

causing 0.55 g. (51% yield) of 4-amino-5-cyano-6-ethoxy-2-methylpyrimidine to precipitate. The infrared spectrum of this sample was identical with the spectrum of the material prepared from acetamidine and dicyanoketene acetal.

Preparation of Amide and Ester Derivatives of the N-(2,2-Dicyano-1-alkoxyvinyl)-imidic Acids.—The same general procedure was used to obtain all the ester and amide derivatives listed in Table I. To illustrate the procedure the preparation of the phenyl ester is described in detail.

Phenol (2.82 g., 0.029 mole) was dissolved in 20 ml. of dry tetrahydrofuran and 0.69 g. (0.03 g.-atom) of sodium was added. The solution was stirred until the sodium had dissolved. N-(2,2-Dicyano-1-methoxyvinyl)-acetimidoyl chloride (5.0 g., 0.027 mole) was added and the solution was stirred for 0.5 hour and then heated to boiling and evaporated to one-half of its original volume. Anhydrous ethyl ether (25 ml.) was added and the mixture was cooled and filtered. The filtrate was evaporated to dryness to obtain a crystalline solid. This material was recrystallized from ether. The physical properties of the phenyl ester of N-(2,2-dicyano-1-methoxyvinyl)-acetimidic acid are reported in Table I.

5-Amino-4-ethoxy-2-methyl-7-phenylpyrimido[4,5-d]pyrimidine (V).—To a solution of 0.70 g. (0.03 g.-atom) of sodium in 25 ml. of ethanol was added 7.61 g. (0.634 mole) of benzamidine hydrochloride trihydrate followed by 3.96 g. (0.02 mole) of N-(2,2-dicyano-1-ethoxyvinyl)-acetimidoyl chloride. The mixture was stirred for two hours at room temperature and then filtered. The solid was collected and washed with water to yield 1.25 g. (22%) of the crude dipyrimidine. Further purification was accomplished by recrystallization from dimethylformamide; m.p. 264.5°.

Anal. Calcd. for $C_{15}H_{15}N_5O$: C, 64.13; H, 5.33; N, 24.91. Found: C, 64.58; H, 5.64; N, 25.03.

The same results were obtained by using N-(2,2-dicyano-1-methoxyvinyl)-acetimidoyl chloride as the starting mate-

rial. The infrared spectrum is in agreement with the above structure, indicating the presence of all the functional groups.

The ethanol filtrate from above was evaporated almost to dryness, treated with water and filtered. The solid that was collected was identified as the ethyl ester of N-(2,2-dicyano-1-ethoxyvinyl)-acetimidic acid; yield 2.70 g. (65%). This latter compound is formed by a competing reaction and is not an intermediate leading to the dipyrimidine. This point was established when it was shown that the ethyl ester of III did not react with benzamidine under the conditions used in formation of the dipyrimidine.

Attempted Preparation of N-(2,2-Dicyano-1-methoxyvinyl)-acetimidoyl Chloride from the Imidic Acid II and Hydrogen Chloride.—N-(2,2-Dicyano-1-methoxyvinyl)-acetimidic acid (2.0 g.) was dissolved in 50 ml. of boiling acetone. The solution was saturated slowly with dry hydrogen chloride. After the solution was cooled and allowed to stand overnight, a crystalline precipitate was obtained (m.p. 148–149°). This solid dissolved rapidly in water to form solutions which gave an immediate precipitate with silver nitrate. Upon careful neutralization of the cold aqueous solution, 1.8 g. of the starting material was obtained and identified by the mixed melting point method.

Attempted Preparation of N-(2,2-Dicyano-1-methoxyvinyl)-acetimidoyl Chloride from the Imidic Acid II and Acetyl Chloride.—N-(2,2-Dicyano-1-methoxyvinyl)-acetimidic acid (1.0 g.) was dissolved in 20 ml. of boiling acetone. Acetyl chloride (15 ml.) was added and the mixture was heated under refluxing conditions for 8 hours. The solution was cooled and allowed to evaporate under a stream of air. The residue weighed 0.93 g. and was identified as the starting material II by mixed melting points and infrared analysis.

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[CONTRIBUTION NO. 518 FROM THE CENTRAL RESEARCH DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DE NEMOURS AND CO.]

