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REACTION OF HYDRAZONOYL CHLORIDES TO TRIMETHYLSILYL HOMOALLYL ETHERS

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Dedicated to Professor Luisa Garanti on the occasion of her retirement.

Abstract – Title reaction gave mainly 4,5-dihydropyrazole derivatives due to nitrilimine cycloaddition onto the ethylenic bond. Cycloaddition regioselectivity was good despite the electronic demands of the substituents placed to the ethylenic dipolarophile are quite similar. Metalated transition states have been proposed in order to account the observed regioselectivity. Highly substituted cyclopropanes were also formed due to the electrophilic attack of a nitrilium-like carbocation to the ethylenic bond.

INTRODUCTION

Nitrilimine cycloadditions to ethylenes constitutes one of the most useful entries to the 4,5-dihydropyrazole ring.[1] A number of examples are available in the literature after Huisgen's fundamental works,[2-4] and several experimental conditions have been exploited for the *in situ* generation of nitrilimines from base treatment of the corresponding hydrazonoyl chlorides; both reaction medium[5] and basic agent[6-8] have been varied in order to achieve better reactivity. It is well known that traditional organic bases like triethylamine or DABCO promote nitrilimine generation, which involves deprotonation of the NH group and the subsequent loss of the halide ion.[1] By contrast, silver carbonate[6,7] or silver acetate[8] can enhance the reactivity of hydrazonoyl chlorides towards ethylenic dipolarophiles due to the well-known ability of the silver ion to facilitate the heterolysis of the carbon-halogen bond.[9] Several years ago, we found that the reaction between hydrazonoyl halides and allylic[10] or homoallylic[11] alcohols in the presence of silver carbonate exhibits some features which were not observed in the presence of triethylamine. However, we pointed out that "as the cycloaddition pyrazolic products are concerned, one

can note that the extent of their formation spreads over a wide range, going from good to null as a function of the substitution degree of the dipolarophile" (sic).[11] In particular, *trans*-3-hexen-1-ol gave an equimolecular mixture of regioisomeric cycloadducts with 26% overall yield. Aimed to achieve better results in terms of both cycloadduct yield and regioselectivity, we have undertaken the present investigation, dealing with the reactions between hydrazonoyl chlorides (**1**) and trimethylsilyl homoallyl ethers (**2**) in the presence of silver acetate.

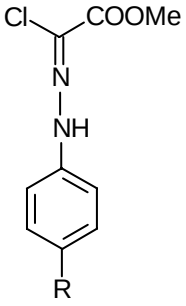
RESULTS AND DISCUSSION

Compounds (**1**) reacted with equimolecular amounts of trimethylsilyl homoallyl ethers (**2**) in ethyl acetate at room temperature by using two mole equivalents of silver acetate. Products and yields are collected in the Table, while experimental details are given in the appropriate section.

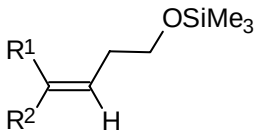
Structural assignement of all products (**3**)-(**8**) rely upon analytical and spectral data. Proton NMR spectroscopy was particularly useful in the elucidation of relative configurations of the two newly-formed stereocentres as well as the regiochemistry of 4,5-dihydropyrazole cycloadducts (**3**)-(**6**). In particular, cycloadduct stereochemistry was suggested from the scalar coupling constants of the hydrogens in the 4- and 5- position of the 4,5-dihydropyrazole ring. *Cis*-cycloadducts (**3**) and (**4**) show J_{cis} between 4.6 and 5.8 Hz, while *trans*-adducts (**5**) and (**6**) exhibit J_{trans} between 6.8 and 9.0 Hz, which agrees with literature values.[12] Regiochemistry of minor cycloadducts (**4**) and (**6**) was unequivocally established by decoupling ^{1}H NMR experiments which showed that the 4-pyrazolinic hydrogen of (**4a**) and (**6a**) lies neighbouring to an ethyl group (see Experimental). The structure of functionalised cyclopropanes (**7**) were proposed on the basis of the observed chemical shifts and multiplicity of two hydrogens, which appear in the range δ 0.34-0.51 according to the shielding effects due to the cyclopropane ring.[13] Here again, scalar coupling constants and decoupling experiments were useful in the determination of relative stereochemistry of products (**7**). J_{vic} values of 9.5 and 9.8 Hz found for cyclopropyl hydrogens clearly speaks in favour of their cis arrangement,[14-16] while the relative configuration of the remaining stereocentre of the cyclopropyl ring remains undetermined.

