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Is anthracene cofactor or spectator for the thermolysis of anthracenyl acylnitroso cycloadducts in the presence of a diene?

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ABSTRACT

Acylnitroso species are very reactive dienophiles broadly used in organic synthesis. They are traditionally prepared from the oxidation of hydroxamic acids at low temperature. When this strategy fails, acylnitroso compounds may be generated from other stable sources, for example, their (9,10-dimethyl)anthracenyl cycloadducts. The thermolysis of such compounds performed in the presence of a diene leads generally to the corresponding hetero Diels–Alder (HD–A) cycloadduct in high yield with concomitant release of anthracene. The most widely accepted mechanism is the postulated slow release of acylnitroso via a retro Diels–Alder process, although the anthracenyl acylnitroso cycloadducts bear intrinsic structural features suggesting another pathway, that is, an exchange process. By using computational chemistry, we have hereby clarified the exact role of anthracene in this reaction.

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1. Introduction

Acylnitroso species are very reactive and unstable compounds. They cannot be observed directly, and concrete proof of their existence has been reported very recently by time-resolved IR spectroscopy.[1] Until this direct proof, only indirect evidences of their exact nature were known (e.g., degradation products, trapping products, etc.).[2,3] Despite their instability, acylnitroso compounds became rapidly popular in organic synthesis.[4,5] Indeed, nitroso compounds allow the direct introduction of both amino and hydroxy functions in one step via a hetero Diels–Alder (HD–A) reaction.[6,7] The synthetic methods for their generation are still limited.[8] As a consequence of their high reactivity, they are traditionally generated in situ in the presence of the diene.[9] In absence of any species susceptible to react with, acylnitroso species undergo rapidly dimerization and degradation. The most widespread method for acylnitroso generation requires the oxidation of the corresponding stable hydroxamic acid, using the modified Moffatt–Swern protocol,[8] organic or inorganic periodates,[8] metal-based oxidation,[10] etc. Sometimes, due to substrate incompatibility or unreactive dienes, they have to be alternatively prepared from other stable sources such as nitrile oxides[11] or from anthracenyl cycloadducts.[12] Anthracene is a masked inner diene reactive towards a wide variety of dienophiles, which leads to the corresponding [4+2] anthracenyl cycloadducts.[13] This D–A process remains a chemical equilibrium, strongly affected by temperature, substitution of the anthracenyl moiety and solvent nature.[13,14] The reversibility of this D–A addition promotes anthracene and derivatives (mainly 9,10-dimethylanthracene) as efficient trapping agents for various transient species. [8,15] Under specific conditions (e.g., thermal decomposition), the trapped species can be released in the reaction medium. When the thermal decomposition of acylnitroso anthracenyl cycloadducts is processed in the presence of another diene, the corresponding cycloadduct is generally observed, with concomitant release of anthracene. This experimental trick has been used a lot when direct oxidation of hydroxamic acids in the presence of the diene remains unsuccessful (Fig. 1).

The retro HD–A process releasing acylnitroso compounds by thermolysis is widely accepted by organic chemists.[4,16] A literature survey reveals some intriguing structural features of these anthracenyl adducts[17] that could suggest another reaction pathway than the classical retro HD–A, that is, an exchange process, in which the trapped acylnitroso behaves as an electrophile (Fig. 2).

2. Results and discussion

Although the two reactions lead to the same cycloadduct, a fine understanding of the incriminated species could have significant importance for reaction optimization and further development.[18] As our research groups are involved in the HD–A reactions of poorly activated dienes[19] with acylnitroso species, we have

