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Reactivity of 2-Pent-4-yn-1-ylpyrimidines in Intramolecular Diels–Alder Reactions. Molecular Mechanics and MNDO Calculations and Crystal Structure Determinations

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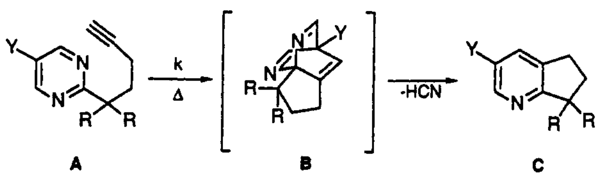
The enhanced reactivity of 2-pent-4-yn-1-ylpyrimidines for intramolecular Diels–Alder reactions to 6,7-dihydro-5*H*-1-pyrindines upon replacement of the α-hydrogens by cyano groups was investigated. The crystal structures of 5-(*p*-nitrophenyl)-2-pent-4-yn-1-ylpyrimidine (1) and 2-(1,1-dicyanopent-4-yn-1-yl)-5-nitropyrimidine (2) showed that 2 adopts a conformation in which the reacting centers are much closer together than in 1. Determination of the energy minima of the related compounds 3 and 4 revealed that the crystal structure conformations of 2 do not constitute the minimum energy conformation of 4. Further calculations show that the enhanced reactivity of the α,α-dicyanopentynyl compounds may be caused by a higher electron-withdrawing effect of the dicyanoalkyne group as revealed by a lower transition state energy (MNDO calculations) and by a higher population of conformations with a short distance between diene and dienophile (MM calculations), caused by the steric influences of the cyano groups.

Introduction

Recently we described intramolecular Diels–Alder reactions of pyrimidines carrying an alkyne-containing dienophilic side chain attached to the 2- or 5-position of the pyrimidine ring.[1,2] Initially, tricyclic intermediate cycloadducts B are believed to be formed (see Scheme I). These intermediates could, however, not be isolated or identified by ^{1}H NMR spectroscopy due to the spontaneous cycloreversion into *b*-annelated pyridines C by expulsion of hydrogen cyanide. This means that the presumed cycloaddition is the rate-determining step in the reaction. In the course of our studies on the intramolecular Diels–Alder conversions of 2-pent-4-yn-1-ylpyrimidines to 6,7-dihydro-5*H*-1-pyrindines we have observed that the reaction is much faster when the α-hydrogen atoms are replaced by cyano groups[2] (see Scheme I and Table I). For the α,α-dicyano-substituted pyrimidine 4, an 18-fold rate enhancement has been observed as compared to the α,α-dihydrogen compound 3 (see Table I).

Although this type of rate enhancement (commonly referred to as the *gem*-dialkyl effect[4] or Thorpe–Ingold effect[5]) is often observed in intramolecular reactions, there is some controversy as to the cause of this phenomenon. One explanation is that due to the presence of substituents at the α-carbon atom, the bond angle between C2–C7 and C7–C8 is diminished, thereby allowing the reacting groups to approach one another better.[5] A different explanation comes from the assumption that, due to the presence of substituents at Cα, the preference for an anti conformation of the groups at Cα and Cβ containing the reacting groups decreases and consequently the percentage of molecules in a syn (syn-clinal and syn-periplanar) conformation, which is considered to be the reactive conformation, increases.[6]

Scheme I



1: Y = *p*-NO$_2$-Ph; R = H
2: Y = NO$_2$; R = CN
3: Y = H; R = H
4: Y = H; R = CN

Table I. Reactivity at 175 °C for the Conversion of the Pyrimidine Compounds 1–4 into the Corresponding Pyrindine Compounds[3]

compd	Y	R	*k*[a]
1	*p*-NO$_2$Ph	H	3.7×10^{-5}
2	NO$_2$	CN	4.8×10^{-3}
3	H	H	4.3×10^{-5}
4	H	CN	7.7×10^{-4}

[a] Values in reciprocal seconds.

