JOURNAL OF PHYSICAL ORGANIC CHEMISTRY, VOL. 5, 819–823 (1992)

SHORT COMMUNICATION

DIASTEREOFACIAL SELECTIVITY IN 1,3-DIPOLAR CYCLOADDITIONS TO CYCLOBUTENES. 8. HF/3–21G TRANSITION STRUCTURES OF THE REACTIONS OF FORMONITRILE OXIDE WITH *CIS*-3,4-DICHLOROCYCLOBUTENE AND NORBORNENE

MARISA BAGATTI AND AUGUSTO RASTELLI*

Dipartimento di Chimica, Università di Modena, Via Campi 183, 41100 Modena, Italy

MARINA BURDISSO AND REMO GANDOLFI*

Dipartimento di Chimica Organica, Università di Pavia, Viale Taramelli 10, 27100 Pavia, Italy

A transition structure for the *syn* and *anti* attack of formonitrile oxide on both *cis*-3,4-dichlorocyclobutene and norbornene was obtained using HF/3–21G method. These calculations correctly predict dominance of the *syn* attack in the reaction of dichlorocyclobutene and 100% *syn* selectivity, with respect to the methano bridge, in the reaction of norbornene. Analysis of the activation energy shows that the inherent facial bias of dichlorocyclobutene is reflected, at the transition state, in a complex way in the deformation energy of both dichlorocyclobutene and formonitrile oxide and in the interaction energy between them. With norbornene the out-of-plane deformation energy of the olefinic hydrogens clearly emerges as the major factor in controlling facial selectivity.

Face selectivity in organic reactions is a topic that has been growing increasingly important in recent years not only from a synthetic but also from a theoretical standpoint. For cycloadditions only very recently have theoretical studies started to appear that address this problem by performing *ab initio* calculations of the transition structures of the two diastereoisomeric attacks on the diastereotopic faces of a double bond[1] or a diene.[2] In particular, no calculations of this type have been reported so far for the very important field of 1,3-dipolar cycloadditions (MM2 calculations on facial selectivity in 1,3-dipolar cycloadditions in which the heavy atoms of the forming five-membered ring are frozen in the geometry of the HF/3–21G transition structure of the reaction of formonitrile oxide with ethylene have been presented[3]).

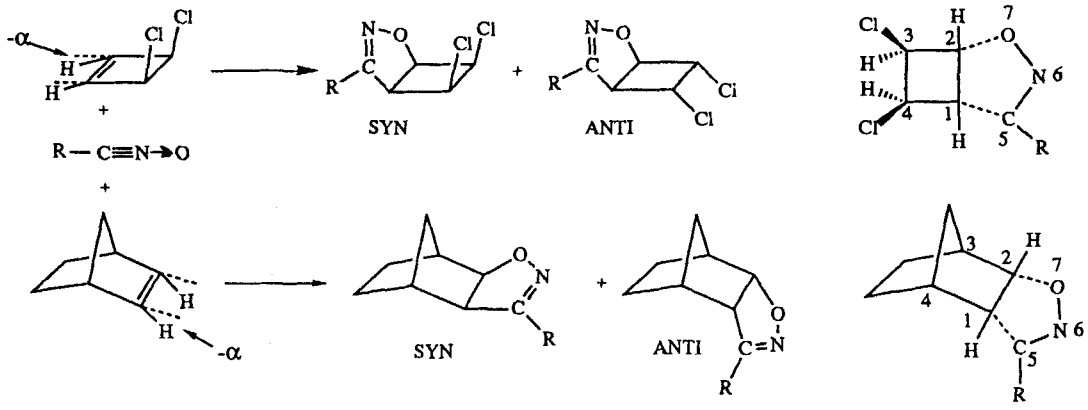
For many years norbornene has played a prominent role in the study of facial selectivity in organic reactions[4] while *cis*-3,4-disubstituted cyclobutenes have recently emerged as compounds for which high contrasteric *syn* selectivity has often been observed.[5] As for 1,3-dipolar cycloadditions, formonitrile oxide, in addition to all nitrile oxides studied to date, reacts with norbornene to afford only the *syn* adduct (with respect to the methano bridge)[6] (for reasons of homogeneity we use *syn* and *anti* descriptors also for facial selectivity of norbornene reactions; *syn* and *anti* correspond to *exo* and *endo* descriptors, respectively, used by other authors[1]). In the reaction of nitrile oxides (and other 1,3-dipoles) with *cis*-3,4-dichlorocyclobutene, *syn* attack (with respect to the chlorine atoms) is always dominant when repulsive through-space steric and electrostatic interactions between the nitrile oxide and the chlorine atoms are not too strong. For example, *syn*/*anti* ratios of *ca* 75:25 for acyl nitrile oxides (R = PhCO, MeCO and COOEt) and of 70:30 for acetonitrile oxide and *p*-nitrobenzonitrile oxide have been observed.[7]