To this point, the thermal lability of cyclopropane derivatives (**7**) needs to be underlined. The NMR sample of these compounds turned from pale yellow to dark brown in a few hours giving unresolved protonic spectra. This behaviour may be a consequence of the known thermal lability of some azo compounds, which undergoes facile loss of nitrogen followed by unselective radical processes.[17]

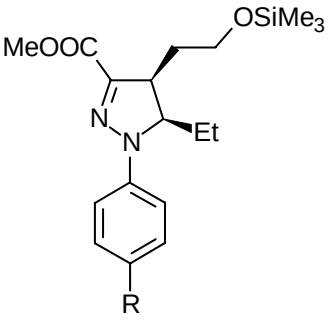
As can be inferred from the Table, 5-ethyl substituted 4,5-dihydropyrazoles (**3**) and (**5**) were obtained as major regioisomers with a product ratio (**3**):(**4**) or (**5**):(**6**) between 90:10 and 92:8. This behaviour is quite unusual since it is known that nitrilimine cycloadditions to 1,2-disubstituted ethylenic dipolarophiles are not regioselective processes.[1] It may be added that preliminary experiments carried out on the reaction



1a: R = H
1b: R = OMe



2a: R^1 = Et, R^2 = H
2b: R^1 = H, R^2 = Et



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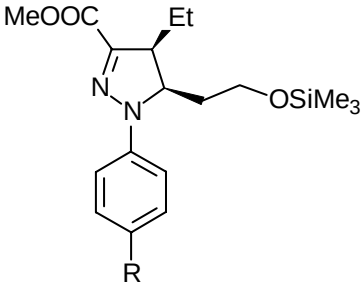

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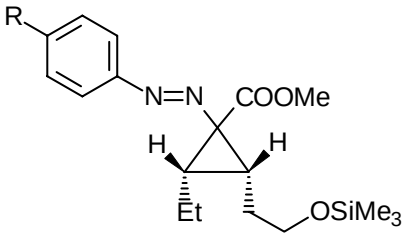

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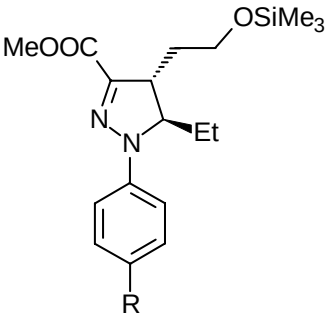

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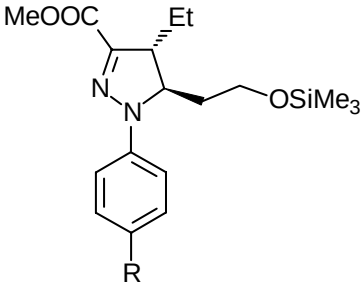

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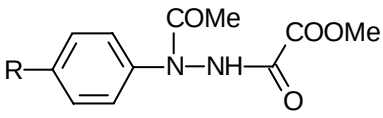

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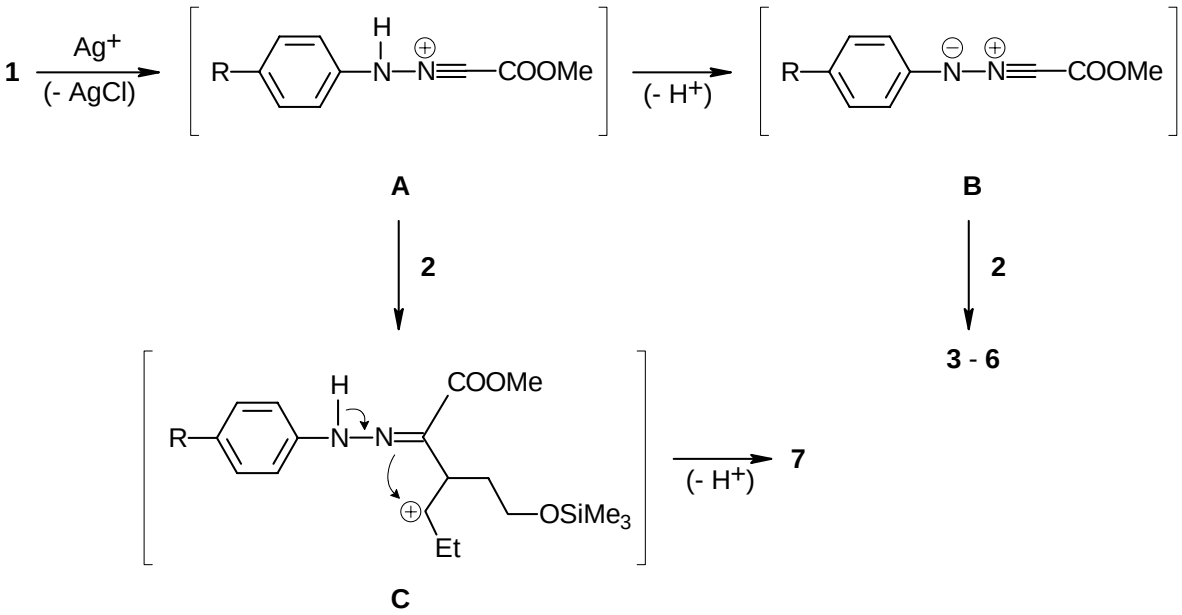
Table. Reaction between hydrazonoyl chlorides (**1**) and trimethylsily homoallyl ethers (**2**) in the presence of AcOAg.

