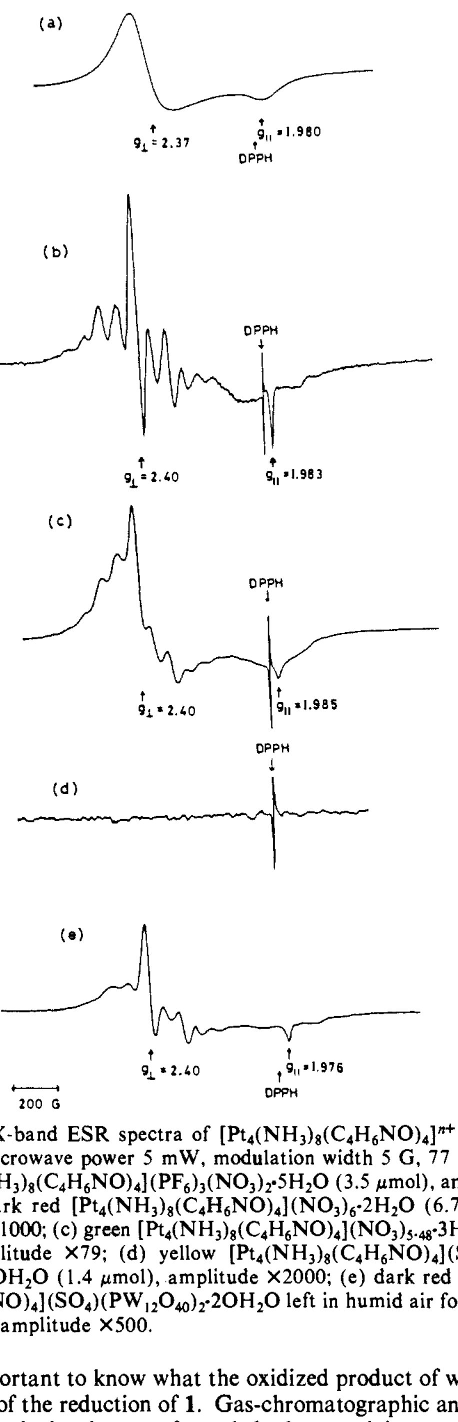

Figure 2. X-band ESR spectra of $[Pt_4(NH_3)_8(C_4H_6NO)_4]^{n+}$ powder samples (microwave power 5 mW, modulation width 5 G, 77 K): (a) blue $[Pt_4(NH_3)_8(C_4H_6NO)_4](PF_6)_3(NO_3)_2 \cdot 5H_2O$ (3.5 μmol), amplitude ×50; (b) dark red $[Pt_4(NH_3)_8(C_4H_6NO)_4](NO_3)_6 \cdot 2H_2O$ (6.7 μmol), amplitude ×1000; (c) green $[Pt_4(NH_3)_8(C_4H_6NO)_4](NO_3)_{5.48} \cdot 3H_2O$ (5.1 μmol), amplitude ×79; (d) yellow $[Pt_4(NH_3)_8(C_4H_6NO)_4](SO_4)(PW_{12}O_{40})_2 \cdot 2OH_2O$ (1.4 μmol), amplitude ×2000; (e) dark red $[Pt_4(NH_3)_8(C_4H_6NO)_4](SO_4)(PW_{12}O_{40})_2 \cdot 2OH_2O$ left in humid air for 7 days (1.4 μmol), amplitude ×500.

