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[8+2] Cycloadditions involving 8-aryl-8-azaheptafulvenes and activated styrenes: efficient synthesis of dihydro-1-azaazulenes

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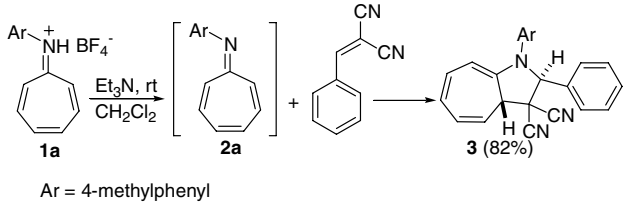
Abstract—Efficient [8+2] cycloaddition reactions of 8-aryl-8-azaheptafulvenes with doubly activated styrenes, leading to a facile synthesis of 1-aza-2-aryl-dihydroazulene derivatives are described.

The azaazulenoid core has been an attractive target in organic synthesis.[1] N-Substituted azafulvenes are very good starting compounds for the synthesis of azaazulenes via [8+2] cycloaddition reactions. Generally, they undergo efficient [8+2] cycloaddition reactions with a range of 2π components such as enamines,[2] allenes,[3] ketenes,[4] isocyanates and isothiocyanates,[5] etc. In rare cases they can participate as 6π components; the reactions with cyclopentadiene and pentafulvenes are examples.[6] Surprisingly, however, there are no reports on the cycloaddition reactions of azafulvenes with activated styrenes. It is evident that such reactions can provide an easy access to functionalized dihydroazaazulene frameworks. In the context of our continued interest in the cycloaddition reactions of fulvenoid compounds in general, and in particular their higher-order cycloaddition reactions,[7] it was decided to undertake a study of such reactions. The results of the investigations leading to an efficient synthesis of 1-aza-2-aryl-dihydroazulene derivatives are presented here.

In an initial experiment, 8-(4-methylphenyl)-8-azaheptafulvenium tetrafluoroborate **1a** was treated with triethylamine, and azafulvene **2a** generated was reacted in situ with dicyanostyrene. The crude reaction mixture, on purification by column chromatography afforded product **3** as a yellow viscous oil in a 82% yield (Scheme 1).[8]

The product was characterized as the [8+2] adduct on the basis of spectroscopic data. In the IR spectrum of **3** the cyano absorption was visible at 2253 cm^{-1}. The ^{13}C NMR spectrum exhibited the cyano carbon signals at δ 112.9 and 113.0. In the ^{1}H NMR spectrum, the signal due to the benzylic proton was observed as a singlet at δ 5.00 and the sp^3 C–H of the cycloheptatriene ring resonated as a doublet at δ 3.12. The methyl group on the aromatic ring appeared as a singlet at δ 2.25. Characteristic cycloheptatriene as well as aromatic resonances were also observed.



Scheme 1. Cycloaddition of azaheptafulvene **2a** with dicyanostyrene.

The relative stereochemistry at C-2 and C-4 was determined to be *trans* from the lack of enhancement of the benzylic proton signal when the molecule was irradiated at the resonance frequency of the C-4 proton (Fig. 1).

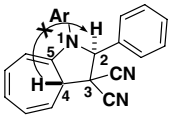


Figure 1. Lack of NOE enhancement in **3**.