In order to gain more insight into the observed rate enhancement by replacing the α-hydrogens in 2-pent-4-yn-1-ylpyrimidines by cyano groups, we determined the crystal structures of a compound with (2) and of a compound without (1) cyano groups at the Cα position. Unfortunately, crystal structures of the computationally more practical compounds 3 and 4 could not be determined, since no appropriate crystals could be obtained. Furthermore, the preferred conformations of 2-pent-4-yn-1-ylpyrimidine (3) and the 2-(1,1-dicyanopent-4-yn-1-yl)pyrimidine (4) were determined (molecular mechanics (MM) calculations). Conformational analyses of these compounds (also MM calculations) were performed in order to com-

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Table II. Some Important Conformational Data from the Crystal Structure Analyses of Compounds 1 and 2

entry	cryst struct	C2–C7[a]	C7–C8[a]	φ^b	α^b	β^b	γ^b
1	1	1.498 (8)	1.510 (8)	115.5 (5)	31.1	−178.8	−171.3
2	**2a**	1.538 (7)	1.570 (8)	110.2 (4)	68.8	62.7	−70.5
3	**2b**	1.527 (7)	1.564 (9)	111.0 (4)	76.5	62.1	−80.8

[a] Bond distances in angstroms. [b] Angles in degrees. Dihedral angles: α, N1–C2–C7–C8; β, C2–C7–C8–C9; γ, C7–C8–C9–C10. Bond angles: φ, C2–C7–C8.

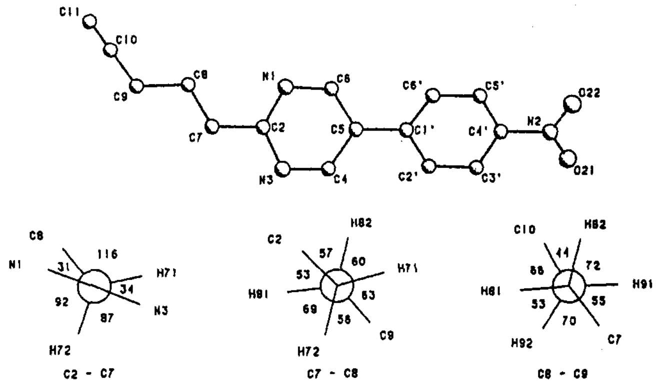


Figure 1. Molecular structure and Newman projections along C2–C7, C7–C8, and C8–C9 of 5-(*p*-nitrophenyl)-2-pent-4-yn-1-ylpyrimidine (1).

pare the amount of molecules in "reactive" conformations. The transition states (MNDO calculations) for the conversion of A to B of both compounds 3 and 4 were determined in order to investigate the electronic effect of the α,α-dicyanopentynyl group on the energy of activation of the rate-determining cycloaddition reaction.

Results and Discussion

Crystal Structure Analyses. Crystals of compounds 1 and 2 were prepared as previously described[2b] and were found suitable for crystal structure analyses. The molecular structure of compound 1 is depicted in Figure 1, together with the atom numbering.

The alkynyl chain is completely stretched as is also clearly seen in the Newman projections along C7–C8 and along C8–C9 where substituents are nearly perfectly anti (see Figure 1). In this structure C11 in the dienophile and C5 in the diene are located at the largest possible distance of 8.46 Å from one another.

The unit cell of crystals of compound 2 contains two independent molecules (**2a** and **2b**). The structure of molecule **2a** is shown in Figure 2, together with the atom numbering. The structures of both molecules show a great resemblance to one another (see Table II). However, the conformations of both molecules **2a** and **2b** are completely different from 1, as is clearly seen in Table II and the Newman projections for molecule 2 along C7–C8, where C2 of the pyrimidine group and C9 are in a syn conformation, and in the Newman projection along C8–C9, where C7 and C10 of the alkyne group are also in a syn conformation (see Figure 2). As a result, the alkyne and the pyrimidine group are much closer together in the molecular structures of **2a** and **2b** than in the molecular structure of 1 (C5···C11 = 3.52 Å for **2a**, 3.87 Å for **2b**, and 8.46 Å for 1). As could be expected, the bond angle C2–C7–C8 (φ) is smaller in **2a** and **2b** (110.2° and 111.0°, respectively) than in 1 (115.5°), due to the bulkiness of the cyano group as compared to a hydrogen.

A comparison of the molecular structures of 1 and 2 seems to lend support to our suggestions about the higher reactivity of 2 in intramolecular cycloaddition reactions, namely a higher population of reactive syn conformers about C7–C8 for 2 than for 1 and a decreased bond angle φ, both caused by the introduction of the two cyano groups. However, the conformations as found in the crystal structure analyses may be influenced by crystal packing effects and may therefore not represent the conformations with minimum energy. Therefore, conformations in the crystals may not be as relevant for the observed rate enhancement as they appear. Another effect that may enhance the intramolecular inverse electron demand reaction of compounds 2 and 4 is the inductive electron-withdrawing effect of the α-cyano groups, which would make the diene more reactive.

