Further Hydrolytic Studies on Tetracyanocyclopropanes[1]

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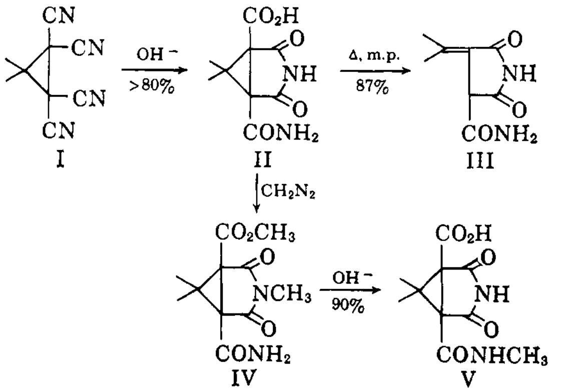
Received February 4, 1963

1,1,2,2-Tetracyanospiro[2.4]heptane has been subjected to a hydrolytic sequence leading ultimately to methyl spiro[2.4]heptane-1,1,2,2-tetracarboxylate. Two additional[2] examples of ring cleavage during the decarboxylation of cyclopropanecarboxylic acids are presented, as is another example of the reaction in which a five-membered imide ring between *cis* substituents is hydrolyzed on one side of a cyclopropane ring plane and formed on the opposite side. N.m.r. evidence for hydrogen bonding in VIII supports a previously proposed mechanism for the latter reaction. The rapid alkaline hydrolysis of 3,3-dialkyltetracyanocyclopropanes to acid amide imides is shown to be general, with three examples in the spiro series.

Several unusual reactions (Scheme 1) were encountered[2] in the hydrolysis of 3,3-dimethyl-1,1,2,2-tetracyanocyclopropane (I) to the corresponding acid. Conversion of I to the acid amide imide (II) was complete after a few minutes of reflux with dilute base, after which further hydrolysis was extremely slow. Prolonged reflux of II with alkali ultimately gave the diacid imide, which failed to hydrolyze further. At its melting point, II lost carbon dioxide with cleavage of the three-membered ring, giving III. Finally, hydrolysis of IV, obtained from the reaction of II with diazomethane, proceeded smoothly to V by cleavage of the N-methylimide ring followed by ring closure to an imide by reaction of the *cis* amide and ester functions on the opposite plane of the cyclopropane ring.

SCHEME 1



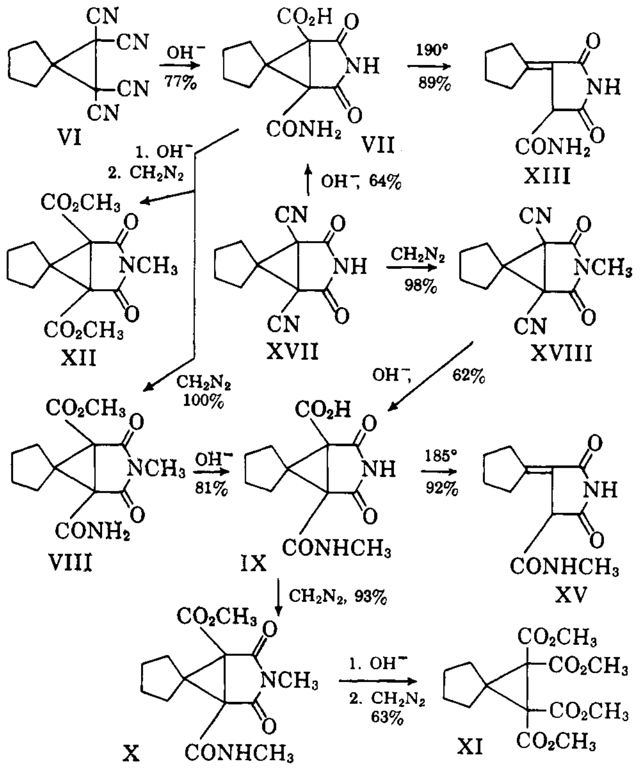
Cessation of the initial hydrolysis at II (and after lengthy reflux, at the diacid imide) can be rationalized in terms of the sluggishness with which hydroxide ion would attack the dianion of II (or the trianion of the diacid imide).[3] Compelling arguments were presented[2] to show that decarboxylation of II to III involves the *cis* amide carbonyl (and not the imide carbonyl) assisting in the proton removal. Finally, hydrogen bonding in IV between the amide nitrogen and the imide carbonyl oxygen closest to it was postulated as the principal reason why attack by base at that imide carbonyl was favored; the product V follows logically from attack by base at that point.

