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[4+2] Cycloaddition on densely functionalized cyclopentadiene

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ABSTRACT

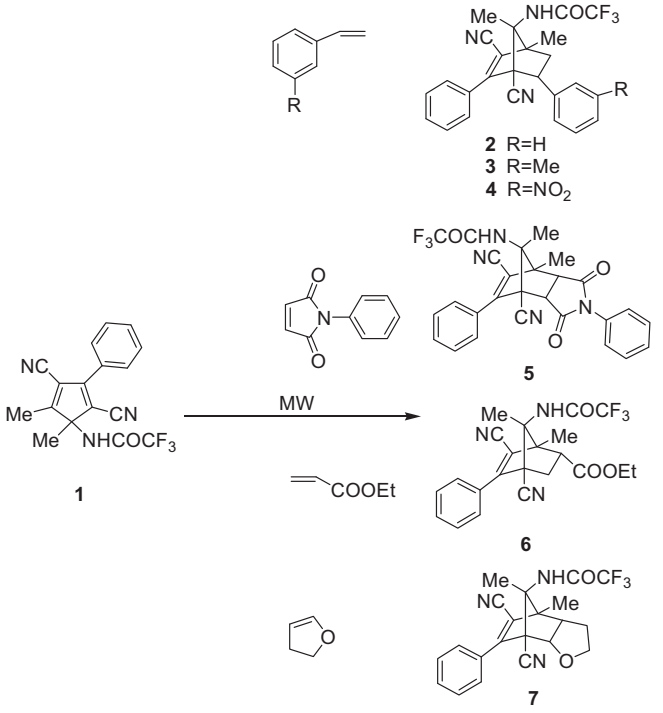
The Diels–Alder (DA) and hetero-Diels–Alder (HDA) reaction of *N*-(2,4-dicyano-1,5-dimethyl-3-phenyl-cyclopenta-2,4-dienyl)-2,2,2-trifluoroacetamide **1** can be conveniently used for the synthesis of biarylic and polycyclic compounds, depending on whether you use alkynes or alkenes as dienophiles. We observe a totally regioselectivity and *endo*-diastereoselectivity of the cycloaddition reactions.

The DA reaction has been widely investigated in the last few decades as one of the most powerful carbon–carbon forming bond. Moreover, the HAD reaction is an useful methodology for the synthesis of many heterocyclic compounds. It is well known that the success of the DA reaction depends on the kind of diene and dienophile used. The cycloaddition has been subjected to different modifications in order to increase the yield, the selectivity and the rate of the reaction: high pressure, ultrasound, Bronsted acids, traditional Lewis acids, special solvent effects, molecular sieves, adsorption on chromatography adsorbents, in situ radical formation and transition metals.[1] The [4+2] cycloaddition is also used to prepare a wide range of substituted biarylic compounds.

Recently, we reported that *N*-trifluoroacetyl-4-aryl-3,5-dicyano-1,4-dihydropyridines undergo a base catalyzed ring contraction to the corresponding *N*-(2,4-dicyano-1,5-dimethyl-3-phenylcyclopenta-2,4-dienyl)-2,2,2-trifluoroacetamide **1**.[2] In this Letter, reactivity of **1** toward different dienophiles has been considered an interesting strategy to synthesize more complex molecular systems.[3,4]

First we have explored the reactivity of **1** toward dienophilic alkenes.

In general the cyclopentadiene system shows low reactivity and the cycloaddition reaction occurs only by heating under microwave irradiation. After two 15 min cycles, the starting material almost disappeared to give compounds **2**–**7** (Scheme 1). The products were isolated as single isomers from the reaction mixture by chromatographic purification and identified by analytical and spectroscopic techniques.[5] Under these conditions compound **1** reacts with



Scheme 1. All reactions were carried out with compound **1** (0.1 mmol) and styrene, 3-methylstyrene, 3-nitrostyrene or *N*-phenyl maleimide, ethyl acrylate and 2,3-dihydrofuran (2 mol) heated in MW (150 °C, 150 W, 2 cycles of 15 min) to give compounds **2**–**7** (**2** = 70%, **3** = 77%, **4** = 68%, **5** = 35%, **6** = 30%, **7** = 30%).

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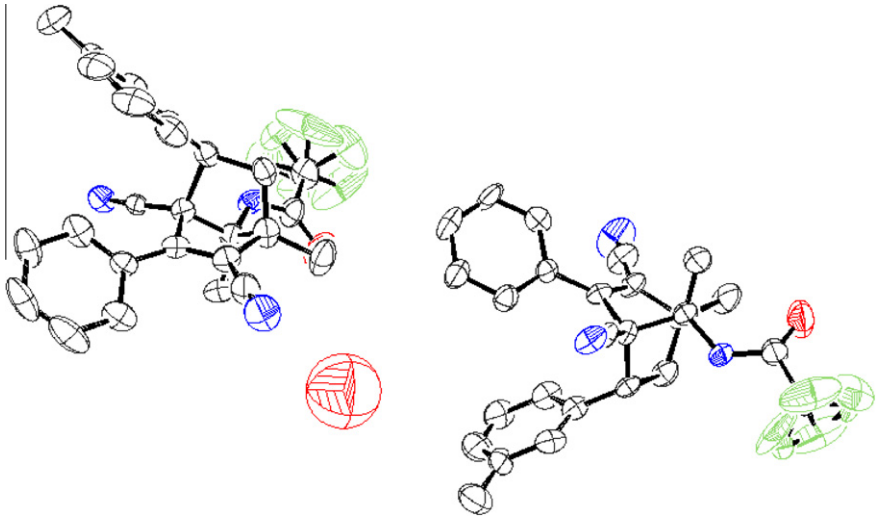


