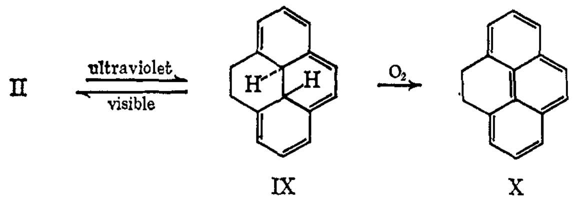
phane. When VIII was treated with sodium in the presence of tetraphenylethylene, the usual conditions for cyclization to form metacyclophanes, cyclization occurred, but it was accompanied by aromatization to give 4,5-dihydropyrene (X) in 50% yield. However, an investigation of other cyclization procedures led to the discovery that the treatment of VIII with phenyllithium in ether gives the desired [2.2]metacyclophane-1-ene (II) as white crystals, mp 82–83°, in 45% yield. It is of interest that in the nmr spectrum of II the signal for the two internal aromatic protons at the 8 and 16 positions is a broad singlet at τ 4.38. In [2.2]metacyclophane itself the internal 8 and 16 protons appear at τ 5.75. Thus, the orientation of the bridging double bond is such that it has a strong deshielding effect on the internal aromatic protons.

Ultraviolet irradiation of stilbene solutions in the absence of oxygen has been shown by a number of investigators to lead to 4a,4b-dihydrophenanthrenes.[9–13] When a solution of II in benzene or carbon tetrachloride was irradiated with ultraviolet light, the solution rapidly became colored, showing the appearance of absorption bands at 237, 305, 318.5, and 500 mμ (broad).[14] This spectrum is in good accord with that reported for the hexamethyldihydrophenanthrene[13] and suggests the formation of the 4,5,15,16-tetrahydropyrene (IX). As would be expected, the formation of IX is readily reversible by visible light. Furthermore, the solutions resulting from irradiation of II are extremely sensitive to traces of oxygen and, in its presence, the product found is 4,5-dihydropyrene (X).



Thus far, attempts (catalytic dehydrogenation and NBS) to effect a dehydrogenation of IX to give *trans*-15,16-dihydropyrene have been unsuccessful and have invariably yielded pyrene. However, in the case where the internal substituents are other than hydrogen, the corresponding irradiation products should be more stable both toward oxygen and toward aromatization to pyrene. Studies on such derivatives are in progress.

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(9) W. M. Moore, D. D. Morgan, and F. R. Stermitz, *J. Am. Chem Soc.*, **85**, 829 (1963).

(10) M. V. Sargent and C. J. Timmons, *ibid.*, **85**, 2186 (1963).

(11) F. B. Mallory, C. S. Wood, and J. T. Gordon, *ibid.*, **86**, 3094 (1964).

(12) G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Cowan, R. C. Counsell, V. Vogt, and C. Dalton, *ibid.*, **86**, 3197 (1964).

(13) K. A. Muszkat, D. Gegiou, and E. Fischer, *Chem. Commun.*, 447 (1965). We are indebted to Professor Fischer for his kindness in making a preprint of their detailed paper on this subject available to us prior to publication.

(14) Since the concentration of IX in the irradiated solutions is not known, extinction coefficients for their absorption bands could not be determined.

(15) We thank the Office of Naval Research for their support under Contract Nonr-2771(OR).NR-055-468, which made this investigation possible.

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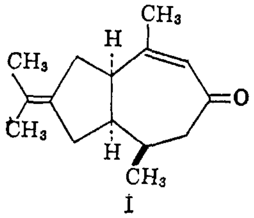
A Stereoselective Synthesis of Hydroazulenes. Grounds for Structure Revision of the Vetivane Sesquiterpenes

Sir:

With a view toward the total synthesis of β-vetivone, a constituent of the essential oil of vetiver,[1] we formulated a new stereoselective route to substituted hydroazulenes and thereby prepared the three 6,10-dimethyl-*cis*-decahydroazulen-8-ones **12a–c**. In this report we describe these synthetic studies and show that none of the aforementioned hydroazulenones corresponds to either of the epimeric desisopropylidenedihydro-β-vetivones prepared from β-vetivone. This finding invalidates not only the structure (I) heretofore accepted[1,2] for β-vetivone but, by virtue of reported chemical correlations, the proposed carbon framework (II) of the entire class of bicyclic vetivane sesquiterpenes as well.[2e,3]