It is important to know what the oxidized product of water is, as a result of the reduction of **1**. Gas-chromatographic analysis[13] of the gas in the head space of a sealed tube containing an aqueous solution of **4** showed that molecular oxygen is generated. Typically, 1.8 × 10^{-5} mol of $[Pt_4(NH_3)_8(C_4H_6NO)_4](SO_4)_2(ClO_4)_4 \cdot 6H_2O$, dissolved in 0.1 mL of H_2O and placed in a 3-mL sealed tube, gradually turned dark red and concomitantly O_2 was generated. The final O_2 amount detected was 2.9 × 10^{-6} mol. The visible and ultraviolet absorption spectrum of the solution after O_2 generation shows that the platinum species in the solution is a mixture of **1** and **4**. Addition of Ce(IV) almost quantitatively restores the original spectrum of **4**. Therefore, the reaction would be described as follows:

$$2[Pt_4(NH_3)_8(C_4H_6NO)_4]^{8+} + 2H_2O \rightleftarrows 2[Pt_4(NH_3)_8(C_4H_6NO)_4]^{6+} + O_2 + 4H^+$$

(13) Column packing, Molecular Sieve 5A; carrier gas, Ar, 50 mL min^{-1}; column temperature, 30 °C; injection port temperature, 30 °C; TCD detector, 70 °C, 80 mA; retention time 1.14 min. Small amount of air leak was estimated by measuring both N_2 and O_2.

The backward reaction has been reported previously.[4] Mass spectrometric analysis[14] of the O_2 gas generated from the reaction of $H_2{}^{18}O$ with **4** confirmed that the oxygen really comes from water.

(14) GC MS was carried out with the same conditions as in ref 13, except that He was used as carrier gas instead of Ar. Both $^{18}O_2$ and $^{18}O^{16}O$ were detected.

Formation of N^{21},N^{22}-Etheno Bridged Porphyrins by the Reaction of Cobalt(III) Porphyrin π-Cation Radicals with Alkynes

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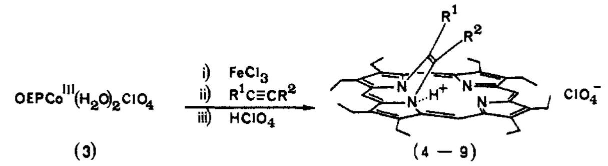
Metalloporphyrin π-cation radicals have been the focus of recent studies directed to elucidate the structure and function of hemoproteins.[1] In the case of cobalt octaethylporphyrin (OEP), two types of Co(III) π-cation radicals, $[OEPCo^{III}]^{2+}2Br^-$ (**1**) and $[OEPCo^{III}]^{2+}2ClO_4^-$ (**2**), have been regarded as representative of $^2A_{1u}$ and $^2A_{2u}$ states, respectively, on the basis of optical and ESR evidence, and the similarity of their optical absorption spectra to those of catalase compound I (CAT-I) and horseradish peroxidase compound I (HRP-I) was noted.[1a] NMR study of **1** and **2** was recently undertaken and the results were interpreted in terms of a thermal equilibrium of $^2A_{1u}$ and $^2A_{2u}$ states with the greater contribution being placed on $^2A_{1u}$ state for **2** in contrast to the previous formulation.[1i] From the viewpoint of reaction behavior, the reaction that is characteristic of metalloporphyrin π-cation radical is rather unknown and the cobalt(III) porphyrin π-cation radicals **1** and **2** have never been reported to react in a different manner, while π-dications of metalloporphyrins are known to react with nucleophiles giving meso-substituted metalloporphyrins via isoporphyrins as intermediates.[1b]

The present study demonstrates that **2** prepared by the oxidation of divalent and trivalent cobalt porphyrins with ferric perchlorate reacted smoothly with alkynes to give N^{21},N^{22}-etheno bridged octaethylporphyrins whereas **1** did not react at all.

An excess amount of alkynes was added to the reaction mixture of $OEPCo^{III}(H_2O)_2ClO_4$[2] (**3**) and $FeCl_3$ (1–2 equiv) in CH_2Cl_2 to result in the color change to reddish green immediately. The mixture was washed with 10% $HClO_4$ solution and then purified by chromatography on silica gel with $CHCl_3$–acetone (5:1). Table I summarizes the yields and the ^1H NMR data of the products **4–9** which were prepared from acetylene, 1-hexyne, propargyl



(3) (4 – 9)

