

The Synthesis of Azulene Derivatives from Troponoids^{*1}

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Various methods for the synthesis of azulene derivatives have in the past been reported by numerous organic chemists. Almost all of these methods required a dehydrogenation reaction in the final stage, and, although many improvements have been effected, these have resulted generally in a poor yield¹⁾.

The present authors have recently found that the condensation of troponoids, such as 2-halo- and 2-methoxytroponone derivatives, with ethyl cyanoacetate or malononitrile, in the presence of a base, afforded 2-amino- and 2-hydroxyazulene derivatives in one step and in a fairly good yield. Although short summaries

of this work have already been published²⁾, a detailed description of the new synthetic method has not yet been given.

In this paper, the authors wish to describe this synthetic procedure in full detail. The reaction of 2-chlorotroponone (Ia) with two molar equivalents of ethyl cyanoacetate in absolute ethanol, in the presence of two molar equivalents of sodium ethoxide, was allowed to stand at room temperature; a sparingly soluble sodium salt, from which an acid substance (II) (m.p. 188~189°C), was liberated by treatment with mineral acid, and orange crystals (III), C₁₆H₁₇O₄N (m.p. 93~94°C) precipitated out. The mother liquor from these precipitates afforded a small amount of colorless crystals (IV), m.p. 135~137°C. The main product III was obtained in about a 70% yield. Under the same conditions, the condensation of 2-bromotroponone (Ib) with ethyl cyanoacetate

^{*1} Presented at the 8th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1955.

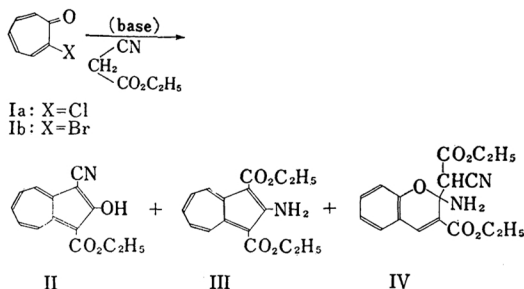
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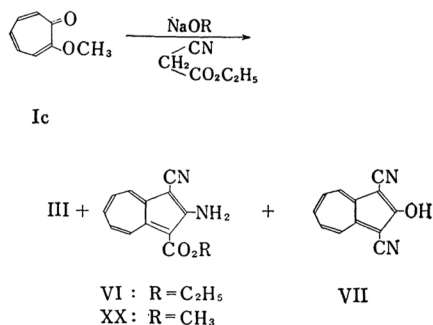
1) a) M. Gordon, *Chem. Revs.*, **50**, 127 (1952); b) W. Keller-Schierlein and E. Heilbronner, "Non-Benzenoid Aromatic Compounds", Ed. by D. Ginsburg, Interscience, New York (1959), p. 277; c) T. Nozoe and T. Asao, "Dai Yuki Kagaku" (Comprehensive Organic Chemistry), Ed. by M. Kotake, Vol. 13, Asakura Shoten, Tokyo (1960), p. 535.

2) a) T. Nozoe, S. Matsumura, Y. Murase and S. Seto, *Chem. & Ind.*, **1955**, 1257; b) T. Nozoe, S. Seto, S. Matsumura and T. Asano, *Proc. Japan Acad.*, **32**, 339 (1956); c) T. Nozoe, S. Seto and S. Matsumura, *Chem. & Ind.*, **1961**, 1715.

gave III in about a 60% yield. The reaction of Ia with two molar equivalents of ethyl sodiocyanoacetate in dehydrated benzene yielded II and III, but not IV.



The use of tertiary amine in place of alkoxide as the condensation agent resulted in the formation of III in a 35% yield and of a small amount of orange crystals (V) (m. p. above 300°C), sparingly soluble in organic solvents. The reaction of 2-methoxytropone (Ic) with two molar equivalents of ethyl cyanoacetate, in the presence of two molar equivalents of sodium ethoxide, afforded III in a 5% yield and a 7% yield of orange crystals (VI), $C_{14}H_{12}O_2N_2$, of m. p. 167~168°C. The remainder



(about 75%) was an acid substance (VII), m. p. above 300°C, sparingly soluble in organic solvents. The application of one molar equivalent of alkoxide to Ic afforded III in over a 70% yield, while the yields of VI and VII were very poor.

It was interesting that the ratio of these products differed markedly according to the amount of alkoxide³⁾.

The ultraviolet absorption spectra⁴⁾ (Fig. 1) of II, III and VII are very similar to each other, and these compounds are assumed to have a common skeletal structure.

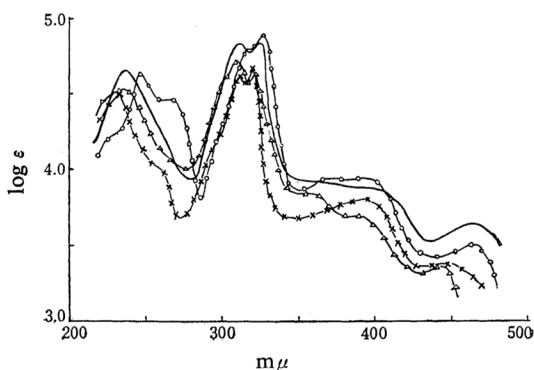


Fig. 1. UV absorption spectra of II, III, VII and XXI in methanol.

— II, —○— III, —△— VII, —×— XXI

The main product III easily formed picrate melting at 125°C and styphnate melting at 150°C. The passage of dry hydrogen chloride gas through a dehydrated benzene solution of III formed reddish orange crystals assumed to be the hydrochloride of III, but the free compound III was easily liberated when the salt was left in the air.

