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Theoretical and Experimental Study of the Regioselectivity of the Reaction of Diazomethane with Allene

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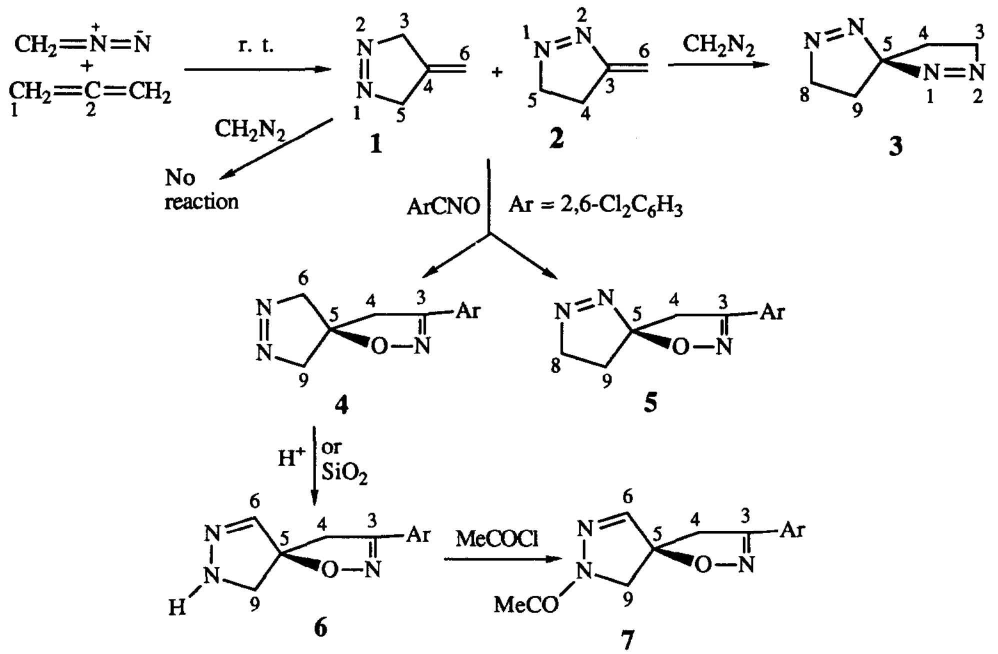
Abstract. *The reaction of diazomethane with allene at room temperature afforded a mixture of 4-methylene-1-pyrazoline (1) and 3-methylene-1-pyrazoline (2) in a 93:7 ratio. This finding revises literature data which describe this reaction as regiospecific with exclusive formation of 1. Good level ab-initio calculations (e.g., HF/6-31G*//HF/6-31G*, MP4SDTQ/6-31G*//HF/6-31G* and MP4SDTQ/6-31G*//MCSCF/3-21G) qualitatively reproduce the experimental regiochemical ratio .*

1,3-Dipolar cycloadditions not only play an increasingly important role in synthetic organic chemistry but they also continue to be a challenging subject for theoretical studies. As for this latter aspect, in 1968 Huisgen stated that "the orientation phenomena (*i.e., regioselectivity*) in 1,3-dipolar cycloadditions offer perhaps the biggest unsolved problem in the field."[1] In the early seventies the advent of FO theory seemed to completely dissipate the fog of uncertainty about regioselectivity in these reactions. In fact, the qualitative FO approach was able to satisfactorily explain the whole set of known regiochemical data.[2] Moreover, since then to find an agreement between FO "predictions" and experimental regiochemical data has become a common practice in the field of cycloadditions.[3] However, it soon became apparent that the astonishing success of this theory was the result of its flexibility; there are too many buttons (orbital energies, coefficients, resonance integrals, secondary orbital interactions, steric effects etc.)[4] to push freely on qualitative grounds so that even opposite regiochemical results for the same reaction can be satisfactorily rationalized.[5] A few quantitative and more "rigid" PMO treatments have also been reported which met with some success in explaining the observed regiochemistry.[4,6] Nevertheless, the Huisgen's statement is as true today as in 1968.

