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Ab Initio and Density Functional Calculations on the Pericyclic vs Pseudopericyclic Mode of Conjugated Nitrile Ylide 1,5-Electrocyclizations[†]

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Ab initio (MP2/6-311+G** and MP4(SDTQ)/6-311+G**//MP2/6-311+G**) and density functional (B3LYP/6-311+G**) calculations on the ring closure reactions of conjugated nitrile ylides **1a**−**e**, **3**, and **6** to the corresponding oxazoles **2a**, **5**, **7**, and **8**; thiazoles **2b** and **4**; imidazole **2c**; and pyrroles **2d** and **2e**, respectively, are reported. Vinyl nitrile ylides **1d** and **1e** cyclize with a substantially higher barrier than nitrile ylides containing a heteroatom. Geometric features as well as electronic structures as obtained by NBO analysis are indicative of a pericyclic, monorotatory 1,5-electrocyclization of **1d** and **1e**. For nitrile ylides where X = heteroatom, a pseudopericyclic heteroelectrocyclization pathway, characterized by in-plane attack of the heteroatom's lone pair at the nitrile ylide group, is found. For **3** and **6**, where two different cyclization products are possible, the calculated barriers and reaction energies are in line with the experimentally observed direction of reaction. Vinyl nitrile ylides **1d** and **1e** are characterized by an allene, acyl substituted derivatives **1a, 1b**, **3**, and **6** by a propargyl type structure. The nitrogen derivative **1c** represents an intermediate case.

Introduction

Nitrile ylides, readily available by a number of methods,[1,2] represent versatile intermediates for the synthesis of heterocyclic molecules, especially via 1,3-dipolar cycloaddition reactions.[3,4] Conjugated (e.g. vinyl) nitrile ylides of type **1**, apart from intermolecular reaction pathways, easily form heterocyclic molecules by 1,5-[2,4,5] and, less frequently, 1,7-electrocyclizations.[6] In compounds where X is a heteroatom (e.g. X = O, NR, S) this intramolecular reaction is especially feasible and largely predominates over cycloadditions. Such heteroelectrocyclizations, as these types of reactions have been dubbed,[7,8] may be regarded as a subset of the so-called pseudopericyclic reactions.[9,10] The key feature of these reactions is a planar (or nearly planar) nonrotatory transition state involving in-plane attack of the lone-pair of the heteroatom X.[5,7,8,11−16] Therefore, in contrast to classical electrocyclic reactions, neither a distinction between conrotatory and disrotatory pathways is possible, nor are there any restrictions imposed by orbital symmetry. In recent years a number of putative pseudopericyclic reactions have been described,[12−14] including so-called lone pair−LUMO mediated pericyclic reactions,[15] and their increas-

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[†] Dedicated to Prof. Dr. Rolf Huisgen on the occasion of his 80th birthday.

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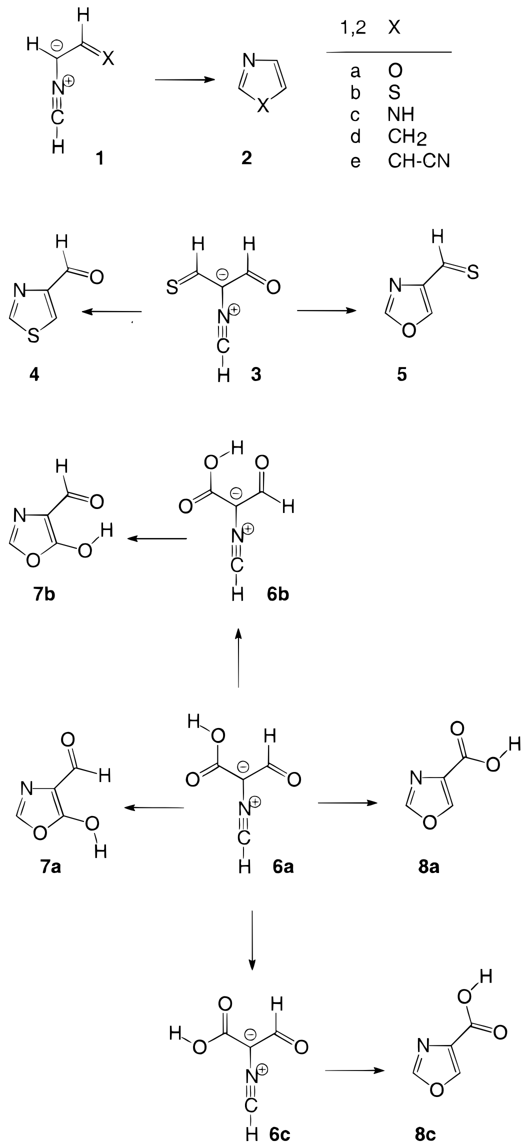
ing importance was pointed out. In continuation of our previous work,[16] we now wish to report the results of ab initio and density functional calculations on 1,5-electrocyclizations of nitrile ylides **1a**−**e** as well as the Cornforth rearrangements[17,18] **4** → **5** and **7** → **8** via nitrile ylides **3** and **6**, respectively. These model systems were chosen on the basis of modeling the commonly found types of nitrile ylide cyclizations. Since nitrile ylides **1a**,**b**, **3**, and **6** lack any geometric feature which would allow distinction between a nonrotatory pseudopericyclic from a classical monorotatory electrocyclization, an analysis of the electronic structure of the nitrile ylide as well as the respective cyclization transition states will be used for a further distinction between these two possible mechanisms.