The infrared absorption spectrum⁵⁾ of III,

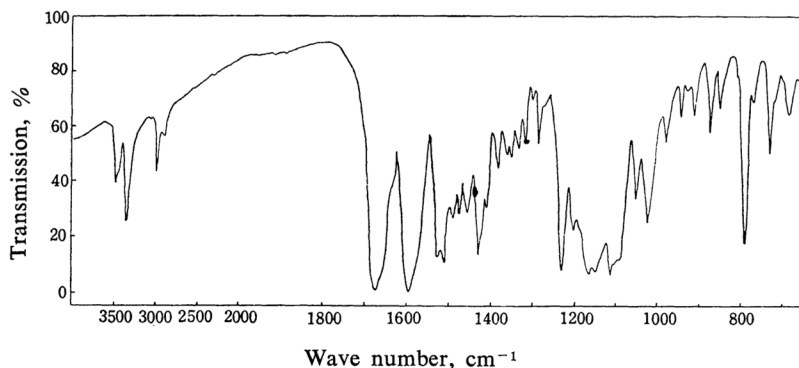
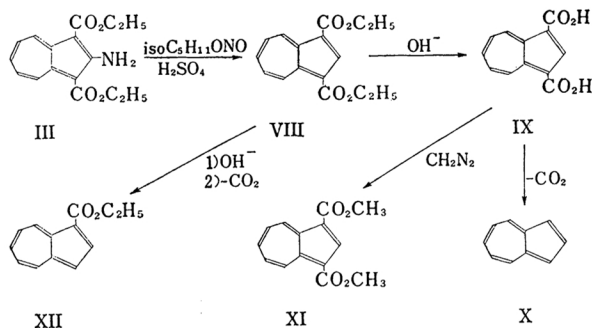


Fig. 2. IR absorption spectrum of III in KBr disk.

3) A similar phenomenon has also been observed in the cases of the reaction of tropone methyl ether (2-methoxytropone) derivatives, such as hinokitiol methyl ether and 4-methyltropone methyl ether etc., with ethyl cyanoacetate (T. Nozoe et al., to be published).

4) Ultraviolet spectra were measured with a Beckman Model DU spectrophotometer.

5) Infrared spectra were measured with a Perkin-Elmer Model 21 double-beam spectrophotometer.



as indicated in Fig. 2, exhibits absorption bands at 3500 and 3310 cm^{-1} for the primary amino group, and at 1660 and 1225 cm^{-1} for the ester group conjugated with the unsaturated bond. The attempted acetylation of III with acetic anhydride containing one drop of pyridine failed to give its acetate. The attempted deamination of the compound III with isoamyl nitrite in its ethanolic solution, in the presence of concentrated sulfuric acid, resulted in changing the color from orange to brownish red, and gave reddish violet crystals (VIII), $\text{C}_{16}\text{H}_{16}\text{O}_4$, of m. p. 120–121°C. The hydrolysis of VIII with an ethanol-aqueous solution of potassium hydroxide afforded a crystalline dicarboxylic acid IX, m. p. 270°C (decomp.), very sparingly soluble in organic solvents.

The thermal decomposition of IX produced blue crystals X, m. p. 98–99°C, with an odor of naphthalene. The ultraviolet (Fig. 3), visible⁶⁾, and infrared absorption spectra of compound X and its melting point are identical with those of azulene; by mixed fusion it was confirmed that X was azulene.

The position of the principal maximum (513 $\text{m}\mu$) in the visible spectrum of compound VIII (Fig. 3) was found to be in excellent agreement with that of dimethyl azulene-1,3-dicarboxylate (511 $\text{m}\mu$), first synthesized by Anderson et al.⁷⁾ The action of diazomethane on IX afforded red crystals XI, m. p. 170–171°C. The melting point of XI was in good agreement with that of dimethyl azulene-1,3-dicarboxylate reported in the literature.

Consequently, compound VIII was diethyl azulene-1,3-dicarboxylate, and IX was its free dicarboxylic acid, azulene-1,3-dicarboxylic acid. The maximum absorption of compound III (465 $\text{m}\mu$) in the visible region causes a shift toward a shorter wavelength (48 $\text{m}\mu$) than that of VIII. The additivity of the spectral shifts in the visible region caused by alkyl groups

on the different positions of azulene ring was first found by Plattner et al.^{1a)} Not only alkyl groups, but also other *o*, *p*-directing groups are found to cause a hypsochromic shift of the absorption bands when substituted at the even-numbered positions in the azulene nucleus^{8,9)}. These considerations supported the view that compound III was diethyl 2-aminoazulene-1,3-dicarboxylate. The hydrolysis of VIII with one molar equivalent of potassium hydroxide gave a red crystalline carboxylic acid sparingly soluble in organic solvents, and its decarboxylation by heating at 240–250°C under a partially reduced pressure afforded, in addition to azulene, ethyl azulene-1-carboxylate (XII) as a reddish violet oil which formed a picrate of m. p. 124°C.

The infrared absorption spectrum of compound VI exhibits the absorption bands due to the primary amino group and to the cyano and ester carbonyl groups conjugated with an unsaturated bond. From these spectral data and from the molecular formula, it was assumed compound (VI) was ethyl 2-amino-3-cyanoazulene-1-carboxylate¹⁰⁾. The hydrolysis of III with an ethanol-aqueous solution of potassium hydroxide afforded 2-aminoazulene-1,3-dicarboxylic acid (XIII), m. p. 158–160°C (decomp.), sparingly soluble in organic solvents. Its decarboxylation by heating at 125–130°C in pyridine or heating at 170–175°C under a reduced pressure gave, in a good yield, 2-aminoazulene (XIV) as red crystals, m. p. 93–94°C, the acetylation of which with acetic anhydride afforded 2-acetamidoazulene (XV) as violet crystals, m. p. 168–169°C. Compound XIV easily formed an unstable picrate of m. p. 145°C (decomp.). 2-Aminoazulene appears more stable than the 1-aminoazulene prepared

8) E. J. Cowles, *J. Am. Chem. Soc.*, **79**, 1095 (1957).

9) T. Nozoe, S. Seto, S. Matsumura and A. Sato, *This Bulletin*, in press.

10) The present authors have previously given an erroneous structure of ethyl 2-amino-3-cyanoazulene-1-carboxylate for compound A of m. p. 135–137°C^{1b)}. Re-examination of the structure of the compound A has shown that A is not an ethyl ester but a methyl ester converted from compound VI by ester exchange reaction.