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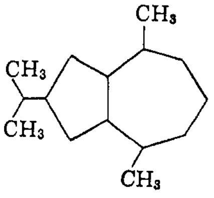

II

Methylation (KO-*t*-Bu, CH_3I)[4] of the known hydrindanone **1**[5] afforded the dimethyl derivative **2** [$\lambda_{\max}^{\text{film}}$ 3.28 (C=CH), 5.84 (CO), 6.09 (C=C), 8.78, 9.21, 9.58, 9.82, 9.92, and 10.05 μ; $\delta_{\text{TMS}}^{\text{CCl}_4} = 5.36$ (H-3, four lines, $J_{3,2} = 2$ Hz, $J_{3,7a} = 2$ Hz), 1.21, and 1.20 ppm (C-4 dimethyl)]. This substance yielded principally the *cis*-hydrindanone **3a** [$\lambda_{\max}^{\text{film}}$ 5.86 (CO), 10.14, 10.86, and 11.59 μ, purified *via* the semicarbazone derivative, mp 207–208°] upon hydrogenation over palladium on carbon in ethanol. The minor hydrogenation product was identified as the *trans*-hydrindanone **3b** by comparison with an authentic sample.[6] Bromination followed by dehydrobromination[4] converted hydrindanone **3a** to the conjugated ketone **4** [$\lambda_{\max}^{\text{film}}$ 5.96 (CO), 6.18 (C=C), 8.91, 10.82, 11.80, and 12.41 μ]. Hydrogenation (Pd–C) regenerated the *cis*-hydrindanone **3a** thus confirming our expectation[4] that isomerization of the ring fusion had not occurred en route to the conjugated ketone **4** (Chart I).

Addition of methylmagnesium iodide to hydrindanone **4** in the initial presence of cupric acetate[4] afforded the 1,4 adduct **5** [$\lambda_{\max}^{\text{film}}$ 5.84 (CO), 8.90, 9.10, 9.63, and 9.95 μ; $\delta_{\text{TMS}}^{\text{CCl}_4} = 1.27$, 0.97 (C-4 dimethyl, two singlets), and 1.01 ppm (C-7 methyl doublet, $J = 5.0$ Hz)]. This

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(1) J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. III, Cambridge University Press, London, 1952, pp 224–232.

(2) (a) A. S. Pfau and P. A. Plattner, *Helv. Chim. Acta*, **23**, 768 (1940), and previous papers; (b) Y. R. Naves and E. Perrottet, *ibid.*, **24**, 3 (1941); (c) Y. R. Naves, *Bull. Soc. Chim. France*, 369 (1951); (d) M. Romaňuk and V. Herout, *Collection Czech. Chem. Commun.*, **25**, 2540 (1960); (e) I. Yosioka and T. Kimura, *Chem. Pharm. Bull.* (Tokyo), **13**, 1430 (1965).

