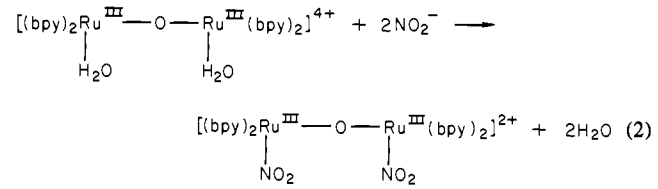


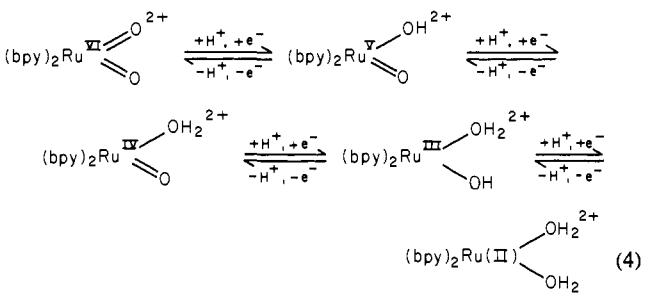
(Ru(III), Ru(III)) couple appears at 0.77 V (vs. SSCE). A second wave appears at 1.20 V, the oxidative component of which appears as a shoulder on a larger catalytic wave involving oxidation of the solvent. Note the solvent background in the absence of dimer and the fact that electrolysis in the presence of dimer leads to visible evolution of O_2 at the electrode.

We have observed that the Ru(III), Ru(III) dimer can also act as a catalyst in the chemical oxidation of H_2O. Upon addition of 50-fold and 100-fold excesses of Ce(IV) to solutions containing 4.1×10^{-5} M dimer in 0.1 M $HClO_4$, O_2 appears rapidly and in the amounts expected based on reaction 3 as monitored by gas

$$4Ce(IV) + 2H_2O \xrightarrow[\text{catalyst}]{Ru} 4Ce(III) + O_2 + 4H^+ \quad (3)$$

chromatography. At the end of the catalytic experiments the dimer was present in its Ru(III), Ru(IV) form as shown spectrophotometrically (λ_{max} 494 nm; ϵ 17 200). With even greater excesses of added Ce(IV), the catalytic ability of the system is eventually lost, apparently due to a breakdown in the dimeric structure. Simple mixing experiments show that addition of 4 equiv of Ce(IV) results in a rapid loss of color followed by a reappearance of color (as the Ru(III), Ru(IV) dimer) both on a time scale of seconds or less. The appearance of O_2 seems to be concomitant with the reappearance of color. The reaction is currently under investigation with use of stopped-flow spectrometry.

There are several available facts that when combined provide a basis for a reasonable understanding of the ability of the dimeric system to oxidize H_2O: (1) The crystal structure of the analogous nitro dimer shows that groups like NO_2 or H_2O are held in close proximity and can approach van der Waals contact distances by allowed molecular motions.[10] It has been concluded that strong electronic coupling across the oxo group exists between ruthenium ions in related oxo-bridged dimers.[8] (2) It is known that higher oxidation states of ruthenium are accessible by a series of sequential electron–proton losses, as observed most dramatically in the $(bpy)_2Ru(H_2O)_2^{2+}$ system[5] (eq 4). Studies of the pH de-



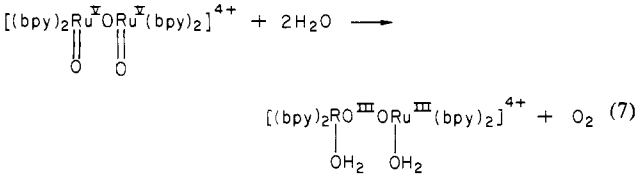
pendences of $E_{1/2}$ values for the dimer over the pH range 0.0–4.6 reveal that the (Ru(III), Ru(IV))/(Ru(III), Ru(III)) and (Ru(IV), Ru(IV))/(Ru(III), Ru(IV)) couples shift reductively by approximately 59 mV/pH decade, suggesting a similar sequence of electron–proton losses for the dimer (eq 5 and 6). It should

$$[(bpy)_2(OH)Ru^{IV}ORu^{III}(H_2O)(bpy)_2]^{4+} + H^+ + e^- \rightarrow [(bpy)_2(H_2O)Ru^{III}ORu^{III}(H_2O)(bpy)_2]^{4+} \quad (5)$$

