Heptafulvenes. II. The Synthesis of 8, 8-Dicyano-2, 3-dihydroxy-isopropylheptafulvenes[1]

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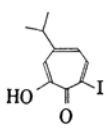
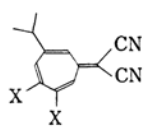
Our recently reported[2] method of synthesizing heptafulvenes has now been applied to two isopropyl derivatives of 3-iodotropolone; the experimental results will be described in this paper.

From the reaction of 3-iodo-6-isopropyltropolone (I) with sodiomalononitrile in liquid ammonia, a yellow product with a poor solubility in common organic solvents was obtained in a 48 per cent yield. Its ultraviolet absorption spectrum (Table I) is similar to that of 8, 8-dicyano-2, 3-dihydroxyheptafulvene,[2] while its infrared spectrum (Table II) indicates the presence of conjugated nitrile groups. This product II gave dimethyl III and diacetyl IV derivatives when treated with diazomethane and acetic anhydride respectively; when treated with dimethylsulfate, II afforded the monomethyl ether X.



I



II: X=OH
III: X=OCH_3
IV: X=OAc

1) This work was presented in part at Tohoku Local Meetings of the Chemical Society of Japan held in June, 1959, and October, 1961.

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

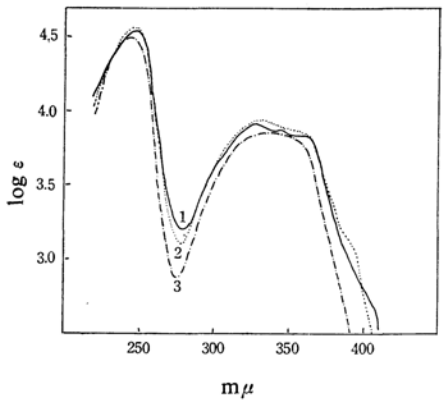
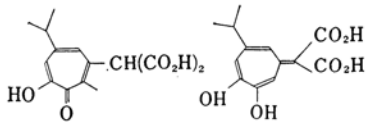
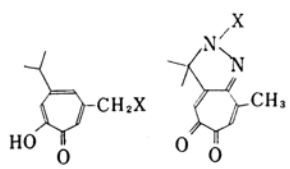


Fig. 1. Ultraviolet absorption spectra of
1: 4-dicarboxymethyl-(V),
2: 4-carboxymethyl-(VII), and
3: 4-methyl-(VIII)-6-isopropyltropolone.

In the preceding paper,[2] it was shown that when 8, 8-dicyano-2, 3-dihydroxyheptafulvene was heated with sulfuric acid, 4-carboxylmethyltropolone was formed as a hydrolysis product. When the heptafulvene (II) was carefully heated with sulfuric acid following the directions previously described,[2] the 4-dicarboxymethyltropolone derivative V was obtained as a hydrolysis product. From the fact that its ultraviolet spectrum (Fig. 1) resembles the spectrum of an alkyltropolone more closely than that of the heptafulvene (II), this hydrolysis product appears to be a tropolone (V) rather than a heptafulvene (VI) derivative. When V was heated to its decomposition point, it gave the 4-carboxymethyltropolone derivative VII, which showed a depression of its melting point on admixture with authentic 3-carboxymethyl-6-isopropyltropolone.[3] The further decarboxylation of VII yielded the 4-methyltropolone derivative VIII, which was not identical with authentic 6-isopropyl-3-methyltropolone.[3]



V VI

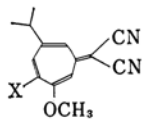


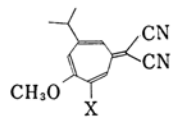
VII: X=CO_2H IX: X=*p*-Tolyl
VIII: X=H

3) K. Takase, This Bulletin, to be published.

