DOI: 10.1002/chem.200903008

The Diels–Alder Reaction of 4,6-Dinitrobenzofuroxan with 1-Trimethylsilyloxybuta-1,3-diene: A Case Example of a Stepwise Cycloaddition

Sami Lakhdar,[a] François Terrier,*[a] Dominique Vichard,[a] Guillaume Berionni,[a]
Nizar El Guesmi,[b] Régis Goumont,*[a] and Taoufik Boubaker[b]

Abstract: The reaction of 4,6-dinitrobenzofuroxan (DNBF) with 1-trimethylsilyloxybuta-1,3-diene (**8**) is shown to afford a mixture of [2+4] diastereomeric cycloadducts (**10**, **11**) through stepwise addition–cyclization pathways. Zwitterionic intermediate σ-adduct **9**, which is involved in the processes, has been successfully characterized by ^{1}H and ^{13}C NMR spectroscopy and UV/visible spectrophotometry in acetonitrile. A kinetic study has been carried out in this solvent that revealed that the rate of formation of **9** nicely fits the three-parameter equation $\log k = s(E+N)$ developed by Mayr to describe the feasibility of nucleophile–electrophile combinations. This significantly adds to the NMR spectroscopic evidence that the overall cycloadditions take place through a stepwise mechanism. The reaction has also been studied in dichloromethane and toluene. In these less polar solvents, the stability of **9** is not sufficient to allow direct characterization by spectroscopic methods, but a kinetic investigation supports the view that stepwise processes are still operating. An informative comparison of our reaction with previous interactions firmly identified as prototype stepwise cycloadditions is made on the basis of the global electrophilicity index, *ω*, defined by Parr within the density functional theory, and highlighted by Domingo et al. as a powerful tool for understanding Diels–Alder reactions.

Keywords: cycloaddition • density functional calculations • Diels–Alder reactions • nitrobenzofuroxans • superelectrophilic heteroaromatics

Introduction

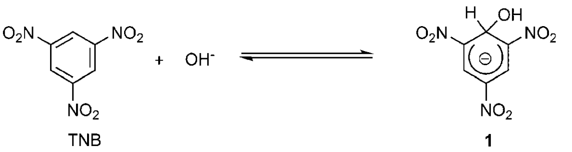
In the last few years, there has been a growing interest in the study of electron-deficient aromatic and heteroaromatic structures that show an extremely high reactivity in nucleophilic aromatic substitutions and related σ-complexation processes.[1–10] Focusing on covalent hydration as a reference process, it has been shown that heteroaromatic compounds, such as nitrobenzofuroxans, nitrobenzofurazans, nitrobenzotriazoles, and nitrotetrazolopyridines, are considerably more electrophilic than 1,3,5-trinitrobenzene (TNB), the conventional aromatic electrophile in σ-complexation chemistry.[1,6,11] Whereas TNB only reacts with the strong oxygen base, hydroxide ion [Eq. (1)],[12] the prototype heteroaromatic 4,6-dinitrobenzofuroxan (DNBF) structure undergoes facile addition of water according to Equation (2) to give hydroxy adduct **2**, which is 10^{10} times more stable than analogous TNB adduct **1**.[11,12] Going along with the ease of σ-complexation with the weak water nucleophile, the high susceptibility of DNBF and related heteroaromatics to undergo facile couplings with weak carbon nucleophiles, such as benzenoid aromatics (phenols, anilines, etc),[2,3,6,10,13] or π-excessive heteroaromatics (pyrroles, indoles, thiophenes, furans, etc)[5,8,10,13] is a remarkable feature in the field of electrophile–nucleophile combinations. This supports the definition of DNBF and a set of structural analogues as superelectrophiles.[6]

Of equal interest, however, is the fact that DNBF behaves as a nitroolefin,[14,15] with its two nitro-activated double bonds contributing formally to normal (NED) and inverse

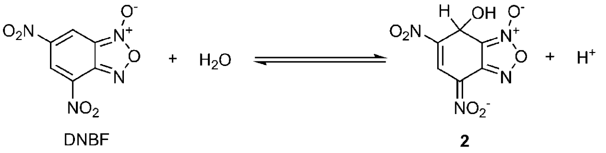
---

[a] Dr. S. Lakhdar, Prof. F. Terrier, D. Vichard, G. Berionni,
Prof. R. Goumont
Institut Lavoisier de Versailles, UMR 8180
Université de Versailles, 45 Avenue des Etats-Unis
78035 Versailles Cedex (France)
Fax: (+33) 139254452
E-mail: terrier@chimie.uvsq.fr
goumont@chemie.uvsq.fr

[b] N. El Guesmi, Prof. T. Boubaker
Unité de Recherche de Physico-Chimie Moléculaire
Faculté des Sciences de Monastir
Avenue de l'Environnement, 5019 Monastir (Tunisia)

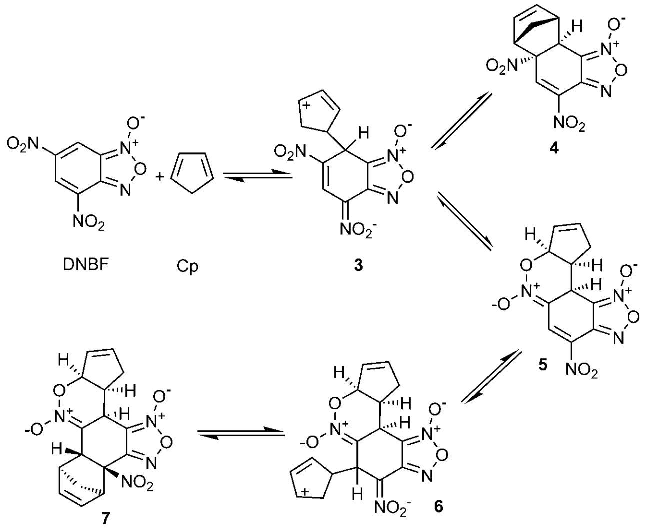


(1)



(2)

(IED) electron-demand Diels–Alder cycloadditions, which in some instances proceed with high regio- and stereoselectivity.[16–18] This is exemplified in Scheme 1, which shows that



Scheme 1.

the reaction of DNBF with cyclopentadiene (Cp) in dichloromethane at room temperature initially affords a 1:1 mixture of the [2+4] and [4+2] monoadducts **4** and **5** in their racemic forms.[18a] Then a second NED process takes place at the remaining and now purely olefinic nitroactivated C_4–C_5 fragment of [4+2] adduct **5** to give an essentially quantitative formation of highly functionalized diadduct **7** in its racemic form.[18a]

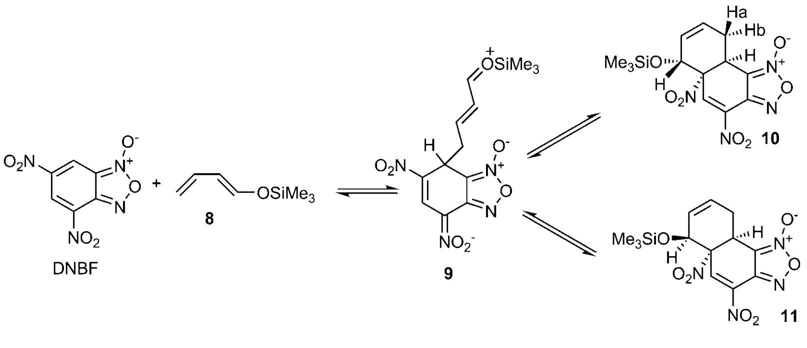
In view of the superelectrophilic behavior of DNBF[6,8] the question of the more-or-less polar character of cycloadditions of the type exemplified in Scheme 1 was posed.[19–31] Recently, a thorough DFT analysis of the DNBF–Cp interaction was made by Domingo et al.[32] While confirming the reactivity patterns and the stereochemical features described in Scheme 1, this study has supported the view that the formation of adducts **4** and **5** must proceed in two steps through the initial formation of zwitterionic σ-complex intermediate **3** in the gas phase. Similarly, formation of diadduct **7** will also involve the formation of a zwitterion, namely **6**, in the gas phase. However, neither **3** nor **6** have been found to be thermodynamically stable enough to accumulate to the extent required for a direct characterization by spectroscopic or kinetic techniques in solution.[32]

Herein, we report on an extensive experimental investigation of the interaction of DNBF with an electron-rich diene, namely 1-trimethylsilyloxybuta-1,3-diene **8**, to afford [2+4] Diels–Alder adducts **10** and **11** according to Scheme 2 in different solvents (acetonitrile, dichloromethane, toluene). As will be seen, the formation of these two diastereomers proceeds through a zwitterionic intermediate, **9**, which has been firmly identified by UV/Vis and ^{1}H NMR spectroscopies in acetonitrile. A kinetic study of the formation of **9** has also been carried out in this solvent with the finding that the rate of C−C coupling of the two partners nicely obeys the relationship recently developed by Mayr and co-workers to describe nucleophilic–electrophilic combinations.[33] Based on the results obtained, the DNBF–1-trimethylsilyloxybuta-1,3-diene system can be classified among the prototype ionic Diels–Alder reactions.