Cyanocarbon Chemistry. XIV.¹ Formation of a Bicyclo[2.2.0]hexane from Tetracyanoethylene

By J. K. WILLIAMS

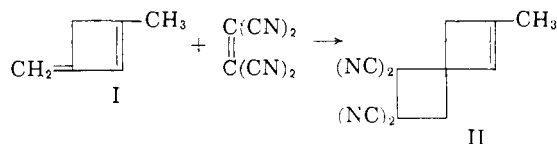
RECEIVED JANUARY 22, 1959

Cyclobutane ring formation occurs when tetracyanoethylene reacts with certain dienes, and in one case a bicyclo[2.2.0]-hexane has been obtained.

Recent reports from this Laboratory have described the chemistry of tetracyanoethylene and have discussed its high reactivity as a dienophile in the Diels-Alder reaction.² Blomquist and Meinwald^{3a,b} have shown that tetracyanoethylene in the presence of a diene that is incapable of forming a Diels-Alder adduct may react by cycloaddition to form a cyclobutane.

We have found that 1-methyl-3-methylenecyclobutene (I)^{4,5} reacts with tetracyanoethylene to give 2-methyl-5,5,6,6-tetracyanospiro[3.3]hept-1-ene (II) in a manner analogous to the formation of 1-methyl-2,3-diphenyl-5,5,6,6-tetracyanospiro[3.3]hept-1-ene from 1-methyl-2,3-diphenyl-4-methyl-

encyclobutene and tetracyanoethylene reported by Blomquist and Meinwald.^{3b} The structure of II is based largely upon infrared and nuclear magnetic



resonance (n.m.r.) spectra. The double bond stretching vibration in the infrared occurs at 6.10μ , a position consistent with an isolated, monosubstituted double bond in a four-membered ring.⁶ The n.m.r. spectrum⁷ of II showed resonance peaks

(1) Paper XIII, H. F. Mower and C. L. Dickinson, *THIS JOURNAL*, **81**, 4011 (1959).

(2) Paper III, W. J. Middleton, R. E. Heckert, E. L. Little and C. G. Krespan, *ibid.*, **80**, 2783 (1958).

(3) (a) A. T. Blomquist and Y. C. Meinwald, *ibid.*, **79**, 5316 (1957); (b) A. T. Blomquist and Y. C. Meinwald, Abstracts of Papers, 133rd Meeting of A.C.S., San Francisco, Calif., 1958, p. 77-N.

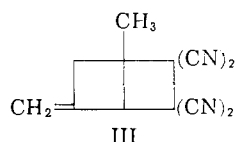
(4) J. K. Williams and W. H. Sharkey, *ibid.*, **81**, in press (1959).

(5) F. F. Caserio, S. H. Parker, R. Piccolini and J. D. Roberts, *ibid.*, **80**, 5507 (1958).

(6) F. F. Cleveland, M. J. Murray and W. S. Gallaway, *J. Chem. Phys.*, **15**, 742 (1947); **16**, 158 (1948).

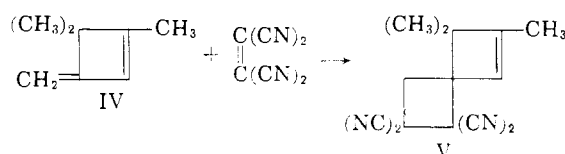
(7) N.m.r. spectra were obtained by means of a high resolution nuclear magnetic resonance spectrometer and associated electromagnet, both manufactured by Varian Associates, Palo Alto, Calif., operating at 40 Mc. and approximately 10,000 gauss. Spectra were calibrated in terms of displacements in cycles per second (c.p.s.) from the proton resonance of H_2O . Negative frequency displacements indicate resonances occurring at higher fields relative to the reference.

of relative area 1:2:2:3 at +46.4 c.p.s. for the single hydrogen at position 1, at -60 and -72 c.p.s. for the four saturated ring-hydrogens, and at -115 c.p.s. for the methyl hydrogens. The alternative methylenebicyclo[2.2.0]hexane (III) structure is eliminated since such a compound would be expected to show absorption in the 11.25 μ region of



the infrared for the out-of-plane bending vibration of the exocyclic methylene hydrogens, and at a lower wave length (*ca.* 5.95 μ) than that observed for the double bond stretching vibration.⁶ In addition, structure III should show an n.m.r. pattern different from that observed, with four resonance peaks of intensity 2:1:2:3, and with the resonance of the two exocyclic methylene hydrogens near 0 c.p.s.⁸

