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Short communication

Ionic Diels-Alder Reactions

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Abstract

The polar cycloaddition reaction of cationic heteroaromatic dienes, the triazoloisoquinolinium ion **1** and the tetramethoxycarbonylquinolizinium ion **4** with electron-rich dienophiles was studied resembling Diels-Alder reactions with inverse electron demand. This was also substantiated by *ab initio* calculations of the FMO energies of the reactants; also the regio- and stereochemistry of the cycloadducts obtained are readily explained in terms of FMO theory.

Keywords: Ionic Diels-Alder, polar cycloaddition reaction, inverse electron demand, cationic heteroaromatic dienes, calculated FMO-energies

In the sixties C. K. Bradsher [1] developed the concept of "ionic polar cycloaddition reactions", [4+2] cycloaddition reactions with inverse electron demand [2] involving cationic hetero 4π-systems. Some proposals concerning the mechanism of these cycloaddition reactions were made to explain their regio- and stereoselectivity, one of them describing these reactions as "ionic Diels-Alder" reactions. Owing to the electrophilic nature of the dienes and the rather nucleophilic character of most dienophiles a stepwise mechanism seemed adequate, but some experimental details made a concerted mechanism more plausible. However, the ionic DA reaction with inverse electron demand is a polar cycloaddition reaction, meaning a concerted but not necessarily synchronous reaction as originally described by R. R. Schmidt. [3] This makes it a limiting case of the DA reaction. The first example of an ionic DA reaction realized in our laboratories was the reaction of the new triazoloisoquinolinium cation **1** with cyclopentadiene **2**. [4] In a regio- and stereoselective cycloaddition reaction only one single product **3** was obtained, the structure was elucidated by means of NMR techniques (NOESY, NOE-DIFF).

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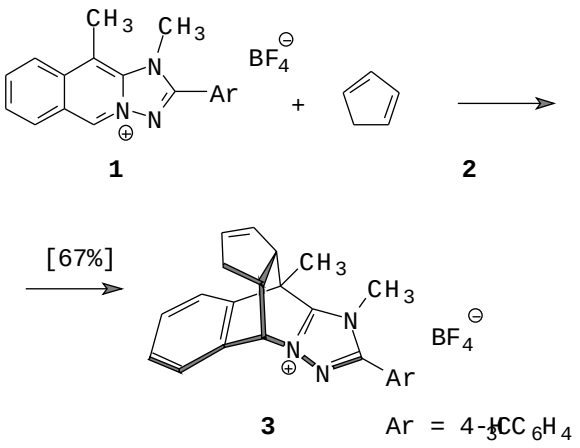


Scheme 1

The spectroscopic structure proof was complemented by an *ab initio* geometry optimization followed by a calculation of the orbital energies. This calculation confirmed the inverse electron demand character of the cycloaddition reaction (Figure 1).

Also the regiochemistry of this reaction can be explained in terms of FMO theory. Following the rules for FMO controlled cycloaddition reactions bond formation between the atoms with the two smaller and between those with the two larger coefficients of the interacting FMOs is energetically favoured and this has been found to be actually the case in this reaction (Figure 2). The stereoselectivity is explained by maximum separation of like charges and by stabilizing secondary orbital interactions in the TS.

Another very effective cationic diene is the tetramethoxycarbonylquinolizinium cation **4**. [5] The reaction of cation **4** with a series of dienophiles affords cycloaddition products usually in good yields (Table 1).

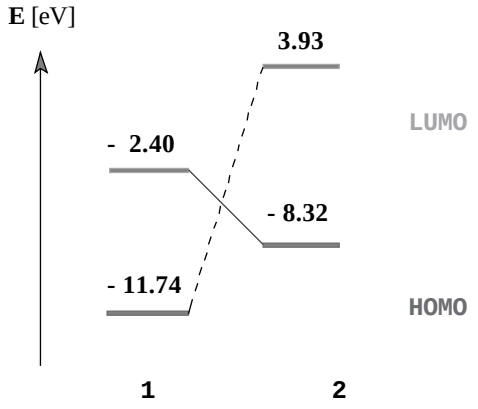
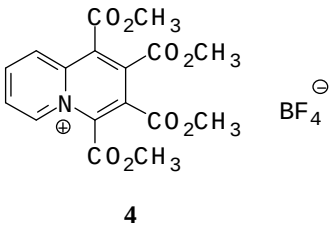


Figure 1. *Ab intio calculation of the FMO energies of the reactants 1 and 2 (RHF/6-31G(d)//RHF/6-31G(d))*

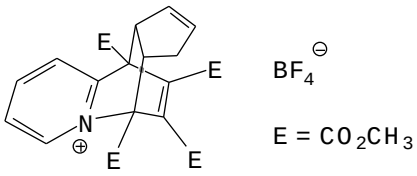


4

Scheme 2

The calculation of the FMO energies of these reactants illustrates the inverse electron demand nature of these cycloaddition reactions involving the LUMO of the diene and the HOMO of the dienophiles (Figure 3).

Likewise, the regioselectivity can be explained by consideration of FMO coefficients. The stereoselectivity of the reaction leading to the norbornene adduct (structure by X-ray analyses) is determined entirely by steric hindrance whereas the cyclopentadiene adduct **5** (structure elucidated by NMR techniques) follows the arguments of electrostatic repulsion and stabilizing secondary orbital interactions in the TS. Calculation of the FMO coefficients revealed the expected stabilizing interaction in the TS leading to **5** and an antibonding and destabilizing interaction in a conceivable TS leading to the stereoisomer with inverse orientation of the cyclopentadiene moiety.



