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Theoretical study of the cycloaddition of nitrones to cinnamonitrile: effect of Lewis acid coordination on the selectivity of the reaction

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Abstract

A number of quantum chemical and density functional methods have been used to study the chemo- and regioselectivity of the uncatalysed and Lewis acid mediated cycloaddition of the nitrone PhCH=N(Me)O with the C=C or the C≡N bond of (*E*)-cinnamonitrile. In agreement with experimental evidence, Lewis acid coordination to the nitrile strongly promotes reaction at the C≡N bond over reaction at the alkene moiety. The main factors responsible for this inversion of the chemoselectivity were identified as the following: (i) the Lewis acid strongly stabilises the product of C≡N addition and the transition state leading to it, thus favouring this reaction both kinetically and thermodynamically. Addition across the C=C bond, in contrast, only receives weak kinetic activation; (ii) the cycloaddition to the C=C or C≡N bonds involves different molecular orbitals at the cinnamonitrile, and the Lewis acid influences the orbital involved in C≡N addition to a larger extent; (iii) the Lewis acid has a stronger effect on the electron distribution of the C≡N bond. As an overall result, the Lewis acid not only promotes the cycloaddition, but also alters the order of functional group reactivity and brings about a complete change in chemoselectivity.

Keywords: Cycloaddition; Quantum chemical calculation; Lewis acid; Nitrones; Nitriles; Alkenes

1. Introduction

Cycloaddition of 1,3-dipolar reagents to C=C and C≡C bonds represents one of the most atom efficient and versatile methods for the synthesis of five-membered heterocycles.[1] Hetero multiple bonds such as nitriles can also act as dipolarophiles in cycloaddition reactions. However, in most cases the reactivity of the C≡N bond is not sufficiently high and applications are limited. Known transformations are restricted to the reactions of electron deficient nitriles with nitrones to form Δ^4-1,2,4-oxadiazolines,[2] with azides to give tetrazoles,[3] addition to nitrile oxides as an alternative route to the well known 1,2,4-oxadiazoles,[4] reaction with *C*,*N*-diacylimines to afford amidooxazoles,[5] or the formal cycloaddition of carbonyl stabilised carbenoids to furnish 1,3-oxazoles.[6]

Our previous work demonstrated that the coordination of nitriles to Lewis acids such as Pt(IV), Pt(II) or Pd(II) promotes the cycloaddition of the C≡N bond with nitrones. Using this technique, a wide range of otherwise inaccessible Δ^4-1,2,4-oxadiazolines and their transition metal complexes have been synthesised.[7] Quantum chemical calculations suggested that the purely organic cycloaddition is a concerted pericyclic reaction, whereas coordination of the nitrile to a model Lewis acid changes the reaction mechanism towards a two-step reaction. The Lewis acid mainly acts by stabilizing the highly polar transition states, intermediates and also the product.[8,9] This activation pathway is markedly different from the traditional interpretation of Lewis acid effects on the cycloaddition to carbonyl conjugated alkenes. In these compounds, the Lewis acid is assumed to activate the C=C bond of the reactant by making it more electron deficient and by lowering the energies of the frontier orbitals involved in the reaction.[10]

With this in mind, we became interested in comparing the behaviour of a C=C and a C≡N bond directly, by studying the

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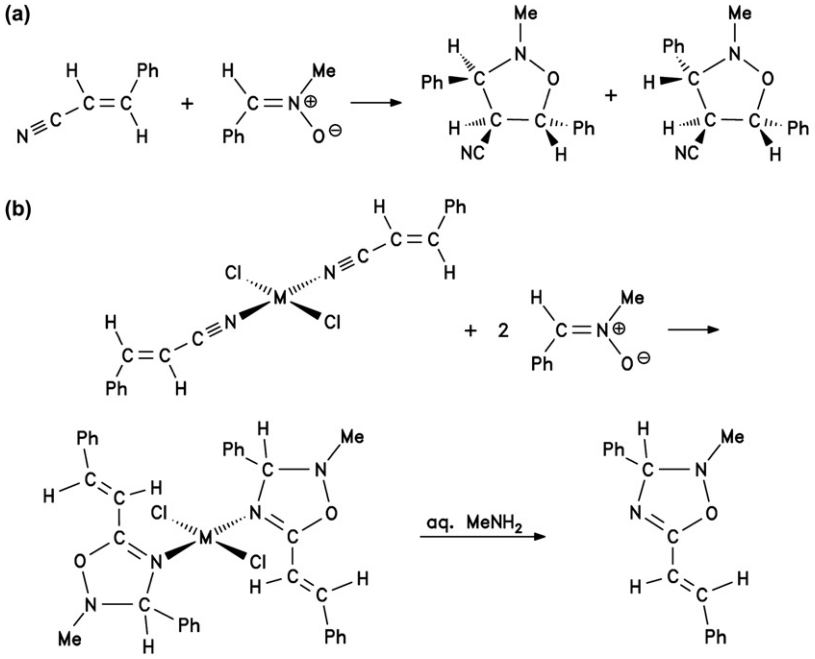


Scheme 1. Experimental results of the [2+3] cycloaddition of nitrones to free or transition metal-bound cinnamonitrile (M=Pt(II), Pd(II)).[11]

reactivity of (*E*)-cinnamonitrile bearing both functional groups conjugated to each other. In this case, one expects a competition between the two different mechanisms, classical C=C activation via Lewis acid coordination to the conjugated functional group, and enhanced reactivity of the C≡N bond due to stabilization of the resulting product by the Lewis acid. In the synthetic experiment,[11] the purely organic reaction produced two diastereomeric isoxazolines as a result of cycloaddition to the C=C bond, whereas platinum- or palladium-coordinated cinnamonitrile reacted exclusively at the C≡N bond. The presence of the Lewis acid thus switches the chemoselectivity of the reaction (see Scheme 1). The present work now aims to explain and understand these experimental results, in particular the observed chemoselectivity and the effect of the Lewis acid transition metal, using quantum mechanical calculations.

2. Computational details

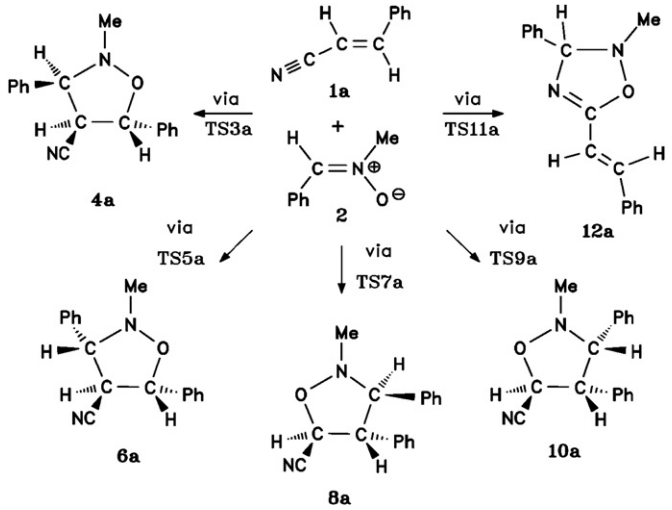
Calculations were performed with GAUSSIAN98[12] (DFT) and the PC GAMESS version[13] of the GAMESS(US)[14] quantum chemistry package (HF and MP). Results were visualised with MOLDEN,[15] MOLEKEL,[16] and PLATON.[17] Full geometry optimizations were performed at HF, MP2 and B3LYP levels of theory, using the standard basis sets LANL2DZ for platinum and 6-31G*[18] for all other atoms. Additionally, single point energies were calculated for the structures obtained from the HF/6-31G* geometry optimization using MP2/6-31G*, MP3/6-31G* and MP4/6-31G*. The geometries optimised with B3LYP/6-31G* were used for single point calculations with MP2/6-31G*, MP3/6-31G* and MP4/6-31G*, and also the different DFT approaches SVWN/6-31G*, SLYP/6-31*, BVWN/6-31*, BP86/6-31*, O3LYP/6-31G*, mPW1PW91/6-31G* and PBE1PBE/6-31G*. The influence of the basis set was studied by single point energy calculations with B3LYP/6-311+G(d,p) and MP3/6-311+G(d,p).

