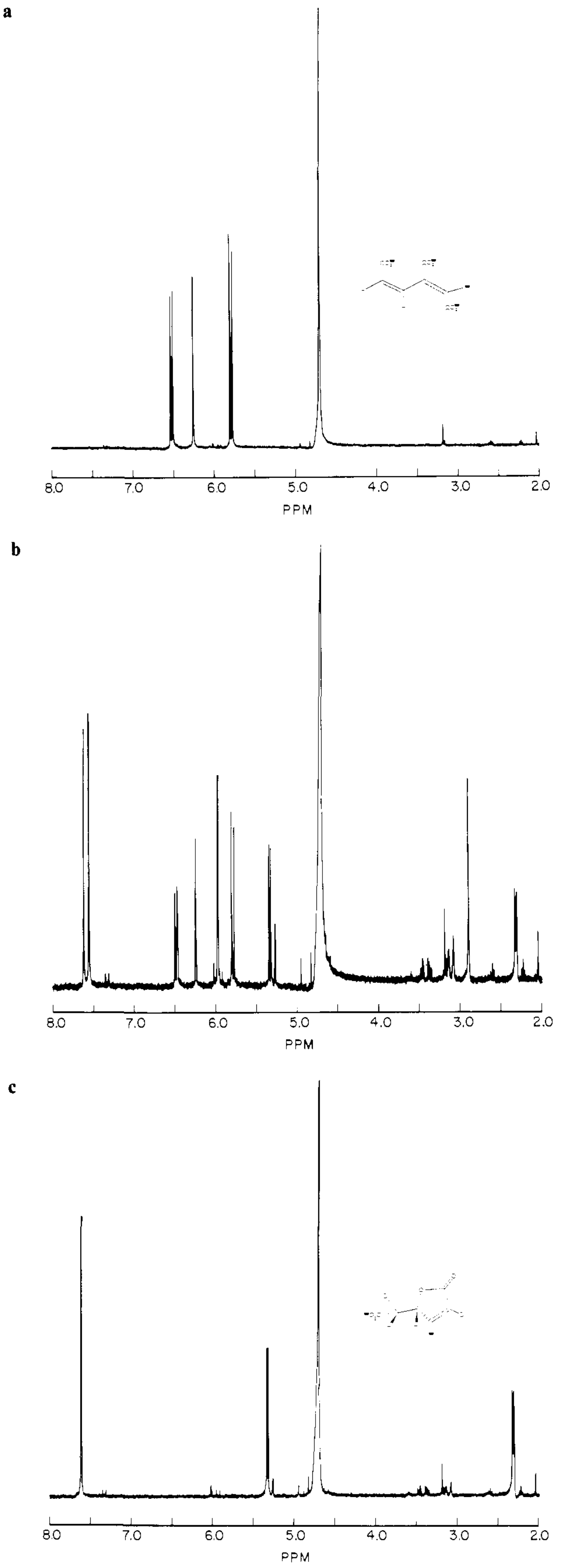
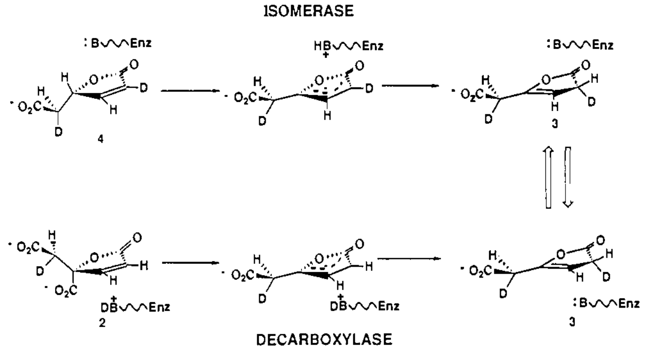


Figure 1. 400-MHz ^1H NMR (^2H_2O) spectra indicating the time course of the "ricochet" experiment for the *P. putida* enzymes: (a) 3-carboxy-*cis,cis*-muconate (**1**) in the presence of isomerase and decarboxylase; (b) 5 min after addition of 3-carboxymuconate cycloisomerase; (c) 15 min after addition of cycloisomerase. Identical results were obtained for the *A. calcoaceticus* enzymes.