$$[(bpy)_2(OH)Ru^{IV}ORu^{IV}(OH)(bpy)_2]^{4+} + H^+ + e^- \rightarrow [(bpy)_2(OH)Ru^{IV}ORu^{III}(H_2O)(bpy)_2]^{4+} \quad (6)$$

be stressed, however, that the precise locations of the protons in the dimer are not known at this point, and only the proton content is. (3) Rapid evolution of oxygen occurs only upon addition of 4 or more equiv of Ce(IV), suggesting that the active entity is a four-electron oxidizied intermediate and that there may be two additional one-electron couples following eq 5 and 6.

Given the structural, redox, and reactivity properties of related Ru=O "ruthenyl" systems, we suggest that the reaction may involve an initial four-electron oxidation to give a Ru(V), Ru(V) dimer, which in turn gives O_2 in a concerted four-electron step (eq 7). The mechanism of the reaction is currently under investigation.



The reaction is not confined to the bpy dimer; the analogous 1,10-phenanthroline (phen) dimer, $[(phen)_2(H_2O)Ru^{III}ORu^{III}(H_2O)(phen)_2]^{4+}$, also acts as a catalyst toward the oxidation of water. It is clear that we will be able to vary the redox potentials of the catalyst by varying substituents on the ligands.

The results reported here are notable in that the dimeric Ru complexes may provide models both for the oxygen-evolving site in photosynthesis, which is thought to involve a Mn dimer,[11] and for surface reactions of RuO_2,[12] where the oxidation of water to oxygen is facile and the oxidation of chloride to chlorine is of commercial importance. It is of interest to note that, when oxidized, the oxo-bridged ruthenium dimers also carry out the oxidation of chloride to chlorine in acidic solution, and clearly they will prove to have an extensive chemistry as oxidants.

Acknowledgments are made to the National Institutes of Health under Grant No. 2 ROI GM 15238-15 for support of this research.

Registry No. $[(bpy)_2(H_2O)RuORu(H_2O)(bpy)_2](ClO_4)_4$, 56110-88-4; H_2O, 7732-18-5; Ce, 7440-45-1.

(11) (a) Shafirovich, V. Ya.; Khannanov, N. K.; Shilov, A. E. *Kinet. Katal.* **1978**, 1502. (b) Shafirovich, V. Ya.; Khannanov, N. K.; Shilov, A. E. *Kinet. Katal.* **1978**, 1591.

(12) (a) Kiwi, J.; Gratzel, M. *Chimia* **1979**, *33*, 289. (b) Kalyanasundaram, K.; Gratzel, M. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 701. (c) Kiwi, J.; Borgarello, E.; Pelizzetti, E.; Visca, M.; Gratzel, M. *Ibid.* **1980**, *19*, 646. (d) Lehn, J. M.; Sauvage, J. P.; Ziessel, R. *Nouv. J. Chim.* **1980**, *4*, 355. (e) Mills, A.; Zeeman, M. L.; *J. Chem. Soc., Chem. Commun.* **1981**, 948. (f) Kiwi, J.; Gratzel, M. *Chem. Phys. Lett.* **1981**, *78*, 241.

Alicyclic Claisen Rearrangement. A General Carbocycle Synthesis Based on Four-Atom-Ring Contractions of Lactones

Matthew M. Abelman, Raymond L. Funk,* and John D. Munger, Jr.

Department of Chemistry
University of Nebraska-Lincoln
Lincoln, Nebraska 68588-0304
Received March 1, 1982

The Claisen rearrangement has enjoyed extensive application in organic synthesis, primarily in the stereocontrolled synthesis of cyclic natural products or acyclic substructural units.[1] In contrast to these examples, the reaction has seen limited application in the construction of the *carbocyclic* ring systems of natural products.[2] However, the exceptional syntheses of aphidicolin and

(1) (a) Rhoads, S. J.; Raulins, N. R. *Org. React. (N.Y.)* **1975**, *22*, 1. (b) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227. (c) Bennett, G. B. *Synthesis* **1977**, 589.

