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Diels-Alder Reactions of Vinyl Fluorides with 1,3-Diphenylisobenzofuran

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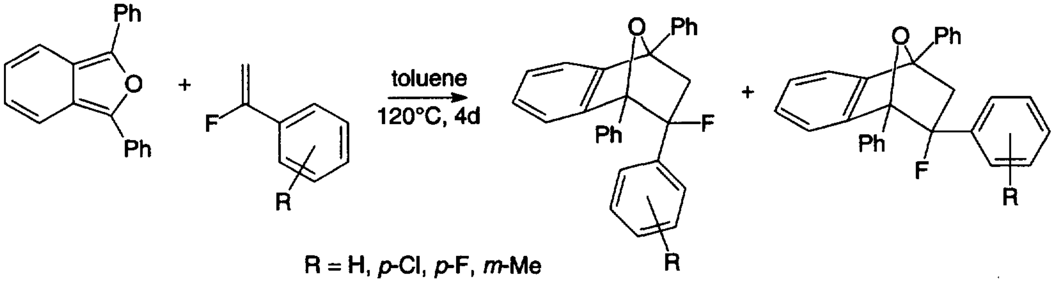
Abstract: α-Fluorostyrenes synthesized from substituted styrenes by a two-step bromofluorination-dehydrobromination procedure and the *E/Z*-isomers of β-fluorostyrene do react in thermal [4+2]-cycloadditions with the super diene 1,3-diphenylisobenzofuran. α-Fluorostyrenes are less reactive and the *endo/exo* ratio is decreased in all cases compared to the parent olefins. Both electron donating and electron withdrawing substituents in the aromatic ring of α-fluorostyrenes accelerate the reaction rate, suggesting a neutral Diels-Alder reaction.

The interest in monofluorinated compounds has widely increased during the last decades.[1] This is caused by the strong effect of the fluorine substituents on the physical, chemical and physiological properties of such substrates.[1,2] Numerous approaches to fluorinated organic compounds have been developed.[3] To synthesize six-membered rings, the Diels-Alder reactions have many advantages comparing to other methods.[4] Two ways are possible to form fluorinated cyclohexenes: i) to locate the fluorine substituent in the diene or ii) to use vinyl fluorides as dienophiles. Shi and Schlosser[5] used dienes bearing the fluorine substituent in the 2-position to synthesize 1-fluorocyclohexenes in good yields. On the other hand only three examples of [4+2]-cycloadditions with monofluorinated α,β-unsaturated carbonyl compounds have been described so far.[6] Simple vinyl fluorides have never been used to now. Moreover, there is very little known about monofluorinated olefins at all, especially about the effect of a single fluorine substituent on the electronic behaviour, the stability and reactivity of the π-system.[7] We wish to present our results on the thermal Diels-Alder reaction of α-fluoro- and β-fluorostyrenes with 1,3-diphenylisobenzofuran.



Substituted α-fluorostyrenes are easily and regioselectivly accessible in two steps from the corresponding styrenes by bromofluorination[8] and subsequent dehydrohalogenation[9] with potassium tert.-butanolate in an 55-75% overall yield. The β-fluorostyrenes are synthesized from the corresponding benzaldehydes through a Wittig reaction as described by Burton *et al.*[10] Unfortunately none of the synthesized vinyl fluorides gave Diels-Alder products with "normal" dienes, neither under high pressure (10 kbar), nor with Lewis acid catalysis, or radical cation initiation. Moreover, no [2+2]-cycloaddition or polymerization products could be detected. Furthermore, our attempts to realize a reverse [4+2]-cycloaddition using hexachlorocyclopentadiene have been unsuccessful, too. Finally 60:40 mixtures of *endo*- and *exo*-Diels-Alder products were formed when the α-fluorostyrenes were treated with the very reactive 1,3-diphenylisobenzofuran. (*E*)-β-Fluorostyrenes gave about 40:60 ratio of the corresponding isomers[11], while styrene itself gave a 70:30 ratio.

According to the FMO theory, the reactivity of a Diels-Alder reaction depends on the energy difference between the HOMO of the diene and the LUMO of the dienophile. From the calculated values it was expected, that α-fluorostyrene would react slightly faster than styrene, because of its lower LUMO energy. However, we measured the reaction rates of these fluorostyrenes[12] and we found that it was not the case here.

Table : Second order rate constants for the reaction of α- and β-fluorostyrenes with 1,3-diphenylisobenzofuran (k [10^{-5} l $mol^{-1}s^{-1}$]) at 72 ± 2 °C

R	H	*p*-Cl	*p*-F	*m*-Me
styrene	---	---	58,5	---
α-fluorostyrene	1,5	5,5	1,9	2,1
β-fluorostyrene	2,8	5,9	5,6	2,1

p-Fluoro-α-fluorostyrene reacts 30 times slower than *p*-fluorostyrene. Furthermore, both the *m*-methyl and the *p*-chloro substituents accelerate the reaction. Thus, it is supposed that this reaction is a neutral Diels-Alder reaction. Further calculations on the reaction pathway and the transition state are in progress.

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11. General procedure : 1 mmol of the vinyl fluoride and 1 mmol (270 mg) of 1,3-diphenylisobenzofuran were dissolved in 3 mL of toluene and heated at 120 °C (bath temperature) for four days. Then the toluene was removed giving 80-85% of crude product mixtures. Recrystallization (2 to 3 times) gave the pure *endo* isomer (R=H, ^{19}F NMR: δ -148.0 ppm, $^{3}J_{FH}$ = 17.9 Hz, $^{3}J_{FH}$ = 32.9 Hz) while the *exo* isomer (R=H, ^{19}F NMR: δ -151.1 ppm, $^{3}J_{FH}$ = 14.8 Hz, $^{3}J_{FH}$ = 21.7 Hz) was enriched in the filtrate to about 80:20 ratio.
12. The reaction rates were determined by ^{19}F-NMR spectroscopy, *m*-fluorotoluene has been used as an internal standard.

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