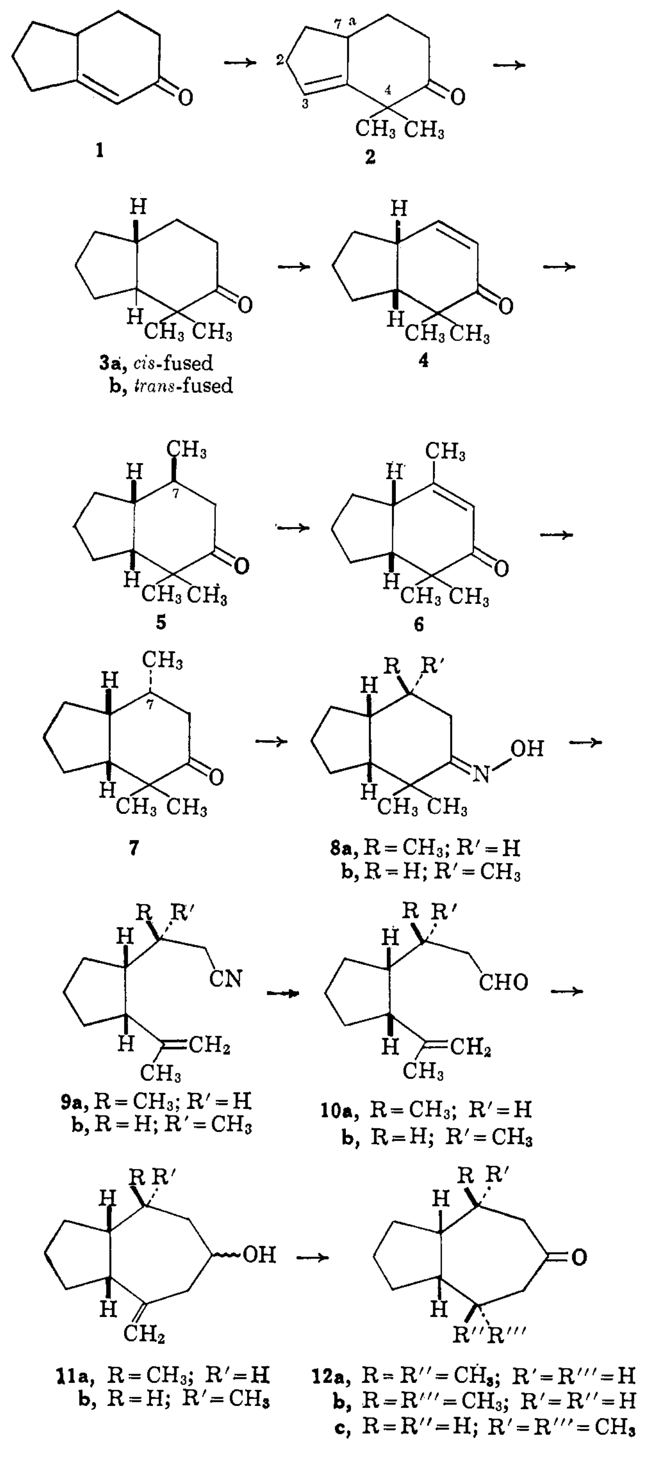
(3) Notably hinesol: W. Z. Chow, O. Motl, and F. Šorm, *Collection Czech. Chem. Commun.*, **27**, 1914 (1962); I. Yosioka, H. Hikano, and Y. Sasaki, *Chem. Pharm. Bull.* (Tokyo), **9**, 84 (1961), and previous papers. Bicyclovetivenol: G. Chiurdoglu and J. Decot, *Tetrahedron*, **4**, 1 (1958). α-Isovetivenene and β-isovetivenene: ref 2d.

(4) *Cf.* J. A. Marshall and N. H. Andersen, *J. Org. Chem.*, **31**, 667 (1966).

(5) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

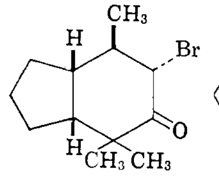
(6) G. Stork, P. Rosen, H. Goldman, R. V. Coombs, and J. Tsuji, *ibid.*, **87**, 275 (1965).

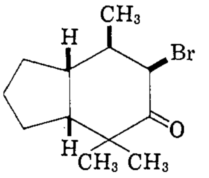
Chart I

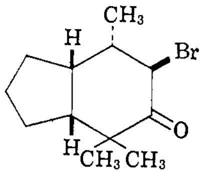


substance yielded the corresponding conjugated ketone **6** *via* bromination and subsequent dehydrobromination.[4] Expectedly, reduction of this conjugated ketone with lithium in ammonia[7] regenerated the saturated ketone **5**, whereas hydrogenation (Pd-C in ethanol) gave a new ketone **7** [$\lambda_{\max}^{\text{film}}$ 5.86 (CO), 8.90, 9.48, and 11.70 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 1.15, 0.98 (C-4 dimethyl, two singlets), and 0.93 ppm (C-7 methyl doublet, J = 5.7 Hz)], which readily afforded its conjugated ketone progenitor **6** upon bromination–dehydrobromination.[4]

