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THE REGIOSELECTIVITY OF [6 + 4] CYCLOADDITIONS OF DIENAMINES TO FULVENES.

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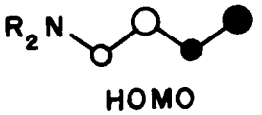
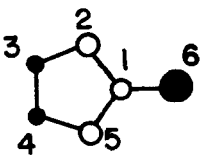
The [6 + 4] cycloadditions of 1-dialkylaminobutadienes to fulvenes constitute an efficient new synthesis of the hydroazulene skeleton, and, in suitably substituted derivatives, of azulenes as well.[1] In order to investigate the suitability of this reaction for the preparation of naturally occurring hydroazulenes and azulenes, such as guaiazulene and chamazulene,[2] the cycloadditions of a variety of substituted aminobutadienes and fulvenes have been investigated. In this communication, we report the results of our studies of the scope and regioselectivities of these reactions, the outcome of which has a bearing on the factors controlling regioselectivity in cycloaddition reactions.[3]

According to a frontier molecular orbital treatment,[4] the most nucleophilic center of the dienamine (the site of the largest HOMO coefficient) should become bonded to the most electrophilic center on fulvene (the site of the largest LUMO coefficient) in the transition state of the cycloaddition. As shown below, these considerations predict that the unsubstituted terminus of the dienamine should become bonded to the C-6 position of fulvene in the transition state.



HOMO

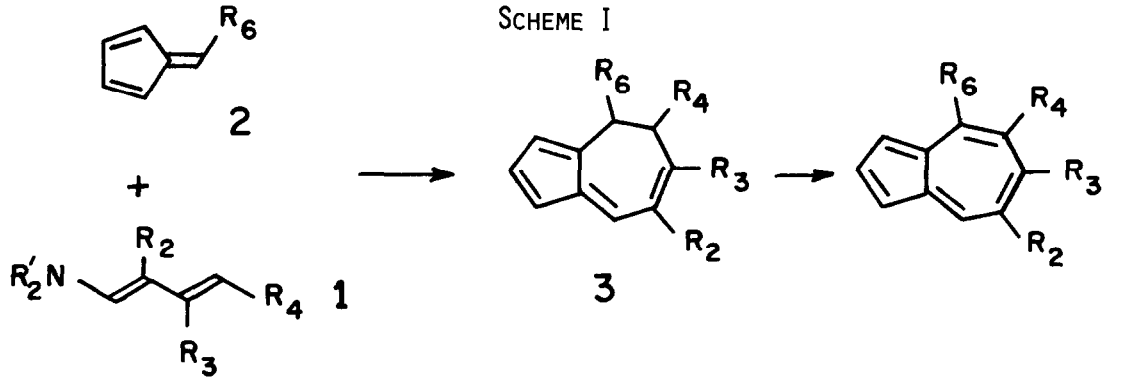


LUMO

The reactions of 4-ethyl, 3-methyl, and 2-ethyl-1-dialkylamino-1,3-butadienes, 1,[5] with 6-

phenyl, 6-isopropyl, and 6-methylfulvenes, 2, gave the dihydroazulenes, 3, which were dehydrogenated with chloranil, sulfur in triglyme, or 5%-Pd/C to give the corresponding azulenes, as shown in Scheme I.[6]

SCHEME I



R_6 = Me ; i-Pr ,or Ph ; R_2 = H or Et ; R_3 = H or Me , R_4 = H or Et

Structure proofs were based on nmr spectral data, which clearly reveal the substitution pattern in the seven-membered ring.[7] The reaction conditions, yields, and physical properties of new azulenes are summarized in Table I.

Table I. Reaction Conditions for Azulenes Prepared According to Scheme I.

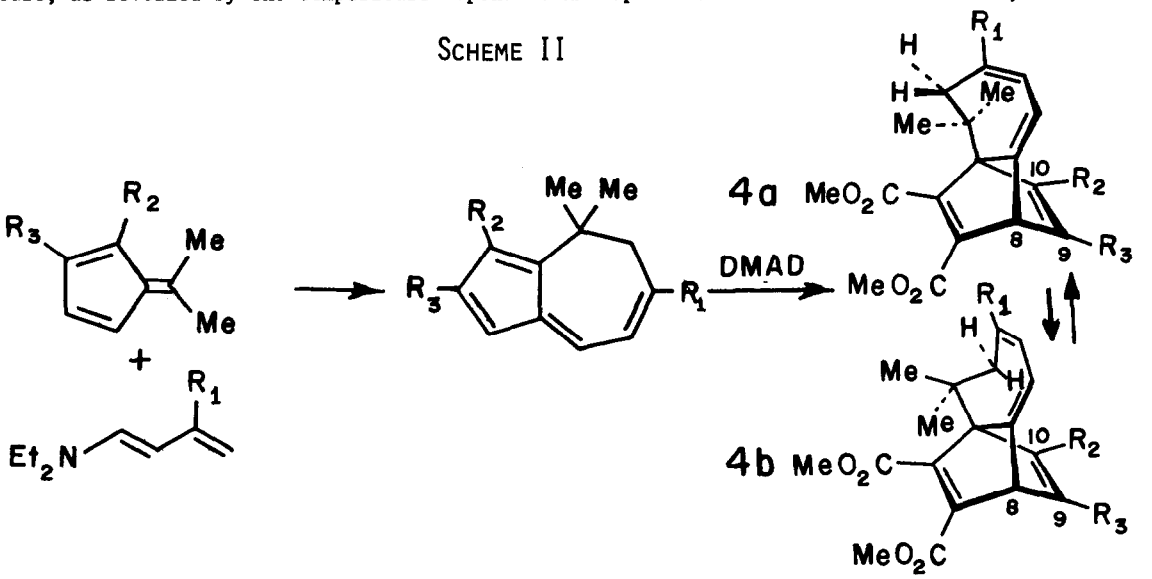
Azulene	Cycloadditions[a]; Dehydrogenations	Azulene Properties[c]
4-Phenyl	24h, 62%; C[b], xylene, 140°C, 15 min., 12%	oil[1]
4-Ethyl-4-phenyl	48h, 43%; S, T[b], 216°C, 1h, <5%	mp 74-75°C
6-Methyl-4-phenyl	24h, 21%; C, C_6H_6, 25°C, 48h, <5%	TNB[b], mp 114-115°C
7-Ethyl-4-phenyl	12h, 46%; S, T, 216°C, 1h, <4%	oil
4-Isopropyl	24h, 23%; S, T, 216°C, 1h, 23%	TNB, mp 140-141°C
4-Isopropyl-6-methyl	48h, 21%; S, T, 216°C, 1h, 21%	TNB, mp 155-156°C
7-Ethyl-4-isopropyl	24h, 34%; S, T, 216°C, 1h, 15%	TNB, mp 103-104°C
7-Ethyl-4-methyl	24h, 52%; Pd-C, T, 216°C, 15 min., 17%	oil[d]