No one good level ab-initio study of a "real" regiochemical problem in intermolecular 1,3-dipolar cycloadditions to carbon-carbon double bonds has been performed yet.[7] Thus, in the context of our effort aimed at rationalizing selectivity aspects of 1,3-dipolar cycloadditions[8] we decided to perform a computational study of the reaction of diazomethane (DZM) with allene to find out whether ab initio calculations could provide an easy answer to the regioselectivity problem.

Only one regioisomer, i.e., the 4-methylene-1-pyrazoline (1) was detected by Crawford et al. in a series of reactions between DZM and excess allene.[9a,b] The same regiochemistry was exhibited by the reaction of allene with diazoethane.[9b,10-12] Pasto rationalized these findings on the basis of a dominant $\mathrm{LUMO_{allene}}$-$\mathrm{HOMO_{DZM}}$ interaction by stating that "the terminal carbon of allene and the terminal nitrogen of DZM have the largest coefficients in their respective orbitals"[13]. Actually, the carbon coefficient of $\mathrm{HOMO_{DZM}}$ is larger than that at the

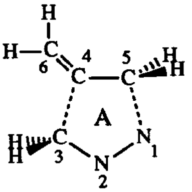


nitrogen atom (STO-3G: $\varepsilon_{HO,DZM} = -6.81$ eV, $c_C = 0.74$ and $c_N = -0.66$) and $LUMO_{allene}$ (STO-3G: $\varepsilon_{LU,allene} = 8.66$ eV, $c_1 = 0.77$ and $c_2 = -0.78$) is almost unpolarized so that the interaction between these two FOs does not favor either of the two regioisomers. Thus, application of FO theory should predict a slight prevalence of the wrong regioisomer **2** as a result of the $LUMO_{DZM}$-$HOMO_{allene}$ interaction (STO-3G; $LUMO_{DZM}$: $\varepsilon = 7.95$ eV, $c_C = 0.66$ and $c_N = 0.61$; $HOMO_{allene}$: $\varepsilon = -8.80$ eV, $c_1 = 0.66$ and $c_2 = 0.56$). This adduct should also slightly be favored by steric effects.[14]

Geometry data for the computed ab initio TSs (transition structures) are reported in Table 1. The TSs correspond to early transition states with all the heavy atoms lying in the same plane. The most relevant geometry difference between the two regioisomeric TSs is to be found in the asynchronicity of bond formation. In fact, at the HF/3-21G level C---C bond formation is more advanced than that of C---N bond in TS A leading to **1** whereas the opposite holds for TS B leading to **2**. On going to higher levels of theory (HF/6-31G* and MCSCF/3-21G) asynchronicity of the former TS is substantially enhanced while that of the latter TS decreases. This observation simply means that these latter calculations, in particular the HF/6-31G* level, tend to favor C---C bond formation over C---N bond formation as compared to the HF/3-21G level.

Anyway, the shorter incipient bond in both TSs at any level of calculations involves the central carbon atom of allene. Notice also that the average bond length of the forming bonds of TS A (2.247, 2.245, 2.278 Å at the HF/3-21G, HF/6-31G* and MCSCF/3-21G levels, respectively) is similar to that of TS B (2.236, 2.228 and 2.248 Å, respectively). Changes in asynchronicity take place in such a way that weakening of one bond is compensated by strengthening of the other in order to keep the energy gain of bond formation as high as possible.

As for bond angles the higher bending (by 5-7°) of the allene moiety in TS A (see C_5-C_4-C_6, Table 1) relative to TS B (C_4-C_5-C_6) is reflected in a very attenuated way in the slightly lower bending (by 1°) of the 1,3-dipole moiety (C_3-N_2-N_1) of the former TS. However, it is worthy to underline that the energy required to deform the isolated educts from ground state geometry to the geometry they adopt in the TS is similar for the two regioisomeric TSs (HF/3-21G//HF/3-21G: 34.2 and 33.9 kcal mol^{-1} for TS A and TS B, respectively).