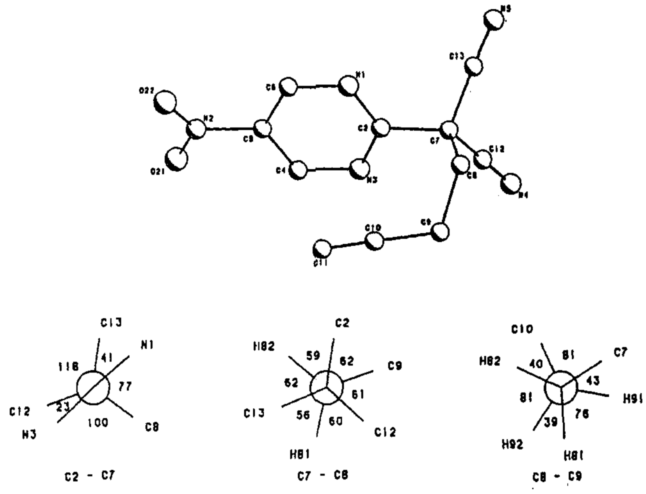


Figure 2. Molecular structure and Newman projections along C2–C7, C7–C8, and C8–C9 of 2-(1,1-dicyanopent-4-yn-1-yl)-5-nitropyrimidine (**2a**).

Computational Analyses. To study the influence of the previously mentioned effects, it was decided to determine the conformations of minimum energy of the compounds 3 and 4. Furthermore, conformational analyses and MNDO calculations of the heats of activation of these molecules were performed. Despite the fact that the X-ray structures of the 5-*p*-nitrophenyl compound 1 and the 5-nitro compound 2 were determined, in the computations the substituents at C5 were not included in order to reduce computation time. Therefore, all calculations in this study were performed with the compounds 3 and 4 with hydrogen at C5. The compounds 3 and 4 have also been prepared earlier,[2b] and their reactivity has been measured (see Table I).

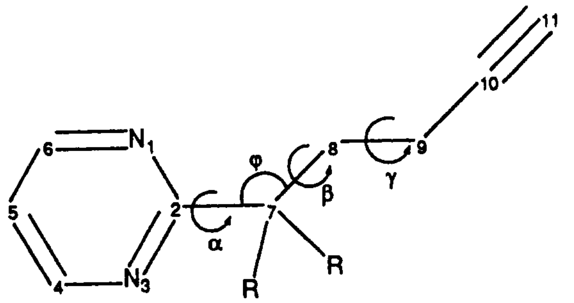
Determination of the Preferred Conformations. In order to determine the preferred conformation (i.e., the conformation with minimum energy), all structures with a staggered conformation along C2–C7 (α), C7–C8 (β), and C8–C9 (γ) (see Figure 3) were optimized with an energy convergence criterion of 0.01 kcal/mol·Å and their MM energies were calculated[7] (see Table III).

From Table III (entry 6) and Table II (entry 1) it is seen that there is a great resemblance between the structure of minimum energy of compound 3 and the structure in the crystals of compound 1. Both the conformation of 1 and the lowest energy conformation of compound 3 have

Table III. Relevant Conformational Data and MM Energies of the Optimized Staggered Conformations of Compounds 3 and 4, As Calculated with the MM Force Field of the CHEMX Program[7]

	initial			3				4			
entry	α^b	β^b	γ^b	α'^b	β'^b	γ'^b	MM energy[a]	α'^b	β'^b	γ'^b	MM energy[a]
1	90	180	180	87.2	175.3	179.5	4.39	89.2	179.5	177.3	3.99
2	90	180	60	85.9	173.4	66.4	3.95	82.9	171.9	85.1	5.52
3	90	60	180	90.4	66.2	175.1	4.28	85.5	58.9	179.1	3.72
4	90	60	60	88.3	60.4	61.8	4.60	89.5	48.3	80.3	5.37
5	90	60	−60	82.7	73.7	−84.3	4.23	72.9	58.4	−81.3	4.94
6	30	180	180	29.9	174.3	176.8	3.90	37.5	176.1	175.9	8.78
7	30	180	60	25.6	177.5	64.5	5.12	29.6	173.7	79.8	6.09
8	30	180	−60	49.8	178.7	−77.0	4.38	40.9	175.4	−87.0	5.69
9	30	60	180	29.6	65.1	176.9	3.95	33.3	59.4	179.9	4.68
10	30	60	60	38.7	57.8	66.7	4.82	32.0	55.0	72.8	7.62
11	30	60	−60	41.2	71.6	−80.5	4.44	34.2	73.1	−76.1	5.54
12	30	−60	180	29.6	−75.4	174.2	6.10	33.9	−71.9	168.0	6.20
13	30	−60	60	43.7	−82.8	106.9	8.18	30.7	−75.3	115.1	8.64
14	30	−60	−60	33.4	−67.6	−54.5	7.00	36.7	−58.4	−74.4	10.70

[a] Values in kilocalories per mole. [b] Angles in degrees.