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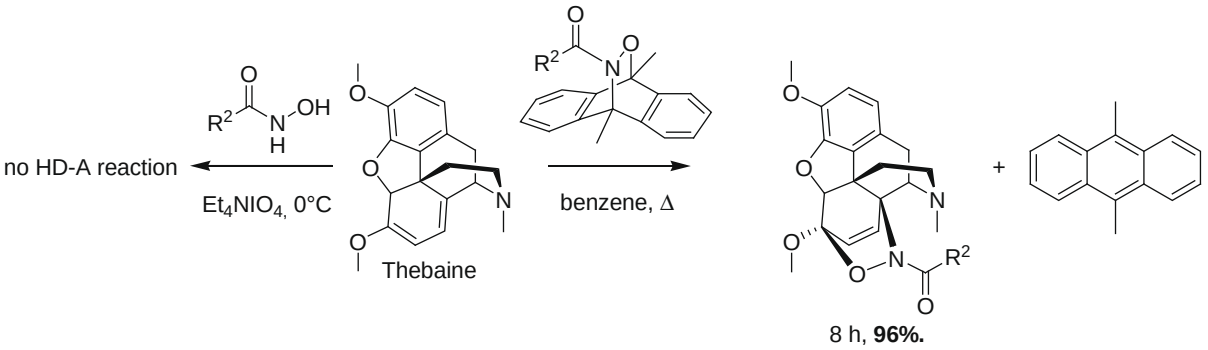


Figure 1. Kirby's functionalization of Thebaine.

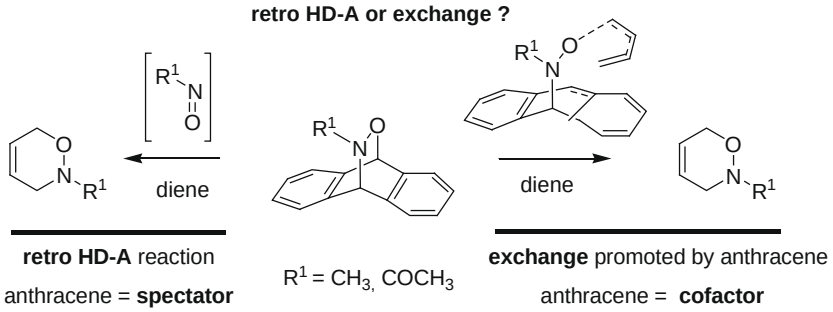


Figure 2. The two possible behaviours for anthracenyl acylnitroso cycloadducts towards dienes.

decided to rationalize the exact role of the anthracene derivative in these reactions. Butadiene (**1**), nitrosomethane (**2**), acetylnitroso (**3**) and anthracene (**6**) were selected as model compounds for this theoretical study.

In view to collect information about the implication of anthracene (cofactor or spectator), we have computed both anthracene-assisted and unassisted pathways (Fig. 3). First, we have studied the exchange barrier for the unassisted reaction, that is, without anthracene, between cycloadducts **4–5** derived from butadiene (**1**) and nitrosomethane (**2**) or acetylnitroso (**3**). The retro HD–A process costs 36.4 kcal mol^{-1} and 50.2 kcal mol^{-1} for the 1,2-oxazine cycloadducts **4**–**5**, respectively. Such values are in good agreement with experimental observations of relative stability of these cycloadducts from acyclic dienes.[3,4] The exchange process between cycloadducts **4** or **5** and butadiene (**1**) is in this case obviously thermoneutral, but its activation barrier indicates that, statistically, the

