salt, 76499-40-6; (*E*)-**9**, 76499-41-7; (*E*)-**10**, 76499-42-8; (*E*)-**11**, 76499-43-9; **12**, 76499-44-0; **13**, 76499-45-1; 3-nitro-2-[2-(1-pyrrolidinyl)ethenyl]benzaldehyde dimethyl acetal, 76499-46-2; (methoxymethyl)triphenylphosphonium chloride, 4009-98-7; (phenylthiomethyl)triphenylphosphonium chloride, 13884-92-9; cyanoacetic acid, 372-09-8.

Structure of a Byproduct Formed during Use of the Robinson Annulation Reaction with 6-Methoxy-1-methyl-2-tetralone[1]

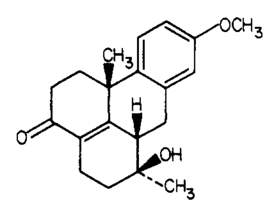
Ajoy K. Banerjee,*[2a] Magaly S. Rizo,[2a] Miguel E. Alonso,[2a]
Anibal Rojas,[2b] John L. Haack,[2c] Herbert O. House,*[2c] and
Don VanDerveer[2c]

Centro de Quimica, Instituto Venezolano de Investigaciones Cientificas, I.V.I.C., Apartado-1827, Caracas-1010A, Venezuela, Escuela de Quimica, Universidad Central de Venezuela, Caracas, Venezuela, and School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332

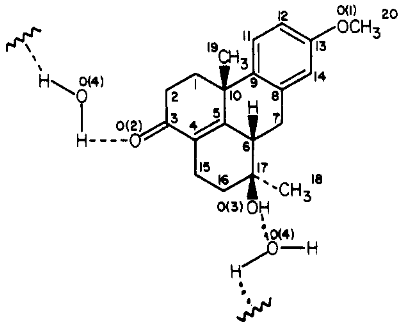
Received September 29, 1980

As part of another synthetic program, the methoxy tetralone **1** was subjected to a Robinson annulation procedure to form the enone **3** by following the procedure of Howell and Taylor.[3] In addition to the enone **3**, isolated in 78% yield, a crystalline C-20 byproduct was isolated in 10% yield. The spectral properties of this byproduct (a conjugated ketone containing a hydroxyl function) were reminiscent of a C-19 crystalline byproduct isolated by Howell and Taylor[3a] when the Robinson annulation procedure was applied to the tetralone **4**. These authors suggested that their byproduct may be derived from the dialkylated product **5** and might have structure **6b**. By analogy, the byproduct from tetralone **1** could be formulated as **6a** or **7** (Scheme I). Alternatively, the initial product **3** could have reacted with more methyl vinyl ketone to form successively the diketone **8** and the hydroxy enone **9** (or one of its stereoisomers).

Since the spectral properties of our byproduct did not unambiguously distinguish among various structures such as **6a**, **7**, and **9**, the structure was determined to be **9** by X-ray crystallographic analyses. The molecule crystallized as a monohydrate with water molecules in the crystal located as shown in structure **10**. A perspective view of the structure of the byproduct **9** is presented in Figure 1.



9



10

Experimental Section[4]

Robinson Annulation with Tetralone 1. A cold (0 °C) solution of 6.71 g (46.9 mmol) of 1-(diethylamino)-3-butanone in 12 mL of Et_2O was treated with 15 mL of MeI in 8 mL of Et_2O and the resulting mixture was stirred at 0 °C for 1 h. After the Et_2O and excess MeI had been removed under reduced pressure, the residual salt **2** was mixed with 10.0 g (53.6 mmol) of the tetralone **1** in 60 mL of PhH. This mixture was cooled to ca. 0 °C and a solution of NaOMe, prepared from 2.4 g (0.1 mol) of Na and 60 mL of anhydrous MeOH, was added. The resulting dark red solution was stirred at 0 °C for 2 h and then refluxed for 10 min. After the reaction mixture had cooled, it was diluted with H_2O and acidified with aqueous 30% H_2SO_4. The organic layer was separated, the aqueous phase was extracted with Et_2O, and the combined organic layers were washed with aqueous NaCl, dried, and concentrated. After the residual oil had been triturated with Et_2O, the solid that separated was recrystallized from an Et_2O–petroleum ether (bp 40–60 °C) mixture. The enone **3** separated as 9.91 g (78%) of crystalline solid: mp 107–108 °C (lit.[3a] mp 106–108 °C); IR (KBr pellet) 1670 cm^{-1} (conjugated C=O); NMR (CCl_4) δ 6.46–7.20 (3 H, m, aryl CH), 5.76 (1 H, s, vinyl CH), 3.72 (3 H, s, OCH_3), 1.52 (3 H, s, CH_3).