Computational Methods

All calculations were done by the Gaussian 98 program suite.[19] The 6-31G* and 6-311+G** basis sets were used throughout. Geometries were completely optimized at the ab initio Hartree−Fock and second-order Møller−Plesset[20] level of theory. In addition, Becke's three-parameter[21] hybrid HF/density functional method with the Lee−Yang−Parr correlation function[22] was also used. All stationary points were characterized as minima or transition states by frequency calculations. Single point computations were done at the MP4(SDTQ)/6-311+G**//MP2/6-311+G** level of theory. Electronic structures were analyzed with the aid of the natural bond orbital (NBO)[23] method (program G94NBO,[24] MP2/6-311+G** geometry, SCF density).

Scheme 1



Results and Discussion

In the following we present first energetic aspects (reaction and activation energies) for the cyclizations **1a**−**e** → **2a**−**e**, **3** → **4**, **3** → **5**, **6** → **7**, and **6** → **8** (Scheme 1). Several of these nitrile ylides may exist in different conformations, leading to different structures of the respective cyclization products. The influence of such conformational isomerism on activation and reaction energies will be illustrated by nitrile ylides **6a**−**c**. Second, molecular structures of nitrile ylides **1a**−**e**, **3**, and **6** as well as those of the respective transition states will be described. Finally, with the aid of the NBO method[23] the electronic structures will be analyzed with special emphasis on the pericyclic vs pseudopericyclic nature of the respective electrocyclization reactions.

Energetic Aspects. Relative energies (reaction and activation energies) with respect to the open isomers **1a**−**e**, **3**, and **6** obtained at various levels of theory (HF/6-311+G**, B3LYP/6-311+G**, MP2/6-311+G**, and MP4-

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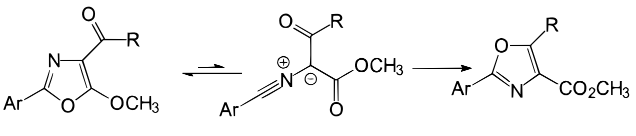
Table 1. Relative Energies (kcal mol^{-1}) for Cyclizations 1 → 2, 3 → 4, 3 → 5, 6 → 7, and 6 → 8 Obtained at Various Levels of Theory[a]

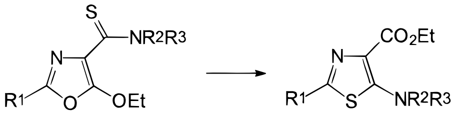
compound	I[b]	II[c]	III[d]	IV[e]
TS(**1a** → **2a**)	6.6	4.4	4.5	3.2
2a	−47.2	−36.9	−45.2	−43.6
TS(**1b** → **2b**)[f]	0.5	0.0	−0.1	−0.1
2b	−54.9	−47.3	−58.9	−56.6
TS(**1c** → **2c**)	10.9	3.4	3.0	2.7
2c	−64.5	−58.3	−64.6	−60.6
TS(**1d** → **2d**)	17.8	13.1	8.8	9.6
2d	−49.5	−37.9	−48.7	−46.5
TS(**1e** → **2e**)	18.9	14.2	9.2	9.4
2e	−43.5	−28.0	−40.0	−39.5
TS(**3** → **4**)	2.7	0.2	0.7	0.3
4	−44.6	−40.9	−50.3	−49.2
TS(**3** → **5**)	10.2	3.7	5.9	3.4
5	−31.8	−28.3	−33.9	−34.0
TS(**6a** → **7a**)	14.1	9.8	13.0	10.2
7a	−17.7	−13.5	−16.7	−16.8
TS(**6a** → **8a**)	8.0	2.8	4.6	2.7
8a	−37.6	−32.7	−38.2	−37.7
6b	3.8	−0.1	1.3	0.6
TS(**6b** → **7b**)	7.6	4.6	7.6	5.3
7b	−28.7	−22.1	−25.8	−25.1
6c	1.1	−0.1	0.6	0.3
TS(**6c** → **8c**)	7.0	2.7	4.3	2.5
8c	−39.2	−33.0	−38.8	−38.1

