SHORT PAPER

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Ab initio calculation of thermodynamic and kinetic quantities for 1,3-dipolar cycloadditions of benzonitrile oxide with various dipolarophiles[†]

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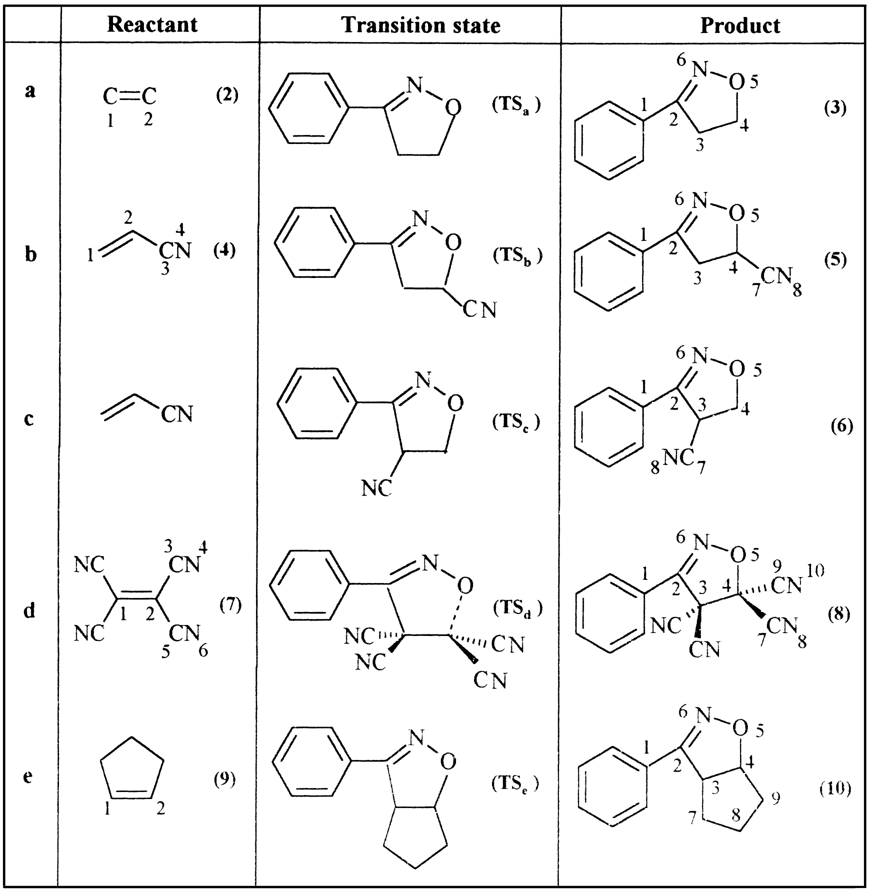
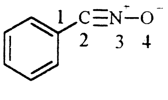
Ab initio molecular orbital calculations have been used to investigate the structures and transition states of 1,3-dipolar cycloadditions between benzonitrile oxide with ethylene, acrylonitrile, tetracyanoethylene and cyclopentene. Geometry optimisations and energy calculations were performed with RHF/6–31*G**//RHF/6–31*G** in each case. Calculation of vibrational frequencies permitted computation of the enthalpies, Gibbs free energies and rate constant of reactions. Cycloadditions of 1,3-dipolar benzonitrile oxide with electron-poor dipolarophiles have higher rates and lower thermodynamic stability than with other dipolarophiles.

Keywords: 1,3-dipolar cycloaddition, regioisomeric cycloadducts

1,3-Dipolar cycloadditions were first studied extensively by Huisgen.[1] The dipoles feature four electrons in three parallel 2p orbitals, similar to the allyl anion, enabling $[\Pi 4_s + \Pi\ 2_s]$ cycloadditions with dipolarophiles, normally alkenes or alkynes. Mechanistic studies have shown that the transition state for 1,3-dipolar cycloaddition is not very polar. The rate of reaction is not strongly sensitive to solvent polarity. Solvent effects on 1,3-dipolar cycloadditions have been less well studied.[2-9] Each 1,3-dipole exhibits a characteristic regioselectivity toward different types of dipolarophile, depending on



