(4-H); b.p., of ethyl ester, 146–148° (10 mm.)] was nitrated using the procedure described above. Two crystallizations of the product from water gave 4.7 g. of 1,5-dimethyl-4-nitropyrazole-3-carboxylic acid, m.p. 153–155° dec., n.m.r. [$(CD_3)_2SO$] 152 and 230 c.p.s. (CH_3 groups).

Anal. Calcd. for $C_6H_7N_3O_4$: C, 38.92; H, 3.81; N, 22.70. Found: C, 39.26; H, 3.90; N,22.87.

1,5-Dimethyl-4-nitropyrazole (XVI).—1,5-Dimethyl-4-nitropyrazole-3-carboxylic acid (60 g.) was decarboxylated in two batches by heating at 150° for 2 hr. Crystallization of the product from methanol gave 39 g. of 1,5-dimethyl-4-nitropyrazole (XVI): m.p. 114–116°; n.m.r. [$(CD_3)_2SO$] 156 and 230 (CH_3 groups), 488 c.p.s. (3-H).

Anal. Calcd. for $C_5H_7N_3O_2$: C, 42.55; H, 5.00; N, 29.78. Found: C, 42.77; H, 4.95; N, 29.67.

Repeated attempts to oxidize this pyrazole to 1-methyl-4-nitropyrazole-5-carboxylic acid by the method described above failed. Approximately 50% of the starting material was recovered from each oxidation.

1,4,6-Triethyl-1H-pyrazolo[4,3-*d*]pyrimidine-5,7(4H,6H)-dione (XVII) and 2,4,6-Triethyl-2H-pyrazolo[4,3-*d*]pyrimidine-5,7-(4H,6H)-dione (XVIII).—1H-Pyrazolo[4,3-*d*]pyrimidine-5,7(4H,-6H)-dione (VI, 30 g.), prepared by the method of Behrend,[4] 2.5 l. of acetone, 500 ml. of ethyl iodide, and 550 g. of anhydrous potassium carbonate were heated under reflux with stirring for 18 hr. The mixture was filtered and the filtrate was evaporated to dryness. The residue was extracted repeatedly with chloroform, and the combined chloroform extracts were evaporated to dryness, finally under vacuum. The residue was chromatographed on 1300 g. of silica gel. The column was eluted with benzene containing increasing amounts of ethyl acetate. The fractions eluted with 20% ethyl acetate in benzene weighed 7.71 g., and after crystallization from petroleum ether (b.p. 28–38°) gave 5.2 g. of 1,4,6-triethyl-1H-pyrazolo[4,3-*d*]pyrimidine-5,7-(4H,6H)-dione (XVII): m.p. 107–108°; λ_{max} 291 mμ (ϵ 5750); n.m.r. (CD_3COOD) 74 (t, $J = 7$ c.p.s.), 245 (q, $J = 7$), 78 (t, $J = 7$), 241 (q, $J = 7$) (4- and 6-CH_3CH_2–), 87 (t, $J = 7$), 277 (q, $J = 7$) (1-CH_3CH_2–), 457 c.p.s. (3-H).

Anal. Calcd. for $C_{11}H_{16}N_4O_2$: C, 55.91; H, 6.83; N, 23.72. Found: C, 55.98; H, 6.59; N, 23.47.

Further elution of the column with 25% ethyl acetate in benzene gave 10.5 g. of a mixture of 2,4,6-triethyl-2H-pyrazolo-[4,3-*d*]pyrimidine-5,7(4H,6H)-dione (XVIII) and a diethylpyrazolo[4,3-*d*]pyrimidinedione. The diethyl compound was isolated from one fraction containing 827 mg. of the mixture. This fraction was dissolved in alcohol (4 ml.) and the resulting solution was diluted with an equal quantity of absolute ether. The resulting precipitate was separated by filtration and washed with ether. The filtrate was cooled and a second crop of the diethyl compound was obtained. Crystallization of the 230 mg. of product so obtained from alcohol gave 175 mg. of 1,4- (or 6-) diethylpyrazolo[4,3-*d*]pyrimidinedione: m.p. 222–225°; λ_{max} 290.5 mμ (ϵ 5800); n.m.r. (CD_3COOD) 79 (t, $J = 7$ c.p.s.), 240 (poor q, $J = 7$) (4- or 6-CH_3CH_2–), 87 (t, $J = 7$), 274 (q, $J = 7$, 1-CH_3CH_2–), 458 c.p.s. (3-H).

Anal. Calcd. for $C_9H_{12}N_4O_2$: C, 51.91; H, 5.81. Found: C, 51.78; H, 5.68.

The remaining fractions (9.7 g.) were dissolved in 40 ml. of ethanol; an equal quantity of absolute ether was added; and the precipitate was separated by filtration. The filtrate was evaporated and the residue was rechromatographed on 800 g. of silica gel. The material eluted with 45% ethyl acetate in benzene was purified, first by precipitation of the diethyl compound present using alcohol and absolute ether, then by two crystallizations from alcohol. In this way 1.5 g. of 2,4,6-triethyl-2H-pyrazolo-[4,3-*d*]pyrimidine-5,7-(4H,6H)-dione (XVIII), m.p. 148–151°, was obtained: λ_{max} 289 mμ (ϵ 5150); n.m.r. (CD_3COOD) 74 (*t*, $J = 7$), 245 (poor q, $J = 7$), 78 (t, $J = 7$), 238 (q, $J = 7$) (4- and 6-CH_3CH_2–), 92.5 (t, $J = 7$), 263 (q, $J = 7$) (2-CH_3CH_2–), 465 c.p.s. (3-H).