Entry	R	Products and Yields (%)					
		3	**4**	**5**	**6**	**7**	**8**
1	H	64	6	—	—	5	7
2	OMe	70	8	—	—	4	8
3	H	—	—	69	7	6	9
4	OMe	—	—	78	7	4	6

between (**1a**) and (**2b**) in dioxane and in the presence of triethylamine or silver carbonate gave disappointing results since: (*i*) isolation yield of 4,5-dihydropyrazole cycloadducts was low, (*ii*) the reaction showed little regioselectivity, and (*iii*) large amounts of tarry materials was formed. To this point, we reasoned that some kind of complexation could be operative between the organic reactants and the silver ion only in the presence of silver acetate, possibly due to the partial solubility of the latter salt in ethyl acetate.

As a possible rationalisation of the above experimental evidences, we propose the mechanistic picture outlined in the Scheme 1. The initial formation of nitrilium cation (**A**) is quite reasonable in the light of the mentioned ability of the silver ion to promote the breaking of the carbon-chlorine bond;[9] it may be added that the intervention of such kind of carbocation in *N*,*N*-disubstituted *C*-halohydrazones is a well-documented matter.[18] To this point, intermediate (**A**) can follow two alternative pathways: (*i*) hydrogen loss with the generation of 1,3-dipole (**B**), (*ii*) electrophilic attack to the C=C double bond of (**2**) giving carbocation (**C**). The occurrence of nitrilimine intermediate (**B**) can be ensured from the the retention of stereochemistry in the formation of cycloadducts (**3**)-(**6**), which points to a classical pericyclic mechanism. A plausible sequence leading to cyclopropane derivatives (**7**) involves proton loss from carbocation (**C**) and subsequent ring closure. This multi-step ionic mechanism could be challenged by invoking the intervention of the carbenic form of nitrilimine (**B**); however, we have recently demonstrated the inconsistency of this latter resonance form in the case of the parent formonitrilimine.[19] The formation of some amount of *N*-oxalylhydrazide by-products (**8**) was unavoidable due to the nucleophilic attack of the acetoxy anion to hydrazonoyl chlorides (**1**) followed by acetyl migration of the resulting acetoxylated intermediates.[20]

Scheme 1



To test the hypothesis that silver ion do have a role in the cycloaddition mechanism, DFT calculations were performed. We computed the minimal energy structures of hexenol (**2b**), nitrilimine (**B**) and the transition state (**TS2**) and compared them with the minimal energy structures of the silver complex (**D**) and the transition state (**TS1**) (see Figure). The effect of the solvent ethyl acetate has been included in the calculations. The silver complex (**D**) can exist in ethyl acetate since its energy is lower than that of the uncomplexed systems by 17.3 kcal/mol. Its structure is not unusual for silver (I) which favors 2-coordinate complexes.[21] This also holds for transition state (**TS1**). Although (**TS1**) is 14.8 kcal/mol lower in energy than (**TS2**), the barrier for the silver-involving cycloaddition (13.9 kcal/mol) is higher by 2.5 kcal/mol than the barrier for the (**2b**) + (**B**) → (**5**) cycloaddition (11.4 kcal/mol), due to intramolecular strain in the complex. Such difference is however small enough to be more than counterbalanced by the entropic effect due to complexation which makes the silver-assisted cycloaddition much more probable than the (**2b**) + (**B**) → (**5**) cycloaddition. Indeed, a difference in activation entropy by 8.4 cal/K/mol is sufficient to favor the former route.