Figure 1. Crystal structure of the asymmetric unit of compound **3** × 0.5 H_2O. (CCDC 830004) Site occupancy factors for the depicted fluorine atoms are 0.52(2) (molecule A) and 0.51(2) (molecule B). Ellipsoids enclose 50% probability.

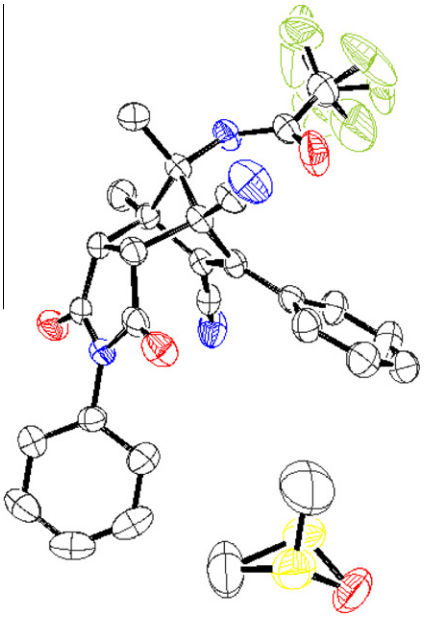


Figure 2. Crystal structure of compound **5** × DMSO. (CCDC 830002) Site occupancy factors for the depicted fluorine and sulfur atoms are 0.77(2) and 0.51(1), respectively. Ellipsoids enclose 50% probability.

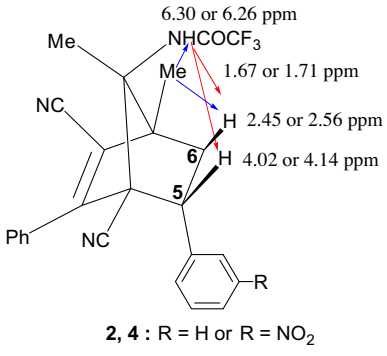


Figure 3. Main NOESY correlation for compounds **2**, **4**.

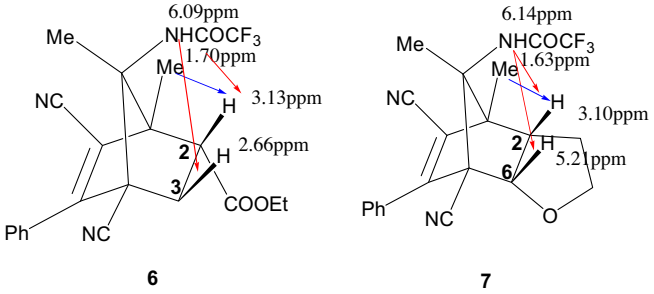
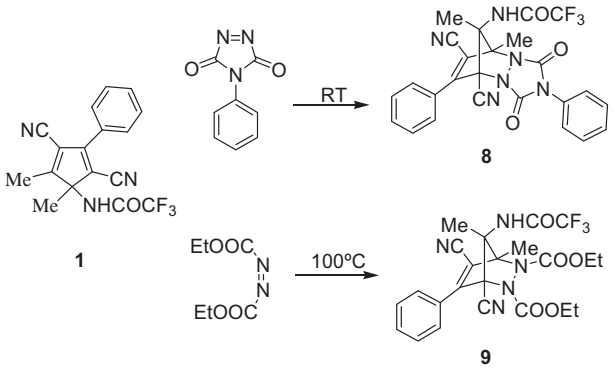


Figure 4. Main NOESY correlation for compounds **6**, **7**.

styrenes in good yields, the presence of electron-withdrawing or electron-donating groups on the aromatic ring does not involve substantial differences. Diene **1** does not react with maleic anhydride and only in low yields with *N*-phenyl maleimide, ethyl acrylate, and 2,3-dihydrofuran.

In these cases the reaction crude shows a mixture of compounds and the main component (**5**–**7**) is recovered after chromatographic purification.



Scheme 2. A solution of compound **1** (0.1 mmol) and 4-phenyl-1,2,4-triazoline-3,5-dione (0.5 mmol) in $CHCl_3$ is stirred at room temperature for 30 min to give compound **8** (68%); A mixture of compound **1** (0.1 mmol) and diethyl azodicarboxylate (0.5 mmol) is heated in an oil bath at 100 °C for two days to give compound **9** (35%).