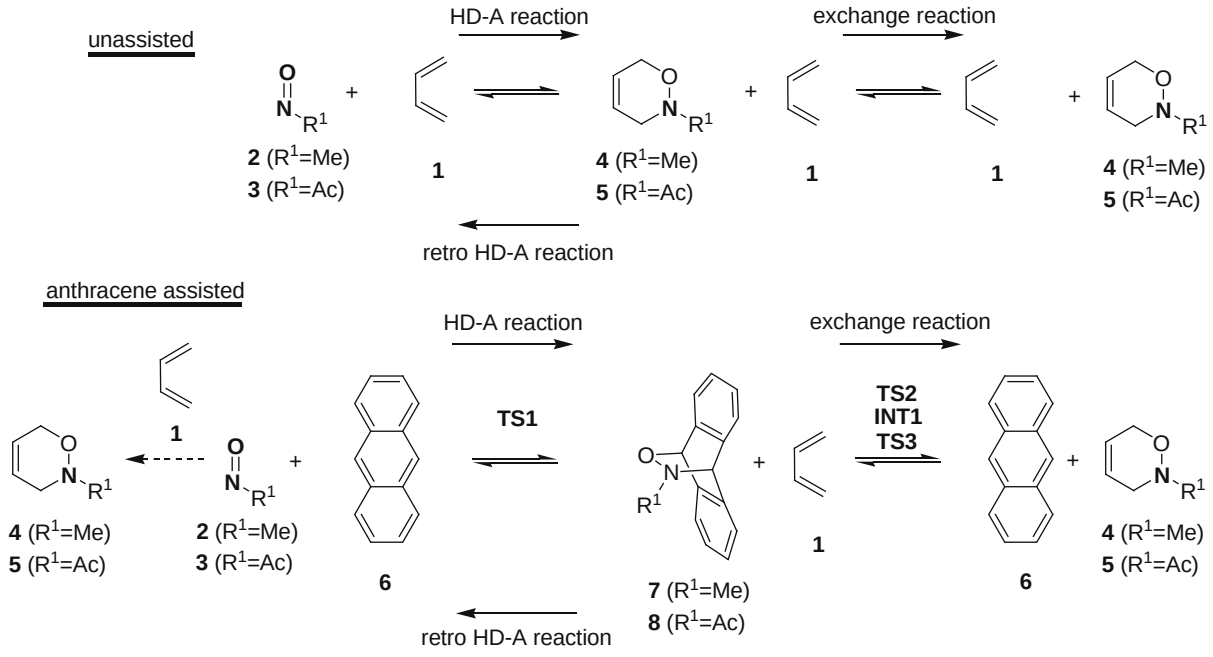


Figure 3. Unassisted and anthracene-assisted reaction pathways for acylnitroso compounds (see also Fig. 4). Keys: TS and INT stand for transition state and intermediate.

exchange would not be a competitive reaction (circa 60 kcal mol^{-1} for both species). The direct exchange between butadiene and the corresponding cycloadduct takes part stepwise. Also, the nitroso substitution (Me or Ac) induces no particular effect for the exchange process, but this substitution induces an important effect for the HD–A step.[20] While the addition of nitrosomethane (**2**) onto anthracene (**6**) appeared to be a nearly thermoneutral process (see Figs. 3 and 4 and Table 1), addition of acetylnitroso (**3**) to anthracene (**6**) is a strongly exothermic reaction.[21]

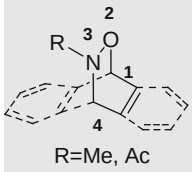
This is in fact the only main difference between the two reaction profiles obtained for nitrosomethane (**2**) and acetylnitroso (**3**) (Fig. 4). Indeed, both exchange processes from cycloadducts **7** (R^1 = Me) or **8** (R^1 = Ac) with butadiene (**1**) cost about 40 kcal mol^{-1} and proceed stepwise. From the electronic point of view, a NBO analysis of the obtained intermediate, as well as the localized orbital description, reveals a three centre delocalization which appears on the diene moiety after formation of the CO bond. Its coupled counterpart is found in the anthracenic moiety opposite to the CN bond. Comparison of the activation barriers for the retro HD–A process for the anthracenyl cycloadducts derived from nitrosomethane and acetylnitroso revealed a difference of about 10 kcal mol^{-1} in favour of nitrosomethane. The retro HD–A process (Fig. 3) costs 21.3 kcal mol^{-1} and 27.6 kcal mol^{-1} for the anthracenyl cycloadducts **7**–**8**, respectively. As it is, the exchange process could not be a competitive process, even for acetylnitroso (**2**).[3f]

The B3LYP/6-31G(d,p) geometries for the important local extrema for the chemical behaviour of anthracenyl cycloadduct **7** (R = Me) are presented in Fig. 4. Some structural data are presented in Table 2 for the cycloadducts derived from butadiene and anthra-

Table 1
Activation barriers and relative energies for the important points of the retro HD–A/exchange sequence assisted by anthracene (see Figs. 3 and 4)