3: R = H, 4: R = CN

Figure 3. Atom numbering and some important conformational parameters of compounds 3 and 4. Dihedral angles: α, N1–C2–C7–C8; β, C2–C7–C8–C9; γ, C7–C8–C9–C10. Bond angles: φ, C2–C7–C8.

an anti conformation about C7–C8 as well as about C8–C9. The conformation with lowest energy of compound 4 (Table III, entry 3) has a syn conformation about C7–C8 and an anti conformation about C8–C9. Therefore, this conformation differs from the conformations of **2a** and **2b**, which have syn conformations about C7–C8 as well as C8–C9 (see Table II, entries 2 and 3). There is an energy difference of 1.22 kcal between the lowest energy conformation of compound 4 and the conformation resembling that in the crystal structure of compound 2 (see Table III, entries 3 and 5). This may indicate that the conformation in the crystal structure of compound 2 about C8–C9 is determined not only by the minimum energy but also by crystal packing effects. Due to the presence of the α-cyano groups, the crystal structure analyses as well as the MM calculations indicate that a syn conformation about C7–C8 is favored. As is seen from Table III, however, there are several conformations of 3 and 4 in local minima whose energies are within 1 kcal/mol from the minimum energy. Therefore, no strong conclusions can be drawn about the minimum energy conformation.[7b] Since the energy differences between several conformations in local minima are small and conformations that are not in a (local) minimum may also play a role in the reactivity of the molecules, other methods were also used to investigate this problem.

Conformational Analyses. The effect of the decreased bond angle C2–C7–C8 (φ) and the bulkiness of the substituents due to the presence of the α,α-dicyano groups was studied for compounds 3 and 4 by molecular mechanics methods. The molecules are considered to be rigid three-rotor structures[8] for which the structural parameters are used as obtained from the crystal structure determinations of the compounds 1 and **2a**.[9] The dihedral angles α, β, and γ (see Figure 3) were rotated with increments of 10°, to represent a three-dimensional conformational surface of these molecules. Due to the mirror symmetry of the pyrimidine group and the acetylene group, the dihedral angles α and γ were rotated only from 0° to 180°. In this manner, 11 665 conformations were generated and their potential energies were calculated in the MM force field of the CHEMX program.[7] Since all the low-energy conformations are thermally accessible, the probability of the molecules to be in a particular conformation can be calculated as function of the dihedral angles[8] α, β, and γ, by the Bolzmann distribution equation (1).

$$P_i(\alpha,\beta,\gamma) = \frac{e^{-dE_i/RT}}{Q} \qquad Q = \sum_{i=1}^{n} e^{-dE_i/RT} \tag{1}$$

In these calculations a temperature of 448 K (175 °C) was used since this is the temperature used for the rate determination in the experimental study (see Table I). The potential energy (E_i) of each conformation was related to the potential energy of the conformation with the lowest energy (E_{min}), to give the potential energy difference ($dE_i = E_i - E_{min}$).

When the distance C5···C11 of each compound is taken as a measure of the proximity of its reacting sites, the distance C5···C11 of a certain conformation can be regarded as a parameter for the reactivity of that conformation.

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(7) (a) The molecular mechanics method was part of the CHEMX program; the MM force field, however, was not specially parameterized for the heteroaromatic structures under study. CHEMX, molecular modeling software: Distributed by Chemical Design, Ltd., Oxford, U.K. Recent reference on the CHEMX MM force field: Davies, E. K.; Murrall, N. W. *Computers Chem.* **1989**, *13*, 149. (b) When other force fields are used for the optimizations of the staggered conformations, slightly other energy differences may be obtained. Furthermore, it should be realized that gas-phase assumptions were used in the calculations. Due to solvent effects or crystal packing effects, the results obtained may not correctly predict the conformations of the molecules in solution or in crystals.

(8) (a) Smeyers, Y. G.; Hernandez-Laguna, A. *Int. J. Quantum Chem.* **1986**, *29*, 553. (b) Miller, K. E.; Rich, D. H. *J. Am. Chem. Soc.* **1989**, *111*, 8351.

(9) The same procedure was repeated with structural parameters obtained from **2b** after the crystal structures were optimized by MM. Although the probability partitions are slightly different from the calculations using the crystal structure parameters from **2a**, the α,α-dicyano compound still has a significantly higher probability to be in a conformation with a short distance C5···C11.