Scheme II



enzyme which was capable of catalyzing both reactions.[9] Our stereochemical analysis suggests an intriguing possiblity to account for this enzymatic divergence. The ancestral enzyme would necessarily have the ability to perform chemistry on either face of a common (carbanionic) intermediate (Scheme II). The divergence of specific enzymatic activities could, therefore, have been due to the development of opposing facial recognition by both enzymes from their progenitor. Recent structural studies on the isomerase[10] and future work on the decarboxylase should be illuminating.

Note Added in Proof. We have recently completed stereochemical analyses of both the isomerase and decarboxylase by independent procedures by using appropriately labeled muconate derivatives. The preliminary results fully corroborate the conclusions of the "ricochet" analysis and will be reported elsewhere.

Acknowledgment. We thank the National Institutes of Health (GM-37210 to J.W.K and GM-33377 to L.N.O.) and the Yale–Celanese Program for support of this research. The Brüker AM 400-MHz spectrometer is supported by a grant from NSF (DMB-84-20175).

[9] Yeh, W. K.; Fletcher, P.; Ornston, N. *J. Biol. Chem.* **1980**, *255*, 6347–6354.

[10] Katz, B. A.; Ollis, D.; Wyckoff, H. W. *J. Mol. Biol.* **1985**, *184*, 311–318.

ESR Investigation of the Cubane Radical Cation ($C_8H_8^+$) in Neon Matrices at 4 K

Lon B. Knight, Jr.,* C. A. Arrington, B. W. Gregory, and S. T. Cobranchi

Chemistry Department, Furman University
Greenville, South Carolina 29613

Shaowo Liang and Leo Paquette*

Chemistry Department, The Ohio State University
Columbus, Ohio 43210

Received January 6, 1987

The high strain energy (166 kcal/mol)[1] of the highly symmetric cubane molecule[2] and the unique bonding adopted by this stable hydrocarbon continues to provide extensive opportunity for fundamental investigation. Detailed analyses of its vibrational[3,4] and photoelectron spectra[5] have recently appeared. Also achieved have

---

[1] (a) Allinger, N. L.; Tribble, M. T.; Miller, M. A.; Wertz, D. *J. Am. Chem. Soc.* **1971**, *93*, 1637. (b) Engler, E. M.; Andose, J. D.; Schleyer, P. v. R. *Ibid.* **1973**, *95*, 8005.

[2] Eaton, P. E.; Cole, T. W., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 3157.

[3] Della, E. W.; McCoy, E. F.; Patney, H. K.; Jones, G. L.; Miller, F. A. *J. Am. Chem. Soc.* **1979**, *101*, 7441.

[4] Pine, A. S.; Maki, A. G.; Robiette, A. G.; Krohn, B. J.; Watson, J. K. G.; Urbanek, Th. *J. Am. Chem. Soc.* **1984**, *106*, 891.

[5] Bischof, P.; Eaton, P. E.; Gleiter, R.; Heilbronner, E.; Jones, T. B.; Musso, H.; Schmelzer, A.; Stober, R. *Helv. Chim. Acta* **1978**, *61*, 547.

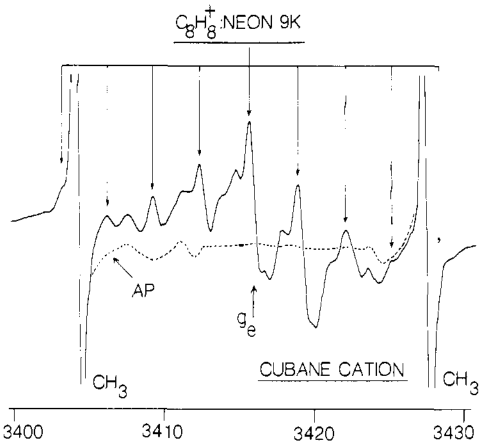


Figure 1. ESR spectrum of $C_8H_8^+$ in neon at 9 K. Dashed line labelled AP was recorded after photolysis with visible light.

been determination of the gas-phase basicity of cubane[6] and systematic substitution of the cubyl framework.[7] The cubane cation radical has been generated by photoionization at 16.8 eV and trapped as a free ion in neon matrices at 4 K for ESR (electron spin resonance) investigation. The apparent equivalency of the hydrogen atoms on the ESR time scale indicates that $C_8H_8^+$ is undergoing fluxional or dynamic Jahn–Teller distortion. Such behavior for the CH_4^+ and $CH_2D_2^+$ radicals prompted this investigation of the highly symmetric cubane molecule.[8,9] MNDO calculations averaged over the different H environments yield a hyperfine-splitting parameter in good agreement with experiment for CH_4^+ and $C_8H_8^+$ cation radicals.