Concentration of the mother liquors from the crystallization of the enone **3** separated 1.61 g (10%) of the crude hydroxy enone **9**, mp 96–101.3 °C. This byproduct was recrystallized from an Et_2O–$CHCl_3$ mixture to separate the monohydrate of hydroxy enone **9** as colorless prisms, mp 98.2–104.6 °C.

Anal. Calcd for $C_{20}H_{24}O_3 \cdot H_2O$: C, 72.70; H, 7.93. Found: C, 72.53; H, 8.14.

After the sample had been dried at 80 °C under reduced pressure for 8 days, the sample melted at 90–92.5 °C. The composition of the sample (Found: C, 75.73; H, 7.94. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74) indicated that about 75% of the water of hydration had been removed. The spectral properties of the monohydrate of hydroxy enone **9** follow: IR ($CHCl_3$) 3685, 3600, 3480 (OH), 1670, 1658 (conjugated C=O), 1626 cm^{-1} (conjugated C=C); UV max (95% EtOH) 229 nm (ϵ 13 400), 247 (15 300), 286 (2030); mass spectrum, *m/e* (relative intensity) 312 (M^+, 55), 297 (49), 280 (20), 279 (100), 241 (25), 239 (25), 237 (35), 227 (21), 43 (33); ^1H NMR ($CDCl_3$) δ 6.5–7.3 (3 H, m, aryl CH), 3.79 (3 H, s, OCH_3), 1.6–3.2 (11 H, m, aliphatic CH), 1.55 (3 H, s, CH_3), 1.37 (3 H, s, CH_3); ^{13}C NMR (Me_2SO-d_6, multiplicity in off-resonance decoupling), 196.0 (s), 160.5 (s), 156.1 (s), 136.4 (s), 135.1 (s), 127.3 (s), 126.6 (d), 112.5 (d), 112.1 (d), 67.4 (s), 54.6 (q), 44.0 (d), 36.5 (t), 34.7 (t), 33.7 (t), 29.6 (q), 27.8 (s), 26.3 (t), 19.5 ppm (t). The last ^{13}C NMR signal may be obscured by absorption of the solvent, Me_2SO-d_6, in the region 37–41 ppm.

Crystal Structure of the Hydroxy Enone 9. A. Data Collection. A crystal of the enone **9** with approximate dimensions 0.75 × 0.35 × 0.35 mm was mounted on a glass fiber, using epoxy cement, such that the longest crystal dimension, 0.75 mm, was approximately parallel to the fiber axis. Unit cell parameters and the orientation matrix were determined on a Syntex $P2_1$ four-circle diffractometer equipped with a graphite monochromator (Bragg 2θ angle = 12.2°), using Mo Kα radiation at a takeoff angle of

---

[1] Portions of this research have been supported by CONICIT (Grant No. 07-35) and by Public Health Service Grant R01-GM-20197 from the National Institute of General Medical Science. The execution of this research was also assisted by Institutional Research Grants from the National Science Foundation for the purchase of a mass spectrometer and a Fourier transform NMR spectrometer.