[a] Energies are given relative to the nitrile ylides **1a**−**e**, **3**, and **6a**, respectively; TS(**6b** → **7b**), **7b**, TS(**6c** → **8c**), and **8c** are given relative to **6b** and **6c**, respectively. Total energies and ZPE values are collected in Table S1 of the Supporting Information. [b] HF/6-311+G**//HF/6-311+G** + ZPE(HF/6-311+G**). [c] B3LYP/6-311+G**//B3LYP/6-311+G** + ZPE(B3LYP/6-311+G**). [d] MP2/6-311+G**//MP2/6-311+G**+ZPE(MP2/6-311+G**). [e] MP4(SDTQ)/6-311+G**//MP2/6-311+G** + ZPE(MP2/6-311+G**). [f] The apparently negative activation energies result from inclusion of unscaled ZPE corrections; however, a genuine transition state was found.

(SDTQ)/6-311+G**//MP2/6-311+G**) are collected in Table 1. Total energies and zero point energy (ZPE) corrections are summarized in Table S1 of the Supporting Information. Conjugated nitrile ylides are highly reactive intermediates which easily cyclize to the corresponding azoles;[5] two acyl substituents have been found to provide sufficient stabilization for a thermal equilibrium, e.g. **9** ⇋ **10** → **11**, between 4-acyloxazoles with a small amount of a diacyl nitrile ylide to be established.[5,17,25] In line with these experimental findings, all the cyclizations treated here are calculated to be substantially exothermic. There seems to be little difference between the ab initio procedures (HF vs MP2 vs MP4(SDTQ)) with the Hartree−Fock method, except for sulfur-containing structures giving the most negative reaction energies. In contrast, at the B3LYP/6-311+G** level of theory up to 10 kcal mol^{-1} less exothermic reactions are calculated. In the case of nitrile ylide **3**, formation of the thiazole **4**, rather than that of oxazole **5**, is predicted to be the more favorable mode of cyclization (see Table 1). Experimentally, the Cornforth rearrangement of 4-(aminothiocarbonyl)-5-ethoxyoxazoles **12** was used to synthesize 5-aminothiazoles **13**.[18d] Thus, the calculated reaction energies are fully in line with these experimental findings. Similarly, in the Cornforth rearrangement **7** ⇋ **8**, which may serve as a model reaction for the transformation of 4-acyl-5-alkoxy oxazoles, e.g. **9** → **11**, the derivative **8** is predicted to be the favored cyclization product, as found also experimentally.[18a] This finding is independent of the conformation of **6**. There is little energy difference between the three conformations **6a**−**c**. The activation energy for the cyclization **6b** → **7b** is ca. one-half that for **6a** → **7a**. Formation of **7b** is calculated to be approximately 10 kcal mol^{-1} more exothermic than formation of **7a**. In contrast, there is little difference in both activation and reaction energies for formation of **8a** or **8c**, respectively. The rather pronounced conformational effect shown by the cyclization **6b** → **7b** might be attributed to the presence of the intramolecular hydrogen bond. Furthermore, in contrast to monoacyl nitrile ylides, intermediate **6** is calculated to be sufficiently stabilized with respect to the 5-hydroxyoxazole **7** (energy difference between **6a** and **7a** <20 kcal mol^{-1} (<30 kcal mol^{-1} for the pair **6b** and **7b**) as opposed to >40 kcal mol^{-1} for **1a** vs **2a**; see Table 1) to allow for the presence of a small amount of **6** in a thermal equilibrium **7** ⇋ **6**.



