Heptafulvenes. I. The Synthesis of 8,8-Dicyano-2,3-dihydroxyheptafulvene[1]

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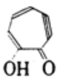
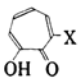
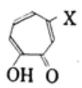
A number of studies of the substitution reactions accompanying rearrangement, which are explainable by an elimination-addition mechanism involving benzyne or its related intermediates, have been made, and a detailed review of this problem has been published.[2] In the field of tropolone chemistry, several reactions deduced to involve analogous intermediate tropolonyne[2] or dehydrotropolone (I, exactly its anion) have also been found: the formations of 3-hydroxy- (III) and 4-hydroxytropolones (IV) from 3-bromotropolone (II) by high-temperature alkaline hydrolysis,[3,4] of 4-cyanotropolone (V) from II reaction with potassium cyanide,[5] and of 4-aminotropolone (VII) from 3-iodotropolone (VI) by treatment with potassium amide in liquid ammonia.[6]



I



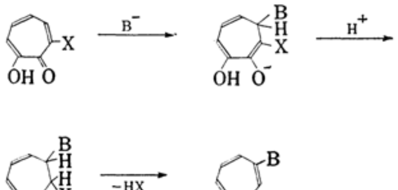
II : X=Br
III : X=OH
VI : X=I



IV : X=OH
V : X=CN
VII : X=NH$_2$

Very recently, novel examples of synthesizing bicyclic tropolones by intramolecular cyclization involving dehydrobromination have also been reported.[7]

In these reactions of halotropolones, however, the following process is also a possible mechanism to explain the above abnormal substitutions:[8]



The Michael-type addition of an anion (B$^-$) to halotropolone, which is an unsaturated conjugated carbonyl compound, would occur, and then hydrogen halide would be eliminated, giving an abnormal substitution product.

No experimental proofs of these possible mechanisms have yet been obtained, so further detailed investigations of these abnormal substitution reactions are desirable. Some compounds containing an active methylene were found to be phenylated in a reaction with benzyne in liquid ammonia.[9] Accordingly,

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[1] This work was presented at the General Meeting of the Hokkaido district of the Chemical Society of Japan, July, 1960.

[2] H. Heaney, *Chem. Revs.*, **62**, 81 (1962).

[3] T. Nozoe and Y. Kitahara, *Proc. Japan Acad.*, **30**, 204 (1954).

[4] Y. Kitahara, *Sci. Repts. Tohoku Univ., Ser. I*, **39**, 258 (1956).

[5] Y. Kitahara, ibid., **40**, 74 (1956).

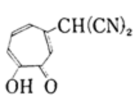
[6] K. Doi, This Bulletin, **34**, 497 (1961).

[7] K. Ogura, ibid., **35**, 808 (1962).

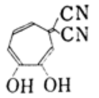
[8] Y. Kitahara, *Sci. Repts. Tohoku Univ., Ser. I*, **39**, 250 (1956).

[9] W. W. Leake and R. Levine, *J. Am. Chem. Soc.*, **81**, 1169, 1627 (1959); J. F. Bunnett and T. K. Brotherton, *J. Org. Chem.*, **23**, 904 (1958).

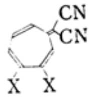
the authors expected to obtain 4-dicyanomethyltropolone (VIII) from the reaction of 3-iodotropolone (VI) with malononitrile under similar conditions. The product actually obtaind, however, was confirmed to be a heptafulvene derivative (IX), and an enolic isomer of VIII, the details of which will be described in this paper.