Anal. Calcd. for $C_{11}H_{16}N_4O_2$: C, 55.91; H, 6.83; N, 23.72. Found: C, 55.94; H, 6.84; N, 23.48.

Reaction of 2-Pyrones with Cyanide Ion[1]

GEORGE VOGEL

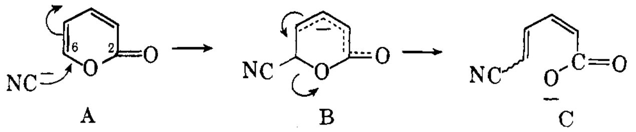
Department of Chemistry, Boston College, Chestnut Hill, Massachusetts 02167

Received September 3, 1964

A number of 2-pyrones are shown to react readily with sodium cyanide in various media to give 5-cyano-2,4-pentadienoic acids. The reaction is stereospecific, and in at least one instance the stereochemistry of the product can be controlled by choice of reaction medium. Intramolecular catalysis of the hydrolysis of a cyano group by a neighboring carboxyl is established and used to distinguish between geometrical isomers.

A 2-pyrone offers two likely points of attack to a nucleophile: the carbon of the carbonyl group (position 2) and the carbon terminating the conjugated carbon chain (position 6). Reactions of the first type have been observed to take place with Grignard reagents,[2] alkoxide ions,[3] and complex metal hydrides under certain conditions.[4] Attack at position 6, to which the effect of the ring carbonyl is transmitted by resonance, occurs with diazomethane (in the presence of suitable activation)[5] and with complex metal hydrides under other conditions.[6,7] The best-known reaction of 2-pyrones with a nucleophile, the conversion into 2-pyridones by the action of ammonia, has been formulated by various workers as proceeding by attack at either position 2 or 6, without experimental evidence for either possibility; the point of attack cannot, of course, be established from the ring-closed product.

The present paper reports on the reaction of a number of readily available 2-pyrones **1** with sodium cyanide, which leads to the corresponding 5-cyano-2-*cis*-4-pentadienoic acids (**2** or **3**), and some further reactions of the latter. The mechanism of the reaction undoubtedly includes attack of the cyanide ion on position 6 of the pyrone A to form a resonance-stabilized carbanion intermediate B, which then breaks down with expulsion of the best leaving group to give the very stable carboxylate anion C.



In accord with this mechanism, the reactivity of 2-pyrones would be expected to be increased by substituents withdrawing electrons from position 6 by resonance, such as a 5-carbalkoxyl group, and de-

---

[1] Presented in part at the 144th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1963; a preliminary report has been published [G. Vogel, *Chem. Ind.* (London), 1829 (1962)].

[2] R. Gompper and O. Christmann, *Chem. Ber.*, **94**, 1784, 1795 (1961).

[3] N. Bland and J. F. Thorpe, *J. Chem. Soc.*, **101**, 1557 (1912).

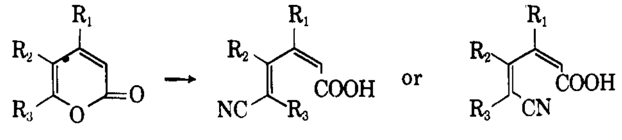
[4] L. R. Morgan, Jr., *J. Org. Chem.*, **27**, 343 (1962).

[5] J. Fried and R. C. Elderfield, *ibid.*, **6**, 577 (1941).

[6] K. Yamada, M. Ishizaka, and Y. Hirata, *Bull. Chem. Soc. Japan*, **34**, 1873 (1961).

[7] G. Vogel, *Chem. Ind.* (London), 268 (1962).

creased by substituents which release electrons to this position or hinder it sterically, such as a 6-methyl. These predictions have been verified in practice. Very surprising, however, is the high reactivity of some of the compounds. Thus, for example, with both the unsubstituted 2-pyrone **1a** and ethyl isodehydroacetate (**1c**), reaction is complete in about 5 min. at or near room temperature, even in a heterogeneous system. It is interesting to compare this with the reaction of a saturated lactone (*e.g.*, phthalide[8]) with an alkali metal cyanide, which requires heating for several hours at temperatures of the order of 180°; this latter reaction is, of course, of the S_N2 type.