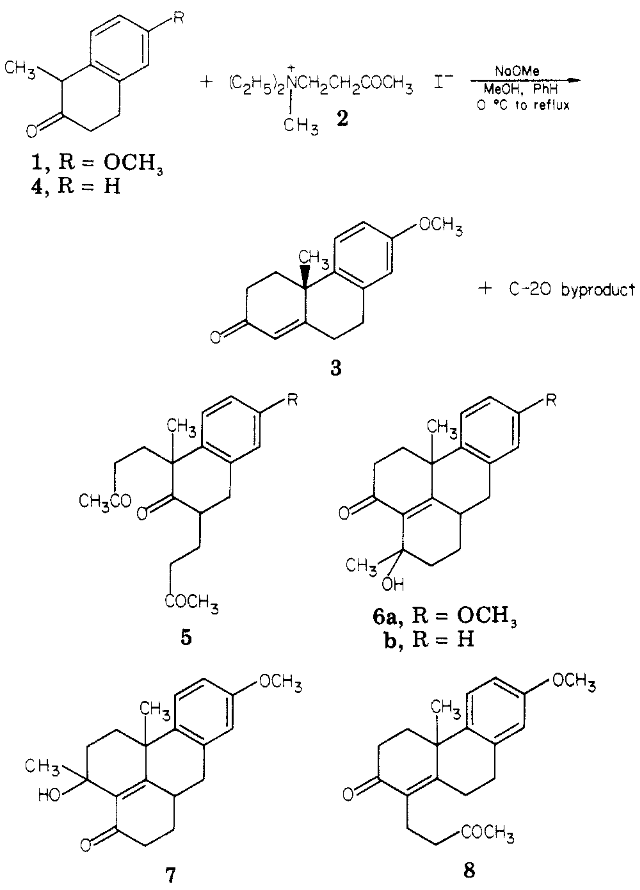
[2] (a) Instituto Venezolano de Investigaciones Cientificas. (b) Universidad Central de Venezuela. (c) Georgia Institute of Technology.

[3] (a) Howell, F. H.; Taylor, D. A. H. *J. Chem. Soc.* **1958**, 1248. (b) also see: Stork, G.; Meisels, A.; Davies, J. E. *J. Am. Chem. Soc.* **1963**, *85*, 3419.

[4] All melting points are corrected; $MgSO_4$ was employed as a drying agent. The IR spectra were determined with a Perkin-Elmer Model 299 infrared recording spectrophotometer fitted with a grating. The UV spectra were determined with a Perkin-Elmer Model 202 recording spectrophotometer. The ^1H NMR spectra were determined at 60 MHz with a Varian Model T-60A NMR spectrometer and the ^{13}C NMR spectra were determined at 25 MHz with a JEOL Fourier transform spectrometer, Model PFT-100. The chemical shift values are expressed in γ values (parts per million) relative to a Me_4Si internal standard. The mass spectra were obtained with a Varian MAT, Model 112S, mass spectrometer. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere.

0022-3263/81/1946-1755$01.25/0

Scheme I



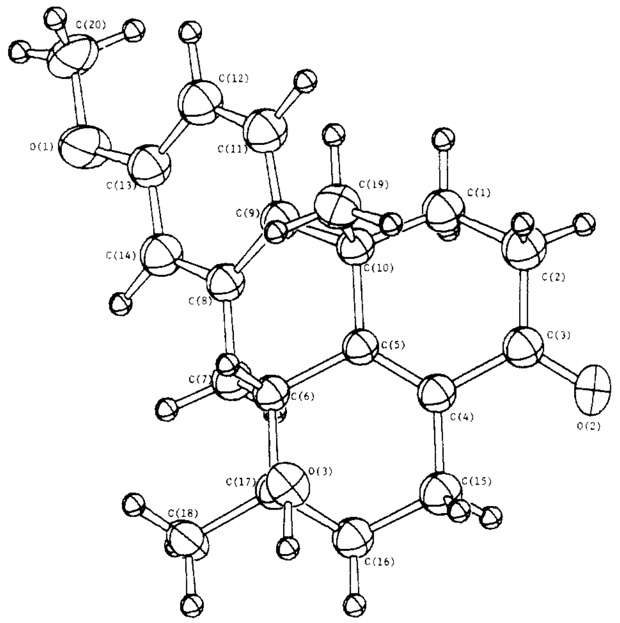


Figure 1. Perspective view of the molecular structure of the hydroxy enone **9**. (For clarity, the H atom thermal parameters have been reduced.)

