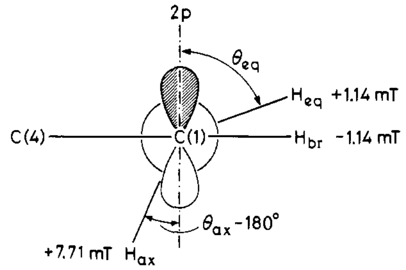
inversion through a planar geometry should be at least 12 kJ mol^{-1} when a relationship between such a barrier and the coalescence temperature is considered.[8] Moreover, the hyperfine data for $\mathbf{1}^{\bullet+}$ are consistent with the unpaired electron residing mainly in the AOs of the two equivalent bridgehead carbon atoms C(1) and C(3). These AOs must have a predominantly p character, because a spin population of 0.5 in each of them can be related to $a(\mathrm{H_{br}})$, $a(\mathrm{H_{eq}})$, and $a(\mathrm{H_{ax}})$ by eq 1 and 2, where a methylene proton $\mathrm{H_m}$

$$a(\mathrm{H_{br}}) = 0.5Q \qquad (1)$$

$$a(\mathrm{H_m}) = B(0.5^{1/2} + 0.5^{1/2})^2 \cos^2\theta_\mathrm{m} = 2B\cos^2\theta_\mathrm{m} \qquad (2)$$

stands for either $\mathrm{H_{eq}}$ or $\mathrm{H_{ax}}$. The parameter Q in the well-known McConnell[9] equation (1) has a negative value ranging from −2.2 to −3.0 mT,[10] and thus a *negative* sign is also required for $a(\mathrm{H_{br}}) = 1.14$ mT with $Q = -2.28$ mT. Equation 2 was first proposed by Whiffen[11] for methylene protons like $\mathrm{H_{eq}}$ and $\mathrm{H_{ax}}$ that are linked to sp^3-hybridized carbon atoms bridging *two* π centers. The parameter B is positive with a value of +4.0 to +4.8 mT appropriate for paramagnetic species of the same structural type as $\mathbf{1}^{\bullet+}$.[4,12] Therefore, the coupling constants $a(\mathrm{H_{eq}}) = 1.14$ mT and $a(\mathrm{H_{ax}}) = 7.71$ mT must also have a *positive* sign. The dihedral angles θ_m between the C(2)–$\mathrm{H_m}$ or C(4)–$\mathrm{H_m}$ bonds and the 2p axes at C(1) or C(3) in $\mathbf{1}^{\bullet+}$[13] cannot comply with the condition $\theta_\mathrm{ax} - \theta_\mathrm{eq} = 120°$, usually applied to unstrained molecules, because this difference is 211.1° − 66.1° = 145.0° in **1** (derived from the microwave data)[2] and it is 153.4° − 26.6° = 126.8° in the planar $\mathbf{2}^{\bullet\bullet}$ (calculated by a UHF-MNDO geometry optimization).[14] Assuming an intermediate value of 135 ± 5° for $\mathbf{1}^{\bullet+}$ and setting the experimental coupling constants $a(\mathrm{H_{ax}})$ and $a(\mathrm{H_{eq}})$ in eq 2, one obtains $\theta_\mathrm{ax} = 204.5 \pm 6°$ and $\theta_\mathrm{eq} = 69.5 \pm 1°$, along with $B = 4.65 \pm 0.5$ mT.

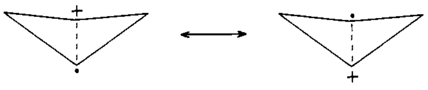


When the geometry of $\mathbf{1}^{\bullet+}$ is MNDO optimized, keeping θ_ax and θ_eq at these values, the flap angle α and the C(1)–C(3) distance come out as 132.2 ± 2.5° and 178.6 ± 3 pm. The coupling constants calculated by INDO[15] for this geometry are $a(\mathrm{H_{br}}) = -1.20 \pm 0.01$, $a(\mathrm{H_{eq}}) = +1.83 \pm 0.20$, and $a(\mathrm{H_{ax}}) = +7.80 \pm 0.25$ mT, in good agreement with experiment.

Two final remarks are in order.

(i) While the C(1)–C(3) distance in $\mathbf{1}^{\bullet+}$ (178.6 pm) lies midway between those of **1** (149.7 pm)[2] and $\mathbf{2}^{\bullet\bullet}$ (UHF-MNDO, this work: 204 pm; ab initio, ref 4: 210 pm), the angles θ_ax, θ_eq, and α in $\mathbf{1}^{\bullet+}$ (204.5, 69.5, and 132.2°) are much closer to the corresponding values in **1** (211.1, 66.1, and 121.7°) than to those in $\mathbf{2}^{\bullet\bullet}$ (153.4, 26.6, and 180°).

