Hz, H-7), 5.54 (J = 7 Hz, vinyl), 4.59 (J = 7 Hz, allyl methylene), 1.78 (C-methyls).

Anal. Calcd for $C_{19}H_{18}N_2O_2$: C, 74.48; H, 5.92; N, 9.14. Found: C, 74.9; H, 6.22; N, 8.29.

Further elution of the column with increasing amounts of benzene in hexane gave fractions from which small amounts of isopimpinellin were obtained. Work-up of fractions eluted with 50% benzene in hexane gave small amounts of aesculetin dimethyl ether, mp 140–142°; infrared and nmr spectra were superimposable on those from a sample of aesculetin dimethyl ether prepared from aesculetin with diazomethane: nmr ($CDCl_3$), δ 7.81 (d, J = 9 Hz, H-4), 6.87, 6.84 (s, H-5 and H-8), 6.27 (d, J = 9 Hz, H-3), 3.95, 3.94 (methoxys).

Hydrolysis of 3.—A solution of 20 mg of **3** in 3 ml of acetic acid containing several drops of concentrated HCl was heated 30 min on a steam bath. The mixture was diluted with sodium carbonate solution and extracted with ethyl acetate. The extracts were washed with 5% sodium carbonate solution and dried and the solvent was removed. The residue was crystallized from methanol, mp 256–258°, and was identical in all respects with an authentic sample of halfordinol (2).

Registry No.—**3,** 17190-80-6; **4,** 17190-81-7.

Acknowledgments.—The author is indebted to Dr. W. D. Crow for an authentic sample of halfordinol and to Dr. D. J. Bertelli for the 100-MHz nmr spectrum.

The Conversion of Cinerone into Cinerolone[1]

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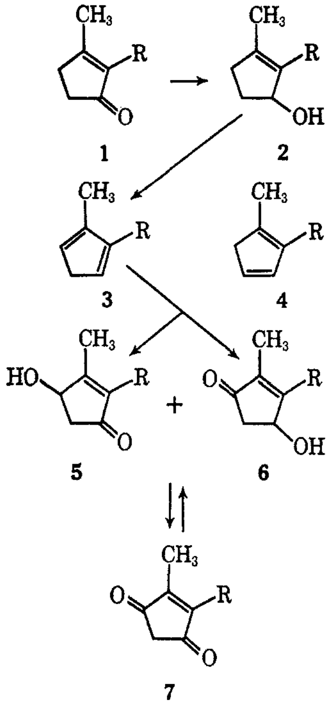
The pyrethrins are the most important natural insecticides and comprise the major active constituents of pyrethrum flowers.[2] *cis*-Cinerolone (**5**) is a valuable intermediate for the preparation of cinerin I and cinerin II both of which are active constituents present in pyrethrum extract.[2] Although the synthesis of *cis*-cinerolone (**5**) has been reported by other workers,[3,4] the routes employed are lengthy and terminate in low over-all yields.

We began our attempt at a synthesis of *cis*-cinerolone (**5**) by investigating various means of introducing a C-4 substituent in cinerone (**1**). Cinerone (**1**) was prepared by alkylation of 2-lithio-5-methylfuran[5] with *cis*-1-bromo-3-pentene[4] followed by acid cleavage and base-catalyzed cyclization, as utilized in a recent synthesis of *cis*-jasmone.[6] Earlier work had shown that bromination with N-bromosuccinimide could not be successfully applied to cyclopentenones with an unsaturated side chain.[7] Treatment of cinerone with lead tetraacetate in benzene, cupric bromide in chloroform and ethyl acetate, *t*-butyl peracetate with cuprous chloride in benzene, *t*-butyl chromate in carbon tetrachloride or selenium dioxide in aqueous ethanol did not succeed in selectively introducing a C-4 substituent.

We have recently developed a novel indirect chemical conversion of cinerone into cinerolone (Scheme I).