Table I. Molecular Geometry of the Monohydrate of Hydroxy Enone 9[a]

A. Bond Lengths, A			
C1-C2	1.534 (4)	C9-C11	1.395 (4)
C2-C3	1.499 (4)	C11-C12	1.394 (5)
C3-C4	1.477 (4)	C12-C13	1.384 (5)
C4-C5	1.345 (4)	C13-C14	1.380 (4)
C5-C6	1.513 (4)	C14-C8	1.392 (4)
C6-C7	1.532 (4)	C15-C4	1.509 (4)
C7-C8	1.506 (4)	C15-C16	1.518 (4)
C8-C9	1.396 (4)	C16-C17	1.523 (4)
C9-C10	1.536 (4)	C17-C18	1.529 (4)
C10-C1	1.541 (4)	C17-C6	1.536 (4)
C10-C5	1.519 (4)	C10-C19	1.546 (4)
O1-C13	1.369 (4)	C1-C20	1.417 (4)
O2-C3	1.233 (4)	O3-C17	1.444 (3)
O3-HO3	1.038 (2)		
B. Bond Angles, deg			
C10-C1-C2	111.9 (3)	O2-C3-C4	120.2 (3)
C1-C2-C3	110.8 (3)	C3-C4-C5	120.6 (3)
C2-C3-C4	118.6 (3)	C3-C4-C15	115.8 (3)
C2-C3-O2	121.2 (3)	C4-C5-C6	121.3 (3)
C5-C4-C15	123.6 (3)	C9-C8-C14	120.2 (3)
C4-C5-C10	124.3 (3)	C8-C9-C10	122.8 (3)
C10-C5-C6	114.4 (2)	C8-C9-C11	117.4 (3)
C5-C6-C7	105.9 (2)	C10-C9-C11	119.8 (3)
C5-C6-C17	114.1 (2)	C9-C10-C5	110.5 (2)
C7-C6-C17	115.1 (2)	C9-C10-C1	108.3 (3)
C11-C12-C13	118.7 (3)	C1-C10-C5	109.8 (2)
C12-C13-C14	119.8 (3)	C1-C10-C19	110.2 (3)
C13-C14-C8	121.2 (3)	C5-C10-C19	108.5 (3)
C4-C15-C16	113.0 (3)	C9-C10-C19	109.5 (2)
C15-C16-C17	111.8 (3)	C9-C11-C12	122.6 (3)
C12-C13-O1	124.1 (3)	C16-C17-C6	110.0 (2)
C14-C13-O1	116.1 (3)	C16-C17-C18	111.3 (3)
C9-C11-HC11	118.7 (2)	C6-C17-C18	112.7 (2)
C12-C11-HC11	118.7 (2)	C16-C17-O3	109.8 (2)
C13-C14-HC14	119.4 (2)	C18-C17-O3	107.9 (2)
C8-C14-HC14	119.4 (2)	C6-C17-O3	105.0 (2)
C6-C7-C8	110.7 (3)	C13-O1-C20	118.0 (3)
C7-C8-C9	121.0 (3)	C11-C12-HC12	120.7 (2)
C7-C8-C14	118.8 (3)	C13-C12-HC12	120.7 (2)
C. Intermolecular Distances (Å) of Monohydrate			
O2-HO4	1.824	O4-HO3	1.746

[a] Numbers in parentheses indicate estimated standard deviations in the least significant digit(s).

6.75°. Fifteen reflections whose 2θ values ranged from 11.56° to 22.64° were machine centered and used in least-squares refinement of the lattice parameters and orientation matrix. Unit-cell parameters obtained were a = 14.881 (4) Å,[5] b = 9.333 (1) Å, c = 14.634 (4) Å, β = 120.46° (2), and V = 1750.3 (7) Å^3. The calculated density of 1.25 g cm^{-3} for four formula units per unit cell agrees with the experimental density of 1.27 g cm^{-3} measured by the flotation method using a mixture of CCl_4 and hexane. ω scans of several low 2θ angle reflections gave peak widths at half-height of less than 0.2°, indicating a satisfactory mosaic spread for the crystal. Axial photographs indicated that the crystal belonged to the monoclinic system. Intensity data for zero and upper levels were collected at a rapid scan rate and the intensities examined carefully for systematic absences. The absence of $h0l$ ($l = 2n + 1$) and $0k0$ ($k = 2n + 1$) reflections is consistent with only space group $P2_1/c$ (No. 14).[6]