The methyltropolone VIII reacted with diazotized *p*-toluidine to yield 4', 6-dimethylhinopurpurin (IX) rather than the expected *p*-tolyazotropolone. On the basis of a comparison of its ultraviolet spectrum with that of hinopurpurin itself,[4] structure IX was assigned to the compound.

In the preceding paper[2] it was also reported that mild hydrolyses of 2, 3-dimethoxy- and 2, 3-diacetoxy-8, 8-dicyanoheptafulvenes gave 8, 8-dicyano-2,3-dihydroxyheptafulvene. On the other hand, the isopropyl-dimethoxy derivative (III) was found to be partially demethylated to X under the same conditions. III was regenerated when X was treated with diazomethane;



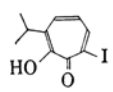


Xa: X=OH Xb: X=OH
XIa: X=OAc XIb: X=OAc

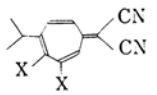
X afforded a monoacetate XI. The further heating of the monomethoxyheptafulvene (X) in dilute alkali gave the dihydroxy derivative II. The careful hydrolysis of the diacetoxy compound IV yielded only II.

The fact that the dimethoxyheptafulvene (III) is easily hydrolyzed to II and then to V suggests that the replacement of the methoxyl groups of the heptafulvene may be possible with other nucleophilic reagents, but no experiments have been undertaken to verify this.

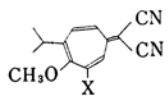
Analogous results were obtained from another isopropyltropolone derivative XII. Dihydroxyheptafulvene (XIII) easily formed a dimethoxy XIV derivative with diazomethane and diacetate XV when reacted with acetic anhydride. It also gave a monomethoxy compound XVI by reaction with dimethyl sulfate; this could be acetylated to XVII.

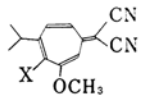


XII



XIII: X=OH
XIV: X=OCH_3
XV: X=OAc





XVIa: X=OH XVIb: X=OH
XVIIa: X=OAc XVIIb: X=OAc

The ultraviolet and infrared absorption maxima for these heptafulvenes are summarized

4) T. Nozoe, T. Ikemi and T. Ozeki, *Proc. Japan Acad.*, 31, 455 (1955).

TABLE I. THE ULTRAVIOLET ABSORPTION MAXIMA

Compound	mμ	log ε	mμ	log ε	mμ	log ε	mμ	log ε
VII	220	4.41	307	4.32			392	4.36
XVIII	220	4.33	300	4.21			390	4.32
VIII	242	4.33	275	4.21	290	4.20	405	4.45
XIX	243	4.20	275	4.18			405	4.40
IX	235	4.17	265	4.12			390	4.37
XX	233	4.20	260	4.15			395	4.42
XV	222	4.39	310	4.40	322	4.41	383	4.45
XXI	223	4.30	240	4.21	293	4.02	433	4.56
XVI	240	4.29	265	4.01			415	4.42
XXII	235	4.15	260	4.10			393	4.40

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

VII	2180 2202	1632	1583	1532	1467	—	1260	875
XVIII	2190 2220	1620	1565	1535	1496	1416	1275	882
VIII	2190 2205	1640	1575	1545	1465	1415	1260	875
XIX	2220	1632	1576	1523	1495	1405	1290	856
XX	2220	1635	1593	1526	1500	1404	1296	868
XV	2185 2202	1632	1595	1545	1485	1418	1275	873
XXI	2210	1632	1576	1540	1502	1402	1285	865
XXII	2218	1632	1588	1525	1495	1400	1295	870

in Tables I and II; these data will be discussed elsewhere.

Experimental

The ultraviolet absorption spectra were measured for methanol solutions on a Hitachi model EPU-2 recording spectrophotometer. The infrared absorption spectra were measured on a Hitachi model EPU-510 infrared spectrometer (rock salt prism, potassium bromide pellet). All melting points are uncorrected.