To determine whether these unusual reactions were general, the tetracyanocyclopropane VI, from cyclopentanone,[4] has been subjected in detail to a similar sequence of conversions, and the present paper describes the results. Limited hydrolytic experiments on tetracyanocyclopropanes from cyclohexanone and cyclobutanone are also described.

Results

The tetracyanocyclopropane VI[5] was prepared from cyclopentanone, bromomalononitrile, and iodide ion.[4] Its ultimate hydrolysis to the corresponding tetracarboxylic acid (methyl ester XI) and various intermediate reactions are shown in Scheme 2.

SCHEME 2



Reflux with potassium hydroxide in aqueous methanol converted VI to the acid amide imide VII. The structure of VII follows from its elemental analysis, neutralization equivalent (dibasic), and from its n.m.r. spectrum, which in dimethyl sulfoxide showed singlets at $-1.12\ \tau$ (imide[2]) and $2.44\ \tau$ (amide) with relative areas 1:2. The same product was obtained by alkaline

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[1] We are indebted to the Petroleum Research Fund, American Chemical Society (grant 488-C), and to the National Science Foundation (G 14289) for financial support.

[2] H. Hart and F. Freeman, *J. Am. Chem. Soc.*, **85**, 1161 (1963).

[3] This is, in fact, an oversimplification, but in the absence of mechanistic studies, further discussion seems at present unwarranted.

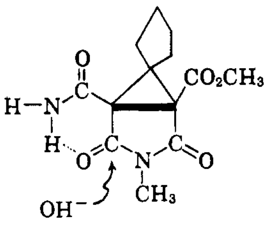
[4] H. Hart and F. Freeman, *J. Org. Chem.*, **28**, 1220 (1963).

[5] Because the systematic names of all compounds described in this paper are cumbersome, they will be given only in the experimental part: otherwise they shall be referred to by number or a trivial name.

hydrolysis of the known[6] dinitrile XVII. Prolonged hydrolysis of VII proceeded only as far as the diacid imide, which was converted by diazomethane to its trimethyl derivative XII, whose n.m.r. spectrum showed sharp singlets at 6.37 τ (O–CH_3) and 7.25 τ (N–CH_3), and a complex multiplet from 8.0–8.5 τ (CH_2), relative areas 6:3:8.

When heated at its melting point for a few minutes, VII lost carbon dioxide and gave XIII. Its n.m.r. spectrum (in dimethyl sulfoxide) showed imide N–H (−1.07 to −0.73 τ), amide N–H (2.43 to 3.53 τ), and a sharp singlet at 4.43 τ (C–H) with relative areas 1:2:1. XIII gave a positive Baeyer test for unsaturation, and with diazomethane gave an N-methyl derivative (XIV).

Reaction of VII with diazomethane afforded a dimethyl derivative VIII, whose n.m.r. spectrum in deuteriochloroform showed sharp singlets at 6.22 τ (O–CH_3) and 7.08 τ (N–CH_3) as well as a broad band in the 8.3-τ region, with relative areas 3:3:8. The n.m.r. also showed broad equal singlets at 2.48 and 3.35 τ, each corresponding to a single proton of the amide group. This supports the postulated[2] hydrogen bonding of one amide hydrogen to the imide carbonyl in such compounds, which should make that carbonyl the most vulnerable position for attack by hydroxide ion.