Intensity data were collected, using θ–2θ scans with X-ray source and monochromator settings identical with those used for determination of the unit-cell parameters. A variable scan rate of from 2.02 to 29.3°/min was used and a scan width of 2° was sufficient to collect all of the peak intensity. Stationary background counts were measured at the beginning (bgd1) and at the end (bgd2) of each scan with a total background to scan time ratio, TR, of 1.0. No significant fluctuations were observed in the intensities of three standard reflections (040, 008, 600) monitored every 97 reflections. Intensities were calculated from the total scan count (CT) and background counts by the relationship in eq 1. The intensities were assigned standard deviations according

$$I = \mathrm{CT} - (\mathrm{TR})(\mathrm{bgd1} + \mathrm{bgd2}) \qquad (1)$$

to eq 2 from a total of 3107 reflections collected in a complete

$$(I) = [\mathrm{CT} + (\mathrm{TR})^2(\mathrm{bgd1} + \mathrm{bgd2})]^{1/2} \qquad (2)$$

---

(5) Numbers in parentheses here and elsewhere in this paper indicate estimated standard deviations in the least significant digit(s).

(6) "International Tables for X-Ray Crystallography"; Kynoch Press: Birmingham, England, 1952; Vol. I.

quadrant of data out to $2\theta = 50°$; 2365 were accepted as statistically above background on the basis that F was greater than $3\sigma(F)$. Lorentz and polarization corrections were made in the usual way.

B. Solution and Refinement of the Structure. Computations were performed by using a standard programs;[7] all computations were carried out on the CDC Cyber 74 System. For structure factor calculations the scattering factors were taken from Cromer and Mann's tabulation.[8] The agreement factors are defined in the usual way as shown in eq 3 and 4. In all least-

$$R = (\Sigma||F_o| - |F_c||)/(\Sigma|F_o|) \tag{3}$$

$$R_w = \frac{[\Sigma(|F_o| - |F_c|)(w^{0.5})]}{[\Sigma(|F_o|)(w^{0.5})]} \tag{4}$$

squares refinement, the quantity minimized was $\Sigma w(|F_o| - |F_c|)^2$. A weighting scheme based on counting statistics ($w = 3.05/[\sigma(F)^2 + 0.0003F^2]$) was employed for calculating R_w and in least-squares refinement.

The structure was solved by using the automatic centrosymmetric direct methods program of SHELX-76. The total number of parameters varied was 147 for 2365 observations. Parameters varied included a scale factor, coordinates of all atoms except hydrogen, anisotropic thermal parameters for all O atoms and methyl group C atoms, and isotropic thermal parameters for all other atoms. The H atoms on the hydroxy group and the water molecule were located from a difference Fourier. The remaining H atom coordinates were determined by using the routine in SHELX-76 that fixes the C–H distance of 1.08 Å and orients the H atom positions to complete the appropriate coordination about each C atom. The full-matrix least-squares refinement converged at $R = 0.072$ and $R_w = 0.074$. The final atomic coordinates and thermal parameters are available as supplementary material in Table 2 and the bond distances and bond angles are in Table I. The list of calculated and observed structure factors is available from the authors as Table 3.

Registry No. 1, 5111-67-1; 2, 43025-83-8; 3, 1910-02-7; 9, 76480-23-4; 1-(diethylamino)-3-butanone, 3299-38-5.

Supplementary Material Available: Table 2 containing atomic coordinates and thermal parameters for hydroxy enone 9 (1 page). Ordering information is given on any current masthead page.

---

[7] Programs utilized were Sheldrick's SHELX-76 program and Johnson's ORTEP program.

[8] "International Tables for X-Ray Crystallography"; Kynoch Press: Birmingham, England, 1974; Vol. IV pp 72–98.

Communications

Palladium(II) Acetate Catalyzed Aromatic Substitution Reaction

Summary: Relative rate measurements indicate that the palladation reaction, although nonselective, adheres to the selectivity relationship for electrophilic aromatic substitution. Kinetic isotope effects and the dependence of the rate on oxidant concentration implicate arylpalladium(II) and arylpalladium(IV) compounds as intermediates in the reactions leading to biaryls and aryl acetates.