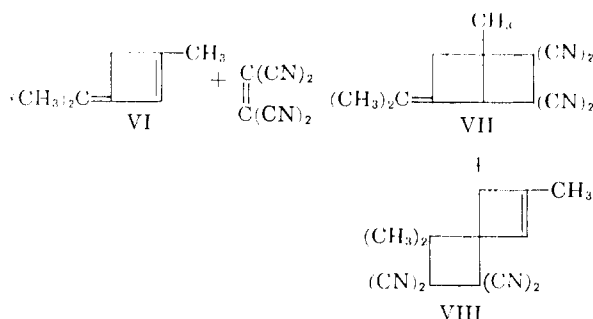
Similarly, tetracyanoethylene reacts with 1,4,4-trimethyl-3-methylenecyclobutene⁴ (IV) to form 2,3,3-trimethyl-5,5,6,6-tetracyanospiro[3.3]hept-1-ene (V). The arguments for structure V parallel



those used in the assignment of structure II. The n.m.r. pattern of V showed a resonance peak at +55 c.p.s. for the single hydrogen at position 1, a weak-strong-strong-weak combination centered at -60 c.p.s. with 11-12 c.p.s. separation for the two saturated hydrogens at position 7, at -132 and -144 c.p.s. for the hydrogens of the *gem*-dimethyl groups, and at -177 c.p.s. for the hydrogens of the methyl group at position 2.

It was of interest to determine if the endocyclic double bond of the diene component could be induced to undergo cycloaddition with tetracyanoethylene by using a diene with a highly substituted exocyclic double bond. The product of such addition would be an example of the difficultly obtainable bicyclo[2.2.0]hexane system.

When 1-methyl-3-isopropylidene-cyclobutene⁴ (VI) was allowed to react with tetracyanoethylene,



(8) H. N. Cripps, J. K. Williams and W. H. Sharkey, *THIS JOURNAL*, **81**, 2723 (1959).

1-methyl-2,2,3,3-tetracyano-5-isopropylidenebicyclo[2.2.0]hexane (VII) was indeed the principal product, obtained as a mixture with a small amount of the spiro isomer VIII formed by addition to the exocyclic double bond. Pure VII was isolated by fractional crystallization. The structure of VII was established by examination of its infrared and n.m.r. spectra and by ozonolysis. The double bond stretching vibration in the infrared occurred at 5.84 μ , as expected for a highly substituted double bond exocyclic to a four-membered ring. No band in the 3.25 μ region was observed, indicating the absence of =CH. The n.m.r. pattern showed the three peaks expected for structure VII in the proper intensity ratio for one tertiary hydrogen (-31 c.p.s.), two saturated ring hydrogens (-56 c.p.s.) and for the nine hydrogens of the three methyl groups (-117 c.p.s.). Ozonolysis of VII gave acetone (isolated as the 2,4-dinitrophenylhydrazone) in 75% yield. Compound VIII was not isolated, but evidence for its presence was found in the infrared spectrum of the crude reaction product which showed bands at 3.30 and 6.08 μ that vanished as VII was isolated by crystallization.

Experimental⁹

2-Methyl-5,5,6,6-tetracyanospiro[3.3]hept-1-ene (II).—When 4.0 g. of 1-methyl-3-methylenecyclobutene^{4,8} (I) and 6.2 g. of tetracyanoethylene were mixed in 50 ml. of tetrahydrofuran, a deep red solution was obtained. After 3 hours at 25°, the red color had been discharged and the clear solution was light amber. The reaction mixture was poured onto a column packed with 350 g. of acid alumina¹⁰ and eluted with 3 l. of ether. When the ether was removed from the eluate, 7.6 g. (75%) of 2-methyl-5,5,6,6-tetracyanospiro[3.3]hept-1-ene (II) was obtained as white needles, m.p. 141.5-142.5°. The melting point was not increased by two recrystallizations from a 1,2-dichloroethane-hexane mixture. The infrared spectrum of II showed absorption at 3.31, 4.47, 6.10 and 7.27 μ . The ultraviolet spectrum had no maxima above 215 m μ .

Anal. Calcd. for C₁₂H₈N₄: C, 69.22; H, 3.87; N, 26.91; mol. wt., 208. Found: C, 69.18; H, 4.00; N, 26.81; mol. wt., 200, 214.