(2) For the synthesis of six- and seven-membered carbocycles using the Claisen rearrangement, see: (a) Buchi, G.; Powell, J. E., Jr. *J. Am. Chem. Soc.* **1967**, *89*, 4559. (b) Buchi, G.; Powell, J. E., Jr. *Ibid.* **1970**, *92*, 3126. (c) Ireland, R. E.; Godfrey, J. D., Thaisrivongs, S. *Ibid.* **1981**, *103*, 2446. (d) Danishefsky, S.; Funk, R. L.; Kerwin, J. R., Jr. *Ibid.* **1980**, *102*, 6889. (e) Danishefsky, S.; Tsuzuki, K. *Ibid.* **1980**, *102*, 6891. (f) Rhoads, S. J.; Watson, J. M. *Ibid.* **1971**, *93*, 5813. (g) Demole, E.; Enggist, P. *J. Chem. Soc., Chem. Commun.* **1969**, 264. (h) Marvell, E. N.; Titterington, D. *Tetrahedron Lett.* **1980**, *21*, 2123.

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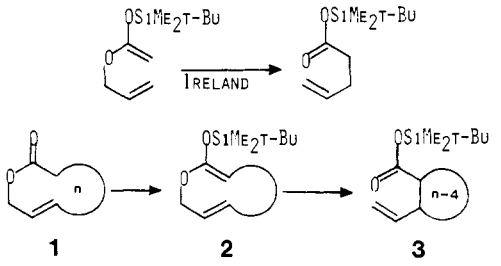
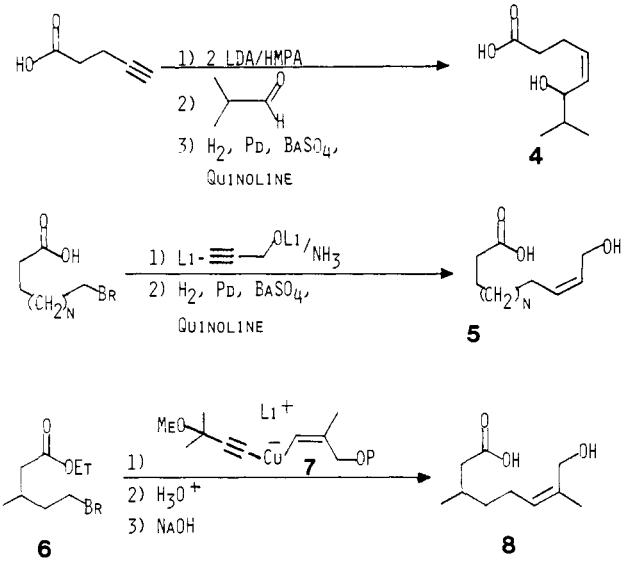
Scheme I



Scheme II

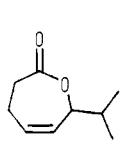
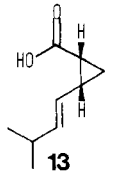
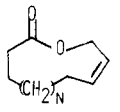
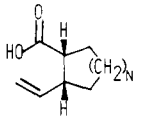
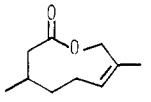
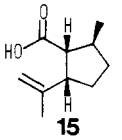
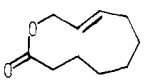
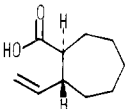


widdrol by the Ireland[2c] and Danishefsky[2e] groups, respectively, document the considerable potential of Claisen-mediated carbocycle synthesis.

Our studies in this area have focused on a new Claisen variant conceptualized in Scheme I. This approach involves the rearrangement of modified Ireland[3] substrates, **2** → **3**, wherein the terminal carbons have been connected by a carbon chain.[4] Thus, all six atoms participating in the sigmatropic rearrangement are incorporated into a ring, hence the term *alicyclic* Claisen rearrangement. The medium- or large-ring lactones[5] **1** are the obvious precursors of the cyclic ketene acetals **2**, and therefore the overall method represents a unique four-atom heterocyclic → carbocyclic ring-contraction procedure.[6] We now report the realization of such a process.

The medium and large ring lactones **9–12** were prepared by cyclization of the corresponding ω-hydroxy acids using the Mukaiyama reagent (2-chloro-1-methylpyridinium iodide).[7] The requisite hydroxy acids were obtained from one of three routes outlined in Scheme II. Full experimental details for the preparation of the hydroxy acids **4**, **5**, and **8** are available in the supplementary material.