8, 8-Dicyano-2, 3-dihydroxy-5-isopropylheptafulvene (II).—The addition of malononitrile (3.3 g.) to a sodium amide solution prepared from sodium (3.4 g.) and liquid ammonia (300 ml.) gave sodiomalononitrile as silver white crystals. I (14.5 g.) was stirred into this mixture at −50°C over a period of 10 min., and the resulting deep red solution was refluxed for 2 hr. under atmospheric pressure. After the addition of ammonium chloride (8 g.), the ammonia was allowed to evaporate. The residue was then washed with water (300 ml.), and the insoluble substance was filtered off. The acidification of the filtrate precipitated a yellow solid which, after recrystallization from methanol, gave II as yellow needles, m. p. 227°C (decomp.), 5.5 g. (48%).

Found: C, 68.85; H, 5.26: N, 12.34. Calcd. for $C_{13}H_{12}O_2N_2$: C, 68.41; H, 5.30; N, 12.27%.

8, 8-Dicyano-2, 3-dimethoxy-5-isopropylheptafulvene (III).—To a cooled, stirred solution of II (0.23 g.) in methanol (10 ml.) an ether solution of diazomethane was added until no more gas was evolved. After 1 hr., the solvent was removed, and a solution of the residue in ethyl acetate was chromatographed over alumina (1.5×10 cm.). The yellowish orange eluate was collected and evaporated under reduced pressure. The recrystallization of the residue from ethyl acetate afforded II as yellowish orange prisms, m. p. 176~177°C, 0.2 g.

Found: C, 70.19; H, 6.32; N, 10.90; mol. wt. (Rast), 263. Calcd. for $C_{15}H_{16}O_2N_2$: C, 70.29; H, 6.29; N, 10.93%; mol. wt. 256.

2, 3-Diacetoxy-8, 8-dicyano-5-isopropylheptafulvene (IV).—II (0.2 g.) in acetic anhydride (5 ml.) was heated under reflux for 2 hr. The removal of the solvent under reduced pressure and the recrystallization of the residue from benzene gave reddish needles, m. p. 138~140°C, 0.1 g.

Found: C, 65.36; H, 4.77; N, 9.03. Calcd. for $C_{17}H_{16}O_4N_2$: C, 65.37; H, 5.16; N, 8.97%.

4-Dicarboxymethyl-6-isopropyltropolone (V).—A mixture of II (0.46 g.) and 75% sulfuric acid (3 ml.) was heated at 80~90°C for 1 hr., and then diluted with water to 10 ml. and cooled. The colorless crystals which separated were filtered and recrystallized from methanol to afford V as colorless prisms, m. p. 135~136°C (decomp.), 0.36 g. A methanol solution of V showed a red coloration with ferric chloride.

Found: C, 51.86; H, 6.29. Calcd. for $C_{13}H_{14}O_6 \cdot H_2O$: C, 51.65; H, 6.00%.

4-Carboxymethyl-6-isopropyltropolone (VII).—V (0.13 g.) was heated at its decomposition point until no more carbon dioxide was evolved. The product formed colorless crystals when allowed to cool under reduced pressure. Recrystallization from a mixture of benzene and methanol gave VII as colorless prisms, m. p. 153~154°C (decomp.), 0.07 g.

Found: C, 64.59; H, 6.49. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35%.

VII decomposes sodium hydrogencarbonate, and its alcoholic solution showed a red coloration with ferric chloride. A mixture of VII and 3-carboxymethyl-6-isopropyltropolone (m. p. 153~154°C (decomp.))[3] had an m. p. of 120~125°C.

6-Isopropyl-4-methyltropolone (VIII).—VII (0.11 g.) was heated at its decomposition point in a sublimation apparatus until the evolution of carbon dioxide ceased; then it was submitted to sublimation in vacuo. The recrystallization of the sublimate from petroleum ether (b. p. 40~60°C) gave VIII as white prisms, m. p. 52~53°C, 0.05 g.

Found: C, 74.16; H, 7.80; mol. wt. (Rast), 192. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92%; mol. wt., 188.