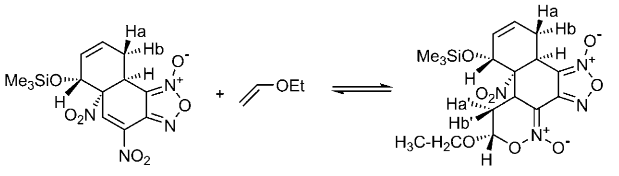
Results and Discussion

Reaction in acetonitrile: In a synthetic context,[17b] Vichard et al. reported in 1998 that dissolution of DNBF in diene **8**, which was used as the solvent at room temperature, leads to the precipitation of pale-yellow crystals that were shown to correspond to the formation of [2+4] adduct **10** in its racemic form and in nearly quantitative yield. Structure **10** was unambiguously established on the basis of a X-ray structure of di-adduct **12**, which was obtained in a subsequent treatment of **10** with vinyl ethyl ether [Eq. (3)].[17b]

In repeating the synthesis of **10** to confirm the unique formation of this diastereomer under the above experimental



Scheme 2.



10 12 (3)

conditions, a most significant feature has emerged, namely, that mixing of the two reagents resulted in the immediate development of a transient red-orange color, which rapidly vanished upon conversion of these materials into adduct **10**. Importantly, all DNBF σ adducts so far reported in the literature are orange-red species with an intense absorption maximum at $\lambda_{max} = 460$ to 490 nm, which depends very little on the solvent.[1–11] On this basis, it was reasonable to envision that the transient color development observed in the DNBF–trimethylsilyloxubutadiene interaction reflected the initial formation of zwitterionic intermediate **9**. Notably, no absorbance was seen in the region typical for the formation of DNBF π complexes.[34,35]

NMR spectroscopic characterization of 9 in acetonitrile: Because it is known that zwitterionic σ adducts, for example, Wheland–Meisenheimer adducts,[5] are strongly stabilized in dipolar aprotic solvents,[1,11b,36] one could reasonably anticipate that acetonitrile would be the most suitable solvent for a successful characterization of intermediate **9**. As a matter of fact, the ^{1}H NMR spectra recorded immediately after mixing the DNBF and diene reagents in a 2:1 ratio ([DNBF] = 0.1 M; [**8**] = 0.05 M) at −40 °C in acetonitrile showed the complete disappearance of the signals due to **8** and the concomitant appearance of a new set of signals that indicate the formation of a new species (Figure 1). A ^{1}H–^{1}H correlation aids in analyzing the spectra to make an unambiguous identification of this species as zwitterionic structure **9**. The data are collected in Table 1. Typical diagnostic features for **9** include: 1) The presence of a singlet at $\delta = 8.30$ ppm and of a multicoupled signal at $\delta = 4.73$ ppm that were assigned to protons H5 and H7, respectively, of the negatively charged DNBF moiety. Similar chemical shifts have been reported for the H5 and H7 protons of a large number of carbon-bonded σ adducts of DNBF, for example, **13** and **14**.[1–11,36,37] 2) The presence of a lowfield resonance at $\delta = 9.32$ ppm assignable to the H13 proton of the exocyclic moiety of **9**. This proton is strongly deshielded by the electron-withdrawing effect of the positively charged oxygen atom of the trimethylsilyloxy group. 3) The finding of clear correlations between H13 and H12 ($\delta = 5.98$ ppm), between H12 and H11 ($\delta = 6.84$ ppm) and between H11 and H10 ($\delta = 3.09$ ppm).

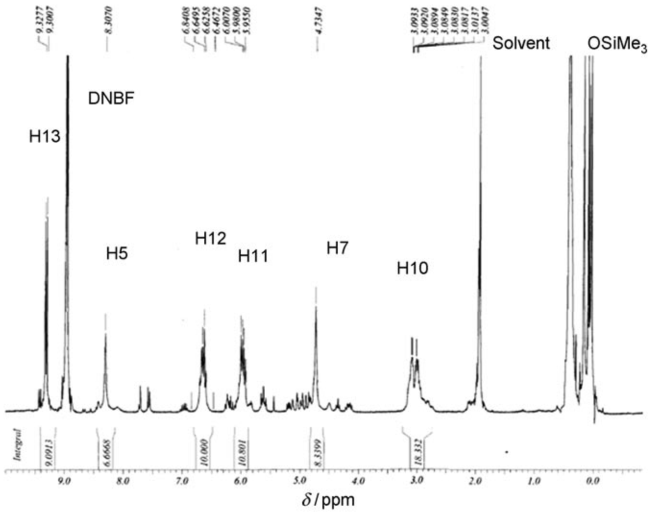
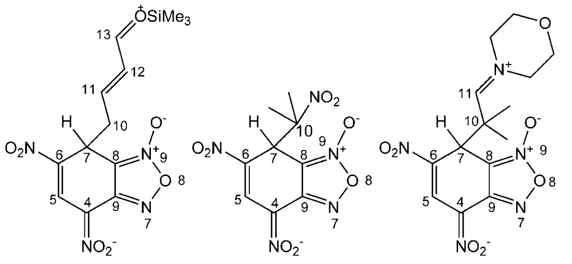


Figure 1. ^{1}H NMR spectrum of zwitterion **9** at −40 °C in CD_3CN.

Table 1. Selected ^{1}H NMR parameters (δ [ppm]) for DNBF, zwitterionic adduct **9**, and two related σ-adducts **13** and **14**.[a]



9 13 14

Compound	δ_{H5}	δ_{H7}	δ_{H10}	δ_{H11}	δ_{H12}	δ_{H13}	δ_{CH_3}	δ_{OSiMe_3}
DNBF[b]	8.95	9.27	–	–	–	–	–	–
9[b]	8.30	4.73	3.09	6.84	5.98	9.32	–	0.11
13[c,d]	8.69	5.27	–	–	–	–	1.49; 1.51	–
14[c,d]	8.41	5.52	–	9.56	–	–	1.03; 1.04	–

[a] Relative to internal $SiMe_4$. [b] Solvent: CD_3CN. [c] Solvent $[D_6]Me_2SO$. [d] Reference [37].