Figure

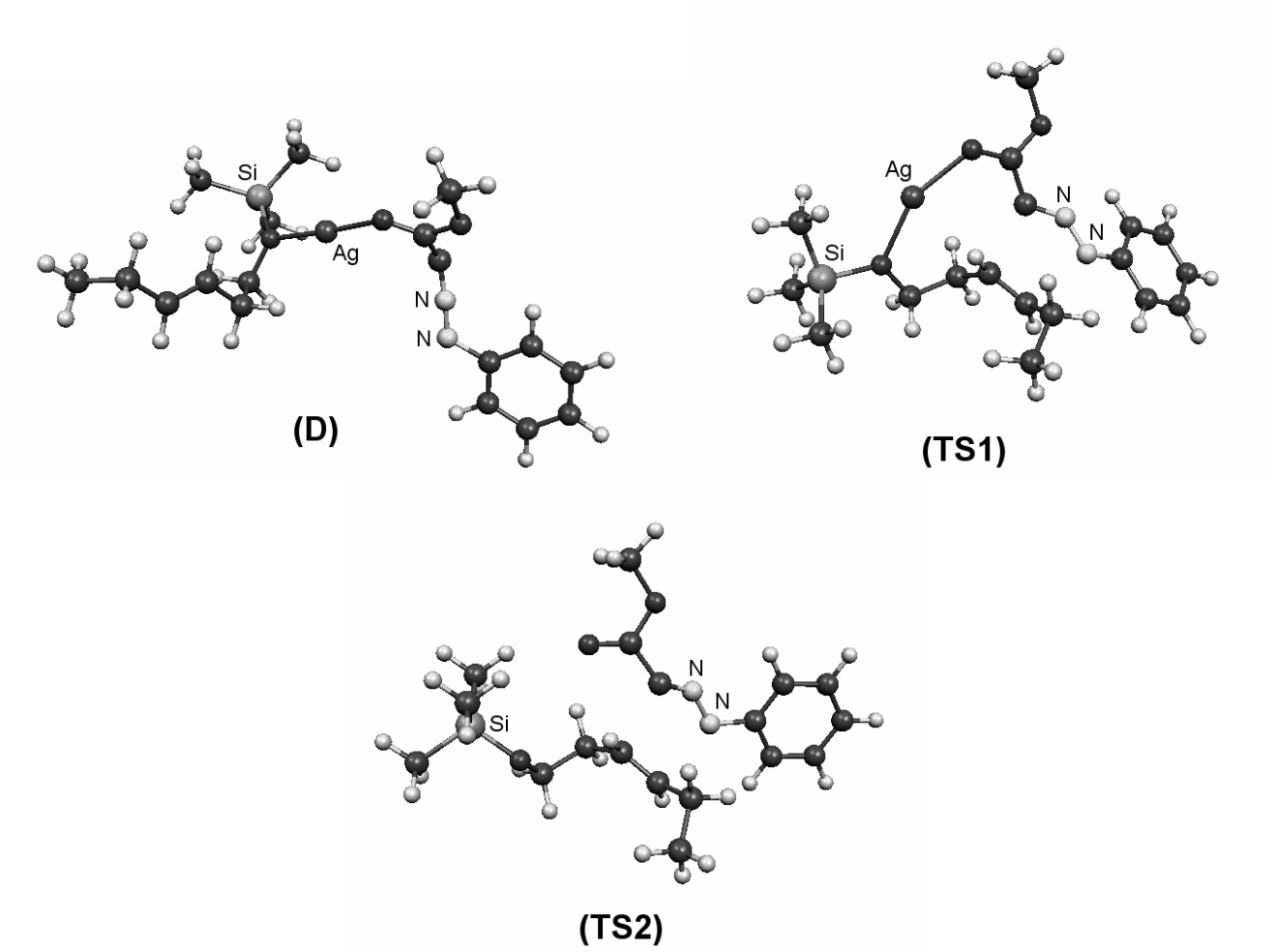
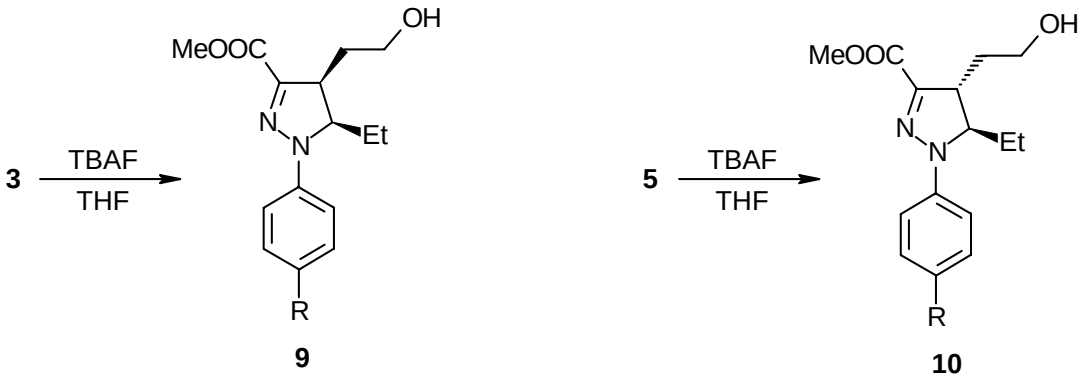


Figure. Structure of the complex (**D**) and of the transition states (**TS1**) and (**TS2**) optimized at the B3LYP/cc-pVDZ level (cc-pVDZ-pp basis and small-core potential for silver). For clarity, silver, silicon, and nitrogen atoms are labelled.

These calculations show that the activation barrier for the silver complex is only slightly larger than that for the free substrates. Since the entropic factor is expected to strongly favor the silver-assisted cycloaddition over both (**2b**) + (**B**) → (**5**) and (**2b**) + (**B**) → (**6**), the observed regioselection can be reasonably attributed to the complexation of silver ions by the reagents.

As a further step of our work, we submitted major cycloadducts (**3**) and (**5**) to treatment with tetrabutyl ammonium fluoride (TBAF) in order to achieve the cleavage of the trimethylsilyl group (Scheme 2). 4-(1-Hydroxy)ethyl-4,5-dihydropyrazoles (**9**) and (**10**) were obtained with very good yields (83-94%); furthermore, the presence of a free hydroxyl group may be of interest for further functionalisations.