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Scheme 3

The reaction of **4** with styrene follows a different stereochemical course. At room temperature a mixture of both

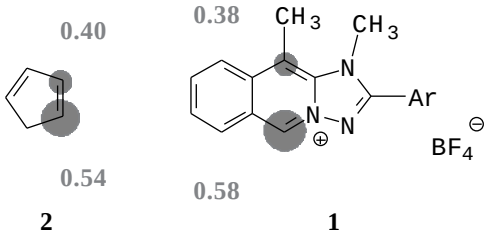
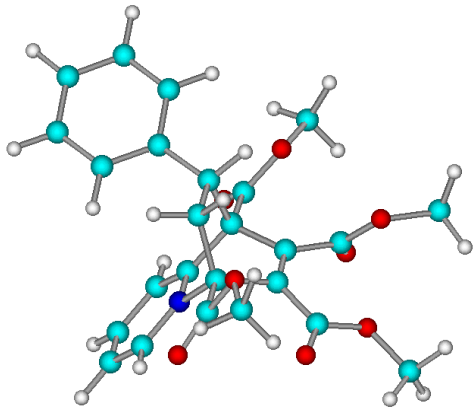


Figure 2

syn and *anti* stereoisomers was obtained (the phenyl ring *syn* or *anti* with respect to the pyridinium moiety). After refluxing the reaction mixture for three days only the *syn* stereoisomer **6a** was isolated.



6a

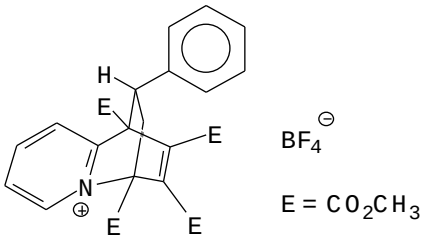
Scheme 4

The distinction between the two stereoisomers was easily achieved by means of NMR techniques because only the *syn* isomer shows anisotropy effects owing to the mutual influences of the phenyl and the pyridinium moieties. The depicted structure **6b** of the *anti* isomer results from an *ab initio* geometry optimisation.

Table 1. *Cycloadducts of* ***4*** *with various dienophiles*

dienophile	**yield [%]**	**mp [°C]**
cyclopentadiene	86 [a]	187-188
styrene	80 [a,b,c]	
	syn : *anti* = 0.7 : 1.0 [b]	150-152
	syn : *anti* = 1.0 : 0.0 [c]	135-137
2,3-dimethylbutadiene	78 [a]	171-172
norbornene	50 [a]	219-221
indene	24 [a]	123-124

[a] 24h reflux [b] 2 weeks RT [c] 3 days reflux



6b

Scheme 5

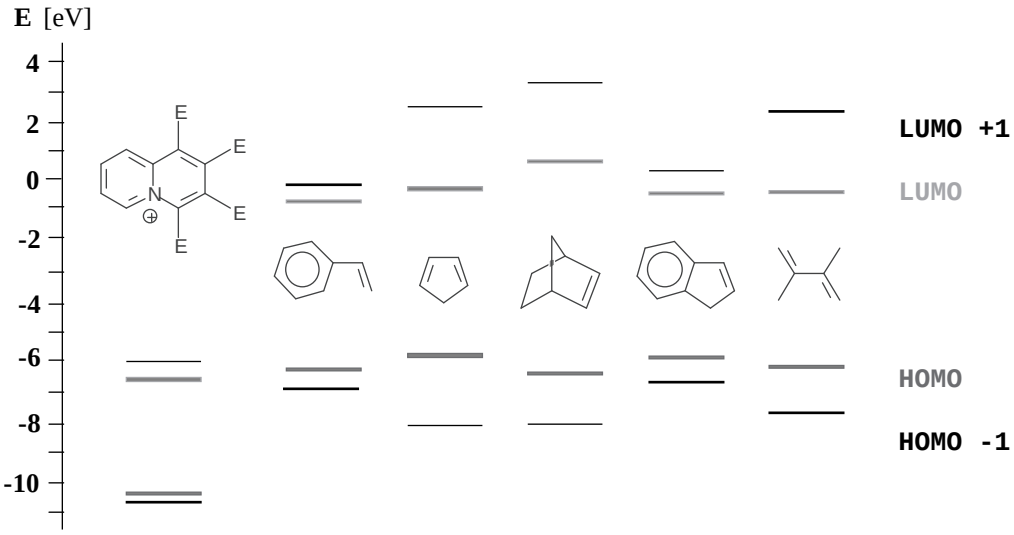


Figure 3. *Ab initio calculation of FMO energies (RB3LYP/3-21G(d)//RB3LYP/3-21G(d))*

Calculations of the energies of **6a**, **6b** and of the TS of both cycloaddition reactions confirmed the expected higher energy of the TS leading to the *syn* adduct **6a** owing to electrostatic repulsion and destabilizing secondary orbital interactions and revealed a lower single point energy for the *syn* adduct **6a** in comparison with the *anti* adduct **6b**. From this can be concluded that in a kinetically controlled reaction (at room temperature or lower) the formation of the thermodynamical less stable product **6b** is favoured due to the lower energy of activation whereas under thermodynamic control (reflux temperature) the thermodynamically more stable product **6a** is obtained.

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