Harmonic vibrational frequencies were computed for all stationary points in order to characterise them as local minima (no imaginary frequency found) or transition states (only one imaginary frequency exists). The vibration associated with the imaginary frequency was found consistent with the ring formation in all cases. Reaction pathways were traced from the transition states towards both reactant and product direction along the imaginary mode of vibration using the algorithm developed by González and Schlegel.[19] All transition states were found to connect reactants and products correctly.

The topological analysis of the charge density was performed with the program MORPHY.[20] Critical points were located by using the eigenvector following method as implemented in the program.[21] The respective wave function input files were generated by GAMESS(US) from single point calculations (MP3/6-31G*//B3LYP/6-31G* and MP3/6-311+G(d,p)//B3LYP/6-31G*). AIM atomic charges were calculated by integration over the atomic basins using the algorithm implemented in MORPHY.[20,22] Natural population analysis (NPA) charges and bond orders were obtained from NBO Version 3.1[23] as implemented in Gaussian 03.

3. Results and discussion

Due to the known dependence of the reactivity on the substituents present in the substrate, the organic reaction was calculated in full rather than as a model system, to keep as close as possible to the experiment. BF_3 was used as a model Lewis acid to reduce the computational effort involved in the calculation of transition metal species, and the corresponding platinum-coordinated species with the $PtCl_2(MeCN)$ fragment as



Scheme 2. Calculated species in the [2+3] cycloaddition of nitrone **2** to uncoordinated cinnamonitrile **1a**.

the Lewis acid was then calculated for comparison. This was expected to show whether the experimentally observed effect can be explained as general Lewis acid activation or whether specific transition metal interactions play a role.

3.1. Cycloaddition of N-methyl-C-phenyl-nitrone to (E)-cinnamonitrile

The starting materials **1a**, **2** and all possible isomeric products **4a**, **6a**, **8a**, **10a**, and **12a**, shown in Scheme 2, were geometry optimised using the HF/6-31G*, MP2/6-31G* and B3LYP/6-31G* methods, and the relative energies of the products were compared (Table 1).

The order of thermodynamic stability of the four isomeric cycloaddition products to the C=C bond follows an order: **6a**>**8a**>**4a**>**10a**, irrespective of the computational method used. However, the energetic position of the cycloadduct to the C≡N bond (**12a**) within this series depends strongly on the computational approach. HF predicts **12a** to be less stable than the C=C adduct **8a** but more stable than **4a**, and MP2 positions it in between **4a** and **10a**. B3LYP, in contrast, seems to overestimate the stability of **12a** and predicts it as the thermodynamically preferred product. Also the relative energy values deviate considerably. The HF and MP2 energies are of an order of −18.6 to −29.7 kcal/mol, but the B3LYP energies are consistently higher, ranging from +4.5 to −13.1 kcal/mol. Again, as shown previously for a similar cycloaddition of benzonitrile oxide to a nitrile, alkyne and alkene,[9] B3LYP calculations of cycloadditions of dipolar reagents to different types of dipolarophiles seem to be not fully comparable with each other, whereas cycloaddition to the same functional group appears to give consistent results.

The large deviation in the energy values and the contradicting results with respect to the relative position of the nitrile cycloadduct among the alkene cycloadducts prompted us to investigate the influence of the computational method in more detail. Firstly, both HF and B3LYP geometries were used for single point calculations on MP2/6-31G*, MP3/6-31G*, and MP4/6-31G* levels of theory, for the purpose of studying

Table 1
Relative energies (kcal/mol) for the reactions of *N*-methyl-*C*-phenyl-nitrone **2** with *E*-cinnamonitrile **1a**

Reaction	HF/6-31G*// HF/6-31G*		MP2/6-31G*// HF/6-31G*		MP3/6-31G*// HF/6-31G*		MP4/6-31G*// HF/6-31G*		MP2/6-31G*// MP2/6-31G*		B3LYP/6-31G*// B3LYP/6-31G*	
	TS	Product	TS	Product	TS	Product	TS	Product	TS	Product	TS	Product
1a+2→4a	+35.4	−18.6	+10.2	−24.2	+19.6	−25.1	+18.8	−23.4	+6.5	−23.6	+23.3	−2.6
1a+2→6a	+32.0	−26.8	+4.8	−30.3	+15.2	−31.8	+14.3	−29.9	+2.0	−29.7	+19.7	−8.5
1a+2→8a	+41.0	−24.1	+5.5	−28.5	+19.0	−29.6	+18.9	−27.8	+2.0	−28.2	+24.4	−6.3
1a+2→10a	+41.9	−10.8	+5.2	−19.0	+19.5	−19.0	+19.2	−17.4	+0.5	−19.4	+24.7	+4.5
1a+2→12a	+33.9	−22.4	+11.7	−21.9	+19.3	−26.5	+18.5	−22.5	+12.6	−19.8	+20.4	−13.1

Reaction	MP2/6-31G*// B3LYP/6-31G*		MP3/6-31G*// B3LYP/6-31G*		MP4/6-31G*// B3LYP/6-31G*		B3LYP/6-311+ G**// B3LYP/6-31G*		MP3/6-311+G**// B3LYP/6-31G*		PBE1PBE/6-31G*// B3LYP/6-31G*	
	TS	Product	TS	Product	TS	Product	TS	Product	TS	Product	TS	Product
1a+2→4a	+8.4	−23.3	+18.7	−25.4	+17.7	−23.4	+27.1	+0.7	+16.6	−27.4	+16.5	−17.5
1a+2→6a	+3.8	−29.3	+14.4	−31.8	+13.8	−29.8	+22.9	−5.7	+12.0	−33.6	+12.6	−23.0
1a+2→8a	+4.0	−27.7	+17.9	−29.7	+18.1	−27.9	+28.0	−3.1	+15.4	−31.9	+17.0	−20.8
1a+2→10a	+3.5	−18.5	+18.5	−19.4	+18.4	−17.7	+28.6	+7.9	+15.5	−22.1	+17.5	−10.5
1a+2→12a	+12.7	−20.0	+20.0	−26.2	+19.1	−21.8	+23.8	−8.7	+19.2	−28.4	+15.0	−26.4