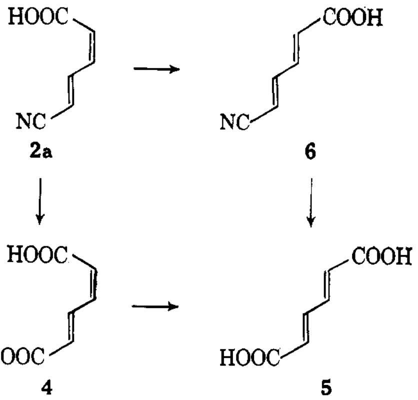


1 **2** **3**

a, $R_1 = R_2 = R_3 = H$
b, $R_1 = R_3 = Me$; $R_2 = H$
c, $R_1 = R_3 = Me$; $R_2 = COOEt$
d, $R_1 = R_3 = Me$; $R_2 = COOH$
e, $R_1 = R_3 = Me$; $R_2 = COOMe$
f, $R_1 = H$; $R_2 = COOMe$; $R_3 = Me$
g, $R_1 = H$; $R_2 = COOH$; $R_3 = Me$
h, $R_1 = R_2 = R_3 = Ph$

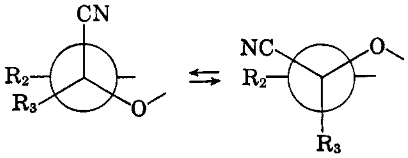
(The formulas of the products are shown in the less likely *s-cis* form solely to stress the relationship to the starting materials.)

The structures assigned to the various 5-cyano-2,4-pentadienoic acids obtained are supported by elemental analyses, neutralization equivalents, and infrared spectra. Moreover, the structure of the simplest of these compounds, 5-*trans*-cyano-2-*cis*-4-pentadienoic acid (**2a**), was established by alkaline hydrolysis to the known *cis,trans*-muconic acid (**4**). The possibility that **2a** is the *cis,cis* isomer (in view of the extremely facile conversion of *cis,cis*-muconic acid into the *cis,-trans* isomer[9]) is ruled out by the presence of a *trans*-olefin band at 970 cm.$^{-1}$ in its infrared spectrum; the reasonable assumption is made that the configuration of the other double bond remains *cis*, as it was in the ring. *cis,trans*-Muconic acid (**4**) was converted[9] into the *trans,trans* isomer **5**, and the latter was compared with an authentic sample. Also, the cyano acid **2a** was isomerized to the *trans,trans* isomer **6**, and this in turn was hydrolyzed to *trans,trans*-muconic acid (**5**).



2a **6** **4** **5**

Interesting questions arise in connection with the geometrical configuration at carbon number 5 of the various 5-cyano-2,4-pentadienoic acids. The intermediate produced by the attack of the cyanide ion on the pyrone would at first have a conformation approximated by the Newman formula D (or its equivalent mirror image). If the stability of the intermediate is so low that it breaks down before conversion into conformation E can take place, departure of the ring oxygen (which must take place in a direction as close to perpendicular to the ring as the ring permits) will leave R_3 on the left and CN on the right, leading to products of the "**3**" series ("retention"). On the other hand, if the intermediate is sufficiently stable to survive one or more oscillations approximately between the conformations D and E (*i.e.*, if the activation energy for the ring opening is much larger than the activation energy for interconversion between D and E), then either of the two possible products (**2** or **3**) can be formed, depending on the relative energies of the transition states preceding products **2** and **3**, as determined by steric and electronic effects; the result may then be either "retention" or "inversion."



D E

Isolation of a "**2**" product from the reaction of 2-pyrone (**1a**) confirms the expectation that the intermediate, at least in this case, is sufficiently stable to survive interconversion between conformations D and E ($R_2 = R_3 = H$), after which ring opens *via* the less hindered conformation E.

Predictions become less secure when (as in all the other cases studied) R_2 or R_3 or both are larger than hydrogen. It is also frequently difficult to establish the configuration of the product reliably. Thus n.m.r. data on 5-cyano-3-methyl-2-*cis*-4-hexadienoic acid (such as obtained here from 4,6-dimethyl-2-pyrone) by Wiley, Balaban, and Crawford[10] favor configuration **2b** over **3b**, but do not rigorously exclude the latter.

However, a most remarkable situation was encountered in the case of ethyl isodehydroacetate (**1c**), with which it is possible not only to steer the reaction toward one or the other geometrical isomer with great stereospecificity by a change in the reaction medium, but also to distinguish unequivocally between the two. Whereas in anhydrous media such as dimethylformamide (DMF) or dimethyl sulfoxide (DMSO) ethyl isodehydroacetate gives with sodium cyanide the isomer **2c** in 70% yield, reaction in aqueous media (aqueous acetone or ethanol) results in a 90% yield of the other isomer, **3c**. Although **3c** can be isomerized to **2c** independently, by heating with a secondary amine or by undergoing a photosensitized reaction in the presence of traces of bromine, no isomerization of preformed **3c** to **2c** takes place under the conditions under which **2c** is obtained in excellent yield, and reaction of ethyl isodehydroacetate with cyanide in aqueous DMF containing a mere 20% of water yields

---

(8) C. C. Price and R. G. Rogers, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 174.

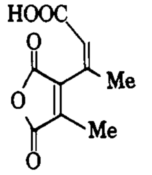
(9) J. A. Elvidge, R. P. Linstead, P. Sims, and B. A. Orkin, *J. Chem. Soc.*, 2235 (1950).

(10) R. H. Wiley, A. T. Balaban, and T. H. Crawford, private communication.