This paper reports the *syn* and *anti* transition structures of the reaction of the parent nitrile oxide, i.e formonitrile oxide (R = H), with norbornene and *cis*-3,4-dichlorocyclobutene calculated using the HF/3–21G model[8] and gradient techniques with optimization of all variables. Critical points were characterized by diagonalizing the Hessian matrices of

* Authors for correspondence.

0894–3230/92/120819–05$07.50

Received 23 April 1992
Revised 3 July 1992



the optimized structures; transition structures have only one negative eigenvalue (first-order saddle points), the corresponding eigenvectors involving the expected concerted formation of the two new bonds. [An MC–SCF study of the reaction of ethylene and acetylene with formonitrile oxide has been carried out by McDouall *et al.*[9a] In the concerted HCNO–ethylene transition structure (obtained using the 4–31G basis set), the length of the forming carbon—carbon bond (2·08 Å) is shorter than that of the carbon—oxygen bond (2·32 Å). Formonitrile oxide is more bent (CNO = 135·4°) than in our transition structures. *Ab initio* calculations on the reactions of diazoalkanes, nitrones and carbonyl ylides have been carried out by Leroy *et al.*[9b] and on the reaction of nitrile oxides by Poppinger,[9c], Kormorniki *et al.*[9d] and Hiberty *et al.*[9e]

The calculations correctly predict a 100% *syn* (to the methano bridge) selectivity for the reaction of norbornene ($E_{a,\,anti} - E_{a,\,syn} = 6{\cdot}1$ kcal mol^{-1}, Table 3). A large difference is also present in HF/AM1 calculations ($E_{a,\,anti} = 21{\cdot}6$ and $E_{a,\,syn} = 18{\cdot}7$ kcal mol^{-1}) and in calculations including MP2 electron correlation (MP2 = FULL/3–21G//HF/3–21G, $E_{a,\,anti} = 11{\cdot}5$ and $E_{a,\,syn} = 6{\cdot}2$ kcal mol^{-1}).*

A mixture of the two diastereoisomers with dominance of the *syn* adduct is predicted for the reaction of dichlorocyclobutene ($E_{a,\,anti} - E_{a,\,syn} = 0{\cdot}6$ kcal mol^{-1}, Table 3). It should be emphasized that the *syn* transition state (TS) of this latter reaction also appears with lower energy than its *anti* counterpart in minimal basis set (HF/STO–3G, $E_{a,\,anti} = 17{\cdot}5$ and $E_{a,syn} = 16{\cdot}0$ kcal mol^{-1}) and also in MP2 = FULL/3–21G//HF/3–21G calculations ($E_{a,\,anti} = 6{\cdot}2$ and $E_{a,\,syn} = 6{\cdot}0$ kcal mol^{-1}). Also Chao *et al.*[2] have recently concluded that the relative energies of competing TSs in Diels–Alder reactions are insensitive to basis set and to inclusion of electron correlation while the absolute activation energies vary widely with the level of *ab initio* calculations. In contrast, HF/AM1 calculations predict as highly prevalent the wrong adduct, that is, the anti adduct ($E_{a,\,anti} = 17{\cdot}8$ and $E_{a,\,syn} = 20{\cdot}1$ kcal mol^{-1}).*

Details of HF/3–21G geometries (Tables 1 and 2) reveal several interesting features. They clearly show that all TSs are early in terms of bond breaking and bond making. Regarding the timing of bond formation, the length of the forming carbon—carbon bond is similar to that of the forming carbon—oxygen bond in both transition structures of norbornene reaction whereas in the dichlorocyclobutene reaction the carbon—oxygen bond is significantly shorter than the carbon—carbon bond.