	Energies (kcal mol^{-1})	
	MeNO	AcNO
TS1	20.7	9.4
7 or **8**	−0.6	−18.2
TS2	42.9	40.8
INT1	38.3	37.0
TS3	42.0	42.8
4 or **5**	−28.9	−33.3
Retro HD–A	21.3	27.6
Exchange	42.0	40.8

Table 2
Structural features for cycloadducts **4**–**8**



	Bond length and atom distance (Å)			
	$d_{1,2}$	$d_{4,3}$	$d_{4,1}$	$d_{3,2}$
4	1.434	1.466	2.866	1.439
5	1.434	1.456	2.897	1.416
7	1.460	1.507	2.513	1.475
8	1.476	1.495	2.523	1.442

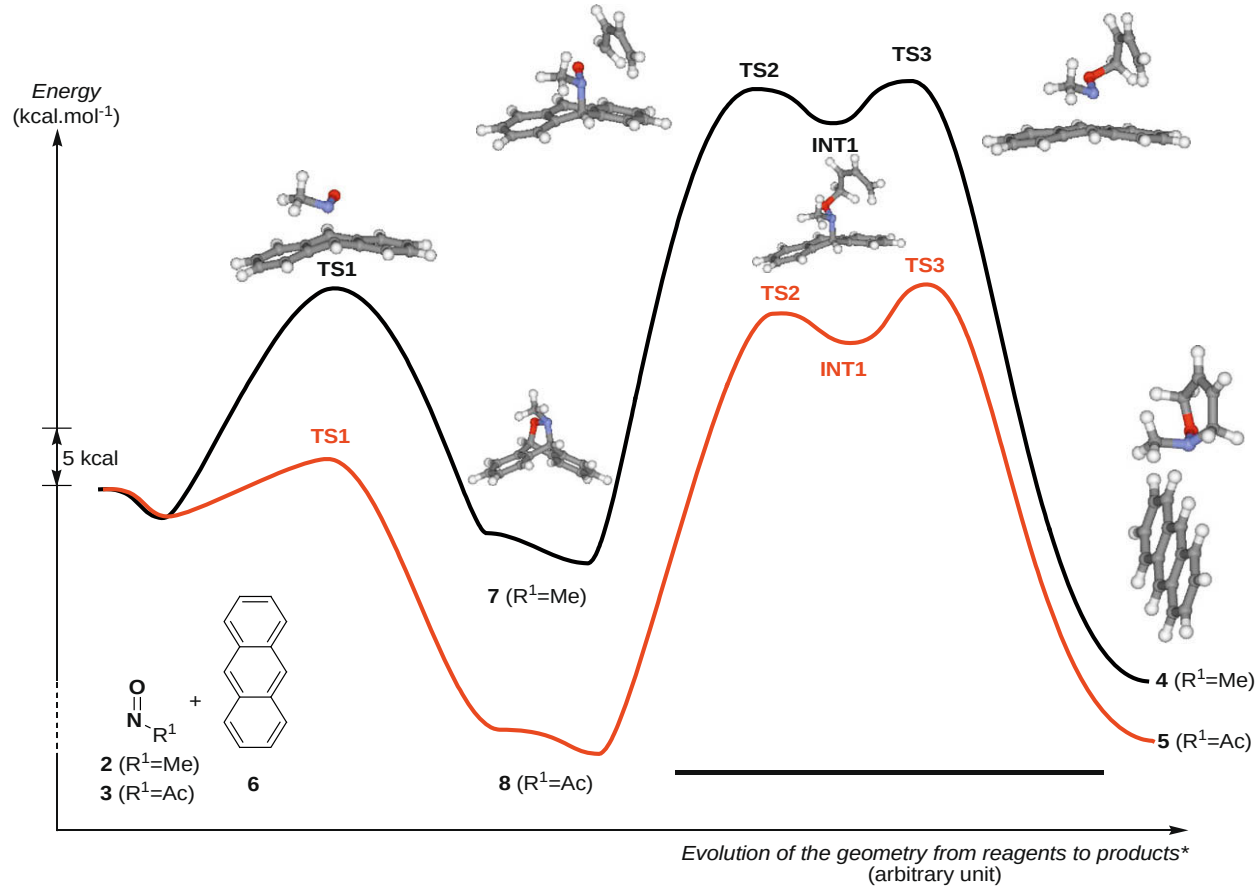


Figure 4. Global reaction profiles for the exchange process promoted by anthracene (B3LYP/6-31G(d,p)). Keys: profile in black: exchange process for anthracenyl nitrosomethane cycloadduct **7** and butadiene; profile in red: exchange process for anthracenyl acetylnitroso cycloadduct **8** and butadiene (*from the concatenation of several reaction coordinates).

cene. Globally, longer bond lengths for anthracenyl derivatives are consistent with an increased tendency for the retro HD–A process (36.4 kcal mol^{-1} for **4**, 50.2 kcal mol^{-1} for **5**, 21.3 kcal mol^{-1} for **7** and 27.6 kcal mol^{-1} for **8**), in good agreement with previous studies.[22]

3. Conclusion

To conclude, anthracenyl acylnitroso cycloadduct **8** behaves well as a stable source for acylnitroso species: the cycloreversion (retro HD–A) performed under thermal conditions needs to overcome an activation barrier of 27.6 kcal mol^{-1}. Statistically, the direct exchange with a diene would not be a competitive reaction (40.8 kcal mol^{-1}). Under conditions of thermolysis, these anthracenyl acylnitroso cycloadducts release slowly acylnitroso species in the reaction medium. This could rationalize why acylnitroso species generated from their stable anthracenyl cycloadducts (i.e., at high temperature) lead more successfully to the corresponding cycloadducts of unconstrained dienes than the classical periodate oxidation of hydroxamic acids (i.e., at low temperature).