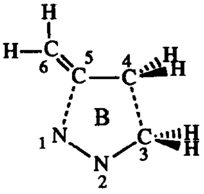


Table 1. Bond lengths (Å),[a] bond angles (°)[b] for the ab-initio TSs A and B.[c]

	TS A			TS B		
	HF/3-21G	HF/6-31G*	MCSCF/3-21G	HF/3-21G	HF/6-31G*	MCSCF/3-21G
C_4-C_5	1.341	1.350	1.356	1.340	1.347	1.355
C_3-N_2	1.330	1.347	1.352	1.322	1.339	1.352
N_1-N_2	1.134	1.122	1.148	1.141	1.130	1.151
C_3---C_4	2.203	2.147	2.201	2.283	2.245	2.269
N_1---C_5	2.291	2.342	2.355	2.189	2.210	2.227
C_5-C_4-C_6 or C_4-C_5-C_6	151.9	149.6	149.3	156.7	156.7	154.5
C_3-C_4-C_5	105.6	107.2	106.1	103.0	103.6	102.7
C_4-C_5-N_1	100.5	98.5	99.6	103.1	102.0	103.3
C_3-N_2-N_1	145.3	143.2	142.8	144.5	141.9	141.5

[a] Allene double bond length: 1.292, 1.296 and 1.302 Å for 3-21G, 6-31G* and MCSCF calculations, respectively. Diazomethane, C-N (N-N): 1.281 (1.131), 1.280 (1.116), 1.287 (1.140) Å for 3-21G, 6-31G* and MCSCF calculations, respectively [b] Allene: C_1-C_2-C_3 = 180°. Diazomethane: C-N-N = 180°. [c] As for dihedral angles all the heavy atoms of A and B lie in the same plane indipendently of the level of calculation. Only in TS A there is a very small deviation from planarity (C_6-C_4-C_5-N_1 = -179.2° and C_4-C_3-N_2-N_1 = -0.6°) at the HF/6-31G* level.

Table 2. Electronic activation energies (kcal mol^{-1}) for the TSs A ($E_{a,A}$) and B ($E_{a,B}$).

Model	$E_{a,A}$	$E_{a,B}$	$E_{a,A}$ - $E_{a,B}$	Model	$E_{a,A}$	$E_{a,B}$	$E_{a,A}$ - $E_{a,B}$
AM1 (opt.)	25.5	25.1	0.4	MP3/6-31G*//[b]	17.8	18.5	-0.7
HF/STO-3G (opt.)	25.5	25.1	0.4	MP4DQ/6-31G*//[b]	18.5	19.2	-0.7
HF/3-21G (opt.)	28.6	28.1	0.5	MP4SDQ/6-31G*//[b]	19.2	19.8	-0.5
HF/6-31G*//[a]	35.2	35.7	-0.5	MP4SDTQ/6-31G*//[b]	12.6	13.0	-0.4
MP2/6-31G*//[a]	8.6	9.4	-0.8	MCSCF/3-21G (opt.)	23.6	23.6	0.0
MP3/6-31G*//[a]	18.2	18.9	-0.7	HF/6-31G*//[c]	35.8	36.0	-0.2
MP4DQ/6-31G*//[a]	18.7	19.4	-0.7	MP2/6-31G*//[c]	8.4	9.2	-0.8
MP4SDQ/6-31G*//[a]	19.5	20.0	-0.5	MP3/6-31G*//[c]	18.3	19.0	-0.7
MP4SDTQ/6-31G*//[a]	13.2	13.6	-0.4	MP4DQ/6-31G*//[c]	18.8	19.7	-0.9
HF/6-31G* (opt.)	35.5	36.0	-0.5	MP4SDQ/6-31G*//[c]	19.7	20.4	-0.7
MP2/6-31G*//[b]	8.2	8.9	-0.7	MP4SDTQ/6-31G*//[c]	12.9	13.5	-0.6