6) Visible absorption spectra were measured with a Beckman DK spectrophotometer.

7) A. G. Anderson, Jr., R. Scotoni, Jr., E. J. Cowles and C. G. Fritz, *J. Org. Chem.*, **22**, 1193 (1957).

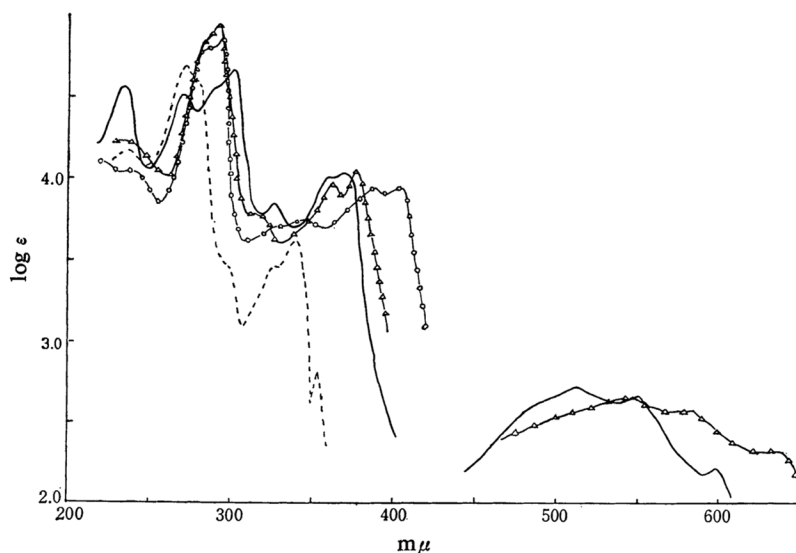
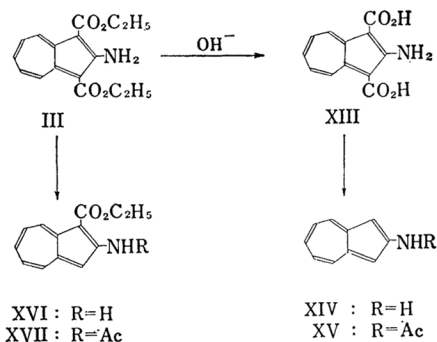


Fig. 3. UV absorption spectra of VIII, X, XIV and XV in methanol.

— VIII, ---- X, —○— XIV, —△— XV

by Schulze and Heilbronner¹¹⁾. However, 2-aminoazulene also becomes a brownish black substance on exposure to air and light for a few days. The hydrolysis of III with one molar equivalent of potassium hydroxide yielded a crystalline carboxylic acid, and its decarboxylation by heating in pyridine afforded ethyl 2-aminoazulene-1-carboxylate (XVI) as red crystals, m. p. 68~70°C. The acetylation of XVI with acetic anhydride gave ethyl 2-acetamidoazulene-1-carboxylate (XVII) as red crystals, m. p. 140~141.5°C.



The ultraviolet and visible absorption spectra of XIV and XV are shown in Fig. 3. The application of nitrous acid to XIV resulted in a change of color from green to dark brown, and no pure product could be isolated.

Although compounds II and VII are acid substances, these compounds do not dissolve

in an aqueous solution of sodium hydrogen-carbonate, but exhibit a dark brown coloration with ferric chloride in ethanol. There are absorption bands for the unsaturated ester carbonyl group at 1655 cm^{-1} , for the unsaturated cyano group at 2200 cm^{-1} , and for the hydroxyl group at 3100 cm^{-1} in compound II, while absorption bands due to unsaturated cyano and hydroxyl groups are present at 2200 and 3100 cm^{-1} respectively in compound VII. The heating of II with an excess of acetic anhydride containing pyridine gave its acetate XVIII as red crystals, m. p. 142°C. Under the same conditions, VII afforded its acetate XIX as red crystals, m. p. 192°C. The infrared absorption band due to the carbonyl group at 1655 cm^{-1} in compound II is displaced to the higher frequency region of 1702 cm^{-1} in compound XVIII. It would be rational to attribute this shift to an intramolecular hydrogen bonding between the carbonyl and hydroxyl groups in compound II. From these facts, it was assumed that compound II was ethyl 3-cyano-2-hydroxyazulene-1-carboxylate and that compound VII was 1,3-dicyano-2-hydroxyazulene (1,3-dicyanoazulene-2-ol).

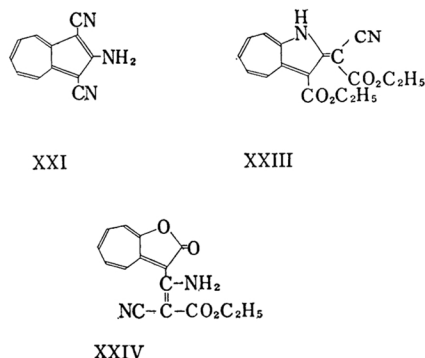
The reaction of Ic with ethyl cyanoacetate, in the presence of two molar equivalents of sodium methoxide in place of sodium ethoxide, afforded methyl 2-amino-3-cyanoazulene-1-carboxylate¹⁰⁾ (XX) as orange crystals, m. p. 135~137°C, in a poor yield, besides III, VI and VII. The condensation of 2-chlorotropone (Ia) with malononitrile, in the presence of sodium ethoxide or tributylamine, afforded, in a quantitative yield, very sparingly soluble orange

11) J. Schulze and H. Heilbronner, *Helv. Chim. Acta*, **41**, 1492 (1958).