[8] Indeed, under thermolysis conditions, the cisoid state of the diene is more populated than the fundamental transoid one; accordingly, generated acylnitroso species could undergo HD–A cycloadditions. At lower temperature, the cisoid state of the diene is not sufficiently populated: acylnitroso species could not cycloadd, accumulate in the reaction medium, dimerize and then undergo degradation.[3] As nitroso compounds are very reactive partners, the fundamental cisoid–transoid equilibrium for unconstrained dienes could act as the rate determining step of the [4+2] cycloaddition.[23] This is also in good agreement with the observation that cisoid constrained dienes (such as cyclopentadiene) are very reactive towards acylnitroso dienophiles generated at low temperature.[8]

4. Computational details

All structures are optimized at B3LYP[24] level of theory using a 6-31G(d,p) basis set and the Gaussian series of programs.[25] All possible conformations have been investigated and the most stable conformer is retained. Reactants are allowed to interact on the Potential Energy Surface (PES) and form a Van der Waals (VDW) intermolecular pre-reaction complex. The rearrangement of such a complex on the (3N-6) singlet hypersurface evolves, passing through the activated complex, to the product. For each species a full optimization was performed using the analytical second derivatives to ensure the quality of the stationary points. For the Transition States (TS), the correctness of the curvature and its corresponding eigenvector were checked in order to guarantee the quality of the obtained results. Accordingly, the Intrinsic Reaction Coordinate (IRC)[26] was followed to highlight the reaction pathway. Natural Bond Orbitals (NBO) analysis brings some further insight on the electronic structure and charge distribution of the considered species.[27]