VIII did not afford a picrate or an *o*-phenylenediamine compound, thus differing from 6-isopropyl-3-methyltropolone (liquid).[3]

The Azo-coupling of 6-Isopropyl-4-methyltropolone (VIII).—A diazonium chloride solution prepared from *p*-toluidine (30 mg.) was stirred into a cooled solution of VIII (45 mg.) in pyridine (2 ml.) over a period of 10 min. After 30 min., the reddish solution was acidified with dilute hydrochloric acid, and the resulting reddish violet solution was extracted with ethyl acetate (30 ml.). The extract was chromatographed over alumina (1×5 cm.), and the reddish violet eluate was collected. After the removal of the solvent under reduced pressure, the residue was recrystallized from cyclohexane, giving the dimethylhinopurpurin compound IX as reddish violet needles, m. p. 130~132°C.

λ_{max}^{MeOH} mμ (log ε): 257 (4.49), 320 (4.09), 360 (3.98), 500 (4.09).

Found: C, 37.67; H, 5.73; N, 9.42. Calcd. for $C_{18}H_{18}O_2N_2$: C, 73.45; H, 6.16; N, 9.52%.

The Alkaline Hydrolysis of 8, 8-Dicyano-2, 3-dimethoxy-5-isopropylheptafulvene (III).—III (0.1 g.) in 2 N methanolic sodium hydroxide (5 ml.) was heated under reflux for 5 min. The neutralization with dilute hydrochloric acid caused the separation of crystals which, after recrystallization from acetic acid, gave 8,8-dicyano-3(or 2)-hydroxy-5-isopropyl-2(or 3)-methoxyheptafulvene (X) as yellow leaflets, m. p. 278°C (decomp.).

Found: C, 69.55; H, 5.74; N, 11.60. Calcd. for $C_{14}H_{14}O_2N_2$: C, 69.40; H, 5.83; N, 11.56%.

Upon treatment with diazomethane in ether, X gave a product which showed no depression of its melting point on admixture with an authentic sample of III. X was soluble in aqueous caustic alkali, and its alcoholic solution did not show any coloration with ferric chloride. When it is heated under reflux in 2 N methanolic sodium hydroxide for 2 hr., III and II are afforded.

3(or 2)-Acetoxy-8, 8-dicyano-5-isopropyl-2(or 3)-methoxyheptafulvene (XI).—A solution of X (0.1 g.) in acetic anhydride (2 ml.) was heated under reflux for 1 hr. The solvent was then evaporated under reduced pressure; the residue after recrystallization from benzene afforded XI as reddish orange needles, m. p. 185~186°C.

Found: C, 67.83; H, 5.18; N, 9.99. Calcd. for $C_{16}H_{16}O_3N_2$: C, 67.59; H, 5.67; N, 9.85%.

The Alkaline Hydrolysis of 2, 3-Diacetoxy-8, 8-dicyano-5-isopropylheptafulvene (IV).—A solution of IV (0.1 g.) in 2 N methanolic sodium hydroxide (5 ml.) was heated under reflux for 10 min. Neutralization with dilute hydrochloric acid afforded II, m. p. and mixed m. p. 227°C (decomp.) with an authentic sample.

The Methylation of 8, 8-Dicyano-2, 3-dihydroxy-5-isopropylheptafulvene (II) with Dimethyl Sulfate.—A mixture of II (0.46 g.), sodium hydroxide (0.2 g.), water (5 ml.), and dimethyl sulfate (0.63 g.) was stirred at room temperature for 2 hr. The crystals which separated out were filtered off and recrystallized from acetic acid to give X (0.42 g.), m. p. and mixed m. p. with an authentic sample, 278°C (decomp.).