(1) (a) Dolphin, D.; Forman, A.; Borg, D. C.; Fajer, J.; Felton, R. H. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 614. (b) Dolphin, D.; Muljiani, Z.; Rousseau, K.; Borg, D. C.; Fajer, J.; Felton, R. H. *Ann. N.Y. Acad. Sci.* **1973**, *206*, 177. (c) Dolphin, D.; Felton, R. H. *Acc. Chem. Res.* **1974**, *7*, 26. (d) Gans, P.; Marchon, J.-C.; Reed, C. A.; Regnard, J. R. *Nouv. J. Chim.* **1981**, *5*, 203. (e) Phillippi, M. A.; Shimomura, E. T.; Goff, H. M. *Inorg. Chem.* **1981**, *20*, 1322. (f) Buisson, G.; Deronzier, A.; Duee, E.; Gans, P.; Marchon, J.-C.; Regnard, J.-R. *J. Am. Chem. Soc.* **1982**, *104*, 6793. (g) Scholz, W. F.; Reed, C. A.; Lee, Y. J.; Scheidt, W. R.; Lang, G. *Ibid.* **1982**, *104*, 6791. (h) Fujita, I.; Hanson, L. K.; Walker, F. A.; Fajer, J. *Ibid.* **1983**, *105*, 3296. (i) Morishima, I.; Takamuki, Y.; Shiro, Y. *Ibid.* **1984**, *106*, 7666. (j) Groves, J. T.; Quinn, R.; McMurry, T. J.; Nakamura, M.; Lang, G.; Bolo, B. *Ibid.* **1985**, *107*, 354.

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Table I. Yields and ^{1}H NMR Data of N^{21},N^{22}-ethenoOEP Hydroperchlorates **4–9**

				^{1}H chem shifts, δ^a		
	R^1	R^2	yield, %	meso H	vinyl H	other R^1 (R^2)
4	H	H	52	10.24 (s, 1 H), 10.60 (s, 2 H) 10.87 (s, 1 H)	−2.60 (s, 2 H)	
5	H	n-C_4H_9	50	10.19 (s, 1 H), 10.55 (s, 1 H) 10.69 (s, 1 H), 10.73 (s, 1 H)	−2.39 (s, 1 H)	−0.26 (t, 3 H), −1.25 (m, 2 H) −1.58 (m, 1 H), −2.03 (m, 1 H) −3.50 (m, 1 H), −3.95 (m, 1 H)
6	H	CH_2OH	48	10.53 (s, 1 H), 10.89 (s, 1 H) 11.08 (s, 1 H), 11.16 (s, 1 H)	−2.14 (s, 1 H)	−1.64 (m, 1 H), −1.92 (m, 1 H)
7	CH_2OH	CH_2OH	50	10.22 (s, 1 H), 10.84 (s, 3 H)		−0.45 (m, 2 H), −2.29 (m, 2 H)
8	H	C_6H_5	44	10.33 (s, 1 H), 10.38 (s, 1 H) 10.72 (s, 1 H), 11.07 (s, 1 H)	−2.34 (s, 1 H)	5.74 (t, 2 H), 6.21 (t, 1 H)^b
9	C_6H_5	C_6H_5	71	10.23 (s, 2 H), 10.48 (s, 1 H) 11.18 (s, 1 H)		2.30 (d, 4 H), 5.67 (t, 4 H) 6.10 (t, 2 H)

^{a}Measured in $CDCl_3$. ^{b}2 H signals due to ortho-phenyl protons are overlapped with the ethyl signals.