Reaction	SVWN/6-31G*// B3LYP/6-31G*		SLYP/6-31G*// B3LYP/6-31G*		BVWN/6-31G*// B3LYP/6-31G*		BP86/6-31G**// B3LYP/6-31G*		O3LYP/6-31G*// B3LYP/6-31G*		mPW1PW91/6-31G*// B3LYP/6-31G*	
	TS	Product	TS	Product	TS	Product	TS	Product	TS	Product	TS	Product
1a+2→4a	+0.3	−26.6	−9.9	−37.8	+32.5	+14.6	+18.6	−4.0	+28.0	−0.2	+18.4	−15.2
1a+2→6a	−3.5	−30.2	−13.3	−40.6	+28.7	+8.0	+14.8	−9.2	+24.0	−7.0	+14.6	−20.9
1a+2→8a	−0.1	−28.2	−10.2	−38.7	+33.1	+10.2	+18.6	−7.3	+28.1	−4.7	+19.1	−18.7
1a+2→10a	−0.2	−10.5	−10.6	−32.2	+33.7	+21.5	+19.0	+2.6	+29.2	−7.6	+19.6	−8.1
1a+2→12a	−2.0	−39.4	−11.3	−49.9	+27.9	+2.0	+15.2	−16.0	+24.4	−12.7	+16.5	−24.5

Relative energy of dipolarophile+dipole=0 kcal/mol.

the effect of dynamic electron correlation estimated through second and higher order perturbation theory. The starting geometry has only minor influence, and the MP2/6-31G* single point energies are in good agreement with the ones obtained from the rather demanding full geometry optimization using MP2/6-31G*. With MP3/6-31G* and MP4/6-31G*, the C=C cycloadducts **4a**, **6a**, **8a** and **10a** are within 1–2 kcal/mol compatible with the MP2 results. Also the MP4 energy of the CN adduct **12a** agrees well with MP2. MP3 predicts this compound to be 5 kcal/mol more stable, but the stability order of **6a**>**8a**>**12a** is still unchanged.

The influence of the basis set was analyzed by comparing B3LYP/6-311+G(d,p) and MP3/6-311+G(d,p) single point calculations on the B3LYP/6-31G* geometry with the corresponding calculations using the 6-31G* basis set. The relative energies are in good agreement, and the products are predicted 2–4 kcal/mol less (B3LYP), or 2 kcal/mol more stable (MP3).

The B3LYP geometry optimised structures were subjected to single point calculations with several 'first generation' DFT approaches, with the aim to separately study the effect of gradient corrections to correlation and exchange, as well as the effect of HF exchange. From these calculations, one would not expect accurate energy values, but the relative stabilities might show whether one of these correction terms can be identified as responsible for the discrepancies. The LDA functional SVWN gives relative energies for the C=C adducts similar to HF, but the CN adduct is predicted to be significantly more stable, like B3LYP. Adding gradient correction to correlation in SLYP lowers the relative energy of all products by approx. 10 kcal/mol without changing their order of stability. Gradient correction to exchange, considered in BVWN, has the opposite effect and strongly destabilises all products. BP86 as a GGA functional with gradient corrections to both correlation and exchange performs quite similar to the hybrid functional B3LYP, and the relative energy values agree well within 3 kcal/mol.

Among the modern DFT methods, the hybrid functionals O3LYP (using the OPTX exchange functional),[24] mPW1PW91[25] and PBE1PBE[26] were chosen. O3LYP performs similarly to B3LYP, but the other two methods seem to be in slightly better agreement with the MP methods, and their relative energies occupy an intermediate position between HF/MP and B3LYP or BP86. The stability trend, however, is the same as with all other DFT methods, but the CN adduct **12a** is only 3.4 kcal/mol more stable than the lowest energy C=C adduct **6a**, compared to other DFT methods where the difference was larger (4.6 kcal/mol with B3LYP, 10 kcal/mol with lower level DFT methods). Other DFT methods such as MPW1K[27] have been recommended for cycloaddition reactions. We have not used these here because the reported energy differences to B3LYP were small.

In summary, all HF and MP methods give consistent values for the relative energies of the products. They appear compatible with the experiment in that the observed C=C addition product **6a** is predicted to be thermodynamically most stable. The DFT methods scatter more widely with respect to the relative energy values. The stability trends, however, are consistent among all DFT methods used. In contrast to HF and MP, DFT predicts the CN adduct **12a** as the thermodynamically most stable product. This is only compatible with the experiment if the reaction was not thermodynamically controlled. Without experimental energy values for comparison it is difficult to assess, which computational approach gives the more accurate result. Still, one would not expect such a large discrepancy for energy minimum structures containing only first and second row main group atoms.

To evaluate the kinetic aspects of the reaction, the transition states for all pathways shown in Scheme 2 were localised and validated by analysis of their imaginary vibrational frequency and their relaxation towards the reactants or products. Their HF structures and relevant bond distances are shown in Figure 1, the corresponding values for the B3LYP transition states are given in parenthesis. All reactions occur in a concerted manner via comparatively early transition states. The bond formation is slightly asynchronous, with the O–C bond being more advanced in all cases. Compared to the HF geometries, the B3LYP transition states are more synchronous whereas the MP2 geometries occupy an intermediate situation.

MP2 gives the expected underestimation of the activation barriers, whereas HF clearly overestimates them. MP3, MP4, BP86, mPW1PW91 and PBE1PBE predict activation energies of 14–20 kcal/mol, which is a plausible range for a reaction that requires 60 °C to take place. The B3LYP values are typically 5–6 kcal/mol higher. The lower level DFT methods perform very badly with respect to energy values for transition states, as expected, but the order is reproduced in close agreement with B3LYP and BP86.

Except for MP2, the activation barrier leading to the C=C addition product **6a** via **TS5a** is always lowest, independent,

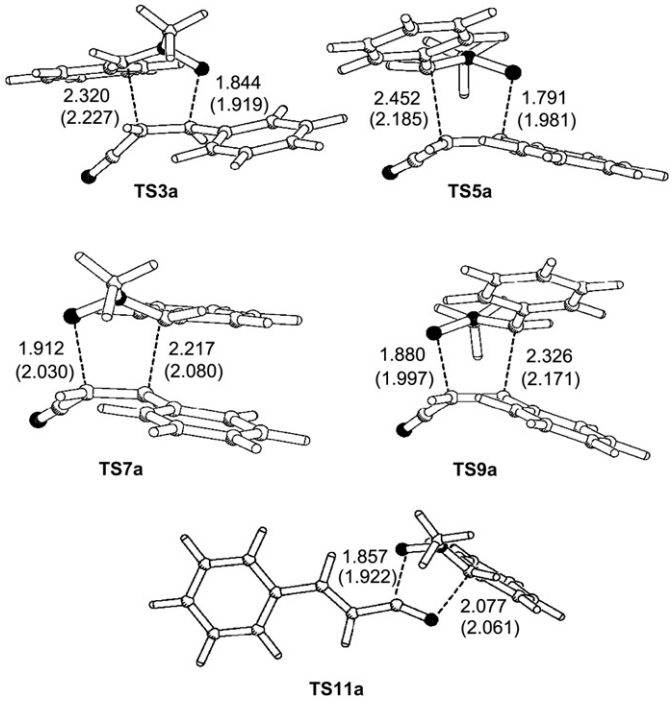


Figure 1. Transition states in the reaction of nitrone **2** with uncoordinated cinnamonitrile **1a**. Relevant bond distances (Å) are stated for the HF geometry, B3LYP values are given in parenthesis.