Table I. Alicyclic Claisen Rearrangements

Entry	Lactone	Yield[a] (%)	Cycloalkane Carboxylic Acid	Yield[a] (%)
1.	 **9**	61	 **13**	89
2.	 **10a** n=1	41	 **14a**	70
3.	**10b** n=2	49	**14b**	81
4.	**10c** n=3	53	**14c**	91
5.	**10d** n=4	45	**14d**	82
6.	**10e** n=7	82	**14e** + TRANS	98 (cis:trans 76:24)
7.	 **11**	72	 **15**	71
8.	 **12**	28	 **16** + **14c**	79 (cis:trans 41:59)

[a] Isolated yields of purified products. Infrared, 90-MHz ^{1}H NMR, ^{13}C NMR, and high-resolution mass spectral data were fully consistent with the assigned structures.

The scope of this new ring-contractive carbocycle synthesis is delineated in Table I. The silyl ketene acetals, prepared from the lactone enolates by using the standard procedure,[3] typically rearranged before or during workup to the corresponding silyl esters, which were then hydrolyzed with HF (2 equiv) in CH_3CN. However, the large-ring ketene acetals derived from lactones **10d** and **10e** were isolable and required heating in toluene at 110 ($t_{1/2}$ ~ 6 h) and 80 °C ($t_{1/2}$ ~ 7 h), respectively, to effect rearrangement. In most of the cases examined only the cycloalkane with cis alkenyl and carboxyl groups is obtained.[8] However, the high internal asymmetric induction[11] erodes significantly when the size of the cyclic ketene acetal is relatively large (entry 6) or when a trans double bond is within the heterocyclic ring (entry 8).

(3) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868.

(4) This type of Claisen rearrangement is not entirely without precedent; e.g., 2,5-dihydrooxepin and *cis*-2-ethenylcyclopropanecarboxaldehyde have been reported to form a 5:95, respectively, equilibrium mixture: Rhoads, S. J.; Cockroft, R. D. *J. Am. Chem. Soc.* **1969**, *91*, 2815.

(5) A number of methods are now available for the synthesis of macrolactones. For two excellent reviews on the subject, see: (a) Nicolaou, K. C. *Tetrahedron* **1977**, *33*, 683. (b) Masamune, S.; Bates, G. S.; Corcoran, J. W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 585.

(6) The analogous Cope rearrangements of 1,5-cyclononadienes and 1,5-cyclodecadienes, a four-carbon carbocyclic → carbocyclic ring-contraction process, have been well studied; see ref 1a. The anionic oxy-Cope ring contraction of *cis,cis,cis*-2,4,7-cyclononatrienol has recently been featured as the key step in the total synthesis of various cyclopentanoid natural products; see: (a) Paquette, L. A.; Crouse, G. D. *Tetrahedron* **1981**, *37*, supp 1, 281. (b) Paquette, L. A.; Crouse, G. D. *J. Org. Chem.* **1981**, *46*, 4272.

(7) Mukaiyama, T.; Usui, M.; Saigo, K. *Chem. Lett.* **1976**, 49. The lactones **10a-d** are quite volatile, and therefore, the yields may actually be higher. The cis double bond apparently facilitates the lactonization since only trace amounts of diolides are formed, and yields for the nine-membered lactones **10a** and **11** are considerably higher than those reported by this and other procedures[5] for the saturated nine-membered lactone.

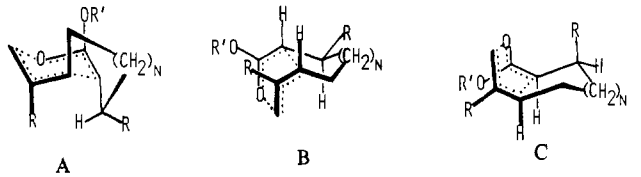
(8) Product stereochemical integrity is based on analysis of the ^{13}C NMR spectra of the cycloalkanecarboxylic acids as well as HPLC and GC analysis of the derived methyl esters (CH_2N_2). The stereochemical assignments for **13**, **14a**, and **14b** are based on the epimerization (NaOMe, MeOH) of the methyl esters to the more stable trans isomers. The assigned (*E*)-olefin stereochemistry of **13** is indicated by a vicinal coupling constant of 15.4 Hz for the olefin protons. The stereochemical assignments for **14c** and **14d** rest on transformation to the corresponding dimethyl *cis*-cycloalkane diesters ((1) CH_2N_2, Et_2O; (2) $RuCl_3$·$(H_2O)_n$, $NaIO_4$, CCl_4, CH_3CN, H_2O;[9] (3) CH_2N_2, Et_2O) and comparison of the ^{13}C NMR spectra with the previously reported ^{13}C NMR data for these diesters.[10] The stereochemical assignment for **14e,f** rests on analogy with **14a–d** and should be regarded as tentative. The stereochemistry of **15** is based on conversion to (±)-dihydronepetalactone and acetate **19**, vide infra.