Scheme 2



As conclusive remarks, it can be stated that regioselective nitrilimine cycloadditions have been performed onto 1,2-disubstituted ethylenic dipolarophiles despite the electronic demands of the substituents are quite similar. As substantiated by the above calculations, this successful behaviour is due to a complexation between the organic reactants and the silver ion which mimic an intramolecular process. Finally, removal of the trimethylsilyl group from the major cycloadducts gave unprotected 4-(1-hydroxy)ethyl-4,5-dihydropyrazoles with good overall yield.

EXPERIMENTAL

Melting points were determined with a Büchi apparatus in open tubes and are uncorrected. IR spectra were recorded with a Perkin-Elmer 1725 X spectrophotometer. MS spectra were determined with a VG-70EQ apparatus. ^{1}H NMR (300 MHz) spectra were taken with a Bruker AMX 300 instrument (in $CDCl_3$ solutions at room temperature). Chemical shifts are given as ppm from tetramethylsilane and *J* values are given in Hz.

Hydrazonoyl chlorides (**1**),[22] *cis*-1-(trimethylsilyloxy)-3-hexene (**2a**)[23] and *trans*-1-(trimethylsilyloxy)-3-hexene (**2b**)[24] were synthesised according to literature procedures.

Cycloaddition between hydrazonoyl chlorides (1) and trimethylsilyl homoallyl ethers (2) in the presence of silver acetate. To a solution of hydrazonoyl chloride (**1**) (2.5 mmol) and silyl ether (**2**) (2.5 mmol) in EtOAc (10 mL) was added silver acetate (0.76 g, 5.0 mmol) and the mixture was stirred in the dark at rt for 2 h. The solid material was filtered off and the organic layer was evaporated under reduced pressure. The residue was chromatographed on a silica gel column with EtOAc -hexane 1:1.

First fractions contained oxalylhydrazides (**8**).

N^1-Acetyl-N^2-methyloxalylphenylhydrazine (**8a**) as colourless needles having mp 118-120°C (from hexane-benzene); IR (Nujol): 3230, 1720, 1665, 1635 (cm^{-1}); ^{1}H-NMR: 2.11 (3H, s, C$\underline{H}_3$CO-), 3.81 (3H, s, C$\underline{H}_3$OCO-), 7.0-7.2 (5H, aromatics), 9.30 (1 H, br s, N_2-H); MS: 236 *m/z* (M^+). *Anal.* Calcd for $C_{11}H_{12}N_2O_4$: C, 55.93; H, 5.12; N, 11.86. Found: C, 55.97; H, 5.09; N, 11.91.

N^1-Acetyl-N^2-methyloxalyl-(4-methoxy)phenylhydrazine (**8b**) as colourless needles having mp 128-131°C (from hexane-benzene); IR (Nujol): 3240, 1725, 1660, 1640 (cm^{-1}); ^{1}H-NMR: 2.08 (3H, s, C$\underline{H}_3$CO-), 3.69 (3H, s, C$\underline{H}_3$O-), 3.93 (3H, s, C$\underline{H}_3$OCO-), 6.7-7.3 (4H, aromatics), 9.20 (1 H, br s, N_2-H); MS: 266 *m/z* (M^+). *Anal.* Calcd for $C_{12}H_{14}N_2O_5$: C, 54.13; H, 5.30; N, 10.52. Found: C, 54.18; H, 5.29; N, 10.45.

Subsequent fractions contained a mixture of regioisomeric cycloadducts (**3**), (**4**) or (**6**), (**7**). Separation of cycloadducts as single regioisomers was achieved by further chromatography on a silica gel column with EtOAc-CH_2Cl_2 10:1. Major cycloadducts (**3**) or (**5**) were eluted first, followed by minor regioisomers (**4**) or (**6**).

1-Phenyl-3-methoxycarbonyl-4-(*S**)-(1-trimethylsilyloxy)ethyl-5-(*R**)-ethyl-4,5-dihydropyrazole (**3a**) (0.56 g, 64%) as a pale yellow oil; IR (Nujol): 1740, 1070 (cm^{-1}); ^{1}H-NMR: 0.04 (9H, s, (C$\underline{H}_3$)$_3$Si-), 0.84 (3H, t, *J*=7.2, C$\underline{H}_3$CH$_2$-), 1.39 (2H, qd, *J*=7.5, 7.2, CH$_3$C$\underline{H}_2$-), 1.60-1.80 (2H, m, -C$\underline{H}_2$CH$_2$O-), 3.28 (1H, ddd, *J*=6.5, 5.8, 2.4, C_4-$\underline{H}$ pyrazoline), 3.41-3.58 (2H, m, -C$\underline{H}_2$OSiMe$_3$), 3.88 (3H, s, C$\underline{H}_3$OCO-), 4.58 (1H, ddd, *J*=6.8, 5.8, 2.7, C_5-$\underline{H}$ pyrazoline), 7.0-7.2 (5H, m, aromatics); MS: 348 *m/z* (M^+). *Anal.* Calcd for $C_{18}H_{28}N_2O_3Si$: C, 62.03; H, 8.09; N, 8.04. Found: C, 61.08; H, 8.12; N, 8.11.