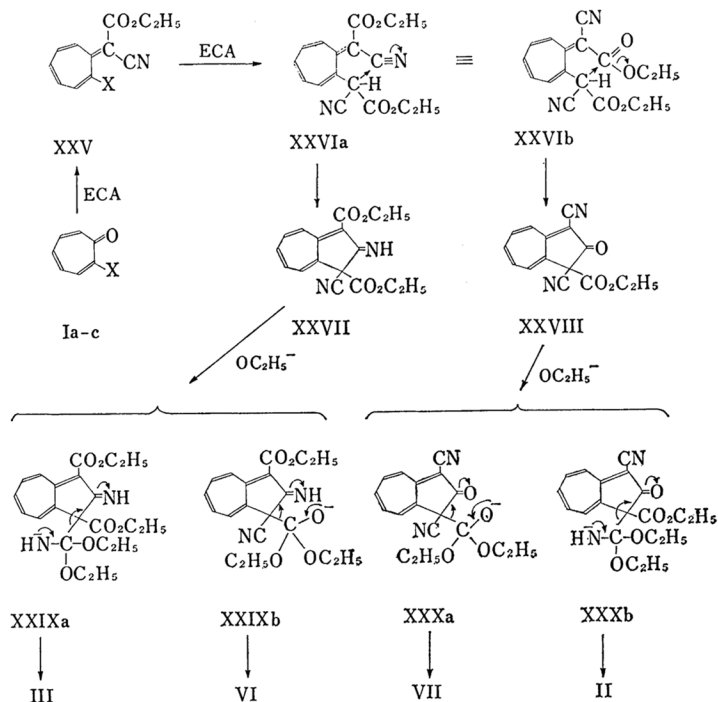
crystals (XXI), m. p. above 300°C. The ultra-violet absorption spectrum of compound XXI, as indicated in Fig. 1, is very similar to that of III; moreover, there are absorption bands for amino and unsaturated cyano groups in the infrared spectrum of compound XXI. Consequently, these observations support the view that compound (XXI) is 2-amino-1,3-dicyanoazulene(1,3-dicyano-2-azulenamine). The hydrolysis of the cyano group of II, VII and XXI by acid or alkali was unsuccessful.

The formation of 2-amino-1,3-dicyanoazulene (XXI) is explained by the reaction of two moles of malononitrile with one mole of 2-chlorotropone; even when one mole of malononitrile was reacted with one mole of 2-chlorotropone the same azulene derivative XXI was formed. The same result was found in the reaction of 2-chloro- or 2-methoxytropone with ethyl cyanoacetate. The use of one mole of the dimer of ethyl cyanoacetate, i.e. ethyl α -cyano- β -aminoglutaconate (XXII), instead of two moles of ethyl cyanoacetate, however, failed to give any azulene; the products were the heterocyclic azulenoid compounds XXIII and XXIV¹².

From the foregoing experimental facts, it is considered that the first intermediate XXV



formed by the reaction of both ethyl cyanoacetate and 2-halo- or 2-methoxytropone is much more reactive than the original troponoids Ia-c and immediately reacts with the second mole of the reagent to form second intermediates such as XXVIa and XXVIb, whose Ziegler-type condensation, forming a five-membered ring, would give a bicyclic intermediate XXVII and XXVIII. By the polarizing effect of the carbonyl or imino group in the 2-position, and the attack on the ethoxycarbonyl or cyano group by the base (alkoxide anion), the intermediate suffers a cleavage of the C-C bond¹³ through the third intermediates, XXIXa-b and



ECA = Ethyl cyanoacetate

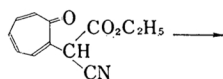
Scheme 1

12) S. Matsumura, This Bulletin, 34, 1361 (1961).

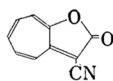
13) A. C. Cope, "Organic Reactions", Ed. by R. Adams,

Band IX, John Wiley & Sons, Inc., New York (1957), p. 107.

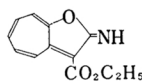
XXXa-b, and forms the final azulenoid products II, III, VI and VII, as is shown in Scheme 1. More recently, it has been found that an application of malonitrile to tropone itself¹⁴, or ethyl cyanoacetate or malonitrile to 8,8-disubstituted heptafulvenes¹⁵ (e.g. XXV: X=H), also gives the afore-mentioned azulene. The structure of the first intermediate might also be tropone derivative XXXI or its cyclization product XXXIIa or b, rather than the afore-mentioned heptafulvene derivative XXV.



XXXI



XXXIIa



XXXIIb

In this connection, it is interesting to note that the compound of the XXXIIa type also gave azulene derivatives in its reaction with ethyl cyanoacetate in the presence of an excess of sodium alkoxide¹⁶. All this evidence seem to confirm the general correctness of our proposed mechanism of this novel azulene synthesis starting with the troponoids.

After the completion of this study^{2a}, Ziegler and Hafner very interestingly reported a practical synthetic method of azulenes; they also found that the alkylation and arylation of the 4- and 8-positions could be effected by the application of organometallic compound to azulenes¹⁷. However, this method would have some disadvantages for the synthesis of special azulene derivatives possessing versatile groups, such as hydroxyl, amino, hydrazino and mercapto groups, on the five or seven-membered ring. In our method, the azulenes first formed always have a versatile functional group, i.e., amino or hydroxyl in the 2-position, which may be easily substituted afterwards by various groups; moreover, such groups may be easily introduced in the seven-membered ring while in the troponoid stage used for this synthesis. Accordingly, our process would complement the Ziegler-Hafner method for azulene synthesis.

As a simpler and more useful process has

recently been found in several laboratories for the synthesis of tropone and tropolone¹⁸, the novel process for the synthesis of azulene derivatives elaborated by us would have a very great significance. Thus, a large number of new azulene derivatives produced by the application of this process are now continuously being synthesized in the authors' laboratory^{15b}.

The yield of compound V is so very poor that further examination of this product was not made. Compound IV is identical with the product obtained by the condensation of salicylaldehyde with ethyl cyanoacetate, and the structure of compound IV was established to be 2-amino-2-(cyano-ethoxycarbonylmethyl)-3-ethoxycarbonyl- α -benzopyran¹⁹.