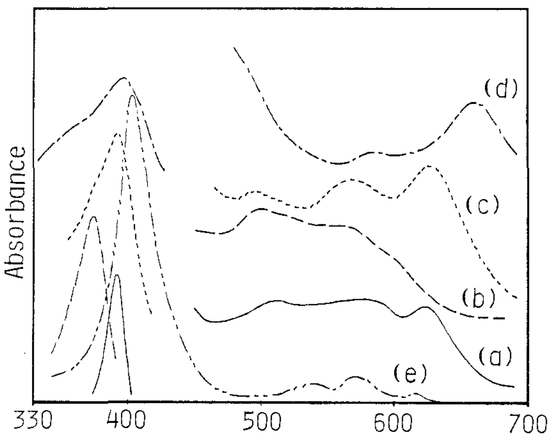
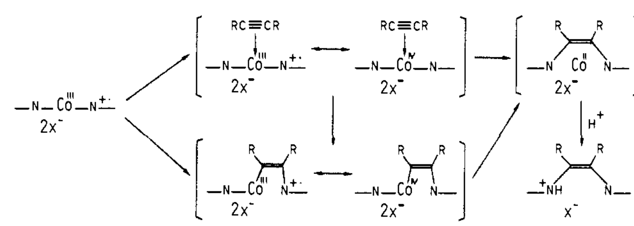


Figure 1. Visible absorption spectra, in CH_2Cl_2, of (a) $[OEPCo^{III}]^{2+}$-$2ClO_4^-$ (—), (b) the reaction mixture of $OEPCo^{II}$ and $FeCl_3$ (– – –), (c) $[OEPCo^{III}]^{2+}Cl^-ClO_4^-$ (- - -), (d) $[OEPCo^{III}]^{2+}2Cl^-$ (– - –), (e) (**9**) (– - - –).

alcohol, 2-butyne-1,4-diol, phenylacetylene, and diphenylacetylene respectively. The visible spectra of these compounds are typical of N-alkyl- and N,N'-dialkylporphyrins[3] (Figure 1e) and the IR spectra showed intense absorptions due to ClO_4^- ion.[4] ^{1}H NMR spectra showed a set of 4 singlets with equal intensity due to the meso protons of the porphyrin ring for **5**, **6**, and **8** which are obtained from unsymmetrical alkynes and a set of three singlets (1:1:2 ratio) for **4** and **9** which are obtained from symmetrical alkynes. A singlet signal at around δ −2.5 is observed for the products obtained from unsubstituted **4** and monosubstituted alkynes **5**, **6**, and **8** but not for those from disubstituted alkynes **7** and **9**. The higher chemical shifts of the protons derived from alkynes attributable to the ring current effect of porphyrin and the splitting patterns of the absorptions due to porphyrin moiety are completely consistent with the structure in which the adjacent two nitrogens of porphyrin are bridged by a 1,2-etheno group with one of the four nitrogens being protonated by $HClO_4$.[5]

When $OEPCo^{II}$ or **3** was treated with ferric perchlorate in CH_2Cl_2, the resulting solution showed the visible spectrum which

Scheme I



is identical with that of the π-cation radical **2**[1a] prepared by electrochemical oxidation in the presence of tetra-n-butylammonium perchlorate (Figure 1a). Whether it is generated chemically by Fe(III) or electrochemically at +1.2 V (vs. Ag/AgCl), the Co(III) π-cation radical **2** reacted with diphenylacetylene to give **9** in 57% or 45% yield.[6] Oxidation of $OEPCo^{II}$ and $OEPCo^{III}Cl$ with $FeCl_3$ in CH_2Cl_2 resulted in the shift of the Soret band to 374 nm (Figure 1b) and this visible spectrum was nearly identical with that observed when **3** was allowed to react with $FeCl_3$. All the cobalt porphyrins treated with $FeCl_3$ gave rise to **9** in similar yields (50–70%) after addition of diphenylacetylene and this is indicative of the formation of similar Co(III) π-cation radicals as active species. Since their optical spectra are quite different from those of the Co(III) π-cation radicals, $[OEPCo^{III}]^{2+}Cl^-ClO_4^-$ and $[OEPCo^{III}]^{2+}2Cl^-$ (Figure 1c,d),[7] the axial coordination sites would not be occupied by chloride, but a noncoordinating counterion like $FeCl_3^-$ seems to exist in these cases. On the other hand, the Co(III) π-cation radical **1**[1a] prepared from $OEPCo^{II}$ and an equimolar amount of Br_2 did not react with diphenylacetylene at all.[8] Thus, the vacancy in the axial coordination site of the Co(III) π-cation radical is crucial for the N-substitution reaction to take place. This points to that the cobalt plays a key role, for example, by forming organocobalt porphyrin intermediates such as an acetylene π-complex of Co(III) π-cation radical and a Co,N-etheno bridged Co(III) π-cation radical.[9] Both intermediates can be described formally as cobalt(IV) porphyrin complexes which rearrange to an N,N'-etheno bridged Co(II) porphyrin via the reductive elimination mechanism as shown in Scheme I.[10]