Scheme 1 Reaction of reactions **a–e** with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whether the dipolarophile has electron-donating or electron-withdrawing substituents. In addition to the role of subsituents in determining regioselectivity, several other structural features affect the reactivity of dipolarophiles. Strain increases reactivity. Norbornene, for example, is consistently more reactive than cyclohexene in 1,3-dipolar cycloadditions. Conjugated functional groups also usually increase reactivity. This increased reactivity has most often been demonstrated with electron-attracting substituents, but, in the case of some 1,3-dipoles, enamines, enol ethers, and other alkenes with donor substituents are also quite reactive. Huisgen *et al.*[10] considered the relative reactivity of benzonitrile oxide with some dipolarophiles. They showed that electron-poor dipolarophiles have a higher relative reactivity than other dipolarophiles. These results led us to investigate 1,3-dipolar cycloadditions between benzonitrile oxide and ethylene, acrylonitrile and tetracyanoethylene and cyclopentene (Scheme 1).

Reaction with acrylonitrile has two regioisomeric cycloadducts (**5**,**6**) corresponding to junction oxygen atom at benzonitrile oxide to C1 or to C2 in acrylonitrile.

Computational details

The *ab initio* molecular orbital calculations were performed with the GAUSSIAN 98 program.[14] Geometries for all structures were fully optimised by means of analytical energy gradients in Restricted Hartree-Fock calculations with the 6–31*G** basis set. The Synchronous Transit-guided Quasi-Newton (STQN) method is used to located transition structure.

Vibrational frequencies were calculated at the 6–31*G** level for all reactions and transition states, which were confirmed to have zero and one imaginary frequency, respectively. The frequencies were scaled by a factor of 0.8929 and used to compute the zero-point vibrational energies, their thermal corrections and vibrational entropies. This enabled calculation of enthalpies, free energies, entropy changes of reactions and free energy changes of activation at 298 K by equations:

$$\Delta_r H°(298\text{K})=\Sigma(\varepsilon_0+H_{\text{corr}})_{\text{Products}} -(\Sigma(\varepsilon_0+H_{\text{corr}})_{\text{Reactants}}$$

$$\Delta_r G°(298\text{K})=\Sigma(\varepsilon_0+G_{\text{corr}})_{\text{Products}} -(\Sigma(\varepsilon_0+G_{\text{corr}})_{\text{Reactants}}$$

$$\Delta_r S(298\text{K})=\Sigma\, S_{\text{Products}} -\Sigma\, S_{\text{Reactants}}$$

$$\Delta G^{\neq}(298\text{K})=\Sigma(\varepsilon_0+G_{\text{corr}})_{\text{TS}} -(\Sigma(\varepsilon_0+G_{\text{corr}})_{\text{Reactants}}$$

Also, rate constants were calculated with the Eyring equation, derived from transition state theory.[11]

$$k = KT/h \exp (-\Delta G^{\neq} / RT)$$

$\Delta G^{\neq}$ is the free energy difference between transition state and reactants.

Results and discussions

The key geometrical parameters for the reactants, products and transition structures are recorded in Table 1.

Almost synchronous transition states structures are obtained with mean bond length values of 2.17, 2.13, 2.13, 2.06 and 2.20 Å for r_{34} and r_{56}, considering reactions of **a, b, c, d, e** respectively. As presented in Table 1, the bond lengths for r_{23} and r_{45} in TS_c are 2.31 and 1.95 Å respectively. However, in the case of TS_b both bond lengths r_{23} and r_{45} are equal to 2.13 Å. The reason might be due to presence of phenyl group attached to the carbon 2 position in the transition states. Because of steric hindrance due to phenyl and nitrile groups in TS_c, the bond length of r_{23} is greater than r_{45}. For the cycloaddition of benzonitrile oxide and tetracyanoethylene (reaction **d**) the bond lengths for r_{23} and r_{45} for TS_d are 2.47 and 1.64 Å respectively. Comparing both bond lengths in reactions **c** and **d**, it is observed that the bond length in r_{45} in the reaction **d** is shorter than reaction **c** which might be due to the presence of two electron withdrawing nitrile groupings attached to carbon at position 4 in TS_d. Bond length r_{23} in reaction **d** is longer than **c** due to higher steric hinderance in the nitrile groups with the phenyl group.