Experimental²⁰

Reaction of 2-Chlorotropone (Ia) and Ethyl Cyanoacetate.—a)

To a suspension of ethyl sodio-cyanoacetate prepared from 5 g. of metallic sodium, 27 g. of ethyl cyanoacetate and 100 ml. of absolute ethanol, a solution of 15 g. of Ia dissolved in 100 ml. of absolute ethanol was added drop by drop under ice-cooling, and the mixture was stirred thoroughly. Immediately the color of the solution changed from yellow to orange. The mixture was allowed to stand at room temperature for 4 hr., and the orange crystals that separated out were then collected by filtration. The collected crystals were dissolved in benzene to be separated into benzene-insoluble and soluble portions. The addition of water to the benzene-insoluble portion precipitated 900 mg. of orange-yellow crystals insoluble in water. This substance was extremely sparingly soluble in various organic solvents. Its recrystallization from a large quantity of ethanol afforded the orange-yellow sodium salt of II, m. p. above 300°C.

Found: N, 4.98. Calcd. for $C_{14}H_{10}O_3NNa$: N, 5.34%.

A mixture of sodium salt of II and 5 ml. of 6 N hydrochloric acid was warmed on a water bath for 1 hr. The orange crystals that separated out were recrystallized from benzene, and 370 mg. of orange needles II, m. p. 188–189°C, was obtained.

Found: C, 69.78; H, 4.63; N, 5.92. Calcd. for $C_{14}H_{11}O_3N$: C, 69.70; H, 4.59; N, 5.80%.

UV λ_{max}^{MeOH} $m\mu$ (log ϵ): 235 (4.53), 311 (4.72), 325 (4.49), 355 (3.77), 470 (3.34).

The evaporation of the solvent of the benzene-soluble portion left orange crystals, m. p. 80–83°C. Repeated recrystallization from ethanol afforded 19 g. of orange prisms III, m. p. 93–94°C.

Found: C, 66.93; H, 6.26; N, 4.82. Calcd. for $C_{16}H_{17}O_4N$: C, 66.88; H, 5.96; N, 4.88%.

14) Y. Kitahara and K. Doi, to be published.

15) a) T. Nozoe and T. Mukai et al., to be published; b) T. Nozoe and S. Ito, *Fortsch. Chem. org. Naturestoffe*, **19**, 32 (1961).

16) T. Nozoe and K. Takase et al., to be published.

17) a) K. Ziegler and K. Hafner, *Angew. Chem.*, **67**, 301 (1955); K. Hafner, *Ann.*, **606**, 69 (1957); b) K. Hafner and H. Weldes, *ibid.*, **606**, 90 (1957); c) K. Hafner, *Angew. Chem.*, **69**, 393 (1957); K. Hafner and H. Kaiser, *Ann.*, **618**, 140 (1958).

18) a) A. P. Ter. Borg, R. van, Helden, A. F. Bickel, W. Renold and A. S. Dreiding, *Helv. Chim. Acta*, **43**, 457 (1960); b) T. Ikemi, T. Nozoe and H. Sugiyama, *Chem. & Ind.*, **1960**, 932.

19) S. Matsumura, *This Bulletin*, **34**, 995 (1961).

20) All melting points are uncorrected. The microanalyses were carried out by Mr. S. Ohyama, Mr. S. Azumi and Miss. A. Iwanaga, to whom the authors are deeply indebted.

UV $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ ($\log \epsilon$): 245 (4.42), 265 (4.36), 315 (4.77), 326 (4.69), 380 (3.84), 465 (3.41).

The mother liquor, after the separation of the above products, was evaporated under a reduced pressure, the residue was dissolved in benzene, and the solution was washed with water. After being dried over anhydrous sodium sulfate, the solvent was evaporated. The orange crystalline residue thereby obtained was recrystallized from ethanol and 5 g. of colorless prisms IV, m. p. 135~137°C, was obtained.

Found: C, 61.37; H, 5.25; N, 8.42. Calcd. for $\text{C}_{17}\text{H}_{18}\text{O}_5\text{N}_2$: C, 61.81; H, 5.49; N, 8.49%.

UV $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ ($\log \epsilon$): 296 (3.72), 305 (3.69), 357 (3.60).

The recrystallization of the mother liquor afforded 2.5 g. of III.

b) To a sodium ethoxide solution prepared from 1 g. of metallic sodium and 20 ml. of absolute ethanol, 5.4 g. of ethyl cyanoacetate was added to form its sodio compound, and the ethanol was evaporated completely. The sodio compound was suspended in 30 ml. of dehydrated benzene, and the solution of 3 g. of Ia dissolved in 50 ml. of dehydrated benzene was stirred into it, by which process the solution became a dark reddish orange and an orange precipitate began to separate out. The orange precipitates were collected by filtration, and the addition of water afforded 200 mg. of sodium salt of II. The reaction mixture left after the removal of the above substance was washed with water. After being dried over anhydrous sodium sulfate, the solution was passed through a column of alumina. The column was eluted with benzene, and the solvent of the effluent was evaporated. The crystalline residue was recrystallized from ethanol to afford 1.2 g. of III.

c) To a solution of 500 mg. of Ia and 2.7 g. of ethyl cyanoacetate dissolved in 10 ml. of absolute ethanol, 1.7 g. of tributylamine was added; the color of the solution gradually changed from yellow to orange. The reaction mixture was allowed to stand overnight at room temperature, and the solvent was evaporated. The orange residue was dissolved in benzene, and the solution was washed with dilute nitric acid and water. After being dried over anhydrous sodium sulfate, the solution was passed through a column of alumina. The column was eluted with benzene, and 350 mg. of III was obtained. Further elution of the column with ethyl acetate afforded ca. 10 mg. of orange crystals. Recrystallization from acetone gave orange scales V, m. p. above 300°C.

Picrate of III.—Found: C, 51.25; H, 3.63; N, 10.64. Calcd. for $\text{C}_{22}\text{H}_{20}\text{O}_{11}\text{N}_4$: C, 51.16; H, 3.90; N, 10.85%. Reddish orange needles, m. p. 125~126°C, as recrystallized from ethanol. The solution of picrate-dissolved ethanol was passed through a column of alumina. The column was eluted with benzene, and III was easily regenerated.

