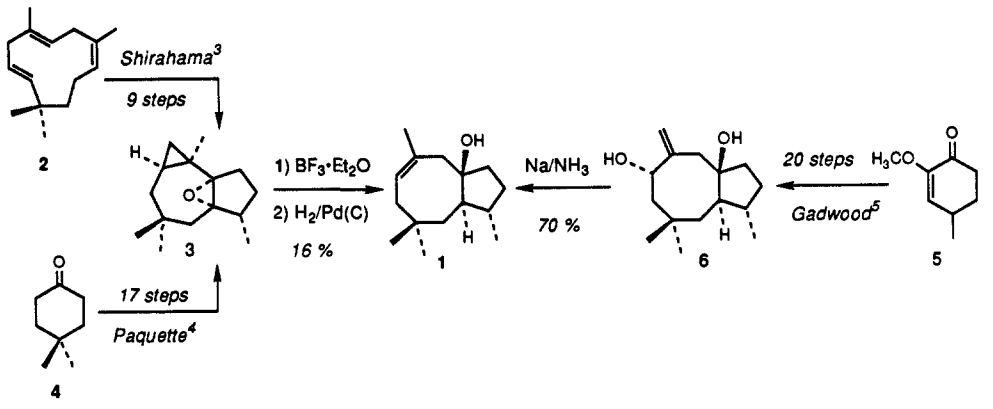
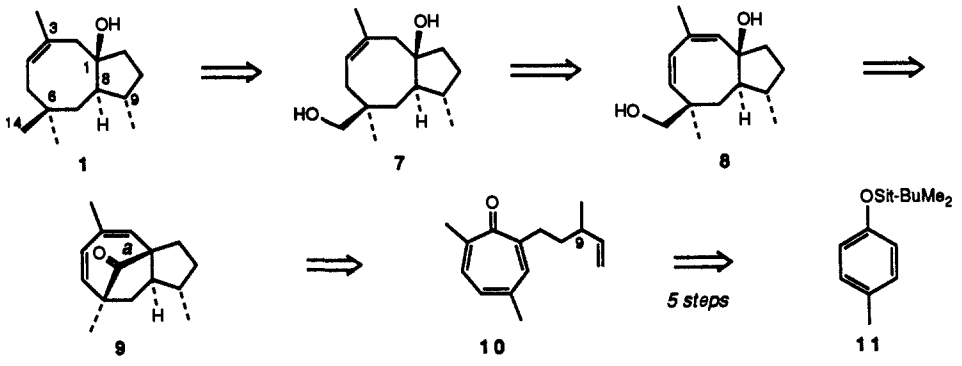
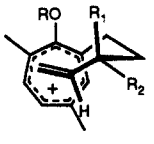
Scheme I



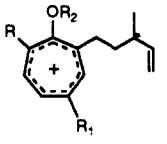
Scheme II



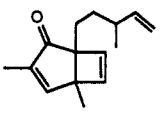
The relative asymmetric induction seen upon formation of the [6π + 2π] adduct **9** (>10:1) can be rationalized by invoking the mechanistic model proposed earlier for these tropone–alkene photocyclizations.[2c] Thus, initial C(1)–C(8) bond formation via either of the diastereomeric conformations **13a** or **13b** will lead to the major and minor C(9) stereoisomeric [6π + 2π] adducts **9** and **9a**, respectively. Steric interactions between the pseudo C(9) axial methyl and the troponoid oxygen (and adjacent C(7) methyl) should raise the energy of a transition state resembling **13a** accordingly, and so product formation will proceed through the relatively less-encumbered alternative species **13b**. While direct evidence for the parallel plane geometry of reactive conformers **13a/b** is lacking, this speculative model conveniently summarizes a host of data.[2a,c]



13a R=H or -, R_1 =CH_3, R_2=H
13b R=H or -, R_1=H, R_2=CH_3



14 R_2=H or -, R=R_1=CH_3
14a R_2=H or -, R_1 =CH_3, R_2=H
14b R_2=H or -, R_1=H, R_2=CH_3



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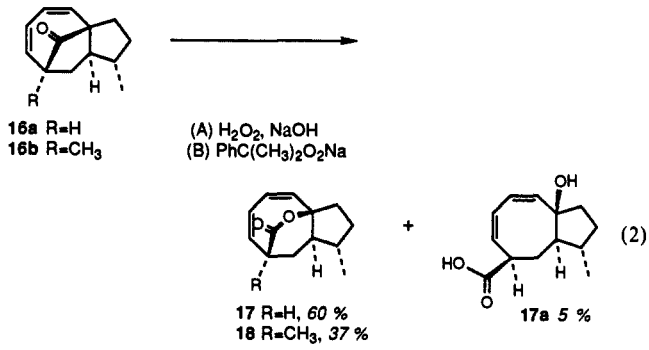
The unprecedented photocyclization under neutral conditions is perhaps related to the stability of the requisite cationic alkoxy(hydroxy)tropylium intermediate **14**, which in turn may be a function of the number of appended electron-donating alkyl substituents. Thus, in the case of mono- or dialkylated tropones, protonation is required to generate useful quantities of hydroxytropylium photochemical precursor **14a** or **14b**, while in the trisubstituted case **10**, the extra methyl may be sufficient to stabilize the intermediate **14** and provide adequate concentrations of this reactive species for efficient photocyclization. Interestingly, photocyclization of **10** in CH_3OH (−60 °C) leads to formation of the bicyclo[3.2.0]heptadienone **15** (16%) along with the usual [6π + 2π] adduct **9** (16% 8:1 at C(9)) and [8π + 2π] adduct **12** (6%). This particular type of tropone photocyclization product had never been detected in our work previously, and only recently has it been identified in the photochemistry of tropone itself.[8] Adduct **15** slowly decomposed under the photolysis conditions to yield intractable material but no [6π + 2π] or [8π + 2π] adducts, and so it is an unlikely intermediate in the photocyclization of interest. The stereochemistry of the major [6π + 2π] adduct **9** was suggested by a comparison of its ^1H NMR and ^{13}C NMR spectra with those of photoadduct **16a** (whose structure and stereochemistry have been secured by ^1H NMR DNOE measurements[2c]), and ultimately confirmed by its conversion into dactylol.

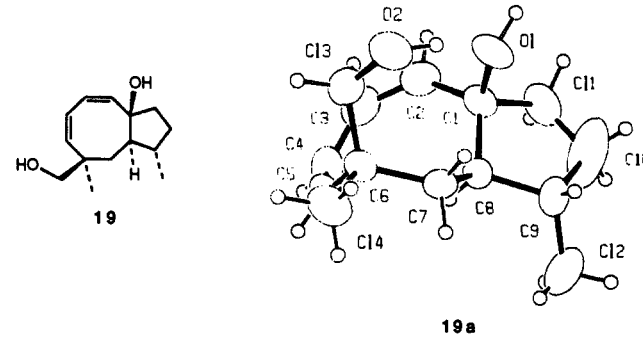
2. Baeyer–Villiger Oxidation of the Tricyclo[5.4.1.0]dodecadienone System

Baeyer–Villiger oxidation of the tricyclo[5.4.1.0]dodecadienone framework of the [6π + 2π] photocyclization adducts proved to be one of the more challenging aspects of the dactylol project. Prior investigations of carbanion nucleophilic addition to the core bicyclo[4.2.1]nonadienone moiety demonstrated that (1) addition is not a facile process and (2) attack occurs exclusively distal to the diene moiety.[2c] Initial attempts to effect oxidation of the relatively unencumbered model photoadduct **16a** with MCPBA led to exclusive alkene epoxidation—thus, the weakly nucleophilic peroxycarboxylate was unable to breach the steric barriers to nucleophilic carbonyl addition. Under basic conditions, the more potent nucleophile HO_2^- (condition A) successfully effected Baeyer–Villiger oxidation to the exclusion of undersired processes and furnished a single lactone regioisomer **17** along with a small amount of the hydrolysis product **17a** (eq 2).

