Heptafulvenes. III.[1] *The Synthesis of 8-Cyanoheptafulvenes*[2]

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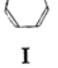
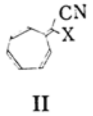
Heptafulvene (I), which is a theoretically-interesting non-benzenoid aromatic hydrocarbon, was synthesized and found to be an extremely unstable liquid.[3] It was discovered,[1,4] however, that its derivatives substituted by two electronegative groups at the 8-position, i. e., 8, 8-dicyano- (II: X=CN) and 8-cyano-8-ethoxycarbonylheptafulvene (II: $X=CO_2Et$), are fairly stable.

In a previous paper,[5] we have reported that the reaction product of 3-iodotropolone (III) with sodiomalononitrile in liquid ammonia is not a tropolone (IV) but its enolic isomer, 8, 8-dicyano-2, 3-dihydroxyheptafulvene (V). Similar results were also found in the case of two isopropyl derivatives of III.[1]



I



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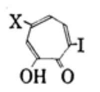

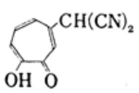

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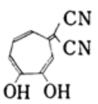
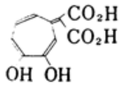


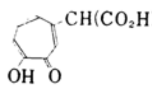
V

III: X=H
IX: $X=CH_3$
X: $X=i\text{-}C_3H_7$

On the other hand, an acid hydrolysis product of V was also found not to be a heptafulvene (VI) but a tropolone derivative (VII).[1] Therefore, it seemed interesting to study keto-enol tautomerisms between tropolone derivatives possessing a side-chain with active hydrogen at the α-position and the corresponding heptafulvenes. We have found that cyanomethyltropolones gave diacetyl derivatives of the heptafulvene-type on acetylation:



VI



VII

Details will be described in this paper.

When 3-iodotropolone (III) reacted with sodioacetonitrile in liquid ammonia, 4-cyanomethyltropolone (VIII) was obtained in a 26 per cent yield. Its structure was confirmed by direct comparison with the dehydration product of 4-carbamoylmethyltropolone.[6] It has been reported that a similar reaction of

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[1] Part II of this series: Y. Kitahara, K. Doi and T. Kato, This Bulletin, 37, 1750 (1964).

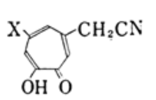
[2] This work was presented at the 14th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1961.

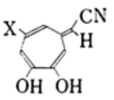
[3] W. von E. Doering and D. W. Wiley, *Tetrahedron*, 11, 183 (1960).

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

[5] Y. Kitahara, K. Doi and T. Kato, This Bulletin, 37, 1747 (1964).

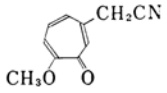
[6] T. Nozoe, Y. Kitahara, K. Doi, M. Funamizu and T. Terasawa, *Bull. Chem. Research Inst. Non-Aqueous Solutions, Tohoku Univ.*, 10, 199 (1961).

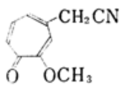




VIII: $X=H$
XI: $X=CH_3$
XII: $X=i\text{-}C_3H_7$

XIII





XIV XV

chlorobenzene and acetonitrile afforded diphenylacetonitrile other than phenylacetonitrile,[7] but in this case no by-products other than VIII were isolated. In a similar manner, alkyl derivatives (IX and X) of 3-iodotropolone also gave corresponding cyanomethyltropolones (XI and XII).

Figure 1 indicates the ultraviolet absorption curves which are characteristic of other alkyltropolones, while Table I shows several principal maxima of the infrared absorption spectra of the cyanomethyltropolones.

This spectral evidence suggests that the above reaction products of iodotropolones and sodioacetonitrile are tropolone derivatives and that they cannot be their enolic forms (XIII). 4-Cyanomethyltropolone (VIII) afforded only two kinds of crystalline monomethoxytropone derivatives on treatment with diazomethane. The structures of these products, 6-cyanomethyl-2-methoxy- (XIV) and 4-cyanomethyl-2-methoxytropone (XV), were determined by a comparison of their absorption peaks based on the CH out-of-plane vibration of the infrared spectra with those of other known substituted tropones[8]: the peaks at 778 (XIV) and 828 (XV) correspond to those at 776 of 2-methoxy-6-methyltropone and 822 cm^{-1} of 2-methoxytropone respectively.