The structure of **9** is further supported by the ^{13}C NMR spectroscopy data summarized in Table 2, with in particular the presence of a C7 resonance at $\delta = 32.9$ ppm typical for a sp^2–sp^3 hybridization change associated with a σ-complexation process.[1,36] Also significant are the C4 and C6 resonances, which are strongly shifted upfield on going from DNBF to **9** ($\delta_{C4} = 136.7$, $\delta_{C6} = 144.9$ ppm for DNBF; $\delta_{C4} = 117$, $\delta_{C6} = 120.5$ ppm for **9**). As has been extensively discussed,[36,38] this shielding reflects the fact that a large portion of the negative charge of DNBF σ adducts is localized onto the oxygen atoms of the 4-nitro and 6-nitro groups. At the same time, the C5 resonance is expected to move downfield, as borne out by experimental evidence: $\delta_{C5} = 126.5$ ppm for DNBF and $\delta_{C5} = 135.8$ ppm for **9**. Such chemical shifts variations are reminiscent of those reported in ^{13}C NMR spectroscopy studies of the formation of picryl σ adducts.[1,36]

Once formed, zwitterion **9** is no longer stable if the temperature is increased to −10 °C; it disappears with a concomitant appearance of two similar sets of resonances that indicate the formation of two products X and Y in an essen-

Table 2. Selected ^{13}C NMR parameters (δ [ppm]) for DNBF, zwitterionic adduct **9**, and two related σ-adducts **13** and **14**.[a]

Compound	δ_{C4}	δ_{C5}	δ_{C6}	δ_{C7}	δ_{C8}	δ_{C9}	δ_{C10}	δ_{C11}	δ_{C12}	δ_{C13}	δ_{CH_3}
DNBF[b]	136.7	126.5	144.9	120.8	116.8	145.0	–	–	–	–	–
9[b]	117.0	135.8	120.5	32.9	112.2	145.1	30.42	151.2	126.4	194.1	–
13[c,d]	110.6	113.3	121.0	41.32	110.1	149.8	92.06	–	–	–	22.23; 23.30
14[c,d]	122.5	133.1	122.5	38.4	111.4	150.1	54.2	201	–	–	13.4; 20.0

[a] Relative to internal $SiMe_4$. [b] Solvent: CD_3CN. [c] Solvent: $[D_6]Me_2SO$. [d] Reference [37].

tially 1:1 ratio. Importantly, the resonances ascribable to X coincided with those seen in the NMR spectrum recorded immediately after dissolution of a sample of isolated adduct **10** at −40 °C in acetonitrile. In this instance, raising the temperature to −10 °C induces the conversion of X into Y and leads to the same 1:1 mixture as the one resulting from the disappearance of the in situ-generated zwitterion. On the other hand, a thorough analysis of the signals ascribable to Y leave little doubt that this species is diastereomeric adduct **11**. The formation of both diastereomers **10** and **11** implies that rotation around the C–C bond of the cationic allylic substructure takes place in zwitterion **9**. In accord with the substantial energy barrier associated with such a process ($\approx$22 kcal mol^{-1}),[39] the isomerization of **10** into **11** proceeds slowly at −40 °C. ^{1}H NMR spectroscopy data for **10** and **11** are given in Table 3, together with those for structurally similar cycloadducts **15** and **16**. As can be seen, there is a close analogy between the chemical shifts and corresponding coupling constants for **10** and **11** and those for cycloadducts **15** and **16**, the stereochemistry of which has been unambiguously established by X-ray crystallography and by NMR spectroscopy investigations.[40] This suggests that the same stereochemistry prevails in the various adducts with, in particular, a *cis* junction between the two rings.[40]

Based on the above discussion, it is clear that **10** is formed under kinetic control and not under thermodynamic control, as initially believed.[17b] Instead, **11** is slowly formed as a product with similar stability to **10** in the overall DNBF–trimethylsilyloxybutadiene interaction. This suggests that the previous isolation of **10** as the unique product resulting from the dissolution of DNBF in the diene itself was probably the reflection of a very low solubility of this adduct, precipitation of which prevented its isomerization into **11**. Notably, the formation of both diastereomers **10** and **11** is in itself evidence for the stepwise character of the cycloaddition.[24,25] Inasmuch as **11** has always been observed in a 1:1 mixture with **10**, we have failed so far to obtain ^{13}C NMR spectroscopy data for this adduct.

UV/Vis characterization of 9 in acetonitrile: Zwitterion **9** has also been characterized by stopped-flow spectrophotometry. Figure 2 exemplifies the set of UV/Vis spectra that

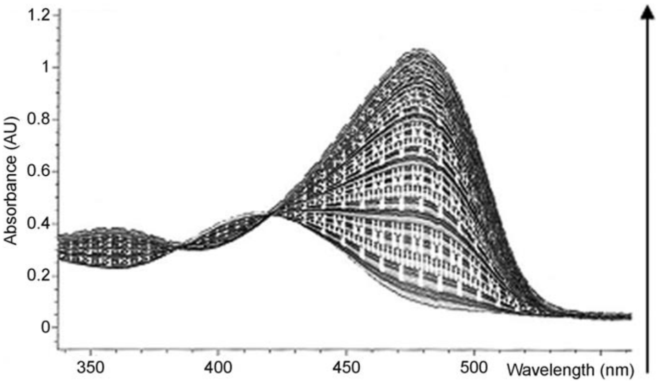
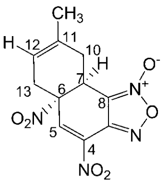


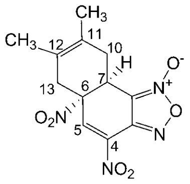
Figure 2. UV/Vis absorption spectra illustrating the formation of zwitterion **9** (3.5×10^{-5} M) in a 10^{-2} M solution of 1-trimethylsyliloxybuta-1,3-diene **8** in acetonitrile. The arrow shows the increase in the absorbance of **9** at 485 nm during the equilibrium approach.

have been recorded after mixing a 3.5×10^{-5} M solution of DNBF in acetonitrile with a large excess of **8** (0.01 M) at 20 °C in this solvent. As can be seen, the observed absorption changes that occur within a few minutes are associated with the formation of a strongly colored species with a λ_{max} (485 nm) that leaves no doubt that we were dealing with the initial equilibrium formation of **9** according to the first step depicted in Scheme 2. Three features are worth mentioning. The first is the presence of two isobestic points at $\lambda = 420$ and 385 nm in Figure 2, which indicates that the observed process is very clean over the time range needed for the equilibrium attainment. The second is that the final absorbance does not change as the diene concen-

Table 3. Selected ^{1}H NMR data (δ [ppm], J [Hz]) for cycloadducts **10** and **11**. Comparison with adducts **15** and **16** of isoprene and 2,3-dimethylbutadiene.[a]



15



16

Solvent	Compound	δ_{H5}	δ_{H7}	δ_{H10}	$\delta_{H11,12}$	δ_{H13}	J(H7,H10)	J(H10a,H10b)	J(H13a,H13b)
CD_3CN	**10**	7.56	4.20	2.85/2.11	6.04	5.04	8.3	18	18
$CDCl_3$		7.33	4.40	3.03/1.93	5.99/6.07	4.88	8.0	19.2	19.1
CD_3CN	**11**	7.77	4.37	3.01/2.15	5.84	4.85	–	–	–
$CDCl_3$	**15**[b]	7.57	4.22	3.32/2.67	5.49	3.14/2.81	7.2	19.0	18.80
$CDCl_3$	**16**[b]	7.54	4.15	2.68/2.28	–	3.09/2.71	7.2	17.7	17.4

[a] Relative to internal $SiMe_4$. [b] Reference [40].

tration is increased from 0.01 to 0.05 M. This shows that the formation of **9** is essentially complete under the experimental conditions at hand. The last feature is that in the above UV/Vis experiments, compound **9** was not subsequently seen to undergo the expected first-order cyclization, presumably because of the very low concentration of DNBF that was used in these experiments.

Kinetic study of the formation of 9: Importantly, the absorption changes pertaining to the formation of **9** at a given diene concentration (Figure 2) go along with oscilloscope traces consisting of a unique first-order relaxation process (Figure 3). For the approach to Equilibrium (4), the observed first-order rate constant, k_{obsd}, is simply given by Equation (5).

$$\mathrm{DNBF}+\mathbf{8}\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}}\mathbf{9} \tag{4}$$

$$k_{obsd} = k_1[\mathbf{8}]+k_{-1} \tag{5}$$

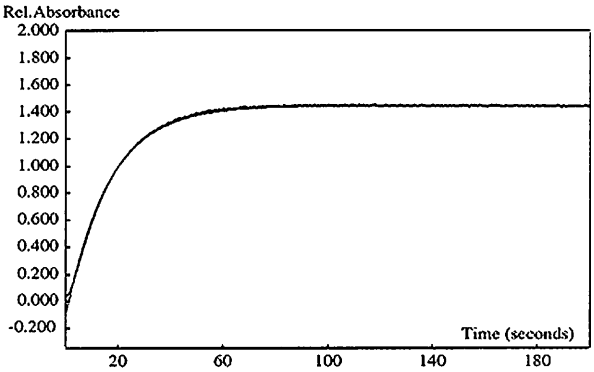


Figure 3. Oscilloscope traces showing the unique relaxation process leading to **9** at $\lambda = 480$ nm in a 2×10^{-2} M solution of **8** in acetonitrile at 20 °C.