Scheme I



R = —$CH_2CH{=}CHCH_3$(*cis*)

The key steps in our synthesis of cinerolone are based on the many examples of Diels–Alder addition of oxygen to cyclic conjugated dienes leading to *endo* peroxides and their subsequent rearrangement in basic media to hydroxyenones.[8] Reduction of cinerone (**1**) with lithium aluminum hydride yielded 2-(2′-*cis*-butenyl)-3-methyl-2-cyclopenten-1-ol (**2**). Dehydration of **2** with *p*-toluenesulfonic acid in benzene proceeded at room temperature to give 2-(2′-*cis*-butenyl)-3-methylcyclopentadiene (**3**), $\lambda_{max}^{C_6H_{12}}$ 243 mμ (ϵ 4000), with nmr absorptions at τ 3.94 (2 H, singlet with fine structure), 4.40 (2 H, multiplet), 8.00 (3 H, singlet with fine structure) and 8.29 (3 H, doublet, J = 5 cps). The nmr spectrum of the alternative structure (**4**) would be expected to be more complex in the region of the cyclopentadiene hydrogens. Elimination of water from **2** is probably assisted by the double bond leading to a tertiary carbonium ion which loses a proton to give **3**.

Irradiation of a methanol solution of **3** containing eosin as a sensitizer with visible light while bubbling a stream of oxygen through the solution gave an oil which was left on a column of basic alumina for 15 hr. Chromatography of the eluent gave an 11% yield of a mixture of two hydroxy cyclopentenones with the same R_f on tlc as that of authentic cinerolone.[9] Small amounts of the two pure compounds were separated by preparative glpc and the major component (58% of the mixture) was identified as cinerolone (**5**) by comparison of its glpc retention time and spectra (ir, nmr, uv, and mass) with those of the authentic material.[9] The

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[1] Presented at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968.

[2] L. Crombie and M. Elliot, *Fortschr. Chem. Org. Naturstoffe*, **19**, 120 (1961).

[3] M. S. Schechter, N. Green, and F. B. LaForge, *J. Amer. Chem. Soc.*, **74**, 4902 (1952).

[4] L. Crombie and S. H. Harper, *J. Chem. Soc.*, 1152 (1950).

[5] Method of V. Ramanathan and R. Levine, *J. Org. Chem.*, **27**, 1216 (1962).

[6] G. Buchi and H. Wuest, *ibid.*, **31**, 977 (1966).

[7] L. Crombie, M. Elliot, and S. H. Harper, *J. Chem. Soc.*, 971 (1950).

[8] Y. A. Arbuzov, *Russ. Chem. Rev.*, **34**, 558 (1965).

[9] M. Elliot, *J. Chem. Soc.*, 5225 (1964).

minor component **6** (42% of the mixture) gave an infrared spectrum differing from **5** only in the fingerprint region and absorbed in the uv region at 232 mμ (ε 13,800). The mass spectrum of **6** was essentially identical with that of **5** except that the peak due to loss of water was stronger in **6** than in **5**. Oxidation of the mixture of hydroxy cyclopentenones gave a 78% yield of a single dione **7** which was identical in all respects with a sample prepared by oxidation of authentic cinerolone (**5**).

Chemical generation of singlet oxygen by the reaction of sodium hypochlorite and hydrogen peroxide[10] in methanol solution containing **3** at −10° gave, after column chromatography, a 40% yield of the hydroxy cyclopentenone mixture (40% of **5** and 60% of **6**).

Reduction of **7** with zinc in acetic acid–methylene chloride at −20° or with aluminum isopropoxide in isopropyl alcohol yielded the hydroxy cyclopentenone mixture which was rich in cinerolone (75–90% of **5** and 10–25% of **6**).

Experimental Section[11]

2-(2′-*cis*-Butenyl)-3-methyl-2-cyclopenten-1-ol (2).—Cinerone (**1**, 30.00 g, 0.2 mol) in 50 ml of anhydrous ether was added dropwise with stirring over a 2-hr period to a suspension of 6.46 g (0.17 mol) of lithium aluminum hydride in 300 ml of anhydrous ether at room temperature in a nitrogen atmosphere. After stirring 15 hr at room temperature, the reaction mixture was cooled in an ice bath while 18 ml of saturated sodium sulfate solution was added dropwise followed by the addition of 20 ml of water. The granular solid was removed by filtration and was washed well with ether. The filtrate was dried ($MgSO_4$) and concentrated under reduced pressure to yield a colorless oil. Distillation gave 28.76 g (94%) of the alcohol (**2**): bp 58–60° (0.3 mm); $n^{24}D$ 1.4902.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.79; H, 10.66.