1-(4-Methoxyphenyl)-3-methoxycarbonyl-4-(*S**)-(1-trimethylsilyloxy)ethyl-5-(*R**)-ethyl-4,5-dihydropyrazole (**3b**) (0.66 g, 70%) as a pale yellow oil; IR (Nujol): 1735, 1070 (cm^{-1}); ^{1}H-NMR: 0.05 (9H, s, (C$\underline{H}_3$)$_3$Si-), 0.81 (3H, t, *J*=7.3, C$\underline{H}_3$CH$_2$-), 1.40 (2H, qd, *J*=7.6, 7.3, CH$_3$C$\underline{H}_2$-), 1.58-1.73 (2H, m, -C$\underline{H}_2$CH$_2$O-), 3.31 (1H, ddd, *J*=6.6, 5.8, 2.3, C_4-$\underline{H}$ pyrazoline), 3.46-3.53 (2H, m, -C$\underline{H}_2$OSiMe$_3$), 3.70 (3H, s, C$\underline{H}_3$O-), 3.88 (3H, s, C$\underline{H}_3$OCO-), 4.58 (1H, ddd, *J*=6.9, 5.8, 2.7, C_5-$\underline{H}$ pyrazoline), 6.8-7.3 (4H, m, aromatics); MS: 378 *m/z* (M^+). *Anal.* Calcd for $C_{19}H_{30}N_2O_4Si$: C, 60.29; H, 7.99; N, 7.40. Found: C, 60.33; H, 8.04; N, 7.48.

1-Phenyl-3-methoxycarbonyl-4-(*S**)-ethyl-5-(*R**)-(1-trimethylsilyloxy)ethyl-4,5-dihydropyrazole (**4a**) (52 mg, 6%) as an yellow oil; IR (Nujol): 1730, 1065 (cm^{-1}); ^{1}H-NMR: 0.02 (9H, s, (C$\underline{H}_3$)$_3$Si-), 0.91 (3H, t, *J*=7.2, C$\underline{H}_3$CH$_2$-), 1.45-1.78 (4H, m, CH$_3$C$\underline{H}_2$- and -C$\underline{H}_2$CH$_2$O-), 3.28 (1H, ddd, *J*=8.5, 4.7, 2.8, C_4-$\underline{H}$ pyrazoline), 3.50-3.70 (2H, m, -CH$_2$C$\underline{H}_2$O-), 3.91 (3H, s, C$\underline{H}_3$OCO-), 4.46 (1H, ddd, *J*=8.8, 4.7, 3.4, C_5-$\underline{H}$

pyrazoline), 7.0-7.3 (5H, m, aromatics); after irradiation of the signal at 3.28 δ: 1.69 (2H, q, *J*=7.2, $CH_3C\underline{H}_2$-) and 4.46 (1H, dd, *J*=8.5, 3.4, C_5-<u>H</u> pyrazoline), after irradiation of the signal at 4.46 δ: 3.28 (1H, dd, *J*=8.5, 2.8, C_5-<u>H</u> pyrazoline); MS: 348 *m/z* (M^+). ***Anal.*** Calcd for $C_{18}H_{28}N_2O_3Si$: C, 62.03; H, 8.09; N, 8.04. Found: C, 62.10; H, 8.14; N, 8.11.

1-(4-Methoxyphenyl)-3-methoxycarbonyl-4-(*S**)-(1-trimethylsilyloxy)ethyl-5-(*R**)-ethyl-4,5-dihydropyrazole (**4b**) (76 mg, 8%) as a yellow oil; IR (Nujol): 1740, 1065 (cm^{-1}); ^{1}H-NMR: 0.05 (9H, s, $(C\underline{H}_3)_3Si$-), 0.88 (3H, t, *J*=7.2, $C\underline{H}_3CH_2$-), 1.49-1.72 (4H, m, $CH_3C\underline{H}_2$- and -$C\underline{H}_2CH_2O$-), 3.20 (1H, ddd, *J*=8.7, 4.6, 3.1, C_4-<u>H</u> pyrazoline), 3.48-3.64 (2H, m, -$CH_2C\underline{H}_2O$-), 3.71 (3H, s, $C\underline{H}_3O$-), 3.86 (3H, s, $C\underline{H}_3OCO$-), 4.40 (1H, ddd, *J*=8.5, 4.6, 3.0, C_5-<u>H</u> pyrazoline), 6.8-7.4 (4H, m, aromatics); MS: 378 *m/z* (M^+). ***Anal.*** Calcd for $C_{19}H_{30}N_2O_4Si$: C, 60.29; H, 7.99; N, 7.40. Found: C, 60.24; H, 7.93; N, 7.47.