[a] HF/3-21G geometry [b] HF/6-31G* geometry [c] MCSCF/3-21G geometry

Inspection of Table 2, which gathers the electronic activation energies, clearly shows that not only semiempirical AM1 and minimal basis set HF/STO-3G methods but also split valence HF/3-21G calculations fail to predict dominance of **1** favoring the wrong regioisomer **2**, i.e., $E_{a,A} - E_{a,B} \approx 0.5$ kcal mol^{-1}. The predictions based on the MCSCF/3-21G model are not much better: the two TSs exhibit the same electronic energy. Introduction of polarization functions not only in a full geometry optimization (HF/6-31G*//HF/6-31G*, $E_{a,A} - E_{a,B} \approx -0.5$ kcal mol^{-1}) but also in a single point calculation using geometries from other models (e.g., HF/6-31G*//HF/3-21G, $E_{a,A} - E_{a,B} = -0.5$ kcal mol^{-1}; HF/6-31G*//MCSCF/3-21G, $E_{a,A} - E_{a,B} = -0.2$ kcal mol^{-1}) led to a substantial improvement of the calculated regioselectivity: now TS A is predicted slightly more stable than TS B. A further step toward a full agreement between theory and experiment seemed to be provided by introduction of correlation energy at the MP2 level (e.g., MP2/6-31G*//HF/6-31G*, $E_{a,A} - E_{a,B} = -0.7$ kcal mol^{-1}; MP2/6-31G*//MCSCF/3-21G, $E_{a,A} - E_{a,B} = -0.8$ kcal mol^{-1}). Disappointingly, a progressively better treatment of electron correlation in single point calculations led $E_{a,A} - E_{a,B}$ to converge to ≈ -0.6 kcal mol^{-1} on the right side but at least 2.0 kcal mol^{-1} higher than that required (≤ -2.7 kcal mol^{-1}) by the reported experimental regiospecificity.

One can argue that activation free enthalpy ($\Delta G^{\neq}$) is more appropriate than electronic activation energy (E_a) to discuss the experimental data and that solvent effects should also be taken into account. We found that consideration of $\Delta G^{\neq}$ in the place of E_a adds a slight preference (≈ -0.5 kcal mol^{-1} independently of the basis set used for corrections) for TS A over TS B (e.g., using the MP4SDTQ/6-31G*//MCSCF/3-21G electronic energy: $\Delta G_A^{\neq} - \Delta G_B^{\neq} = -1.1$ kcal mol^{-1} at 298 K).[15] However, inclusion of the solvent (diethyl ether, dielectric constant = 4.3) through self consistent reaction field[16] favors TS B over TS A by 0.27 kcal mol^{-1} [SCRF/6-31G*; dipole moment: 2.49 (2.57) D for TS B and 1.87 (1.82) D for TS A at the HF/6-31G*(HF/3-21G) level] thus partly cancelling the improvement obtained by the use of $\Delta G^{\neq}$.

At this point it was mandatory to confirm the experimental result. In our hands the reaction of ethereal diazomethane with a large excess of allene at room temperature afforded a mixture of **1** and **2** (**1**/**2** = 93:7, $\Delta G_A^{\neq} - \Delta G_B^{\neq} = -1.5$ kcal mol^{-1}). Although compound **2** could not be isolated in a pure state, its structure was firmly established on the basis of spectroscopic data and by trapping reactions with diazomethane and 2,6-dichlorobenzonitrile oxide (Scheme) to give the fully characterized adducts **3** and **5** (see EXPERIMENTAL). For example, the presence of a symmetry plane in **2** (the molecular plane), of a C_2 axis in **3** and the absence of symmetry elements in **5** can easily be inferred from ^1H and ^{13}C NMR spectra. Moreover, the chemical shifts of C_3 [δ ($CDCl_3$) 145.1 (s)] in **2** and of C_5 in **3** [δ ($CDCl_3$) 131.1 (s)] and in **5** [δ ($CDCl_3$) 121.2 (s)] as compared to the chemical shifts of the related carbons in **1** [δ ($CDCl_3$) 137.8 (s, C_4)] and **4** [δ ($CDCl_3$) 85.7 (s, C_5)] provide convincing evidence of the presence of an olefinic carbon bearing an electron attracting group in **2** and of a quaternary carbon atom bearing two heteroatoms in **3** and **5**. Actually the **1**/**2** ratio changed from 93:7 at the beginning (after 2 h) of the reaction to 97:3 at the end (after 36 h) of the reaction. This change in the regioisomer ratio could easily be rationalized by the observation that pyrazoline **2** reacted easily with diazomethane to give **3** whereas pyrazoline **1** proved unreactive toward this 1,3-dipole. It is well known that electron-attracting conjugating substituents, such as the azo group in **2**, highly enhance the reactivity of double bonds toward diazoalkanes.[17]

The revised regiochemical ratio does not completely reconcile theory with experiment but the gap between the calculated and observed regioselectivity is reduced to less than 0.9 kcal mol^{-1} (somewhat lesser if one considers calculated $\Delta G^{\neq}$ and solvent effects).

