The Reaction of 5- and 6-Acetylazulene Derivatives with Hydrazines. The Formation of Azuleno[4, 3-f]pyrazoles

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In a previous report[1], 5- and 6-acetylazulene derivatives were derived from 4-acetyltropolone. The present paper deals with the reaction of these acetylazulenes with various hydrazines and hydroxylamine. The reaction with unsubstituted hydrazine resulted in the formation of azulenopyrazoles.

The reaction of hydrazine hydrate with diethyl 5-acetylazulene-1, 3-dicarboxylate (I) yielded dull reddish crystals II. When II was heated with potassium hydroxide in ethylene glycol, deep violet crystals III were

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[1] T. Nozoe, K. Takase and M. Tada, This Bulletin, 36, 1010 (1963).

formed; III was also obtained by the alkaline hydrolysis of II and the subsequent decarboxylation in quinoline of the resultant dicarboxylic acid IV.

III contains nitrogen and shows a sharp N–H band at 3135 cm^{-1} which disappears upon acetylation to form *N*-acetate (V). The carbonyl frequency (1724 cm^{-1}) of the acetate indicated the attachment of an aromatic system or an electron-attracting group to the imino nitrogen[2]. These spectral observations reveal the structure of III to be that of a methylazulenopyrazole. The infrared spectra of II and its acetate VI exhibited ν_{NH} at 3230 cm^{-1} and ν_{NCOCH_3} at 1733 cm^{-1}, which facts suggest presence of the same ring system in both II and III. The conclusive evidence for the presence of a pyrazole ring was obtained by the alkaline permanganate oxidation of II, upon which 5-methylpyrazole-3, 4-dicarboxylic acid (VII) was obtained. The stability of II to chloranil indicated that II must be a pyrazole and not a pyrazoline derivative. Therefore, II can be formulated as IIa or IIb (see Chart I). Although definite evidence is lacking, we prefer IIa, that is, diethyl 3-methylazuleno [4, 3-f] pyrazole-5, 7-dicarboxylate, to IIb on the basis of the steric hindrance of ethoxycarbonyl at Position 3. Thus, the structures of 3-methylazuleno [4, 3-f]-pyrazole shown in Chart I were assigned to III and IV.

On hydrolysis with a limited amount of alkali, II yielded an ester acid VIII which, on heating in quinoline, gave a monoester IX, althougth the exact position of the ethoxycarbonyl group is not known.

The ultraviolet and visible absorption spectra of these 3-methylazuleno[4, 3-f]pyrazole derivatives are shown in Figs. 1 and 2.

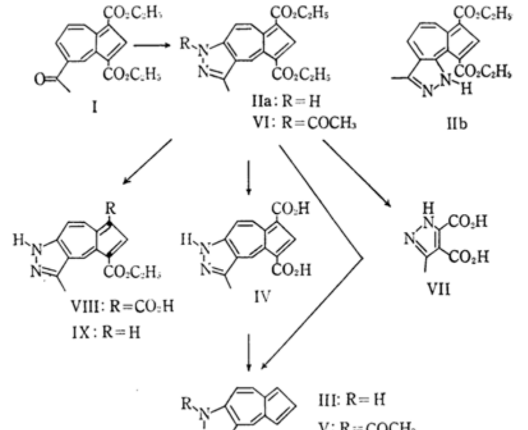


Chart I

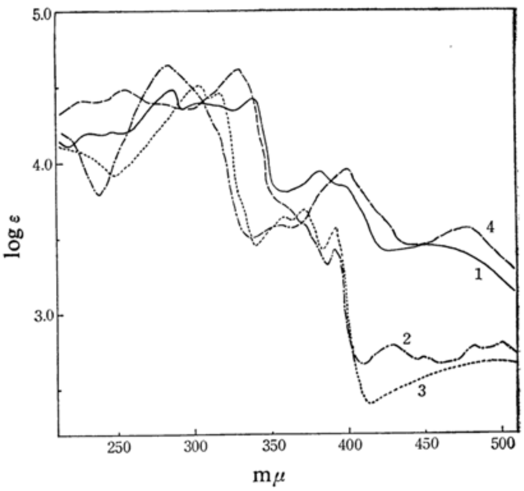


Fig. 1. Ultraviolet absorption spectra in methanol.
1 Diethyl 3-methylazuleno[4,3-f]pyrazole-5,7-dicarboxylate (II)
2 3-Methylazuleno[4, 3-f]pyrazole (III)
3 Acetate (V) of III
4 Acetate (VI) of II