Extension of this simple procedure (condition A) to the more sterically hindered carbonyl in **16b** was not fruitful. After considerable experimentation, a related experimental protocol which utilizes either $PhC(CH_3)_2O_2Li$ or $(CH_3)_3CO_2Li$ (procedure B)

(8) Reingold, I. D.; Kwong, K. S.; Menard, M. M. *J. Org. Chem.* **1989**, *54*, 708.

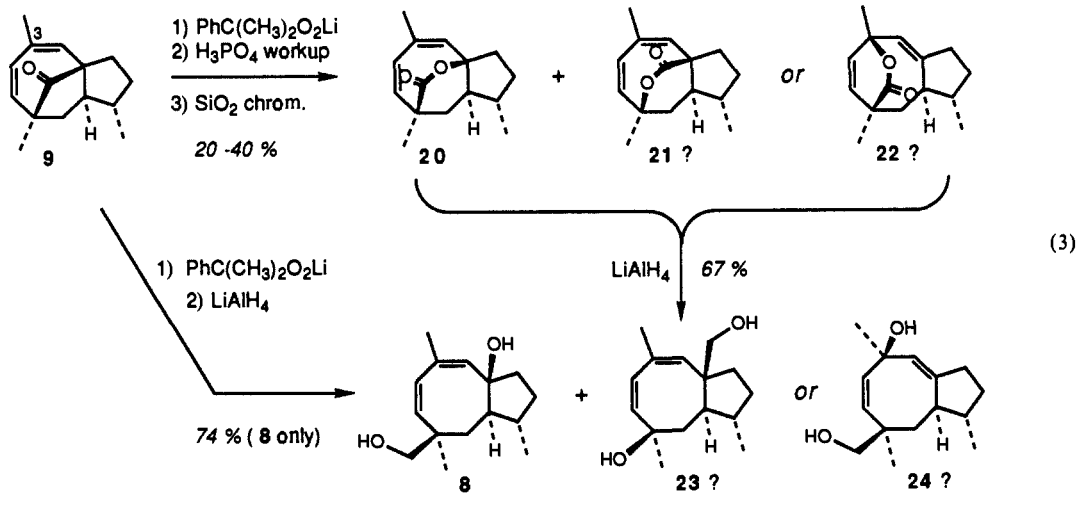




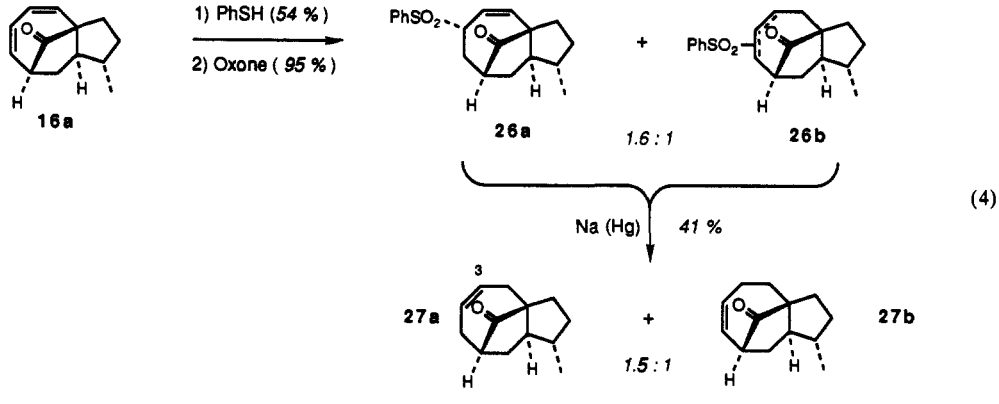
as the nucleophilic peroxide source proved modestly successful and afforded 20–40% yields of a single lactone regioisomer. Unlike the desmethyl case **17** where regiochemistry of oxygen insertion could be discerned by the position of the C(6)–H signal in the proton NMR spectrum, the regiochemistry of the lactone prepared from **16b** could not readily be assigned. However, $LiAlH_4$ reduction of **18** led to a diol **19** whose structure and stereochemistry were unambiguously established by single crystal X-ray analysis[9] (cf., **19a**), thus defining the connectivity (O–C(1) rather than O–C(6)) of the lactone **18** as well.

Oxidation of the fully methylated dactylol precursor **9** via procedure B affords modest yields (20–40%) of a mixture of lactone regioisomers following aqueous workup and SiO_2 chromatography (eq 3, Scheme III). The inseparable lactone isomers typically were obtained in ca. 1:1 to 3:1 ratios under varying experimental conditions and were tentatively assigned the structures **20** and **21** corresponding to the two alternate modes of oxygen insertion into the carbonyl bridge. This lactone mixture

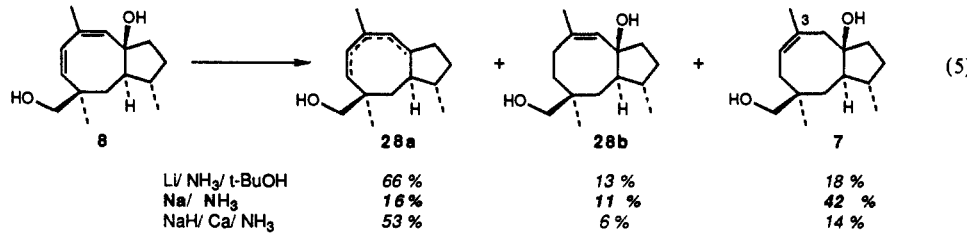
Scheme III



Scheme IV



Scheme V



could be reduced to chromatographically separable diols which were fully characterized. It was not clear, however, why introduction of a remote methyl substituent at C(3) should so drastically alter the course of the Baeyer Villiger oxidation of **9** compared with **16b**. This puzzle was clarified by subjecting the crude lactone product, without benefit of aqueous workup or exposure to SiO_2, to $LiAlH_4$ reduction. In this instance, only a *single diol*, **8**, was obtained (74% yield). Thus, the Baeyer–Villiger oxidation was, in fact, completely regiospecific, and an isomerization, aided by the cation stabilizing ability of the C(3) methyl, must have resulted during the workup/chromatography sequence. In this secondary process, the lactone regioisomer **22** (and not **21**) was formed, and from it the diol **24**. The structural and stereochemical assignment of diol **8** rests upon a comparison of spectral data with the C(3) desmethyl analogue **19** whose structure is secure and upon its eventual conversion to dactylol. The structure of the second diol (**23** or **24**?) in fact could not be unambiguously determined on the basis of spectral data alone—the assignment cited, **24**, is based solely on the reduction experiments described above (i.e., lactone **21** was not formed).