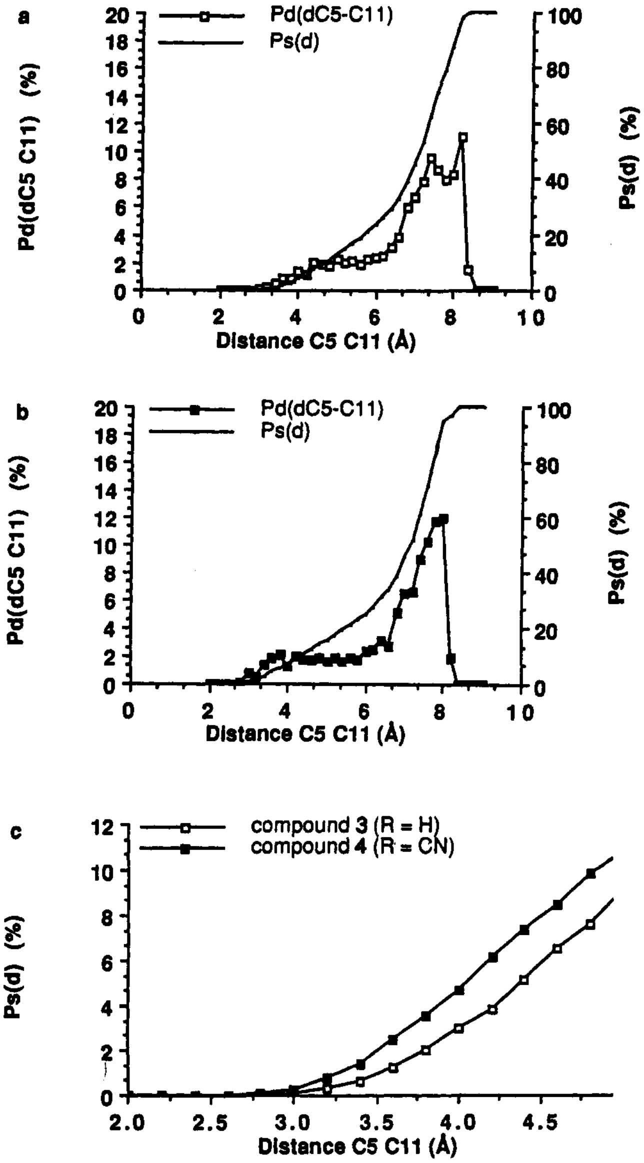

Figure 4. Probability partition related to the distance C5⋯C11, $P_d(d(\mathrm{C5}\cdots\mathrm{C11}))$ (according to eq 2; left *y*-axis) and $P_s(d)$ (according to eq 3; right *y*-axis), of compound 3 (a) and compound 4 (b) and comparison of the summed probabilities of both compounds for short distances (c).

Sorting the conformations as a function of the distance C5⋯C11, in arbitrary intervals of 0.2 Å, results in a probability partition of the conformations of each compound related to the distance C5⋯C11 (eq 2).

$$P_d(d(\mathrm{C5}\cdots\mathrm{C11})) = \sum_{d=d-0.2}^{d} P_i(d) \qquad (2)$$

To give better insight into the reactivity of each compound (i.e., the probability to be in a conformation with a short distance between the reactants), the sum of the probabilities ($P_s(d)$) having a distance C5⋯C11 shorter than a certain value is calculated according to eq 3.

$$P_s(d) = \sum_{d=0}^{d} P_d(d(\mathrm{C}_5\cdots\mathrm{C11})) \qquad (3)$$

The results of these calculations for compounds 3 and 4 are depicted in parts a and b, respectively, of Figure 4. From Figure 4a,b it is seen that the probability partitions of compounds 3 and 4 are more or less the same. Both molecules have the highest probability for conformations with a large distance between the alkyne group and the pyrimidine ring. At short distance, C5⋯C11 of 2.5 Å or less, the probability decreases to zero. When the summed probabilities ($P_s(d)$) of compounds 3 and 4 are compared (Figure 4c), it is clearly seen that the α,α-dicyano compound 4 has a higher probability to be in a conformation with a distance C5⋯C11 of less than 4 Å than the α,α-dihydrogen compound 3.

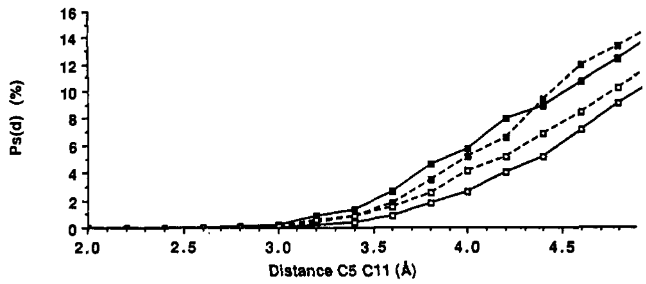

Figure 5. Summed probability partitions ($P_s(d)$) related to short (reactive) distances C5⋯C11 of the structures 3 (R = H, φ = 115.5°; -□-), 3′ (R = CN, φ = 115.5°; --■--), 4 (R = CN, φ = 110.2°; -■-), and 4′ (R = H, φ = 110.2°; --□--).