Styphnate of III.—Found: N, 10.15. Calcd. for $\text{C}_{22}\text{H}_{20}\text{O}_{12}\text{N}_4$: N, 10.52%. Orange scales, m. p. 147~150°C, as recrystallized from ethanol.

Hydrochloride of III.—Dry hydrogen chloride gas was passed through a solution of III dissolved in dehydrated benzene, and the reddish orange prisms

that separated out were collected by filtration. The product underwent a change to the starting material by atmospheric moisture.

Action of Acetic Anhydride on III.—A solution of 100 mg. of III dissolved in 1 ml. of acetic anhydride, in the presence of one drop of pyridine, was heated at 120~130°C for 3 hr. The excess acetic anhydride was evaporated under a reduced pressure, and the residues were recrystallized from ethanol, by which 80 mg. of III was recovered.

Reaction of 2-Bromotropone (Ib) with Ethyl Cyanoacetate.—To a suspension of ethyl sodio-cyanoacetate prepared from 780 mg. of metallic sodium, 4 g. of ethyl cyanoacetate and 10 ml. of absolute ethanol, a solution of 3 g. of Ib dissolved in 7 ml. of absolute ethanol was added and the mixture was stirred thoroughly. Immediately the color of the solution changed from yellow to a dark reddish orange. After the solution had stood overnight at room temperature, the orange crystals that separated out were collected by filtration. The collected crystals were dissolved in benzene, and the solution was passed through a column of alumina. The column was eluted with benzene, and the solvent was evaporated. The crystallized residue was recrystallized from ethanol, and 2.6 g. of III was obtained. The mother liquor, after the separation of the above crystals, was concentrated, and the residue thereby obtained was dissolved in benzene. The solution was passed through a column of alumina, and the column was eluted with benzene. Evaporation of the solvent from the effluent afforded 400 mg. of III.

Reaction of 2-Methoxytropone (Tropolone Methyl Ether) (Ic) with Ethyl Cyanoacetate.—

a) Into a suspension of ethyl sodiocyanoacetate prepared from 600 mg. ($2.6/10^2$ mol.) of metallic sodium, 3.0 g. ($2.67/10^2$ mol.) of ethyl cyanoacetate and 10 ml. of absolute ethanol, a solution of 1.8 g. ($1.3/10^2$ mol.) of Ic dissolved in 10 ml. of absolute ethanol was stirred under ice-cooling. After allowing the solution to stand overnight at room temperature, a large amount of precipitate separated out and was collected by filtration. The collected precipitate was dissolved in benzene to be separated into benzene-soluble (A) and benzene-insoluble (B) portions. Evaporation of the solvent of A portion left orange crystals, m. p. 160~164°C. Four recrystallizations from ethanol afforded 210 mg. of orange scales VI, m. p. 167~168°C.

Found: C, 69.41; H, 4.88; N, 11.82. Calcd. for $\text{C}_{14}\text{H}_{12}\text{O}_2\text{N}_2$: C, 69.99; H, 5.03; N, 11.66%.

UV $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ ($\log \epsilon$): 238 (4.06), 310 (4.75), 322 (4.78), 368 (3.81), 445 (3.04).

The benzene-insoluble portion was dissolved in water, and the solution was neutralized with dilute sulfuric acid, from which 2.1 g. of a brown precipitate was obtained. This substance was sparingly soluble in organic solvents. Its recrystallization from a large quantity of acetone afforded 1.92 g. of orange-yellow scales VII, m. p. above 300°C.

Found: C, 73.98; H, 3.42; N, 14.06. Calcd. for $\text{C}_{12}\text{H}_6\text{ON}_2$: C, 74.22; H, 3.11; N, 14.43%.

UV $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ ($\log \epsilon$): 233 (4.35), 311 (4.72), 322 (4.62), 362 (3.86), 448 (3.50).

The mother liquor, after the separation of the

above products, was evaporated under reduced pressure. The orange residue thereby obtained was dissolved in benzene; the evaporation of the benzene left an oily substance. The residue was repeatedly digested with hot petroleum ether (b. p. 60~70°C) to be separated into petroleum ether-soluble and insoluble portions. The solvent of the petroleum ether-soluble portion was evaporated. The orange crystalline residue hereby produced was recrystallized from ethanol to give 190 mg. of III. Recrystallization of the petroleum ether-insoluble portion from the ethanol-benzene mixture afforded ca. 10 mg. of VI.

b) To a suspension of ethyl sodiocyanoacetate prepared from 600 mg. (2.59/10² mol.) of metallic sodium, 6.04 g. (5.34/10² mol.) of ethyl cyanoacetate and 10 ml. of absolute ethanol, 3.64 g. (2.74/10² mol.) of Ic was added, drop by drop under ice-cooling, and the mixture was stirred thoroughly. When the reaction mixture was treated as in the foregoing case, 5.5 g. of III, 100 mg. of VI and 500 mg. of VII were obtained.

c) To a suspension of ethyl sodiocyanoacetate prepared from 1.42 g. of sodium methoxide, 3.02 g. of ethyl cyanoacetate and 5 ml. of absolute ethanol, a solution of 1.8 g. of Ic dissolved in 10 ml. of absolute ethanol was added, and the mixture was treated as in the foregoing cases. The orange crystals were separated out from the benzene-soluble portion, besides 200 mg. of III, and 120 mg. of VI. The orange crystals were recrystallized from ethanol to afford 40 mg. of orange scales XX, m. p. 135~137°C.

Found: C, 68.98; H, 4.36; N, 12.56. Calcd. for C₁₃H₁₀O₂N₂: C, 69.01; H, 4.46; N, 12.38%.

UV $\lambda_{\text{max}}^{\text{MeOH}}$ m μ (log ϵ): 238 (4.05), 310 (4.73), 322 (4.77), 368 (3.79), 445 (3.03).