The computed thermodynamic properties of reactants, products and transition structures in 1,3-dipolar cycloadditions are recorded in Table 2. These properties contain electronic energies, enthalpies, free energies and entropies computed from the vibrational frequencies, and Table 3 lists the computed thermodynamic quantities and rate constants for 1,3-dipolar cycloadditions with benzonitrile oxide as the dipolar reagent.

Comparing the electronic energy, enthalpy and free energy changes of the reactions shows that the relative order of decreasing magnitude of these quantities is as follows: **a**>**e**>**b**>**c**>**d**. Consequently, cycloaddition of 1,3-dipoles with electron-poor dipolarophiles has less thermodynamic stability than for other dipolarophiles. Furthermore, steric hindrance of substituents is effective. But comparing kinetic data, the activation free energy changes and rate constants show that the

Table 1 Key geometrical parameters for the reactants and transition structure[a]

Parameter	1	2	3	4	5	6	7	8	9	10	TS_a	TS_b	TS_c	TS_d	TS_e
r_{12}	1.44	1.32	1.48	1.32	1.48	1.48	1.34	1.48	1.32	1.48	1.46	1.46	1.45	1.42	1.46
r_{23}	1.13	–	1.51	1.44	1.51	1.52	1.44	1.54	1.51	1.51	2.18	2.13	2.31	2.47	2.19
r_{34}	1.21	–	1.53	1.14	1.53	1.53	1.13	1.57	1.55	1.55	1.36	1.37	1.38	1.43	1.37
r_{45}	–	–	1.42	–	1.41	1.41	–	1.39	–	1.42	2.16	2.13	1.95	1.64	2.21
r_{56}	–	–	1.37	–	1.38	1.37	1.13	1.38	–	1.37	1.24	1.23	1.25	1.26	1.24
r_{26}	–	–	1.26	–	1.26	1.26	–	1.26	–	1.26	1.18	1.18	1.17	1.17	1.18
r_{37}	–	–	–	–	–	1.47	–	1.49	–	1.55	–	–	1.44	1.44	1.52
r_{78}	–	–	–	–	1.13	1.13	1.13	1.13	–	1.54	–	1.14	1.14	1.14	1.54
r_{47}	–	–	–	–	1.48	–	–	–	–	–	–	1.44	–	–	–
a_{123}	179.99	–	125.37	122.3	125.07	125.37	–	125.89	112.23	125.51	113.39	114.25	114.72	114.72	112.7
a_{234}	179.99	–	99.1	179.2	98.96	98.57	179.16	96.8	102.89	99.22	100.44	101.54	97.11	97.11	100.34
a_{345}	–	–	104.64	–	104.7	104.3	–	102.41	105.59	105.48	103.14	102.15	106.46	106.46	102.64
a_{265}	–	–	110.75	–	110.44	111.24	–	110.97	–	111.18	137.09	136.98	137.95	137.95	136.73
a_{347}	–	–	–	–	112.01	113.89	–	114.74	–	106.44	–	120.36	120.16	120.16	109.77
a_{489}	–	–	–	–	–	–	–	–	–	103.71	–	–	–	–	–
a_{874}	–	–	–	–	178.05	–	–	178.93	–	–	–	178	–	–	–
a_{873}	–	–	–	–	–	178.91	–	–	–	104.12	–	–	178.56	178.56	102.53
a_{947}	–	–	–	–	–	–	–	109.26	–	–	–	–	–	–	–
a_{523}	–	–	–	–	–	–	116.37	–	–	–	–	–	–	–	–

[a] Bond lengths (*r*) in Å, bond angles (*a*) in degrees.

Table 2 Computed thermodynamic properties of reactants, products and transition state structures in 1,3–dipolar cycloadditions [a]