2,3,3-Trimethyl-5,5,6,6-tetracyanospiro[3.3]hept-1-ene (V).—When 11.0 g. of 1,4,4-trimethyl-3-methylenecyclobutene (IV)⁴ and 12.8 g. of tetracyanoethylene were added to 100 ml. of tetrahydrofuran, a deep orange-red solution was obtained. The reaction mixture was stirred at 25° until its color had faded to pale amber (2-3 hours). Most of the tetrahydrofuran was removed by distillation. When 100 ml. of ether was added to the dark-colored residue, crystals of V were deposited. The crystalline material was collected and washed with ether to give 20.7 g. (88%) of 2,3,3-trimethyl-5,5,6,6-tetracyanospiro[3.3]hept-1-ene as colorless prisms, m.p. 160.5-162°. A sample prepared for characterization by three crystallizations from 1,2-dichloroethane melted at 161-162°. The infrared spectrum of V had bands at 4.47, 6.07, 7.20 and 7.30 μ . The ultraviolet spectrum in acetonitrile had no maxima above 215 m μ .

Anal. Calcd. for C₁₄H₁₂N₄: C, 71.16; H, 5.12; N, 23.72; mol. wt., 236. Found: C, 70.83; H, 5.36; N, 23.65; mol. wt., 237.

1-Methyl-2,2,3,3-tetracyano-5-isopropylidenebicyclo[2.2.0]hexane (VII).—When 12.8 g. of tetracyanoethylene was added to a solution of 11.0 g. of 1-methyl-3-isopropylidene-cyclobutene⁴ in 50 ml. of tetrahydrofuran, an intense blue color developed immediately. The mixture was stirred at room temperature for 4.5 hours, at which point the blue color had faded and the mixture was dark amber. The reaction mixture was diluted with 3 l. of absolute ether and passed through a column packed with 750 g. of alumina.¹⁰ An additional 5 l. of absolute ether was passed through the

(9) All melting points are uncorrected.

(10) Aluminum oxide, Woelm, acid (anionotropic), activity grade 1 for chromatographic analysis.

column. The combined ether solutions were evaporated to give 16.7 g. (71%) of white solid, m.p. 99–111°. This material had bands in the infrared at 3.30, 4.46, 5.84 and 6.08 μ . Four recrystallizations of a 5.0-g. sample of the product, m.p. 99–111°, from 1:6 methylene chloride–ether mixture gave 2.2 g. of VII, m.p. 120–121°. The infrared spectrum of VII showed absorption in the infrared at 4.46 and 5.84 μ but none at 3.30 and 6.08 μ . The ultraviolet spectrum of VII in acetonitrile showed no maxima above 215 m μ .

Anal. Calcd. for C₁₄H₁₂N₄: C, 71.16; H, 5.12; N, 23.72; mol. wt., 236. Found: C, 71.33; H, 5.13; N, 23.57; mol. wt., 227.

The crude product, m.p. 99–111°, was estimated to contain 80% of VII by intensity measurements of the 5.84 μ band in the infrared using 1,2-dichloroethane solvent and

solutions of known concentration of pure VII as references.

Ozonolysis of VII.—Ozone was passed into a solution of 1.0 g. of VII in 50 ml. of absolute methanol at –80° until a blue color persisted (0.5 hour). While a slow stream of nitrogen was passed through the mixture, it was allowed to warm to room temperature over the course of 0.5 hour. To the methanolic suspension of ozonide was added 150 ml. of methanol and 0.25 g. of 10% palladium-on-charcoal. This mixture was shaken under 2.5 atm. of hydrogen for 0.25 hour and then filtered to remove the catalyst. When 200 ml. of this solution was distilled into a solution of 1.6 g. of 2,4-dinitrophenylhydrazine in 8 ml. of sulfuric acid, 12 ml. of water and 40 ml. of methanol, 0.75 g. (75%) of acetone 2,4-dinitrophenylhydrazone was obtained, m.p. 123.5–124.5°, alone or mixed with an authentic sample.

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[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, CIBA PHARMACEUTICAL PRODUCTS, INC.]

Amphenone Analogs. III. Pinacol–Pinacolone Type Rearrangement in the Pyridine Series¹

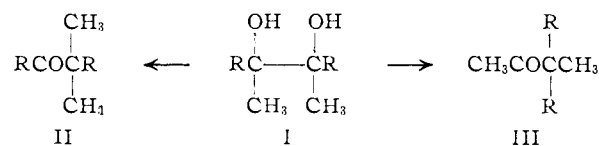
BY W. L. BENCZE AND M. J. ALLEN

RECEIVED JANUARY 12, 1959

The three isomeric acetylpyridines were reduced to the corresponding pinacols which in turn were rearranged.

