Retrograde Michael Reaction in Additions of Active Methylene Compounds to Tetracyanoethylene[1]

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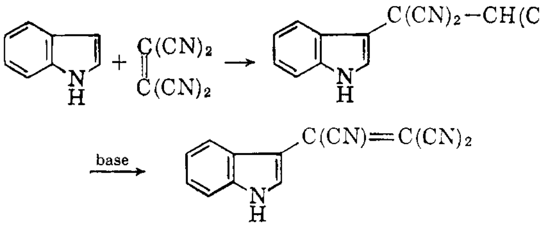
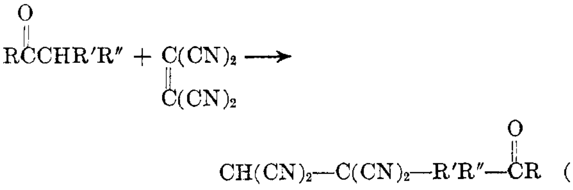
Tetracyanoethylene reacts with 2*H*,3*H*-thieno[3,2-*b*]pyrrol-3-one and 2*H*,3*H*-benzo[*b*]thiophene-3-one to give 2-dicyanomethylene-2*H*,3*H*-thieno[3,2-*b*]pyrrol-3-one (II) and 2-dicyanomethylene-2*H*,3*H*-benzo[*b*]thiophene-3-one (VI), respectively. Compounds II and VI undergo Diels-Alder reactions giving adducts containing spiro systems.

Tetracyanoethylene (TCNE) has been reported to react with aromatic or heterocyclic nuclei to introduce a tricyanovinyl group into the ring system.[3-5] The mechanism proposed for this reaction involves initial addition across the double bond in tetracyanoethylene, followed by the base-induced elimination of hydrogen cyanide (equation 1). The tricyanovinyl group can be converted to a carbethoxyl group by a series of solvolytic steps.[3]



(1)

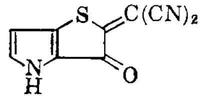
Ketones possessing an α-hydrogen react with tetracyanoethylene to yield substituted tetracyanoethanes (equation 2).[6] The reaction is very slow when no catalyst is used but can be accelerated by addition of the "molecular" silver catalyst of Gomberg and Cone[7] or by volatile acid catalysts, such as hydrogen chloride or boron trifluoride. The adducts with ketones, however, were found to be unstable to basic catalysts and elevated temperatures.[6]



$$R\overset{O}{\overset{\|}{C}}CHR'R'' + \underset{C(CN)_2}{\underset{\|}{C(CN)_2}} \longrightarrow CH(CN)_2{-}C(CN)_2{-}R'R''{-}\overset{O}{\overset{\|}{C}}R \quad (2)$$

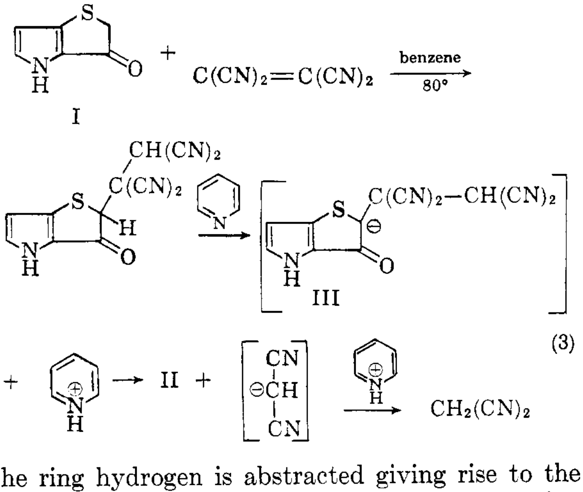
Results and Discussion

It was to be expected that the reaction of 2*H*,3*H*-thieno[3,2-*b*]-pyrrol-3-one (I) with tetracyanoethylene would follow one of the above patterns; reaction according to scheme (1) would afford a means of introduction of the carbethoxyl group into the pyrrole ring of the heterocyclic ketone. When I was refluxed with tetracyanoethylene in dry benzene, a deep maroon solution resulted. After all solid had dissolved, a small quantity of pyridine was added and a maroon solid precipitated. The n.m.r. spectrum possessed doublets at τ = 2.35 p.p.m. (J = 2.4 c.p.s.) and τ = 3.56 p.p.m. (J = 2.4 c.p.s.), consistent with the presence of hydrogen in the α- and β-position of the pyrrole ring, respectively. The product was, therefore, not a tricyanovinyl derivative; the n.m.r. spectrum, the composition, and the reactions mentioned below indicated it to be 2-dicyanomethylene-2*H*,3*H*-thieno[3,2-*b*]-pyrrol-3-one (II).