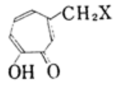


VIII



IX



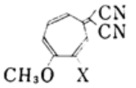


X : X=OCH_3 XII : X=CO_2H
XI : X=OAc XIII : X=H
XVI : X=H

3-Iodotropolone (VI) reacted with sodiomalononitrile in liquid ammonia to give a yellow product with the composition of $C_{10}H_6O_2N_2$ in about a 30 per cent yield. Its ultraviolet absorption maxima (Fig. 1) are at a longer wavelength region than those anticipated for the structure VIII, and its infrared spectrum indicates the presence of the conjugated nitrile grouping (Table I). Therefore, this product is deduced not to be the expected tropolone derivative (VIII) but its enolic isomer, 8, 8-dicyano-2, 3-dihydroxyheptafulvene (IX). This deduction is strongly supported by the fact that IX reacted with diazomethane and acetic anhydride to yield the dimethoxy (X) and diacetoxy (XI) derivatives respectively. On being heated in concentrated sulfuric acid, IX was hydrolyzed and partially decarboxylated to give 4-carboxymethyltropolone (XII), which led to 4-methyltropolone (XIII). From the above facts, the position of the dicyanomethylene grouping of IX can also be elucidated. In the course of the formation of the carboxymethyl derivative (XII) from IX, the corresponding dicarboxymethyltropolone or its isomeric heptafulvene derivative was assumed as an intermediate, but it has not yet been actually isolated.

On being treated with dilute alkali under mild conditions, both X and XI were readily hydrolyzed to give IX, maintaining the dicyanoheptafulvene skeleton. It is possible that the reactivities of the methoxyl and acetoxyl groups of the above heptafulvenes, X and XI, depend on their positions, but in alkaline hydrolyses of X and XI no partially hydrolyzed products other than IX have been isolated.

The methylation of IX with dimethyl sulfate give a yellow monomethylated product (XIV), which led to the dimethoxy derivative (X) upon reaction with diazomethane and to the acetoxy derivative (XV) upon heating with acetic anhydride. These facts indicate that the reactivities of the two hydroxyl groups of IX depend on their positions in the heptafulvene nucleus. A study attempting to determine the position of methoxyl group of the partially-methylated product, XIV, will be reported elsewhere.



XIVa : X=OH XIVb : X=OH
XVa : X=OAc XVb : X=OAc

Figure 1 indicates the ultraviolet absorption spectra of three heptafulvene derivatives, the features of which resemble those of 8, 8-dicyanoheptafulvene[10] (XVI).

Table I indicates some principal absorption maxima of the infrared spectra of the heptafulvenes compared with those[10] of XVI. The details of these spectroscopic analyses will be described in the near future.

As has been described hitherto, it has been clarified that 3-iodotropolone (VI) reacts with sodiomalononitrile in liquid ammonia to yield an abnormally-substituted product, 8, 8-dicyano-2, 3-dihydroxyheptafulvene (IX), which is an enol form of 4-dicyanomethyltropolone (VIII). For the following reasons, this reaction presumably proceeds by way of an intermediate dehydrotropolone or tropolonyne (I), as has been stated by other authors.[2,6] First, this

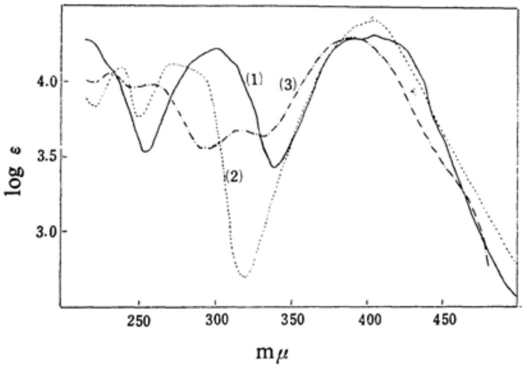


Fig. 1. The ultraviolet absorption spectra of 8, 8-dicyanoheptafulvene derivatives.

(1) 2, 3-Dihydroxy-(IX)
(2) 2, 3-Dimethoxy-(X)
(3) 2, 3-Diacetoxy-(XI)

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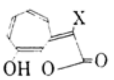
[10] T. Nozoe, T. Mukai, K. Osaka and N. Shishido, This Bulletin, 34, 1384 (1961).