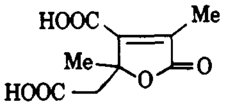
a mixed product in which the "aqueous" product, **3c**, predominates approximately 3:1 over the other. This supports the view that the decisive factor is the presence of water, and it is proposed that the cyano group, normally smaller than the methyl group, becomes effectively larger than the methyl group upon hydration, so that in an anhydrous medium the sterically favored transition state is that derived from E, and, in aqueous media, that derived from D.

Regrettably no other case is known at this time on which this hypothesis could be verified. Methyl 6-methylcoumalate (**1f**) reacted with cyanide in both types of media to give the same product **3f**, which could not be isomerized to **2f** by the methods that were successful with **3c**. A plausible explanation is that the 4-methyl group of ethyl isodehydroacetate, by which the latter differs from methyl 6-methylcoumalate,[11] almost certainly prevents coplanarity of the 5-carbalkoxyl group with the ring, so that the latter group plays merely a steric role; by contrast, absence of this methyl group in methyl 6-methylcoumalate should permit coplanarity of the ester group with the double bond being formed to the cyano group, favoring the more stable *trans* orientation between the two polar groups. This interesting problem needs further study.

Unequivocal distinction between the isomers **2c** and **3c** (and the assignment of correct configuration to **3f**) is possible on the basis of their behavior upon hydrolysis. While both compounds are stable enough to be recrystallized from boiling water (or even 10% hydrochloric acid), one of the two corresponding dicarboxylic acids, which must have the formula **2d**, is hydrolyzed almost instantaneously by mineral acid at the cyano group to give the anhydride **7** (which is also obtained directly when the saponified mixture is acidified without great care). Facile hydrolysis of a cyano group next to a carboxyl has been observed, *e.g.*, in *o*-cyanobenzoic acid,[12] and undoubtedly follows a mechanism closely related to that proposed by Bender, *et al.*,[13] for the hydrolysis of phthalamic acid. The anhydride **7**, which in the present case is the final product rather than an intermediate, exhibits the stability normally associated with dialkylmaleic anhydrides; for example, only the free carboxyl can be esterified by methanol and sulfuric acid, although three acidic groups are present by titration with alkali. This behavior, in addition to the facile hydrolysis of the cyano group in **2d** but not in **2c**, naturally rules out the six- and seven-membered anhydrides which in principle are also possible.



7



8

In contrast to **2d**, the dicarboxylic acid **3d** obtained by saponification of the isomeric half-ester **3c** is largely insensitive to mineral acid, and is hydrolyzed only by refluxing with concentrated hydrochloric acid, to a product to which the structure **8** is assigned tentatively on the basis of ultraviolet and infrared spectra, elemental analysis, and neutralization equivalent. A similar lack of sensitivity to acid leads to assignment of the configurations of **3g** and **3f**, obtained from methyl 6-methylcoumalate.

Experimental[14]

5-*trans*-Cyano-2-*cis*-4-pentadienoic Acid (2a).—To a solution of 2.6 g. (27 mmoles) of 2-pyrone (**1a**)[15] in 6.5 ml. of DMF, 1.59 g. (1.2 moles/mole) of sodium cyanide was added with stirring. In about 5 min., the temperature rose from 25 to 52° and the mixture turned dark brown, most of the solid having gone into solution. After 15–20 min., the mixture was diluted with ice and water, acidified with concentrated hydrochloric acid, and extracted with methylene chloride. The organic layer was extracted with 10% sodium carbonate solution, and the alkaline extract was acidified, precipitating 2.13 g. (64%) of crude **2a**. Recrystallization from benzene yielded 1.74 g. (53%) of slightly off-white needles, m.p. 110–111°, which upon recrystallization from hot water with charcoal afforded a pure white product with m.p. 110–111°, $\lambda_{\max}^{\mathrm{EtOH}}$ 259 mμ (ϵ 23,200).

Anal. Calcd. for $C_6H_5NO_2$: C, 58.54; H, 4.09; N, 11.38. Found: C, 58.2; H, 4.3; N, 11.4.

The methyl ester of **2a** (by diazomethane) had m.p. 51–53° (from hexane).

***cis,trans*-Muconic Acid (4).**—The cyano acid **2a** (0.1 g.) was heated with 0.65 ml. of 20% (w./v.) sodium hydroxide on a steam bath for 15 min.; the odor of ammonia was noticeable almost at once. Acidification and recrystallization from hot water afforded 0.1 g. of *cis,trans*-muconic acid (**4**), m.p. 189–190° (lit.[9] m.p. 190–191°).

Anal. Calcd. for $C_6H_6O_4$: C, 50.71; H, 4.26. Found: C, 50.6; H, 4.2.

The dimethyl ester of **4** (by diazomethane) had m.p. 74–75° (lit.[9] m.p. 75°).

5-*trans*-Cyano-2-*trans*-4-pentadienoic Acid (6).[16]—A solution of 0.80 g. (6.5 mmoles) of the cyano acid **2a** in 3.2 ml. of 25% aqueous dimethylamine was heated on a steam bath for 30 min. and acidified, and the crude product was recrystallized twice from hot water with charcoal to give 0.51 g. (64%) of **6**, white needles, m.p. 175–177°, $\lambda_{\max}^{\mathrm{EtOH}}$ 260 mμ (ϵ 30,400).