Figure 4 shows a plot of k_{obsd} versus the diene concentration for the DNBF reaction. As called for by Equation (5), it is linear, which allows a straightforward determination of the second-order rate constant k_1 from the slope of the observed line: $k_1 = 0.31\,\mathrm{M}^{-1}\mathrm{s}^{-1}$. In this instance, the intercept of the k_{obsd} versus [**8**] plot is too low for a meaningful determination of the rate constant k_{-1} by measuring the tendency of **9** to undergo a spontaneous or solvent-assisted return to the starting materials. This feature is consistent with the experimental evidence that the formation of **9** is essentially complete in the range of concentrations of **8** (0.01–0.05 M) employed in our study. The k_{obsd} values are collected in Table 4.

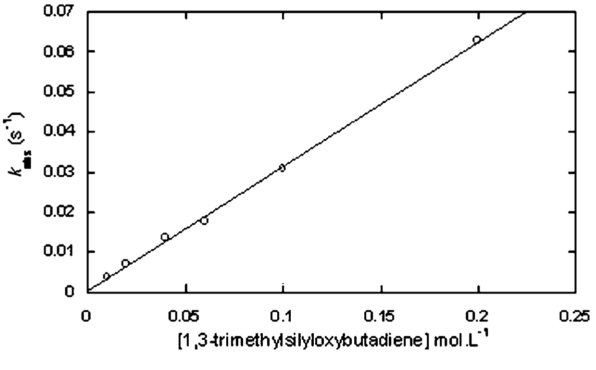


Figure 4. Effect of the concentration of **8** on the observed first-order rate constant k_{obsd} for the formation of zwitterion **9** at $T = 20$ °C in acetonitrile; ——: $y = 0.00044239+0.30983x$, $R^2 = 0.99868$.

Table 4. k_{obsd} values for the reaction of DNBF with **8** in acetonitrile, dichloromethane, and toluene at $T = 20$ °C.

Diene concentration [M]	CH_3CN k_{obsd} [s^{-1}]	CH_2Cl_2 k_{obsd} [s^{-1}]	Toluene k_{obsd} [s^{-1}]
5×10^{-3}	–	1.77×10^{-3}	–
1×10^{-2}	3.60×10^{-3}	3.75×10^{-3}	3.18×10^{-4}
2×10^{-2}	7.28×10^{-3}	7.24x 10^{-3}	6.37×10^{-4}
3×10^{-2}	–	1.06×10^{-2}	–
4×10^{-2}	1.35×10^{-2}	–	1.26×10^{-3}
5×10^{-2}	–	1.62×10^{-2}	–
6×10^{-2}	1.76×10^{-2}	–	1.80×10^{-3}
1×10^{-1}	3.11×10^{-2}	–	3.17×10^{-3}
2×10^{-1}	6.28×10^{-2}	–	–

Mayr et al. have successfully developed the three-parameter relationship of Equation (6) to describe the feasibility and rate of a large variety of electrophile–nucleophile combinations.[33]

$$\log k_1 = s(E+N) \tag{6}$$

In Equation (6), the E parameter measures the strength of the electrophilic partner, whereas the N and s parameters characterize the sensitivity of the nucleophile. Based on this equation, general electrophilicity (E) and nucleophilicity (N) scales, each covering a reactivity range of about 40 orders of magnitude, have been defined. Interestingly, these include a calibration of the E value for DNBF ($E = -5.06$),[40] as well as of the N and s values for 1-trimethylsilyloxybuta-1,3-diene acting as a nucleophile ($N = 4.60$; $s = 0.90$).[41] Combining the above parameters thus allows us to estimate the rate constant, k_1, for the nucleophilic addition step of **8** to DNBF, resulting in the formation of intermediate zwitterion **9** in acetonitrile, a suitable solvent for the application of Equation (6). One thus obtains a value of $k_1 = 0.38\,\mathrm{M}^{-1}\mathrm{s}^{-1}$, which is in remarkable agreement with the measured rate constant $k_1 = 0.31\,\mathrm{M}^{-1}\mathrm{s}^{-1}$and, therefore, with the recognition of the DNBF–**8** interaction as a prototype example for stepwise Diels–Alder cycloadditions. A similar consistency between calculated and experimentally determined rate constants has been reported by Mayr, Ofial et al. in investigations of the Diels–Alder reactions of iminium ions and 1,1,3-triarylallyl cations.[41,42]

Reactions in dichloromethane and toluene: Figure 5 shows the UV/Vis spectra recorded when carrying out the reactions of DNBF (3.5×10^{-5} M) with **8** (0.005–0.05 M) at 20 °C in toluene, a solvent of lower polarity than acetonitrile. In this instance in which the DNBF concentration is very low,

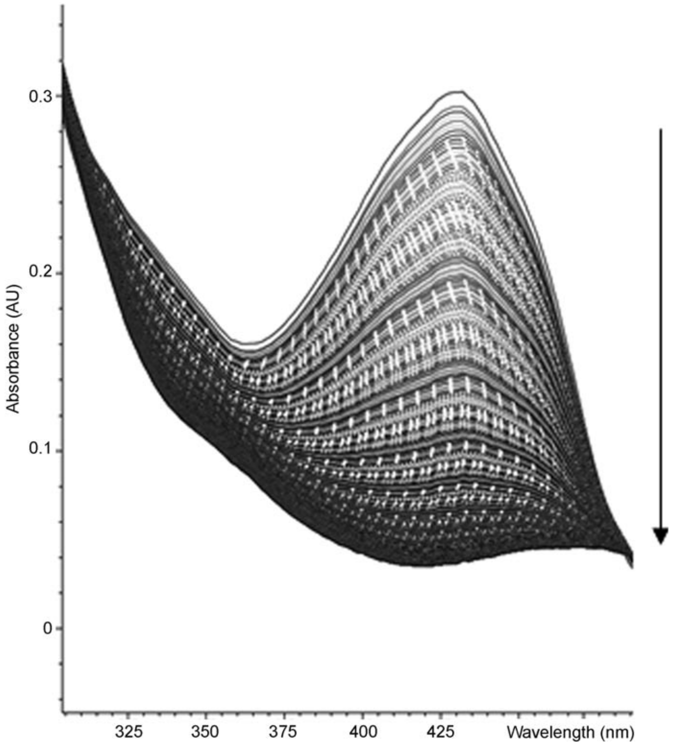


Figure 5. UV/Vis absorption spectra illustrating the conversion of DNBF (3×10^{-5} M) into Diels–Alder adduct **10** in a 10^{-2} M solution of diene **8** at 20 °C in toluene. The arrow shows the decrease in the absorbance of DNBF at 425 nm.

no transient absorption assignable to an initial formation of **9** could be detected. A similar situation prevails in CH_2Cl_2. The rate of disappearance of DNBF was followed at 425 nm. Values of the corresponding pseudo-first-order rate constants, k_{obsd}, measured in these two solvents are collected in Table 4. In each of the two solvents, plotting k_{obsd} versus the diene concentration afforded a nice straight line from which the second-order rate constant k_1 was readily determined: $k_1 = 0.32\,M^{-1}s^{-1}$ in CH_2Cl_2; $k_1 = 0.03\,M^{-1}s^{-1}$ in toluene (Figure 6).

Formally, these rate constants can be interpreted as representative of the initial formation of **9** or of a concerted process. An interesting feature, however, is that the rate constant k_1 measured in CH_2Cl_2 is essentially the same as that measured in acetonitrile; this fits Mayr's relationship nicely. These findings strongly favor the view that we are still dealing with stepwise cycloadditions in which the first step is a nucleophile–electrophile combination. Note that Sustmann et al. reported a well-established stepwise cycloaddition of *trans*-1-(dimethylamino)-1,3-butadiene with dimethyl dicyanofumarate that also proceeds with similar rates in acetonitrile and dichloromethane.[26] In this instance, it was suggested that the zwitterionic intermediate is less stabilized by solvation in CH_2Cl_2 than in acetonitrile. As a result, the ring closure of this intermediate is faster, thereby preventing sufficient accumulation of this species for its direct characterization in this solvent. The 10-fold decrease in k_1 on going from dichloromethane to toluene seems equally consistent with an ionic pathway in the latter solvent.

