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THE FACILE SYNTHESIS OF 1- AND 2-ALKYLAZULENES BY THE REACTIONS OF 2H-CYCLOHEPTA[b]FURAN-2-ONES WITH ENAMINES OF ALDEHYDES AND ACYCLIC KETONES[1)]

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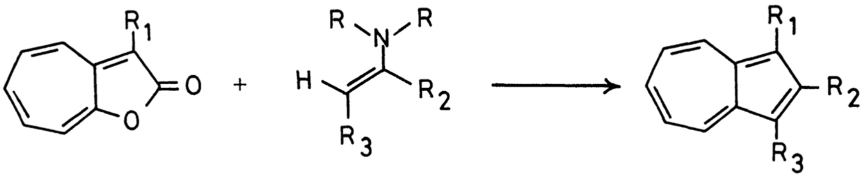
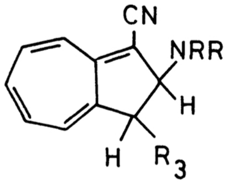
The reactions of 2H-cyclohepta[b]furan-2-one and its 3-cyano derivatives with enamines derived from aldehydes and acyclic ketones were investigated. On the reactions, 1- and 2-alkylazulenes were easily synthesized.

Azulenic hydrocarbons are of interest in their chemical and physical properties as a fundamental system of nonbenzenoid aromatic compounds. The favorable methods for synthesizing azulenic compounds have been found by Ziegler and Hafner,2) utilizing the condensation of pyridinium or pyrylium salts with cyclopentadiene, and by Nozoe and his co-workers,3) utilizing the reaction of reactive troponoids with active methylene compounds. These mothods have also been applied for the syntheses of some alkylazulenes having the alkyl substituents at the seven-membered ring, by the use of alkyl derivatives of pyridinium or pyrylium salts2) or alkyltropolones.3) Recently, Houk and his co-worker have reported4) that the cycloaddition of fulvenes with substituted aminobutadienes gave alkylazulenes having the alkyl substituents at the seven-membered ring. The synthesis of 1- and 2-alkylazulenes, however, is rather difficult because of the formation of 1-alkylazulenes in poor yields on alkylation of azulenes by Friedel-Crafts reaction with alkylhalides,5) although some 1- and 2-alkylazulenes have been obtained in about 50% yields by Hafner's method2) using alkylcyclopentadienes. On the other hand, the reaction of 2H-cyclohepta[b]furan-2-one (1) with enamines of cyclic ketones has been found to give 1,2-polymethylenazulenes in excellent yields.6) This reaction is expected to be applicable for the facile synthesis of 1- and 2-alkylazulenes. This communication describes the synthesis of 1- and





1: R_1=H 3: NRR=Pyrrolidinyl 5: R_1=H 7a: R_3=Et

2: R_1=CN 4: NRR=Morpholino 6: R_1=CN 7b: R_3=isoPr

NRR=Morpholino

a: R_2=H, R_3=Et, b: R_2=H, R_3=isoPr, c: R_2=H, R_3=Ph
d: R_2=Et, R_3=H, e: R_2=R_3=Me, f: R_2=Et, R_3=Me
g: R_2=Ph, R_3=H, h: R_2=Ph, R_3=Me

Table 1. The Formation of Alkylazulenes by the Reaction of 1 and 2 with Enamines

Compound	Enamine	Product Azulene	Form	Yield % a)	
1	3a (4a)	1-ethyl- (5a)[8]	blue oil	90.0	(26.0)
1	3b (4b)	1-sipropyl- (5b)[9]	blue oil	72.7	(18.0)
1	3c	1-phenyl- (5c)[10]	blue scales mp 58°C	40.6	
1	3d (4d)	2-ethyl- (5d)[12]	blue needles mp 44-46°C	76.8	(28.0)
	3e (4e)	1,2-dimethyl- (5e)[11]	blue scales mp 59-61°C		
1	3f (4f)	2-ethyl-1-methyl- (5f)	blue oil	83.4	(19.0)
1	3g	2-phenyl- (5g)[10]	blue scales mp 230°C	29.0	
1	3h	1-methyl-2-phenyl- (5h)	blue scales mp 72°C	14.0	
2	3a (4a)	1-cyano-3-ethyl- (6a)	blue needles mp 64-65°C	22.0	(86.1)[b]
2	(4b	1-cyano-3-isopropyl- (6b)	blue needles mp 62-63°C		(79.1)[b]
2	3f (4f)	1-cyano-2-ethyl- 3-methyl- (6f)	blue needles mp 61-62°C	7.4	(40.7)

a) The data in parentheses indicate the yields on the reaction with morpholino enamines (4).

b) The yields after treatment with a silica gel column.