2-(2′-*cis*-Butenyl)-3-methylcyclopentadiene (3).—*p*-Toluenesulfonic acid monohydrate (0.580 g) was suspended in 600 ml of anhydrous benzene and was heated until solution was achieved. After cooling to room temperature, 26.14 g (0.17 mol) of **2** was added dropwise with stirring over a 1-hr period. After stirring for 3 hr at room temperature, the mixture was washed with 100 ml of saturated sodium bicarbonate solution, dried ($MgSO_4$), and concentrated on the water aspirator. The resultant oil was transferred to a Vigreux distillation apparatus (6-in. column) and the distillation flask was packed loosely with glass wool to prevent foaming. The apparatus was connected to the water aspirator and heated at 30° for 30 min to remove the residual benzene. The condenser was then wrapped with crushed Dry Ice and the receiving flask was cooled in a Dry Ice bath. Distillation gave 19.76 g of colorless liquid, bp 17–27° (0.05 mm), which was redistilled to yield 17.70 g (77%) of the diene **3**: bp 21–23° (0.04 mm); $_{\max}^{C_6H_{12}}$ 243 mμ (ε 4000); nmr ($CDCl_3$), singlet with fine structure (2 H) at τ 3.94, multiplet (2 H) at 4.40, singlet with fine structure (3 H) at 8.00, and doublet (J = 5 cps, 3 H) at 8.29. The mass spectrum had a strong molecular ion peak at *m/e* 134 with relatively abundant fragment peaks at *m/e* 119 s (C_9H_{11}), 105 m (C_8H_9), 91 s (C_7H_7), 79 m (C_6H_7), and 77 m (C_6H_5).

Anal. Calcd for $C_{10}H_{14}$: C, 89.49; H, 10.51. Found: C, 89.32; H, 10.71.

Oxidation of 2-(2′-*cis*-Butenyl)-3-methylcyclopentadiene (3) A.—A solution of 2.00 g (0.015 mol) of **3** in 200 ml of methanol containing 50 mg of eosin Y was irradiated for 4 hr with a 200-W bulb clamped 3 in. below the flask. A slow stream of oxygen was bubbled through the mixture which was cooled slightly to maintain a temperature of 25°. The methanol was then removed on the water aspirator and the residual oil was dissolved in chloroform and left on a column of 15 g of basic alumina for 16 hr. Elution with chloroform yielded 1.663 g of crude product which was chromatographed on 30 g of silica gel. Solvent polarity was gradually increased and the fractions obtained were examined by thin layer chromatography. Finally elution with ether gave 310 mg of material with an R_f identical with that of authentic cinerolone. Molecular distillation gave a colorless oil (274 mg, 11% yield) which exhibited two peaks on glpc (0.5% PEG 4000 MS + 0.5% NPGS on Anak. ABS). Pure samples of both compounds were separated by preparative glpc. The first peak (retention time 12.2 min, 42% of mixture) exhibited the following spectral data: $\lambda_{\max}^{CHCl_3}$ 2.76 (sharp), 2.90 (broad), 5.87, and 6.06 μ; $\lambda_{\max}^{EtOH}$ 232 mμ (ε 13,800); nmr ($CDCl_3$), multiplet (2 H) at τ 4.45, broad doublet (1 H) at 5.20, doublet (2 H) at 6.75, singlet (3 H) at 8.25, and doublet (3 H) at 8.30. The mass spectrum had a weak molecular ion peak *m/e* 166 with relatively abundant fragment peaks at *m/e* 148 s ($C_{10}H_{12}O$), 137 w ($C_8H_9O_2$), 133 w (C_9H_9O), 123 w ($C_8H_{11}O$), and 119 w (C_9H_{11}). The second peak (retention time 13 min; 58% of mixture) exhibited $\lambda_{\max}^{CHCl_3}$ 2.76 (sharp), 2.90 (broad), 5.88, and 6.06 μ, $\lambda_{\max}^{EtOH}$230 mμ (ε 11,300), and was identified as cinerolone (**5**) by comparison of its infrared and nmr spectra with those of the authentic compound.[1] The mass spectrum had a strong molecular ion peak at *m/e* 166 with relatively abundant fragment peaks at *m/e* 151 m ($C_9H_{11}O_2$), 148 w ($C_{10}H_{12}O$), 137 m ($C_8H_9O_2$), 133 m (C_9H_9O), 123 ($C_8H_{11}O$), and 119 w (C_9H_{11}). The above mixture was oxidized, as described below, to give a single diketone (**7**). This fact along with the spectral data permit assignment of structure **6** to the first peak.