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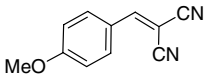
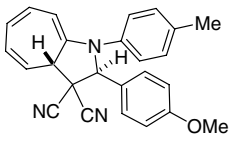
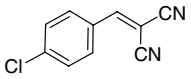
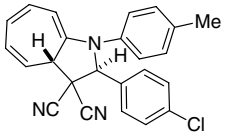
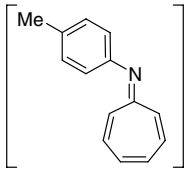
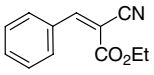
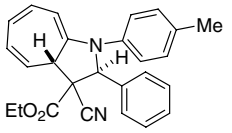
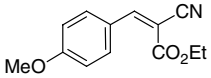
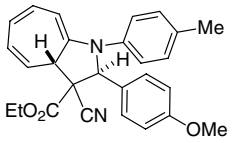
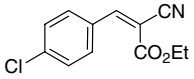
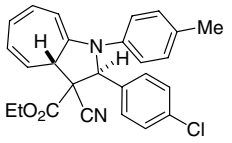
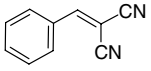
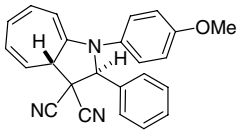
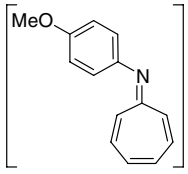
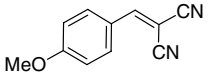
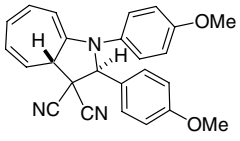
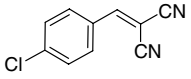
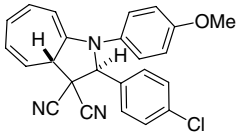
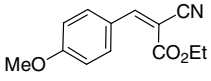
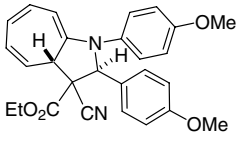
Table 1. Cycloaddition products of azaheptafulvenes with activated styrenes

Entry	Azaheptafulvene	Styrene	Product	Yield (%)
1				83
2				76
3				89
4				84
5				80
6				96
7				92
8				86
9				79

The reaction was found to be applicable to various substituted dicyanostyrenes as well as cyano carboethoxy styrenes. The presence of two electron withdrawing groups on the styrene was found to be necessary for the reaction to take place. The *N*-aryl group on the azafulvene could also be varied. The results are presented in Table 1.

In conclusion, we have found that 8-aryl-8-azaheptafulvenes undergo a very efficient [8+2] cycloaddition reaction with activated styrenes, leading to a facile synthesis of 1-aza-2-aryl-dihydroazulene derivatives.

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8. *General procedure*: The azaheptafulvenium fluoroborate was prepared following a literature procedure.[9] Representative procedure and data for compound **3**: The azaheptafulvenium fluoroborate **1a** (170 mg, 0.6 mmol) was dissolved in 15 mL dry dichloromethane in a RB flask under argon. To this, triethylamine (76 mg, 0.75 mmol) was added followed by dicyanostyrene (52 mg, 0.5 mmol) and the mixture was allowed to stir at room temperature for 12 h. The solvent was then removed and the residue, on column chromatography (using 100–200 mesh silica gel and 90:10 hexane–ethyl acetate solvent mixture), afforded product **3** (143 mg, 82%) as a pale yellow viscous liquid. IR (thin film) ν_{max}: 3032, 2920, 2253, 1621, 1509, 1382, 1348, 1188, 1115, 1022, 818, 701 cm^{-1}. ^1H NMR: δ 2.25 (s, 3H), 3.12 (d, 1H, $J = 4.2$ Hz), 5.00 (s, 1H), 5.56 (dd, 1H, $J_1 = 4.2$ Hz, $J_2 = 9.3$ Hz), 5.65 (d, 1H, $J = 6.6$ Hz), 6.32 (dd, 1H, $J_1 = 6.0$ Hz, $J_2 = 11.1$ Hz), 6.41–6.46 (m, 1H), 6.58 (dd, 1H, $J_1 = 7.2$ Hz, $J_2 = 11.1$ Hz), 6.94 (d, 2H, $J = 8.4$ Hz), 7.04 (d, 2H, $J = 8.4$ Hz), 7.39–7.41 (m, 3H), 7.49–7.51 (m, 2H). ^{13}C NMR: δ 20.9, 44.8, 48.9, 74.1, 97.6, 110.4, 112.9, 113.0, 123.1, 123.9, 124.5, 128.1, 129.1, 129.3, 130.0, 131.2, 132.7, 135.8, 137.8, 138.3. HRMS (EI): Calcd. for $C_{24}H_{19}N_3$: 349.1579. Found: 349.1561.
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