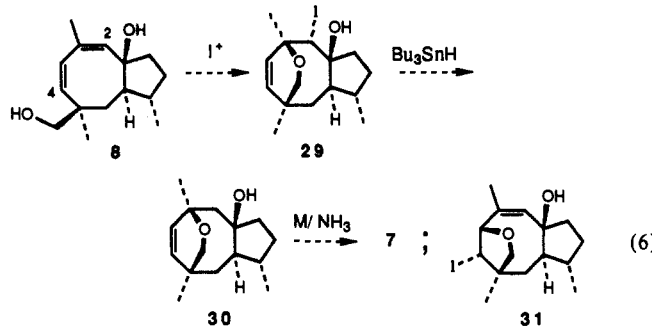
The strict regiospecific oxygen insertion into bond a (cf. Scheme II) of the doubly quaternary ketone in **9** was unanticipated. Post facto rationalization of this selectivity is hampered by uncertainties not only in the facial selectivity of peroxide anion (as opposed to carbanion) addition to the carbonyl but also in the precise location of the atoms (especially the lithium counterion) when carbon migration occurs. Nevertheless, this interesting outcome proved crucial for the successful completion of the dactylol synthesis.

3. Diene Reduction

Several distinct approaches for regioselective diene reduction were explored by using both the dienone photoadduct **16a** and the cyclooctadiendiol **8** as substrates. Initial attempts to partially reduce the diene moiety of photoadduct **16a** relied on a PhSH addition/reductive desulfurization sequence to deliver the required cyclooctene moiety (eq (4, Scheme IV)). Thus, free-radical-mediated thiophenol addition produced a complex mixture of monosulfide adducts which were subsequently oxidized to the corresponding sulfones **26** (5:2:1 ratio of isomers). The major isomer **26a** could be isolated in pure form, and structurally characterized via analysis of ^1H NMR decoupling and DNOE data (see Experimental Section). Reduction of the sulfone mixture **26a/b** afforded the mono olefins **27a** and **27b** in a 1.5:1 ratio, suggesting that one and possibly both of the minor sulfone isomers had the gross structures shown as **26b**. In any event, the lack of selectivity for Δ^3-alkene formation and the modest yields of alkenes obtained forced us to pursue alternative reduction procedures.

Dissolving metal reduction of diene **8** has the potential for delivering the desired Δ^3-cyclooctene moiety provided that overreduction (deoxygenation at C(1)) is suppressed. In an effort to identify experimental conditions which favor formation of the desired alkene product **7** over other possible products (**28a** or **28b**), several reducing agents (Na, Li, K, Ca), temperatures (−90, −78, −35 °C), additives (*t*-BuOH, CH_3OH), or initial bases (NaH, BuLi → alkoxide substrate) were examined. A survey of several experiments (eq 5, Scheme V) indicated that (1) overreduction to form **28a** is a serious complication in all cases, and (2) selectivity for the Δ^3-cyclooctene product **7** is not sufficiently high to incorporate this experimental approach into the dactylol synthesis.

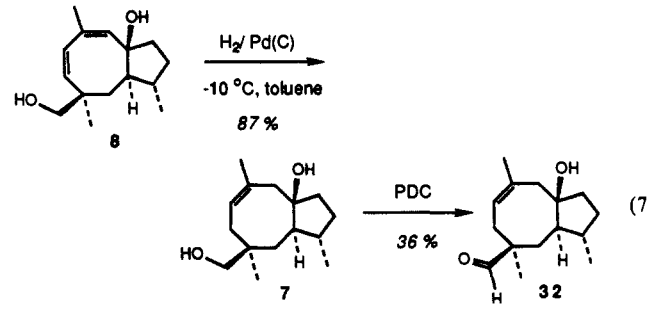
One potential solution to the lack of selectivity seen in direct diene reduction with metals (eq 5) is shown in eq 6. This three step procedure, if successful, would necessarily eliminate the formation of overreduction product **28a** or Δ^2-cyclooctene product **28b**. Furthermore, inspection of the X-ray crystal structure of the analogous C(3) desmethyl species **19a** revealed that (1) the primary oxygen is in a pseudoaxial orientation and should have ready access to C(3), and (2) the distal face of the Δ^2-olefin is available for I^+ attack. In the event, addition of *N*-iodosuccinimide to the diene diol **8** resulted in a smooth reaction to afford a single iodoether in 97% yield. Unfortunately, analysis of ^1H NMR



(6)

decoupling and DNOE data led inevitably to the structural assignment shown as **31** (see Experimental Section). Thus, iodoether formation occurred at the Δ^4-alkene in a formal 5-endo trigonal type cyclization process, rather than the expected 6-exo trigonal closure at the Δ^2-alkene. The reasons behind this unusual cyclization selectivity remain obscure at present—while hydrogen bonding clearly plays a role in fixing the conformation of **19** in the solid state,[9] MM2 calculations on **8** support this conformational preference as well. Unfortunately, iodo ether **31** does not contain a disposition of functionality appropriate for eventual selective conversion into the desired Δ^3-cyclooctene **7**, and so this approach was also abandoned.

After exhausting these unproductive attempts at selective diene reduction, we were delighted to find that simple hydrogenation of diene diol **8** at −10 °C[10] afforded the desired Δ^3 cyclooctene product **7** entirely free of overreduction products, alkene isomers, or unreacted starting material (eq 7). Presumably, the trisubstituted alkene moiety in **7** cannot effectively compete for catalyst sites with diene **8** under the low-temperature reaction conditions. In any event, with alkene **7** in hand, the synthesis of (±)-dactylol could be readily completed.



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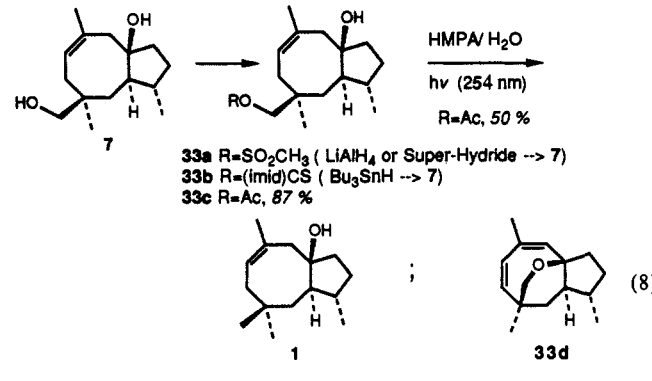
4. Deoxygenation at C(14)

Initial attempts to effect deoxygenation at C(14) relied on Wolf–Kishner reduction of aldehyde **32** (eq 7). Unfortunately, all experimental variants examined led to uncharacterizable material from which no dactylol, even in trace amounts, could be identified. Likewise, deoxygenation approaches utilizing the mesylate **33a** or thiocarbamate **33b** did not lead to any products derived from cleavage of the C(14)–O bond (eq 8). In addition,



(8)

(9) Parvez, M. *Acta Cryst.* **1990**, *C46*, 150.

(10) Takahashi, A.; Kirio, Y.; Sodeoka, M.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1988**, *111*, 643.

attempts to manipulate the diene diol intermediate **8** in a similar manner were foiled by a facile intramolecular cyclization leading to the dienyl ether **33d**. Fortunately, simple photoreduction of the acetate **33c** in HMPA/H_2O[11] furnished (±)-dactylol (**1**) in moderate yield as the only identifiable organic product. Both the mildness of this procedure and its ability to induce cleavage of this particularly refractory primary C–O bond are noteworthy.

5. Conclusion

The total synthesis of (±)-dactylol (**1**) has been achieved in six steps from trisubstituted tropone **10**, itself available from 4-(*tert*-butyldimethylsiloxy)toluene (**11**) in five steps. The synthesis is approximately half as long as previous syntheses of dactylol,[4,5] and features several highly stereoselective transformations, including tropone–alkene [6π + 2π] photocyclization of **10**, regioselective Baeyer–Villiger oxidation of **9** and regioselective diene semireduction of **8**.