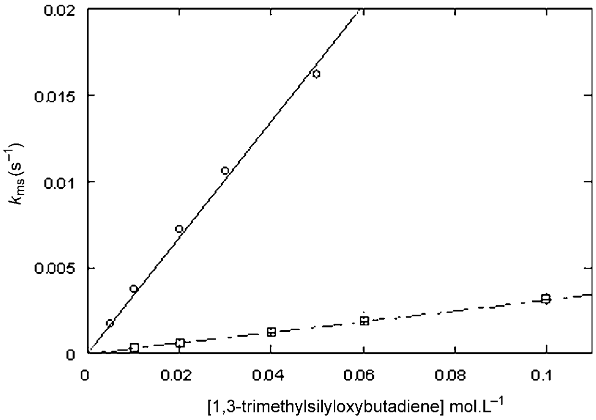


Figure 6. Effect of the concentration of diene **8** on the observed first-order rate constant k_{obsd} for the formation of Diels–Alder adduct **10** at 20 °C in toluene (□) and dichloromethane (○); ——: $y = 0.33609x$, $R^2 = 0.99579$; – – –: $y = 0.031294x$, $R^2 = 0.99846$.

Predicting stepwise cycloadditions through Parr's model: Stereochemical studies and trapping of the zwitterionic intermediates by appropriate reagents have proved to be the most used criteria to identify stepwise cycloadditions.[19,21–24,27] Theoretical calculations have also played a major role in the recognition of ionic pathways, especially in the last decade.[19,21–24,32] By comparison, the number of polar cycloadditions in which a direct observation of the zwitterionic intermediate could be achieved by spectroscopic and/or kinetic methods remains rather sparse. Among the most representative systems in which this observation has been successful, there are those involving electron-deficient dienophiles, such as tetracyanoethylene (TCNE), dimethyl dicyanofumarate, or electron-deficient heteroaromatic structures, such as aryl-substituted 1,2,4-triazines, 1,2,4,5-tetrazines, or 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD).[23–26,29,31] These compounds favor the stability of the zwitterionic intermediates by efficiently stabilizing the negative charge. In this context, Sustmann has characterized some zwitterionic intermediates by using stopped-flow spectrophotometry.[26,31] In a thorough investigation of the reactions of a variety of aryl-substituted 1,2,4-triazines with 2-cyclopropylidene-1,3-dimethylimidazolidine, a very electron-rich olefin, Heuschmann and Zipse have also detected a number of zwitterions that have been characterized spectroscopically and, in some cases, isolated at low temperatures.[29] In exploring the synthetic potential of the Diels–Alder reactivity of 2,4,6-tris(trifluoromethyl)-1,3,5-triazine towards 2-aminopyrroles, De Rosa and Arnold have recently characterized the zwitterionic Wheland–Meisenheimer-type intermediates **17** by using ^1H, ^{13}C, ^{15}N, and ^{19}F NMR spectroscopy.[43] In an earlier work, Hartmann and Heuschmann firmly characterized zwitterionic Wheland–Meisenheimer adducts, namely **18**, as intermediates in the reactions of 3,6-diphenyl-1,2,4,5-tetrazine with 2-cyclopropylidene-1,3-dimethylimidazolidine.[29b]

It is interesting to relate the present work to the above systems. This can be done by using the approach recently developed by Domingo et al. on the basis of two reactivity indexes defined within the DFT theory and found to be very useful for predicting the feasibility of many nucleophile–electrophile combinations and the more-or-less polar character of Diels–Alder reactions.[44–47] A first key parameter is the global electrophilicity index, ω, introduced by Parr and defined in Equation (7).[48–50] In this equation, the electronic chemical potential μ and the chemical hardness η of a substrate are two parameters that were evaluated in terms of the one-electron energies of the frontier molecular orbitals (FMO) HOMO and LUMO at the ground state of the molecules. The second informative index used by Domingo et al. in several investigations is the so-called $\Delta N_{\max}$ parameter defined in Equation (8), which is a measure of the maximum amount of electronic charge that an electrophilic partner can accept.[44–46] Recent investigations have used the ω and $\Delta N_{\max}$ values to classify dienes and dienophiles on a unique electrophilicity scale.[44–47,51] According to the model, the polar character of a Diels–Alder interaction can be assessed from the difference in the global electrophilicities of the two reagents, $\Delta\omega$, and the $\Delta N_{\max}$ values for the system at hand. Thus, it is anticipated that reactions involving a diene and a dienophile located at the ends of the ω scale will proceed with an especially strong polar character.[45,46] In turn, reactions associated with small $\Delta\omega$ values should be prototypes of non-polar processes. The calculated values of ω and $\Delta N_{\max}$ of relevance for our comparison of the DNBF–**8** system with well-established stepwise cycloadditions are collected in Table 5, together with reported data for a few reference cycloadditions.[45–47] All structures quoted in Table 5 are shown in Chart 1 in the Supporting Information.

$$\omega = \frac{\mu^2}{2\eta} \tag{7}$$

$$\Delta N_{\max} = -\frac{\mu}{\eta} \tag{8}$$

With an ω value of 5.46, which approaches that of TCNE and surpasses those of other strongly electron-deficient olefinic structures, such as dimethyl dicyanofumarate or dicyanomaleate and 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD), DNBF appears to be an especially strong electrophilic dienophile. As a result, its reactions with **8** and most of the dienic structures listed in Table 5 are characterized by large $\Delta\omega$ values (≥ 4.5) and $\Delta N_{\max}$ values, which leaves little doubt that the related cycloadditions will exhibit a large polar character.[44–47] Consistent with this anticipation, the experimental evidence reported in this work is that the reaction of DNBF with **8** ($\Delta\omega = 4.73$) proceeds stepwise through a relatively stable zwitterionic intermediate. Interestingly, a DFT study of the reaction of DNBF with cyclopentadiene (Cp) has been made that suggests that decreasing the electron-rich character of the diene on going from **8** to Cp or other common dienes, such as 2,3-dimethyl-butadiene, should not change the mechanism of the DNBF cycloadditions, even though the intermediates are no longer stable enough to be experimentally observed.[18a,44a] Thorough kinetic investigations are presently carried out in different solvents to test whether this conclusion can be confirmed or not through use of Mayr's equation.

Table 5. Global electrophilicity (ω) and $\Delta N_{\max}$ parameters for dienophile and dienes discussed herein.[a]

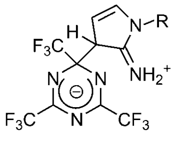
Compound	ω [eV]	$\Delta N_{\max}$ [eV]	Ref.
2-cyclopropylidene-1,3-dimethylimidazolidine	0.18	0.25	[b]
trans-1-dimethylamino-1,3-butadiene	0.57	0.48	–
Danishefsky diene	0.65	0.51	[b]
1-trimethylsilyloxy-1,3-butadiene	0.73	0.52	[45]
1,1-dimethoxy-1,3-butadiene	0.83	0.58	[b]
1-methoxy-1,3-butadiene	0.77	0.548	[45]
cyclopentadiene	0.83	0.55	[45]
cyclohexadiene	0.90	0.59	[47]
Isoprene	0.94	0.57	[45]
2,3-dimethylbutadiene	0.97	0.58	[47]
3,5-diphenyl-1,2,4-triazine	2.09	1.00	[b]
nitroethylene	2.61	0.98	[40]
trans-β-nitrostyrene	2.70	1.11	[47]
3-(*p*-nitrophenyl)-5-phenyl-1,2,4-triazine	2.80	1.19	[b]
2,4,6-tris(trifluoromethyl)-1,3,5-triazine	3.14	1.04	[b]
1,1-dinitro-2,2-diphenylethylene	3.16	1.27	[47]
tetrazine	3.38	1.36	[46]
nitroethylene/BH_3	4.33	1.55	[40]
4-nitrobenzodifuroxan (NBDF)	4.80	1.65	[47]
4-aza-6-nitrobenzofuroxan (ANBF)	4.81	1.64	[47]
4-phenyl-1,2,4-triazoline-3,5-dione (PTAD)	4.92	1.8	[b]
4,6-dinitrobenzofuroxan (DNBF)	5.46	1.85	[40]
tetracyanoethylene (TCNE)	5.96	1.695	[45]

[a] ω is defined by Equation (7), in which μ and η refer to the electronic chemical potential and the hardness of the substrates, respectively (see ref. [45a]). [b] Values calculated in this work.