9 **10** **11**



12 **13**

Apart from the planarity or near-planarity of pseudopericyclic transition structures, such reactions also may have quite low activation energies.[12,13a,14,15] Thus, we anticipated that the cyclizations of vinyl nitrile ylides **1d** and **1e**, for which at least a monorotatory pathway is required, should have significantly higher activation energies. As can be seen from the data presented in Table 1, the calculated barriers for these two reaction are at least twice those for the cyclizations of (thio)acyl or imino nitrile ylides **1a**−**c**, **3**, and **6**. Experimentally, for X = CHR (R = electron withdrawing group), intermolecular reactions, e.g. 1,3-dipolar cycloadditions, can compete with or even suppress cyclization; in contrast, for X = O or NR, the intramolecular reaction prevails.[3b] With respect to the level of theory used, HF/6-311+G** calculations invariably yield the highest activation energies (about twice those obtained by B3LYP or MP2 computations). Except for the vinyl nitrile ylide cyclizations, where the B3LYP/6-311+G** results more closely match the HF/6-311+G** ones, results obtained at the B3LYP/6-311+G**, MP2/6-311+G**, and MP4(SDTQ)/6-311+G**// MP2/6-311+G** levels of theory, respectively, are rather similar. 1,5-Electrocyclization of thioformyl nitrile ylides **1b** and **3** to thiazoles **2b** and **4** is predicted to occur essentially without barrier (the marginally negative activation energies obtained for the cyclization of **1b** by MP2 and MP4 calculations (see Table 1) result from the inclusion of unscaled ZPE corrections; see also Figure S1 of the Supporting Information). Experimentally, for the enthalpy of activation $\Delta H^{\ddagger}$ for the disappearance of 2-(4-trifluoromethylphenyl)-5-methoxy-4-(*N*-phenyl-*N*-methyl)oxazolecarboxamide (**9**, Ar = 4-$CF_3C_6H_4$, R = N(Me)Phe), a value of $\Delta H^{\ddagger}$ = 28.2 kcal mol^{-1} has been found.[18a] The calculated barrier [23 kcal mol^{-1} (B3LYP/6-311+G**) to 32 kcal mol^{-1} (HF/6-311+G**)]

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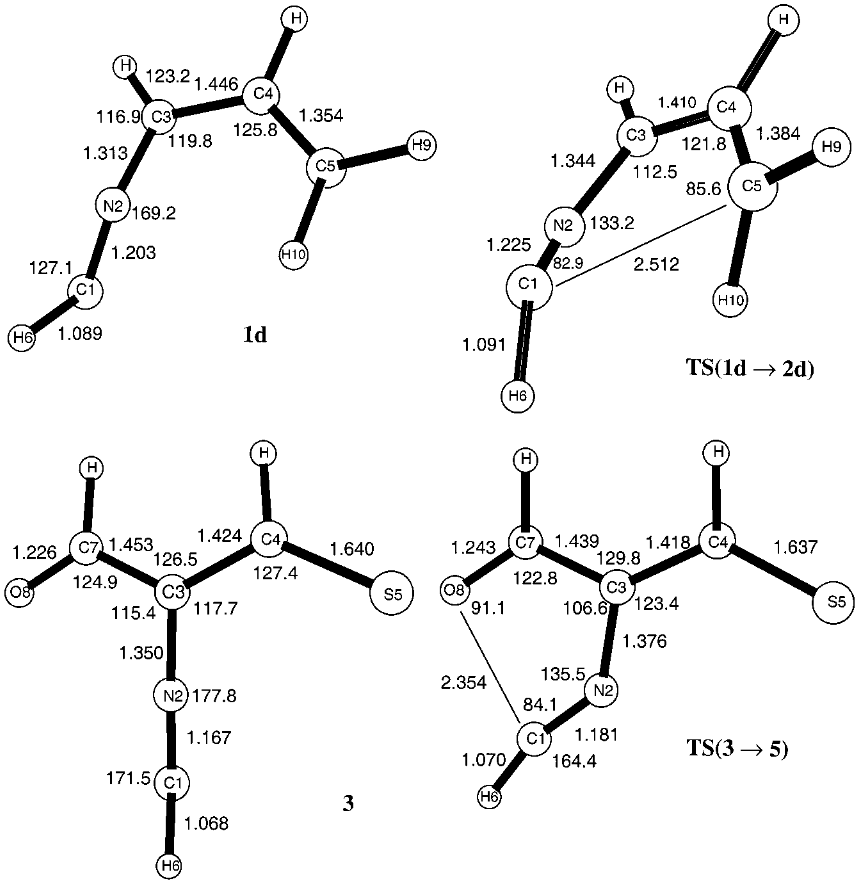
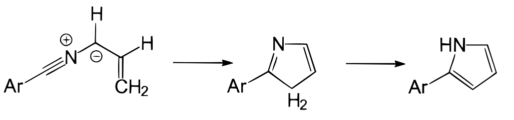


Figure 1. MP2/6-311+G** calculated structures of nitrile ylides **1d** and **3** and cyclization transition states TS(**1d** → **2d**) and TS(**3** → **5**) (Distances are in Å, angles in degrees).