6. Experimental Section

Only characteristic IR, ^{1}H NMR, and MS signals are reported (copies of ^{1}H NMR and ^{13}C NMR spectra can be found in the supplementary material). Gas–liquid chromatography (GLC) was performed on a Hewlett-Packard 5890A instrument equipped with a capillary cross-linked methyl silicone column (25 m; i.d. 0.20 mm; film thickness 0.33 mm) and a flame-ionization detector. Helium was used as carrier gas, and the chromatograms were recorded on an HP 3390A integrator. Liquid (flash)[34] chromatography was carried out by using 32–63-μm silica gel (Woelm-Pharma) and the indicated solvent. High-pressure liquid chromatography (HPLC) was performed on a Waters 6000A semipreparative instrument equipped with an R-400 refractometer and 440 UV detector, using a ZORBAX-SIL silica gel column (25 cm × 20 mm, Dupont). Elemental analyses were performed by Micro-Tech Laboratories, Inc., Skokie, IL. Photochemical reactions were carried out with a 450-W Hanovia medium-pressure lamp filtered through uranium glass (Corning). Ether, tetrahydrofuran, and benzene were purified by distillation from sodium/benzophenone under nitrogen, while methylene chloride was distilled from CaH_2 under nitrogen. Moisture-sensitive reactions were carried out in predried glassware and under an inert atmosphere (N_2, Ar). Reactions were worked up by one of the following standard procedures: (A) the organic phase was washed with an equivalent volume of ice cold 1 M H_3PO_4, which was in turn back-extracted with an equivalent volume of organic solvent. The combined organic solvents were washed with saturated brine, dried over Na_2SO_4, filtered, and concentrated in vacuo, and the residue was purified by flash chromatography on SiO_2 with the indicated solvent; (B) As per procedure A, but substituting H_2O for 1 M H_3PO_4.

Photocyclization of 2,5-Dimethyl-7-(3-methyl-4-pentenyl)-2,4,6-cycloheptatrienone (10). A 0.003 M $CHCl_3$ solution of alkenyltropone **10** (58 mg, 0.27 mmol) in the annulus of the Hanovia photoreactor immersed in a −65 °C bath was subject to irradiation under a continuous Ar purge. After GLC analysis indicated that starting material was consumed (1.5 h), the solution was concentrated and the residue was purified via flash chromatography on SiO_2 with 5% Et_2O in hexane as eluent to afford 24 mg (41%) of [6π + 2π] cycloadduct **9** and 7 mg (12%) of [8π + 2π] cycloadduct **12** as colorless oils. **9**: IR (neat) 1740 (C=O) cm^{-1}; ^{1}H NMR (360 MHz, C_6D_6) δ 5.41 (d, J = 11.6 Hz, 1 H, —C*H*=CH—), 5.24 (br s, 1 H, —C*H*=C(CH$_3$)—), 4.96 (d, J = 11.6 Hz, 1 H, —CH=C*H*—), 1.47 (d, J = 1.4 Hz, 3 H, —CH=C(C*H*$_3$)—), 1.14 (s, 3 H, CH$_3$), 0.78 (d, J = 6.9 Hz, 3 H, —CH(C*H*$_3$)—); ^{13}C NMR (75 MHz, $CDCl_3$) δ 216.4, 133.7, 132.3, 131.2, 126.8, 61.0, 56.7, 55.6, 47.7, 41.3, 33.3, 32.5, 24.5, 20.4, 19.1; MS m/z (relative intensity) 216 (M$^+$, 51), 188 (M$^+$ − CO, 49); HRMS calcd for $C_{15}H_{20}O$ 216.1514, found 216.1513. **12**: IR (neat) 1640 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.19 (d, J = 11.3 Hz, 1 H, —C*H*=CH—), 6.04 (d, J = 11.3 Hz, 1 H, —CH=C*H*—), 5.26 (s, 1 H, —C*H*=C(CH$_3$)—), 4.13 (dd, J = 8.9, 7.1 Hz, 1 H, —OC(*H*)H—), 4.05 (dd, J = 8.9, 3.6 Hz, 1 H, —OC(H)*H*—), 1.89 (d, J = 1.2 Hz, 3 H, —CH=C(C*H*$_3$)—), 1.85 (s, 3 H, C=C-(CH$_3$)), 1.06 (d, J = 6.8 Hz, 3 H, —C(H)C*H*$_3$—); ^{13}C NMR (90 MHz, $CDCl_3$) δ 156.0, 133.1, 131.9, 126.4, 125.9, 101.4, 74.7, 60.5, 55.0, 40.2, 36.6, 34.1, 22.4, 19.6, 16.0; MS m/z (relative intensity) 216 (M$^+$, 66), 201 (M$^+$ − CH$_3$, 82); HRMS calcd for $C_{15}H_{20}O$ 216.1514, found 216.1516.

In multiple runs utilizing up to 200 mg of alkenyltropone **10** per run, 30–40% yields of cycloadduct **9** were reproducibly obtained.

In methanol as solvent (−65 °C, 0.01 M **10**), the bicyclo[3.2.0]heptane cycloadduct **15** (as a 1:1 mixture of diastereomers at C(9)) was obtained (16%) along with the expected [6π + 2π] adduct **9** (16%) and [8π + 2π] adduct **12** (6%). **15**: IR (neat) 1690 (C=O), 1635 (C=C) cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.26 (s, 1 H, —COC(CH$_3$)=C*H*—), 5.83 (d, J = 1.6 Hz, 1 H, —C*H*=C(CH$_3$)—), 5.63 (m, 1 H, C*H*=CH$_2$), 4.94 (dd, J = 15.7, 1.6 Hz, 1 H, CH=C(*H*)H), 4.86 (dd, J = 9.9, 0.9 Hz, 1 H, CH=C(H)*H*), 3.24 (s, =CHC*H*C(CH$_3$)=), 1.74 (s, 3 H, CH$_3$), 1.73 (s, 3 H, C′H$_3$), 0.94 (m, 3 H, —C(C*H*$_3$)H—, 2 diast); ^{13}C NMR (90 MHz, $CDCl_3$) δ 208.7, 154.3, 144.3, 142.9, 131.2, 130.5, 112.8, 58.3, 53.8, 38.2, 32.4, 28.4, 20.1, 16.0, 11.1; MS m/z (relative intensity) 216 (M$^+$, 13); HRMS calcd for $C_{15}H_{20}O$ 216.1514, found 216.1515.

Baeyer–Villiger Oxidation of 1,2,3,8,9,9a-Hexahydro-1-methyl-3a,8-methano-3a*H*-cyclopentacycloocten-10-one (16a). A 30% aqueous solution of H_2O_2 (326 mg, 9.57 mmol) was added dropwise to a room temperature solution of dienone **16a** (120 mg, 0.64 mmol) and NaOH (255 mg, 6.38 mmol) in 7 mL of CH_3OH and 1 mL of water. After 40 h at room temperature, the reaction solution was diluted with 10 mL of Et_2O and worked up as per general procedure A with use of 20% Et_2O in hexane as chromatography eluent to furnish 78 mg (60%) of lactone **17** and 5 mg (4%) of the corresponding hydroxyacid **17a**. **17**: IR (CH-Cl$_3$) 1730 (C=O) cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.00–5.80 (m, 3 H, —*H*C=C*H*—, —C′H=C′—), 5.81 (m, 1 H, —C′H=C′*H*—), 3.37 (dt, J = 7.5, 4.5 Hz, 1 H, —COC*H*—), 2.53 (ddd, J = 13.1, 7.6, 2.4 Hz, 1 H, —COCHC(*H*)H—), 1.03 (d, J = 6.6 Hz, 3 H, —C(CH$_3$)H—); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 139.1, 131.9, 127.4, 126.4, 88.8, 46.6, 42.3, 42.0, 37.5, 32.2, 29.6, 19.1; MS m/z (relative intensity) 204 (M$^+$, 7), 176 (M$^+$ − CO, 32), 160 (M$^+$ − CO_2, 13).