B.—To a stirred solution of 5.36 g (0.04 mol) of **3** in 400 ml of methanol at −10° was added 9.12 g (0.08 mol) of 30% hydrogen peroxide. The solution was stirred at −10°, and 37 ml (0.084 mol) of 2.27 *M* sodium hypochlorite solution was added in the course of 2 hr. After stirring at −10° for 30 min, the reaction mixture was acidified with dilute hydrochloric acid and the methanol was removed on a rotary evaporator at ~1 mm. The residual oil was taken up in 50 ml of ether and washed with 25 ml of saturated brine, dried ($MgSO_4$), and concentrated at reduced pressure to yield a yellow oil (6.45 g). Distillation through a Vigreux column gave three fractions: (1) bp 50–93° (0.20 mm), 1.24 g; (2) bp 93–115° (0.20 mm), 1.03 g; and (3) bp 115–120° (0.20 mm), 2.66 g of silica gel. Elution with solvents of gradually increasing polarity and examination of each fraction by thin layer chromatography gave 0.80 g of unidentified products in several fractions. Finally elution with 10% ether–benzene and then 100% ether gave 2.64 g of an oil with an R_f identical with authentic cinerolone. Distillation gave a colorless liquid [bp 117–120° (0.15 mm)] which by glpc analysis contained 36% of **5** and 64% of **6**.

2-(2′-*cis*-Butenyl)-3-methyl-2-cyclopentene-1,4-dione (7).—To a stirred solution of 1.0133 g (0.006 mol) of hydroxy ketone mixture (40% of **5** and 60% of **6**) in 20 ml of acetone at 5° was added 1.62 ml (0.0065 equiv) of Jones reagent[12] over a 20-min period. After stirring at room temperature for 15 min, the acetone was removed at reduced pressure. Water (10 ml) was added and the product was extracted with three 25-ml portions of ether. The combined extract was dried ($MgSO_4$) and concentrated at reduced pressure to yield a yellow oil. Distillation gave 0.777 g (78%) of **7**: bp 72–78° (0.20 mm); $\lambda_{\max}^{CHCl_3}$ 5.72, 5.88, and 6.09 μ; $\lambda_{\max}^{EtOH}$ 242 mμ (ε 11,400). The infrared, ultraviolet, and nmr spectra and glpc retention time were identical with those of a sample of **7** prepared by oxidation of authentic cinerolone. The monosemicarbazone of **7** was prepared and recrystallized from acetic acid, mp 260–262° dec.

Anal. Calcd for $C_{11}H_{15}N_3O_2$: C, 59.71; H, 6.83; N, 18.99. Found: C, 59.65; H, 6.87; N, 18.81.

Reduction of 2-(2′-*cis*-Butenyl)-3-methyl-2-cyclopenten-1,4-dione (7) A.—To a stirred solution of 0.500 g of **7** in 25 ml of methylene chloride and 7 ml of acetic acid at −20° was added zinc dust (0.986 g) in portions over a 20-min period. After stirring at −20° for 1 hr, the solvents were removed on the rotary evaporator at ~1 mm. Ether (30 ml) was added and the excess zinc was removed by filtration. The filtrate was washed with two 10-ml portions of 10% sodium carbonate, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was distilled to give 0.290 g (58% yield) of colorless oil, bp 106–108° (0.05

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[10] C. S. Foote and S. Wexler, *J. Amer. Chem. Soc.*, **86**, 3879 (1964).