The ESR matrix apparatus at Furman and ion-trapping techniques have been described in previous reports.[10,11] The cubane molecule was synthesized at Ohio State through adaptations of the original procedure[2] as given by Stock[12] and by Chapman.[13] The cubane sample (~3 mg), supplied in a sealed glass vial, was placed inside a small copper tube. Prior to releasing the cubane sample, several "blank" neon matrix depositions were conducted under exactly the same experimental conditions to be employed with cubane vapor present. Any volatile impurities in the copper tube or on the outside of the glass vial that could have produced spurious radical signals would have been detected under these conditions. The photoionization source, an open-tube neon resonance lamp (16.8 eV), irradiated the 4 K matrix target during the deposition process. ESR signals detected in these blank experiments could be assigned to commonly occurring background impurity radicals such as CH_3, ^{14}N atoms, and trace amounts of the $^{14}N_2^+$ molecular cation.[14] Following these blank experiments, the crystalline cubane sample was released by crimping the outer copper tube which in turn broke the inner glass vial. A quadrupole mass spectrometer permanently installed in the ESR matrix apparatus was used to monitor the gases present in the copper tube. Other than normal amounts of background gases, intense signals characteristic of cubane were observed at m/e values of 104 and 88. Typical background pressures in the matrix apparatus were 2×10^{-7} Torr. Three separate neon matrix depositions were conducted for ESR investigation before the cubane sample was depleted. The relative concentration of neutral cubane to neon was varied from approximately $^1/_{2000}$ to $^1/_{200}$ with no significant differences observed in the ESR results except for intensity changes in the absorption features assigned to the cubane cation radical. The ratio of trapped $C_8H_8^+$ to neon is estimated to be about $1/10^6$ based on previous calculations for similar experimental conditions.[10] As previously discussed, the identity of the counter anion trapped in a separate neon matrix site could not be established.[11,15] Likely candidates include OH^-, N_2^-, or O_2^- which are either not radicals or do not have the proper electronic ground state to be detected by ESR under these conditions.

The ESR spectrum assigned to $C_8H_8^+$ (Figure 1) is apparently described by nine equally spaced hydrogen hyperfine lines which would be expected for eight equivalent H atoms. By a distortion of the cubic structure, the triple degeneracy of the HOMO's in neutral cubane is removed in the paramagnetic cation. However, fluxional behavior can cause averaging of the different H environments on the ESR time scale. Seven of the nine nuclear hf lines exhibiting approximately the expected relative intensities were observed with the extremely weak first and ninth lines obscured by the second and third lines of the intense methyl quartet. (CH_3 is usually present as a background impurity radical in such deposition experiments involving a high energy source.) The expected relative intensity distribution for completely isotropic lines is 1:8:28:56:70:56:28:8:1 compared to the observed peak-to-peak intensities of –:9:24:54:75:66:33:6:– where the 5th and 6th lines which occur right at the g_e position had to be corrected in a highly approximate manner for overlap with impurity signals. Residual anisotropy and slight line width variations possibly due to incomplete averaging would be expected to cause some deviation from the theoretical ratios. The dashed line ESR spectrum labeled AP in Figure 1 was recorded after photolyzing the matrix sample with low intensity visible light for 20 min. All ESR lines assigned to $C_8H_8^+$ were eliminated while those of the background neutral radicals were unchanged. Such a photobleaching response is a well-established property of charged species in matrices.[16-18] Other experimental evidence corroborating the assignment include a similar response of the different lines of $C_8H_8^+$ to variations in the applied microwave power, similar line widths, consistency in relative intensities on different depositions, and similar line narrowing upon warming the neon matrix from 4 to 9 K, which is the highest temperature obtainable for neon without significant diffusion. The blank experiments combined with the photobleaching results account for all unassigned ESR lines except for two shoulder features on the central line which occurs very close to the g_e magnetic field position. The observed magnetic parameters for $C_8H_8^+$ in neon are $g = 2.0022$ (2) and $|A(\mathrm{H})| = 3.2$ (1) G.