Baeyer–Villiger Oxidation of 1,2,3,8,9,9a-Hexahydro-1,8-dimethyl-3a,8-methano-3a*H*-cyclopentacycloocten-10-one (16b). A solution of dienone **16b** (52 mg, 0.25 mmol) in 1 mL of Et_2O was added to a stirring 0 °C solution of PhC(CH$_3$)$_2$O$_2$Li (prepared by addition of *n*-BuLi (0.58 mL of a 1.6 M solution in hexanes, 0.94 mmol) to PhC(CH$_3$)$_2$O$_2$H (137 μL, 0.75 mmol) in 1 mL of Et_2O). The solution was warmed to room temperature and held there for 20 h. General workup A with 10% Et_2O in hexane as chromatography eluent furnished 20 mg (37%) of lactone **18** along with 23 mg of recovered dienone **16b**. **18**: IR (neat) 1740 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.96–5.87 (m, 2 H, —CH=CH—), 5.77 (dd, J = 11.7, 7.0 Hz, 1 H, —C′*H*=C′H—), 5.64 (d, J = 11.8 Hz, 1 H, —C′H=C*H*CCO—), 1.41 (s, 3 H, CH$_3$), 1.00 (d, J = 6.6 Hz, 3 H, —C(C*H*$_3$)H—); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2, 139.3, 139.1, 126.3, 126.1, 88.6, 47.4, 45.6, 43.9, 42.3, 42.0, 31.9, 26.8, 19.2; MS m/z (relative intensity) CI 219 (M + 1, 100).

Baeyer–Villiger Oxidation of 1,2,3,8,9,9a-Hexahydro-3a,8-methano-1,5,8-trimethyl-3a*H*-cyclopentacycloocten-10-one (9). A solution of dienone **9** (69 mg, 0.32 mmol) in 3 mL of THF was added to a stirring, 0 °C solution of (CH$_3$)$_3$CO$_2$Li (prepared from *n*-BuLi (0.63 mL of a 1.6 M solution in hexanes, 1.0 mmol) and (CH$_3$)$_3$CO$_2$H (0.33 mL of a 3M solution in toluene, 1.0 mmol) in 3 mL of THF). The solution was warmed to room temperature and held there for 72 h. General workup A with 10% Et_2O in hexane as eluent led to isolation of 27 mg (36%) of lactones **20** and **22** (1.6:1 ratio) along with 18 mg of starting dienone **9**. Repeated flash chromatography furnished an enriched sample (~10:1) of lactone **20**. **20**: IR (neat) 1735 (C=O) cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.79 (d, J = 12.5 Hz, CH, —C*H*=CH—), 5.77 (s, 1 H, —C*H*=C(CH$_3$)—), 5.57 (d, J = 12.5 Hz, 1 H, —CH=C*H*—), 1.80 (d, J = 1.4 Hz, 3 H, —CH=C(C*H*$_3$)—), 1.39 (s, 3 H, CH$_3$), 1.00 (d, J = 6.5 Hz, 3 H, —C(C*H*$_3$)H—); ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.8, 137.5, 134.9, 132.7, 130.0, 88.6, 47.1, 45.3, 44.2, 42.6, 42.3, 31.8, 26.6, 26.0, 19.2; MS m/z (relative intensity) 232 (M$^+$, 19), 188 (M$^+$ − CO_2, 22); HRMS calcd for $C_{15}H_{20}O_2$ 232.1463, found 232.1464.

In a separate experiment, dienone **9** (130 mg, 0.60 mmol) was oxidized with 5 equiv of PhC(CH$_3$)$_2$O$_2$Li for 20 h at room temperature as described above. After the reaction mixture was cooled to 0 °C, a solution of $LiAlH_4$ (4 mL of a 1 M THF solution, 4.0 mmol) was added dropwise, stirring was continued for 1 h at 0 °C, and the mixture was worked up per the method of Fieser.[12] The residue was purified by flash chromatography on SiO_2 with 50% Et_2O in hexane as eluent to afford 105 mg (74%) of diol **8**, mp 63–66 °C (recrystallization benzene/hexane). **8**: IR (neat) 3400 cm^{-1} (OH); ^{1}H NMR (360 MHz, C_6D_6) δ 5.74 (d, J = 12.1 Hz, 1 H, —C*H*=CH—), 5.40 (br s, 1 H, —C*H*=C(CH$_3$)—), 5.36 (d, J = 12.1 Hz, 1 H, —CH=C*H*—), 3.23 (d, J = 10.2 Hz, 1 H, C(*H*)-HOH), 3.14 (d, J = 10.2 Hz, 1 H, C(H)*H*OH), 1.58 (br s, 3 H, —CH=C(C*H*$_3$)—), 0.97 (d, J = 6.7 Hz, 3 H, —C(C*H*$_3$)H—), 0.92 (s, 3 H, CH$_3$); ^{13}C NMR (90 MHz, C_6D_6) δ 138.0, 135.6, 133.5, 130.7, 81.2, 73.3, 50.9, 42.8, 40.5, 39.6, 32.5, 31.4, 23.5, 20.6, 19.1; MS m/z (relative intensity) 326 (M$^+$, 3), 218 (M$^+$ − H_2O, 54); HRMS calcd for $C_{15}H_{22}O$ (M$^+$ − H_2O) 218.1671, found 218.1643.

$LiAlH_4$ Reduction of (1α,3aβ,8β,9aα)-1,2,3,8,9a-Hexahydro-1,8-dimethyl-3a,8-(epoxymethano)-3a*H*-cyclopentacycloocten-10-one (18). A

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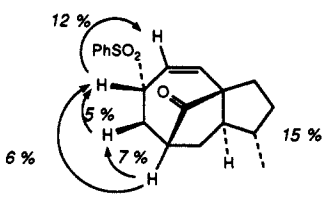
(12) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; John Wiley and Sons: New York, NY, 1967; Vol. 1, p 581.

solution of lactone **18** (15 mg, 0.07 mmol) in 0.5 mL of Et_2O was added dropwise into an ice-cooled suspension of $LiAlH_4$ (6 mg, 0.2 mmol) in 0.5 mL of Et_2O. After 1 h, TLC indicated complete consumption of starting material, and so application of the standard Fieser[12] workup yielded 11 mg (73%) of pure diol **19**. Vapor diffusion crystallization with benzene/hexane furnished a sample suitable for X-ray analysis[9], mp 100–104 °C. **19**: IR (CCl_4) 3400 (OH) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 5.81 (dd, J = 12.3, 4.2 Hz, 1 H, —C*H*=CH—), 5.65 (dd, J = 11.8, 4.3 Hz, 1 H, —C′*H*=C′H—), 5.56 (d, J = 11.8 Hz, 1 H, —C′H=C′*H*—), 5.23 (d, J = 12.2 Hz, 1 H, —CH=C*H*—), 3.43 (d, J = 10.4 Hz, 1 H, C(*H*)HOH), 3.13 (d, J = 10.4 Hz, 1 H, C(H)*H*OH), 0.96 (s, 3 H, CH_3), 0.93 (d, J = 6.7 Hz, 3 H, —C(CH_3)H—); MS m/z (relative intensity) 222 (M^+, 3), 205 ($M^+ - OH$, 30), 204 ($M^+ - H_2O$, 21).

