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THE REACTION OF 3-CYANO-2H-CYCLOHEPTA[b]FURAN-2-ONE WITH β,β-DISUBSTITUTED ENAMINES [1)]

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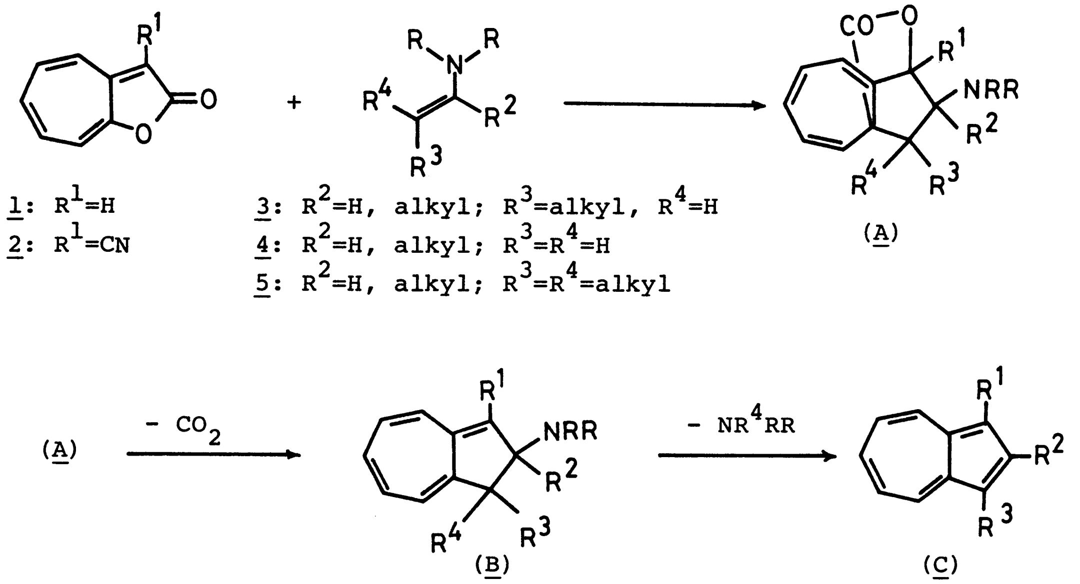
The reaction of 3-cyano-2H-cyclohepta[b]furan-2-one with enamines derived from isobutyraldehyde gave 2-amino derivatives of 3-cyano-1,1-dimethyl-1,2-dihydroazulene, which on heating with sulfuric acid underwent the elimination of amines accompanied by the migration of the methyl group to give 1,2-dimethylazulenes.

In the preceding papers,[2)] we have reported the facile method for synthesis of azulene derivatives utilizing the reaction of 2H-cyclohepta[b]furan-2-one (1) and its 3-cyano derivative (2) with β-monosubstituted (3) and β-non-substituted enamines (4). The mechanism for the formation of azulene derivatives (C) in this reaction has also been presumed to proceed with the elimination of amines from the dihydroazulene-type intermediates (B) which are formed by decarboxylation from the primarily produced intermediates (A). In addition, such dihydroazulene-type intermediates have been isolated in the reaction of 1 with pyrrolidinyl enamines derived from cyclopentanone[2a)] and 1-indanone[2b)] and also in the reaction of 2 with morpholino enamines derived from some aldehydes,[2d)] and are found to undergo the elimination of amines to give azulene derivatives in excellent yields when treated with silica gel or p-toluenesulfonic acid. In the viewpoint on the scope and limitation of this azulene formation reaction, an additional interest is aroused in the reaction of 1 and 2 with β,β-disubstituted enamines (5): this should give only dihydroazulene-type compounds (B: R^3,R^4=alkyl) in which the 1,2-elimination of amines can not take place to give azulene derivatives. This communication describes the reaction of 1 and 2 with enamines (6) derived from isobutyraldehyde.

A suspension of 2 in ethanol, containing 3 molar equivalents of 1-morpholinoisobutene (6a), was refluxed for 8 hr. After evaporation of the solvent the residue was chromatographed (alumina, benzene) to give 3-cyano-1,1-dimethyl-2-morpho-