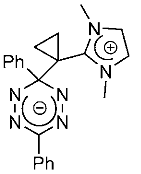
As revealed by Table 5, the electron-deficient olefins involved in previously recognized stepwise cycloadditions, notably dimethyl dicyanofumarate, PTAD, and TCNE are all highly electrophilic dienophiles with ω values in the range of 4 to 5.9. This corresponds to $\Delta\omega$ values in the range of 3.5 to 5 for their reactions with the most reactive dienes studied, such as the Danishefsky diene, 1,1-bis(dimethylamino)-1,3-butadiene, or 2-cyclopropylidene-1,3-dimethylimidazolidine. Based on these $\Delta\omega$ values, which are similar to those for the DNBF–**8** interaction, a similar feasibility of stepwise cycloadditions could be expected because it is actually borne out by the experiments. An interesting feature is that other nitrobenzofuroxan structures, for example, 4-aza-6-nitrobenzofuroxan (ANBF) or 4-nitrobenzodifuroxan (NBDF), are also characterized by high ω values of ≈ 4.8.[51] This allows us to predict the occurrence of stepwise cycloadditions upon reaction of these derivatives with the most reactive dienes.

For the best evaluation of the Diels–Alder reactivity of the aforementioned electron-deficient olefinic structures, it is worth noting that the corresponding ω values are all considerably high compared with that of the reference nitroolefin, namely nitroethylene ($\omega = 2.61$).[44a] This olefin itself is not always very reactive in terms of Diels–Alder reactivity and it is only in the presence of a Lewis acid catalyst that it can be involved in a number of normal or inverse electron demand cycloadditions.[14,15] Interestingly, a Lewis acid catalyst has the effect of enhancing ω up to 4.33 eV (for the nitroethylene/BH_3 complex), a value that is now greater than that for dimethyl dicyanofumarate and compares well with those for ANBF or NBDF. This makes it possible to engage this olefin in many C–C coupling reactions, including polar Diels–Alder reactions.[14,15,45] Similarly, appropriate Lewis acid catalysts have to be employed to enhance the electrophilicity of nitro-activated olefins, such as *trans*-β-nitrostyrene and 1,1-dinitrodiphenylethylene, and cyano- and carbonyl-activated olefins, for example, benzylidenemalonitrile, which have ω values comparable to that of nitroethylene (see Table 5).[52–54]

As also shown in Table 5, the electrophilicity of representive 1,3,5-triazines, 1,2,4-triazines, and 1,2,4,5-tetrazines is associated with rather moderate ω values. The ω values for the two most electrophilic compounds, namely, 2,4,6-tris(trifluoromethyl)-1,3,5-triazine and unsubstituted 1,2,4,5-tetrazine, are equal to 3.14 and 3.37, respectively. This implies that even with electron-rich olefins, the coupling of these compounds goes along with moderate $\Delta\omega$ values ($\Delta\omega \leq 3$). On this basis, should the ω scale be considered as a good monitor to predict the mechanism of all Diels–Alder reactions, one would suggest that the triazine and tetrazine systems exhibit a more-or-less polar character excluding, however, two-step addition–cyclization pathways.[29,31,43,55,56] Obviously, the experimental evidence does not fit this expectation because zwitterionic intermediates, such as **17** or **18**, have been firmly characterized.[29b,43] It follows that the ω scale, a parameter referring to calculations in the gas phase, is certainly useful for understanding the mechanism of a number of electrophile–nucleophile combinations. However, it does not seem to be a universal criterion, maybe because the solvent can play a major role in determining the stability of the reaction partners within this class of reactions. A very recent proposal by Domingo and Saez that consideration of the extent of charge transfer at the transition state might be a better descriptor of polar Diels–Alder reactions than the aforediscussed ω values based on molecular orbital interactions, might be a useful tool to get further information on this point.[57]



17



18

Conclusion

4,6-Dinitrobenzofuroxan, a superelectrophilic heteroaromatic, is found to behave as a formal dienophile upon reaction with the electron-rich 1-trimethylsilyloxybuta-1,3-diene in different solvents (acetonitrile, dichloromethane, and toluene). The interaction afforded a 1:1 mixture of two diastereomers of [2+4] cycloadducts **10** and **11**, which are shown to result from a stepwise process through initial formation of zwitterion **9**. This zwitterion has been structurally characterized by ^1H and ^{13}C NMR spectroscopy at −40 °C in acetonitrile and by UV/Vis stopped-flow spectrophotometry at room temperature. The kinetics of the formation of **9** in acetonitrile has allowed the determination of a second-order rate constant that agrees nicely with the value of the rate constant predicted by Mayr's three-parameters equation [Eq. (6)], thereby supporting the nucleophile–electrophile character of the reaction. Contrasting with the situation in acetonitrile, zwitterion **9** is not stable enough to form to a sufficient extent for a room-temperature characterization in toluene or CH_2Cl_2. Importantly, however, the kinetics of formation of cycloadduct **10** (under kinetic control) have been measured and the related second-order rate constant is found to fit Equation (6). On these grounds, it is concluded that a stepwise mechanism is also operating in these two less-polar solvents.

Experimental Section

General: DNBF was available from a recent study.[6a] ^1H and ^{13}C NMR spectra were recorded by using a 300 MHz spectrometer.

The synthesis and characterization of the cycloadduct **10** has been previously described.[17b]

The in situ NMR spectroscopic characterization of transient zwitterion **9** and cycloadduct **11** was carried out as follows: Freshly distilled 1-trimethylsilyloxybuta-1,3-diene **8** (1 equiv) was added to a NMR tube under argon to a cooled solution (−40 °C) of DNBF (2 equiv) in CD_3CN (1 mL). As illustrated in Figure 1, the NMR spectra recorded immediately after mixing of the reagents shows the complete formation of zwitterion **9**, allowing a full ^1H and ^{13}C NMR spectroscopic characterization of this species (Tables 1 and 2). As elaborated in detail in the main text, increasing the temperature to −10 °C resulted in the formation of a 1:1 mixture of cycloadduct **10**, which was previously obtained as a pure species under other experimental conditions,[17b] and of diasteomer **11**. Although we failed to separate these two cycloadducts, a detailed analysis of the recorded ^1H NMR spectra has allowed a full characterization of **11**.

Kinetic measurements: Kinetic measurements pertaining to the interaction of DNBF with 1-trimethylsilyloxybuta-1,3-diene in MeCN, CH_2Cl_2, and toluene were performed by using a stopped-flow or a conventional spectrophotometer, the cell compartments of which were maintained at 20 ± 0.1 °C. All kinetic runs were carried out in triplicate under pseudo-first-order conditions with a DNBF concentration of approximately 3.5–5×10^{-5} M and a diene concentration in the range of 5×10^{-3}–0.2 M. The rates were measured by monitoring either the increase in absorbance at λ_{max} of zwitterion **9** in MeCN (see Figure 2) or the decrease in absorbance at λ_{max} of the parent DNBF molecule in CH_2Cl_2 and toluene (see Figure 5). In a given experiment, the rates were always found to be reproducible to within ±2–3 %.

Computational information: Full geometry optimizations for the dienes and dienophiles not yet studied (see footnote [c] in Table 5) have been performed at the B3LY8/6-31G* level of theory,[58,59] which was implemented in the Gaussian 03 package of programs.[60] The global electrophilicity power (ω) was evaluated by means of Equation (7). The electronic chemical potential (μ) and chemical hardness (η) values were approximated in terms of the one-electron energies of the HOMO and LUMO FMOs, ε_H and ε_L, respectively, by using $\mu=(\varepsilon_H+\varepsilon_L)/2$ and $\eta=\varepsilon_H-\varepsilon_L$[57] at the ground state of the molecules.

Acknowledgements

The authors are grateful for the support of this research by CNRS and the Ministry of Research.

---

[1] a) F. Terrier in *Nucleophilic Aromatic Displacement, The Influence of the Nitro Group*, Wiley-VCH, Weinheim, **1991**; b) E. Buncel, J. M. Dust, F. Terrier, *Chem. Rev.* **1995**, *95*, 2261–2280.