$LiAlH_4$ Reduction of Lactones 20 and 22. A solution of lactones **20** and **22** (ca. 2:1 ratio, 37 mg, 0.16 mmol) in 1 mL of Et_2O was reduced with $LiAlH_4$ (8 mg, 0.2 mmol) as described above to furnish, after chromatography with 50% Et_2O in hexane, 18 mg of diol **8** (48%), and 7 mg (19%) of diol **24**, mp 99–102 °C (recrystallized from benzene/hexane). **24**: IR (CCl_4) 3300 (OH) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 5.57 (d, J = 12.9 Hz, 1 H, —C*H*=CH—), 5.34 (dd, J = 4.2, 2.7 Hz, 1 H, —C=CH—), 5.27 (dd, J = 13.0, 1.4 Hz, 1 H, —CH=CH—), 4.4 (br s, 2 H, OH, OH′), 3.44 (s, 2 H, CH_2OH), 1.37 (s, 3 H, CH_3), 0.89 (d, J = 6.4 Hz, 3 H, —C(CH_3)H—), 0.82 (s, 3 H, C′H_3); ^{13}C NMR (90 MHz, C_6D_6) δ 154.0, 137.7, 135.3, 125.7, 69.2, 69.0, 47.5, 44.0, 43.0, 39.4, 36.0, 34.9, 33.6, 27.9, 18.2; MS m/z (relative intensity) 236 (M^+, 1), 218 ($M^+ - H_2O$, 20); HRMS calcd for $C_{15}H_{22}O$ ($M^+ - H_2O$) 218.1671, found 218.1661.

Thiophenol Addition/Sulfide Oxidation of 1,2,8,9,9a-Hexahydro-1-methyl-3a,8-methano-3a*H*-cyclopentacycloocten-10-one (16a). A mixture of dienone **16a** (28 mg, 0.15 mmol) and thiophenol (49 mg, 0.45 mmol) in a sealed vial was heated at 110 °C for 2 h. The reaction solution was then cooled to room temperature and purified via flash chromatography on SiO_2 with 3% Et_2O in hexane as eluent to afford 24 mg (54%) of an isomeric mixture of sulfide adducts: IR ($CHCl_3$) 1730 (C=O) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.58–7.22 (m, 5 H, Ar-H), 5.81–5.55 (m, 2 H, —CH=), 4.01 (br s, 1 H, CHSPh), 3.84 (m, 1 H, C′HSPh), 1.18–0.88 (m, 3 H, —C(CH_3)H—). A solution of the sulfide mixture (29 mg, 0.097 mmol) in 1.5 mL of CH_3OH was added dropwise to a 0 °C suspension of oxone (179 mg, 0.29 mmol) in 3 mL of H_2O. The suspension was brought to room temperature and held there with stirring for 1 h. At that time, TLC indicated consumption of starting sulfide, and so the reaction solution was poured into 10 mL of Et_2O and worked up as per general procedure B to afford, following chromatography with 40% Et_2O in hexane as eluent, 29 mg (92%) of a mixture of sulfone isomers (ca. 5:2:1 ratio) **26** as a colorless oil. **26**: IR (CCl_4) 1740 (C=O), 1305, 1125 (SO_2) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.88–7.82 (m, 2 H, ArH), 7.68–7.53 (m, 3 H, ArH′), 6.15 (m, 1 H, —C*H*=CH—), 5.72 (m, 1 H, —CH=C*H*—), 3.54 (m, 1 H, $CHSO_2Ph$), 0.94 (m, 3 H, —C(CH_3)H—); MS m/z (relative intensity) 330 (M^+, 14), 189 ($M^+ - SO_2Ph$, 50), 188 ($M^+ - HSO_2Ph$, 28). A pure sample of the major sulfone isomer **26a** could be obtained after HPLC with 25% Et_2O in hexane as eluent. **26a**: ^1H NMR (360 MHz, $CDCl_3$) δ 7.88–7.84 (m, 2 H, ArH), 7.71–7.62 (m, 1 H, ArH′), 7.62–7.56 (m, 2 H, ArH″), 6.16 (dd, J = 9.0, 7.4 Hz, 1 H, —C(SO_2Ph)HC*H*=CH—), 5.73 (d, J = 9.0 Hz, 1 H, —C(SO_2Ph)HCH=C*H*—), 3.54 (ddd, J = 7.3, 7.0, 3.5 Hz, 1 H, —C(SO_2Ph)*H*—), 3.25 (dd, J = 12.3, 5.1 Hz, 1 H, —CHCO—), 2.98 (dd, J = 15.4, 12.4 Hz, 1 H, —C(*H*)HCO—), 2.32 (dd, J = 15.4, 4.8 Hz, 1 H, —C(H)*H*CO—), 2.08 (ddd, J = 15.5, 5.1, 0.4 Hz, 1 H, —C(H)*H*C(SO_2Ph)H—), 0.96 (d, J = 6.0 Hz, 3 H, —C(CH_3)H—).

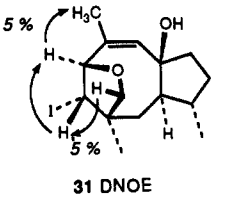


26a DNOE

Reductive Desulfurization of the Sulfone Mixture 26. Sodium amalgam (6%, 1.08 g, 2.73 g atom Na) was added to a slurry of Na_2HPO_4 (177 mg, 1.25 mmol) and the sulfone mixture **26** (90 mg, 0.27 mmol) in 5 mL of CH_3OH at 0 °C. After 1 h, TLC indicated that sulfone had been consumed, and so the reaction solution was poured into 10 mL of Et_2O and worked up as per general procedure B to furnish, following chromatography with 5% Et_2O in hexane as eluent, 21 mg (41%) of alkenes **27a** and **27b** in a 1.5:1 ratio (GLC) as colorless oils. The isomers could be obtained in pure form via HPLC with 2.5% Et_2O in hexane. **27a**: IR (CCl_4) 1740 (C=O) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.65–5.61 (m, 2 H, —CH=CH—), 2.68 (m, 1 H, CHCO), 0.97 (d, J = 6.6 Hz, 3 H, —C(CH_3)H—); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.2, 127.4, 126.3, 53.1, 47.4, 44.4, 38.6, 34.0, 33.3, 32.3, 30.9, 30.7, 29.7; MS (**27a** + **27b**) m/z (relative intensity) 190 (M^+, 100), 175 ($M^+ - CH_3$, 21), 162 ($M^+ - CO$, 15). **27b**: IR (CCl_4) 1740 cm^{-1} (C=O) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.95 (ddd, J = 11.1, 8.8, 2.5 Hz, 1 H, —C*H*=CH—), 5.80 (ddd, J = 11.0, 7.7, 4.0 Hz, 1 H, —CH=C*H*—), 2.95 (td, J = 8.7, 1.8 Hz, 1 H, CHCO), 1.01 (d, J = 6.6 Hz, 1 H, —C(CH_3)H—); ^{13}C NMR (90 MHz, $CDCl_3$) δ 214.2, 130.2, 130.0, 51.8, 50.1, 43.5, 38.8, 33.8, 32.6, 29.7, 24.5, 18.5; MS (see **27a**). Homodecoupling experiments established the connectivity between —C*H*CO— and —C*H*=CH— for **27b**.