II

The course of the reaction can be explained by a mechanism similar to the formation of the tricyanovinyl derivatives. After the addition across the double bond of tetracyanoethylene, instead of abstraction of the terminal hydrogen by the base, the ring hydrogen is abstracted giving rise to the anion III. The loss of the malononitrile anion gives the product II (equation 3).



(3)

The presence of malononitrile was detected by the use of thin layer chromatography on silica gel

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[1] Supported in part by a research grant [C3969-Bio] from the National Cancer Institute, Public Health Service.

[2] National Science Foundation Cooperative Fellow, 1960–1961.

[3] B. C. McKusick, R. E. Heckert, T. L. Cairns, D. D. Coffman, and H. F. Mower, *J. Am. Chem. Soc.*, **80**, 2806 (1958).

[4] G. N. Sausen, V. A. Engelhardt, and W. J. Middleton, *ibid.*, **80**, 2815 (1958).

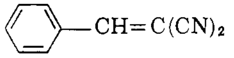
[5] W. E. Noland, W. C. Kuryla, and R. F. Lange, *ibid.*, **81**, 6010 (1959).

[6] W. J. Middleton, R. E. Heckert, E. L. Little, and C. G. Krespan, *ibid.*, **80**, 2783 (1958).

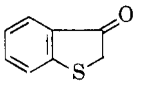
[7] M. Gomberg and M. Cone, *Ber.*, **39**, 3286 (1906).

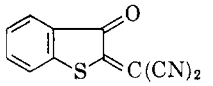
with dioxane as solvent. The solvent was allowed to travel 10 cm. After being dried, the plate was sprayed with basic potassium permanganate. A brown spot in the reaction mixture corresponded to a control of malononitrile ($R_f = 0.67$).

The reaction between I and tetracyanoethylene was repeated, but this time benzaldehyde was introduced immediately after the addition of pyridine. After II was removed, the reaction mixture was concentrated to dryness and benzylidenemalononitrile (IV) was isolated.

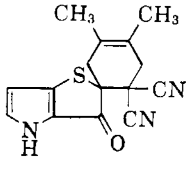

IV

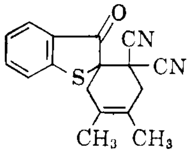
When 2*H*,3*H*-benzo[*b*]thiophene-3-one (V) was treated with tetracyanoethylene, 2-dicyanomethylene-2*H*,3*H*-benzo[*b*]thiophene-3-one (VI) was obtained.


V


VI

Since II and VI contain reactive carbon–carbon double bonds, it was of interest to examine the Diels-Alder reaction with 2,3-dimethylbutadiene. When II and VI were refluxed with the diene for forty-eight hours in ethanol the Diels-Alder adducts VII and VIII, respectively, were obtained.


VII


VIII

The n.m.r. spectrum of VII showed doublets at $\tau = 2.35$ p.p.m. ($J = 2.42$ c.p.s.) and $\tau = 3.68$ p.p.m. ($J = 2.42$ c.p.s.) in good agreement for α- and β-pyrrole hydrogen, respectively. One of the methylene groups showed a singlet at $\tau = 6.90$ p.p.m. The other methylene group, having nonequivalent hydrogens, was split into two doublets; this probably is the methylene group adjacent to the dicyanomethylene group. The two doublets were found at $\tau = 6.89$ and 7.57 p.p.m. ($J = 19$ c.p.s.). The relative area of the outer peak to that of the inner peak was found to be 0.44 (calcd. 0.41).[8] The two methyl groups showed a singlet at $\tau = 8.24$ p.p.m.

The n.m.r. spectrum of VIII also showed similar splitting. The aromatic hydrogen absorption was centered at $\tau = 2.39$ p.p.m. One methylene group had a singlet at $\tau = 6.98$ p.p.m. and the two methyl groups had a singlet at $\tau = 8.23$ p.p.m. The other methylene group was again split into two doublets at $\tau = 6.86$ and 7.66 p.p.m. ($J = 17$ c.p.s.). The relative area of the outer peak to that of the inner peak was equal to 0.50 (calcd. 0.50).[8]

Experimental[9]

2-Dicyanomethylene-2*H*,3*H*-thieno[3,2-*b*]pyrrol-3-one (II).—To a boiling solution of tetracyanoethylene[10] (0.46 g.) in 25 ml. of dry benzene was added 0.5 g. of 2*H*,3*H*-thieno-[3,2-*b*]pyrrol-3-one. The mixture was heated at reflux for 10 min. (or until all solid dissolved) forming a dark maroon solution. Two drops of pyridine were added and the solution refluxed for 15 min., during which time maroon solid started precipitating. The mixture was cooled in a refrigerator and the solid was filtered and dried. The yield of II was 0.72 g. (99.5%). An analytical sample was prepared by two recrystallizations from 95% ethyl alcohol; m.p. 278–279° dec. The infrared spectrum of II showed absorption at 3180 (N—H), 2210 ($C\equiv N$), and 1672 cm.$^{-1}$ (C=O). In the ultraviolet spectrum in ethanol maxima were located at 247 mμ (log ε, 4.16), 281 mμ (log ε, 3.97), 345 mμ (sh.) (log ε, 3.96), and 365 mμ (log ε, 3.98).