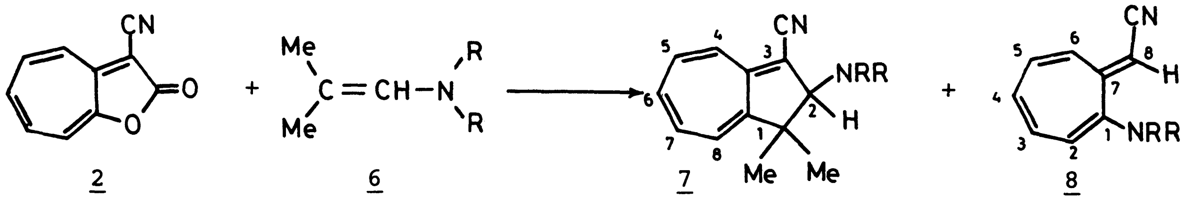


1: R^1=H
2: R^1=CN

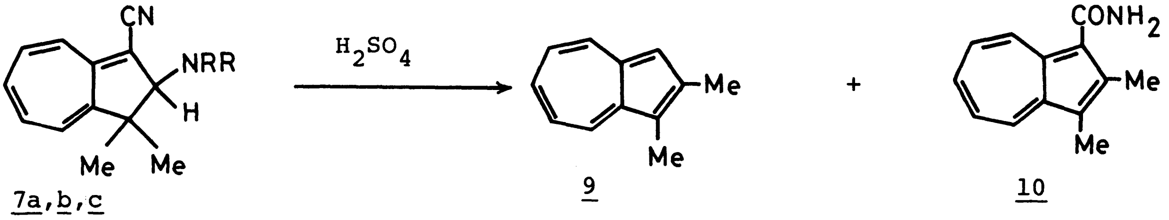
3: R^2=H, alkyl; R^3=alkyl, R^4=H
4: R^2=H, alkyl; R^3=R^4=H
5: R^2=H, alkyl; R^3=R^4=alkyl

lino-1,2-dihydroazulene (7a) [red needles, mp 105°C] in a 64% yield, together with 8-cyano-1-morpholinoheptafulvene (8a) in a 2% yield. Similarly, the reaction of 2 with 1-piperidino- (6b) and 1-N-pyrrolidinylisobutene (6c) gave 3-cyano-1,1-dimethyl-2-piperidino- (7b) [red needles, mp 61°C] and 3-cyano-1,1-dimethyl-2-N-pyrrolidinyl-1,2-dihydroazulenes (7c) [red needles, mp 58°C] in 60 and 66% yields, together with 8-cyano-1-piperidino- (8b) and 8-cyano-1-N-pyrrolidinylheptafulvenes (8c) in 5 and 2% yields, respectively. On the other hand, under similar reaction conditions as with 2, 1 also reacted with 6a, but yielded an unstable oily substance which changed into a resinous substance over an alumina column.

The structures of 7a,b,c and 8a,c[4] were established on the basis of the spectral data (Table 1) and the chemical evidence described below, as well as the elemental analyses.[5] The UV spectra of 7a,b,c and 8a,c are similar to that of 8-cyanoheptafulvene,[6] and their ^{1}H-NMR spectral data are in accord with the assigned heptafulvene structures. Further, 7a,b could be converted into azulene derivatives as follows: A solution of 7a in conc. sulfuric acid was heated at 90°C for 6 hr, then the mixture was diluted with water and extracted with benzene. The extract was chromatographed (alumina, benzene) to give 1,2-dimethylazulene (9) [blue scales, mp 61°C][7] in a 35% yield. A similar treatment of 7b also give 9 in a 32% yield. When 7a was treated with 75% sulfuric acid under a procedure similar to that described above, 9 and 3-carbamoyl-1,2-dimethylazulene (10)[8] [violet needles, mp 230°C(dec.)] was obtained in 8 and 13% yields, respectively. The formation of 1,2-dimethylazulenes, 9 and 10, from 7a,b is presumed to proceed with the elimination of amines accompanied by the migration of methyl group to the

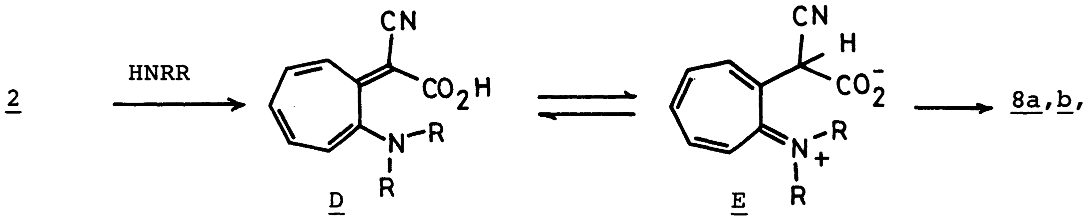


a: NRR=morpholino; b: NRR=piperidino; c: NRR=pyrrolidinyl



produced cationic center. Under these reaction conditions, the elimination or hydrolysis of the cyano group takes place simultaneously to give 9 and 10. A similar type of elimination and hydrolysis reaction has been observed for 1-cyano-2-methylazulene.9)

On the other hand, the minor products, 8a [red prisms, mp 102°C] and 8c [red scales, mp 96°C], were also obtained when a suspension of 2 in ethanol, containing merely the corresponding amines, was refluxed for 8 hr, in 38 and 35% yields, respectively. From this finding the formation of 8a,b,c in the reaction of 2



with enamines is presumed to be caused by the attack of not enamines, but free amines produced by hydrolysis of enamines onto 2 and subsequent decarboxylation from the resulting heptafulvene-8-carboxylic acids (D). An easy decarboxylation from D seems to proceed through the cyanoacetate intermediates (E).