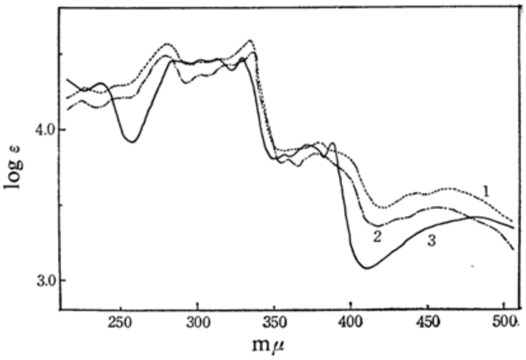
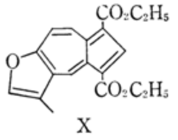


Fig. 2. Ultraviolet absorption spectra in methanol.
1 3-Methylazuleno[4, 3-f]pyrazole-5, 7-dicarboxylic acid (IV)
2 3-Methylazuleno[4, 3-f]pyrazole-5, 7-dicarboxylic acid monoethyl ester (VIII)
3 Ethyl 3-methylazuleno[4, 3-f]pyrazole-5(or 7)-carboxylate (IX)

This rather unusual ring formation on an azulene nucleus (though such a formation is not without precedent[3], azulenofurane derivative (X)), can be rationalized by the electrophilic nature of the seven-membered ring in



X

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[2] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London (1958), p. 213.

[3] T. Nozoe, S. Seto and S. Matsumura, *Chem. & Ind.*, **1961**, 1715.

azulene enhanced by the presence of the two ethoxycarbonyl groups at Positions 1 and 3, and by the facility of the dehydrogenation of dihydroazulene to azulene. This reaction path is shown in Chart II.

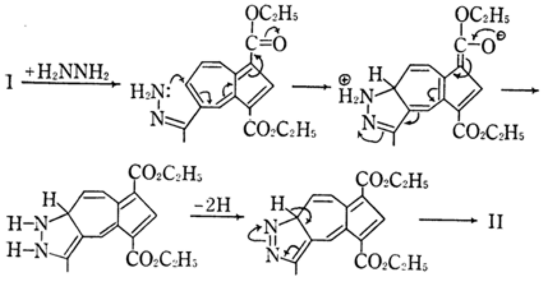
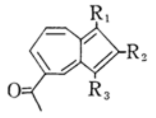


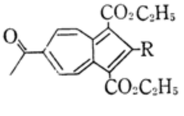
Chart II

This interesting behaviour of I toward hydrazine prompted us to extend our study to other acetylazulenes and other reagents related to hydrazine.

Several experiments revealed that hydrazine is the only reagent to form pyrazole; thus, I gave a normal phenylhydrazone(ν_{NH} 3210 cm^{-1}), a normal *p*-tolylsulfonylhydrazone (ν_{NH} 3210 cm^{-1}) and a normal oxime (ν_{OH} 3350 cm^{-1}). Moreover, 2-amino (XI, XII), 2-acetamido (XIII) or 2-hydroxyl (XIV, XV) groups inhibit the ring formation, giving the normal ketonic derivatives (see the Experimental section). There seems to be no difference if the ethoxycarbonyl or the cyano groups occupy at Positions 1 and 3, inasmuch as electron-releasing amino or the hydroxyl group is situated at Position 2. Furthermore, it is a rather interesting difference that diethyl 6-acetylazulene-1, 3-dicarboxylate (XVI), the position isomer of I, gives only normal hydrazone. According to the SCF electron density calculation for the ground state of azulene[4], the density at Position 6 (0.938) is comparatively lower than that at Position 5 (1.034). The findings described above are consistent with the theoretical calculation.