During the last eight years Amphenone B, a pinacolone-type ketone, was widely investigated in numerous biological and clinical studies due to the striking endocrine effects exerted by this compound in animals as well as in man.²

Amphenone B was prepared by subjecting the butanediol (I) (R = *p*-dimethylaminophenyl) to the pinacol–pinacolone rearrangement.³ The *p*-aminophenyl group was observed to migrate exclusively, hence structure III recently has been assigned to Amphenone B.⁴ The isomeric pinacolone II also has been prepared and was found to possess a narrower spectrum of endocrine activity.¹



The present report deals with the pinacol–pinacolone rearrangement of the butanediols I (R = 2-, 3-, and 4-pyridyl) which gave the pyridyl analogs of Amphenone B. The three diols used were first prepared by bimolecular electrolytic reduction of the respective pyridyl ketones.⁵ Subsequently it was found that these diols could also be prepared photochemically.

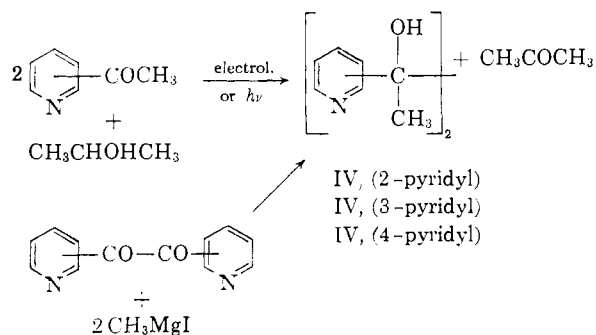
(1) Amphenone Analogs. 11. W. L. Bencze, L. I. Barsky, M. J. Allen and E. Schlittler, *Helv. Chim. Acta*, **41**, 882 (1958).

(2) (a) M. J. Allen, R. Hertz and W. W. Tullner, *Proc. Soc. exp. Biol. Med.*, **74**, 632 (1950); (b) R. Hertz, W. W. Tullner, J. A. Schrickler, F. G. Dhyse and L. F. Hallman, "Recent Progr. in Hormone Research," G. Pincus, ed., Academic Press, Inc., New York, N. Y., 1955, Vol. XI, p. 119; (c) O. Picinelli, *Farmaco (Pavia) Ed. Sci.*, **12**, 428 (1957); (d) H. Kless, *Arzneimittel-Forsch.*, **8**, 83 (1958).

(3) M. J. Allen and A. H. Corwin, *THIS JOURNAL*, **72**, 117 (1950).

(4) (a) W. L. Bencze and M. J. Allen, *J. Org. Chem.*, **22**, 352 (1957); (b) J. Korman and E. C. Olson, *ibid.*, **22**, 870 (1957).

(5) (a) M. J. Allen, *ibid.*, **15**, 435 (1950); (b) M. J. Allen, *Can. J. Chem.*, **37**, 257 (1959); (c) M. J. Allen and H. Cohen, *J. Amer. Electrochem. Soc.*, **106**, 451 (1953).



The photochemical reduction⁶ could be rendered more efficient by irradiating the samples with ultraviolet lamps rather than sunlight. The 2-pyridylbutanediol was also obtained by reaction of α -pyridyl with methylmagnesium iodide. Unfortunately the difficulty in obtaining the β - and γ -pyridyl precluded investigation of this reaction in the 3- and 4-pyridyl-series. The 2-pyridylbutanediol thus obtained was not identical with the product obtained from the photochemical reduction of 2-acetylpyridine. No attempt has thus far been made to investigate the resolvability of these pinacols in order to assign to them the *meso* or *racemic* structure, respectively.

Concentrated sulfuric acid was used as the rearranging agent for all three isomeric butanediols IV. The rearrangement of IV (3-pyridyl) resulted in a binary mixture of pinacolones V and VI. Their separation was accomplished by chromatography on aluminum oxide, or by converting them to their oximes with subsequent fractional recrystallization and hydrolysis to the parent ketones. A partial separation also was achieved by distillation, whereby ketone V appeared in the first fractions followed by a distillate composed of the two com-

(6) W. E. Bachmann, "Organic Syntheses," Coll. Vol. 11, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 71.