(9) Carlsen, P. H. J.; Katsuki, R.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

(10) James, D. E.; Stille, J. K. *Ibid.* **1976**, *41*, 1504.

(11) For a definition of this term, see: Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2.

The preferential formation of the *cis*-2-alkenylcycloalkanecarboxylic acids (entries 1–7) can be understood by examining the possible transition states for rearrangement of the ketene acetals obtained upon silylation of the assumed (*Z*)-lithio lactone enolates.[12] Molecular models indicate the chairlike transition-state A to be much more strained than the boatlike transition-state B.

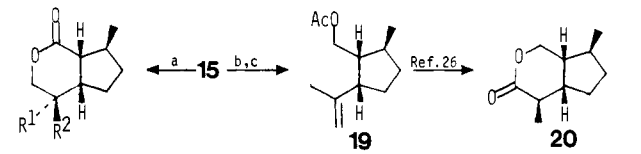


A B C

R′ = $SiMe_2T$-Bu

Transition-state A is accessible only when the diaxially bridging methylene chain becomes sufficient in length (n = 7, R = H). The preferential formation of the trans isomer from lactone **12** (entry 8) can be similarly rationalized. In this case, the analogous boatlike transition state for the ketene acetal derived from lactone **12** (not shown) ultimately leads to the trans carboxylic acid **16**. This boatlike transition state is understandably less highly favored since the analogous chairlike transition state now has a less strained axial, equatorial bridging methylene arrangement. Finally, the exclusive (>98%) formation of the *cis,trans*-cyclopentanecarboxylic acid **15** is a consequence of preferential rearrangement through boatlike transition state B (n = 1, R = Me) as opposed to the alternative boat conformer C (n = 1, R = Me) in which a serious $A^{(1,3)}$ type interaction[14] between the endocyclic oxygen atom and pseudoaxial methyl group is encountered, thereby precluding the eventual formation of the *cis,cis*-cyclopentanecarboxylic acid isomer. Similar relative asymmetric induction[11] is involved in the exclusive formation of the (*E*)-olefin stereochemistry in cyclopropanecarboxylic acid **13**.

The cyclopentanecarboxylic acid **15** is a useful substrate for the preparation of cyclopentanoid terpene lactones.[15] Thus, stereoselective hydroboration (2 equiv of $(C_6H_{11})_2BH$) of **15** with oxidative workup (NaOH, H_2O_2) directly provided the previously unsynthesized terpenes of *Nepeta cataria* (catnip oil),[16] (±)-dihydronepetalactone (**17**) and (±)-isodihydronepetalactone (**18**),



17 R^1=Me, R^2=H

18 R^1=H, R^2=Me

a) $(C_6H_{11})_2BH$; H_2O_2, NaOH b) LAH c) Ac_2O, pyr

in a 93:7 ratio, respectively (75%).[17] Alternatively, reduction ($LiAlH_4$) of carboxylic acid **15** followed by acetylation provided the known acetate **19**,[18] which was identical (^1H NMR, ^{13}C NMR, IR) with an authentic sample.[18] The acetate **19** has been converted to iridomyrmecin (**20**),[18] an insecticidal iridoid isolated from the Argentinian ant *Iridomyrmex humilis*. Therefore, this route constitutes a formal total synthesis of this cyclopentanoid terpene as well.

In summary, the methodology described herein represents a general and stereocontrolled route to multisubstituted cycloalkanes. Additional stereochemical control by remote chirality seems possible. Moreover, the potential for extending this process to the synthesis of heterocycles clearly exists. These topics in addition to the application of this methodology in natural product synthesis are under investigation.

Acknowledgment. We thank the University of Nebraska Research Council for initial financial and material support and the National Institutes of Health (Grant No. GM 28663) for current support. High-field (360 MHz) ^1H NMR spectra were obtained on a spectrometer purchased with funds provided, in part, by the National Science Foundation (CHE-80-24328). We thank Professor J. Wolinsky for furnishing authentic spectra of iso- and dihydronepetalactone.