As for absolute activation energies it should be remembered that known experimental $\Delta H^{\neq}$ for diazomethane cycloadditions in solution range from 7.5 ± 0.6 kcal mol^{-1} for the highly reactive ethyl acrylate to 13-14 kcal mol^{-1} for norbornene and 1-phenylbutadiene.[18] It is reasonable to assume that $\Delta H^{\neq}$ of the allene-DZM reaction resembles these latter figures. All calculations (see electronic activation energies of Table 2) without electron correlation perform very poorly (e.g., $E_a \approx 35$-36 kcal mol^{-1} at the HF/6-31G* level) in predicting absolute activation energies. Inclusion of the MP2 contribution (no matter which geometry is used) overestimates the correlation energy changes leading to too low E_a figures ($E_a \approx 8$-9 kcal mol^{-1}). MP3 ($E_a \approx 18$-19 kcal mol^{-1}), MP4DQ and MP4SDQ levels underestimate electron correlation effects and the MP4SDTQ method ($E_a \approx 13$ kcal mol^{-1}) eventually led to a reasonable convergence[19] to the experimental data.[20-21] It is interesting to notice that the figures at the MP4SDTQ level are similar (slightly lower) to the average of the values obtained at the related MP2 and MP3 levels. Moreover, it should be emphasized that notwithstanding very large changes in absolute activation energies on going from, for example, HF/6-31G* to MP2/6-31G*//HF/6-31G* and then to MP4SDTQ/6-31G*//HF/6-31G*levels the relative activation energies, i. e., $E_{a,A} - E_{a,B}$, oscillate in the range of a few tenths of a kcal mol^{-1}.

To conclude it is quite evident that one cannot confidently rely neither on semiempirical MO methods nor on split valence small basis set ab initio methods to theoretically predict regiochemistry in 1,3-dipolar cycloadditions. Also relatively high level ab initio calculations may not give a completely satisfactory answer to this problem. However, this study and preliminary ab-initio results for other 1,3-dipolar cycloadditions[22] show that the MP4SDTQ/6-31G*//HF/6-31G* provides a sufficient level of theory to qualitatively reproduce both experimental activation energies and regiochemical ratios at least for reactions not highly affected by solvent polarity.

COMPUTATIONAL METHODS

The ab initio molecular orbital calculations were executed with the GAUSSIAN 92 program.[23] The geometries of reactants and TSs were fully optimized at different level of theory (AM1, HF/STO-3G, HF/3-21G, HF/6-31G*, MCSCF/3-21G) utilizing gradient techniques and default thresholds for convergence. The search was limited to concerted TSs, since there is now general agreement that simple 1-3-dipolar cycloadditions are concerted reactions with no comparable alternative. Critical point were fully characterized by diagonalizing the hessian matrices of the optimized structures. TSs were found to have only one negative eigenvalue (first order saddle point), the corresponding eigenvectors involving the expected concerted formation of the two new bonds. Vibrational frequencies were calculated at the HF/3-21G and HF/6-31G* levels for all reactants and transition structures. This enabled calculation of the enthalpies and entropies of activation at 298 K.

The numbers of active electrons and orbitals for MCSCF calculations were chosen to include all the π-electrons and π-orbitals involved in the new ring formation [CAS(6,5) for TSs, CAS(2,2) for allene and CAS(4,3) for diazomethane.

The whole set of theoretical data is available on request.