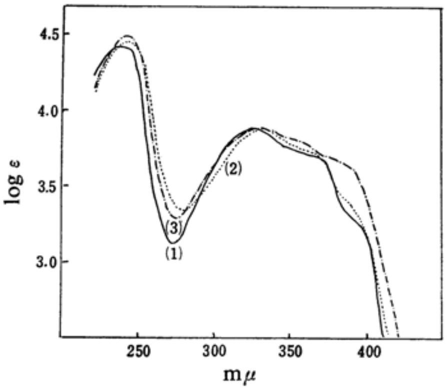
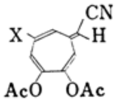


Fig. 1. Ultraviolet absorption spectra of
(1) 4-cyanomethyl-(VIII),
(2) 4-cyanomethyl-6-methyl-(XI), and
(3) 4-cyanomethyl-6-isopropyl-(XII) tropolone.

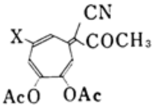
TABLE I. INFRARED ABSORPTION MAXIMA OF 4-CYANOMETHYLTROPOLONES (cm^{-1})

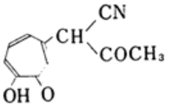
	ν_{OH}	$\nu_{C\equiv N}$	$\nu_{C=O}$	$\nu_{C=C}$	δ_{CH_2}
VIII	3200	2255	1613	1553	1410
IX	3200	2260	1613	1546	1413
XII	3150	2255	1608	1535	1420

On the other hand, we have found that cyanomethyltropolones yielded products of the heptafulvene-type on acetylation. When 4-cyanomethyltropolone (VIII) was treated in pyridine with acetic anhydride at room temperature, 8-cyano-2, 3-diacetoxyheptafulvene (XVI) and 8-acetyl-8-cyano-2, 3-diacetoxyheptafulvene (XVII) were obtained. The structures of these products were easily drawn out from their analytical values, ultraviolet (Figs. 2 and 3) and infrared spectra (Table II), and hydrolyzed to the starting material VIII under mild conditions.



XVI: $X=H$
XIX: $X=CH_3$
XXI: $X=i\text{-}C_3H_7$





XVII: $X=H$
XX: $X=CH_3$

XVIII

An attempted further acetylation of the diacetyl compound XVI to the triacetyl derivative (XVII) was found to result in only the recovery of the starting material. In the course of the formation of XVII from VIII, there may exist an intermediate, such as XVIII or its enol isomer, which has not yet been isolated.

The similar acetylation of two other alkyl-4-cyanomethyltropolones afforded also similar results: XI yielded both diacetyl (XIX) and triacetyl (XX) derivatives, but XII only a diacetyl compound (XXI). The ultraviolet absorption spectra of these heptafulvenes are shown in Figs. 2 and 3.

Table II indicates some principal maxima of

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[7] F. W. Bergstrom and R. Agostinho, *J. Am. Chem. Soc.*, 67, 2152 (1945).

[8] K. Takase, M. Yasunami and T. Nozoe, to be published.

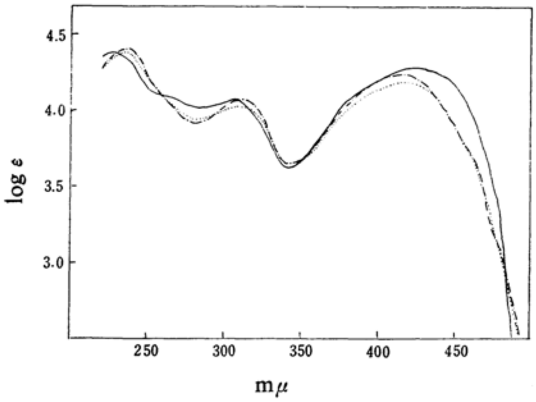

Fig. 2. Ultraviolet absorption spectra of 8-cyanoheptafulvenes (XVI, ——; XIX, ------; XXI, —·—·—).

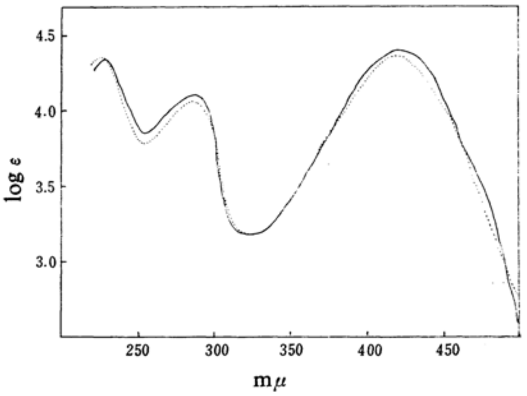

Fig. 3. Ultraviolet absorption spectra of 8-acetylheptafulvenes (XVII, ——; XX, ------).