As already stated, the reason for this higher probability is possibly due to be the smaller bond angle C2–C7–C8 of the α,α-dicyano compound, or a higher syn population about C7–C8 due to the steric influence of the cyano groups. The effect of the bond angle C2–C7–C8 and the steric hindrance on the probability of the molecule to have a short distance C5⋯C11 can be assessed by taking the conformational parameters of compounds 3 (R = H, φ = 115.5°) and 4 (R = CN, φ = 110.2°) and interchanging the substituents on C7, while keeping the rest of the parameters the same. In this manner, structures 3′ (R = CN, φ = 115.5°) and 4′ (R = H, φ = 110.2°) are generated. For both structures 3′ and 4′ the probability calculations, as described above, have also been performed. In Figure 5 the summed probabilities ($P_s(d)$) of all four compounds 3, 3′, 4, and 4′ are depicted for small (reactive) C5⋯C11 distances.

Structures 3 and 4′ and also structures 4 and 3′ are the same with the exception of their geometry around Cα (C7). The differences in the summed probability partitions (see Figure 5) of 3 and 4′ (both R = H) and 4 and 3′ (both R = CN) are only due to the difference in their bond angle C2–C7–C8 (Thorpe–Ingold effect). It is seen from Figure 5 that the structures with a smaller bond angle, 4 and 4′, have a higher probability as compared to their counterparts 3′ and 3, respectively, at C5⋯C11 distances smaller than 4.4 Å. On the other hand, structures 3 and 3′ and also 4 and 4′ have the same angles about Cα, but different substituents. Therefore, the differences between the summed probability partitions of 3 and 3′ and also between 4 and 4′, respectively, are only due to the steric influences of the substituents (*gem*-dialkyl effect). From Figure 5 it is clearly seen that the structures with the cyano substituents (4 and 3′) have a higher probability to be in conformations with a short distance C5⋯C11 than their counterparts with the hydrogen substituents 4′ and 3, respectively.

From the examination of Figure 5, the conclusion can be drawn that both a reduction of the bond angle C2–C7–C8 and the presence of the sterically hindering cyano groups increase the probability of the molecule to have a short distance C5⋯C11. For the compounds under investigation, the bulkiness of the substituents on C7 seem to have more effect than the effect of a decreased bond angle, even though a cyano group is one of the least sterically hindering groups (E_s = −0.51; this is comparable to a fluorine group[10]).

Table IV. Some Important Conformational Data and Energies for the Cycloaddition Reaction of A to B (Starting (A), Transition State (TS), and Intermediate (B) Conformations)

entry	conformn	α^a	β^a	γ^a	φ^a	C2⋯C10[b]	C5⋯C11[b]	H_{formn}[c]	H_{activn}[c]
1	3 A	88.7	177.7	179.7	113.2	5.06	7.81	72.1	0.0
2	3 TS	89.4	33.2	−45.2	112.1	2.29	2.41	123.8	51.7
3	3 B	107.1	17.5	−17.7	105.8	1.56	1.54	64.2	−7.9
4	4 A	89.2	177.6	177.6	109.0	5.01	8.22	155.1	0.0
5	4 TS	84.9	39.5	−49.3	108.5	2.31	2.44	204.8	49.7
6	4 B	103.2	22.8	−22.7	103.0	1.56	1.53	144.3	−10.8

[a] Angles in degrees. [b] Bond distances in angstroms. [c] Values in kilocalories per mole.

Determination of the Transition States and Heats of Activation. Besides the determination of the probability of the molecules to be in a reactive conformation, the transition states and the accessory heats of activation of compounds **3** and **4** were also determined, since the difference in reactivity between various species also depends on the difference between their heats of activation.