(3) Grigg, R.; Shelton, G.; Sweeney, A.; Johnson, A. W. *J. Chem. Soc., Perkin Trans 1* **1972**, 1789.

(4) Visible spectrum of **9** in CH_2Cl_2: λ_{max} (log ϵ) 401 (5.13), 535 (3.94), 569 (4.06), 614 (3.63) nm. IR of **9**: 1090, 622 cm^{-1}.

(5) Although one of the authors (J.-i.S.) and Professor D. Dolphin (U.B.C., Vancouver, Canada) reported the formation of N^{21},N^{22}-ethenooctaethylporphyrin from [N-(formylmethyl)octaethylporphyrinato]cobalt(II) complex and described the compound as a $CHCl_3$ adduct of the free base (Setsune, J.-i.; Dolphin, D. *Organometallics* **1984**, *3*, 440), reinvestigation of its IR and microanalysis data has unambiguously shown that it is a monocation with perchlorate, the spectroscopic properties of which proved totally identical with those of **4** obtained here. Satisfactory (C, H, N) analyses were obtained for **4–9**. Free bases of **4–9** turned out to be difficult to isolate because of decomposition during neutralization as is frequently seen for N,N'-disubstituted porphyrins (see ref 9).

(6) This shows that there is no critical role for Fe(III) or Fe(II) and this N-alkylation reaction is essentially due to Co(III) π-cation radicals. When $OEPFe^{III}ClO_4$ or $OEPH_2$ was treated with $FeCl_3$ and diphenylacetylene as a control experiment, there was formed no N-alkylated porphyrin.

(7) $[OEPCo^{III}]^{2+}2Cl^-$ was prepared by the reactions of $OEPCo^{II}$ and $OEPCo^{III}Cl$ with Cl_2 and its visible spectrum is virtually the same as that of $[OEPCo^{III}]^{2+}2Br^-$ (**1**).[1a] $[OEPCo^{III}]^{2+}Cl^-ClO_4^-$ prepared from $OEPCo^{III}Cl$ with ferric perchlorate showed the same optical spectrum as that obtained from **3** with Cl_2, and it reacted with diphenylacetylene to afford **9** in 50% yield.

(8) When triethylbenzylammonium bromide was added to **2** prepared from $OEPCo^{II}$ and ferric perchlorate, the optical spectrum changed stepwisely to that of **1** and the resulting mixture no longer reacted with diphenylacetylene.

(9) The failure for a bulky alkyne such as bis(trimethylsilyl)acetylene to react with the Co(III) porphyrin π-cation radicals is also consistent with the organocobalt intermediate formation rather than electron transfer between acetylene and the π-cation radical as an initial step.

While the syntheses of *N,N'*-bridged porphyrins so far reported are quite limited because of their low yields and poor generality,[11] this work provides a facile synthetic method of novel *N,N'*-ethenoporphyrins with various substituents on the bridge, the structure of which is also of considerable significance in view of the formation of *N,N'-o*-phenylene bridged protoporphyrin IX when cytochrome P-450 enzymes were inactivated with 1-aminobenzotriazole known as a precursor of benzyne.[12] Our efforts to discover the reaction behaviors of metalloporphyrin π-cation radicals are curently in progress.

Acknowledgment. We are grateful to Prof. David Dolphin for providing us with a sample of N^{21},N^{22}-ethenoOEP hydroperchlorate derived from *N*-(formylmethyl)$OEPCo^{II}$.