TABLE II. PRINCIPAL MAXIMA OF THE INFRARED SPECTRA OF 8-CYANOHEPTAFULVENES (cm^{-1})

	$\nu_{C\equiv N}$	$\nu_{C=O}$	$\nu_{C=O}$	$\nu_{C=C}$	ν_{C-O}
XVI	2210	1760		1640	1210
XIX	2200	1762		1635	1188
XXI	2200	1766		1635	1195
XVII	2200	1775	1650	1615	1215
XX	2195	1770	1650	1640	1200

the infrared absorption spectra of these heptafulvenes. The bands based on the stretching vibration of nitrile groups correspond to the conjugated cyano groups and satisfy their presumed structures. The maxima in the second and fifth columns have strong intensities and can be assigned to acetate groups. The bands at 1650 cm^{-1} of XVII and XX, which are sharp and moderately strong, probably indicate the conjugated ketones. The maxima in the fourth column, based on carbon-carbon double bonds, are medium or weak and are distinguishable from those at 1650 cm^{-1}. Bands corresponding to these have also been discussed in 8, 8-dicyanoheptafulvenes,[1,5)] fulvene[9)] and 6, 6-dialkylfulvenes.[10)] The band of heptafulvene itself has been reported to appear at 1585 cm^{-1} (strong).[3)]

Experimental

The ultraviolet absorption spectra in methanol were measured with a Hitachi model EPU-2 recording spectrometer. The infrared spectra were measured with a Perkin-Elmer model 21 infrared spectrometer (rock salt prism and potassium bromide pellets). All melting points are uncorrected.

4-Cyanomethyltropolone (VIII).—Into a sodium amide solution prepared from liquid ammonia (400 ml.) and sodium (9.2 g.) acetonitrile (7 g.) at −50°C was stirred. After 10 min., iodotropolone (III, 25 g.) was added to the above mixture, and then it was stirred while the ammonia was refluxed at atmospheric pressure for 2 hr. After ammonium chloride was added, ammonia was evaporated. The residue was dissolved in water (500 ml.), and the insoluble matter was filtered off. The filtrate was acidified and extracted with ethyl acetate (500 ml.). After the solvent had been removed, the residue was recrystallized from a mixture of benzene and methanol, giving VIII as colorless scales; m. p. and mixed m. p.[6)] 134∼135°C; 4.2 g. (26% yield).

4-Cyanomethyl-6-methyltropolone (XI). — This was prepared from IX (26.2 g.) under the same conditions as those used for III. Recrystallization from ethyl acetate gave XI (2.6 g., 15%) as colorless prisms; m. p. 154∼155°C.

Found: C, 68.72; H, 5.07; N, 8.01. Calcd. for $C_{10}H_9O_2N$: C, 68.56; H, 5.18; N, 8.00%.

4-Cyanomethyl-6-isopropyltropolone (XII).—This was prepared from X (29 g.) under the conditions used for III. Recrystallization from benzene gave XII as colorless needles; m. p. 83∼84°C; 8.2 g. (40%).

Found: C, 70.67; H, 5.78; N, 6.66. Calcd. for $C_{12}H_{13}O_2N$: C, 70.91; H, 6.45; N, 6.89%.

XII (0.19 g.) in 75% sulfuric acid (2 ml.) was heated at 150°C for 1 hr., diluted with water, and extracted with ethyl acetate. After the solvent had been removed, the residue was recrystallized from petroleum ether, giving 6-isopropyl-4-methyltropolone; m. p. and mixed[1)] m. p. 42∼43°C.

The Methylation of 4-Cyanomethyltropolone (VIII). — The addition of an ethereal solution of diazomethane to a cooled suspension of VIII (2 g.) in methanol (5 ml.) caused a violent evolution of gas, and the mixture became a clear solution. When the colorless crystals which separated out soon were filtered, a crude mixture of methoxytropones, m. p. 105∼115°C, was obtained (1.9 g.). Fractional crystallization from ethyl acetate gave 6-cyanomethyl-2-methoxytropone (XIV) as colorless prisms from the less soluble portion, m. p. 130∼131°C; 0.7 g.; Found: C, 68.66; H, 4.85; N, 8.07. Calcd. for $C_{10}H_9O_2N$: C, 68.56; H, 5.18;

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9) J. Theic and J. Wiemann, *Bull. soc. chim. France*, **1956**, 177.

10) J. H. Day and R. Jennkins, *J. Org. Chem.*, **23**, 2039 (1958).