The out-of-plane bending of the olefinic hydrogen (as described by α_1 and α_2, Tables 1 and 2) in the TSs of the two dipolarophiles differs considerably. (α_1 and α_2 are the same angles as used in Refs 1 and 4i for out-of-plane bending of the olefinic hydrogens of norbornene. Houk *et al.*[4f] measure this bending by a different angle: $\sin\alpha_{1,\text{Houk}} = (H_1{-}C_1{-}C_2{-}C_4) \times \sin(H_1{-}C_1{-}C_2)$. α_1 and α_2 are also a measure of the degree of pyramidalization of C-1 and C-2. For a discussion of this problem, see Ref. 10.) In fact, with norbornene the *syn* attack by the 1,3-dipole brings about a bending of these hydrogens which is either slightly smaller (by 0·7° for α_1) or slightly larger (by 2·2° for α_2) than that in the *anti* attack, whereas in the reaction of dichlorocyclobutene the out-of-plane bending of the olefinic hydrogens is always larger in the *syn* TS (by 2·9° for α_1 and by 13·0° for the α_2) than in the *anti* TS. In the reaction of norbornene the olefinic hydrogen attached to the carbon atom involved in formation of a carbon—carbon bond experiences substantially greater bending in both TSs than that attached to the carbon

* A complete study of these reactions has also been done by the use of HF/AM1 and HF/STO–3G models; structure and energy results are available on request. The MP2 = FULL/3–21G//HF/3–21G total energies of formonitrile oxide, norbornene and dichlorocyclobutene are −167·026960, −270·004303 and −1067·923594 hartree, respectively.

Table 1. Bond lengths (Å), bond angles (°) and dihedral angles (°)[a] for the HF/3–21G optimized geometries of educts, transition structures and products of the reaction of formonitrile oxide with norbornenene

	Educts	Transition structures		Adducts	
		Syn	*Anti*	*Syn*	*Anti*
C_1—C_2	1·32	1·36	1·36	1·56	1·56
C_5—N_6	1·14	1·16	1·17	1·26	1·26
N_6—O_7	1·29	1·32	1·33	1·45	1·46
C_1—C_5		2·29	2·24	1·50	1·50
C_2—O_7		2·26	2·29	1·47	1·46
C_5—N_6—O_7	180·0	139·8	137·8	108·7	108·9
H_5—C_5—N_6	180·0	156·6	153·7	119·5	119·1
α_1	−4·8	−26·1	26·8	−57·2	59·8
α_2	−4·8	−17·3	15·1	−50·0	57·1
$\beta = C_4$—C_1—C_2—C_3	0·0	0·9	−1·9	−2·0	−0·3
$\gamma_1 = C_5$—C_1—C_2—C_4		−108·8	115·4	−117·0	120·7
$\gamma_2 = O_7$—C_2—C_1—C_3		103·6	−110·9	111·4	−119·5

[a] α_1 and α_2 give the out-of-plane bending of the olefinic hydrogens H_1 and H_2. α_1 (α_2) is the difference between 180° and the absolute value of the dihedral angle H_1—C_1—C_2—C_4 (H_2—C_2—C_1—C_3). α_1 (α_2) is given a positive sign when H_1 (H_2) is bent in a *syn* direction and a negative sign when H_1 (H_2) is bent in an *anti* direction with respect to the methano bridge.