Table 3. Electronic energies (hartrees) of allene and diazomethane

Model	Allene	DZM	Model	Allene	DZM
AM1 (opt.)	0.073454	0.099735	MP3/6-31G*//[b]	-116.257622	-148.297541
HF/STO-3G (opt.)	-114.421719	-145.920607	MP4DQ/6-31G*//[b]	-116.259900	-148.300483
HF/3-21G (opt.)	-115.219044	-146.995820	MP4SDQ/6-31G*//[b]	-116.264357	-148.307591
HF/6-31G*//[a]	-115.860302	-147.843199	MP4SDTQ/6-31G*//[b]	-116.279073	-148.329186
MP2/6-31G*//[a]	-116.231622	-148.296578	MCSCF/3-21G (opt.)	-115.247100	-147.027140
MP3/6-31G*//[a]	-116.256186	-148.298850	HF/6-31G*//[c]	-115.860990	-147.842291
MP4DQ/6-31G*//[a]	-116.258423	-148.301979	MP2/6-31G*//[c]	-116.233402	-148.297634
MP4SDQ/6-31G*//[a]	-116.262820	-148.309553	MP3/6-31G*//[c]	-116.257904	-148.299343
MP4SDTQ/6-31G*//[a]	-116.277397	-148.331737	MP4DQ/6-31G*//[c]	-116.260193	-148.302602
HF/6-31G* (opt.)	-115.861100	-147.843784	MP4SDQ/6-31G*//[c]	-116.264708	-148.310483
MP2/6-31G*//[b]	-116.233074	-148.294585	MP4SDTQ/6-31G*//[c]	-116.279538	-148.333118

[a] HF/3-21G geometry [b] HF/6-31G* geometry [c] MCSCF/3-21G geometry

EXPERIMENTAL

Melting points are uncorrected. Elemental analyses were made on a Carlo Erba CHN analyser, model 1106. Infrared spectra were recorded as either Nujol suspensions or films on a Perkin-Elmer 881 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AE 300 (operating at 300.3 and 75.5 MHz, respectively) spectrometer with tetramethylsilane as internal standard for $CDCl_3$ solutions unless otherwise stated. Protons were correlated by decoupling experiments. Assignments were secured by ^{1}H/^{13}C heterocorrelated spectra. ^{1}H NMR spectra were evaluated as first order spectra. GC analyses were carried out with a DANI 6500, PTV injector, CP-Sil-19CB (25 m) capillary column and carrier H_2. GC mass spectra were measured on a Finnigan ITS40 using electron impact mode. Thin-layer chromatograms were done on plates precoated with silicagel 60 GF_{254} (Merck). Spots were visualized either by spraying with 3% chromic oxide in sulphuric acid (50%) followed by heating at 120 °C or under UV light. Column chromatography was performed with Silicagel 60 (70-230 mesh) Merck.

Reaction of diazomethane with allene.

Allene (30 ml) was condensed into a stainless steel bomb at - 70 °C and a solution of diazomethane ($\approx$ 1.0 g) in ethyl ether (20 ml) was added. The bomb was closed and kept at room temperature for 36 h . After that time the bomb was recooled at -70 °C and opened. The yellow color of diazomethane had disappeared. GC analysis of the crude reaction mixture allowed an easy (pyrazoline **2** had a slightly longer retention time) evaluation of the regioisomer ratio: **1**/**2** = 97:3 (average of three runs). Then the reaction mixture was allowed to warm slowly to room temperature under stirring at atmospheric pressure in order to remove excess allene. The residue was subjected to a fractional distillation under reduced pressure to give a mixture of **1** and **2** [colorless oil, 1.3 g (65%); IR ν_{max} = 1535 cm^{-1} (N=N)] whose ratio (^{1}H NMR and GC) was very similar to that evaluated before the work-up. Also the ethyl ether fractions contained small amounts of **1** and **2** once again in a $\approx$ 97:3 ratio (GC).

The reaction was also stopped after two hours. A 93:7 (average of two runs) ratio between **1** and **2** was evaluated by GC analysis of the yellow solution. Reaction times intermediate between 2 h and 36 h led to **1**/**2** ratios in the range 93:7-97:3 (^{1}H NMR and GC).

The **1**/**2** ratio did not change appreciably when solutions of **1** and **2** in ethyl ether or ethyl acetate were left at room temperature in the dark for 36 h.

