

THE INFLUENCE OF CAPTODATIVE EFFECT ON THE DIENOPHILICITY OF OLEFINS.
THE EASY DIELS-ALDER REACTION OF α -METHYLTHIOACRYLONITRILE WITH CYCLOHEXADIENE¹

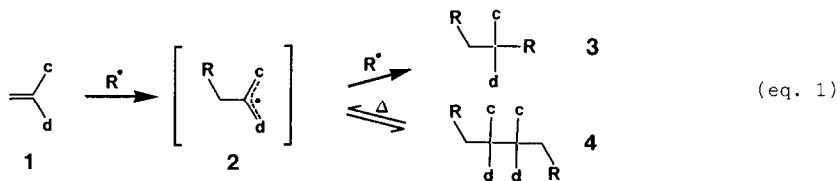
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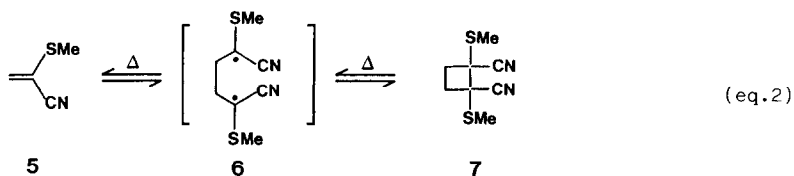
Abstract : We show that the cycloaddition of α -methylthioacrylonitrile to cyclohexadiene is faster than that of acrylonitrile. This indicates that the captodative substitution exerts an accelerating effect on the Diels-Alder reaction despite the larger steric bulk of the methylthio group compared to hydrogen.

The Diels-Alder reaction is one of the most useful reactions in preparative organic chemistry². Consequently, the improvements which increase its efficiency or enlarge its applicability are always desirable³. The reaction mechanism still is a subject of pre-eminent interest to both organic and physical-organic chemists because of its usefulness in predicting the relative rate, the regioselectivity and the stereoselectivity of this ring formation process⁴. Dewar and Pierini have lately stressed^{4d} that all the available evidence concerning the Diels-Alder reaction can be interpreted in terms of a very unsymmetrical transition state close to a biradical or zwitterion. In the context of our studies on the captodative effect⁵ and its application to organic synthesis⁶, we found that Diels-Alder cycloadditions can be accelerated by using captodative olefins such as 5. This result supports Dewar's conclusion in a typical case where the transition state can be regarded as a weakly perturbed biradical.

Captodative olefins 1, *i.e.* olefins which are geminally disubstituted by both an electron-withdrawing (*captor*) and an electron-releasing (*donor*) group have been defined as radicophiles⁷ because of their efficient radical-trap properties⁸. The thermodynamic stabilization⁹ of the captodative radical adducts 2 allows selective coupling reactions leading to the formation of double-adducts 3 and/or adduct-dimers 4 without side reaction (eq. 1). Butadiene is known for an analogous behaviour which has been described in term of "resonance effect"¹⁰. Kinetic studies¹¹ show that, beyond expectation from polar effects, rate accelerations are observed when captodative olefins 1 undergo radical additions.



It has been qualitatively proposed^{7b} and experimentally supported^{6b,8e,11a} that relative to the frontier orbital of ethylene, the orbital scheme of the captodative olefins should show the simultaneous lowering of the LUMO and rising of the HOMO. This narrowing of the HOMO-LUMO gap characterises also the butadiene. Regardless to the steric effect, a lowering of the LUMO energy level compared to ethylene suggests that the captodative olefins **1**, like butadiene, will be more potent dienophiles and undergo easier Diels-Alder reactions due to favorable LUMO (olefin) HOMO (diene) interactions^{4c}. Furthermore, an easy and efficient twofold CC bond formation process, thermodynamically and even kinetically^{11a} promoted by the captodative effect, would also be expected in cycloaddition reactions which develop a biradical intermediate or a weakly perturbed biradical transition state. Effectively, the spontaneous head-to-head cyclodimerisation of the α -methylthioacrylonitrile **5**, a typical captodative olefin, leads almost quantitatively to the cyclobutane derivative **7**¹² (eq. 2).



The comparison with the very sluggish cyclodimerisation of acrylonitrile¹³ leads to assume that the captodative stabilization of the 1,4-biradical **6** must be the driving force for the easy two-step process.

On the other hand, the good reactivity of acrylonitrile in Diels-Alder reactions is a familiar feature. Since it is well established that the two major limitations imposed on the generality of the Diels-Alder reaction are the inherent inefficiency of electron-rich olefins and its pronounced sensitivity to steric effect², then the question about the dienophilicity of the α -methylthioacrylonitrile compared with acrylonitrile is of great significance: if both π -donor electronic effect and steric effect of the methylthio group are dominant in the Diels-Alder reactions involving the olefin **5**, one might then reasonably expect that the formation of cycloadducts would be disfavored, whereas, if the captodative effect comes into play in stabilizing a transition state close to a biradical, the dienophilicity of the olefin **5** would be enhanced.