(10) *N,N'*-Etheno bridged cobalt porphyrins could not be isolated but the hydroperchlorate **9** was obtained even if the 10% $HClO_4$ treatment was omitted in the workup procedure of the reaction of $OEPCo^{II}$, ferric perchlorate, and diphenylacetylene. A similar reductive elimination mechanism can explain the Co-to-N ethyl migration upon one-electron electrochemical oxidation of ethyl(*meso*-tetraphenylporphinato)cobalt(III) giving (*N*-ethyl-*meso*-tetraphenylporphinato)cobalt(II) and cobalt(III) porphyrin π-cation radical has been suggested as an intermediate (Dolphin, D.; Halko, D. J.; Johnson, E. *Inorg. Chem.* **1981**, *20*, 4348).

(11) (a) Johnson, A. W.; Ward, D.; Batten, P.; Hamilton, A. L.; Shelton, G.; Elson, C. M. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2076. (b) Johnson, A. W.; Ward, D. *Ibid.* **1977**, 720. (c) Wisnieff, T. J.; Gold, A.; Evans, S. A., Jr. *J. Am. Chem. Soc.* **1981**, *103*, 5616. (d) Latos-Grazynski, L.; Cheng, R.-J.; La Mar, G. N.; Balch, A. L. *Ibid.* **1981**, *103*, 4270. (e) Lange, M.; Mansuy, D. *Tetrahedron Lett.* **1981**, *22*, 2561. (f) Callot, H. J.; Fischer, J.; Weiss, R. *J. Am. Chem. Soc.* **1982**, *104*, 1272.

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Total Synthesis Necessitates Revision of the Structure of Robustadials

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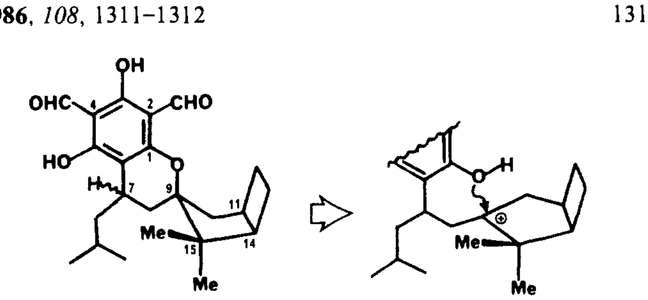
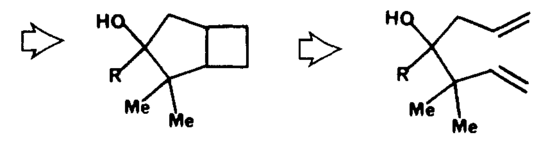
A global resurgence of malaria and the appearance of strains that are resistant to quinine and its analogues provide an urgent need for the identification and total synthesis of new antimalarial natural products. Several active compounds are contained in an antimalarial extract of *Eucalyptus robusta* leaves, a plant used in Chinese herbal medicine.[1] Recently two new compounds isolated from this plant, robustadial A and robustadial B, were assigned bicyclo[3.2.0]heptane structures **1a** and **1b**, respectively, on the basis of NMR, UV, IR, and mass spectral data.[2] We now report the total synthesis of **1a** which we find *not* to be identical with robustadial A, and we postulate a new structure for the natural product.

Presuming that the pyran ring in **1a** could be generated by cyclization of a phenol as in X, our synthetic strategy envisioned a key copper(I)-catalyzed photobicyclization[3] of a diene Z to provide the requisite bicyclo[3.2.0]heptane ring system of Y. Our synthesis of **1a**, outlined in Scheme I[4], built the diene **7** from 1,3,5-trimethoxybenzene (**2**). Friedel-Crafts acylation provided the ketone **3** in which the carbonyl carbon is shielded sterically by two adjacent methoxy groups. Low yields were obtained upon cyanomethylenation of **3** with the anion of (dimethylphosphono)acetonitrile presumably owing to steric congestion.