[11] All melting points were taken in glass capillaries and are corrected; all boiling points are uncorrected. The infrared spectra were determined using a Beckman IR-9 spectrophotometer. The nuclear magnetic resonance spectra were determined using a Varian A-60 spectrometer with tetramethylsilane as the internal standard. The ultraviolet spectra were determined with a Cary 14 spectrophotometer. The high-resolution mass spectra were obtained with a Consolidated Electrodynamics Corporation 21-110 mass spectrometer.

[12] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

mm). Glpc analysis showed the distillate to contain 74% of **5** and 26% of **6**. Smaller scale experiments gave mixtures containing 80–90% **5** and 10–20% **6**.

B.—A solution of 220 mg (1 mmol) of freshly distilled aluminum isopropoxide in 10 ml of anhydrous isopropyl alcohol (distilled from calcium hydride) was heated to reflux and 73.2 mg (0.44 mmol) of **7** in 0.5 ml of anhydrous isopropyl alcohol was added by syringe over 15 min. The isopropyl alcohol was distilled slowly through a Claisen head over 2 hr keeping the volume in the reaction flask constant by the addition of fresh isopropyl alcohol (25 ml was distilled after 2 hr). The remaining isopropyl alcohol was removed on the rotary evaporator at ~1 mm. Ether (20 ml) and water (5 ml) were added and the mixture was acidified with dilute hydrochloric acid. The organic layer was dried ($MgSO_4$) and concentrated to yield a colorless oil (65.5 mg, 90%) which was shown by glpc to contain 84% of **5** and 16% of **6**.

Registry No.—**1**, 17190-71-5; **2**, 17190-72-6; **3**, 17190-73-7; **5**, 17190-74-8; **6**, 17190-75-9; **7**, 17190-76-0.

Acknowledgment—We thank Dr. A. Steyermark and his staff for the microanalyses, Dr. F. Vane for the mass spectra, Dr. T. Williams for the nmr spectra, Dr. V. Toome for the uv spectra, Mr. S. Traiman for the ir spectra, and Mr. H. Jenny for the gas–liquid partition chromatography. We are indebted to Dr. A. Brossi for his encouragement during the course of this work.

Synthesis of $\Delta^{\alpha,\beta}$-Butenolides[1]

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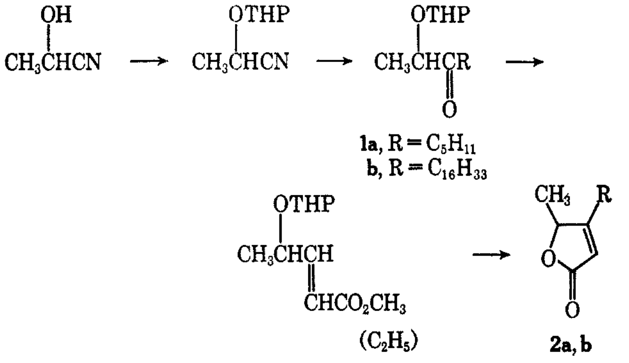
A relatively useful method for the preparation of β,γ-dialkyl-$\Delta^{\alpha,\beta}$-butenolides (γ-lactones of 3,4-dialkyl-4-hydroxycrotonic acids) has been devised in which aldehydes or aldehyde cyanohydrins and alkyl halides are used as starting materials. The condensation reaction between **1** and the Wadsworth–Emmons reagent[2]



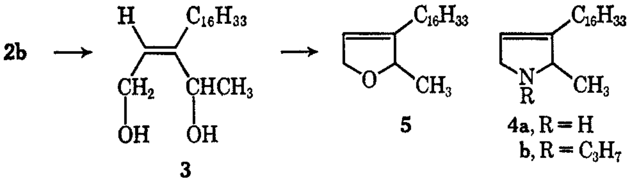
1a, R = C_5H_{11}
b, R = $C_{16}H_{33}$

2a,b

THP = tetrahydropyranyl

is expected to provide a mixture of geometrical isomers. Hence, a considerable quantity of substituted *trans*-4-hydroxycrotonic acid should be present. Further treatment of the acid residue with HCl did not provide any lactone. Recently Epstein and Sonntag[3] transformed methyl *trans*-4-hydroxy-3-methylcrotonate into the γ-lactone of the *cis* isomer by irradiation, in the presence of a trace of HCl, in a quartz cell with a high-pressure mercury arc. We found that treatment with BF_3 etherate in benzene under reflux produced a mixture of polyester and $\Delta^{\alpha,\beta}$-butenolide from which the latter could be distilled. Since the acid fraction may have contained γ-keto acid (5.84 μ) as well as the expected *trans*-4-hydroxycrotonic acid (5.96, 6.09 μ) and the former can be cyclized to $\Delta^{\beta,\gamma}$-butenolides it is not certain that isomerization of the *trans*-4-hydroxycrotonic acid occurred.