Registry No. (±)-**4**, 81987-42-0; (±)-**8**, 81987-43-1; (±)-**9**, 81987-44-2; **10a**, 41979-97-9; **10b**, 41979-98-0; **10c**, 41979-99-1; **10d**, 81987-45-3; **10e**, 81987-46-4; **10e** *tert*-butyldimethylsilyl ketene acetal, 81987-47-5; (±)-**11**, 81987-48-6; **12**, 41980-03-4; (±)-**13**, 81987-49-7; (±)-**14a**, 81987-50-0; (±)-**14b**, 81987-51-1; (±)-**14c**, 81987-52-2; (±)-**14d**, 81987-53-3; (±)-*cis*-**14e**, 82010-05-7; (±)-*trans*-**14e**, 82043-25-2; (±)-**15**, 82041-92-7; (±)-**16**, 81987-54-4; 4-pentynoic acid, 6089-09-4; isobutyraldehyde, 78-84-2; (±)-6-hydroxy-7-methyl-4-octynoic acid, 81987-55-5; (*Z*)-3-iodo-2-methyl-2-propen-1-ol ethoxyethyl ether, 81987-56-6; 3-methyl-3-methoxy-1-butyne, 13994-57-5; ethyl 4-iodo-3-methylpentanoate, 81987-57-7; ethyl (±)-*Z*-8-hydroxy-3,7-dimethyl-6-octenoate, 81987-58-8; **10d** *tert*-butyldimethylsilyl ketene acetal, 81987-59-9.

Supplementary Material Available: Experimental details for the preparation of hydroxy acids **4**, **5**, and **8**, and full spectral data for all compounds listed in Table I (9 pages). Ordering information is given on any current masthead page.

Mechanism of Carbon Monoxide Substitution in a Metal Radical: Vanadium Hexacarbonyl

Qi-Zhen Shi,[1a] Thomas G. Richmond,[†1b] William C. Trogler,*[1b] and Fred Basolo*[1b]

Department of Chemistry, Northwestern University Evanston, Illinois 60201

Received April 9, 1982

Metal carbonyl radicals are postulated intermediates in a variety of catalytic and stoichiometric chemical transformations.[2] Although the substitution lability of 17-electron organometallic radicals has been recognized,[3,4] the precise mechanisms available are not well defined. For example, for the group 7 radicals $M(CO)_5$· (M = Mn, Re) both dissociative[3] and associative[4] substitution pathways have been proposed. Recent work favors an associative mechanism for substitution processes in $Re(CO)_5$·[4a] and $Mn(CO)_3L_2$·[4c] species. Part of the difficulty in quantitatively discerning reactivity patterns of these radicals lies in the inherent

(12) Molecular mechanics calculations predict the (*Z*)-enolate of macrolactones to be highly preferred over the (*E*)-enolate isomer.[13] Highly stereoselective kinetic alkylations of nine- and thirteen-membered lactone enolates support this prediction.[13] Furthermore the (*Z*)-enolate is kinetically preferred even in acyclic ester enolizations.[3]

(13) Still, W. C.; Galynker, I. *Tetrahedron* **1981**, *37*, 3981.

(14) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

(15) For reviews see: (a) Taylor, W. I.; Battersby, A. R. "Cyclopentanoid Terpene Derivatives"; Marcell Dekker: New York, 1961. (b) Ap Simon, J. "The Total Synthesis of Natural Products"; Wiley-Interscience: New York, 1973, Vol. 2, p 62. (c) Wagner, H.; Wolff, P. "New Natural Products and Plant Drugs with Pharmacological Biological or Therapeutical Activity"; Springer-Verlag: Berlin, 1977; p 137.

(16) Wolinsky, J.; Dickerson, D.; Slabaugh, M.; Nelson, D.; Sakan, T.; Isoe, S.; Hyeas, S. B.; Katsumura, R. *Tetrahedron Lett.* **1965**, *46*, 4097.

(17) The ^1H NMR and IR spectra were identical with authentic spectra kindly provided by J. Wolinsky, Purdue University.

(18) Wolinsky, J.; Gibson, T.; Chan, D.; Wolf, H. *Tetrahedron* **1965**, *21*, 1247.

[†] NSF Predoctoral Fellow, 1980–1983.

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