1: GC/MS, m/z 83 (M^++1,100%), 54 (20%), 53 (22%), 39 (72%); ^{1}H NMR, δ ($CDCl_3$) 4.98 (t, 4 H, H-3 and H-5, J = 2.7 Hz), 5.18 (quintet, 2 H, H-6, J = 2.7 Hz); ^{13}C NMR, δ ($CDCl_3$) 78.4 (t, C-3 and C-5), 105.9 (t, C-6), 137.8 (s, C-4). **2**: GC/MS, m/z 83 (M^++1, 100%), 54 (22%), 53 (33%), 39 (58%); ^{1}H NMR, δ ($CDCl_3$) 2.30 (m, 2 H, H-4, $J_{4,6}$ = 2.0 Hz, $J_{4,6'}$ = 2.8 Hz, and $J_{4,5} + J_{4,5'}$ = 14.0 Hz), 4.49 (m, 2 H, H-5), 5.60 (m, 1 H, H-6, $J_{6,6'}$ = 0.8 Hz) and 6.15 (m, 1 H, H-6'); δ (C_6D_6) 1.48 (m, 2 H, H-4), 3.83 (m, 2 H, H-5), 5.08 (m, 1 H, H-6), 6.00 (m, 1 H, H-6');^{13}C NMR, δ ($CDCl_3$) 20.4 (t, C-4), 74.0 (t, C-5), 110.6 (t, C-6), 145.1 (s, C-3).

Reaction of diazomethane with 1 and 2.

A mixture of **1** and **2** (96:4, 0.500 g) was treated with a high excess of diazomethane in ethyl ether at room temperature and the reaction followed by GC. After 2 h an increase in the regioisomer ratio was observed (97:3) and after further 10 h the peak of pyrazoline **2** had disappeared while the area of that of pyrazoline **1** did not change appreciably. Column chromatography (eluant cyclohexane:ethyl acetate = 8:2) led to isolation of **3** (15 mg) as colorless viscous oil. IR ν_{max} = 1542 cm^{-1} (N=N); ^{1}H NMR, δ ($CDCl_3$) 1.63 (ddd, 2 H, H-4 and H-9, J = 13.5, 9.2 and 7.3 Hz), 2.32 (ddd, 2 H, H-4' and H-9', J = 13.5, 8.8 and 4.7 Hz), 4.79 (ddd, 2 H, H-3' and H-8', J = 18.0, 8.8 and 7.3 Hz) and 4.90 (ddd, 2 H, H-3 and H-8, J = 18.0, 9.2 and 4.7 Hz); ^{13}C NMR, δ ($CDCl_3$) 26.9 (t, C-4 and C-9), 77.8 (t, C-3 and C-8) and 131.1 (s, C-5). Anal. Calcd for $C_5H_8N_4$: C, 48.4; H, 6.5; N 45.1. Found: C, 48.5; H, 6.4; N, 44.8.

Even in a reaction mixture kept for 5 days at room temperature we were not able to detect any adduct of diazomethane to pyrazoline **1**.

*Reaction of 2,6-dichlorobenzonitrile oxide with **1** and **2**.*

A solution of a mixture of **1** and **2** (97:3, 0.400 g) and 2,6-dichlorobenzonitrile oxide (0.800 g) in ethyl ether (15 ml) was left at room temperature for 36 h. The precipitated colorless solid (0.814 g of **4** with very small amounts of **5** as shown by ^{1}H NMR analysis) was crystallized from cyclohexane/benzene to give colorless needles of pure **4** (mp 124-126 °C). The mother liquors were concentrated under reduced pressure and column chromatographed (eluant cyclohexane:ethyl acetate = 7:3) to give in order of elution: small amounts of the nitrile oxide dimer and of two not characterized products, **5** (15 mg, colorless prisms from benzene, mp 177 ° dec.), **4** (20 mg) and **6** (10 mg, glassy solid). Both compounds **4** and **6** were quantitatively transformed into **7** (colorless needles from MeOH, mp 156-157 °C) when treated with acetyl chloride.