Anal. Calcd. for $C_9H_3N_3OS$: C, 53.73; H, 1.50; N, 20.89; S, 15.93; mol. wt., 201.2. Found: C, 53.44; H, 1.63; N, 20.86; S, 15.95; mol. wt., 194.8, 219.3.

Isolation of Benzylidenemalononitrile (IV).—The above procedure was repeated using 2.0 g. of I and 1.84 g. of tetracyanoethylene. Immediately after the addition of the pyridine, 1.48 g. of benzaldehyde was added. The precipitated solid (II) was filtered (2.28 g.). The filtrate was concentrated to dryness under vacuum at room temperature. The residue was recrystallized from ethanol–water, filtered, and dried. The yield of IV was 1.05 g. (59% based on yield of II obtained). An analytical sample was prepared by two recrystallizations from ethanol–water; m.p. 84–85°. A mixed melting point with an authentic sample of benzylidenemalononitrile showed no depression. The infrared spectra were also identical.

Anal. Calcd. for $C_{10}H_6N_2$: C, 77.90; H, 3.92; N, 18.18. Found: C, 77.61; H, 3.96; N, 17.77.

Diels-Alder Adduct of II (VII).—A solution of 0.6 g. of II, 0.02 g. of hydroquinone, and 4.5 ml. of 2,3-dimethylbutadiene in 30 ml. of ethyl alcohol was refluxed for 48 hr. The solvent was removed under vacuum on a hot water bath. The residue was twice recrystallized from ethanol–water. The yield of VII was 0.47 g. (55.7%). The white needles were recrystallized once more from ethanol–water to give an analytical sample; m.p. 220–221°.

Anal. Calcd. for $C_{16}H_{13}N_3OS$: C, 63.59; H, 4.62; N, 14.83. Found: C, 63.62; H, 4.46; N, 14.84, 14.76.

2-Dicyanomethylene-2*H*,3*H*-benzo[*b*]thiophene-3-one (VI).—To a boiling solution of tetracyanoethylene (0.92 g.) in 45 ml. of benzene was added 0.93 g. of 2*H*,3*H*-benzo[*b*]-thiophene-3-one (V)[11] in 10 ml. of benzene. The mixture was heated for 10 min. forming a deep maroon solution. Four drops of pyridine were added and the solution was refluxed for 15 min. After cooling, the solid was filtered and dried. The yield of VI was 1.2 g. (91.7%). An analytical sample

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(8) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Inc., New York, N. Y., 1959, pp. 89–90.

(9) All melting points are uncorrected. Microanalyses and molecular weight determinations were performed by Mr. Josef Nemeth and his associates. N.m.r. spectra were measured by O. W. Norton and his associates on a Varian Associates A-60 spectrometer. Infrared spectra were measured by D. H. Johnson and his associates on a Perkin-Elmer Model 21 spectrophotometer.

(10) T. L. Cairns, R. A. Carboni, D. D. Coffman, V. A. Engelhardt, R. E. Heckert, E. L. Little, E. G. McGeer, B. C. McKusick, W. J. Middleton, R. M. Scribner, C. W. Theobald, and H. A. Winberg, *J. Am. Chem. Soc.*, **80**, 2775 (1958); R. A. Carboni, *Org. Syn.*, **39**, 64 (1959).

(11) C. Hansch and H. G. Lindwall, *J. Org. Chem.*, **10**, 381 (1945).

was obtained by one recrystallization from 95% ethanol; m.p. 263–264° dec. The infrared spectrum of VI showed absorption at 2220 (C≡N) and 1685 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{11}H_4N_2OS$: C, 62.25; H, 1.89; N, 13.20; S, 15.10. Found: C, 62.15; H, 1.81; N, 13.04; S, 15.49.

Diels-Alder Adduct of VI (VIII).—A solution of 0.5 g. of VI, 0.02 g. of hydroquinone, and 4.5 ml. of 2,3-dimethylbutadiene in 50 ml. of ethyl alcohol was refluxed for 48 hr. The solvent was removed under vacuum on a hot water bath. The residue was recrystallized from ethanol–water. The yield of VIII was 0.65 g. (93.8%). The white needles were recrystallized twice from ethanol–water to give an analytical sample; m.p. 157–158°.