Previous studies[4] provide a basis for the *a priori* assignment of stereochemistry to ketone **5**. The spectral properties of the α-bromo ketones derived from **5** and **7** support this assignment. Thus ketone **5** affords bromo derivatives **13a** [mp 97–98°, $\lambda_{\max}^{\text{KBr}}$ 5.81 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 4.77 ppm (H-6 doublet, $J_{6,7}$ = 11.2 Hz)], an equatorial α-bromo ketone,[4] and **13b** [$\lambda_{\max}^{\text{film}}$ 5.86 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 4.20 ppm (H-6 doublet, $J_{6,7}$ = 2.4 Hz)], an axial α-bromo ketone,[4] in the ratio 6:1 upon bromination in acetic acid. In contrast, ketone **7** yields only an equatorial bromo ketone **14** [$\lambda_{\max}^{\text{film}}$ 5.81 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 4.10 ppm (H-6 doublet, $J_{6,7}$ = 12.2 Hz)] under these conditions.


13a


13b


14

We recently reported[8] the conversion of hydrindanone **5** to hydroazulenol **11a** *via* fragmentation of the oxime derivative **8a** (mp 150°) to nitrile **9a** in pyridine containing *p*-toluenesulfonyl chloride, reduction of this nitrile with diisobutylaluminum hydride,[9] and cyclization of the resulting aldehyde **10a** with stannic chloride in benzene. The epimeric hydrindanone **7** was transformed in a similar manner to the oxime **8b** (mp 98°), nitrile **9b**, aldehyde **10b**, and hydroazulenol **11b** [$\lambda_{\max}^{\text{film}}$ 2.95 (OH), 3.25 (C=CH$_2$), 6.11 (C=C), 9.45, 9.61, 9.75, 11.23 (C=CH$_2$), 12.42, and 12.55 μ]. Aldehyde **10b**, like its methyl epimer **10a**, afforded principally one isomer (95% according to the gas chromatogram) in the cyclization step.

Catalytic hydrogenation (Pt in ethanol) of unsaturated alcohol **11a** afforded a mixture (*ca.* 1:1) of two dihydro compounds (methyl epimers) which, in turn, gave ketones **12a** [$\lambda_{\max}^{\text{film}}$ 5.88 (CO), 8.86, 9.12, 9.32, and 9.60 μ] and **12b** [$\lambda_{\max}^{\text{film}}$ 5.88 (CO), 8.85, and 9.32 μ], respectively, upon oxidation with chromic acid. Similar treatment of unsaturated alcohol **11b** likewise afforded two ketones (in the ratio 40:60) of which the major component was identified by spectra comparison and gas chromatographic behavior (peak enhancement) as one of the ketones obtained from **11a**. This substance must therefore possess *trans* oriented methyl groups as in **12b**. The stereochemistry of the minor ketone **12c** [$\lambda_{\max}^{\text{film}}$ 5.90 (CO), 8.50, 8.70, 8.9, 9.21, and 9.34 μ] follows from its hydrindanone precursor **7**.

(−)-β-Vetivone was secured from vetivert acetate, Java origin, and identified by its melting point,[2a,b] optical rotation,[2a,b] infrared spectrum,[2e,10] and nmr spectrum.[2e]

Following the hydrogenation–ozonolysis sequence reported by Pfau and Plattner,[2a] we converted (−)-β-vetivone first to the *meso*-dihydro alcohol [a 65:35 mixture of alcohol epimers, mp 68–74°; $\lambda_{\max}^{\text{KBr}}$ 3.1 (OH), 9.7, 10.40, 10.61, 10.93, and 12.61 μ], and then to the desisopropylidene compound [$\lambda_{\max}^{\text{film}}$ 2.94 (OH), 5.77 (CO), 9.74, 10.92, and 12.18 μ]. The thioketal derivative of this hydroxy ketone afforded the alcohol upon desulfurization (H$_2$, Raney nickel). Oxidation with chromic acid then gave the desired ketone, *meso*-desisopropylidenedihydro-β-vetivone [$\lambda_{\max}^{\text{film}}$ 5.81 (CO), 8.63, 8.75, 10.24, 10.72, and 11.67 μ]. The infrared spectrum

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(7) *Cf.* G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, **86**, 1761 (1964).