1-Phenyl-3-methoxycarbonyl-4-(*R**)-(1-trimethylsilyloxy)ethyl-5-(*R**)-ethyl-4,5-dihydropyrazole (**5a**) (0.60 g, 69%) as a colourless oil; IR (Nujol): 1740, 1080 (cm^{-1}); ^{1}H-NMR: 0.05 (9H, s, $(C\underline{H}_3)_3Si$-), 0.80 (3H, t, *J*=7.3, $C\underline{H}_3CH_2$-), 1.48 (2H, qd, *J*=7.6, 7.3, $CH_3C\underline{H}_2$-), 1.65-1.82 (2H, m, -$C\underline{H}_2CH_2O$-), 3.34 (1H, ddd, *J*=7.0, 6.3, 2.5, C_4-<u>H</u> pyrazoline), 3.43-3.60 (2H, m, -$C\underline{H}_2OSiMe_3$), 3.94 (3H, s, $C\underline{H}_3OCO$-), 4.50 (1H, ddd, *J*=7.0, 6.6, 2.9, C_5-<u>H</u> pyrazoline), 7.0-7.2 (5H, m, aromatics); MS: 348 *m/z* (M^+). ***Anal.*** Calcd for $C_{18}H_{28}N_2O_3Si$: C, 62.03; H, 8.09; N, 8.04. Found: C, 62.11; H, 8.13; N, 8.12.

1-(4-Methoxyphenyl)-3-methoxycarbonyl-4-(*R**)-(1-trimethylsilyloxy)ethyl-5-(*R**)-ethyl-4,5-dihydropyrazole (**5b**) (0.74 g, 78%) as a colourless oil; IR (Nujol): 1730, 1065 (cm^{-1}); ^{1}H-NMR: 0.04 (9H, s, $(C\underline{H}_3)_3Si$-), 0.88 (3H, t, *J*=7.2, $C\underline{H}_3CH_2$-), 1.56 (2H, qd, *J*=7.5, 7.2, $CH_3C\underline{H}_2$-), 1.70-1.95 (2H, m, -$C\underline{H}_2CH_2O$-), 3.40 (1H, ddd, *J*=6.8, 6.4, 2.6, C_4-<u>H</u> pyrazoline), 3.49-3.58 (2H, m, -$C\underline{H}_2OSiMe_3$), 3.69 (3H, s, $C\underline{H}_3O$-), 3.85 (3H, s, $C\underline{H}_3OCO$-), 4.48 (1H, ddd, *J*=6.8, 6.3, 3.0, C_5-<u>H</u> pyrazoline), 6.8-7.3 (4H, m, aromatics); MS: 378 *m/z* (M^+). ***Anal.*** Calcd for $C_{19}H_{30}N_2O_4Si$: C, C, 60.29; H, 7.99; N, 7.40. Found: C, 60.35; H, 7.92; N, 7.31.

1-Phenyl-3-methoxycarbonyl-4-(*R**)-ethyl-5-(*R**)-(1-trimethylsilyloxy)ethyl-4,5-dihydropyrazole (**6a**) (61 mg, 7%) as a pale yellow oil; IR (Nujol): 1735, 1080 (cm^{-1}); ^{1}H-NMR: 0.05 (9H, s, $(C\underline{H}_3)_3Si$-), 0.98 (3H, t, *J*=7.3, $C\underline{H}_3CH_2$-), 1.50-1.80 (4H, m, $CH_3C\underline{H}_2$- and -$C\underline{H}_2CH_2O$-), 3.11 (1H, ddd, *J*=8.6, 8.5, 3.6, C_4-<u>H</u> pyrazoline), 3.51-3.64 (2H, m, -$CH_2C\underline{H}_2O$-), 3.89 (3H, s, $C\underline{H}_3OCO$-), 4.49 (1H, ddd, *J*=8.6, 8.5, 3.3, C_5-<u>H</u> pyrazoline), 7.0-7.2 (5H, m, aromatics); after irradiation of the signal at 3.11 δ: 1.72 (2H, q, *J*=7.3, $CH_3C\underline{H}_2$-) and 4.49 (1H, dd, *J*=8.6, 3.3, C_5-<u>H</u> pyrazoline), after irradiation of the signal at 4.49 δ: 3.11 (1H, dd, *J*=8.6, 3.6, C_5-<u>H</u> pyrazoline); MS: 348 *m/z* (M^+). ***Anal.*** Calcd for $C_{18}H_{28}N_2O_3Si$: C, 62.03; H, 8.09; N, 8.04. Found: C, 61.95; H, 8.04; N, 8.10.