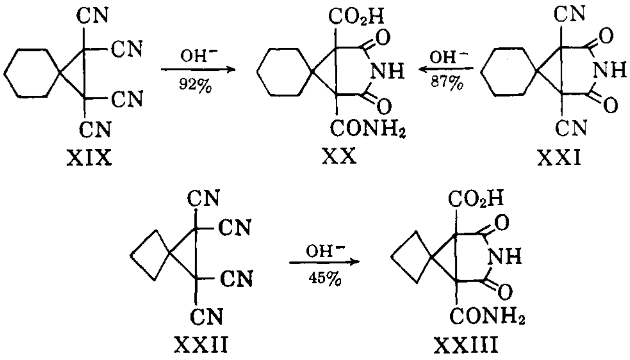
Hydrolysis of VIII by brief reflux with dilute aqueous methanolic alkali gave IX. Its structure follows from its analysis, neutralization equivalent, and additional conversions; its n.m.r. spectrum in dimethylsulfoxide showed one imide (singlet, −0.85 τ) and one amide (poorly resolved symmetrical multiplet, 2.32 τ) proton. Alkaline hydrolysis of XVIII (synthesized from known XVII and diazomethane) also gave IX.

IX was dibasic, and reacted with two moles of diazomethane to give the dimethyl derivative X, which still showed the N–H stretch at 2.95 μ in the infrared, due to the secondary amide group; its n.m.r. spectrum in carbon tetrachloride clearly established its structure as formulated. It showed a single amide proton (complex symmetrical multiplet centered at 2.78 τ), O–CH_3 (singlet, 6.40 τ), imide–N–CH_3 (singlet, 7.23 τ), amide–N–CH_3 (unequal doublet at 7.30 and 7.58 τ; J = 17 c.p.s.), and CH_2 (broad band, 8.13–8.58 τ) with the calculated relative areas. Hydrolysis of X gave the tetracarboxylic acid, which was converted to its tetramethyl ester XI. In contrast to previous intermediates in its synthesis, XI showed a single sharp carbonyl band, at 5.75 μ. Its n.m.r. spectrum in carbon tetrachloride had a single sharp peak at 6.45 τ (OCH_3), and a complex multiplet, 8.12–8.42 τ (CH_2), relative areas 3:2, as expected.

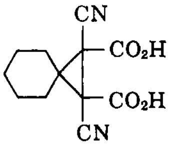
As with VII, IX lost one mole of carbon dioxide when heated just above its melting point and gave the cyclopentylidene derivative XV; the latter was monobasic and, with diazomethane, gave an N-methyl derivative XVI.

Reactions of tetracyanocyclopropanes from cyclohexanone and cyclobutanone are summarized in Scheme 3.

SCHEME 3



XIX[7] was hydrolyzed rapidly in excellent yield to the acid amide imide XX, which also was obtained from the previously known[8] dinitrile XXI. The imide and amide hydrogens of XX appeared at −1.14 and 2.47 τ, respectively, relative areas 1:2, in dimethyl sulfoxide. This compound previously had been assigned[8] the incorrect structure XXIV.



XXIV

The structure XXIII is assigned to the hydrolysis product of XXII[4] on the basis of elemental analysis, infrared spectrum, analogy with the hydrolysis of I, VI, and XIX, and an n.m.r. spectrum in dimethyl sulfoxide which showed imide (−0.78 τ) and amide (2.72 τ) nitrogen, relative areas 1:2.

In summary, the rapid alkaline hydrolysis of tetracyanocyclopropanes derived from ketones leads to acid amide imides (I → II, VI → VII, XIX → XX, and XXII → XXIII).[9] The cyclopropane ring cleavage in the decarboxylation of a cyclopropanecarboxylic acid with a fused five-membered ring and a carbonyl group situated favorably for proton removal is also general (three examples previously given,[2] to which VII → XIII and IX → XV may be added). Finally another example (VIII → IX) is presented of the previously observed (IV → V[2]) ring opening and closing reactions on opposite sides of the cyclopropane plane. Studies of the mechanisms of these reactions are in progress.