The $\Delta^{\alpha,\beta}$-butenolides would appear to be useful synthetic intermediates for other partially dehydrogenated heterocyclic ring systems such as 2,5-dihydrofurans and 3-pyrrolines. In particular, a route was sought to 2-methyl-3-hexadecyl-3-pyrroline which has been proposed[4] as the structure of a component of the venom of the imported fire ant, *Solenopsis saevissima richteri* (Faril). Treatment of **2b** with lithium aluminum hydride gave diol **3** which, with *p*-toluenesulfonyl chloride and excess pyridine, yielded the corresponding 2,5-dihydrofuran. As we had been unable to convert 2-methyl-3-hexadecylpyrrole into its 3-pyrroline,[5] we attempted to prepare it from **3** in analogy to the method of Bobbitt, *et al.*[6] Reaction of **3** with thionyl chloride and pyridine, followed by heating in propylamine, produced **4b**. The 3-pyrroline **4a**, however, was not obtained by similar treatment of **3** with ammonia.



3 **5** **4a**, R = H
b, R = C_3H_7

Experimental Section

Infrared spectra were determined on both Perkin-Elmer Model 137 and 521 infrared spectrophotometers. Ultraviolet spectra were obtained with a Beckman DK-2 spectrophotometer. Nmr spectra were obtained with a Varian HA 100 instrument and chemical shifts are reported in parts per million from tetramethylsilane; carbon tetrachloride was employed as the solvent unless otherwise indicated. Gas chromatograms were obtained with Aerograph Model A-700 and Varian Aerograph Model 204 B instruments employing various columns as indicated below. Elemental analyses were carried out by Galbraith Laboratories, Inc., Knoxville, Tenn.

2-[(Tetrahydropyranyl)oxy]propionitrile.—Lactonitrile[7] (142 g, 2.00 mol) was converted into its tetrahydropyranyl ether in the usual manner. The product was distilled through an 8-in. column packed with helices. After a small forerun, 264 g (85.3%) of product was obtained, bp 58–64° (0.35 mm). The ir spectrum (film) lacked OH absorption, CN was undetectable,[8] and a series of intense bands appeared between 970 and 1120 cm^{-1}. The nmr spectrum showed bands at 1.44 and 1.48 (2 CH_3 doublets—compound is a mixture of diastereomers), 4.28 and 4.48 (two quartets—the H on the neighboring carbon), and 4.72 ppm (multiplet—H on carbon bonded to two oxygens).

Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 62.18; H, 8.49; N, 8.81.

2-[(Tetrahydropyranyl)oxy]-3-octanone (1a).—Pentylmagnesium bromide (from 58.1 g of 1-bromopentane, 9.72 g of magnesium turnings, and 1 l. of anhydrous ether), in a nitrogen at-

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[1] See P. E. Sonnet, *Chem. Ind.* (London), 1296 (1967), for a preliminary communication.

[2] W. S. Wadsworth, Jr., and W. D. Emmons, *J. Amer. Chem. Soc.*, **83**, 1733 (1961).

[3] W. W. Epstein and A. C. Sonntag, *J. Org. Chem.*, **32**, 3390 (1967).

[4] G. A. Adrouny, *Bull. Tulane Univ. Med. Fac.*, **25** (1), 67 (1966).

[5] P. E. Sonnet, *Science*, **156**, 1759 (1967).

[6] J. M. Bobbitt, L. H. Amundsen, and R. I. Steiner, *J. Org. Chem.*, **25**, 2230 (1960).

[7] Obtained from Columbia Organic Chemicals, Inc., Columbia, S. C.

[8] The presence of an oxygenated group, especially on the same carbon that bears CN, results in marked "quenching" of the CN absorption intensity: L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, p 266.