Anal. Calcd. for $C_6H_5NO_2$: C, 58.54; H, 4.09; N, 11.38. Found: C, 58.49; H, 4.03; N, 11.24.

The methyl ester of **6** (by diazomethane) had m.p. 92–93° (from methanol).

Hydrolysis of a sample of acid **6** by the method used for the isomer **2a** afforded *trans,trans*-muconic acid, m.p. about 300°, identified by comparison of the dimethyl ester, m.p. 154–155°, with that of an authentic specimen.

5-Cyano-3-methyl-2-*cis*-4-*cis*-hexadienoic Acid (2b).[17]—A mixture of 6.2 g. (50 mmoles) of 4,6-dimethyl-2-pyrone (**1b**) in 12 ml. of DMF and 2.94 g. (1.2 moles/mole) of sodium cyanide was stirred in an oil bath at 180°. Reaction took place rapidly at about 150°, and after stirring for a total of 5 min. at this temperature, the mixture was cooled, poured on ice, and acidified. The crude product was recrystallized from hot water with charcoal to give 4.10 g. (54%) of **2b** as colorless needles, m.p. 117–118° (lit.[18] m.p. 118°), $\lambda_{\max}^{\mathrm{EtOH}}$ 269 mμ (ϵ 17,700).

Anal. Calcd. for $C_8H_9NO_2$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.4; H, 5.9; N, 9.4.

The methyl ester of **2b** (by diazomethane) had m.p. 52–53.5° (from aqueous methanol).

---

[11] Methyl isodehydroacetate (**1e**) reacts with the same stereospecificity as the ethyl ester **1c**.

[12] S. Wideqvist, *Arkiv Kemi*, **2**, 383 (1950).

[13] M. L. Bender, Y.-L. Chow, and F. Chloupek, *J. Am. Chem. Soc.*, **80**, 5380 (1958).

[14] Melting points were determined with a Fisher-Johns apparatus calibrated with standard substances. Elemental analyses were performed by Dr. Carol M. Fitz and Schwarzkopf Microanalytical Laboratory. Satisfactory neutralization equivalents were obtained for all the acidic products. DMF was distilled at atmospheric pressure and a center cut used. Sodium cyanide was powdered reagent grade, dried *in vacuo* at 100°. Pyrone starting materials were prepared by published methods except as noted.

[15] The author is indebted to Dr. H. E. Zimmerman for directions for the preparation of 2-pyrone by decarboxylation of coumalic acid.

[16] Mr. Arthur Girard assisted with this reaction.

[17] The opposite configuration for the cyano group has not been rigorously excluded; see text.

[18] A. T. Balaban and C. D. Nenitzescu, *J. Chem. Soc.*, 3566 (1961).

4-Carbethoxy-5-cyano-3-methyl-2-*cis*-4-*cis*-hexadienoic Acid (2c).—To a stirred solution of 19.6 g. (0.1 mole) of ethyl isodehydroacetate (**1c**) in 40 ml. of DMF, 5.4 g. (1.1 moles/mole) of sodium cyanide was added at 20°. In the course of 5 min., the temperature rose to a maximum of 42°; after a further 15 min., the mixture was diluted with ice and water and acidified. The product, which initially separated as an oil, soon crystallized; it was filtered off and washed with water and with benzene to remove a small amount of an oily by-product. After drying, there was obtained 15.7 g. (70%) of substantially pure **2c**, m.p. 158–160°. Recrystallization from hot water with charcoal afforded pure white needles, m.p. 160–161°, $\lambda_{\max}^{\text{EtOH}}$ 210 mμ (ε 15,000).[19]

Anal. Calcd. for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87; N, 6.28. Found: C, 59.3; H, 5.8; N, 6.3.

Essentially the same results were obtained using DMSO as the solvent.

Reaction of methyl isodehydroacetate (**1e**) with sodium cyanide in DMF similarly gave in 60% yield compound **2e**, m.p. 182–185° (from water).

Hydrolysis of 4-Carbethoxy-5-cyano-3-methyl-2-*cis*-4-*cis*-hexadienoic Acid (2c). A. To 2,4-Dimethyl-3-carboxy-*trans,cis*-muconic Acid 2,3-Anhydride (7).—The half-ester **2c** (2.23 g., 10 mmoles) was dissolved in 12 ml. of 20% sodium hydroxide (6 moles/mole), the solution was cooled to room temperature, and 10 ml. of concentrated hydrochloric acid was added in one portion without cooling. An oil separated, which slowly crystallized (crystallization is made instantaneous by addition of a few drops of benzene). The material was taken up in methylene chloride and the aqueous layer was extracted lightly with the same solvent. After the organic layer was dried, evaporation of the solvent left 1.83 g. (94%) of a crude yellowish product, m.p. 100–105°. Two recrystallizations from chloroform afforded, with considerable losses, the anhydride **7** in colorless needles, m.p. 111–112°, $\lambda_{\max}^{\text{EtOH}}$ 211 mμ (ε 13,500). The infrared spectrum shows anhydride bands at 1850 and 1770 cm.$^{-1}$. The compound decomposes slowly at room temperature.