Experimental[10]

2-Carboxamido-1,2-dicarboximidospiro[2.4]heptane-1-carboxylic Acid (VII). From 1,1,2,2-Tetracyanospiro[2.4]heptane (VI).—A solution of 3.14 g. (0.016 mole) of VI[4] in 30 ml. of methanol and 30 ml. of 25% aqueous potassium hydroxide was

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[6] S. S. G. Sircar, *J. Chem. Soc.*, 1257 (1927).

[7] S. Wideqvist, *Arkiv Kemi, Mineral. Geol.*, 20B, 4, 8 (1945).

[8] S. F. Birch, W. H. Gough, and G. A. R. Kon, *J. Chem. Soc.*, 119, 1315 (1921).

[9] Preliminary experiments on the alkaline hydrolysis of tetracyanocyclopropanes from aldehydes shows that the reaction takes a different course and, with aromatic aldehydes, leads to dihydroxypyridine derivatives.

refluxed for 3 hr. The alcohol was removed on a rotary evaporator and the remaining liquid extracted continuously with ether for 4 hr. to remove nonacidic products. The aqueous solution was acidified (congo red) with dilute hydrochloric acid and once again extracted with ether for 24 hr. Filtration of the extract gave a solid which, on recrystallization from water, gave 3.1 g. (76.9%) of white crystals of VII, m.p. 187–188° dec.

Anal. Calcd. for $C_{11}H_{12}N_2O_5$: C, 52.37; H, 4.80; N, 11.10; neut. equiv., 126.1. Found: C, 52.17; H, 4.88; N, 11.08; neut. equiv., 124.6.

Its n.m.r. spectrum in dimethyl sulfoxide showed singlets at -1.12 and 2.44 τ, relative areas 1:2.

From 3,3-Pentamethylene-1,2-dicyanocyclopropane-1,2-dicarboximide (XVII).—A solution of 1.9 g. (0.01 mole) of XVII[6] in 15 ml. of 10% aqueous sodium hydroxide was refluxed for 30 min., made strongly acidic with dilute hydrochloric acid, and allowed to stand in the refrigerator for 2 days. The resulting crystals (1.62 g., 64%), m.p. 187–188°, were identical with those described previously.

VII was quantitatively converted to **methyl 2-carboxamido-1,2-(N-methyl)dicarboximidospiro[2.4]heptane-1-carboxylate (VIII)** by reaction with excess diazomethane in methanol, followed by recrystallization from methanol, m.p. 133–134°.

Anal. Calcd. for $C_{13}H_{16}N_2O_5$: C, 55.70; H, 5.75; N, 10.00. Found: C, 55.61; H, 5.77; N, 10.06.

The n.m.r. spectrum of VIII had broad singlets at 2.48 and 3.35 τ, sharp singlets at 6.22 and 7.08 τ, and a multiplet centering around 8.3 τ, relative areas 1:1:3:3:8, in deuteriochloroform.

1,2-Dicarboximidospiro[2.4]heptane-1,2-dicarboxylic Acid and Methyl 1,2-(N-Methyl)dicarboximidospiro[2.4]heptane-1,2-dicarboxylate (XII).—A solution of 1.26 g. (5 mmoles) of VII in 30 ml. of 10% sodium hydroxide was refluxed for 3.25 hr., acidified with dilute hydrochloric acid, and extracted continuously with ether for 36 hr. The resulting acid (0.99 g.) was recrystallized from ethyl acetate–pentane and had a m.p. 135–136.5° dec. It was not analyzed, but converted with diazomethane in methanol to XII, m.p. 101–102°, in 83.5% yield.

Anal. Calcd. for $C_{14}H_{17}NO_6$: C, 56.94; H, 5.80; N, 4.74. Found: C, 56.73; H, 5.85; N, 4.78.

The n.m.r. spectrum (in carbon tetrachloride) had bands at 6.37 and 7.25 τ (sharp singlets) and 8.0–8.5 τ (multiplet), with relative areas 6:3:8.

Decarboxylation of VII.—Heating VII (2.52 g., 0.01 mole) just above its melting point (188–190°) for a few minutes in a nitrogen atmosphere gave, upon cooling and recrystallization from water, 1.85 g. (89%) of **4-carboxamido-3-cyclopentylidenesuccinimide (XIII)**, m.p. 137–138°.