3-Iodo-7-isopropyltropolone (XII).—To a refluxing mixture of 3-isopropyltropolone (41 g.), anhydrous potassium carbonate (72 g.) and methanol (300 ml.), a solution of iodine (64 g.) and potassium iodide (42 g.) in methanol (300 ml.) was added drop by drop; refluxing was then continued for an additional 4 hr. After most of the methanol had been removed under reduced pressure, the residue was diluted with dilute sulfuric acid and then extracted with chloroform. The extract was washed with sodium hydrogen sulfite and then dried. The removal of the solvent gave crude XII as a dark red oil, 58 g.

Into a cooled solution of the oil (0.2 g.) in pyridine (3 ml.) a solution of *p*-toluenediazonium chloride prepared from *p*-toluidine (0.11 g.) was stirred. After 1 hr. the mixture was diluted with dilute hydrochloric acid, and the crystals which separated out were recrystallized from acetone to give 3-iodo-7-isopropyl-5-*p*-tolylazotropolone as orange needles, m. p. 167~168°C; 90% yield.

Found: C, 50.35; H, 4.29; N, 6.88. Calcd. for $C_{17}H_{17}O_2N_2I$: C, 50.01; H, 4.19; N, 6.86%.

8, 8-Dicyano-2, 3-dihydroxy-4-isopropylheptafulvene (XIII).—XII (41 g.) was added to a mixture of malononitrile (14 g.), liquid ammonia (500 ml.) and sodium amide prepared from sodium (16 g.). The subsequent procedure is the same as that used in the case of I. After recrystallization from a mixture of methanol and acetone, XIII was obtained as yellowish orange needles, m. p. 242°C (decomp.), 13 g.

Found: C, 68.75; H, 5.19; N, 12.28. Calcd. for $C_{13}H_{12}O_2N_2$: C, 68.41; H, 5.30; N, 12.27%.

8, 8-Dicyano-2, 3-dimethoxy-4-isopropylheptafulvene (XIV).—A solution of diazomethane in ether was added to a mixture of XIII (0.7 g.) and ethanol (3 ml.) with stirring and cooling. After the removal of the solvent under reduced pressure, the product was dissolved in ethyl acetate and chromatographed over alumina. The reddish orange eluates were evaporated to afford XIV as reddish prisms, m. p. 124~125°C, 0.25 g.

Found: C, 70.08; H, 5.89; N, 10.59. Calcd. for $C_{15}H_{16}O_2N_2$: C, 70.29; H, 6.29; N, 10.93%.

2, 3-Diacetoxy-8, 8-dicyano-4-isopropylheptafulvene (XV).—A mixture of XIII (0.2 g.) and acetic anhydride (5 ml.) was heated under reflux for 3 hr., and then the solvent was removed under reduced pressure. The residue was recrystallized from ethyl acetate to give XV (0.1 g.) as reddish prisms, m. p.

183~184°C, 0.1 g.

Found: C, 65.46; H, 5.06; N, 8.93. Calcd. for $C_{17}H_{16}O_4N_2$: C, 65.37; H, 5.16; N, 8.97%.

The Methylation of 8, 8-Dicyano-2, 3-dihydroxy-4-isopropylheptafulvene (XIII) with Dimethyl Sulfate.—To a solution of XIII (0.45 g.) in 2 N sodium hydroxide (6 ml.) dimethyl sulfate (1.6 g.) was added, and then the mixture was stirred at room temperature for 6 hr. The crystals which separated out were filtered and recrystallized from methanol to give XVI as yellow prisms, m. p. 254~255°C (decomp.), 0.4 g.

Found: C, 69.34; H, 5.86; N, 11.79. Calcd. for $C_{14}H_{14}O_2N_2$: C, 69.40; H, 5.83; N, 11.56%.

The treatment of XVI with diazomethane in ether afforded XIV. When XVI was heated in acetic anhydride, the acetyl derivative XVII was yielded as reddish orange needles, m. p. 176~178°C.

Found: C, 67.75; H, 5.47; N, 9.55. Calcd. for $C_{16}H_{16}O_3N_2$: C, 67.59; H, 5.67; N, 9.85%.

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