Anal. Calcd. for $C_9H_8O_5$: C, 55.10; H, 4.11; neut. equiv. (mol. wt./3), 65.3. Found: C, 55.02; H, 3.98; neut. equiv., 64.8.

Attempted Conversion of 7 into the Free Tricarboxylic Acid.—The anhydride **7** (0.196 g.) was dissolved in 1.2 ml. of 20% sodium hydroxide, and the solution was carefully acidified while cooling in ice. Nothing separated immediately, but, after about 30 min., separation of the starting material set in and appeared essentially complete at the end of 2 hr.

Attempted Esterification to Trimethyl Ester.—The anhydride **7** (0.3 g.), 2.5 ml. of absolute methanol, and 1 drop of concentrated sulfuric acid were refluxed for 3 hr. After distilling off the bulk of the alcohol and adding ice and water, about 0.3 g. of a product crystallized, which after recrystallization from hexane melted at 41–42°. The product showed anhydride bands similar to those of the anhydride **7** in the infrared, and analysis and comparison with the product of the action of diazomethane on anhydride **7** showed that only the free carboxyl group had been esterified.

Anal. Calcd. for $C_{10}H_{10}O_5$: C, 57.14; H, 4.80. Found: C, 57.3; H, 4.8.

The same anhydride **7** was obtained by hydrolysis of the methyl half-ester **2e**, proving its configuration.

B. To 4-Carboxy-5-cyano-3-methyl-2-*cis*-4-*cis*-hexadienoic Acid (2d).—The half-ester **2c** (1.12 g., 5 mmoles) was dissolved in 6 ml. of 20% sodium hydroxide (6 moles/mole) at room temperature, and while cooling in ice and stirring, 3 ml. of concentrated hydrochloric acid was added very slowly. The fine white precipitate that separated was filtered off (the filtrate gave a very strong test with Nessler's reagent, indicating some hydrolysis of the cyano group), washed with water and ether, and dried *in vacuo* to give 0.7 g. (70%) of **2d** as a slightly off-white powder, which turned progressively yellow on heating and melted indistinctly at about 130° with profound decomposition. Since the compound could not be recrystallized from any of several solvents, it was analyzed directly.

Anal. Calcd. for $C_9H_9NO_4$: C, 55.38; H, 4.65; N, 7.18. Found: C, 55.1; H, 4.6; N, 7.2.

The dimethyl ester of **2d** (by diazomethane), needles, had m.p. 62–63° (from methanol).

An attempt to prepare the same dimethyl ester of **2d** by esterification–transesterification of the ethyl half-ester **2c** failed; after refluxing 2.3 g. of **2c** with 0.2 ml. of concentrated sulfuric acid and 10 ml. of methanol for 11 hr., only the methyl ethyl ester, m.p. 37–38°, was obtained, which was identical with the product obtained by the action of diazomethane on the ethyl half-ester **2c**. The carbethoxyl group of **2c** is apparently highly hindered.

4-Carbethoxy-5-cyano-3-methyl-2-*cis*-4-*trans*-hexadienoic Acid (3c).—A stirred solution of 9.8 g. (50 mmoles) of ethyl isodehydroacetate (**1c**) in a mixture of 5 ml. of water and 12.5 ml. of acetone was cooled to 5°, and 2.75 g. (1.1 moles/mole) of sodium cyanide was added in one portion. The temperature reached a maximum of about 33° in 4–5 min.; after a total of 15 min., the acetone was evaporated *in vacuo*, and the mixture was diluted with water and acidified. The product, which initially separated as an oil, soon crystallized; it was filtered off, washed with water and hexane, and dried to give 10.0 g. (90%) of a slightly yellowish product, m.p. 67–77°. Recrystallization from hot water with charcoal afforded 8.0 g. (72%) of the ethyl half-ester **3c**, white needles, m.p. 77–79°, $\lambda_{\max}^{\text{EtOH}}$ 210 mμ (ε 15,500).

Anal. Calcd. for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87; N, 6.28. Found: C, 58.95; H, 5.82; N, 6.21.

Methyl isodehydroacetate (**1e**) reacted similarly to give in 62% yield the methyl half-ester **3e**, needles, m.p. 97–98° (from water).

4-Carboxy-5-cyano-3-methyl-2-*cis*-4-*trans*-hexadienoic Acid (3d).—A solution of 2.23 g. (10 mmoles) of the half-ester **3c** in 6 ml. of 20% sodium hydroxide (3 moles/mole) was allowed to stand for 5 min., and then cooled and acidified with concentrated hydrochloric acid. The crystals that separated rather slowly upon standing in ice were filtered off (the filtrate gave a negative Nessler test) and dried to give 1.62 g. (83%) of essentially pure **3d**, which after recrystallization from hot water with charcoal afforded 1.38 g. (70%) of pure **3d**, white needles, m.p. 149–150° dec., $\lambda_{\max}^{\text{EtOH}}$ 210 mμ (ε 12,700).

Anal. Calcd. for $C_9H_9NO_4$: C, 55.38; H, 4.65; H, 7.18. Found: C, 54.95; H, 4.68; N, 6.78.