The benzene-insoluble portion was acidified with dilute sulfuric acid, from which 2 g. of VII was obtained.

Diethyl Azulene-1,3-dicarboxylate (VIII).—To a solution of 1 g. of III dissolved in 100 ml. of ethanol containing 500 mg. of concentrated sulfuric acid, 500 mg. of isoamyl nitrite was added. The reaction mixture was allowed to stand overnight at room temperature. The color of the solution gradually changed from an orange, reddish green, to a brownish red. The ethanol was then evaporated under reduced pressure. The dark red residue was suspended in water, and the suspension was neutralized with an aqueous solution of sodium carbonate. The residue thereby formed was extracted with benzene and the extract was dried over anhydrous sodium sulfate. The solution was passed through a column of alumina, and the column was eluted with benzene, by which 450 mg. of red crystals was obtained. Recrystallization from ethanol afforded 400 mg. of reddish violet prisms VIII, m. p. 120~121°C.

Found: C, 70.88; H, 5.71. Calcd. for C₁₈H₁₆O₄: C, 70.57; H, 5.92%.

UV $\lambda_{\text{max}}^{\text{MeOH}}$ m μ (log ϵ): 234 (4.56), 271 (4.50), 302 (4.67), 326 (3.83), 365 (3.99), 371 (4.03), [513 (2.71), 550 (2.65), 604 (2.21) in cyclohexane].

Azulene-1,3-dicarboxylic Acid (IX).—A solution of 1 g. of VIII dissolved in 10 ml. of a 10% ethanol-

water (4:1) solution of potassium hydroxide was warmed on a water bath for 30 min. The color of the solution changed from red to violet. After being cooled, the solution was acidified with 6N hydrochloric acid. The precipitate thereby formed was collected by filtration and repeatedly washed with water, by which 800 mg. of a sparingly soluble red substance IX, m. p. 270°C (decomp.), was obtained.

Azulene (X).—The low-pressure (200 mmHg) sublimation of 500 mg. of IX by heating at 270~280°C produced blue crystals. The crystals were dissolved in petroleum ether (b. p. 50~60°C), and the solution was passed through a column of alumina. The column was eluted with petroleum ether, and the solvent was cautiously removed. The crystalline residue was recrystallized from a methanol-water (4:1) mixture to afford 250 mg. of X as blue leaflets, m. p. 98~99°C, which showed no depression on admixture with an authentic specimen of azulene.

UV $\lambda_{\text{max}}^{\text{MeOH}}$ m μ (log ϵ): 238 (4.17), 273 (4.68), 279 (4.64), 295 (3.55), 326 (3.45), 341 (3.60), 352 (2.70), 580 (2.50), 633 (2.41), 700 (1.98).

Dimethyl Azulene-1,3-carboxylate (XI).—An ether solution of diazomethane was added to 100 mg. of IX suspended in 10 ml. of methanol, and the mixture was allowed to stand overnight. The solvent was evaporated, and the residue was dissolved in benzene. The solution was passed through a column of alumina. The column was eluted with benzene, and the solvent was distilled off. The crystallized residue was recrystallized from methanol to give 80 mg. of reddish violet scales XI, m. p. 171~172°C.

Found: C, 68.64; H, 4.86. Calcd. for C₁₄H₁₂O₄: C, 68.84; H, 4.95%.

Ethyl Azulene-1-carboxylate (XII).—To a solution of 100 mg. of potassium hydroxide dissolved in 5 ml. of an ethanol-water (4:1) mixture, 500 mg. of VIII was added; the mixture was then warmed on a water bath for 15 min. After being cooled, the solution was acidified with 6N hydrochloric acid. The precipitate thereby formed was collected by filtration and repeatedly washed with water, by which 60 mg. of crystalline carboxylic acid was obtained. The low-pressure (100 mmHg) sublimation of the carboxylic acid by heating at 240~250°C produced a violet oil. The oil was dissolved in petroleum ether (b. p. 60~70°C) and chromatographically purified through an alumina column. The product separated into blue and reddish violet bands. The elution of the blue band with petroleum ether afforded ca. 10 mg. of X. The further elution of the reddish violet oil produced XII.

UV $\lambda_{\text{max}}^{\text{Cyclohexane}}$ m μ (log ϵ): 234 (4.30), 291 (4.61), 296 (4.65), 351 (3.76), 365 (3.95), 545 (2.65), 588 (3.60), 645 (2.23).

Picrate of XII.—Found: C, 53.41; H, 5.48; N, 9.81. Calcd. for C₁₉H₁₅O₉N₃: C, 53.15; H, 3.52; N, 9.79%. Red needles, m. p. 123~124°C, as recrystallized from ethanol.

2-Aminoazulene-1,3-dicarboxylic Acid (XIII).—To a solution of 200 mg. of potassium hydroxide in 5 ml. of an ethanol-water (4:1) mixture, 500 mg. of III was added; the mixture was then refluxed in a water bath for 3 hr., by which the solution clearly colored orange-yellow. The solution was

acidified with 6 N hydrochloric acid. The precipitate hereby formed was collected by filtration and repeatedly washed with water; 350 mg. of crude 2-aminoazulene-1,3-dicarboxylic acid (XIII), m. p. 158~160°C (decomp.), sparingly soluble in organic solvents, was obtained.

2-Aminoazulene (XIV).—a) A suspension of 400 mg. of XIII in 2 ml. of pyridine was heated at 125~130°C for 15 min. to effect decarboxylation. The residue obtained by evaporation of the excess pyridine was dissolved in benzene, and the solution was passed through a column of alumina. The column was eluted with benzene. Evaporation of the solvent from the effluent afforded red crystals. Recrystallization from benzene-cyclohexane mixture gave 200 mg. of red needles (XIV), m. p. 93~94°C.

Found: C, 83.31; H, 6.44; N, 9.40. Calcd. for $C_{10}H_9N$: C, 83.88; H, 6.34; N, 9.78%.