Anal. Calcd. for $C_{10}H_{12}N_2O_3$: C, 57.68; H, 5.81; N, 13.46. Found: C, 57.79; H, 5.68; N, 13.38.

Its n.m.r. spectrum in dimethyl sulfoxide showed an unequal doublet (-0.97 and -0.80 τ), two unequal doublets centered at 2.77 and 3.07 τ (J = 32 c.p.s.), and a sharp singlet at 4.43 τ, with relative areas 1:2:1. XIII gave a positive permanganate test for unsaturation; with an excess of diazomethane in absolute methanol, it was converted to **4-carboxamido-3-cyclopentylidene-1-methylsuccinimide (XIV)**, m.p. 148.5–149°, from methanol.

Anal. Calcd. for $C_{11}H_{14}N_2O_3$: C, 59.44; H, 6.35; N, 12.61. Found: C, 59.51; H, 6.26; N, 12.77.

2-(N-Methyl)carboxamido-1,2-dicarboximidospiro[2.4]heptane 1-carboxylic Acid (IX). From VIII.—A solution of 2.80 g. (0.01 mole) of VIII in 35 ml. of methanol and 25 ml. of 10% aqueous sodium hydroxide was refluxed for 30 min., cooled to room temperature, and the methanol removed on a rotary evaporator. The solution was made strongly acidic (hydrochloric acid) and refrigerated overnight. The resulting crystals, recrystallized from methanol, were obtained in 80.6% yield, m.p. 180–181° dec.

Anal. Calcd. for $C_{12}H_{14}N_2O_5$: C, 54.13; H, 5.30; N, 10.52; neut. equiv., 133.1. Found: C, 54.43; H, 5.10; N, 10.54; neut. equiv., 133.3.

The n.m.r. spectrum in dimethyl sulfoxide showed equal peaks at -0.85 τ (singlet) and 2.32 τ (multiplet).

From XVIII. 3,3-Tetramethylene-1,2-dicyanocyclopropane-1,2-(N-methyl)carboximide (XVIII) was prepared (98%) by adding ethereal diazomethane to a methanolic solution of XVII.[6] Recrystallization from methanol gave white crystals, m.p. 247–248° (dec.).

Anal. Calcd. for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.84; N, 18.33. Found: C, 62.81; H, 4.90; N, 18.28.

When 2.29 g. (0.01 mole) of XVIII was refluxed in 15 ml. of 10% sodium hydroxide for 30 min., cooled, acidified with hydrochloric acid, and refrigerated overnight, there was obtained 1.65 g. (62%) of IX, recrystallized from water. Its m.p. and m.m.p. with a sample prepared from VIII was 180–181°.

Decarboxylation of IX.—When IX (2.66 g., 0.01 mole) was heated just above its melting point (185°) for a few minutes in a nitrogen atmosphere, there was obtained, on cooling and recrystallization from water, 2.05 g. (92.4%) of **4-(N-methyl)-carboxamido-3-cyclopentylidenesuccinimide (XV)**, m.p. 131–132°.

Anal. Calcd. for $C_{11}H_{14}N_2O_3$: C, 59.44; H, 6.35; N, 12.61. Found: C, 59.30; H, 6.28; N, 12.70.

XV gave the N-methyl derivative XVI on treatment with diazomethane, m.p. 93.3–94.0°, from methanol.

Anal. Calcd. for $C_{12}H_{16}N_2O_3$: C, 61.08; H, 6.82; N, 11.68. Found: C, 60.80; H, 6.80; N, 11.79.

Methyl Spiro[2.4]heptane-1,1,2,2-tetracarboxylate (XI).—A solution of 0.26 g. (1 mmole) of IX in 5 ml. of absolute methanol was treated with excess ethereal diazomethane, and the resulting product recrystallized from methanol, giving 0.27 g. (93.1%) of **methyl 2-(N-methyl)carboxamido-1,2-(N-methyl)dicarboximidospiro[2.4]heptane-1-carboxylate (X)**, m.p. 118–119°.