XI: $R_1=R_3=CO_2C_2H_5$; $R_2=NH_2$
XII: $R_1=CN$, $R_3=CO_2C_2H_5$ or $R_1=CO_2C_2H_5$, $R_3=CN$; $R_2=NH_2$
XIII: $R_1=R_3=CO_2C_2H_5$; $R_2=NHCOCH_3$
XIV: $R_1=CN$, $R_3=CO_2C_2H_5$ or $R_1=CO_2C_2H_5$, $R_3=CN$; $R_2=OH$
XV: $R_1=R_3=CN$; $R_2=OH$



XVI: R=H
XVII: $R=NH_2$

Experimental[5]

Diethyl 3-Methylazuleno[4, 3-f]pyrazole-5, 7-dicarboxylate (II).—To a solution of diethyl 5-acetylazulene-1, 3-dicarboxylate (I) (130 mg.) in ethanol (2 ml.), 80% hydrazine hydrate (0.1 g.) was added, and the mixture was warmed for 30 min., by which process II (40 mg.) was obtained as dull red micro-prisms (m. p. 252~253°C, after recrystallization from ethanol).

Found: C, 65.99; H, 5.73; N, 8.56. Calcd. for $C_{18}H_{18}O_4N_2$: C, 66.24; H, 5.56; N, 8.58%.

λ_{max}^{MeOH} mμ (log ε): 232 (4.18), 218 (4.44), 307 (4.39), 339 (4.45), 384 (3.94), 460 (3.45). IR (Nujol): 3230, 1692, 1656 cm^{-1}.

Acetate (VI).— Reddish orange micro-prisms (from ethanol); m. p. 121~122°C.

Found: C, 65.46; H, 5.61; N, 8.04. Calcd. for $C_{20}H_{20}O_5N_2$: C, 65.46; H, 5.47; N, 7.61%.

λ_{max}^{MeOH} mμ (log ε): 255 (4.48), 275 (4.38), 328 (4.62), 404 (3.95), 480 (3.53). IR (Nujol): 1733, 1689, 1669 cm^{-1}.

3-Methylazuleno[4, 3-f]pyrazole-5, 7-dicarboxylic Acid (IV).—A solution of II (150 mg.) and potassium hydroxide (200 mg.) in 50% aqueous ethanol (8 ml.) was refluxed for 8 hr. After being cooled, the solution was acidified with 6 N sulfuric acid to give IV (110 mg.) as a brownish red crystalline powder (m. p. above 270°C) which is sparingly soluble in organic solvents.

Found: C, 59.55; H, 4.00; N, 8.90. Calcd. for $C_{14}H_{12}O_4N_2$-$2H_2O$: C, 59.78; H, 4.66; N, 9.96%.

λ_{max}^{MeOH} mμ (log ε): 230 (4.25), 284 (4.54), 304 (4.41), 338 (4.56), 363 (3.82), 460 (3.53). IR (Nujol): 3155, 1661 cm^{-1}.

3-Methylazuleno[4, 3-f]pyrazole (III).—*i) From II.*—To a solution of potassium hydroxide (110 mg.) in ethylene glycol (3 ml.), II (180 mg.) was added, and the mixture was heated at 140~150°C for 6 hr. After being cooled, this solution was diluted with water (40 ml.) and extracted with benzene. Removal of the solvent from the extract gave III (50 mg.) (m. p. 185~186°C), which was recrystallized from aqueous ethanol in the form of purplish red needles (m. p. 186~187°C).

Found: C, 79.20; H, 4.91; N, 15.47. Calcd. for $C_{12}H_{10}N_2$: C, 79.09; H, 5.72; N, 15.38%.

λ_{max}^{MeOH} mμ (log ε): 280 (4.64), 352 (3.59), 370 (3.63), 390 (3.46), 430 (2.79), 500 (2.79). IR (Nujol): 3135, 1613 cm^{-1}.

Acetate (V).—Pale purple scales (from ethanol); m. p. 158~159°C.

Found: C, 75.46; H, 5.56; N, 12.70. Calcd. for $C_{14}H_{12}ON_2$: C, 74.99; H, 5.38; N, 12.49%.