Isomerization of 3c to 2c. A.—A solution of 0.7 g. of **3c** in 2 ml. of benzene containing a trace of bromine was allowed to stand on an ordinary fluorescent tube for 24 hr., adding more bromine after about 12 hr. Filtration and washing with benzene afforded 0.42 g. (60%) of essentially pure **2c**, identified by mixture melting point with an authentic sample.

B.—A solution of 0.5 g. of **3c** in 13 ml. of 10% aqueous piperidine was heated on a steam bath for 1.5 min. After cooling, acidification afforded 0.34 g. of a solid which after washing with benzene weighed 0.18 g. (36%) and was identical with **2c** (by mixture melting point). When the time of heating was extended to 30 min., **2c** was no longer obtained upon acidification but instead the product was **2b** (0.12 g., 24%), by loss of carbethoxyl. The same compound was obtained when **2c** was treated similarly.[20]

Simultaneous Formation of 2c and 3c in Aqueous DMF.—Benzene extraction of the crude product from 1.96 g. of **1c** and sodium cyanide in aqueous DMF (1:4) (see preparation of **2c**) left undissolved 0.41 g. of substantially pure **2c**; evaporation of the extract and recrystallization from hot water afforded 1.21 g. of pure **3c**.

4-Carbomethoxy-5-cyano-2-*cis*-4-*trans*-hexadienoic Acid (3f). A. In DMF.—To a solution of 3.36 g. (20 mmoles) of methyl 6-methylcoumalate (**1f**)[21] in 7 ml. of DMF, 1.03 g. (1.05 moles/mole) of sodium cyanide was added with cooling at 3–7° over a period of 4 min., during which the cyanide went almost completely into solution. The mixture was allowed to come to room temperature, and at the end of about 25 min. the mixture was cooled in ice and diluted with about 125 ml. of dry ether.[22] The reddish salt that separated was filtered off, washed with ether, and dissolved in 25 ml. of water; the solution was acidified to yield, after drying, 2.83 g. of the crude product. Recrystallization from benzene–cyclohexane (1.5:1) with charcoal yielded 2.69 g. (69%) of pure **3f**, white needles, m.p. 99–100°,

---

[19] For a discussion of the anomalously low absorption maxima of some of the compounds, see G. Vogel, *Chem. Ind.* (London), 1954 (1964).

[20] Although this suggests that **2b** is formed *via* **2c**, it does not prove its configuration, in view of the possibility of a second isomerization taking place.

[21] This compound is readily obtained in about 50% yield by a natural extension of the observations of Fried and Elderfield[6]: Excess ethereal diazomethane is added to coumalic acid at 0–10°, insoluble impurities are filtered off, and the residue after evaporation of ether is recrystallized from methanol: m.p. 83–85° (lit.[5] m.p. 86–87°).

[22] This method of isolation can also be used to advantage in the other reactions in DMF.

$\lambda_{\max}^{\mathrm{EtOH}}$ 260 mμ (ε 12,000). (Attempted recrystallization from hot water caused darkening and a less pure product.)

B. In Aqueous Acetone.—To a partial solution of 1.68 g. (10 mmoles) of methyl 6-methylcoumalate (**1f**) in 4 ml. of acetone and 4 ml. of water, 0.54 g. (1.1 mole/mole) of sodium cyanide was added over a period of 4 min. at 5–10°. The mixture became homogeneous after about 10 min., when cooling was removed; at the end of 20 min., acetone was removed *in vacuo* and the residual aqueous solution was acidified to give 1.44 g. (74%) of a slightly impure product, which after recrystallization from benzene–cyclohexane proved to be identical with the product obtained in DMF solvent.

Anal. Calcd. for $C_9H_9NO_4$: C, 55.38; H, 4.65; N, 7.18. Found: C, 55.58; H, 4.69; N, 7.37.

4-Carboxy-5-cyano-2-*cis*-4-*trans*-hexadienoic Acid (3g).—The preceding half-ester **3f** (0.56 g., 2.87 mmoles) was dissolved in 1.7 ml. of 20% sodium hydroxide (3 moles/mole), and after 5 min. the solution was cooled in ice and acidified to congo red with the calculated amount of concentrated hydrochloric acid added over a period of 3–5 sec. (slow acidification in another run resulted in the precipitation of a salt, probably the monosodium salt, which was not converted readily into the diacid upon standing in the solution). The crystals, which separated rather slowly at ice temperature, were filtered off and washed with a few drops of ice-cold water, and the crude product after drying in a vacuum desiccator was recrystallized from benzene with charcoal to give 0.21 g. (40%) of **3g**, colorless needles, m.p. about 125° dec., $\lambda_{\max}^{\mathrm{EtOH}}$ 256 and 209 mμ (ε 9200 and 8500).

Anal. Calcd. for $C_8H_7NO_4$: C, 53.04; H, 3.90; N, 7.73. Found: C, 53.16; H, 4.13; N, 8.01.