Anal. Calcd. for $C_{14}H_{18}N_2O_5$: C, 57.13; H, 6.16; N, 9.52. Found: C, 57.25; H, 6.02; N, 9.48.

Its n.m.r. spectrum in carbon tetrachloride showed bands at 2.78 τ (multiplet), 6.40 and 7.23 τ (equal singlets), 7.30 and 7.58 τ (together account for three protons), and a broad band at 8.13–8.58 τ, relative areas 1:3:3:3:8.

A solution of 1.47 g. (5 mmoles) of X in 13 ml. of 10% sodium hydroxide and 20 ml. of methanol was refluxed for 30 min., cooled, and the methanol removed using a rotary evaporator, after which the residue was extracted for 6 hr. with ether. The aqueous solution was acidified with hydrochloric acid and again continuously extracted with ether (36 hr.). Evaporation of the ether, Norit treatment of the residue in ethyl acetate solution, and reaction with diazomethane in ether, followed by recrystallization from methanol, gave 1.04 g. (63.1%) of XI, m.p. 103–104°, carbonyl absorption at 5.75 μ.

Anal. Calcd. for $C_{15}H_{20}O_8$: C, 54.87; H, 6.14. Found: C, 55.01; H, 6.23.

Its n.m.r. spectrum in carbon tetrachloride showed a sharp singlet at 6.45 τ and a broad multiplet, 8.1–8.4 τ, with relative areas 3:2.

2-Carboxamido-1,2-dicarboximidospiro[2.5]octane-1-carboxylic Acid (XX). From 1,1,2,2-Tetracyanospiro[2.5]octane (XIX).—A solution of 3.36 g. (0.016 mole) of XIX[4] in 30 ml. of 25% aqueous potassium hydroxide and 40 ml. of methanol was refluxed for 3 hr., the alcohol removed with a rotary evaporator, and the remaining solution extracted for 4 hr. with ether to remove nonacidic products. After acidification to congo red with hydrochloric acid, the solution was extracted continuously with ether for 24 hr., the solid filtered from the extract and recrystallized from water, giving 3.92 g. (92.4%) of white crystals, m.p. 202.5–203° dec., with n.m.r. bands (dimethyl sulfoxide solvent) at -1.14 and 2.47 τ, relative areas 1:2.

Anal. Calcd. for $C_{12}H_{14}N_2O_5$: C, 54.13; H, 5.30; N, 10.52. Found: C, 54.24; H, 5.20; N, 10.50.

From XXI.—An identical product (XX), m.p. and m.m.p., was obtained in 87.2% yield by refluxing 2.29 g. (0.01 mole) of XXI[8] in 15 ml. of 10% sodium hydroxide for 30 min., followed by acidification, refrigeration, and recrystallization from water. With diazomethane, XX was converted in 97% yield to **methyl 2-carboxamido-1,2-(N-methyl)dicarboximidospiro[2.5]octane-1-carboxylate**. m.p. 147–148°, from methanol.

Anal. Calcd. for $C_{14}H_{18}N_2O_5$: C, 57.13; H, 6.16; N, 9.52. Found: C, 57.21; H, 5.96; N, 9.50.

2-Carboxamido-1,2-dicarboximidospiro[2.3]hexane-1-carboxylic Acid (XXIII).—A solution of 2.82 g. (0.01 mole) of 1,1,2,2-tetracyanospiro[2.3]hexane (XXII)[4] in 40 ml. of 2 N aqueous potassium hydroxide was refluxed for 25 min., cooled, acidified to congo red with 4 N hydrochloric acid, and refrigerated for 2 days, during which time white crystals deposited. Recrystallization from methanol gave 1.14 g. (44.9%) of XXIII, m.p. 218–219° dec.

Anal. Calcd. for $C_{10}N_{10}N_2O_5$: C, 50.42; H, 4.23; N, 11.76. Found: C, 50.55; H, 4.34; N, 11.62.

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(10) Melting points are uncorrected. Analyses are by Spang Microanalytical Laboratories, Ann Arbor, Mich. N.m.r. spectra were obtained on a Varian Model A-60 instrument.