(8) J. A. Marshall and N. H. Andersen, *Tetrahedron Letters*, 1219 (1967).

(9) *Cf.* L. I. Zakharkin and I. M. Khorlina, *Dokl. Akad. Nauk SSSR*, 116, 422 (1957); *Chem. Abstr.*, 52, 8040*f* (1958).

(10) J. C. Nigam and L. Levi, *Can. J. Chem.*, 40, 2083 (1962).

of this substance clearly differed from that of its alleged synthetic counterpart **12a** and the isomers thereof (**12b** and **c**).

Reduction of (−)-β-vetivone with lithium in ammonia–ethanol afforded principally a new dihydro alcohol [40% yield, $\lambda_{\max}^{\text{film}}$ 3.00 (OH), 9.71, 10.38, and 11.05 μ] along with one of the previously obtained *meso* dihydro alcohols (15% yield) and recovered starting material. Degradation of this new dihydro alcohol along the lines described above for the *meso* compound afforded a new desisopropylidenedihydro-β-vetivone [$\lambda_{\max}^{\text{film}}$ 5.81 (CO), 8.64, and 9.6 μ] whose infrared spectrum bore no close resemblance to that of its supposed racemic counterpart **12b** or the synthetic *meso* compounds **12a** and **c**.

In view of the nonidentity of our naturally derived and synthetic ketones we must conclude that β-vetivone cannot be represented by I or a stereoisomer thereof. Evidence which supports a spiro[4.5]decane skeleton for this substance and its relatives is presented in the following paper.

Acknowledgments. We thank the Public Health Service for supporting this work through a research grant (AI04965, Division of Allergy and Infectious Diseases) and predoctoral fellowships. We are indebted to Dr. S. K. Freeman (International Flavors and Fragrances, Inc., New York, N. Y.) for generous samples of vetivert acetate.

(11) (a) Alfred P. Sloan Foundation Fellow; (b) Public Health Service Fellow of the National Institute of General Medical Sciences.

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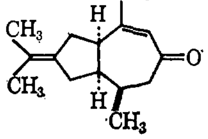
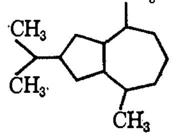
The Structure of β-Vetivone and Related Vetivane Sesquiterpenes

Sir:

The preceding report[1] summarizes synthetic and degradative work refuting the previously proposed structure (I) for β-vetivone[2] and those related sesquiterpenes whose carbon skeletons hinge on their correlation with "isovetivane" (II).[3] In this earlier work we noted that the carbonyl absorption ($\lambda_{\max}$ 5.81 μ) of dihydro-β-vetivone and desisopropylidenedihydro-β-vetivone seemed better accommodated by a cyclohexanone than a cycloheptanone as previously formulated.[1] We therefore sought alternative structures for these substances based on cyclohexanone. With this in mind and after considering the wealth of chemical and physical data recorded for β-vetivone,[1,2] we decided on the spiro[4.5]decanes III and IV as likely possibilities.

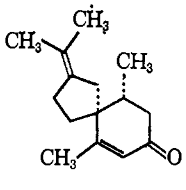


I

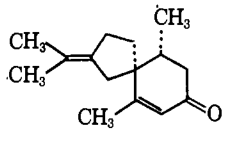


II

Chart I summarizes the transformations which verify this proposal and allow us to choose III as the correct structure.