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[References and Notes]

1) Part V of the series of the synthesis of azulene derivatives by the reaction of 2H-cyclohepta[b]furan-2-one with enamines. For part IV see ref. 2d.

2) a) P. W. Yang, M. Yasunami, and K. Takase, Tetrahedron Lett., 1971, 4725; b) Alice Chen, M. Yasunami, and K. Takase, ibid., 1974, 2581; c) M. Yasunami, P. W. Yang, Y. Kondo, Y. Noro, and K. Takase, Chemistry Lett., 1980, 167; d) M. Yasunami, Alice Chen, P. W. Yang, and K. Takase, ibid., 1980, 579.

Table 1. The Spectral Data of 7a, 7b, 7c, 8a, and 8c

7a	IR(KBr): 2175, 1640, 1602, 1550, 1110, 769, 740, 690 cm^{-1} UV in MeOH, λmax nm (log ε): 234(4.05), 243(4.04), 258(3.95), 359(4.17) ^{1}H-NMR in CDCl$_3$, δ ppm, 60 MHz: 1.16(6H, s, Me), 2.55-2.80(4H, m, N-CH$_2$), 3.19(1H, s, H-2), 3.51-3.76(4H, m, O-CH$_2$), 5.75-6.89(5H, m, H-4,5,6,7,8)
7b	IR(KBr): 2170, 1640, 1599, 1545, 1091, 770, 743, 698 cm^{-1} UV in MeOH, λmax nm (log ε): 235(4.03), 243(4.01), 260(3.89), 356(4.08) ^{1}H-NMR in CDCl$_3$, δ ppm, 60 MHz: 1.12(6H, s, Me), 1.33-1.78(6H, m, CH$_2$) 2.42-2.75(4H, m, N-CH$_2$), 3.19(1H, s, H-2), 5.77-6.83(5H, m, H-4,5,6,7,8)
7c	IR(KBr): 2157, 1640, 1601, 1550, 1110, 772, 745, 695 cm^{-1} UV in MeOH, λmax nm (log ε): 235(3.97), 242(3.95), 269(3.68), 356(4.10) ^{1}H-NMR in CDCl$_3$, δ ppm, 60 MHz: 1.12(6H, s, Me), 1.58-2.09(4H, m, CH$_2$), 2.58-2.95(4H, m, N-CH$_2$), 3.58(1H, s, H-2), 5.72-6.86(5H, m, H-4,5,6,7,8)
8a	IR(KBr): 2180, 1582, 1526, 1505, 1460, 1258, 1214, 1198, 1155, 1105, 872, 804, 738, 698 cm^{-1} UV in MeOH, λmax nm (log ε): 228(4.08), 276(4.01), 374(4.01), 400(3.76) ^{1}H-NMR in CDCl$_3$, δ ppm, 60 MHz: 2.77-3.04(4H, m, N-CH$_2$), 3.64-3.91(4H, m, O-CH$_2$), 5.47(1H, s, H-8), 5.84(1H, dm, J=8 Hz, H-2), 6.19-6.60(3H, m, H-3,4,5), 6.87(1H, dm, J=12 Hz, H-6)
8c	IR(KBr): 2180, 1570, 1510, 1496, 1450, 1418, 1340, 1240, 1140, 890, 840, 740, 712 cm^{-1} UV in MeOH, λmax nm (log ε): 226(4.11), 281(4.06), 387(3.95) ^{1}H-NMR in CDCl$_3$, δ ppm, 60 MHz: 1.82-2.13(4H, m, CH$_2$), 3.03-3.40(4H, m, N-CH$_2$), 4.78(1H, s, H-8), 5.72(1H, dm, J=8 Hz, H-2), 6.73(4H, m, H-3,4,5,6)

3) E. Benzing, Angew. Chem., 71, 521 (1959).

4) The UV spectra of 8b is similar to those of 8a,c, but further details of its properties could not be examined because of a small amount of the sample.

5) All new compounds gave satisfactory results of elemental analyses in accord with the assigned structures.

6) M. Oda and Y. Kitahara, Chem. Commun., 1969, 352.

7) Pl. A. Plattner and J. Wyss, Helv. Chim. Acta, 24, 483 (1941).

8) The spectral data of 10: IR(KBr): 3360, 3170, 1639, 1600, 1452, 731, 690, and 660 cm^{-1}; UV: λmax in MeOH 239 nm (log ε 4.13), 291(4.66), 340(3.51), 355(3.60), 375(3.39), 572(2.44), and 620(2.34); ^{1}H-NMR in CDCl$_3$, δ ppm, 60 MHz: 2.52(3H, s, Me), 2.72(3H, s, Me), 5.52-5.92(2H, m, CONH$_2$), 7.04-7.70(3H, m, H-5,6,7), 8.21(1H, dm, J=10 Hz, H-8), and 8.89(1H, dm, J=10 Hz, H-4).

9) T. Nozoe, K. Takase, T. Nakazawa, and S. Fukuda, Tetrahedron, 27, 3357 (1971).

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