4: IR ν_{max} = 1555 cm^{-1} (N=N); ^{1}H NMR, δ ($CDCl_3$) 3.39 (s, 2 H, H-4), 4.38 and 5.23 (AA'XX' pattern, 4 H, H-6 and H-9), 7.3-7.5 (3H, aromatic protons); ^{13}C NMR, δ ($CDCl_3$) 43.0 (t, C-4), 85.4 (t, C-6 and C-9), 85.7 (s, C-5), 127.7, 127.9, 131.2, 134.6 (aromatic carbons) and 154.0 (s, C-3). Anal. Calcd for $C_{11}H_9Cl_2N_3O$: C, 48.9; H, 3.3; N 15.6. Found: C, 48.6; H, 3.2; N, 15.4. **5**: IR ν_{max} = 1554 cm^{-1} (N=N); ^{1}H NMR, δ ($CDCl_3$) 1.90 (ddd, 1 H, H-9, J = 14.5, 8.8 and 5.9 Hz), 2.20 (ddd, 1 H, H-9', J = 14.5, 8.7 and 5.5 Hz), 3.52 (d, 1 H, H-4, $J_{4,4'}$ = 17.9 Hz), 3.73 (d, 1 H, H-4'), 4.56 (ddd, 1 H, H-8, J = 18.2, 8.8 and 5.5 Hz) and 4.65 (ddd, 1 H, H-8', J = 18.2, 8.7 and 5.9 Hz), 7.3-7.5 (3H, aromatic protons); ^{13}C NMR, δ ($CDCl_3$) 27.0 (t, C-9), 45.6 (t, C-4), 75.6 (t, C-8), 121.2 (s, C-5), 127.6, 128.0, 131.3, 135.0 (aromatic carbons) and 154.5 (s, C-3). Anal. Found: C, 48.7; H, 3.4; N, 15.7. **6**:^{1}H NMR, δ ($CDCl_3$) 3.31 (d, 1 H, H-4, $J_{4,4'}$ = 17.4 Hz), 3.49 (d, 1 H, H-4'), 3.53 (d, 1 H, H-9, $J_{9,9'}$ = 12.4 Hz), 3.89 (d, 1 H, H-9'), 5.73 (bs which exchanged with D_2O, 1 H, H-8), 6.98 (s, 1 H, H-6), 7.3-7.5 (3H, aromatic protons). **7**: IR ν_{max} = 1671 cm^{-1} (MeCON); ^{1}H NMR, δ ($CDCl_3$) 2.37 (s, 3 H, Me), 3.33 (d, 1H, H-4, $J_{4,4'}$ = 17.5 Hz), 3.62 (d, 1 H, H-4'), 3.93 (d, 1 H, H-9, $J_{9,9'}$ = 14.0 Hz), 4.38 (d, 1 H, H-9'), 7.05 (s, 1 H, H-6), 7.3-7.5 (3H, aromatic protons). Anal. Calcd for $C_{13}H_{11}Cl_2N_3O_2$: C, 50.0; H, 3.9; N 13.4. Found: C, 50.3; H, 3.6; N, 13.6.

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19. When the HF/6-31G* contributions described in note 15 are taken into account (and by using the MP4SDTQ/6-31G*//MCSCF/3-21G electronic energy) one gets for gas phase: 14.6, 24.6, -33.5 for $\Delta H^{\neq}$ (kcal mol^{-1}), $\Delta G^{\neq}$ (kcal mol^{-1}) and $\Delta S^{\neq}$ (e.u.), respectively, of TS A and 15.4, 25.7, -34.2, respectively, for those of TS B. The experimental activation entropies for the cited DZM reactions in solution are as follows: -33 ± 2 (DZM + ethyl acrylate), -31 ± 3 (DZM + norbornene) and -29 ± 3 (DZM + 1-phenylbutadiene) e.u..[18] For a discussion about the uncertainty in comparing activation entropies for bimolecular reactions in the gas phase and solution see ref. 21.
20. Very recently it was concluded that MP3/6-31G*//HF/6-31G* calculations can accurately predict relative reactivities and diastereoselectivities in Diels-Alder reactions and also to provide quantitatively reasonable estimates of enthalpies and entropies of activation.[21]

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