Hydrolysis of 4-Carboxy-5-cyano-3-methyl-2-*cis*-4-*trans*-hexadienoic Acid (3d).—A mixture of 3 g. of the acid and 12 ml. of concentrated hydrochloric acid was refluxed for 1.5 hr. and cooled in an ice–salt mixture, and the crystals that separated were filtered off and washed with a little ice-cold water. After drying there was obtained 0.6 g. of a material which after recrystallization from water with charcoal weighed 0.42 g. (13%) and had m.p. 214–216°, $\lambda_{\max}^{\mathrm{EtOH}}$ 228 mμ (ε 9600).

Anal. Calcd. for $C_9H_{10}O_6$: C, 50.47; H, 4.71; neut. equiv. (mol. wt./2), 107. Found: C, 50.70; H, 4.90; neut. equiv., 107.

5-*trans*-Cyano-3,4,5-triphenyl-2-*cis*-4-pentadienoic Acid (2h).[23]—To a solution of 3.36 g. (10.4 mmoles) of 4,5,6-triphenyl-2-pyrone (**1h**) in 8 ml. of DMF, 0.53 g. (1.05 moles/mole) of sodium cyanide was added and the mixture was heated with stirring for 3 hr. at 150°. After the mixture was poured into water, a little tarry material was removed with methylene chloride, and the aqueous layer was acidified to give an oil which slowly solidified. After grinding this with water and drying, **2h** was obtained as a grayish powder; recrystallization from methanol with charcoal yielded 2.93 g. (80%) of **2h**, white needles, m.p. 197–201°.

Anal. Calcd. for $C_{24}H_{17}NO_2$: C, 82.00; H, 4.88; N, 4.01. Found: C, 81.65; H, 4.64; N, 3.93.

Acknowledgment.—The author wishes to thank the National Science Foundation for generous support of this research through Grant GP-1072, and Dr. A. T. Balaban for helpful discussion and a sample of 5-cyano-3-methyl-2,4-hexadienoic acid.

[23] This configuration of the cyano group is the more likely one for steric reasons (see text), but a rigorous proof is lacking.

Bridged Polycyclic Compounds. XXVII. Addition of Thiophenol to 5-Methylenenorbornene[1]

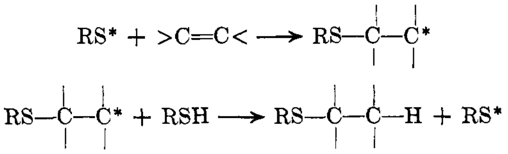
STANLEY J. CRISTOL, THOMAS W. RUSSELL, AND DAVID I. DAVIES

Department of Chemistry, University of Colorado, Boulder, Colorado 80304

Received September 1, 1964

Free-radical addition of thiophenol to 5-methylenenorbornene (XI) gives three products, all resulting from preliminary attack of the phenylmercapto radical on the endocyclic double bond. Two of the products are formed by 1,2-addition and the third by homoconjugate addition. Dilution experiments indicate that classical radical intermediates are involved. These results are compared with those with trichloromethyl radical.

The mechanistic details of the addition of mercaptans to olefins *via* a free-radical chain mechanism have been well investigated. Kharasch, Read, and Mayo[2] have proposed the following mechanism.

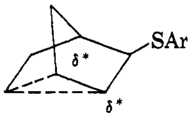


$$RS^* + {>}C{=}C{<} \longrightarrow RS{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{}^*$$

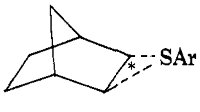
$$RS{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{}^* + RSH \longrightarrow RS{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}H + RS^*$$

We have been interested in the nature of the free-radical intermediate, in particular, the question of whether nonclassical structures analogous to those proposed for ionic additions need to be considered for free-radical addition reactions.

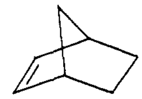
Evidence against the existence of carbon-bridged structures, such as I,[3] or sulfur-bridged structures, such as II,[4] as product-determining intermediates has already been adduced. Thus, addition of *p*-thiocresol to norbornene (III) gave only unrearranged *exo*-2-norbornyl *p*-tolyl thio ether,[3] and addition of *p*-thiocresol to a substituted norbornene (6-chloroaldrin) gave *exo–cis* addition of the thiyl radical and the hydrogen atom.[4] Addition of *p*-thiocresol to norbornadiene (IV) has also been described[5] and provided no evidence for a homoallylic nonclassical radical, V. As the ratio of the two products, *exo*-5-dehydronorbornyl *p*-tolyl thio ether and 3-nortricyclyl *p*-tolyl thio ether, varied with changes



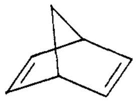
I



II



III



IV

---

[1] Previous paper in series: S. J. Cristol and D. D. Tanner, *J. Am. Chem. Soc.*, **86**, 3122 (1964). The work described in this paper was presented at the 146th National Meeting of the American Chemical Society, Denver, Colo., Jan. 1964.

[2] M. S. Kharasch, A. T. Read, and F. R. Mayo, *Chem. Ind.* (London), 752 (1938).

[3] S. J. Cristol and G. D. Brindell, *J. Am. Chem. Soc.*, **76**, 5699 (1954).

[4] S. J. Cristol and R. P. Arganbright, *ibid.*, **79**, 6039 (1957).

[5] S. J. Cristol, G. D. Brindell, and J. A. Reeder, *ibid.*, **80**, 635 (1958).