MNDO calculations[19] of the geometry of $C_8H_8^+$ indicate a distortion of the cubic symmetry by lengthening one of the C–C bonds from 1.57 to 1.99 Å with a resulting C_{2v} symmetry. Restricted HF MNDO calculations yield hyperfine splittings for the hydrogen atoms ranging from 2.1 to 5.0 G with an average of 3.9 G. Unrestricted HF calculations give A values from –5.3 to 4.9 G with an average of 1.5 G. These theoretical comparisons together with the observed spectral characteristics indicate that the cubane cation is undergoing dynamic Jahn–Teller distortion at low temperatures in neon matrices. To gauge the reasonableness of the approximate theoretical procedure used in estimating A, calculations were also conducted in a similar manner for CH_4^+ in its C_{2v} geometry.[20] At the UHF MNDO level the average A was found to be 49 G while the RHF A value is 57 G compared to 54.8 (2) G observed in neon matrix ESR experiments at 4 K. The A values were obtained by multiplying the H 1s spin populations by the atomic parameter of 508 G for the free H atom.

---

(6) Santos, I.; Balogh, D. W.; Doecke, C. W.; Marshall, A. G.; Paquette, L. A. *J. Am. Chem. Soc.*, in press.

(7) Eaton, P. E.; Castaldi, G. *J. Am. Chem. Soc.* **1985**, *107*, 724.

(8) Knight, L. B., Jr.; Steadman, J.; Feller, D.; Davidson, E. R. *J. Am. Chem. Soc.* **1984**, *106*, 3700.

(9) Paddon-Row, M. N.; Fox, D. J.; Pople, J. A.; Houk, K. N.; Pratt, D. W. *J. Am. Chem. Soc.* **1985**, *107*, 7696.

(10) Knight, L. B., Jr.; Steadman, J. *J. Chem. Phys.* **1982**, *77*, 1750.

(11) Knight, L. B., Jr. *Acc. Chem. Res.* **1986**, *19*, 313.

(12) Luh, T.-Y.; Stock, L. M. *J. Org. Chem.* **1972**, *37*, 338.

(13) Chapman, N. B.; Key, J. M.; Toyne, K. J. *J. Org. Chem.* **1972**, *35*, 3860.

(14) Knight, L. B., Jr.; Bostick, J. M.; Woodward, R. J.; Steadman, J. *J. Chem. Phys.* **1983**, *78*, 6415.

(15) Knight, L. B., Jr.; Earl, E.; Ligon, A. R.; Cobranchi, D. P. *J. Chem. Phys.* **1986**, *85*, 1228.

(16) Andrews, L. *Annu. Rev. Phys. Chem.* **1979**, *30*, 89.

(17) Bondybey, V. E.; English, J. H. *J. Chem. Phys.* **1979**, *71*, 777.

(18) Knight, L. B., Jr.; Steadman, J. *J. Chem. Phys.* **1983**, *78*, 5940.

(19) Dewar, M. J. S.; Stewart, J. J. P. *QCPE Bulletin* **1986**, *6*, 24.

(20) Whiteside, R. A.; Frisch, M. J.; Binkley, J. S.; Krishnan, R.; DeFrees, D. J.; Schlegel, H. B.; Pople, J. A. *Carnegie-Mellon Quantum Chemistry Archive*, 2nd ed.; Department of Chemistry, Carnegie-Mellon University: Pittsburgh, Pa, p 15213.

Deuterium substitution experiments and attempts to observe the ^{13}C hfs are planned for cubane.[21] Hopefully, deuterium substitution because of zero-point energy differences will prevent the fluxional averaging and provide information about the type of static distortion that occurs in the unusual $C_8H_8^+$ cation radical. This type of isotopic effect was observed in in $CH_4^+/CH_2D_2^+$ and allowed its ground state to be established as C_{2v}.

Acknowledgment. Project support from the National Science Foundation (CHE-8508085) is gratefully acknowledged. We (L.B.K. and C.A.A.) express our appreciation to the Camille and Henry Dreyfus Foundation for the computer equipment used to conduct the theoretical calculations.