[2] a) E. Buncel, R. A. Renfrow, M. J. Strauss, *J. Org. Chem.* **1987**, *52*, 488–495; b) E. Buncel, R. A. Manderville, J. M. Dust, *J. Chem. Soc., Perkin Trans. 2* **1997**, 1019–1026.

[3] a) M. R. Crampton, L. C. Rabbitt, *J. Chem. Soc., Perkin Trans. 2* **2000**, 2169–2171; b) M. R. Crampton, L. M. Pearce, L. C. Rabbitt, *J. Chem. Soc., Perkin Trans. 2* **2002**, 257–261; c) M. R. Crampton, R. E. A. Lunn, D. Lucas, *Org. Biomol. Chem.* **2003**, *1*, 3438–3443; d) B. H. M. Asghar, M. R. Crampton, C. Isanbor, *Can. J. Chem.* **2008**, *86*, 225–229.

[4] G. Ya. Remmennikov, B. Kempf, A. R. Ofial, K. Polborn, H. Mayr, *J. Phys. Org. Chem.* **2003**, *16*, 431–437.

[5] a) C. Boga, E. Del Vecchio, L. Forlani, A. Mazzanti, P. E. Todesco, *Angew. Chem.* **2005**, *117*, 3349–3353; *Angew. Chem. Int. Ed.* **2005**, *44*, 3285–3289; b) C. Boga, L. Forlani, *J. Chem. Soc., Perkin Trans. 2* **2001**, 1408–1414; c) L. Forlani, A. L. Tocke, E. Del Vecchio, S. Lakhdar, R. Goumont, F. Terrier, *J. Org. Chem.* **2006**, *71*, 5527–5537; d) C. Boga, E. Del Vecchio, L. Forlani, A. Mazzanti, C. M. Lario, P. E. Todesco, S. Tozzi, *J. Org. Chem.* **2009**, *74*, 5568–5575.

[6] a) S. Lakhdar, M. Westermaier, F. Terrier, R. Goumont, T. Boubaker, A. R. Ofial, H. Mayr, *J. Org. Chem.* **2006**, *71*, 9088–9095; b) S. Lakhdar, R. Goumont, T. Boubaker, M. Mokhtari, F. Terrier, *Org. Biomol. Chem.* **2006**, *4*, 1910–1925; c) S. Lakhdar, R. Goumont, F. Terrier, T. Boubaker, J. M. Dust, E. Buncel, *Org. Biomol. Chem.* **2007**, *5*, 1744–1751.

[7] a) M. I. Evgen'ev, S. Yu. Garmonov, I. I. Evgen'eva, *Zh. Anal. Khim. Int. Ed.* **2002**, *57*, 159–163; b) M. I. Evgen'ev, I. I. Evgen'eva, F. S. Levinson, E. A. Ermolaeva. Ya. R. Valitova, *Zh. Anal. Khim.* **2006**, *61*, 133–138.

[8] a) S. Kurbatov, P. Rodriguez-Dafonte, R. Goumont, F. Terrier, *Chem. Commun. (Cambridge)* **2003**, 2150–2151; b) S. Kurbatov, A. Tatarov. R. Goumont, V. Minkin, F. Terrier, *Chem. Commun. (Cambridge)* **2006**, 4279–4281; c) P. Rodriguez-DaFonte, F. Terrier, S. Lakhdar, S. Kurbatov, R. Goumont, *J. Org. Chem.* **2009**, *74*, 3305–3315.

[9] R. W. Read, W. P. Norris, *Aust. J. Chem.* **1985**, *38*, 435–445.

[10] a) F. Terrier, M. J. Pouet, J. C. Halle, E. Kizilian, E. Buncel, *J. Phys. Org. Chem.* **1998**, *11*, 707–714; b) F. Terrier, E. Kizilian, J. C. Hallé, E. Buncel, *J. Am. Chem. Soc.* **1992**, *114*, 1740–1742; c) F. Terrier, M. J. Pouet, J. C. Halle, S. Hunt, J. R. Jones, E. Buncel, *J. Chem. Soc., Perkin Trans. 2* **1993**, 1665–1672; d) F. Terrier, M. J. Pouet, E. Kizilian, J. C. Hallé, F. Outurquin, C. Paulmier, *J. Org. Chem.* **1993**, *58*, 4696–4702.

[11] a) F. Terrier, F. Millot, W. P. Norris, *J. Am. Chem. Soc.* **1976**, *98*, 5883–5890; b) F. Terrier, *Chem. Rev.* **1982**, *82*, 77–152.

[12] C. F. Bernasconi, *J. Am. Chem. Soc.* **1970**, *92*, 4682–4688.

[13] M. R. Crampton, L. C. Rabbitt, F. Terrier, *Can. J. Chem.* **1999**, *77*, 639–646.

[14] a) S. E. Denmark, A. Thorarensen, *Chem. Rev.* **1996**, *96*, 137–166; b) S. E. Denmark, J. A. Dixon, *J. Org. Chem.* **1998**, *63*, 6167–6177; S. E. Denmark, J. A. Dixon, *J. Org. Chem.* **1998**, *63*, 6178–6195; c) S. E. Denmark, J. J. Cottell, *J. Org. Chem.* **2001**, *66*, 4276–4284; d) S. E. Denmark, A. R. Hurd, H. J. Sacha, *J. Org. Chem.* **1997**, *62*, 1668–1674; e) S. E. Denmark, L. R. Marcin, *J. Org. Chem.* **1997**, *62*, 1675–1686.

[15] D. B. Boger, S. N. Weinreb in *Hetero Diels–Alder Methodology in Organic Synthesis*, Academic Press, New-York, **1987**, pp. 71–93.

[16] G. Kresze, H. Bathelt, *Tetrahedron* **1973**, *29*, 1043–1045.

[17] a) J. C. Hallé, D. Vichard, M. J. Pouet, F. Terrier, *J. Org. Chem.* **1997**, *62*, 7178–7182; b) D. Vichard, J. C. Halle, B. Huguet, M. J. Pouet, D. Riou, F. Terrier, *Chem. Commun. (Cambridge)* **1998**, 791–792.

[18] a) P. Sepulcri, J. C. Hallé, R. Goumont, D. Riou, F. Terrier, *J. Org. Chem.* **1999**, *64*, 9254–9257; b) R. Goumont, M. Sebban, P. Sepulcri, J. Marrot, F. Terrier, *Tetrahedron* **2002**, *58*, 3249–3262; c) R. Goumont, M. Sebban, F. Terrier, *Chem. Commun. (Cambridge)* **2002**, 2110–2111.

[19] For reviews of Diels–Alder reactions, see: a) J. Sauer, *Angew. Chem.* **1967**, *79*, 76–94; *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 16–33; b) J. Sauer, R. Sustmann, *Angew. Chem.* **1980**, *92*, 773–801; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 779–807; c) "Intermolecular Diels–Alder Reactions": W. Oppolzer in *Comprehensive Organic Synthesis, Vol. 5* (Ed.: B. M. Trost), Pergamon Press, Oxford, **1991**, Chapter 4.1, pp. 315–399; d) K. N. Houk, J. Gonzalez, Y. Zi, *Acc. Chem. Res.* **1995**, *28*, 81–90; e) K. N. Houk, J. D. Evanseck, *Angew. Chem.* **1992**, *104*, 711–739; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 682–708; f) M. J. S. Dewar, C. Jie, *Acc. Chem. Res.* **1992**, *25*, 537–543; g) D. H. Ess, G. O. Jones, K. N. Houk, *Adv. Synth. Catal.* **2006**, *348*, 2337–2361.

[20] a) R. Huisgen, *Acc. Chem. Res.* **1977**, *10*, 117–124; b) R. Huisgen, *Acc. Chem. Res.* **1977**, *10*, 199–206.

[21] E. Goldstein, B. Beno, K. N. Houk, *J. Am. Chem. Soc.* **1996**, *118*, 6036–6043.

[22] D. A. Singleton, B. E. Schulmeier, C. Hang, A. A. Thomas, S.-W. Leung, S. R. Merrigan, *Tetrahedron* **2001**, *57*, 5149–5160.