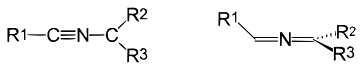
for ring opening of **7** [$\Delta E^{\ddagger} = E(\mathrm{TS}(\mathbf{6} \rightarrow \mathbf{7})) - E(\mathbf{7})$ in Table 1] is completely compatible with this experimental result. The 3*H*-pyrroles **2d,e** formed by 1,5-electrocyclizations of vinyl nitrile ylides **1d,e** may be further stabilized by aromatization, e.g. **14** → **15**.[1c] Incidentally, we have found



14 **15**

for **2e**, at the MP2/6-311+G** level of theory, the transition state for a [1,5] H-shift to give 3-cyano-2H-pyrrole (barrier, 20.9 kcal mol^{-1}, i.e., less than half the barrier for ring opening; reaction energy with respect to **2e**, −8.4 kcal mol^{-1}). Thus, the ease of this subsequent rearrangement to aromatic products makes the reaction, i.e., ring closure of **1d**, proceed.

Molecular Structures of Nitrile Ylides and Cyclization Transition States. According to Houk[26] nitrile ylides belong to the class of 1,3-dipoles with the least diradical character. Depending on the substituents R^2 and R^3, they are either of the propargyl type **A** or the



A **B**

allenyl type **B**. The parent nitrile ylide (R^1 = R^2 = R^3 = H) can be best characterized as a 2-azonia-allenyl anion (**B**).[26] Electron-withdrawing substituents at the ylide carbon (C3; see Figure 1 for atom numbering) lead to a stabilization of the propargyl type structure **A**.[26] However, MINDO/3 calculations on 3-aminocarbonyl-3-methoxycarbonyl nitrile ylide[18c] gave a significantly bent geometry with some pyramidalization at C3 and, thus, a structure more closely resembling the allenyl type **B**. Relevant structural features, obtained at the MP2/6-311+G** level of theory, are summarized in Table 2. The corresponding HF/6-311+G** and B3LYP/6-311+G** values are collected in Table S2 of the Supporting Information. Representative structures of nitrile ylides (**1d** and **3**) as well as the corresponding cyclization transition states [TS(**1d** → **2d**) and TS(**3** → **5**)] are depicted in Figure 1. Like the parent nitrile ylide, all substituted derivatives **1a**−**e**, **3**, and **6** are also comparably bent (~ 170°) at N2 (angle α in Table 2; see Figure 1 for atom numbering). The values for α obtained at different levels of theory are rather similar (<5° difference; see Table 2 and Table S2 of the Supporting Information). The monosubstituted derivatives **1a**−**e**, especially **1d**,**e** (i.e. those with X ≠ heteroatom), are also significantly bent at C1 (angle β in Table 2); nitrile ylide **1c** (X = NH) appears to be intermediate between **1a**,**b** and **1d**,**e**. The diacyl nitrile ylide **3** is almost linear at C1 (see Table 2). In contrast, for **6**, a bent structure is obtained at both the MP2/6-311+G** and B3LYP/6-311+G** level of theory (Table 2 and Table S2 of the Supporting Information). However, HF/6-311+G** calculations lead to a linear geometry like **3**. Generally, in

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[26] Houk, K. N.; Yamaguchi, K. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2, p 407.

Table 2. Selected Structural Features (MP2/6-311+G Geometries) of Nitrile Ylides and Cyclization Transition States (Distances in Å, Angles in Deg; for Atom Numbering see Figure 1)**

compound	α[a]	β[b]	Δ*q*[c]	*R*(C1−N2)	*R*(N2−C3)	*R*(C1−X5)[d]	τ[e]
nitrile ylide	172.0	122.4	0.008	1.210	1.299		
1a	170.9	140.9	0.014	1.184	1.326	3.435	−137.1
TS(1a → 2a)	138.8	149.7	0.056	1.189	1.348	2.436	156.2
1b	167.0	141.0	0.017	1.187	1.327	3.533	−141.8
TS(1b → 2b)	159.8	142.1	0.027	1.188	1.328	3.298	145.4
1c	169.8	135.7	0.016	1.190	1.321	3.397	−134.4 (178.5)[f]
TS(1c → 2c)	142.6	138.4	0.052	1.197	1.333	2.542	−146.7 (173.6)[f]
1d	169.3	127.1	0.018	1.203	1.313	3.567	−124.3 (178.3)[f] (−1.5)[g]
TS(1d → 2d)	133.2	127.3	0.055	1.225	1.344	2.512	144.1 (−164.3)[f] (33.3)[g]
1e	169.7	132.8	0.014	1.196	1.321	3.555	−129.2 (178.5)[f] (−1.5)[g]
TS(1e → 2e)	133.8	130.3	0.048	1.219	1.352	2.525	147.9 (−161.5)[f] (37.0)[g]
3	177.8	171.5	0.052	1.167	1.350	3.690 (3.489)	−171.6 (170.6)[h]
TS(3 → 4)	158.0	172.0	0.051	1.170	1.354	3.197 (3.812)	−178.5 (178.1)[h]
TS(3 → 5)	135.3	164.4	0.036	1.181	1.376	4.307 (2.353)	−179.0 (−179.8)[h]
6a	173.8	156.9	0.017	1.173	1.339	3.410 (3.521)	−153.7 (151.8)[h]
TS(6a → 7a)	128.5	162.1	0.001	1.187	1.376	4.077 (2.165)	−179.9 (179.9)[h]
TS(6a → 8a)	137.2	165.6	0.026	1.179	1.364	2.400 (4.022)	−178.4 (177.3)
6b	173.3	154.0	0.002	1.175	1.338	4.652 (3.388)	54.2 (150.5)[h]
TS(6b → 7b)	131.6	164.3	0.021	1.184	1.366	4.653 (2.277)	173.4 (178.6)[h]
6c	172.5	154.1	0.011	1.175	1.337	3.401 (4.668)	150.8 (52.7)[h]
TS(6c → 8c)	137.4	165.5	0.020	1.180	1.363	2.409 (4.709)	−178.4 (−161.5)[h]