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References and notes

1. Cohen, A.; Zeng, B.; King, S.; Toscano, J. *J. Am. Chem. Soc.* **2003**, *125*, 1444–1445.
2. Kirby, G. *Chem. Soc. Rev.* **1977**, *6*, 12–22.
3. (a) Corrie, J.; Kirby, G.; Mackinnon, J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 883–886; (b) Kirby, G.; Mackinnon, J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 887–892; (c) Kirby, G.; Mcguigan, H.; Mclean, D. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1961–1966; (d) Christie, C.; Kirby, G.; Mcguigan, H.; Mackinnon, J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2469–2473; (e) Corrie, J.; Kirby, G.; Sharma, R. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1571–1572; (f) Kirby, G.; Sweeny, J. *J. Chem. Soc., Perkin Trans. 1* **1981**, 3250–3254; (g) Horsewood, P.; Kirby, G.; Sharma, R.; Sweeny, J. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1802–1806.
4. (a) Ganga, V. B.; Sreeja, T.; Suresh, E.; Varma, R. L. *Tetrahedron* **2007**, *63*, 4134–4143; (b) Bodnar, B. S.; Miller, M. J. *J. Org. Chem.* **2007**, *72*, 3929–3932; (c) Adam, W.; Krebs, O. *Chem. Rev.* **2003**, *103*, 4131–4146.
5. Yamamoto, H.; Kawasaki, M. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 595–607.
6. (a) Yamamoto, Y.; Yamamoto, H. *Eur. J. Org. Chem.* **2006**, 2031–2043; (b) Yamamoto, Y.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 7082–7085.
7. (a) Zhu, L.; Lauchli, R.; Loo, M.; Shea, K. J. *Org. Lett.* **2007**, *9*, 2269–2271; (b) Kibayashi, C.; Aoyagi, S.; Abe, H. *J. Synth. Org. Chem. Jpn.* **2007**, *65*, 805–819; (c) Fokin, A. A.; Yurchenko, A. G.; Rodionov, V. N.; Gunchenko, P. A.; Yurchenko, R. I.; Reichenberg, A.; Wiesner, J.; Hintz, M.; Jomaa, H.; Schreiner, P. R. *Org. Lett.* **2007**, *9*, 4379–4382; (d) Jiang, M. X.; Jin, B.; Gage, J. L.; Priour, A.; Savela, G.; Miller, M. J. *J. Org. Chem.* **2006**, *71*, 4164–4169; (e) Li, F.; Warshakoon, N.; Miller, M. *J. Org. Chem.* **2004**, *69*, 8836–8841.
8. Iwasa, S.; Fakhruddin, A.; Nishiyama, H. *Mini-Rev. Org. Chem.* **2005**, *2*, 157–175; Streith, J.; Defoin, A. *Synthesis* **1994**, 1107–1117.
9. (a) Defoin, A.; Fritz, H.; Schidlin, C.; Streith, J. *Helv. Chim. Acta* **1987**, *70*, 554–569; (b) Boger, D. L.; Patel, M.; Takusagawa, F. *J. Org. Chem.* **1985**, *50*, 1911–1916.
10. (a) Adamo, M. F. A.; Bruschi, S. *J. Org. Chem.* **2007**, *72*, 2666–2669; (b) Chow, C.; Shea, K. *J. Am. Chem. Soc.* **2005**, *127*, 3678–3679.
11. (a) Quadrelli, P.; Mella, I.; Carosso, S.; Bovio, B.; Caramella, P. *Eur. J. Org. Chem.* **2007**, 6003–6015; (b) Quadrelli, P.; Invernizzi, A.; Caramella, P. *Tetrahedron Lett.* **1996**, *37*, 1909–1912.
12. Keck, G.; Webb, R.; Yates, J. *Tetrahedron* **1981**, *37*, 4007–4016. See also Ref.[4].
13. (a) Atherton, J.; Jones, S. *Tetrahedron* **2003**, *59*, 9039–9057; (b) Chung, Y.; Duerr, B.; Mckelvey, T.; Nanjappan, P.; Czarnik, A. *J. Org. Chem.* **1989**, *54*, 1018–1032.
14. Manoharan, M.; De Proft, F.; Geerlings, P. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1767–1773.
15. Kitamura, T.; Yamane, M.; Inoue, K.; Todaka, M.; Fukatsu, N.; Meng, Z.; Fujiwara, Y. *J. Am. Chem. Soc.* **1999**, *121*, 11674–11679.