[23] J. S. Chen, K. N. Houk, C. S. Foote, *J. Am. Chem. Soc.* **1998**, *120*, 12303–12309.

[24] F. Jensen, C. S. Foote, *J. Am. Chem. Soc.* **1987**, *109*, 6376–6385.

[25] R. Sustmann, S. Tappanchai, H. Bandmann, *J. Am. Chem. Soc.* **1996**, *118*, 12555–12561.

[26] a) R. Sustmann, M. Rogge, U. Nächter, J. Harvey, *Chem. Ber.* **1992**, *125*, 1665–1667; b) R. Sustmann, H. G. Kôrth, U. Nächter, I. Siangouri-Feulner, W. Sicking, *Chem. Ber.* **1991**, *124*, 2811–2814; c) M. Rese, M. Dern, K. Lücking, R. Sustmann, *Liebigs Ann.* **1995**, 1139–1152.

[27] H. Quast, M. Seefelder, S. Ivanova, M. Heubes, E.-M. Peters, K. Peters, *Eur. J. Org. Chem.* **1999**, 3343–3351.

[28] G. Orlova, J. D. Goddard, *J. Org. Chem.* **2001**, *66*, 4026–4035.

[29] a) M. Heuschmann, *Chem. Ber.* **1988**, *121*, 39–49; b) K. P. Hartmann, M. Heuschmann, *Angew. Chem.* **1989**, *101*, 1288–1290; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1267–1268; c) M. Ernd, M. Heuschmann, H. Zipse, *Helv. Chim. Acta* **2005**, *88*, 1491–1518; d) K. P. Hartmann, M. Heuschmann, *Tetrahedron* **2000**, *56*, 4213–4218.

[30] H. Quast, D. Regnat, E.-M. Peters, K. Peters, H. G. Von Schnering, *Angew. Chem.* **1990**, *102*, 724–726; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 695–697.

[31] a) R. Sustmann, M. Rogge, *Tetrahedron Lett.* **1990**, *31*, 2265–2268; b) R. Sustmann, M. Rogge, U. Nâchter, H. Bandmann, *Chem. Ber.* **1992**, *125*, 1657–1664.

[32] P. Arroyo, M. T. Picher, L. R. Domingo, *J. Mol. Struct.* **2004**, *687–708*, 45–52.

[33] a) H. Mayr, M. Patz, *Angew. Chem.* **1994**, *106*, 990–1010; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 938–957; b) H. Mayr, B. Kempf, A. R. Ofial, *Acc. Chem. Res.* **2003**, *36*, 66–77; c) H. Mayr, M. Patz, M. F. Gotta, A. R. Ofial, *Pure Appl. Chem.* **1998**, *70*, 1993–2000; d) H. Mayr, A. R. Ofial in *Carbocation Chemistry* (Eds.: G. A. Olah, G. K. S. Prakash), Wiley, New York, **2004**, Chapter 13, pp. 331–358; e) H. Mayr, A. R. Ofial, *Pure Appl. Chem.* **2005**, *77*, 1807–1821;

f) B. Kempf, N. Hampel, A. R. Ofial, H. Mayr, *Chem. Eur. J.* **2003**, *9*, 2209–2218.

[34] a) A. S. Bailey, J. R. Case, *Tetrahedron* **1958**, *3*, 113–131; b) A. S. Bailey, J. R. Case, *Proc. R. Chem. Soc.* **1957**, 176.

[35] A. S. Bailey, M. W. Heaton, J. I. Murphy, *J. Chem. Soc. C* **1971**, 1211–1213.

[36] E. Buncel, M. R. Crampton, M. J. Strauss, F. Terrier in *Electron-Deficient Aromatic and Heteroaromatic Base Interactions*, Elsevier, Amsterdam, **1984**.

[37] a) F. Terrier, S. Lakhdar, T. Boubaker, R. Goumont, *J. Org. Chem.* **2005**, *70*, 6242–6253; b) F. Terrier, R. Goumont, M.-J. Pouet, J. C. Hallé, *J. Chem. Soc., Perkin Trans. 2* **1995**, 1629.

[38] a) H. Hosoya, S. Hosoya, D. Nagakura, *Theor. Chim. Acta* **1968**, *12*, 117–122; b) H. Wennerström, O. Wennerström, *Acta. Chem. Scand.* **1972**, *26*, 2833–2890.

[39] a) J. M. Bollinger, J. M. Brinich, G. A. Olah, *J. Am. Chem. Soc.* **1970**, *92*, 4025–4033; b) N. C. Deno, E. Nowak, R. C. Haddon, *J. Am. Chem. Soc.* **1970**, *92*, 6691–6693.

[40] R. Goumont, M. Sebban, J. Marrot, F. Terrier, *ARKIVOC* **2004**, 85–100.

[41] H. Mayr, A. R. Ofial, J. Sauer, B. Schmid, *Eur. J. Org. Chem.* **2000**, 2013–2020.

[42] C. Fichtner, H. Mayr, *J. Chem. Soc., Perkin Trans. 2* **2002**, 1442–1444.

[43] a) M. De Rosa, D. Arnold, *J. Org. Chem.* **2009**, *74*, 319–328; b) M. de Rosa, D. Arnold, *Tetrahedron Lett.* **2007**, *48*, 2975–2977.

[44] a) P. Arroyo, M. T. Picher, L. R. Domingo, *J. Mol. Struct.* **2004**, *687–708*, 45–52; b) P. Arroyo, M. T. Picher, L. R. Domingo, F. Terrier, *Tetrahedron* **2005**, *61*, 7359–7365.

[45] a) L. R. Domingo, M. J. Aurell, P. Perez, R. Contreras, *Tetrahedron* **2002**, *58*, 4417–4423; b) P. Perez, L. R. Domingo, M. J. Aurell, R. Contreras, *Tetrahedron* **2003**, *59*, 3117–3125; c) L. R. Domingo, M. J. Aurell, P. Perez, R. Contreras, *J. Phys. Chem. A* **2002**, *106*, 6871–6875.

[46] L. R. Domingo, P. Perez, R. Contreras, *Tetrahedron* **2004**, *60*, 6585–6591.

[47] a) D. V. Steglenko, M. E. Kletsky, S. V Kurbatov, A. V. Tatarov, V. J. Minkin, R. Goumont, F. Terrier, *J. Phys. Org. Chem.* **2009**, *22*, 298–307; b) S. Kurbatov, R. Goumont, S. Lakhdar, J. Marrot, F. Terrier, *Tetrahedron* **2005**, *61*, 8167–8176.

[48] R. G. Parr, L. Von Szentpaly, S. J. Liu, *J. Am. Chem. Soc.* **1999**, *121*, 1922–1924.

[49] R. G. Parr, W. Yang in *Density Functional Theory of Atoms and Molecules*, Oxford University Press, New York, **1989**.

[50] R. G. Parr, R. G. Pearson, *J. Am. Chem. Soc.* **1983**, *105*, 7512–7516.

[51] S. Lakhdar, R. Goumont, G. Berionni, T. Boubaker, S. Kurbatov, F. Terrier, *Chem. Eur. J.* **2007**, *13*, 8317–8324.

[52] K. B. Jensen, J. Thorhauge, R. G. Hazell, K. A. Jørgensen, *Angew. Chem.* **2001**, *113*, 164–167; *Angew. Chem. Int. Ed.* **2001**, *40*, 160–163.

[53] J. Zhou, Y. Tang, *J. Am. Chem. Soc.* **2002**, *124*, 9030–9031.

[54] S. Otto, J. B. F. N. Engberts, J. C. T. Kwak, *J. Am. Chem. Soc.* **1998**, *120*, 9517–9525.

[55] D. V. Sadasivam, E. Prasad, R. A. Flowers, D. M. Birney, *J. Phys. Chem. A* **2006**, *110*, 1288–1294.

[56] L. R. Domingo, M. T. Picher, J. A. Saez, *J. Org. Chem.* **2009**, *74*, 2726–2735.

[57] L. R. Domingo, J. A. Saez, *Org. Biomol. Chem.* **2009**, *7*, 3576–3583.

[58] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652.

[59] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789.

[60] Gaussian 03, Revision B.04, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C.Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, Gaussian, Inc., Pittsburgh PA, **2003**.

Received: October 30, 2009