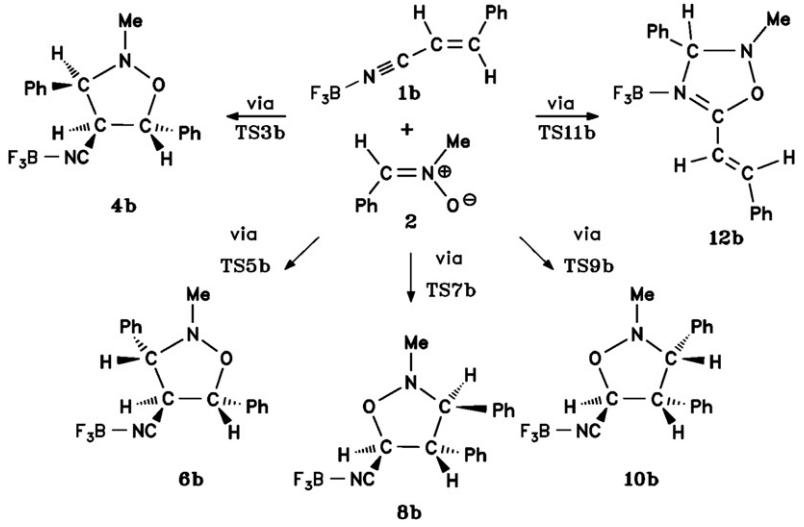
which DFT or higher order Møller–Plesset method was used. This is in clear agreement with the experiment where **6a** was one of the observed products. The formation of the by-product **4a**, however, is more difficult to motivate because its relative activation energy depends on the computational method. All DFT methods used consistently rank **TS3a** leading to **4a** as second most favourable, which is in agreement with the experiment. All MP methods predict very similar activation barriers for the formation of **4a**, **8a** and **10a**, so that no clear decision can be made. On the other hand, the MP methods seem to perform far better than HF or DFT with respect to the relative position of the transition state **TS11a** leading to C≡N addition. HF and most DFT methods do not discriminate clearly between **TS5a** and **TS11a**, and the two activation energies typically differ by less than 1 kcal/mol. This would hardly be enough to explain the experimental selectivity in favour of C=C addition. Compared to this, MP2 predicts a more drastic difference of 6–8 kcal/mol. MP3 and MP4 give intermediate values of 4–5 kcal/mol, which appear more in agreement with the experiment. Among the DFT methods, PBE1PBE and mPW1PW91 come closest to the MP results with an activation energy difference between **TS5a** and **TS11a** of approx. 2 kcal/mol.

In an attempt to analyze solvent effects, B3LYP/6-31G* single point calculations were performed using the Kirkwood–Onsager model,[28] which places the solute in a spherical cavity within the solvent reaction field. A dielectric constant of 8.93 (CH_2Cl_2) and a solute radius of 6.0 Å was used for all transition states. The results have to be interpreted with care since most of the transition states, in particular **TS11a**, deviate strongly from a spherical shape. The solvent effect was assessed by looking at the activation energy differences relative to the preferred **TS5a**. For **TS3a**, the relative activation energy decreases by 0.1 kcal/mol, whereas there is an increase by 0.6, 0.5 and 0.3 kcal/mol for **TS7a**, **TS9a** and the **TS11a** leading to C≡N addition. Although the effects are very small, a polar solvent tends to favour the formation of the observed regioisomeric C=C adducts **4a** and **6a**, whereas formation of the regioisomers **8a** and **10a** becomes less favourable. The activation energy for reaction at the C≡N bond, however, is still unrealistically close to the one for C=C addition.

3.2. Cycloaddition to BF_3- and platinum-coordinated (*E*)-cinnamonitrile

BF_3-coordinated (*E*)-cinnamonitrile **1b**, the BF_3-coordinated cycloaddition products **4b**, **6b**, **8b**, **10b**, and **12b**, as well as the transition states leading to these products were geometry optimised with HF/6-31G* and B3LYP/6-31G*, and their relative energy was compared with single point calculations obtained with MP2/6-31G*//HF/6-31G* and MP3/6-31G*//B3LYP/6-31G* (see Scheme 3 and Table 2). The relative energies of the uncoordinated compounds **4a**, **6a**, **8a** and **10a** and their BF_3-coordinated counterparts **4b**, **6b**, **8b** and **10b** are practically the same. The presence of the Lewis acid neither stabilises these products nor changes the thermodynamics of the cycloaddition to the C=C bond. The product of C≡N addition, however, is far more stable in its coordinated state **12b**. Depending on the computational method, the difference in relative energy between **12a** and **12b** is 15–20 kcal/mol, hence formation of **12b** becomes thermodynamically clearly preferred over the formation of the C=C cycloadducts.

Also with respect to the relative activation energies and transition state geometries (Fig. 2), the HF, B3LYP and MP3 results are quite consistent, although the numerical values vary strongly. Overall, the energy values obtained with B3LYP seem to be in best agreement with the experiment. The cycloaddition to the C=C bond still occurs in a concerted but less synchronous manner. In the formation of **4b** and **6b** via **TS3b** and **TS5b**, the C–O bond is more advanced than the C–C bond. In the case of the regioisomers **8b** and **10b**, this effect is less pronounced. The activation barriers for the C=C attack are 2–10 kcal/mol lower than in the uncatalysed case, indicating that the Lewis acid activates the C=C bond. The order of activation energy is the same as for the uncatalysed reaction. **TS3b** and **TS5b** benefit more from the Lewis acid activation



Scheme 3. Calculated species in the [2+3] cycloaddition of nitrone **2** to BF_3-coordinated cinnamonitrile **1b**.

Table 2
Relative energies (kcal/mol) for the reactions of *N*-methyl-*C*-phenyl-nitrone **2** with BF_3-coordinated (*E*)-cinnamonitrile **1b**

Reaction	HF/6-31G*//HF/6-31G*		MP2/6-31G*//HF/6-31G*		B3LYP/6-31G*//B3LYP/6-31G*		MP3/6-31G*//B3LYP/6-31G*	
	TS	Product	TS	Product	TS	Product	TS	Product
1b+2→4b	+25.2	−18.7	+6.1	−25.2	+17.4	−3.6	+10.3	−26.8
1b+2→6b	+20.1	−26.5	+0.04	−30.2	+12.6	−8.1	+5.2	−31.6
1b+2→8b	+40.5	−23.9	+4.3	−28.5	+22.4	−6.5	+23.1	−30.7
1b+2→10b	+41.4	−16.2	+3.7	−22.6	+21.4	+0.9	+13.7	−23.2
1b+2→12b	+8.9	−36.9	+3.8	−42.6	+6.6	−28.5	+2.2	−45.2
1c+2→4c					+23.9	−1.4	+11.2	−28.3
1c+2→6c					+18.9	−6.2	+6.4	−39.4
1c+2→8c					+27.6	−3.0	+18.1	−29.6
1c+2→10c					+27.4	+3.4	+14.9	−23.2
1c+2→12c					+11.3	−21.6	+0.9	−44.5

Relative energy of dipolarophile+dipole=0 kcal/mol.

than **TS7b** and **TS10b**, so the regioselectivity would be expected even more pronounced than in the uncatalysed case, if the cycloaddition did in fact occur at the C=C bond. So far, the Lewis acid activation mechanism resembles closely that of other cycloadditions to conjugated C=C bonds, as, for example, the Diels–Alder reaction of methyl cinnamate with cyclopentadiene,[29] the reaction of butadiene with acrolein,[30] or the addition of nitrones to electron deficient alkenes.[31]

In the presence of the Lewis acid, the formation of the C≡N cycloadduct occurs via a mechanism that is very close to a two-step reaction, as described previously for the reaction of nitrones with acetonitrile.[8] The activation barrier is significantly lower than in the uncatalysed case (order 14–18 kcal/mol), and this leads to a high preference for this pathway also from a kinetic point of view. Overall, Lewis acids have been frequently used to accelerate cycloaddition reactions, and to direct their regio- and stereochemistry.[10] The present case is one of the rare ones where the Lewis acid can be used to alter the chemoselectivity to induce a reaction at an otherwise unreactive functional group in the presence of a more reactive one.