Sir: Palladium(II)-catalyzed aromatic substitution reactions have been widely studied.[1] Henry recently reviewed these contributions.[2] In brief, many substituents including the halogens[3,4] and the nitro,[1j,k,5] acetate,[1b,j,m] cyano,[1j,6,7] and phenyl groups[1l,8] can be introduced into the aromatic nucleus under the influence of this reagent. The reaction between benzene and palladium(II) acetate yields biphenyl in the absence of an added oxidant. In the presence of an oxidant, the reaction yields substitution products. Indeed, phenyl acetate and nitrobenzene are formed in efficient catalytic reactions in the presence of strong oxidants.[1f,j] Several different suggestions have been advanced concerning the role of the oxidant. Some attribute the influence of the oxidant to the conversion of Pd(II) compounds to more electrophilic Pd(IV) species, others to the conversion of arylpalladium(II) compounds to the observed oxidation products. The role of the oxidant in biaryl and aryl acetate formation remains puzzling. The isomer distributions obtained in these processes are rich in the meta isomer even when the substituent in the aromatic nucleus is an ortho,para directing group. Such observa-

Table I. Isomer Distributions for the Palladium(II) Acetate Catalyzed Oxidation of Benzene Derivatives in Acetic Acid at 90 °C for 16 h[a]

compd	aryl acetate, % 2-	3-	4-	% yield[b]
chlorobenzene	38	23	35	15
toluene	26	36	38	212
tert-butylbenzene	0	58	42	125

[a] A solution of the aromatic compound (33 mmol), palladium(II) acetate (0.5 mmol), methanesulfonic acid (3.1 mmol), and sodium dichromate dihydrate (15 mmol) in acetic acid (25 mL) with benzonitrile (3 mmol) used as a complexing reagent. [b] Based upon palladium(II) acetate.

---

[1] (a) Davidson, J. M.; Triggs, C. *J. Chem. Soc. A* **1968**, 1324. (b) Davidson, J. M.; Triggs, C. *Ibid.* **1968**, 1331. (c) Eberson, L.; Gomez-Gonzalez, L. *Acta Chem. Scand.* **1973**, *27*, 1162. (d) Eberson, L.; Gomez-Gonzalez, L. *Ibid.* **1973**, *27*, 1249. (e) Eberson, L.; Gomez-Gonzalez, L. *Ibid.* **1973**, *27*, 1255. (f) Eberson, L.; Jonsson, E. *Acta Chem. Scand., Ser. B* **1974**, *28*, 771. (g) Eberson, L.; Jonsson, L. *J. Chem. Soc., Chem. Commun.* **1974**, 885. (h) Eberson, L.; Jonsson, L. *Acta Chem. Scand., Ser. B* **1976**, *30*, 361. (j) Henry, P. M. *J. Org. Chem.* **1971**, *36*, 1886. (k) Norman, R. O. C.; Parr, W. J. E.; Thomas, C. B. *J. Chem. Soc., Perkin Trans. 1* **1974**, 369. (l) Clark, F. R. S.; Norman, R. O. C.; Thomas, C. B.; Willson, J. S. *Ibid.* **1974**, 1289. (m) Eberson, L.; Jonsson, L. *Justus Liebigs Ann. Chem.* **1977**, 233.

[2] Henry, P. M. "Palladium Catalyzed Oxidation of Hydrocarbons"; D. Reidel Publishing Company: Dordrecht, Holand, 1980; pp 306–338.

[3] Fahey, D. R. *J. Organomet. Chem.* **1971**, *27*, 283.

[4] Allison, J. A. C.; El Khadem, H. S.; Wilson, C. A. *J. Heterocycl. Chem.* **1975**, *12*, 1275.

[5] Tisue, T.; Downs, W. J. *J. Chem. Soc., Chem. Commun.* **1969**, 410.

[6] Takagi, K.; Okamoto, T.; Sakakibara, Y.; Oka, S. *Chem. Lett.* **1973**, 471.

[7] Nakamura, S. Japan Patent 74 41,426 (1974); *Chem. Abstr.* **1975**, *82*, 170443*g*.

[8] van Helden, R.; Verberg, G. *Recl. Trav. Chim. Pays-Bas* **1965**, *84*, 1263.

[9] Wright, T. L. Ph.D. Thesis, University of Chicago, 1978.

[10] Olah, G. A.; Hashimoto, I.; Lin, H. C. *Proc. Natl. Acad. Sci. U.S.A.* **1977**, *74*, 4121.

[11] Brown, H. C.; Wirkkala, R. A. *J. Am. Chem. Soc.* **1966**, *88*, 1447.

[12] Stock, L. M.; Brown, H. C. *Adv. Phy. Org. Chem.* **1963**, *1*, 35.

0022-3263/81/1946-1757$01.25/0