[a] ∠(C3−N2−C1). [b] ∠(N2−C1−H6). [c] Height of C3 above plane formed by N2−C4−R7. [d] R(C1−O8) in parentheses; In **6**, **TS(6 → 7)**, and **TS(6 → 8)**, X5 and O8 represent the aldehyde and carbonyl oxygen of the carboxyl group, respectively. [e] Torsional angle ∠(C4−X5−C1−H6). [f] Torsional angle ∠(C3−C4−X5−H9); for **1e** and TS(**1e** → **2e**) ∠(C3−C4−X5−C9). [g] Torsional angle ∠(C3−C4−X5−H10). [h] Torsional angle ∠(C7−O8−C1−H6).

contrast to the angle α, some dependence of the amount of bending at C1 (angle β) on both the method and basis set used is found. Compared to the unsubstituted nitrile ylide, for acyl and—even more so—diacyl derivatives, distances *R*(C1−N2) and *R*(N2−C3) are significantly shorter and longer, respectively. For comparison purposes, the calculated (MP2/6-311+G**) C−N distances *R*(C1−N2) in vinyl isonitrile and 2-azabutadiene are *R* = 1.188 and 1.283 Å, respectively. For ketenimine, *R*(N1−C2) = 1.234 Å. Thus, despite the bend at C1, acyl-substituted nitrile ylides appear to correspond more closely to the propargyl type **A**, whereas (cyano)vinyl nitrile ylide **1d** and **1e** resemble the allenyl type **B.** The results of the NBO analysis (see below) corroborate this assertion.

In line with the exothermic nature of all the cyclizations considered here, the distances *R*(C1-X5) between the atoms involved in the forming bond are still quite long, indicating a rather early transition state. Correspondingly, changes in *R*(C1−N2) and *R*(N2−C3), especially for the (di)acyl derivatives, are also quite small in going from the nitrile ylides to the respective cyclization transition states. Although the cyclization transition states involving nitrile ylides **1a**,**1b**, **3**, and **6** are characterized by a nearly planar arrangement of the heavy atom skeleton, they lack any geometrical probe which could be reliably used as an indicator for a pericyclic or pseudopericyclic mode of electrocyclization; a distinction between these two mechanistic pathways, thus, has to rely on an analysis of the electronic rather than the geometric structure of the corresponding transition states (see below). In contrast, **1c**−**e** offer the possibility to use the torsion angles τ(C3−C4−X5−H9) (τ(C3−C4−X5−C9) for **1e**) and, for **1d,e**, in addition τ(C3−C4−X5−H10) as a measure for the nonrotatory or monorotatory character of these cyclizations. In the transition state for the cyclization of **1c** there is little change in τ(C3−C4−N5−H9) compared to its value in **1c** (173.6° vs 178.5°; see Table 2). In stark contrast, TS(**1d** → **2d**) and TS(**1e** → **2e**) show substantial torsion of the vinyl group as well as pyramidalization at C5 (see Table 2). Clearly, thus, the cyclizations of **1d** and **1e** follow the classic pericyclic, i.e., monorotatory, mode, whereas the geometrical features of TS($\mathbf{1c} \rightarrow \mathbf{2c}$) are indicative of a nonrotatory pseudopericyclic 1,5-heteroelectrocyclization.