Because the conversion of A to B (see Scheme I) involves the interaction between the π system of the ethynyl group and that of the pyrimidine ring, it was decided to use the VAMP program,[11a] which makes use of the semiempirical MNDO force field of Dewar and Thiel[11b] and the Davidon–Fletcher–Powell (DFP) geometry optimization routine.[12] The transition states of the Diels–Alder reaction were determined with use of the saddle-point method of McIver and Komornicki,[13] which was also implemented in the VAMP program. For reasons of computation time, the saddle-point calculations were not performed between the conformations of A and B, but between the conformations of A′[14] and B. Conformation A′ is characterized by a distance of 4 Å between C5 and C11, at which distance there was not yet any interaction between the diene and dienophile systems. The conformation of the intermediate B was also determined by the DFP geometry optimization routine[12] in the VAMP program. The saddle-point determination and the subsequent calculation of the transition-state geometries of **3** and **4** provided their heats of formation (see Table IV). The heats of formation of the starting geometries A were determined by reoptimizing the conformations of minimum energy, as found in the determination of the preferred conformation, in the MNDO force field of the VAMP program. The semiempirical MNDO method results in slightly different conformations of minimum energy (see Table IV, entries 1 and 4), as compared to the MM-optimized conformations (see Table III, entries 6 and 3). The heats of activation of each intramolecular cycloaddition were calculated by subtracting the heats of formation of the starting point geometries from those of the transition-state geometries (see Table IV).

As is seen from Table IV, the heat of activation of the α,α-dicyano system is 2.0 kcal/mol lower than that of the α,α-dihydrogen system. This difference has to be attributed to both the electron-withdrawing effect of the α,α-dicyanopentynyl group on the pyrimidine ring ($\sigma_p = 0.34$),[15] which is comparable to the electronic effect of a halogen or ester group, and the electron-donating effect of a pentynyl group ($\sigma_p = -0.14$). Therefore, the α,α-dicyanopentynyl group will enhance the Diels–Alder reaction with inverse electron demand, whereas the pentynyl group slightly decreases the reactivity of the system.

From the differences in the heat of activation it is clear that the reactivity-enhancing effect of the α-cyano groups as compared to the α-hydrogen atoms is a substantial part of the overall effect, which makes the α,α-dicyano system more reactive (see Table I).

Conclusions

The relative contributions of the different effects (a decreased bond angle φ, a preference for the syn conformation about C7–C8, and a lower heat of activation) of the cyano groups on the enhanced reactivity of the α,α-dicyano compounds ($k_4/k_3 = 18$, see Table I) are not easy to estimate. Each effect alone does not seem to be responsible for the observed rate enhancement, since introduction of a strongly activating nitro group (which is more activating than the α,α-dicyanopentynyl group) in the pyrimidine system generally gives only 5–10-fold rate enhancements.[1c] Also, substitution of the α-hydrogen atoms by methyl groups (which are significantly more sterically demanding than the cyano groups) gives only about 10-fold rate enhancements in intramolecular Diels–Alder reactions of the related 5-[(propynyloxy)methyl]pyrimidines.[1c]

The calculations as presented in this study suggest that the 18-fold rate enhancement observed for compound **4** as compared to **3** (see Table I) is supported by (i) the lower heat of activation, (ii) the preference for the syn conformation about C7–C8 (*gem*-dialkyl effect), and (iii) the decreased bond angle φ (Thorpe–Ingold) effect), which is due to the presence of the α-cyano groups.

Experimental Part

Crystal Structure Determinations. The X-ray intensities were measured on a Nonius CAD-4 diffractometer using graphite-monochromated Mo Kα (λ = 0.71069 Å) radiation. Intensities below the $2.5\sigma(I)$ level were treated as unobserved. The non-hydrogen atoms were found by means of the symbolic addition program set SIMPEL.[16] The hydrogen atoms were found in a ΔF synthesis. The structure was refined by a block-diagonal least-

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(14) The geometries of the A′ conformations of **3** and **4** were determined by the common reaction coordinate method, starting with the MNDO reoptimized A geometries of **3** and **4**. To bring the reaction centers together with as little restriction to the geometry as possible, dummy atoms were centered between the diene system (C2–C5) and the dienophile system (C10–C11) and brought together in increments of 0.5 Å. As the reaction coordinate, the distance C5⋯C11 was monitored. References on the reaction coordinate method: (a) Muller, K. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1. (b) Ermer, O. *Struct. Bonding (Berlin)* **1976**, *27*, 161. (c) Dewar, M. J. S.; Kirschner, S. *J. Am. Chem. Soc.* **1971**, *93*, 4290. (d) Sharma, K. K.; Aggarwal, A. K. *Indian J. Chem.* **1987**, *26A*, 906. (e) Dorweiler, C.; Holderbaum, M.; Muenzmay, T.; Spang, P.; Duerr, H.; Krueger, C.; Raabe, E. *Chem. Ber.* **1988**, *121*, 843.