UV λ_{max}^{MeOH} $m\mu$ (log ϵ): 218 (4.10), 240 (4.08), 284 (4.80), 294 (4.89), 345 (3.74), 387 (3.92), 403 (3.83).

b) The low-pressure (2 mmHg) sublimation of 60 mg. of XIII by heating at 170~175°C afforded red crystals. Their recrystallization from the benzene-cyclohexane mixture gave 20 mg. of XIV.

2-Acetamidoazulene (XV).—When 2-aminoazulene (200 mg.) was added to 0.2 ml. of acetic anhydride, the mixture colored violet immediately. After allowing the mixture to stand at room temperature for 2 hr., the violet crystals that separated out were collected by filtration; recrystallization from benzene afforded 200 mg. of violet needles XV, m. p. 168~169°C.

Found: C, 77.49; H, 5.80; N, 7.49. Calcd. for $C_{12}H_{11}ON$: C, 77.81; H, 5.99; N, 7.56%.

UV λ_{max}^{MeOH} $m\mu$ (log ϵ): 240 (4.23), 285 (4.84), 294 (4.97), 345 (3.73), 363 (3.94), 379 (4.06), 548 (2.64), 584 (2.57), 640 (2.31).

Ethyl 2-Aminoazulene-1-carboxylate (XVI).—To a solution of 250 mg. of potassium hydroxide dissolved in 4 ml. of an ethanol-water (4:1) mixture, 1.3 g. of III was added, and the mixture was refluxed in a water bath for 3 hr. The solution was acidified with 6 N hydrochloric acid. The precipitate thereby obtained was collected by filtration and washed with water. After being dried, the precipitate was suspended in 2 ml. of pyridine, and the suspension was heated at 120~130°C to effect decarboxylation. The residue produced by evaporation of the excess pyridine was dissolved in benzene, and the solution was passed through a column of alumina, by which the products were separated into red, reddish-orange and orange bands. Elution of the red band with benzene gave a small amount of XIV. Elution of the reddish orange band with benzene afforded a reddish orange oil which was crystallized from cyclohexane to crystals of m. p. 60~65°C. Recrystallization from cyclohexane afforded 400 mg. of reddish orange needles (XVI), m. p. 68~70°C.

Found: C, 72.48; H, 5.97; N, 6.67. Calcd. for $C_{13}H_{13}O_2N$: C, 72.54; H, 6.09; N, 6.51%.

UV λ_{max}^{MeOH} $m\mu$ (log ϵ): 304 (4.76), 314 (4.93), 358 (3.96), 378 (3.86).

Ethyl 2-Acetamidoazulene-1-carboxylate (XVII).—A mixture of 200 mg. of XVI and 2 ml. of acetic

anhydride was treated as in the preparation of XV, and 200 mg. of XVII as red leaflets, m. p. 140~141.5°C, was obtained.

Found: C, 69.96; H, 5.85; N, 5.15. Calcd. for $C_{15}H_{15}O_3N$: C, 70.02; H, 5.88; N, 5.44%.

UV λ_{max}^{MeOH} $m\mu$ (log ϵ): 246 (4.32), 304 (4.82), 314 (4.97), 356 (3.96), 371 (3.96), 503 (2.55).

Ethyl 2-Acetoxy-3-cyanoazulene-1-carboxylate (XVIII).—A mixture of 50 mg. of II and 0.2 ml. of acetic anhydride containing one drop of pyridine was heated at 120~130°C for 3 hr., by which the II dissolved completely. The mixture was evaporated under reduced pressure, and the crystalline residue was recrystallized from ethanol to give 40 mg. of XVIII as reddish orange needles, m. p. 141~142°C.

Found: C, 67.74; H, 4.61; N, 4.81. Calcd. for $C_{16}H_{13}O_4N$: C, 67.84; H, 4.63; N, 4.95%.

2-Acetoxy-1,3-dicyanoazulene (XIX).—A mixture of 50 mg. of VII and 1 ml. of acetic anhydride was treated as in the foregoing case, and 30 mg. of reddish orange scales XIX, m. p. 191~192°C, was obtained.

Found: C, 70.97; H, 3.67; N, 11.63. Calcd. for $C_{14}H_8O_2N_2$: C, 71.18; H, 3.41; N, 11.86%.

Reaction of 2-Chlorotropone (Ia) with Malononitrile.—a) Into a suspension of sodiummalononitrile prepared from 320 mg. (1.4/10² mol.) of metallic sodium, 920 mg. (1.4/10² mol.) of malononitrile and 10 ml. of absolute ethanol, a solution of 1 g. (7/10³ mol.) of Ia dissolved in 8 ml. of absolute ethanol was stirred, drop by drop, ice-cooling. The mixture was allowed to stand at room temperature for 1 hr., by which the solution became clearly a green color and orange crystals began to separate out. The crystals were collected by filtration and washed with water. Their recrystallization from a large quantity of acetone afforded 1.2 g. of orange needles XXI, m. p. above 300°C.

Found: C, 74.83; H, 3.41; N, 21.62. Calcd. for $C_{12}H_7N_3$: C, 74.60; H, 3.65; N, 21.75%.

UV λ_{max}^{MeOH} $m\mu$ (log ϵ): 231 (4.50), 309 (4.58), 322 (4.64), 393 (3.75), 445 (2.90).

b) To a solution of 500 mg. (3.5/10³ mol.) of Ia and 460 mg. (7/10³ mol.) of malononitrile dissolved in 10 ml. of absolute ethanol or dehydrated benzene was added 1.3 g. (7/10³ mol.) of tributylamine, by which the solution immediately turned reddish-orange and a precipitate gradually deposited. The precipitate was collected by filtration and recrystallized from acetone to give 700 mg. of XXI.

c) When a solution of 500 mg. (3.5/10³ mol.) of Ia, 230 mg. (3.5/10³ mol.) of malononitrile and 650 mg. (3.5/10³ mol.) of tributylamine dissolved in 5 ml. of absolute ethanol was treated as in the foregoing cases, 300 mg. of XXI was obtained.

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