Structure	E_{elec}	H (298)	G (298)	S (298) $\times 10^4$
Benzonitrile oxide	–397.19	–397.07	–397.113	1.3168
Ethylene	–78.032	–77.973	–77.9978	0.8305
Benzonitrile oxide–Ethylene [TS_a]	–475.17	–474.99	–475.038	1.5556
Benzonitrile oxide–Ethylene [product (a)]	–475.3	–475.12	–475.165	1.4655
Acrylonitrile	–169.77	–169.71	–169.739	1.0288
Benzonitrile oxide – Acrylonitrile [TS_b]	–566.9	–566.72	–566.775	1.7207
Benzonitrile oxide – Acrylonitrile [product (b)]	–567.03	–566.85	–566.895	1.6049
Benzonitrile oxide – Acrylonitrile [TS_c]	–566.91	–566.73	–566.781	1.6582
Benzonitrile oxide – Acrylonitrile [product (c)]	–567.03	–566.85	–566.893	1.6011
Tetracyanoethylene	–444.92	–444.86	–444.9	1.4281
Benzonitrile oxide –Tetracyanoethylene [TS_d]	–842.07	–841.89	–841.95	2.0669
Benzonitrile oxide–Tetracyanoethylene[product (d)]	–842.16	–841.97	–842.031	1.9861
Cyclopentene	–193.98	–193.85	–193.879	1.0939
Benzonitrile oxide–Cyclopentene [TS_e]	–591.11	–590.86	–590.914	1.7177
Benzonitrile oxide–Cyclopentene [product (e)]	–591.25	–590.99	–591.042	1.6353

[a] Scaled vibrational frequencies from 6–31G* calculations, energies in Hartree, entropies in eu (hartree/K).

Table 3 Computed thermodynamic quantities and rate constants for 1,3-dipolar cycloaddition with benzonitrile oxide as dipole reagent.[a]

Dipolarophile	$\Delta_r E_{elec}$	$\Delta_r H$ (298)	$\Delta_r G$ (298)	ΔS (298)	$\Delta G^{\#}$ (298)	k (298)$\times 10^{20}$
Ethylene	–50.64	–46.62	–33.87	–42.78	45.65	0.205
Acrylonitrile(b)	–44.71	–41.28	–27.44	–46.48	48.01	0.004
Acrylonitrile(c)	–43.42	–39.79	–25.86	–46.72	44.44	1.58
Tetracyanoethylene	–27.86	–25.72	–11.53	–47.61	39.46	7101.4
Cyclopentene	–49.39	–45.89	–31.39	–48.65	48.55	0.0015

[a] Energy in kcal/mol, entropy in eu (cal/molK) and rate constants in $M^{-1}\ s^{-1}$

rate of cycloadditions of the 1,3-dipoles with electron-poor dipolarophiles is greater than for other dipolarophiles. Saver and Wuest[12] determined the rate constant ratio of tetracyanoethylene to acrylonitrile in their reactions with cyclopentene at 20°C in dioxane (4.3×10^7) and we obtained this ratio for reaction **c** of acrylonitrile with benzonitrile oxide (4.49×10^3) and for reaction **b** of acrylonitrile (1.87×10^6) at 25°C in the gas phase.

These results can be explained in terms of the frontier molecular orbital (FMO) theory. This theory states that the Gibbs energy of activation is related to the energy gap between the dominant interacting HOMO and LUMO. The energies of HOMO and LUMO can be experimentally or theoretically estimated. For a number of common reactions in 1,3-dipolar cycloadditions, Houk[13] has calculated the energy of the FMOs. The relative levels of the HOMO and LUMO of both reactants determine whether the HOMO (dipole) – LUMO (dipolarophile) interactions or the LUMO (dipole) – HOMO (dipolarophile) interactions are dominant. Furthermore, the levels of the FMOs can be affected by stabilising factors. For example, electron-withdrawing substituents stabilise the FMOs, whereas electron-donating subtituents raise the FMO energy. Thus for cycloaddition with tetracyanoethylene (including four electron-withdrawing substituents), the energy gap between HOMO (benzonitrile oxide) – LUMO (tetracyanoethylene) is less than other dipolarophiles.

Also, Table 2 shows that the entropy changes of reactions are negative, since 1,3-dipolar cycloadditions are characterised by a negative volume.

It is considered that in the cycloaddition of benzonitrile oxide with acrylonitrile, the product of reaction **b** has more thermodynamic stability than that of reaction **c**, probably because of lower steric hindrance of nitrile and phenyl groups. Also, the rate of reaction **c** is more than reaction **b**. This result could be related to 6–31G* Mulliken charges. C1 at acrylonitrile has more positive charge (0.096) than C2 (0.072), so the oxygen atom of benzonitrile oxide is inclined to attack C1 and its transition state will be more stable than that for reaction **b**.

We intend to study these reactions in the solution phase and predict the rate of reactions in different solvents.

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