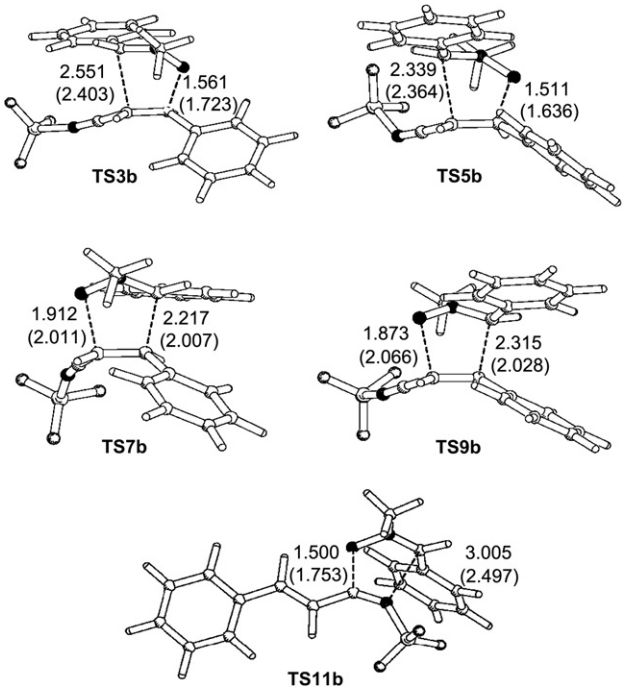


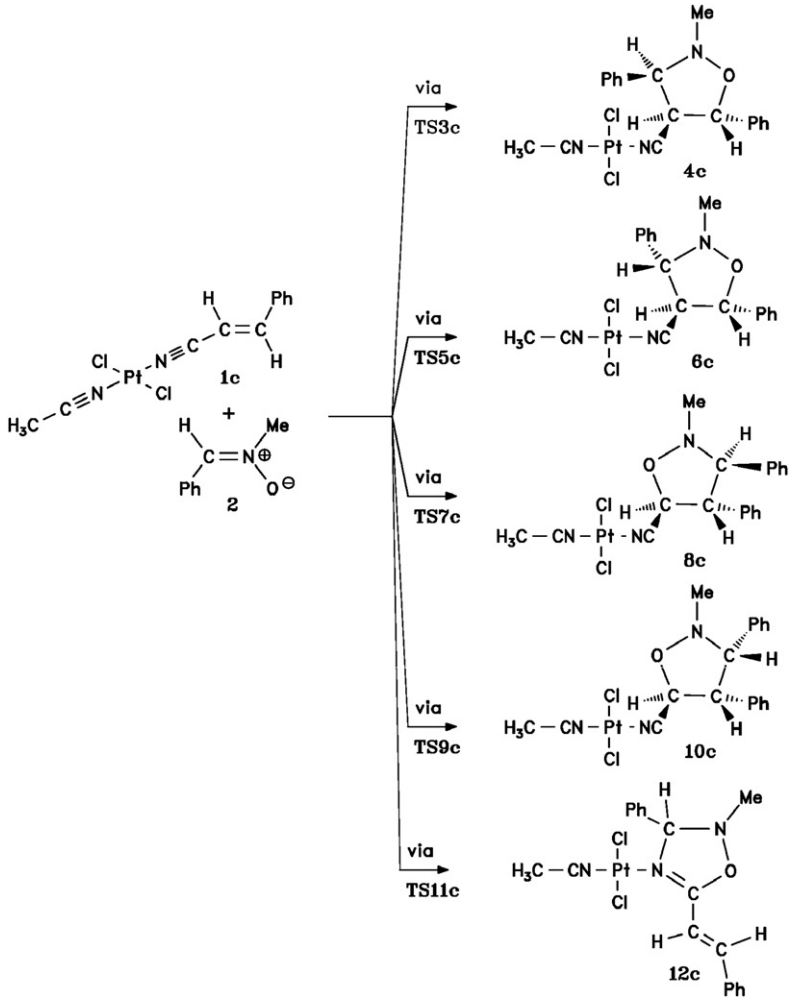
Figure 2. Transition states in the reaction of nitrone **2** with BF_3-coordinated cinnamonitrile **1b**. Relevant bond distances (Å) are stated for the HF geometry, B3LYP values are given in parenthesis.

The results obtained with BF_3 coordination suggest that Lewis acidity might be sufficient to explain the experimental effect observed with Pt coordinated species. To confirm this hypothesis, the reaction of nitrone **2** with the cinnamonitrile ligand in the platinum complex **1c** was calculated, and the pathways leading to the C=C cycloadducts **4c**, **6c**, **8c**, **10c** and the nitrile addition product **12c** were considered (see Scheme 4).

The relative product energies and activation barriers show same trend as in the case of BF_3 coordination, and also the numerical values of the energy values match fairly well. The transition states **TS3c** and **TS5c**, shown in Figure 3, are slightly more synchronous than the ones observed with BF_3, but otherwise their geometries are in very close agreement. Similar results have been obtained previously for the transition states of nitrone addition to acetonitrile coordinated to BF_3 or the $PtCl_2$(MeCN) fragment.[8,32] This suggests that BF_3 can indeed be used to model the platinum centre in this type of reactions.

3.3. Orbital involvement

If the addition to the C=C or C≡N bond involved the same cinnamonitrile FMO orbital, one should expect the Lewis acid to promote both reactions to a similar extent, and a change of chemoselectivity would be difficult to motivate. We therefore analyzed the relevant molecular orbitals of free and BF_3-coordinated (*E*)-cinnamonitrile with a π-contribution at the C=C or the C≡N bond, shown in Figure 4, together with the corresponding orbital energies obtained from HF/6-31G* calculations. MP2/6-31G* orbital energies are given in parenthesis, Kohn–Sham orbital energies from B3LYP/6-31G* calculations are in square brackets. The HOMO/LUMO pair is orthogonal to the plane of the phenyl ring and delocalised over the entire molecule. In terms of symmetry, it is suited for cycloaddition to the C=C bond but unsuited for reaction at the nitrile because of the nodal plane passing through the nitrile carbon. The next lower occupied orbital (HOMO−1) and the next higher unoccupied



Scheme 4. Calculated species in the [2+3] cycloaddition of nitrone **2** to platinum-coordinated cinnamonitrile **1c**.

orbital (LUMO+1) are located at the aromatic ring and irrelevant to cycloadditions. The HOMO−2/LUMO+2 pair is again orthogonal to the phenyl plane and delocalised, but its symmetry makes it suited for cycloadditions at the C═C or the C≡N bond. The HOMO−3/LUMO+3 orbital pair has its major contribution at the nitrile and is in plane with the aromatic ring. It has the correct symmetry for reaction at the C≡N moiety.