2-alkylazulenes utilizing the reactions of 1 and its 3-cyano derivative (2) with enamines of aldehydes and acyclic ketones.

A solution or suspension of 1 or 2 and 3 molar equivalents of pyrrolidinyl (3) or morpholino enamines (4) of aldehydes or ketones in anhydrous ethanol was caused to reflux for 6 ~ 8 hr. After evaporation of the solvent, the residue was dissolved in benzene, washed with water, and then chromatographed (alumina or silica gel, benzene); the blue colored fraction afforded alkylazulenes (5 and 6). The results are summerized in Table 1. The reactions of 1 or 2 with enamines of aldehydes (3a,b,c, and 4a,b) gave only the azulenes having the alkyl(or aryl) substituents at the 1-position, that is, 1-alkyl(or aryl)- (5a,b,c) and 1-cyano-3-alkylazulenes (6a,b), while the reactions with enamines of ketones (3d,e,f,g,h, and 4d,e,g) gave azulenes having the alkyl(or aryl) substituents at the 2- or 1,2-positions, that is, 2-alkyl(or aryl)-(5e,g), 1,2-dialkyl(or 1-alkyl-2-aryl)-(5d,f,h), and 1-cyano-2,3-dialkylazulenes (6f). A mixture of two azulenes, 5d, and 5e (1 : 1),[7] was obtained on the reaction with enamines of 2-butanone: these azulenes are corresponding to two kinds of enamines from 2-butanone which are known to exist in a tautomeric mixture of 1- and 2-buten-2-ylamines, 3d and 3e (or 4d and 4e).[8] The alkyl(or aryl) substituents at the 1(or 3)- and 2-positions in these azulenes are corresponding to those at the β- and α- positions of enamines, respectively. These findings indicate that the reaction of 1 with enamines proceeded in an extremely regioselective mode.[6]

The reactions of 1 with pyrrolidinyl enamines of aliphatic aldehydes or ketones, 3a,b,d,e,f, gave the corresponding alkylazulenes, 5a,b,d,e,f, in excellent yields, respectively, while those with morpholino enamines, 4a,b,d,e,f, gave the alkylazulenes in low yields, accompanied by considerable amounts of the recovery of 1. This fact indicates that morpholino enamines are less reactive toward 1 than pyrrolidinyl enamines. The inferior reactivities of the aryl-conjugated enamines are also shown from the fact that the reactions of 1 with enamines, 3c,g,h, gave arylazulenes, 5c,g,h, in low yields, accompanied by the recovery of 1. On the other hand, the reactions of 2 with pyrrolidinyl enamines, 3a,f, gave azulenes, 6a,f, in low yields, while those with morpholino enamines, 4a,b,f, gave azulenes, 6a,b,f, in good yields. However, in the former case, the reactions gave no recovery of 2, but yielded resinous substances as well as azulenes. These facts indicate that 2 is more reactive than 1 toward enamines.

The high reactivities of 2 toward enamines are presumable due to the contribution of an electron-with-drawing effect of the cyano group. In the case of the reaction of 2 with morpholino enamines, dihydroazulene-type intermediates (7a)[red oil] and 7b[red oil] could be isolated in 74 and 75% yields, respectively, as well as azulenes, 6a,b, when the reaction mixtures were chromotographed over an alumina column. These compounds resulted in easy elimination of morpholine to give azulenes 6a,b, in quantitative yields when passed through a silica gel column.

In the present experiments, it should be noted that 1- and 2-alkylazulenes have been easily synthesized by the reaction of 2H-cyclohepta[b]furan-2-ones with enamines in high yields. The detailed studies on this reaction, involving the influence of substituents at the 3-position of 1 as well as the amine moiety of enamines on this reaction, are now in progress.

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References and Notes

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