Table 2. Bond lengths (Å), bond angles (°) and dihedral angles (°)[a] for the HF/3–21G optimized geometries of educts, transition structures and products of the reaction of formonitrile oxide with dichlorocyclobutene

	Educts	Transition structures		Adducts	
		Syn	*Anti*	*Syn*	*Anti*
C_1—C_2	1·33	1·38	1·37	1·56	1·56
C_5—N_6	1·14	1·15	1·16	1·26	1·26
N_6—O_7	1·29	1·32	1·32	1·46	1·46
C_1—C_5		2·37	2·29	1·51	1·50
C_2—O_7		2·01	2·16	1·44	1·45
C_5—N_6—O_7	180·0	141·6	139·7	109·0	109·2
H_5—C_5—N_6	180·0	161·0	156·8	119·6	119·3
α_1	−1·9	−26·3	23·4	−58·9	58·6
α_2	−1·9	−31·0	18·0	−61·1	59·1
$\beta = C_4$—C_1—C_2—C_3	0·0	2·6	−2·6	8·0	−10·3
$\gamma_1 = C_5$—C_1—C_2—C_4		−104·7	101·6	−114·4	112·5
$\gamma_2 = O_7$—C_2—C_1—C_3		110·7	−98·2	117·2	−113·1

[a] α_1 and α_2 give the out-of-plane bending of the olefinic hydrogens H_1 and H_2. α_1 (α_2) is the difference between 180° and the absolute value of the dihedral angle H_1—C_1—C_2—C_4 (H_2—C_2—C_1—C_3). α_1 (α_2) is given a positive sign when H_1 (H_2) is bent in a *syn* direction and a negative sign when H_1 (H_2) is bent in an *anti* direction with respect to the chlorine atoms.

atom involved in the formation of a carbon—oxygen bond ($\alpha_1 = -26·1°$ and $\alpha_2 = -17·3°$ for the *syn* attack and $\alpha_1 = +26·8°$ and $\alpha_2 = +15·1°$ for the *anti* attack). In the *anti* TS of the reaction of dichlorocyclobutene, once again α_1 is higher than α_2 ($\alpha_1 = 23·4°$ and $\alpha_2 = 18·0°$) but in the *syn* TS the opposite holds ($\alpha_1 = -26·3°$ and $\alpha_2 = -31·0°$).

The 1,3-dipole suffers high bending (by *ca* 40°) in all TSs. This bending is slightly smaller (by *ca* 2°) in the TSs of the cyclobutene reaction than in those of the norbornene reaction and in the *syn* than in the *anti* attack (again by *ca* 2°) for both dipolarophiles. Finally, the dihedral angles γ_1 and γ_2 are larger when formonitrile oxide attacks the sterically more congested face of the dipolarophile, namely the *anti* face of norbornene and the *syn* face of dichlorocyclobutene, as a result of its attempt to keep steric interactions as low as possible.

In order to achieve a deeper insight into the factors that control facial selectivity, we carried out an analysis of activation energies according to Koga *et al.*[1] (Table 3). In this analysis deformation energies are provided

by the energies required to deform the isolated molecules to the geometries they adopt in the transition state. The contribution of out-of-plane bending of the olefinic hydrogens is given by the difference between the energy of the deformed (to TS geometry) dipolarophile and that of a dipolarophile in which all the geometrical parameters are those of the TS with the exception of olefinic hydrogen bending angles. These latter were assumed to be those of the dipolarophile equilibrium geometry (i.e. $-4{\cdot}8^{\circ}$ for norbornene and $-1{\cdot}9^{\circ}$ for dichlorocyclobutene). Likewise, a bending of the three heavy atoms of formonitrile oxide from the linear ground state geometry to the transition-state angle allowed us to evaluate the role played by this deformation. The difference between the activation energy and the whole deformation energy gives the interaction energy which reflects steric and electrostatic interactions and stabilization due to incipient bond formation and to the consequent electron delocalization between the deformed reaction partners.