The transition state geometries for cycloaddition to the C═C bond (**TS3a**, **TS5a**, **TS7a** and **TS9a**) reveal that the nitrone, in all cases, approximates from a direction orthogonal to the plane through the alkene moiety of the cinnamonitrile, as expected. The C−O bond forms at a slightly earlier stage than the C−C bond, indicating that the reaction is initiated by a nucleophilic attack of the nitrone oxygen. The relevant orbital interaction therefore involves an occupied orbital at the nitrone (HOMO) and an unoccupied orbital at the cinnamonitrile, which is most likely the LUMO, although the LUMO+2 cannot be excluded on the basis of transition state geometry consideration.

Cycloaddition to the nitrile occurs via the transition state **TS11a**. The C−O bond is more advanced than the C−N bond, and the reaction is also dominated by an interaction of an occupied orbital at the nitrone with an unoccupied orbital at the cinnamonitrile. The nitrone, however, approaches the nitrile from a direction *orthogonal* to the one in the reaction with the alkene. This clearly suggests involvement of different orbitals for the two reactions, and the only suitable orbital compatible with the direction of attack of the nitrone at the C≡N bond is the LUMO+3. This orbital is energetically less favourable and interaction with the nitrone HOMO is expected to lead to a smaller overlap. The approach of the reagent to LUMO+3 also appears more difficult because of potential steric interaction with the C═C bond of the cinnamonitrile. On the other hand, use of the LUMO+3 for the bond formation does not disturb the extended conjugated π system during the reaction. Overall, the choice of the interacting orbitals appears to depend on a delicate balance between all energetic contributions.

The Lewis acid mediated reactions show the same effect, and comparison of the BF_3-coordinated transition states **TS3b**, **TS5b**, **TS7b** or **TS9b** versus **TS11b** or the platinum species **TS3c**, **TS5c**, **TS7c** or **TS9c** versus **TS11c**, confirms that the reaction at the C═C or C≡N bond involves different orbitals of the cinnamonitrile since the attack of the nitrone at these two groups occurs from orthogonal directions. The presence of the Lewis acid does not change the orbital coefficients to

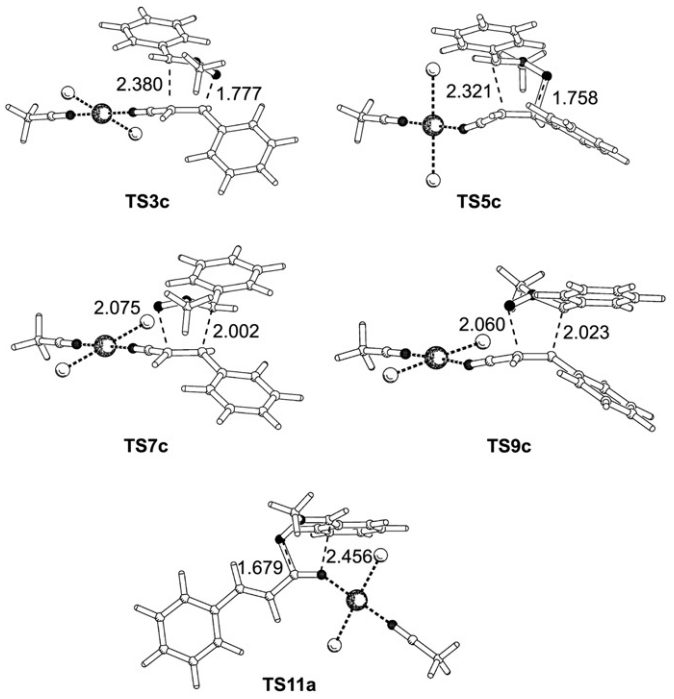


Figure 3. Transition states in the reaction of nitrone **2** with the platinum-coordinated cinnamonitrile **1c**. Relevant bond distances (Å) are stated for the B3LYP geometry.

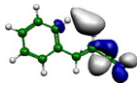
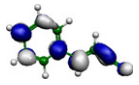
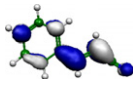
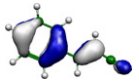
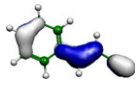
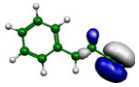
Orbital		*E* in **1a** (eV)	*E* in **1b** (eV)
LUMO+3		5.6 (5.4) [1.0]	5.2 (4.1) [–0.2]
LUMO+2		4.9 (4.6) [0.5]	4.7 (4.0) [–0.4]
LUMO		1.7 (1.6) [–2.2]	1.5 (0.7) [–2.9]
HOMO		–8.8 (–8.8) [–6.6]	–9.1 (–9.4) [–7.3]
HOMO-2		–11.4 (–11.1) [–8.4]	–11.7 (–12.1) [–8.9]
HOMO-3		–12.6 (–12.2) [–8.8]	–13.2 (–13.8) [–9.2]

Figure 4. Relevant orbitals and HF/6-31G* orbital energies of free and BF_3-coordinated *E*-cinnamonitrile **1a** and **1b** (MP2/6-31G* values are given in parenthesis, B3LYP/6-31G* values in square brackets).

any significant extent. However, the orbital energies are lowered, and the HOMO−3/LUMO+3 pair is affected to a larger extent than the FMO or FMO±2 orbitals. The activation of the C≡N is thus expected to be stronger and this favours an inversion of the selectivity of the reaction towards formation of the oxadiazoline.

Interactions with non-FMOs seem to be comparatively common in cycloadditions involving triple bonds with non-degenerated π systems, as, for example, in the reaction of nitrones with benzonitrile,[8] benzonitrile oxide with carbon−carbon or carbon−hetero multiple bonds,[9a] or phenylazide with alkenes.[33] However, there are also cases where FMO interaction is preferred, as in the reaction of mesitonitrile oxide with alkynes,[34] or the Lewis acid mediated variant of the above mentioned cycloaddition of benzonitrile oxide with carbon−carbon or carbon−hetero multiple bonds.[9b] In these cases, the approach of the reagent to the non-FMO is sterically hindered, and interaction with the FMO seems to be accepted as the second best choice. Analysis of this effect and its influence on the reactivity and selectivity of cycloadditions did not receive overly much attention so far.