1a, 7α-H
1b, 7β-H

X



Y Z

However, lithioacetonitrile,[5] a less bulky nucleophile, added to this carbonyl group to give the benzylic alcohol **4** in excellent yield. After reductive removal of the vestigial hydroxyl group, ketone **6** was elaborated from nitrile **5** by reaction with prenylmagnesium chloride. This appears to be the first example of such a regioselective reaction of this Grignard reagent with a nitrile.[6] The observed preferential electrophilic attack at the more substituted allylic terminus presumably results from pseudointramolecular C-C bond formation as in **14**.

14

Copper(I)-catalyzed photobicyclizations are not known for dienes as functionally complex as **7**. The synthetic versatility of this reaction is now demonstrated by the production of **8** in reproducibly good yield upon UV irradiation of **7** in the presence of copper(I) trifluoromethanesulfonate. Monodemethylation of **8** with NaSEt set the stage for generation of the pyran ring. The favorable regioselectivity of this demethylation results from a novel remote neighboring group effect of the tertiary alcohol.[7] Treatment of **9** with $BF_3 \cdot OEt_2$ generated an 8:1:1 mixture of diastereomeric pyrans **10**. The major diastereomer (mp 80-82 °C) was readily isolated by HPLC on a Whatman M-20 μ-porasil column eluting with 35% toluene in hexane. Fortunately this diastereomer has the correct relative configurations for **1a**. This was unambiguously established by X-ray crystal structural analysis (Figure 1) of the derived dibromide **11** (mp 131-133 °C). Lithium-bromine exchange followed by carboxylation, acidification, and O-methylation delivered the diester **12** (mp 135 °C). The dimethyl ether **13** (mp 40-42 °C) of **1a** was obtained from **12** by reduction to a diol which was oxidized to the dialdehyde with pyridinium dichromate. ^1H and ^{13}C NMR analysis clearly show that **13** and robustadial A dimethyl ether are *not* identical. Notably, the ^1H NMR spectrum of the latter only shows resonances for aldehydic, benzylic, and methoxy hydrogens downfield of δ 2.3. In contrast, the ^1H NMR spectrum of **13** shows ab-

(1) Qin, G. W.; Chen, H. C.; Wang, H. C.; Qian, M. K. *Acta Chim. Sin.* **1981**, *39*, 83.

(2) Xu, R.; Snyder, J. K.; Nakanishi, K. *J. Am. Chem. Soc.* **1984**, *106*, 734.

(3) For a recent review, see: Salomon, R. G. *Tetrahedron* **1983**, *39*, 485.

(4) New compounds were characterized by ^1H and ^{13}C NMR spectroscopy as well as elemental analysis or high-resolution mass spectra. See supplementary material.

(5) Kaiser, E. M.; Hauser, C. R. *J. Org. Chem.* **1968**, *33*, 3402.

(6) (a) Analogous reactions of allylic zinc reagents are known;[6b] however, crotylmagnesium bromide in diethyl ether undergoes regioselective electrophilic attack by propionitrile at the *less* substituted allylic terminus.[6c] (b) Rousseau, G.; Conia, J. M. *Tetrahedron Lett.* **1981**, 649. (c) Andrac, M. *Ann. Chim.* **1964**, 287.

(7) Cannon, J. R.; Feutrill, G. I.; Wong, L. C. *Aust. J. Chem.* **1983**, *36*, 2575.

(8) X-ray analysis (Mo Kα radiation): **11** crystallizes from hexane in the triclinic space group $P\bar{1}$, with a = 9.148 (2) Å, b = 10.052 (2) Å, c = 13.376 (4) Å, α = 93.38 (2)°, β = 107.13 (2)°, γ = 104.25 (2)°, V = 1158.0 (5) Å^3, ρ_{obsd} = 1.48 g/cm^3, ρ_{calcd} = 1.48 g/cm^3, Z = 2. Standard direct and difference Fourier methods and least-squares refinement on the basis of 1976 ($I \geq 3\sigma$) reflections led to a final R = 0.037.