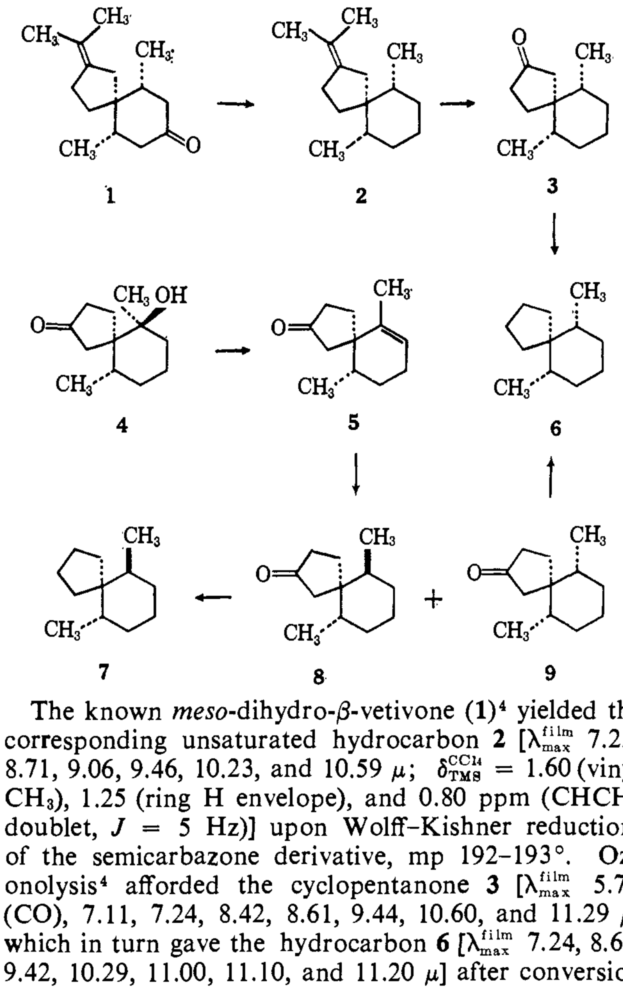


III



IV

Chart I



The known *meso*-dihydro-β-vetivone (**1**)[4] yielded the corresponding unsaturated hydrocarbon **2** [$\lambda_{\max}^{\text{film}}$ 7.25, 8.71, 9.06, 9.46, 10.23, and 10.59 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 1.60 (vinyl CH_3), 1.25 (ring H envelope), and 0.80 ppm ($CHCH_3$ doublet, J = 5 Hz)] upon Wolff–Kishner reduction[5] of the semicarbazone derivative, mp 192–193°. Ozonolysis[4] afforded the cyclopentanone **3** [$\lambda_{\max}^{\text{film}}$ 5.75 (CO), 7.11, 7.24, 8.42, 8.61, 9.44, 10.60, and 11.29 μ] which in turn gave the hydrocarbon **6** [$\lambda_{\max}^{\text{film}}$ 7.24, 8.68, 9.42, 10.29, 11.00, 11.10, and 11.20 μ] after conversion to the ethylene thioketal derivative and desulfurization with W-2 Raney nickel[6] in refluxing ethanol.

We secured an authentic sample of the spiro[4.5]decane **6** from hydroxy ketone **4**,[7] a known photochemical transformation product of *trans*-4a,8-dimethyl-5,6,7,8-tetrahydro-2(4aH)-naphthalenone. Dehydration with thionyl chloride in pyridine led to a mixture of olefins [$\lambda_{\max}^{\text{film}}$ 5.75 (CO), 7.11, 7.24, 8.6, 10.12, 10.25, 10.36, 11.06, 11.79, and 12.42 μ], mainly **5** along with a minor amount of the exocyclic double bond isomer. Hydrogenation over palladium on carbon in ethanol afforded a mixture of ketones **8** [$\lambda_{\max}^{\text{film}}$ 5.75 (CO), 7.11, 7.24, 8.53, 8.67, 10.20, 10.50, 10.74, and 11.25 μ] and **9** [$\lambda_{\max}^{\text{film}}$ 5.75, 7.11, 7.24, 8.53, 8.67,

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[1] J. A. Marshall, N. H. Andersen, and P. C. Johnson, *J. Am. Chem. Soc.*, **89**, 2748 (1967).

[2] J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. III, Cambridge University Press, London, 1952, pp 224–232.

[3] *Cf.* M. Romañuk and V. Herout, *Collection Czech. Chem. Commun.*, **25**, 2540 (1960).

[4] A. S. Pfau and P. A. Plattner, *Helv. Chim. Acta*, **23**, 768 (1940).

[5] Huang-Minlon, *J. Am. Chem. Soc.*, **68**, 2487 (1946).

[6] R. Mozingo, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 181.

[7] P. J. Kropp and W. F. Erman, *J. Am. Chem. Soc.*, **85**, 2456 (1963).