---

(21) The d_1, *sym-d_2*, *sym-d_6*, and d_8 isotopic forms of cubane have previously been reported: (a) Luh, T.-Y.; Stock, L. M. *J. Am. Chem. Soc.* **1974**, *96*, 3712. (b) Della, E. W.; Patney, H. K. *Austr. J. Chem.* **1976**, *29*, 2469.

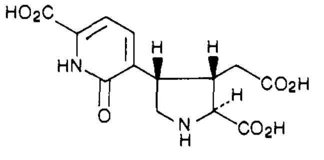
A Concise Enantioselective Synthesis of Acromelic Acid A

Seiichi Takano,* Yoshiharu Iwabuchi, and Kunio Ogasawara

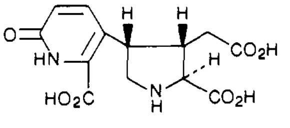
Pharmaceutical Institute, Tohoku University
Aobayama, Sendai 980, Japan

Received April 1, 1987

Acromelic acid A (**1**), isolated along with acromelic acid B (**2**) from the poisonous Japanese mushroom *Clitocybe acromelalga*,[1] has been revealed to exhibit the most potent depolarizing effect[2] among the kainoid amino acids ever found.[3] The structure and stereochemistry of acromelic acids A (**1**) and B (**2**) have been established through efforts of Matsumoto and co-workers on the basis of chemical conversion of natural kainic acid into these amino acids.[4,5] This conversion implies their formal total synthesis as kainic acid has been synthesized in natural forms;[6] however, more straightforward preparation is currently required for neurochemical investigations of these interesting amino acids. We report here a concise synthesis of acromelic acid A (**1**) in natural forms starting from (*S*)-*O*-benzylglycidol (**3**) employing the intramolecular 1,3-dipolar addition[7] as the key reaction.



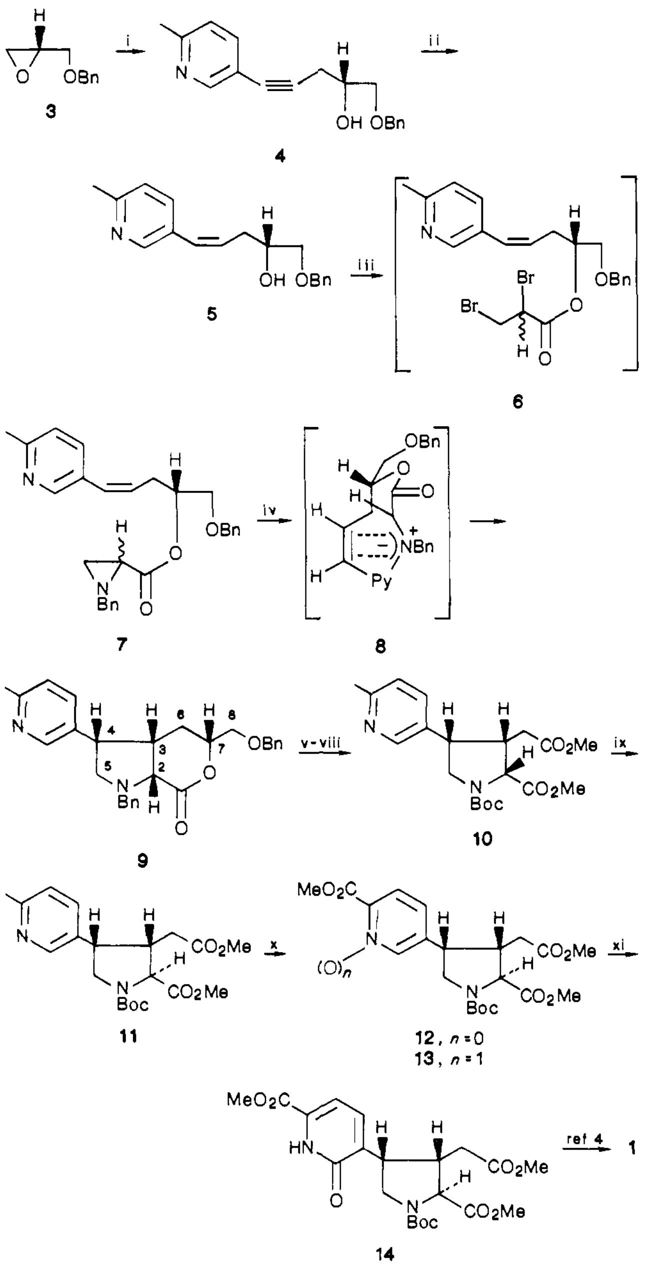
acromelic acid A (1)