λ_{max}^{MeOH} mμ (log ε): 300 (4.50), 316 (4.44), 359 (3.62),

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[4] A. Julg, *J. chim. phys.*, 52, 377 (1955).

[5] All melting points are uncorrected.

371 (3.67), 391 (3.55), 495 (2.64). IR (Nujol): 1724, 1684 cm^{-1}.

ii) From IV. — A mixture of IV (120 mg.) and quinoline (1 ml.) was heated at 230~250°C for 2 hr. to effect decarboxylation. The residue produced by the evaporation of the quinoline was dissolved in ethyl acetate and passed through a column of alumina to give III (10 mg.).

The Permanganate Oxidation of II. — Into a solution of II (400 mg.) in a 0.25 N potassium hydroxide solution (100 ml.), finely powdered potassium permanganate (2.32 g.) was added in small portions with stirring at room temperature; the mixture was then stirred a further 6 hr. and allowed to stand overnight. The excess permanganate was decomposed on the addition of methanol, and the precipitated manganese dioxide was filtered off. The filtrate was slightly acidified with 6 N hydrochloric acid and concentrated under a reduced pressure until crystal had begun to separate out. Acetone was added, and the inorganic salts thereby separated were filtered off. After the mother liquor was treated repeatedly in the same way as above, the combined acetone solution was evaporated to dryness; the subsequent addition of a small amount of water gave oxalic acid. From the water-soluble part, 5-methylpyrazole-3, 4-dicarboxylic acid (VII) (20 mg.) was obtained (m. p., 233°C (decomp.)); this acid was identified as identical with an authentic specimen[6] by a comparison of the infrared spectra.

3-Methylazuleno[4, 3-f]pyrazole-5, 7-dicarboxylic Acid Monoethyl Ester (VIII). — To a solution of potassium hydroxide (150 mg.) in 75% aqueous ethanol (8 ml.), II (200 mg.) was added, and the mixture was refluxed for 4 hr. This solution was acidified with 6 N sulfuric acid to give VIII (150 mg.) as brownish red crystals (m. p. 247~250°C (decomp.)).

Found: C, 60.95; H, 4.92; N, 8.58. Calcd. for $C_{16}H_{14}O_4N_2$-H_2O: C, 60.75; H, 5.10; N, 8.86%.

$\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 230 (4.19), 284 (4.55), 304 (4.37), 321 (4.42), 363 (3.79), 380 (3.86), 460 (3.51).

Ethyl 3-Methylazuleno[4, 3-f]pyrazole-5 (or 7)-carboxylate (IX). — A mixture of VIII (100 mg.) and quinoline (1.5 ml.) was heated at 230~250°C for 2 hr. to effect decarboxylation. The residue, obtained by the evaporation of the quinoline, was dissolved in benzene and passed through a column of alumina to give red crystals (20 mg.) (m. p. 162 ~168°C) which were then recrystallized from benzene to form IX (15 mg.) as red prisms (m. p. 202~203°C).

Found: C, 71.03; H, 5.46; N, 10.71. Calcd. for $C_{15}H_{14}O_2N_2$: C, 70.85; H, 5.55; N, 11.02%.

$\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 235 (4.32), 286 (4.47), 302 (4.45), 315 (4.30), 333 (4.29), 373 (3.92), 390 (3.92), 484 (3.41). IR (Nujol): 3145, 1647 cm^{-1}.

Ketonic Derivatives of I.—*a) Phenylhydrazone.*— Violet brown micro-prisms (from ethanol); m. p. 181~182°C.

Found: C, 71.24; H, 5.90; N, 6.54. Calcd. for $C_{24}H_{24}O_4N_2$: C, 71.27; H, 5.98; N, 6.93%.

IR (Nujol) 3310, 1686, 1667 cm^{-1}.

b) p-Tolylsulfonylhydrazone.—Brown micro-prisms (from ethanol); m. p. 206~207°C.

Found: C, 62.16; H, 5.13; N, 5.67. Calcd. for $C_{25}H_{26}O_6N_2S$: C, 62.23; H, 5.43; N, 5.80%.