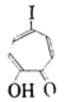
TABLE I. THE INFRARED ABSORPTION MAXIMA OF 8,8-DICYANOHEPTAFULVENES (cm^{-1})

XVI	2205	1633	1585	1520	1490	1406	1269	885
IX	2190 2215	1626	1570	1550	1485	1410	1260	874
X	2205	1630	1564	1550	1487	1412	1284	862
XI	2220	1645	1597	1560	1490	1405	1265	870

reaction proceeds under as mild conditions as in the amination of halobenzenes.[2)] Second, the addition of a carbanion to the intermediate (I) would be expected to occur at the 4-position rather than the 3-position because of the polar effect of the carbonyl group. Third, under forced conditions, 3-halotropolones were found to react with carbanions to give normal substitution products: for example, when 3-bromotropolone (II) was heated with a sodium compound of acetoacetate or malonate in dioxane, a normally-substituted product (XVII: X=$COCH_3$ or $CO_2C_2H_5$) was obtained, although ring closure was followed.[11)]



XVII



XVIII

Under conditions similar to those in the case of VI, however, 5-iodotropolone (XVIII) has been found not to react with sodio- or potassiomalononitrile. Taking this fact into account, we can say that the above abnormal substitution reaction, which led to an enolic form (IX) of VIII from a reaction of 3-iodotropolone (VI) and malononitrile, presumably proceeds by way of the above-mentioned addition-elimination mechanism, involving the Michael-type reaction rather than elimiation-addition-involving tropolonyne (I). Some efforts to resolve this problem are now being made.

Heptafulvene itself was first synthesized in 1954 and found to be an extremely unstable liquid,[12)] in spite of having 13.2 kcal./mol. of stabilization energy based on the heat of hydrogenation.[13)] Nozoe and his collaborators indicated, however, that some heptafulvenes having two electronegative groups at the 8-position are fairly stable, and that especially 8,8-dicyanoheptafulvene (XVI) resists bromination, Diels-Alder addition, and catalytic hydrogenation over palladium carbon.[10)] The present authors have been able to synthesize many heptafulvenes by the new synthetic method described above and have studied their properties as a new system of non-benzenoid aromatic compounds. Details will be reported in the following papers.

Experimental

The ultraviolet absorption spectra were measured in a methanol solution with a Hitachi model EPU-2A spectrophotometer. The infrared absorption spectra were measured on potassium bromide disks with a Hitachi model EPI-2 infrared spectrometer, using rock salt prisms. All melting points are uncorrected.

8,8-Dicyano-2,3-dihydroxyheptafulvene (IX).—The addition of malononitrile (4 g.) to a sodium amide solution prepared from liquid ammonia (300 ml.), sodium (5.6 g.) and a catalytic amount of ferric nitrate gave sodiomalononitrile as silver-white crystals. Into this mixture 3-iodotropolone (VI, 15 g.) was stirred at −50°C over a period of a few minutes, and then the mixture was gently refluxed at −33°C for 2 hr. After ammonium chloride (4.8 g.) had been added, the ammonia was allowed to evaporate. The solid residue was washed out with water (300 ml.) and some insoluble solid (6 g.), which consisted mainly of ammonium salt of VI, was removed by filtration. When this filtrate was acidified with dilute hydrochloric acid, yellow solids separated out; these solids, after filtration and recrystallization from acetone, gave IX (3.6 g.) as yellow prisms; m. p. 222°C (decomp.)

Found: C, 64.58; H, 3.56; N, 15.22. Calcd. for $C_{10}H_6O_2N_2$: C, 64.51; H, 3.25; N, 15.05%.

λ_{max} $m\mu$ (log ε): 300 (4.19), 390 (4.25), 405 (4.26).

8,8-Dicyano-2,3-dimethoxyheptafulvene (X).—To a stirred suspension of IX (1.2 g.) in ethanol (50 ml.) an excess of diazomethane in ether was added with ice cooling. The evaporated residue in vacuo was dissolved in ethyl acetate, the solution was chromatographed over alumina using ethyl acetate, and the reddish effluents were collected; these effluents, after evaporation in vacuo and recrystallization from the same solvent, yielded X (0.6 g.) as orange needles; m. p. 227∼228°C.

Found: C, 67.44; H, 4.42; N, 13.32. Calcd. for $C_{12}H_{10}O_2N_2$: C, 67.28; H, 4.71; N, 13.08%.

λ_{max} $m\mu$ (log ε): 238 (4.09), 273 (4.11), 405 (4.38).

