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THE FORMATION OF AZULENE DERIVATIVES BY THE REACTION OF 2H-CYCLOHEPTA[b]FURAN-2-ONES WITH ENAMINES

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2H-Cyclohepta[b]furan-2-one derivatives, which had been obtained by the reaction of 2-halotropones with diethyl malonate or its related active methylene compounds (1), have been found to be important intermediates of synthesizing azulenoid compounds from troponoid compounds (2) and a number of azulene derivatives has been synthesized by the reaction of 2H-cyclohepta[b]furan-2-one derivatives with active methylene compounds, such as diethyl malonate, ethyl cyanoacetate or malononitrile (2,3,4). This communication will describe a new reaction of 2H-cyclohepta[b]furan-2-ones with enamines for synthesizing azulene derivatives from troponoid compounds.

When a solution of 2H-cyclohepta[b]furan-2-one (I) (lb) in anhydrous ethanol was refluxed in the presence of 3 molar equivalents of 1-N-pyrrolidinyl-1-cycloheptene, it was changed to a blue-colored solution with an evolution of gases. After being refluxed for 2 hr, the product was isolated by an alumina column chromatography to give a hydrocarbon (II); blue prisms, m.p. 84.5-85°, in an excellent yield. A similar treatment of I with 1-N-pyrrolidinyl-1-cyclohexene also gave a hydrocarbon (III); blue prisms, m.p. 77-78°, in an excellent yield. On the other hand, the reaction of I with 1-N-pyrrolidinyl-1-cyclopentene under a similar condition gave only a minor amount of a hydrocarbon (IV); blue prisms, m.p. 41°, but a major amount of a reddish oily compound (V).

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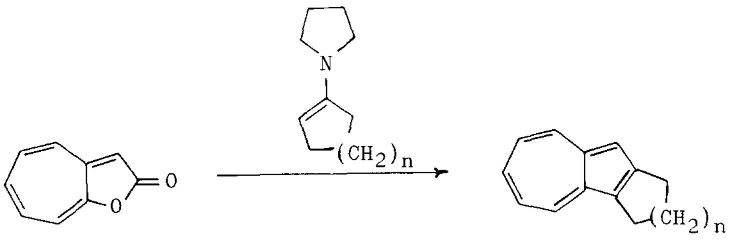
The UV and visible absorption spectra (Table 1) show that the hydrocarbons, II, III, and IV, must be alkyl azulene derivatives (5). Their nmr spectral data (Table 2) indicate that II, III, and IV must be disubstituted azulenes bearing pentamethylene, tetramethylene, and trimethylene substituents respectively. On the basis of these spectral data and the elementary analyses, as well as on a consideration of the structural relation with the starting materials, these hydrocarbons are assigned the structures of 1,2-pentamethylene-, 1,2-tetramethylene-, and 1,2-trimethyleneazulenes respectively.

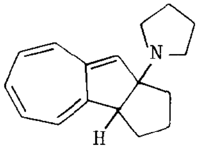
On the other hand, the compound, V, was gradually changed to IV upon allowing to stand at room temperature or passing through an alumina column. When its ethanolic solution was refluxed, especially in the presence of p-toluenesulfonic acid, V easily gave IV in a good yield. These facts suggest that V must be a precursor of the azulene, IV. Although a pure sample of V could not be obtained because of its easy changeability to IV, the UV absorption curve of a crude sample (6) suggests that V is a heptafulvene derivative (7). Furthermore, its nmr spectrum ($CDCl_3$) reveals three multiplets at 1.3-2.2 (10H, m, $-CH_2-$), 2.4-3.0 (5H, m, two $-CH_2-N$ and a methine proton) and 5.16-6.20 ppm (5H, ring protons of the heptafulvene), and a singlet at 5.03 ppm (1H, a vinylic proton) (8). From these facts, the structure of V is assumed to be 2(or 1)-N-pyrrolidinyl-1,2-trimethylene-1,2-dihydroazulene, being a reaction intermediate in the formation of azulene, IV, from I by the reaction with the enamine. The position of the pyrrolidinyl group of V was assumed to be at the 2-position from the evidence to be presented below. The reaction of I with a piperidino enamine of α-phenylacetaldehyde gave only 1-phenylazulene (VI) (3,9), in a 10% yield, whereas that with a pyrrolidinyl enamine of acetophenone gave only 2-phenylazulene (VII) (3,9), in a 13% yield. These findings indicate that enamines must be added on I in such a way that α- and β-carbons of the enamines are connected with the C_3- and C_9(or C_4)-positions of I, respectively, to give 1,2-dihydroazulene-type intermediate.

In this azulene formation reaction, 1,2-dihydroazulene-type intermediate, such as V, could be only isolated in the case of a five-membered ring enamine, but not in the case of larger ring-size enamines or acyclic enamines. This remarkable difference in reaction modes is thought to be due to a ring-size effect,

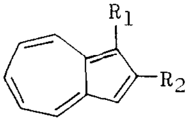


(I)

(II) n=3
(III) n=2
(IV) n=1



(V)



(VI) R_1=Ph, R_2=H
(VII) R_1=H, R_2=Ph

Table 1. The UV and Visible Absorption Maxima of Azulene Derivatives

Compounds	λ_{max} (MeOH) nm (log ε)
II	281 (4.60), 289 (4.70), 309 (3.60), 340 (3.47), 355 (3.57), 371 (2.23), 604 (2.38)
III	242 (3.93), 279 (4.57), 289 (4.76), 305 (3.49), 336 (3.32), 351 (3.38), 367 (2.60), 588 (2.07)
IV	242 (3.98), 278 (4.64), 286 (4.77), 304 (3.58), 335 (3.33), 350 (3.40), 365 (2.56), 582 (2.15)

Table 2. The NMR Data of Azulene Derivatives, δ ($CDCl_3$) ppm (intensity, signal pattern[a]), coupling constant, assignment).

Compounds	Methylene protons	Ring protons
II	1.50-2.15 (6H, m, $-CH_2-$) 2.93-3.26 (4H, m, $=C-CH_2-$)	6.76-7.60 (4H, m, $H_{3,5,6,7}$) 8.10 (2H, bd, 10 Hz, $H_{4,8}$)
III	1.80-2.07 (4H, m, $-CH_2-$) 2.93-3.26 (4H, m, $=C-CH_2-$)	6.76-7.60 (4H, m, $H_{3,5,6,7}$) 8.05 (1H, bd, 9 Hz, H_4 or H_8) 8.10 (1H, bd, 9 Hz, H_4 or H_8)
IV	2.25-2.75 (2H, m, $-CH_2-$) 2.93-3.26 (4H, m, $=C-CH_2-$)	6.76-7.60 (4H, m, $H_{3,5,6,7}$) 7.96 (1H, bd, 9 Hz, H_4 or H_8) 8.10 (1H, bd, 9 Hz, H_4 or H_8)

a) bd; broad doublet, m; multiplet

depending on the ring strains of the final products; the ring strain in IV is expected to be larger than those in the others. The mechanistic investigation of this reaction is now in progress.

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6. A crude sample of V shows such an UV absorption curve, λ_{max} (MeOH) nm (relative absorption); 224 (0.467), 231 (0.352), 257 (0.125), 267 (0.148), *279* (0.201), *287* (0.225), *305* (0.164), 406 (0.020), 440 (0.022), 473 (0.019), 500 (0.012), 533 (0.0055), that is estimated to be a superposition of that of the heptafulvent, V, and that of a minor amount of the azulene, IV, (underlined).
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