IR (Nujol): 3210, 1689 cm^{-1}.

c) Oxime. — Brown needles (from ethanol); m. p. 162.5~164°C.

Found: C, 65.38; H, 5.47; N, 4.65. Calcd. for $C_{18}H_{19}O_5N$: C, 65.64; H, 5.82; N, 4.25%.

IR (Nujol): 3350, 1672 cm^{-1}.

Oxime Acetate: Dull red crystals (from ethanol); m. p. 126.5~128°C.

Found: N, 3.77. Calcd. for $C_{20}H_{21}O_6N$: N, 3.33%. IR (Nujol): 1789, 1686 cm^{-1}.

Ketonic Derivatives of XI. — *a) Hydrazone.* — Orange yellow fine crystals (from ethanol); m. p. 128~129°C.

Found: C, 63.01; H, 5.80; N, 11.73. Calcd. for $C_{18}H_{21}O_4N_3$: C, 62.96; H, 6.16; N, 12.24%.

IR (Nujol): 3320, 3250, 3160, 3100, 1667 cm^{-1}.

Hydrazone Monoacetate: Orange yellow fine crystals (from ethanol); m. p. 193~194°C.

Hydrazone Diacetate: Yellow orange needles (from a mixture of ethyl acetate and benzene); m. p. 223~224°C.

Found: C, 62.02; H, 6.04; N, 10.34. Calcd. for $C_{22}H_{25}O_6N_3$: C, 61.81; H, 5.90; N, 9.83%.

IR (Nujol): 3280, 3135, 1730, 1712, 1658 cm^{-1}.

b) Azine. — Orange red micro-prisms (from ethanol); m. p. 224~225°C.

Found: C, 65.12; H, 5.67; N, 8.75. Calcd. for $C_{36}H_{38}O_8N_4$: C, 66.04; H, 5.85; N, 8.56%.

IR (Nujol): 3400, 3250, 1650 cm^{-1}.

Azine Diacetate: Orange red silky needles (from ethyl acetate); m. p. 179.5~181°C.

Found: C, 64.77; H, 5.36; N, 8.12. Calcd. for $C_{40}H_{42}O_{10}N_4$: C, 65.03; H, 5.73; N, 7.58%.

Picrate of Azine Diacetate: Scarlet crystals (from ethanol); m. p. 153~155°C.

Found: N, 9.52. Calcd. for $C_{48}H_{51}O_{18}N_7$: N, 9.67%.

c) p-Tolylsulfonylhydrazone.—Yellow micro-prisms (from ethyl acetate); m. p. 209°C (decomp.).

Found: C, 60.41; H, 5.23; N, 8.63. Calcd. for $C_{25}H_{27}O_6N_3S$: C, 60.35; H, 5.47; N, 8.45%.

IR (Nujol): 3330, 3160, 3100, 1672 cm^{-1}.

p-Tolylsulfonylhydrazone Acetate: Pale red micro-prisms (from ethyl acetate); m. p. 210~210.5°C.

Found: C, 59.39; H, 5.31; N, 7.39. Calcd. for $C_{27}H_{29}O_7N_3S$: C, 60.10; H, 5.42; N, 7.79%.

d) Oxime. — Orange yellow micro-prisms (from ethanol); m. p. 155~156.5°C.

Found: C, 62.50; H, 5.34; N, 7.81. Calcd. for $C_{18}H_{20}O_5N_2$: C, 62.78; H, 5.85; N, 8.14%.

IR (Nujol): 3390, 3260, 1669 cm^{-1}.

Oxime Acetate: Orange needles (from ethanol); m. p. 153~154°C.

Found: C, 62.03; H, 5.46; N, 7.10. Calcd. for $C_{20}H_{22}O_6N_2$: C, 62.16; H, 5.74; N, 7.25%.

IR (Nujol); 3380, 3260, 1756, 1667 cm^{-1}.

e) Phenylhydrazone.—Orange micro-prisms (from ethanol); m. p. 139~139.5°C.

Found: C, 66.79; H, 5.38; N, 8.44. Calcd. for $C_{26}H_{31}O_5N_3$: C, 67.08; H, 6.71; N, 9.03%.