Dissolving Metal Reduction of (3α,3aα,5β,9aβ)-2,3,3a,4,5,9a-Hexahydro-9a-hydroxy-3,4,8-trimethyl-1*H*-cyclopentacyclooctene-5-methanol (8). A solution of diol **8** (49 mg, 0.2 mmol) in 3 mL of THF was added dropwise to a blue solution of Na (26 mg, 1.1 mg atom) in 15 mL of NH_3 at −78 °C. After an additional 5 min, the blue color was discharged, and so the ammonia was allowed to evaporate after removal of the −78 °C bath, and the residue was worked up as per general procedure A to yield, following chromatography with 50% Et_2O in hexane as eluent, 25 mg (53%) of monoalkene diols **7** and **28b** (4:1 ratio by ^1H NMR), 7 mg (16%) of overreduction product **28a** (GLC ratio of isomers 5.4:1.6:1), and 7 mg of recovered starting diene **8**. The alkene isomers **7** and **28b** could be separated by HPLC with 50% Et_2O in hexane as eluent to furnish pure samples. **28a**: IR (CCl_4) 3400 (OH) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 5.2–4.9 (m, 1 H, =CH—), 3.4–2.9 (m, 2 H, CH_2OH), 1.70 (s, 3 H, —C(CH_3)=CH—, major isomer), 1.0–0.8 (m, 6 H, CH_3, —C(CH_3)H—); MS m/z (relative intensity) 222 (M^+, 25), 207 ($M^+ - CH_3$, 4), 204 ($M^+ - H_2O$, 4), 191 ($M^+ - CH_3OH$, 58). **7**: IR (CCl_4) 3618 (OH) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 5.48 (t, J = 8.4 Hz, —C(CH_3)=C*H*—), 3.20 (d, J = 10.4 Hz, 1 H, C(*H*)HOH), 3.05 (d, J = 10.7 Hz, 1 H, C(H)*H*OH), 2.20 (d, J = 13.6 Hz, 1 H, —C=CHC(*H*)H—), 2.06 (d, J = 13.4 Hz, 1 H, —C=CHC(H)*H*—), 1.83 (s, 3 H, —C(CH_3)=CH—), 0.91 (d, J = 6.5 Hz, 3 H, —C(CH_3)H—), 0.89 (s, 3 H, CH_3); ^{13}C NMR (90 MHz, C_6D_6) δ 136.0, 124.1, 82.8, 70.8, 52.0, 43.0, 40.5, 40.4, 39.5, 34.1, 31.5, 29.5, 27.9, 23.5, 19.2; MS m/z (relative intensity) 238 (M^+, 6), 220 ($M^+ - H_2O$, 8%); HRMS calcd for $C_{15}H_{26}O_2$ 238.1933, found 238.1928. **28b**: IR (CCl_4) 3300 (OH) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 5.30 (d, J = 1.4 Hz, 1 H, —C(CH_3)=C*H*—), 3.01 (s, 2 H, CH_2OH), 2.52 (ddd, J = 13.8, 10.3, 3.4 Hz, 1 H), 1.64 (d, J = 1.3 Hz, 3 H, —C(CH_3)=CH—), 0.97 (d, J = 6.3 Hz, 3 H, —C(CH_3)H—), 0.84 (s, 3 H, CH_3); MS m/z (relative intensity) 238 (M^+, 16), 220 ($M^+ - H_2O$, 34); HRMS calcd for $C_{15}H_{26}O_2$ 238.1933, found 238.1928.

Iodoetherification of (3α,2aα,5β,9aβ)-2,3,3a,4,5,9a-Hexahydro-9a-hydroxy-3,5,8-trimethyl-1*H*-cyclopentacyclooctene-5-methanol (8). A solution of diol **8** (10 mg, 0.04 mmol) in 1.5 mL of CH_2Cl_2 was added to a stirring suspension of *N*-iodosuccinimide (15 mg, 0.07 mmol) at room temperature. After 15 min, the reaction solution was diluted with 10 mL of Et_2O and 10 mL of 10% $Na_2S_2O_3$ solution and worked up as per general procedure B to furnish 14 mg (97%) of iodo ether **29** following chromatography with 20% Et_2O in hexane as eluent. **29**: IR (CCl_4) 3400 (OH) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.61 (s, 1 H, —C(CH_3)=C*H*—), 4.95 (d, J = 4.3 Hz, 1 H, —CHO—), 4.58 (d, J = 4.3 Hz, 1 H, —CHI—), 3.54 (d, J = 10.9 Hz, 1 H, —C(*H*)HO—), 3.36 (d, J = 10.9 Hz, 1 H, —C(H)*H*O—), 2.06 (s, 3 H, —C(CH_3)=CH—), 0.96 (s, 3 H, CH_3), 0.95 (d, J = 6.1 Hz, 3 H, —C(CH_3)H—); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.0, 135.1, 95.5, 89.0, 76.1, 53.0, 43.8, 42.8, 41.7, 37.2, 36.1, 34.4, 18.8, 17.9, 17.1; MS m/z (relative intensity) 362 (M^+, 0.07), 235 ($M^+ - I$, 30), 217 ($M^+ - I$, H_2O, 18), 205 ($M^+ - I$, CH_2O, 100).



31 DNOE

Semihydrogenation of (3α,2aα,5β,9aβ)-2,3,3a,4,5,9a-Hexahydro-9a-hydroxy-3,5,8-trimethyl-1*H*-cyclopentacyclooctene-5-methanol (8). A solution of diol **8** (45 mg, 0.19 mmol) in 4 mL of toluene was added to a stirring −10 °C suspension of 10% Pd/C (23 mg, 0.02 mmol) in 4 mL of toluene which had been pretreated with H_2 (1 atm) for 1 h. After stirring under 1 atm of H_2 for 1.5 h, the solution was filtered and concentrated, and the residue was purified by flash chromatography on SiO_2 with 50% Et_2O in hexane as eluent to afford 40 mg (89%) of monoalkene **7** as a clear oil.

Attempted Iodide Formation from (3α,2aα,5β,9aβ)-2,3,3a,4,5,9a-Hexahydro-9a-hydroxy-3,5,8-trimethyl-1*H*-cyclopentacyclooctene-5-methanol (8). Methane sulfonyl chloride (12 μL, 0.15 mmol) was added to a stirring 0 °C solution of diol **8** (24 mg, 0.1 mmol) and triethylamine (18 μL, 0.23 mmol) in 1 mL of CH_2Cl_2. After 2 h, the solution was worked up as per general procedure A to yield the crude mesylate: ^{1}H NMR (360 MHz, C_6D_6) δ 5.67 (d, J = 12.1 Hz, 1 H, —C*H*=CH—), 5.33 (s, 1 H, —C(CH_3)=C*H*—), 5.23 (d, J = 12.1 Hz, 1 H, —CH=C*H*—), 3.78 (d, J = 9.1 Hz, 1 H, C(*H*)HOMs), 3.70 (d, J = 9.1 Hz, 1 H, C(H)*H*OMs), 2.30 (s, 3 H, SO_2CH_3), 1.52 (s, 3 H, —C(C*H*$_3$)=CH—), 0.92 (d, J = 6.8 Hz, 3 H, —C(C*H*$_3$)H—), 0.86 (s, 3 H, CH_3). A solution of LiI (49 mg, 0.37 mmol) and $NaHCO_3$ (5 mg) in 1 mL of THF was added to the crude mesylate (ca. 0.15 mmol) in 1 mL of THF. After stirring at room temperature for 5 h and then warming to 50 °C for 12 h, the reaction solution was poured into 10 mL of Et_2O and 10 mL of 10% $Na_2S_2O_3$ solution and worked up as per general procedure B to yield 10 mg (42%) of cyclic ether **33d** as a colorless oil following chromatography with 5% Et_2O in hexane as eluent. **33d**: ^{1}H NMR (360 MHz, C_6D_6) δ 5.55 (d, J = 12.0 Hz, 1 H, —C*H*=CH—), 5.33 (s, 1 H, —C(CH_3)=C*H*—), 5.20 (d, J = 12.1 Hz, 1 H, —CH=C*H*—), 4.28 (dd, J = 11.0, 1.0 Hz, 1 H, —C(*H*)HO—), 3.32 (dd, J = 11.0, 1.0 Hz, 1 H, —C(H)*H*O—), 1.71 (d, J = 1.5 Hz, 3 H, —C(C*H*$_3$)=CH—), 0.91 (d, J = 6.5 Hz, 3 H, —C(C*H*$_3$)H—), 0.79 (s, 3 H, CH_3); MS m/z (relative intensity) 218 (M^+, 100), 203 ($M^+ - CH_3$, 19), 188 ($M^+ - CH_2O$, 16).