The 100% *syn* selectivity in the reaction of norbornene with formonitrile oxide clearly appears to be primarily dictated by the deformation energy of the dipolarophile, and in particular by the easier *anti* than *syn* deformation of the olefinic hydrogens. This finding is in agreement with a similar observation (based on HF/3–21G calculations) by Koga *et al.*[1] for the hydroboration reaction of norbornene and can be traced back to the well established ground-state pyramidalization of the double bond of norbornene.[1,4] In fact, very recent neutron diffraction data indicate that the *anti* bending of its olefinic hydrogens may be even higher than that evaluated by molecular orbital calculations.[4i] Interestingly, the deformation (in particular the bending of its three heavy atoms) energy of formonitrile oxide is significantly smaller in the *syn* than in the *anti* TS and cooperates with the deformation energy of the dipolarophile in making the *syn* attack so highly favoured. In fact, deformation energies as a whole strongly overcome the interaction energy which stabilizes the *anti* TS more than its *syn* counterpart.

In contrast, in the reaction of dichlorocyclobutene the stabilizing interaction energy favours the *syn* over the *anti* attack. Moreover, while the deformation energy of the 1,3-dipole is smaller in the *syn* than in the *anti* TS (as the norbornene reaction), the opposite is true not only for the whole deformation energy of cyclobutene but also for the out-of-plane bending of the olefinic hydrogens. At first sight the latter observation is surprising in the light of the fact that in the ground state of dichlorocyclobutene the olefinic hydrogens are already bent in the *anti* direction (by $-1{\cdot}9^{\circ}$). However, we feel that all these observations can be consistently explained. In the *syn* attack cyclobutene prefers to deform in order to reduce steric interactions and to achieve a much higher pyramidalization of the double bond carbon atoms than in the *anti* attack. This will cost a relatively small amount of energy as a consequence of the easier *anti* than *syn* deformability of the olefinic hydrogen atoms[5d] and will result in a higher interaction energy (stabilizing) in the former than in the latter TS. Moreover, as a result of the larger pyramidalization of the dipolarophile this higher interaction in the *syn* attack can be achieved with a smaller 1,3-dipole deformation compared with that in the *anti* attack.

Our results clearly show that the inherent facial bias of a double bond is reflected, in the diastereoisomeric transition states of its 1,3-dipolar cycloadditions, in a complex way in the deformation energy of both the partner reagents and in the interaction energy between

Table 3. Deformation and interaction energy contribution to activation energy (kcal mol^{-1})[a] of *syn* and *anti* transition structures (HF/3–21G//HF/3–21G)[b]

Parameter	Norbornene		Dichlorocyclobutene	
	Syn	*Anti*	*Syn*	*Anti*
Deformation energy (dipolarophile	4·4	9·3	10·0	6·5
Deformation energy (1,3-dipole)	23·7	26·4	20·9	24·0
Σ (Deformation energies)	28·1	35·7	31·0	30·6
Out-of-plane bending (olefinic hydrogens)	3·0	6·7	6·4	4·8
Bending of the CNO moiety	24·9	27·5	22·5	25·1
Interaction energy	−6·9	−8·5	−10·0	−9·0
Activation energy[c]	21·2	27·3	21·0	21·6
Heat of reaction (adducts)	−72·3	−70·0	−66·5	−69·5

[a] 1 kcal = 4·184 kJ.
[b] The total energies of formonitrile oxide, norbornene and dichlorocyclobutene are −166·678766, −269·369086 and −1067·462186 hartree, respectively.
[c] The activation energies for the two *syn* attacks are virtually identical, suggesting that norbornene and dichlorocyclobutene should exhibit very similar reaction rates in their reactions with nitrile oxides. Unfortunately, experimental evidence on this point is lacking.

them. The reacting system finds its way to TSs through a delicate balance of energy gains and energy losses which is not easily predictable only on the basis of calculations on the isolated molecules.

ACKNOWLEDGEMENTS

We thank MURST and CNR for financial support.