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squares refinement, anisotropic for the C, O, and N atoms and isotropic for the H atoms. The calculations were carried out with XRAY76 and scattering factors from Cromer and Mann.[17]

5-(*p*-Nitrophenyl)-2-pent-4-yn-1-ylpyrimidine (1). Crystals of 1 are orthorhombic, space group *Pbca* with 8 molecules in the unit cell with dimensions a = 10.066 (2) Å, b = 34.428 (6) Å, c = 7.647(3) Å, V = 2650 (1) Å^3, μ = 0.86 cm^{-1}, and d_{calc} = 1.34 g cm^{-3}. Crystal dimensions are 0.18 × 0.20 × 0.50 mm. A total of 2437 intensities were measured, from which 1466 were below the 2.5$\sigma(I)$ level. The final R value was 0.052 (R_w = 0.062, using a weighing scheme $w = (85 + F_o + 0.003F_o^2)^{-1}$).

2-(1,1-Dicyanopent-4-yn-1-yl)-5-nitropyrimidine (2). Crystals of 2 are monoclinic, space group $P2_1/n$, with 8 molecules in the unit cell with dimensions a = 22.604 (2) Å, b = 10.271 (2) Å, c = 10.146 (2) Å, β = 98.75 (2)°, V = 2328.1 (7) Å^3, μ = 0.73 cm^{-1}, and d_{calc} = 1.32 g cm^{-3}. Crystal dimensions are 0.15 × 0.25 × 0.30 mm. A total or 4051 intensities were measured, from which 2286 were below the 2.5$\sigma(I)$ level. The final R value was 0.054 (R_w = 0.094, using a weighing scheme $w = (3.98 + F_o + 0.0216F_o^2)^{-1}$).

Computations. All molecular mechanics calculations were performed on the VAX cluster of the CAOS/CAMM Centre, University of Nijmegen, The Netherlands, with the MM force field of the CHEMX program.[7a] The MNDO calculations were carried out on a CONVEX C120 computer, with use of the VAMP program.[11]

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Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond distances, and bond angles (12 pages). Ordering information is given on any current masthead page.

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Indirect Electrooxidation of Alcohols by a Double Mediatory System with Two Redox Couples of $[R_2N^+{=}O]/R_2NO^\bullet$ and $[Br^\bullet$ or $Br^+]/Br^-$ in an Organic–Aqueous Two-Phase Solution

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An indirect electrooxidation method for alcohol to aldehyde or ketone conversion has been developed. This method, applicable to chemoselective oxidation, employs two redox couples, consisting of 2,2,6,6-tetramethylpiperidine-1-oxyl derivatives 6 and active bromine species. The former is required for the chemical process and recycled, whereas the latter is to be involved in the electrochemical process. Three chemical events play an important role in this system: (1) the formation of [$Br^\bullet$ or Br^+] from bromide ion by discharge on the anode in an aqueous solution, (2) the reaction of *N*-oxyl compounds 6 with active bromine species to generate *N*-oxoammonium ion 7, and (3) the oxidation of alcohols with 7 in an organic phase. Optimum conditions were established as follows: an aqueous 25% NaBr solution buffered at pH 8.6 in a binary system, the use of 1–10 mol % of 4-(benzoyloxy)piperidine derivatives 6, and adjustment of an electric current at 10–100 mA/cm^2. The successful applications of the present method to the oxidation of a variety of primary and secondary alcohols including 1,*n*-diols, giving the corresponding carbonyl compounds, have delineated its synthetic utility. The chemoselective oxidation of a primary hydroxy group in the presence of secondary one has been achieved with a high selectivity by the present procedure.

The development of practical electrooxidation methods for alcohols is one of desirable goals in synthetic chemistry.[1] In this context, a double mediatory system which features two redox couples consisted of Ru(VIII)/Ru(IV) and $[Cl^+]/Cl^-$ has been developed in our laboratory prior to the present work. This idea provided a considerable advantage that the chemical and the electrochemical processes took place separatedly in an organic and aqueous phase, respectively, by use of a two-phase solution.[2] Indeed, this procedure bears a practical aspect that it is capable of oxidizing secondary alcohols in a large-scale work.[2b] However, it is still desirable to find a more efficient system for selective aldehyde synthesis, which motivated us to examine the role of a nonmetallic redox reagent such as *N*-oxoammonium salts 7 as a mediator[3,4] for the chemical process to circumvent the problems imposed by the high-valency ruthenium compounds.

N-Oxoammonium salts 7 are highly useful for the oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones, respectively. For this purpose, aprotic media are usually employed, probably because they are labile in water.[5] However, it became feasible to manipulate this reagent in an aqueous–organic two-phase system because 7 can be revived, after oxidizing alcohols, by being oxidized with reagents such as NaOCl–KBr,[6] $NaBrO_2$,[7] $Ca(OCl)_2$,[7] and R_4NBr_3,[8] which occurs

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