Oxidation of (3α,3aα,5β,9aβ)-2,3,3a,4,5,6,9,9a-Octahydro-9a-hydroxy-3,5,8-trimethyl-1*H*-cyclopentacyclooctene-5-methanol (7). A solution of diol **7** (32 mg, 0.13 mmol) in 1 mL of CH_2Cl_2 was added to a stirring suspension of pyridinium dichromate (50 mg, 0.26 mmol Cr^{VI}) in 1 mL of CH_2Cl_2. After the solution was stirred at room temperature for 5 h, 10 mL of Et_2O were added, and the solution was filtered through a plug of SiO_2 and concentrated, and the residue was purified via flash chromatography on SiO_2 with 25% Et_2O in hexane as eluent to furnish 11 mg (36%) of aldehyde **32**. **32**: IR (neat) 3480 (OH), 1716 (C=O) cm^{-1}; ^{1}H NMR (360 MHz, C_6D_6) δ 9.29 (s, 1 H, CHO), 5.35 (t, J = 8 Hz, 1 H, —C(CH_3)=C*H*—), 1.72 (s, 3 H, —C(C*H*$_3$)=CH—), 0.77 (d, J = 6.5 Hz, 3 H, —C(C*H*$_3$)H—), 0.72 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, C_6D_6) δ 204.6, 137.3, 122.8, 82.5, 51.6, 50.5, 42.7, 40.4, 39.3, 33.9, 29.2, 28.1, 27.7, 20.8, 19.0; MS m/z (relative intensity) 236 (M^+, 1), 218 ($M^+ - H_2O$, 2); HRMS calcd for $C_{15}H_{24}O_2$ 236.1776, found 236.1780.

Acetylation of (3α,3aα,5β,9aβ)-2,3,3a,4,5,6,9,9a-Octahydro-9a-hydroxy-3,5,8-trimethyl-1*H*-cyclopentacyclooctene-5-methanol (7). Pyridine (13 μL, 0.15 mmol) was added dropwise to a stirring 0 °C solution of diol **7** (34 mg, 0.14 mmol) and acetyl chloride (12 μL, 0.15 mmol). After 1 h at 0 °C, the reaction was diluted with 10 mL of Et_2O and worked up as per general procedure A to furnish 34 mg (87%) of acetate **33c** following chromatography with 50% Et_2O in hexane as eluent. **33c**: IR (neat) 3500 (OH), 1730 (C=O) cm^{-1}; ^{1}H NMR (360 MHz, C_6D_6) δ 5.44 (t, J = 8.5 Hz, 1 H, —C*H*=C(CH_3)—), 3.97 (d, J = 10.8 Hz, 1 H, C(*H*)HOAc), 3.76 (d, J = 10.8 Hz, 1 H, C(H)-*H*OAc), 2.15 (d, J = 13.5 Hz, 2 H, —C(*H*)HC(CH_3)=CH—), 2.03 (d, J = 13.5 Hz, 1 H, —C(H)*H*C(CH_3)=CH—), 1.88 (m, 1 H, —C(*H*)-HCH=C—), 1.81 (m, 1 H, —C(H)*H*CH=C—), 1.77 (br s, 3 H, —CH=C(C*H*$_3$)—), 1.72 (s, 3 H, O_2CCH_3), 0.87 (s, 3 H, CH_3), 0.86 (d, J = 6.7 Hz, 3 H, —CH(C*H*$_3$)—); ^{13}C NMR (90 MHz, C_6D_6) δ 170.2, 136.8, 123.4, 82.7, 71.5, 51.9, 43.0, 40.4, 39.4, 38.9, 34.4, 31.4, 29.4, 27.9, 23.7, 20.5, 19.2; MS m/z (relative intensity) 280 (M^+, 2), 262 ($M^+ - H_2O$, 5); HRMS calcd for $C_{17}H_{28}O_3$ 280.2038, found 280.2046.

Photochemical Reductive Deacetylation of (3α,3aα,5β,9aβ)-2,3,3a,4,5,6,9,9a-Octahydro-9a-hydroxy-3,5,8-trimethyl-1*H*-cyclopentacyclooctene-5-methanol, α-Acetate. A solution of acetate **33c** (10 mg, 0.036 mmol) in 1.5 mL of 95:5 HMPA–H_2O in a quartz tube was irradiated for 1 h with a 450-W Hanovia Hg lamp. The crude photolysate solution was poured into 10 mL of Et_2O and worked up as per general procedure B to afford 4 mg (50%) of (±)-dactylol (**1**) after chromatography with 50% Et_2O in hexane as eluent: mp 50–52 °C (lit.[1a] mp 50.3–51.5 °C); IR (CCl_4) 3440 (OH) cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.49 (t, J = 8.4 Hz, 1 H, C(*H*)=C), 2.21 (d, J = 13.7 Hz, 1 H, —C(CH_3)=CHC(*H*)H—), 2.05 (d, J = 13.7 Hz, 1 H, —C(CH_3)=CHC(H)*H*—), 1.90 (m, 2 H, C*H*$_2$CH=C), 1.83 (br s, 3 H, —C-(C*H*$_3$)=CH—), 1.77 (m, 1 H, —C(*H*)CH$_3$—), 0.90 (d, J = 6.4 Hz, 3 H, —C(H)C*H*$_3$—), 0.89 (s, 3 H, C**H**$_3$), 0.85 (s, 3 H, CH_3); ^{13}C NMR (90 MHz, C_6D_6) δ 135.9, 124.6, 82.8, 52.9, 43.0, 40.4, 39.4, 39.3, 36.5, 35.2, 29.5, 29.3, 28.9, 27.9, 19.2; MS m/z (relative intensity) 222 (M^+, 3); HRMS calcd for $C_{15}H_{26}O$ 222.1984, found 222.1976.

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Supplementary Material Available: ^{1}H NMR and ^{13}C spectra for **1**, **7–9**, **12**, **15**, **17**, **18**, **20**, **24**, **27b**, **31**, **32**, and **33c** and ^{1}H NMR spectra for **19**, **26**, **27a**, **28a**, **28b**, and **33d** (34 pages). Ordering information is given on any current masthead page.