Electronic Structures of Nitrile Ylides and Cyclization Transition States. To further strengthen the arguments based on molecular geometries, an analysis of the respective electronic features of nitrile ylides and the cyclization transition states with the aid of the NBO procedure[23,24] was performed (for details see Table S3 of the Supporting Information). The electronic structure of the unsubstituted nitrile ylide is characterized by two orthogonal π-bonds between C1−N2 and N2−C3, respectively, and a lone pair at C1 with an occupation number of 1.69e; approximately 0.36e of the lone pair at C1 is delocalized into the antibonding π^* (N2−C3) orbital. Thus, the results of the NBO analysis of the parent nitrile ylide are completely compatible with the allenyl type structure **B**. Most of the negative charge [see Table S4 of the Supporting Information for natural charges (NPA)] resides on N2 and, to a lesser extent, on C3. Vinyl nitrile ylide **1d** shows a rather similar electronic structure as the parent molecule itself. A significant amount of negative charge is accommodated by the vinyl carbon atoms (C4 and C5; Table S4). Introduction of the cyano group at C5 completely alters the electronic structure: the nitrile ylide functionality resembles a propargyl type (two orthogonal π-bonds between C1 and N2); C3 and the vinyl carbons are part of a three-center bond). The "nonbonding" three-center orbital has, however, a rather low occupation number (1.26e) with a substantial delocalization into the antibonding π_z^*(C1−N2) orbital (0.66e). The acyl substituted nitrile ylides **1a**,**b**, **3**, and **6** are characterized by a propargyl type (**A**) electronic structure with a "lone pair" (occupation number ≈ 1.3e) at C3 with significant delocalization into the C1−N2 and C4−X5 π_z^*-orbitals. Interestingly, **1c** (X = NH), like **1d**, also corresponds to a 2-azonia-allenyl anion (**B**) with a "lone pair" (occupation number 1.33e) at C1. On the basis of substituent and solvent effects on the kinetics of the Cornforth rearrangement of 4-acyl-5-alkoxy oxazoles $\mathbf{9} \rightarrow \mathbf{11}$, it was concluded that either the intermediate **10** must be relatively nonpolar or the transition state leading to it must occur early in the reaction.[18a,c] Given the endothermic nature of the ring-opening process, this latter possibility was dismissed as unlikely.[18c] The calculated (see above) structures of the cyclization transition states corroborate this argument. Insofar as dipole moments μ are indicative for the polar nature of a molecule, the calculated (MP2/6-311+G**) values for μ (**6**, 3.19 D; **7**, 6.65 D; **8**, 3.66 D) also point to a rather low polarity of nitrile ylide **6**. The effect of variation of substituents in the 2-aryl group in oxazoles of type **9** on the kinetics of the ring opening was interpreted in terms of development of a small positive charge at the substituted carbon.[18a] The NPA charges (see Table S4 of the Supporting Information) at the corresponding carbon C1 of **6** are 0.324 and 0.464. Thus, these model systems also show the experimentally found small increase of positive charge at C1.