Anal. Calcd. for $C_{17}H_{14}N_2OS$: C, 69.35; H, 4.79; N, 9.52. Found: C, 69.57; H, 4.97; N, 9.52.

The Preparation of *s*-Triazine Derivatives Containing the N—O Bond. I. Mono-*N*-oxides of Amino-substituted *s*-Triazine Derivatives[1]

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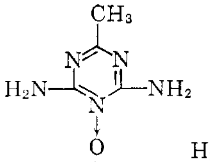
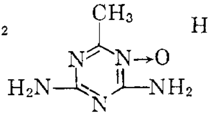
The preparation of mono-*N*-oxides of amino-substituted *s*-triazine derivatives by two methods is reported: peracetic acid oxidation of aminotriazines and cyclization of dicyanoamidine salts with hydroxylamine hydrochloride. Both methods give the same *N*-oxide. The dicyanoamidine salts were obtained by reaction of alkyl imidate hydrochlorides with sodium acid cyanamide (limited to lower alkyl) or by reaction of alkyl- or arylamidines with cyanogen chloride. The latter method appears to be general.

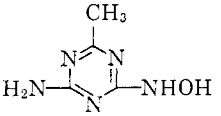
The objective of this investigation was the preparation of mono-*N*-oxides of amino-substituted *s*-triazine derivatives. A review of the literature uncovered only one reference to the preparation of an *s*-triazine mono-*N*-oxide. In this work, by Kaiser and Roemer,[2] a good yield of melamine *N*-oxide was obtained by slurrying an equimolar mixture of potassium dicyanoguanidine and hydroxylamine hydrochloride in Cellosolve. This cyclization method was not chosen initially primarily because the dicyanoamidines required in the reaction were themselves unknown. An alternative route to the *N*-oxides was an oxidative procedure. Grundmann and Schroeder[3] had shown that Caro's acid oxidation of 2-amino-4,6-bis-*p*-chlorophenyl-*s*-triazine gave a tris-*N*-oxide. It was hoped that the use of a milder peracid like peracetic acid under the proper reaction conditions would lead to mono-*N*-oxide formation.

The Peracetic Acid Oxidation of Amino-substituted *s*-Triazines.—The reaction of acetoguanamine (1 mole) with peracetic acid (1.5 moles) was carried out in acetic acid at 40–45° for about twenty-four hours. The compound isolated was a white crystalline solid, whose elemental analysis gave the empirical formula $C_4H_7N_5O$; no water present. The material was soluble in dilute acid and base and gave a deep red color with ferric chloride. To confirm the assumption that the triazine ring was still intact, the oxidized product was treated with phosphorus trichloride in chloroform to deoxygenate it. Acetoguanamine was identified as the resulting product by melting point, elemental analysis, and infrared comparisons with an authentic sample.

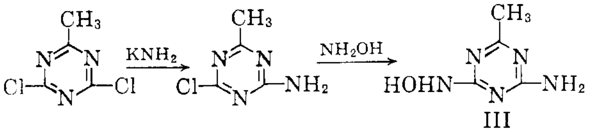
With the previous data in mind, the structural possibilities $C_4H_7N_5O$ appeared to be I, II, or III


I


II


III

and tautomers thereof. The normal triazine *N*-oxide structures are shown for sake of simplicity. The other triazine isomer of $C_4H_7N_5O$, 2,4-diamino-6-hydroxymethyl-*s*-triazine (which was not really expected), was eliminated on the basis of recovering acetoguanamine from the phosphorus trichloride reaction.



III

In the synthesis of III, freshly prepared potassium amide was added in the cold to 2,4-dichloro-6-methyl-*s*-triazine[4] in ether, followed by the addition of an intimate mixture of hydroxylamine hydrochloride and sodium carbonate. The usual physical properties of melting point, infrared, and solubility of III did not agree with those of the peracetic acid–acetoguanamine oxidation product. Furthermore, III gave a blue color with ferric chloride in contrast to the red color of the acetoguanamine product.

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[1] Presented in part before the Division of Organic Chemistry at the 140th National Meeting of the American Chemical Society, Chicago, Ill., September, 1961.

[2] D. W. Kaiser and J. J. Roemer, U. S. Patent 2,729,640 (January 3, 1956).

[3] C. Grundmann and H. Schroeder, *Chem. Ber.*, **87**, 747 (1954).

[4] R. Hirt, H. Nidecker, and R. Berchtold, *Helv. Chim. Acta*, **33**, 1365 (1950).