IR (Nujol): 3380, 3240, 1667 cm^{-1}.

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[6] K. v. Auwers and E. Cauer, *Ann.*, **470**, 304 (1929).

f) Semicarbazone.— Yellowish orange micro-prisms (from aqueous ethanol); m. p. 245∼246°C.

Found: C, 59.05; H, 5.35; N, 14.03. Calcd. for $C_{19}H_{22}O_5N_4$: C, 59.00; H, 5.74; N, 14.50%.

IR (Nujol): 3350, 3300, 3160, 3100, 1712, 1664 cm^{-1}.

Ketonic Derivatives of XII. — *a) Hydrazone.* — Yellowish orange micro-prisms (from ethanol); m. p. above 270°C.

Found: N, 16.28. Calcd. for $C_{18}H_{22}O_3N_4$: N, 16.36%.

IR (Nujol): 3300, 3230, 2208, 1667 cm^{-1}.

Hydrazone diacetate: Dull orange micro-prisms (from eshanol); m. p. 192∼193°C.

Found: N, 14.49. Calcd. for $C_{20}H_{20}O_4N_4$: N, 14.73%.

IR (Nujol): 3300, 3200, 2193, 1876, 1661 cm^{-1}.

b) Azine. — Orange micro-prisms (from ethyl acetate); m. p. 168°C.

Found: N, 14.53. Calcd. for $C_{32}H_{28}O_4N_6$: N, 14.99%.

IR (Nujol): 3420, 3300, 3200, 2193, 1661 cm^{-1}.

Azine of XIV. — Pale yellowish brown micro-prisms (from ethyl acetate); m. p. 194∼195°C (decomp.).

Found: N, 7.47. Calcd. for $C_{40}H_{38}O_{10}N_4$: N, 7.63%.

IR (Nujol): 2222, 1650 cm^{-1}.

Hydrazone of XV. — Orange red powder (from ethanol); m. p. above 265°C.

Found: N, 23.07. Calcd. for $C_{14}H_{10}ON_4$: N, 22.39%.

IR (Nujol): 3380, 3330, 3210, 2193 cm^{-1}.

Hydrazone Acetate.—Pale red micro-prisms (from ethanol); m. p. above 265°C.

Found: C, 63.55; H, 4.37; N, 15.03. Calcd. for $C_{20}H_{20}O_4N_4$: C, 63.15; H, 5.30; N, 14.73%.

IR (Nujol): 3350, 3200, 2208, 1776, 1718, 1684 cm^{-1}.

Hydrazone of XVI. — Dull yellow leaflets (from ethanol); m. p. 232∼233°C (decomp.).

Found: C, 65.93; H, 5.93; N, 8.85. Calcd. for $C_{18}H_{20}O_4N_2$: C, 65.84; H, 6.14; N, 8.53%.

IR (Nujol): 3330, 3300, 3250, 1684 cm^{-1}.

Hydrazone Acetate.—Dull yellowish orange micro-needles (from ethanol); m. p. 220°C (blackened).

Found: N, 7.83. Calcd. for $C_{20}H_{22}O_5N_2$: N, 7.56%.

IR (Nujol): 3300, 1706, 1669 cm^{-1}.

Hydrazone of XVII.—Orange micro-prisms (from ethanol); m. p. 125∼126°C.

Found: C, 63.39; H, 5.92; N, 12.60. Calcd. for $C_{18}H_{21}O_4N_3$: C, 62.96; H, 6.16; N, 12.24%.

IR (Nujol): 3380, 3250, 3100, 1667 cm^{-1}.

Hydrazone Acetate.—Reddish orange prisms (from ethanol); m. p. 218∼219°C.

Found: C, 62.60; H, 5.99; N, 10.80. Calcd. for $C_{20}H_{23}O_5N_3$: C, 62.32; H, 6.02; N, 10.90%.

IR (Nujol): 3350, 3250, 3100, 1724, 1675 cm^{-1}.

Picrate of Hydrazone Acetate: Deep red crystals (from ethanol); m. p. 252.5∼253.5°C.

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