In the cyclization transition states of acyl substituted nitrile ylides **1a**,**b**, **3**, and **6** the electronic features of the open isomers are largely preserved. Specifically, in going from the nitrile ylide to the respective transition state, no discernible bonding between C1 and X5 is yet developed. The transition state TS($\mathbf{1c} \rightarrow \mathbf{2c}$) shows a striking peculiarity: whereas **1c** more closely resembles the 2-azonia-allenyl anion type **B**, TS($\mathbf{1c} \rightarrow \mathbf{2c}$)—like those of acyl derivatives—corresponds to a propargyl type structure **A** with a "lone pair" (occupation number 1.27e) at C3. By comparison of the NBO's of these transition states [i.e. TS($\mathbf{1a} \rightarrow \mathbf{2a}$), TS($\mathbf{1b} \rightarrow \mathbf{2b}$), TS($\mathbf{1c} \rightarrow \mathbf{2c}$), TS($\mathbf{3} \rightarrow \mathbf{4}$), TS($\mathbf{3} \rightarrow \mathbf{5}$), TS($\mathbf{6} \rightarrow \mathbf{7}$), and TS($\mathbf{6} \rightarrow \mathbf{8}$)] with those of the ring-closed products, it becomes clear that the new C1−X5 (or C1−O8) bond is formed by interaction of the lone pair at the heteroatom X5 (or O8) and the in-plane π-orbital of the nitrile ylide group. In contrast, the cyclization of vinyl nitrile ylide **1d** is accompanied by a rather substantial reorganization of the electronic structure: the π(N2−C3) bond is broken, instead an additional π(C1−N2) bond, leading to a propargyl type structure for the nitrile ylide group, as well as a three-center bond involving the p_z- AO's at C3 and C4 and a p_x−p_z hybrid at C5, is formed. The "non-bonding" combination of this three-center bond is significantly delocalized into the π^*-(C1−N2) orbital (0.83e; bond order C1−C5 = 0.354), providing the sp^3(C5)−sp^2(C1) single bond as well as the sp^2-type lone pair at N2 of the product **2d**. Thus, to give **2d** via TS($\mathbf{1d} \rightarrow \mathbf{2d}$), at least rotation of the vinyl group is essential. Similarly, in TS($\mathbf{1e} \rightarrow \mathbf{2e}$), with the three-center bond already present in **1e**, its nonbonding combination—again via rotation of the vinyl group—provides a C1−C5 bonding interaction (bond order = 0.355). In addition, for TS($\mathbf{1d} \rightarrow \mathbf{2d}$) and TS($\mathbf{1e} \rightarrow \mathbf{2e}$), there is substantial $\pi_{x,z}$-mixing in the C1−N2 moiety. In contrast, in TS($\mathbf{1a} \rightarrow \mathbf{2a}$), TS($\mathbf{1b} \rightarrow \mathbf{2b}$), TS($\mathbf{1c} \rightarrow \mathbf{2c}$), TS($\mathbf{3} \rightarrow \mathbf{4}$), TS($\mathbf{3} \rightarrow \mathbf{5}$), TS($\mathbf{6} \rightarrow \mathbf{7}$), and TS($\mathbf{6} \rightarrow \mathbf{8}$), this mixing is quite small. Thus, the NBO analysis of the electronic structures of these cyclization reactions corroborates the pseudopericyclic, nonrotatory 1,5-heteroelectrocyclization pathway in the case of nitrile ylides for which X is a heteroatom. In contrast, the reaction of vinyl nitrile ylides **1d** and **1e** follows the classical pericyclic monorotatory, or possibly even bisrotatory, mechanism. Finally, according to the magnetic criterion of aromaticity,[27] the transition states of thermally allowed pericyclic reactions have aromatic transition states which can have not just π but also σ or hybrid character, e.g. the so-called in-plane aromaticity postulated for certain 1,3-dipolar cycloadditions.[13b] In line with these findings, all the transition states treated here have calculated magnetic anisotropies (see Table S5 of the Supporting Information) comparable to those for 1,3-dipolar cycloadditions,[13b] independently of the aromatic character (or lack thereof, e.g. **2a** vs **2d**) of the respective cyclization product.

Conclusion

The main conclusions emerging from the present computational study can be summarized as follows: (i) The calculated activation energies for cyclization of conjugated nitrile ylides where X = heteroatom are substantially lower than those where X = CHR. Experimentally, when X = CHR, intermolecular reactions, e.g. 1,3-dipolar cycloadditions with dipolarophiles compete or even suppress cyclization, whereas for X = heteroatom the intramolecular reaction is favored. [3b] (ii) In the Cornforth rearrangements $\mathbf{4} \leftrightharpoons \mathbf{5}$ and $\mathbf{7} \leftrightharpoons \mathbf{8}$ via nitrile ylides **3** and **6**, respectively, thiazole **4** and oxazole-4-carboxylic acid **8** are calculated to be the favored cyclization products, as is also found experimentally. (iii) Vinyl nitrile ylides **1d** and **1e** are best characterized as 2-azo-

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[27] Jiao, H.; Schleyer, P. v. R. *J. Phys. Org. Chem.* **1998**, *11*, 655.

nia-allenyl anions (structure B), whereas acyl derivatives correspond to the propargyl type A. (iv) In agreement with conclusions derived from substituent and solvent effects on the kinetics of the Cornforth rearrangement of 4-acyl-5-alkoxyoxazoles,[18a] the nitrile ylide intermediates are considerably less polar than a zwitterionic formula would suggest. (v) 1,5-Electrocyclization of vinyl nitrile ylides **1d** and **1e** proceed via a pericyclic, monorotatory (or possibly even bisrotatory) mechanism. The respective transition states involve rotation of the vinyl group with a concomitant pyramidalization of the terminal carbon atom. (vi) The analogous reactions of acyl nitrile ylides are characterized by an almost planar transition state. Analysis of the electronic structures reveal in-plane attack of the heteroatom's lone pair onto the $\pi_{x,y}$(C1−N2) orbital as the key feature. For TS(**1c** → **2c**) the molecular structure (planar NH) further corroborates the description of these latter 1,5-electrocyclizations as pseudopericyclic heteroelectrocyclizations.

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Supporting Information Available: Total energies including ZPE values (Table S1), structural data (Table S2) and results of NBO analysis (Tables S3 and S4), and magnetic anisotropies (Table S5) of the electronic structures of reactants, transition states, and products. This material is available free of charge via the Internet at http://pubs.acs.org.

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