(ii) The reasonable fit of $a(\mathrm{H_{eq}})$ and $a(\mathrm{H_{ax}})$ to eq 2, which requires *twice* the value B as the proportionality factor, is not compatible with a fast interconversion between charge- and spin-localized structures $\mathbf{1a}^{\bullet+}$ and $\mathbf{1b}^{\bullet+}$.[5] These structures should thus represent mesomeric formulas of $\mathbf{1}^{\bullet+}$.



$\mathbf{1a}^{\bullet+}$ $\mathbf{1b}^{\bullet+}$

Acknowledgment. This work was supported by the Swiss National Science Foundation. We thank Prof. E. Haselbach, Université de Fribourg, for permission to use his ^{60}Co source of γ-rays. We are also obliged to the two Referees for their constructive criticism.

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Application of an Intramolecular Tropone–Alkene Photocyclization to the Total Synthesis of (±)-Dactylol

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Intramolecular tropone–alkene [6π + 2π] photocycloaddition[1,2] (eq 1) represents an efficient complement to classical acyclic closure,[3] fragmentation,[4] or ring expansion[5] strategies for the construction of the bicyclo[6.3.0]undecane skeleton characteristic of several terpenoid natural products. An exemplary member of this class of compounds is dactylol (**3**), a marine sesquiterpene isolated from *Aplysia dactylomela*,[6] which features three contiguous stereogenic centers embedded with the *trans*-bicyclo-

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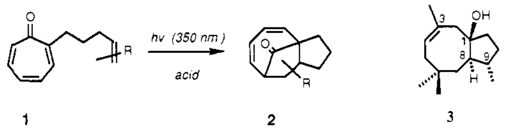
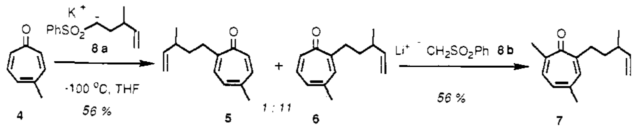
[6.3.0]undecane framework. Herein we describe an efficient (12 steps from 1,4-cyclohexadiene), stereoselective synthesis of this structurally interesting target molecule in which a tropone–alkene photocyclization not only assembles the 5-8 ring system but also correctly sets the relative stereochemistry at C(1), C(8), and C(9).[7]



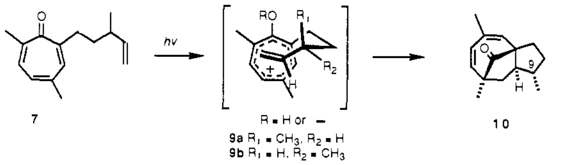
(1)

The synthesis of dactylol can be considered in three stages: (1) regioselective preparation of the requisite 2,4,7-trisubstituted tropone **7**, (2) stereoselective photocyclization to furnish the bicyclo[6.3.0]undecane-containing intermediate **10**, and (3) processing tricycle **10** into the target **3**. In each stage, high levels of selectivity in the desired sense for dactylol were realized by judicious choice of reaction conditions, as described below.



(2)

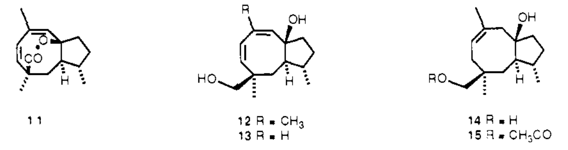
Synthesis of tropone **7** commenced with 4-methyltropone (**4**)[8] and utilized the sulfone-stabilized anion methodology recently reported by Funk[9] for successive introduction of the alkyl appendages (eq 2). Thus, combination of potassium anion **8a**[9] with tropone **4** led to the regioisomeric 2,4- and 2,5-disubstituted tropones **6** and **5**, respectively, in an 11:1 ratio. Use of alternate counterions or solvents, or reaction at higher temperatures, resulted in diminished regioselectivity. This inseparable mixture of regioisomers was treated with the methylsulfone anion **8b** to complete preparation of the 2,4,7-trisubstituted tropone **7**.[10]



(3)