a) All cycloadditions were carried out at 25°C from the time specified.
b) C = chloranil; T = triglyme; TNB = trinitrobenzene complex.
c) All new azulenes or the TNB complexes listed gave satisfactory elemental analyses.
d) Characterized by conversion to chamazulene.[2]

Cycloadditions were also studied with 6,6-dimethylfulvene. The structures of the dihydroazulenes were proven by conversion to the dimethyl acetylenedicarboxylate (DMAD) adducts, as shown

in Scheme II. As reported earlier for the compound formed from 6,6-dimethylfulvene and 1-diethylaminobutadiene,[1] the DMAD adducts exist as two slowly interconverting conformers at room temperature, as revealed by the temperature dependent nmr spectra. The reaction conditions, ratios of

SCHEME II



conformers present at room temperature, and coalescence temperatures for the methyl resonances as well as estimated free energies for conformational inversion are shown in Table II.

Table II. Reaction Conditions and Conformational Barriers (Scheme II).

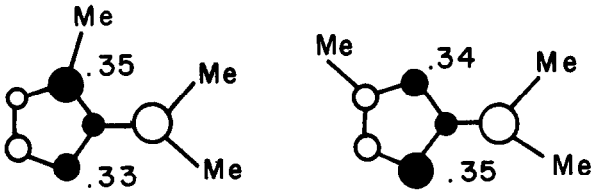
R_1	R_2	R_3	Dihydroazulene Formation	DMAD Reaction[a]	4a : 4b	T_c(±5°C)	$\Delta G^{\neq}$[b]
H	H	H	25°, 48 hrs, 65%	24h, 79%, mp 62-63°	2:1	100	20
H	H	Me	35-40°, 4 days, 40%	12h, 12%, mp 79.5-80.5°	2:1	100	20
H	Me	H	25°, 2 weeks, 9%	12h, 9%, oil	1:1	135	21
Me	H	H	25°, 24 hrs, 43%	24h, 42%, oil	2:1	—	—

a) In CCl_4 at 80°C.
b) ±0.5 kcal/mol.

Regioselectivity with respect to secondary bond formation at the fulvene ring was tested using 2,6,6- and 3,6,6-trimethylfulvene. The reactions of these compounds proceeded as shown in Scheme II to give dihydroazulenes in lower yields than usual, and these were converted to the DMAD adducts. The nmr spectrum of the parent DMAD adduct has $J_{8,9}$=3.2Hz, $J_{8,10}$=1.1Hz, and $J_{9,10}$= 5.0Hz.[1] In the DMAD adduct from 3,6,6-trimethylfulvene, the CH_3 group is vinylic (δ=1.9) and has an allylic coupling of 2Hz to H-10, $J_{8,10}\cong$2Hz, and there is no resonance corresponding to a

hydrogen at C-9. This implies that the [6 + 4] cycloaddition occurs at C-5, not C-2, of 3,6,6-trimethylfulvene. In the DMAD adduct from 2,6,6-trimethylfulvene, there is again a vinyl methyl (2.0δ), with an allylic coupling to H-9 (J=2Hz), which in turn is coupled to the bridgehead proton ($J_{8,9}$=3.5Hz). Bond formation occurs at C-5 in the [6 + 4] cycloaddition.

Secondary bond formation seems to occur in such a way to minimize steric repulsions. That is, the LUMO's of these species, shown below, suggest that bond formation should occur at C-2 in 2,6,6-trimethylfulvene and at C-5 in 3,6,6-trimethylfulvene, although the polarizations of the LUMO's by the ring methyls are extremely small. While the latter case occurs as expected, the former does not.



Finally, it is interesting to note that the barrier for conformational inversion of 4a and 4b is only slightly increased by a methyl substituent at C-10. It has been proposed that the conformational freedom of rotation about a single bond joining a quaternary carbon to an aromatic ring is severely hindered by an ortho-methyl substituent, and that this "trialkyl lock" has a significant effect on various intramolecular reactions.[8] Our results suggest that in a sterically similar situation, a "pseudo-ortho" methyl has a very small influence on the rotational barrier.

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