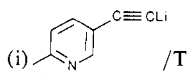


acromelic acid B (2)

(*S*)-*O*-Benzylglycidol[8] (**3**) is reacted with the lithium acetylide generated in situ from 2-methyl-5-ethynylpyridine[9] to afford (76%) the (*R*)-alcohol[10] **4** (Scheme I). Partial hydrogenation of **4** gives (85%) the *Z*-olefin **5**, mp 93–94 °C, $[\alpha]^{25}_{D}$ −10.2° (*c* 1.0, $CHCl_3$). Treatment[7] of **5** with 2,3-dibromopropionyl chloride followed by benzylamine in the same flask yields (65% overall) the aziridine **7**. Thermolysis[7] of **7** in *o*-dichlorobenzene[11] in a sealed tube affords

Scheme I



(i) 

/THF-HMPA/−70 °C-room temperature/8 h. (ii) H_2/Lindlar catalyst/benzene/quinoline (catalytic)/room temperature/24 h. (iii) $BrCH_2CHBrCOCl/Et_3N/CH_2Cl_2$/0 °C/2 h, then $C_6H_5CH_2NH_2$/0 °C/2 h. (iv) 200 °C/1.7% in *o*-$C_6H_4Cl_2$/1.5 h. (v) H_2/10%Pd-C/MeOH-HCl/room temperature/3 days. (vi) $(Boc)_2O$/3 N NaOH-dioxane (1:1)/room temperature 1 h, then aqueous $NaIO_4$/0 °C/15 min, then aqueous $KMnO_4$/0 °C/2 h. (vii) concentrated H_2SO_4 (catalyst)/MeOH/reflux/24 h. (viii) $(Boc)_2O/Et_3N/CH_2Cl_2$/room temperature/15 min. (ix) NaH (2.1 equiv)/DBU (2.5 equiv)/benzene/room temperature/5 h. (x) *m*-CPBA/CH_2Cl_2/room temperature/24 h. (xi) $(CF_3CO)_2O$(10 equiv)/DMF/room temperature/45 h.

---

(1) (a) Konno, K.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1983**, *24*, 939. (b) Konno, K.; Hayano, K.; Saito, H.; Shirahama, H.; Matsumoto, T. *Tetrahedron* **1982**, *38*, 3281. (c) Konno, K.; Shirahama, H.; Matsumoto, T. *Phytochemistry* **1984**, *23*, 1003.

(2) Cf.: (a) McGeer, E. G.; Olney, J. W.; McGeer, P. L. *Kainic Acid as a Tool in Neurobiology*; Raven Press: New York, 1978. Watkins, J. C. *Glutamate Transmitter in the Central Nervous System*; Roberts, P. J. Storm-Mathisen, J., Johnston, G. A. R., Eds.; Wiley: Chichester, 1981; p 1.

(3) Konno, K.; Hashimoto, K.; Shirahama, H.; Matsumoto, T.; Ohfune, Y. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **1985**, *27*, pp 252–258.

(4) Konno, K.; Hashimoto, K.; Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1986**, *27*, 607.

(5) Hashimoto, K.; Konno, K.; Shirahama, H.; Matsumoto, T. *Chem. Lett.* **1986**, 1399.

(6) Oppolzer, W.; Thirring, K. *J. Am. Chem. Soc.* **1982**, *104*, 4978.

(7) DeShong, P.; Kell, D. A.; Sidler, D. R. *J. Org. Chem.* **1985**, *50*, 2309.

(8) Cf.: Takano, S.; Akiyama, M.; Ogasawara, K. *Synthesis* **1985**, 503.

(9) Prepared (67% overall) from 2-methyl-5-acetylpyridine by a conventional manner: (i) PCl_5, toluene, 12 h; (ii) *t*-BuOK, *t*-BuOH, 30 min.

(10) All new isolated compounds reported herein exhibited satisfactory ^1H NMR, IR, optical rotation, and MS or combustion analytical data.

0002-7863/87/1509-5523$01.50/0