Acrylonitrile reacts with cyclohexadiene (120°, 12h) to give the mixture (46:54) of *exo-endo*-cyano diastereoisomers **8-9** in 80% yield¹⁴. On the other hand, the reaction of **5** with cyclohexadiene (80°, 18h) leads to the *exo-endo*-cyano Diels-Alder mixture **10-11** (84:16) in 91% yield¹⁵. We will report elsewhere¹⁶ that no sign of epimerisation was observable when the isolated isomer adducts were heated up to 160° and that the stereospecificity of the reaction was confirmed with E and Z α -methylthiocrotonitriles. This indicates that the cycloaddition of olefin **5** to cyclohexadiene is a concerted, kinetically controlled reaction.

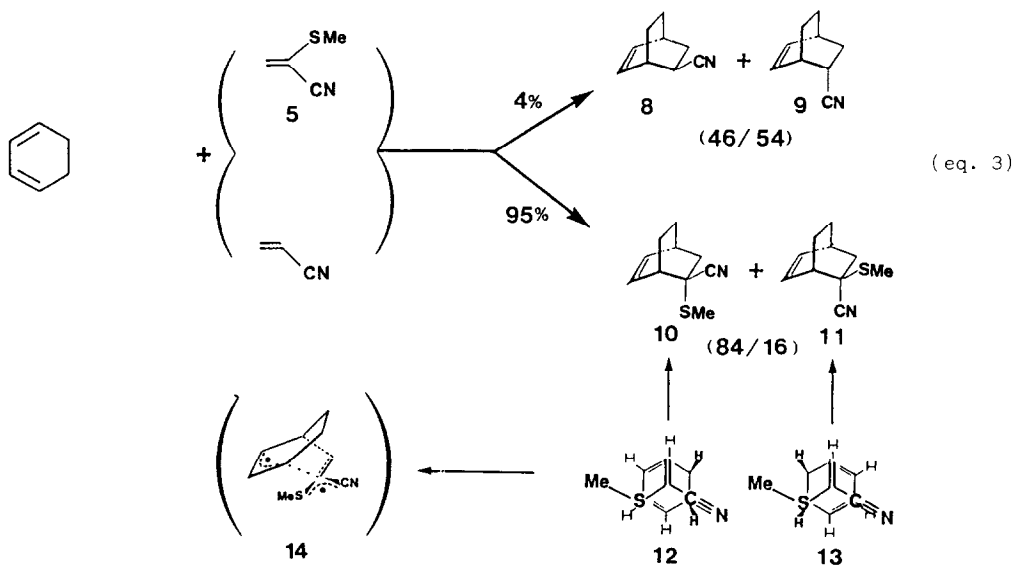
In the asymmetric *endo*-cyano approach **13**, secondary orbital interaction between the dienophile cyano carbon and a diene sp² carbon should lead to stabilization, but the methylthio group acts in the opposite direction by interfering sterically with the out-of-plane methylene hydrogens of the cyclohexadiene. Consequently, the cyano group must assume preferentially the asymmetric *exo* approach **12** such that minimal steric repulsion

occurs.

When equimolecular amounts of cyclohexadiene, acrylonitrile and **5** are heated for 6h at 80°, the mixture of cycloadducts shown in eq.3 is formed. It was easy to confirm the greatest reactivity of **5** by measuring, in an excess of cyclohexadiene, the rate of appearance of the adduct couples **8-9** and **10-11**. During the first six hours, the cycloadditions follow pseudo-first-order kinetics for both **5** and acrylonitrile and the rate of appearance of the adducts **10-11** is about 7 to 6 times greater than that of adducts **8-9**¹⁷.

It is not surprising that steric repulsion¹⁸ or attractive interactions¹⁹ may influence the *endo-exo* stereoselectivity of Diels-Alder reactions. Thus, it is well known that while acrylonitrile reacts with the cyclopentadiene affording a 57:33 mixture of *endo-exo* -cyano cycloadducts^{19a}, methacrylonitrile reacts *seven times slower*²⁰ to give a 12:88 mixture of the corresponding *endo-exo* -cyano adducts^{19a}. In contrast, it is actually noteworthy that the methylthio group, which apparently acts as a bulky substituent which governs to stereoselectivity, does not reduce the reactivity of **5** but, on the contrary enhances it. As for the methylthio ethylene, both the σ and π electron transfer occur in the same direction²¹, *i.e.*, from the heteroatom to the adjacent ethylene fragment, it appears that an interpretation of our result based upon a simple additivity of classical polar effects does not hold. The enhanced reactivity of **5** compared with acrylonitrile may be well interpreted by employing a model of a concerted reaction with an unsymmetrical transition state having biradical character^{4d}: the steric bulk of methylthio group predisposes the reactants to adopt the *exo* -cyano approach **12**. This approach leads to the transition state **14** in which one of the new CC bonds have been almost completely formed while the other is very weak. Such a transition state, close to a biradical, is stabilized by both allylic resonance and captodative effect and, consequently is easily reached in the cycloaddition of **5**.

The Diels-Alder reactions of captodative olefins appears to be of substantial synthetic, mechanistic and theoretical interest. We are currently investigating all of these aspects together with the exploitations of the versatility of the adducts.



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References and notes

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