2,3-Diacetoxy-8,8-dicyanoheptafulvene (XI).—IX (0.1 g.) and acetic anhydride (4 ml.) were heated under reflux for 1 hr. The excess acetic anhydride was then removed under reduced pressure, and the residue was crystallized from ethyl acetate to give XI as red needles; m. p. 166∼167°C.

Found: C, 62.36; H, 3.76; N, 10.36. Calcd. for $C_{14}H_{10}O_4N_2$: C, 62.22; H, 3.73; N, 10.37%.

λ_{max} $m\mu$ (log ε): 230 (4.03), 260 (3.96), 315 (3.67), 390 (4.28).

The Acid Hydrolysis of 8,8-Dicyano-2,3-Dihydroxyheptafulvene (IX).—A mixture of IX (0.56 g.) and 75% sulfuric acid (4 ml.) was heated at 100°C for 1 hr., diluted with water (10 ml.), and then cooled. 4-Carboxymethyltropolone (XII, 0.25 g.)

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11) K. Takase, ibid., to be published.

12) W. von E. Doering and D. W. Wiley, *Tetrahedron*, **11**, 183 (1960).

13) R. B. Turner, W. R. Meador, W. von E. Doering, J. R. Mayer and D. W. Wiley, *J. Am. Chem. Soc.*, **79**, 4127 (1957).

precipitated out as colorless needles; m. p. 154~155°C (decomp.). When heated at its decomposition point, XII gave 4-methyltropolone (XIII), m. p. 76~77°C. The melting points of XII and XIII did not show any depression on admixture with respective authentic samples.[14]

The Alkaline Hydrolysis of 8, 8-Dicyano-2, 3-dimethoxyheptafulvene (X).—A mixture of X (0.1 g.) and 2 N methanolic sodium hydroxide (10 ml.) was heated under reflux for 5 min., and then the solvent was removed under reduced pressure. The acidification of the residue with dilute sulfuric acid afforded IX (0.08 g.) m. p., alone and mixed, 222°C (decomp.).

The Alkaline Hydrolysis of 2, 3-Diacetoxy-8, 8-dicyanoheptafulvene (XI).—A mixture of XI (0.1 g.) and 2 N sodium hydroxide (5 ml.) was heated on a water bath for 1 hr.; neutralization with dilute sulfuric acid then yielded IX, m. p., alone and mixed, 222°C (decomp.).

The Methylation of 8, 8-Dicyano-2, 3-dihydroxyheptafulvene (IX) with Dimethyl Sulfate.—Dimethyl sulfate (1 g.) was added to the solution of IX (0.2 g.) in 2 N sodium hydroxide (2 ml.) under ice cooling, and then the mixture was stirred for 4 hr. The precipitated solid, after collection by filtration and subsequent recrystallization from acetone, gave a monomethylated product (XIV, 0.2 g.) as yellow prisms; m. p. 164~165°C.

Found: C, 65.73; H, 4.23; N, 13.86. Calcd. for $C_{11}H_8O_2N_2$: C, 65.99; H, 4.03; N, 13.99%.

XIV reacted with an excess of diazomethane in ether to give the dimethoxyl derivative (X), m. p., alone and mixed, 227~228°C.

3 (2)-Acetoxy-8, 8-dicyano-2 (3)-methoxyheptafulvene (XV).—A mixture of XIV (0.08 g.) and acetic anhydride (1 ml.) was heated under reflux for 1 hr.; the residue obtained after the removal of acetic anhydride under reduced pressure was crystallized from ethyl acetate, giving XV as red needles; m. p. 141~142°C.

Found: N, 11.57. Calcd. for $C_{13}H_{10}O_3N_2$: N, 11.33%.

The Reaction of 5-Iodotropolone (XVIII) and Sodiomalononitrile.—To a mixture of sodium amide or potassium amide and malononitrile in liquid ammonia, XVIII was added; the following procedure was essentially that used in the case of VI. No reaction product other than the starting material was isolated.

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[14] T. Nozoe, Y. Kitahara, K. Doi, M. Funamizu and T. Terasawa, *Bull. Chem. Res. Inst. Non-Aqueous Solutions, Tohoku Univ.*, **10**, 199 (1961).