3.4. Charge density and distribution in free and coordinated cinnamonitrile

To study the nature of the activating effect of the Lewis acid in more detail, the topology of the charge density in free and BF_3-coordinated cinnamonitrile was examined, by using the theory of 'Atoms in Molecules' (AIM) introduced by Bader.[35] The charge densities of relevant bond critical points of *trans*-cinnamonitrile **1a** and its BF_3-adduct **1b** are given in Table 3. The ρ_{BCP} values for C−C, C=C and C≡N bonds are in the normal range expected for these types of bonds.[35] The N−B bond is relatively weak with a ρ_{BCP} of only 0.066 a.u., however, this value is in good agreement with the one found previously for MeCN−BF_3.[9b,36] Compared to other boron coordinated species,[37] the N−B bond in nitrile complexes is best characterised as electrostatic interaction with partial covalent contribution. The charge transfer from the Lewis base to the Lewis acid moiety was determined to be 0.094 a.u. (AIM charges), as compared to 0.197 a.u. based on NPA charges,[23] respectively. As expected, these values are lower than the ones found for the strong Lewis acid adduct between BF_3 and ammonia (0.011−0.13 a.u. (AIM) or 0.27−0.33 a.u. (NPA), depending on the basis set used).[38] Comparison of the charge densities of bonds in coordinated and free cinnamonitrile reveals that the Lewis acid withdraws more electron density from the C≡N bond than from the C=C bond, suggesting a stronger activation of the C≡N bond. This is further confirmed from the atomic charges and bond orders. The atom−atom net linear NLMO/NPA bond order[23] of the C=C bond decreases only slightly upon BF_3 coordination whereas the C≡N bond weakens drastically. Both AIM and NPA atomic charges change considerably at the C≡N bond, leaving the N1 atom with a higher negative charge whereas the C2 atom becomes significantly more positive. The C≡N bond is strongly polarised upon BF_3 coordination, which motivates the tendency towards a two-step cycloaddition induced by nucleophilic attack at the C2 atom, and the increased reactivity. The charges at the carbons of the C=C bond, in contrast, are only weakly affected by the presence of the Lewis acid, resulting in a weaker activation and a less pronounced asynchronicity.

Table 3
Charge densities ρ (a.u.) of relevant bond critical points, NLMO bond orders, and atomic charges q (a.u.) of selected bonds and atoms of *trans*-cinnamonitrile **1a**, its BF_3-adduct **1b** and the complex *trans*-$PtCl_2$(MeCN)(*trans*-cinnamonitrile) **1c**

	Ph–C	C=C	C–C	C≡N	N–B/N–Pt
ρ_{BCP} (MP3/6-31G*)[a]					
ρ(**1a**)	0.28786	0.34297	0.29291	0.46476	—
ρ(**1b**)	0.29056	0.34099	0.29188	0.46037	0.06604
ρ(**1c**)	0.29030	0.34023	0.29308	0.45213	0.11999
$\Delta\rho=\rho$(**1b**)$-\rho$(**1a**)	0.00270	−0.00198	−0.00103	**−0.00439**	(0.06604)
$\Delta\rho=\rho$(**1c**)$-\rho$(**1a**)	0.00244	−0.00274	0.00017	**−0.01263**	(0.11999)
ρ_{BCP} (MP3/6-311+G**)[a]					
ρ(**1a**)	0.28576	0.33946	0.28962	0.47063	—
ρ(**1b**)	0.28830	0.33745	0.28811	0.46490	0.06680
$\Delta\rho=\rho$(**1b**)$-\rho$(**1a**)	0.00254	−0.00201	−0.00151	**−0.00573**	(0.06680)
NLMO bond orders					
b(**1a**)	1.0470	1.7885	1.0552	2.5988	—
b(**1b**)	1.0664	1.7063	1.0574	2.3125	0.2043
b(**1c**)	1.0636	1.7050	1.0654	2.2705	0.2538
$\Delta b=b$(**1b**)$-b$(**1a**)	0.0194	−0.0822	0.0022	**−0.2863**	(0.2043)
$\Delta b=b$(**1c**)$-b$(**1a**)	0.0166	−0.0835	0.0102	**−0.3283**	(0.2538)

	Ph, C_{ipso}	C4	C3	C2	N1	B/Pt
AIM (MP3/6-31G*)[a]						
q(**1a**)	0.0164	0.0171	−0.1241	1.0721	−1.4475	—
q(**1b**)	0.0227	0.0254	−0.1955	1.0836	−1.5630	2.5815
$\Delta q=q$(**1b**)$-q$(**1a**)	0.0063	0.0083	−0.0714	0.0115	**−0.1155**	(2.5815)
NPA (MP3/6-31G*)[a]						
q(**1a**)	−0.10867	−0.09266	−0.36195	0.30864	−0.36823	—
q(**1b**)	−0.13323	−0.03422	−0.41654	0.53310	−0.45755	1.57005
q(**1c**)	−0.13051	−0.03572	−0.41666	0.53357	−0.46999	0.96792
$\Delta q=q$(**1b**)$-q$(**1a**)	−0.02456	0.05844	−0.05459	**0.22446**	**−0.08932**	(1.57005)
$\Delta q=q$(**1c**)$-q$(**1a**)	−0.02184	0.05694	−0.05471	**0.22493**	**−0.10176**	(0.96792)

[a] From single point calculation performed on the B3LYP/6-31G* geometry.

The charge densities at bond critical points, and also the NLMO bond orders and atomic charges of the Pt–cinnamonitrile complex **1c** show essentially the same trends as in the BF_3-coordinated species, suggesting a similar type of interaction. The $PtCl_2$(MeCN) moiety seems to act as a slightly stronger Lewis acid as the change in electronic properties appear more pronounced than with BF_3. This, however, does not reflect in the energy considerations, which predict the Pt complex to act similarly (MP3) or as a weaker Lewis acid (B3LYP) than BF_3.

4. Concluding remarks

We have shown in this work that the selectivity of the cycloaddition of nitrones to cinnamonitrile can be switched from reaction at the C=C to an exclusive C≡N attack if the cinnamonitrile is coordinated to a Lewis acid, which does not necessarily have to be a platinum species used in the experiment.[11] This change in chemoselectivity is motivated by a number of factors. (i) The cycloaddition to the C=C or C≡N bond involves different activation mechanisms; in the reaction with the C=C bond, the Lewis acid stabilises the reactant and the products to a very similar extent because the functional group attached to the Lewis acid is not altered. The thermodynamic driving force of the reaction is thus relatively unaffected by the Lewis acid. The activation barrier is smaller because the Lewis acid lowers the orbital energies so that the overlap with the orbitals of the nitrone is more efficient. The cycloaddition to the C≡N bond, in contrast, occurs under conversion of the weakly Lewis basic nitrile into an imine, which acts as a stronger Lewis base. As a result, the product is far more stabilised by coordination to the Lewis acid, and this reflects in a significantly enhanced thermodynamic driving force. In addition, the Lewis acid also stabilises the transition states so that the activation barrier is significantly decreased. Overall, the C≡N activation mechanism outperforms the C=C activation pathway. (ii) The cycloaddition to the C=C or C≡N bond involves different molecular orbitals: the Lewis acid induced lowering of the orbital energy is more pronounced for the orbital used for C≡N addition, and much weaker for the one relevant to the reaction with the C=C bond. Hence, C≡N addition is promoted more efficiently than C=C addition. (iii) Lewis acid coordination to the starting material (**1a**) causes larger electronic changes to the C≡N bond, as compared to the weak effect on the C=C bond: the C≡N bond is weakened and becomes strongly polarised, it is therefore easier to attack for the nucleophilic oxygen atom of the nitrone. This also motivates the change from a concerted nearly synchronous C≡N cycloaddition towards an almost two-step reaction and a similar but weaker trend for the reaction at the C=C bond.

Although the reaction studied would appear fairly standard for modern computational techniques, the choice of the

computational method requires care. In particular, the approach to electron correlation seems crucial, and rather high level methods such as MP3 or MP4 are required to achieve convergent results. The basis set dependence is negligible, and the results from 6-31G* calculations are in good agreement with the ones obtained with 6-311+G**. DFT methods, including the commonly used B3LYP, give results that do not fully agree with the experiment. As previously observed for the reactions of acetonitrile, propene and propyne with benzonitrile oxide,[9] a comparison of different dipolarophiles is difficult whereas all trends for the same type of dipolarophile are correctly reproduced.