Irradiation of a regiochemically pure[10] sample of trisubstituted tropone **7** with a 450 W medium pressure Hg lamp filtered through uranium glass (350 nm cutoff) at –60 °C in $CHCl_3$ led to formation of the [6π + 2π] photoadduct **10** in 41% yield as an 11:1 mixture of stereoisomers at C(9), along with 12% of a tricyclic [8π + 2π] adduct. The major [6π + 2π] stereoisomer was assigned the structure depicted in eq 3 based initially on DNOE analysis and ultimately on a comparison of the spectral data of a later intermediate (**12**, vide infra) with that of the des 3-methyl analogue **13** whose structure was unambiguously established by single-crystal X-ray analysis.[11] The observed stereoselectivity can be rationalized by consideration of a mechanistic model proposed earlier for this transformation.[1] We believe that the accumulated evidence to date is best accommodated by a stepwise reaction sequence initially involving a hydroxytropylium ion (or related zwitterion) as the photoactive species, followed by reaction through a conformation such as **9** (R = H or –) which places the alkene moiety at least partially over the troponoid ring. Collapse of an excited state resembling **9** eventually leads to carbocyclic products through stepwise bond formation. Substituents placed on the propane tether that connects the alkene with the tropone nucleus can adopt either pseudoaxial (**9a**, $R_1 = CH_3$, $R_2 = H$) or pseudoequatorial (**9b**, $R_1 = H$, $R_2 = CH_3$) orientations. Unfavorable steric interactions in the conformer **9a** ($R_1 = CH_3 \leftrightarrow OR$) should raise its energy relative to the alternative **9b**, and so the product derived from **9b**, with the pseudoequatorial disposition of the C(9) methyl, is favored.

Conversion of the dienylketone **10** into dactylol requires a regioselective Baeyer–Villiger oxidation for introduction of oxygen at C(1) and a regioselective 1,4-reduction of the diene moiety to furnish the Δ^3 olefin in the target structure. Initial attempts to effect Baeyer–Villiger oxidation of the particularly refractory ketone in **10** with CF_3CO_3H, MCPBA, $(TMSO)_2$/TMSOTf, or $PhSeO_3H$ led to either competitive reaction at the diene or recovery of starting material and forced us to consider a novel, strongly nucleophilic alternative to these standard reagents. After much experimentation, recourse was eventually made to $PhC(CH_3)_2O_2^-Li^+$ in THF,[12] which cleanly furnished the desired lactone **11** in a regiospecific manner. While this sensitive lactone could be isolated, immediate reduction ($LiAlH_4$) of the crude product led to the more conveniently isolable diol **12** in 73% yield from ketone **10**. 1,4-Reduction of the diene portion of diol **12** was effected by hydrogenation (1 atm) over Pd(C) in toluene at –10 °C.[13] The desired Δ^3 monoolefin **14** was isolated in 89% yield, unaccompanied by any alkene isomers or overreduction products. Esterification (AcCl/pyridine, 87%) of the primary hydroxyl of diol **14**, followed by irradiation of this acetate **15** at 254 nm in $HMPA/H_2O$,[14] led to clean reductive deacetylization and afforded (±)-dactylol (**3**) in 50% yield (mp 50–52 °C) following purification by silica gel chromatography and recrystallization from hexane. The synthetic material exhibited spectral data (^1H NMR, ^{13}C NMR, IR, MS) identical with those provided by Schmitz.[6]



11

12 R = CH_3
13 R = H

14 R = H
15 R = CH_3CO

In summary, the marine sesquiterpene dactylol has been synthesized in racemic form in an concise and selective manner. Notable features of the synthesis include consecutive regioselective alkylations of the tropone nucleus, a stereoselective tropone–alkene intramolecular photocyclization, and the development of a novel Baeyer–Villiger oxidation protocol useful for sterically hindered ketones which proceeds, in the case of **10**, with complete regioselectivity. Efforts to extend this strategy to the synthesis of more complex bicyclo[6.3.0]undecane-containing natural products are underway and will be reported in due course.

Acknowledgment. We thank the National Institutes of Health (GM35727) for financial support and Dr. F. Schmidtz for providing copies of spectral data for dactylol.

Supplementary Material Available: Spectral data (IR, ^1H NMR, ^{13}C NMR, MS, HRMS) for **3**, **6**, **7**, **10**, **11**, **12**, **14**, and **15** (2 pages). Ordering information is given on any current masthead page.

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(7) Other approaches to the synthesis of dactylol can be found in the following: (a) Gadwood, R. C. *J. Chem. Soc., Chem. Commun.* **1985**, 123. (b) References 4t and 4u. (c) Hayasaka, K.; Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1985**, *26*, 873.

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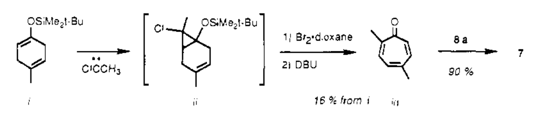
(10) An alternative synthesis of isomerically pure trisubstituted tropone **7** is shown below:



(11) Parvez, M. *Acta Crystallogr., Sect. C*, in press.

(12) Recently, the use of Ph_3CO_2H/NaOH in a Baeyer–Villiger oxidation was described. However, no reaction between this reagent combination and ketone **10** was observed: Corey, E. J.; Kang, M.-C.; Desai, M. C.; Ghosh, A. K.; Houpis, I. N. *J. Am. Chem. Soc.* **1988**, *110*, 649.

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