16. Leach, A.; Houk, K.; Reymond, J. *J. Org. Chem.* **2004**, *69*, 3683–3692.
17. X-ray data for several acylnitroso anthracenyl cycloadducts show unprecedented N–O bond length (1.48 Å instead of 1.41 Å as observed in classical 3,4-dihyro-1,2-oxazine patterns). This enhancement of the N–O bond length can also be interpreted as a consequence of a reduced bond order for the oxazine bond (i.e., it suggests both activation of the oxygen and the nitrogen atoms). (a) Chen, W.; Day, C. S.; King, S. B. *J. Org. Chem.* **2006**, *71*, 9221–9224; (b) Kirby, G.; Mcguigan, H.; Mackinnon, J.; Mclean, D.; Sharma, R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1437–1442.
18. (a) Liu, X.; Snyder, J. K. *J. Org. Chem.* **2008**, *73*, 2935–2938; (b) Adams, H.; Bawa, R. A.; McMillan, K. G.; Jones, S. *Tetrahedron: Asymmetry* **2007**, *18*, 1003–1012; (c) Adams, H.; Bawa, R. A.; Jones, S. *Org. Biomol. Chem.* **2006**, *4*, 4206–4213; (d) Adams, H.; Jones, S.; Ojea-Jimenez, I. *Org. Biomol. Chem.* **2006**, *5*, 2296–2303; (e) Sasaoka, A.; Uddin, M. I.; Shimomoto, A.; Ichikawa, Y.; Shiro, M.; Kotsuki, H. *Tetrahedron: Asymmetry* **2006**, *17*, 2963–2969; (f) Burgess, K.; Lajkiewicz, N.; Sanyal, A.; Yan, W.; Snyder, J. *Org. Lett.* **2005**, *7*, 31–34; (g) Sanyal, A.; Yuan, Q.; Snyder, J. *Tetrahedron Lett.* **2005**, *46*, 2475–2478; (h) Burgess, K.; Corbett, M.; Eugenio, P.; Lajkiewicz, N.; Liu, X.; Sanyal, A.; Yan, W.; Yuan, Q.; Snyder, J. *Bioorg. Med. Chem.* **2005**, *13*, 5299–5309.
19. (a) Monbaliu, J.-C.; Marchand-Brynaert, J. *Tetrahedron Lett.* **2008**, *49*, 1839–1842; (b) Robiette, R.; Defacqz, N.; Peeters, D.; Marchand-Brynaert, J. *Curr. Org. Synth.* **2005**, *2*, 453; (c) Robiette, R.; Marchand-Brynaert, J.; Peeters, D. *J. Mol. Struct. (THEOCHEM)* **2002**, *587*, 159–169.
20. Reaction with acetylnitroso **3** is strongly exothermic ($\Delta G = -48.3$ kcal mol^{-1}) because the final product is an amide rather than an amine, as for MeNO **2** ($\Delta G = -28.2$ kcal mol^{-1}).
21. For the formation of **8** (R^1 = Ac), $\Delta G = -18.2$ kcal mol^{-1}. For the formation of **7** (R^1 = Me), $\Delta G = -0.6$ kcal mol^{-1}. See also note 20.
22. (a) Birney, D.; Lim, T.; Koh, J.; Pool, B.; White, J. *J. Am. Chem. Soc.* **2002**, *124*, 5091–5099; (b) Pool, B.; White, J. *Org. Lett.* **2000**, *2*, 3505–3507.
23. For butadiene, this cisoid–transoid equilibrium costs about 2 kcal mol^{-1}, as the HD–A process with acetylnitroso **3**.
24. Becke, A. *J. Chem. Phys.* **1993**, *98*, 5648–5652.
25. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. J. A.; 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.; 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. *Gas Phase Calculations Were Done Using the Gaussian Suite of Programs, Revision A.7*; Gaussian: Pittsburgh PA, 1998.
26. (a) Gonzalez, C.; Schlegel, H. B. *J. Chem. Phys.* **1990**, *94*, 5523–5527; (b) Gonzalez, C.; Schlegel, H. B. *J. Chem. Phys.* **1989**, *4*, 2154–2161.
27. Reed, A. E.; Weinstock, F.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735–746.