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References and notes

1. (a) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 565; (b) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 633; (c) *1,3 Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley-Interscience: New York, NY, 1984; Vols. 1–2.
2. (a) Samuilov, Ya. D.; Solov'eva, S. E.; Konovalov, A. I. *Dokl. Akad. Nauk. SSSR Ser. Khim.* **1980**, *255*, 606; (b) Padwa, A.; Kline, D. N.; Koehler, K. F.; Matzinger, M.; Venkatramanan, M. K. *J. Org. Chem.* **1987**, *52*, 3909; (c) Hermkens, P. H. H.; van Maarseveen, J. H.; Kruse, C. G.; Scheeren, H. W. *Tetrahedron* **1988**, *44*, 6491; (d) Eberson, L.; McCullough, J. J.; Hartshorn, C. M.; Hartshorn, M. P. *J. Chem. Soc., Perkin Trans 2* **1998**, 41.
3. (a) Herbst, R. M.; Wilson, K. R. *J. Org. Chem.* **1957**, *22*, 1142; (b) Demko, Z. P.; Sharpless, K. B. *Org. Lett.* **2001**, *3*, 4091.
4. (a) Leandri, G.; Pallotti, M. *Ann. Chim. (Roma)* **1957**, *47*, 376; (b) Huisgen, R.; Mack, W.; Anneser, E. *Tetrahedron Lett.* **1961**, 587.
5. Fischer, B.; Hassner, A. *J. Org. Chem.* **1990**, *55*, 5225.
6. (a) Huisgen, R.; Sturm, H. J.; Binsch, G. *Chem. Ber.* **1964**, *97*, 2864; (b) Armstrong, R. K. *J. Org. Chem.* **1966**, *31*, 618; (c) Doyle, M. P.; Buhro, W. E.; Davidson, J. G.; Elliott, R. C.; Hoekstra, J. W.; Oppenhuizen, M. *J. Org. Chem.* **1980**, *45*, 3657.
7. (a) Wagner, G.; Haukka, M. *J. Chem. Soc., Dalton Trans.* **2001**, 2690; (b) Wagner, G.; Haukka, M.; Fraústo da Silva, J. J. R.; Pombeiro, A. J. P.; Kukushkin, V. Yu. *Inorg. Chem.* **2001**, *40*, 264; (c) Wagner, G.; Pombeiro, A. J. P.; Kukushkin, V. Yu. *J. Am. Chem. Soc.* **2000**, *122*, 3106; (d) Wagner, G. *Inorg. Chim. Acta* **2004**, *357*, 1320; (e) Desai, B.; Danks, T. N.; Wagner, G. *Dalton Trans.* **2004**, 166.
8. Wagner, G. *Chem.—Eur. J.* **2003**, *9*, 1503.
9. (a) Vullo, V.; Danks, T. N.; Wagner, G. *Eur. J. Org. Chem.* **2004**, 2046; (b) Wagner, G.; Danks, T. N.; Vullo, V. *Tetrahedron* **2007**, *63*, 5251.
10. (a) Gothelf, K. V.; Jørgensen, K. A. *Chem. Commun.* **2000**, 1449; (b) Gothelf, K. V.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 863.
11. Desai, B.; Danks, T. N.; Wagner, G. *J. Chem. Soc., Dalton Trans.* **2003**, 2544.
12. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Salvador, P.; Dannenberg, J. J.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *GAUSSIAN*; Pittsburgh, PA, 2001.
13. Granovsky, A. A. http://classic.chem.msu.su/gran/gamess/index.html. See also: Nemukhin, A. V.; Grigorenko, B. L.; Granovsky, A. A. *Moscow Univ. Chem. Bull.* **2004**, *45*, 75.
14. Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. H.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Su, S. J.; Windus, T. L.; Dupuis, M.; Montgomery, J. A. *J. Comput. Chem.* **1993**, *14*, 1347.
15. Schaftenaar, G.; Noordik, J. N. *J. Comput.-Aided Mol. Des.* **2000**, *14*, 123.
16. Flükiger, P.; Lüthi, H. P.; Portmann, S.; Weber, J. *MOLEKEL 4.0*; Swiss Center for Scientific Computing: Manno, Switzerland, 2000.
17. Spek, A. L. http://www.cryst.chem.uu.nl/platon/.
18. (a) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213; (b) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654.
19. González, C.; Schlegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5523.
20. *MORPHY98* a program written by P. L. A. Popelier with a contribution from R. G. A. Bone; UMIST: Manchester, England, EU, 1998.
21. Popelier, P. L. A. *Chem. Phys. Lett.* **1994**, *228*, 160.
22. Popelier, P. L. A. *Comput. Phys. Commun.* **1998**, *108*, 180.
23. (a) Reed, A. E.; Weinhold, F. *J. Chem. Phys.* **1983**, *78*, 4066; (b) Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735; (c) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.
24. Handy, N. C.; Cohen, A. J. *Mol. Phys.* **2001**, *99*, 403.
25. Adamo, C.; Barone, V. *J. Chem. Phys.* **1998**, *108*, 664.
26. Perdew, J. P.; Burke, K.; Ernzerhof, M. *Phys. Rev. Lett.* **1996**, *77*, 3865.
27. (a) Ess, D. H.; Houk, K. N. *J. Phys. Chem.* **2005**, *109*, 9542; (b) Lynch, B. J.; Fast, P. L.; Harris, M.; Truhlar, D. G. *J. Phys. Chem. A* **2000**, *104*, 4811.
28. (a) Kirkwood, J. K. *J. Chem. Phys.* **1934**, *2*, 351; (b) Onsager, L. *J. Am. Chem. Soc.* **1936**, *58*, 1486.
29. Alves, C. N.; Camilo, F. F.; Gruber, J.; da Silva, A. B. F. *Chem. Phys.* **2004**, *306*, 35.
30. Garcia, J. I.; Martinez-Merino, V.; Mayoral, J. A.; Salvatella, L. *J. Am. Chem. Soc.* **1998**, *120*, 2415.
31. Tanaka, J.; Kanemasa, S. *Tetrahedron* **2001**, *57*, 899.
32. Kuznetsov, M. L.; Kukushkin, V. Yu. *J. Org. Chem.* **2006**, *71*, 582.
33. Klicić, J. J.; Friesner, R. A. *J. Phys. Chem.* **1999**, *103*, 1276.
34. Hu, Y. F.; Houk, K. N. *Tetrahedron* **2000**, *56*, 8239.
35. (a) Bader, R. F. W. *Atoms in Molecules: A Quantum Theory*; Clarendon: Oxford, UK, 1990; (b) Bader, R. F. W. *Acc. Chem. Res.* **1985**, *18*, 9; (c) Wiberg, K. B.; Bader, R. F. W.; Lau, C. D. H. *J. Am. Chem. Soc.* **1987**, *109*, 985.
36. Giesen, J. D.; Phillips, J. A. *J. Phys. Chem. A* **2003**, *107*, 4009.
37. Jonas, V.; Frenking, G.; Reetz, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 8741.
38. Szefczyk, B.; Sokalski, W. A.; Leszczynski, J. *J. Chem. Phys.* **2002**, *117*, 6952.