N, 8.00%. λ_{max} mμ (log ε) : 237 (4.42), 320 (3.93). ν_{max} cm^{-1}: 2250, 1630, 1410, 778; and 4-cyanomethyl-2-methoxytropone (XV) as colorless needles from the more soluble portion, m. p. 139~140°C; 0.9 g.; Found: C, 68.64; H, 4.83; N, 7.98%. λ_{max} mμ (log ε): 240 (4.43), 320 (3.89). ν_{max} cm^{-1}: 2258, 1630, 1425, 828.

The Acetylation of 4-Cyanomethyltropolone (VIII).—To a solution of VIII (0.2 g.) in pyridine (3 ml.), acetic anhydride (0.5 g.) was added. The mixture was stirred at room temperature for 3 hr., and then acidified with cold dilute hydrochloric acid and extracted with ethyl acetate. The addition of benzene to the residue of the evaporation of the solvent separated out a yellowish solid. Filtration and recrystallization from acetone gave 2, 3-diacetoxy-8-cyanoheptafulvene (XVI) as yellow needles; m. p. 172°C; 0.05 g.

Found: C, 63.95; H, 4.20; N, 5.64. Calcd. for $C_{13}H_{11}O_4N$: C, 63.67; H, 4.52; N, 5.71%.

The benzene filtrate, from which XVI had been removed, was chromatographed on alumina using benzene, and red effluents were collected. The benzene was removed from the effluent, and the residue was recrystallized from a mixture of benzene and cyclohexane to give 8-acetyl-8-cyano-2, 3-diacetoxyheptafulvene (XVII) as reddish orange needles; m. p. 154°C; 0.1 g.

Found: C, 62.41; H, 4.40; N, 4.99. Calcd. for $C_{15}H_{13}O_5N$: C, 62.71; H, 4.56; N, 4.88%.

Further reaction of XVI with acetic anhydride in pyridine resulted in the recovery of only the starting material.

The Alkaline Hydrolysis of XVI and XVII.—XVI (0.12 g.) in 2 N sodium hydroxide (5 ml.) was heated at 50°C for 20 min., and then the solution was acidified with dilute hydrochloric acid, giving 4-cyanomethyltropolone (VIII). The hydrolysis of XVII under the same conditions resulted in the formation of VIII.

The Acetylation of 4-Cyanomethyl-6-methyltropolone (XI).—A solution of XI (0.35 g.), pyridine (4 ml.) and acetic anhydride (0.6 g.) was stirred at room temperature for 3 hr., neutralized by dilute hydrochloric acid, and then extracted with ethyl acetate. The evaporation of the solvent and fractional recrystallization from ethyl acetate gave the following products, which are arranged in the order of increasing solubility to the solvent:

i) 8-Acetyl-8-cyano-2, 3-diacetoxy-5-methylheptafulvene (XX); m. p. 151~152°C; reddish orange needles; 0.2 g.

Found: C, 63.80; H, 4.56; N, 4.93. Calcd. for $C_{16}H_{15}O_5N$: C, 63.78; H, 5.02; N, 4.65%.

ii) 8-Cyano-2, 3-diacetoxy-5-methylheptafulvene (XIX); m. p. 150~151°C; yellow prisms; 0.08 g.

Found: C, 65.17; H, 5.03; N, 5.54. Calcd. for $C_{14}H_{13}O_4N$: C, 64.86; H, 5.05; N, 5.40%.

iii) 4-Cyanomethyl-6-methyltropolone acetate; m. p. 118~119°C; colorless needles; 0.03 g.

Found: C, 66.20; H, 5.09; N, 6.69. Calcd. for $C_{12}H_{11}O_3N$: C, 66.35; H, 5.10; N, 6.45%. λ_{max} mμ (log ε): 235 (4.43), 318 (3.90). ν_{max} cm^{-1}: 2255, 1755, 1615, 1406.

The Acetylation of 4-Cyanomethyl-6-isopropyltropolone (XII).—A solution of XII (0.38 g.), pyridine (4 ml.) and acetic anhydride (0.6 g.) was stirred at room temperature for 3 hr. and then treated in the same manner as was used in the case of VIII. After recrystallization from ethyl acetate, 8-cyano-2, 3-diacetoxy-5-isopropylheptafulvene (XXI) was obtained as yellow needles; m. p. 154~155°C; 0.16 g.

Found: C, 67.10; H, 5.74; N, 5.05. Calcd. for $C_{16}H_{17}O_4N$: C, 66.88; H, 5.96; N, 4.88%.

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