REFERENCES

1. N. Koga, T. Ozawa and K. Morokuma, *J. Phys. Org. Chem.* **3**, 519–532 (1990).
2. T. M. Chao, J. Baker, W. J. Hehre and S. D. Kahn, *Pure Appl. Chem.* **63**, 283–288 (1991).
3. K. N. Houk, H.-Y. Duh, Y.-D. Wu and R. M. Moses, *J. Am. Chem. Soc.* **108**, 2754–2755 (1986), and references cited therein.
4. (a) P. von R. Schleyer, *J. Am. Chem. Soc.* **89**, 701–703 (1967); (b) H. C. Brown, P. Geohegan, *J. Am. Chem. Soc.* **89**, 1522–1524 (1967); (c) S. Inagaki, K. Fujimoto and K. Fukui, *J. Am. Chem. Soc.* **98**, 4054–4062 (1976); (d) G. Wipff and K. Morokuma, *Tetrahedron Lett.* **21**, 4445–4448 (1980); (e) R. Huisgen, P. H. Ooms, M. Mingin and N. L. Allinger, *J. Am. Chem. Soc.* **102**, 3951–3953 (1980); (f) K. N. Houk, N. G. Rondan and F. K. Brown, *Isr. J. Chem.* **23**, 3–9 (1983); (g) J. Spanget-Larsen and R. Gleiter, *Tetrahedron* **20**, 3345–3350 (1983); (h) K. N. Houk, in *The Stereochemistry and Reactivity of Systems Containing π Electrons*, edited by W. H. Watson, pp. 1–40. Verlag Chemie International, Deerfeld Beach, FL (1983); (i) O. Ermer, P. Bell and S. A. Mason, *Angew. Chem., Int. Ed. Engl.* **28**, 1239–1241 (1989).
5. (a) M. Frank-Neumann, *Angew. Chem., Int. Ed. Engl.* **8**, 210–211 (1969); (b) M. Burdisso, R. Gandolfi, M. Lucchi and A. Rastelli, *J. Org. Chem.* **53**, 2123–2125 (1988); (c) A. Rastelli, M. Burdisso and R. Gandolfi, *J. Phys. Org. Chem.* **3**, 159–173 (1990); (d) M. Burdisso, A. Gamba, R. Gandolfi, L. Toma, A. Rastelli and E. Schiatti, *J. Org. Chem.* **55**, 3311–3321 (1990), and references cited therein; (e) H. Landen, B. Margraf, H.-D. Martin and A. Steigel, *Tetrahedron Lett.* **29**, 6597–6601 (1988); (f) M. Burdisso, R. Gandolfi and A. Rastelli, *Tetrahedron Lett.* **32**, 2659–2662 (1991).
6. (a) G. Bianchi, R. Gandolfi, P. Grunanger, in *The Chemistry of Functional Groups*, edited by S. Patai, pp. 737–804. Wiley, New York (1985); (b) P. Caramella and P. Grunanger, in *1,3-Dipolar Cycloaddition Chemistry*, edited by A. Padwa, Vol. 1, pp. 291–392. Wiley-Interscience, New York (1984).
7. G. Bianchi, C. De Micheli, A. Gamba and R. Gandolfi, *J. Chem. Soc., Perkin Trans. 1* 137–140 (1974); M. Burdisso and R. Gandolfi, unpublished results.
8. M. J. Frisch, M. Head-Gordon, H. B. Schlegel, K. Raghavacari, J. S. Binkley, C. Gonzales, D. J. Defrees, D. J. Fox, R. A. Whiteside, R. Seeger, C. F. Melius, J. Baker, R. Martin, L. R. Kahn, J. J. P. Stewart, E. M. Fluder, S. Topiol and J. A. Pople, *Gaussian 88*. Gaussian, Pittsburgh, PA (1988).
9. (a) J. J. McDouall, M. A. Robb, U. Niazi, F. Bernardi and H. B. Schlegel, *J. Am. Chem. Soc.* **109**, 4642–4648 (1987); (b) G. Leroy, M. T. Nguyen and M. Sana, *Tetrahedron* **34**, 2459–2468 (1978), and references cited therein; (c) D. Poppinger, *Aust. J. Chem.* **29**, 465–473 (1976); (d) A. Kormorniki, J. D. Goddard and H. F. Schaefer, *J. Am. Chem. Soc.* **102**, 1763–1769 (1980); (e) P. C. Hiberty, G. Ohanessian and H. B. Schlegel, *J. Am. Chem. Soc.* **105**, 719–723 (1983).
10. R. C. Haddon, *J. Am. Chem. Soc.* **112**, 3385–3389 (1990).