1-(4-Methoxyphenyl)-3-methoxycarbonyl-4-(*R**)-ethyl-5-(*R**)-(1-trimethylsilyloxy)ethyl-4,5-dihydropyrazole (**6b**) (66 mg, 7%) as a yellow oil; IR (Nujol): 1730, 1075 (cm^{-1}); ^{1}H-NMR: 0.03 (9H, s, $(C\underline{H}_3)_3Si$-), 0.90 (3H, t, *J*=7.2, $C\underline{H}_3CH_2$-), 1.48-1.84 (4H, m, $CH_3C\underline{H}_2$- and -$C\underline{H}_2CH_2O$-), 3.21 (1H, ddd,

J=9.0, 8.4, 3.1, C_4-H pyrazoline), 3.50-3.60 (2H, m, -CH_2CH_2O-), 3.68 (3H, s, CH_3O-), 3.90 (3H, s, CH_3OCO-), 4.50 (1H, ddd, *J*=9.0, 8.3, 3.7, C_5-H pyrazoline), 6.8-7.4 (4H, m, aromatics); MS: 378 *m/z* (M^+). *Anal.* Calcd for $C_{19}H_{30}N_2O_4Si$: C, 60.29; H, 7.99; N, 7.40. Found: C, 60.21; H, 8.05; N, 7.48.

Further elution gave cyclopropane derivatives (**7**).

1-Phenylazo-1-methoxycarbonyl-2-(*S**)-(1-trimethylsilyloxy)ethyl-3-(*S**)-ethylcyclopropane (**7a**) as an yellow oil; IR (Nujol): 1740, 1080, 1021 (cm^{-1}); ^{1}H-NMR: 0.02 (9H, s, $(CH_3)_3Si$-), 0.37 (1H, ddd, *J*=9.8, 7.6, 3.7, C_3-H cyclopropyl), 0.49 (1H, ddd, *J*=9.8, 7.5, 3.1, C_2-H cyclopropyl), 0.88 (3H, t, *J*=7.3, CH_3CH_2-), 1.40-1.64 (4H, m, CH_3CH_2- and -CH_2CH_2O-), 3.48-3.62 (2H, m, -CH_2CH_2O-), 3.94 (3H, s, CH_3OCO-), 7.1-7.3 (5H, m, aromatics); after irradiation of the signal at 0.37 δ: 0.49 (1H, dd, *J*=7.5, 3.1 C_2-H cyclopropyl) and 1.57 (2H, q, *J*=7.3, CH_3CH_2-), after irradiation of the signal at 0.49 δ: 0.37 (1H, dd, *J*=7.6, 3.7, C_3-H cyclopropyl), and 1.47 (2H, t, *J*=7.4, -CH_2CH_2O-); MS: 348 *m/z* (M^+). *Anal.* Calcd for $C_{18}H_{28}N_2O_3Si$: C, 62.03; H, 8.09; N, 8.04. Found: C, 62.10; H, 8.00; N, 8.12.

1-(4-Methoxyphenyl)azo-1-methoxycarbonyl-2-(*S**)-(1-trimethylsilyloxy)ethyl-3-(*S**)-ethylcyclopropane (**7b**) as an yellow oil; IR (Nujol): 1735, 1070, 1025 (cm^{-1}); ^{1}H-NMR: 0.05 (9H, s, $(CH_3)_3Si$-), 0.34 (1H, ddd, *J*=9.5, 7.4, 3.2, C_3-H cyclopropyl), 0.51 (1H, ddd, *J*=9.5, 7.5, 3.0, C_2-H cyclopropyl), 0.91 (3H, t, *J*=7.2, CH_3CH_2-), 1.38-1.59 (4H, m, CH_3CH_2- and -CH_2CH_2O-), 3.48-3.60 (2H, m, -CH_2CH_2O-), 3.64 (3H, s, CH_3O-), 3.91 (3H, s, CH_3OCO-), 6.7-7.3 (4H, m, aromatics); MS: 378 *m/z* (M^+). *Anal.* Calcd for $C_{19}H_{30}N_2O_4Si$: C, 60.29; H, 7.99; N, 7.40. Found: C, 60.36; H, 8.07; N, 7.49.

Cleavage of the silyl ether linkage of major cycloadducts (3) and (5) with TBAF. A solution of major cycloadducts (**3**) or (**5**) (1.0 mmol) in dry tetrahydrofuran (9 mL) and 1 M tetrabutylammonium fluoride (TBAF) (1.0 mL, 1.0 mmol) was stirred for 1 h at rt. The solvent was removed at reduced pressure, the residue was washed with water (2 mL) and crystallised from diisopropyl ether/isopropanol affording pure (**9**) or (**10**).

1-Phenyl-3-methoxycarbonyl-4-(*S**)-(1-hydroxy)ethyl-5-(*R**)-ethyl-4,5-dihydropyrazole (**9a**) (0.26 g, 94%) as white needles having mp 76-78°C; IR (Nujol): 3450, 1735 (cm^{-1}); ^{1}H-NMR: 0.92 (3H, t, *J*=7.2, CH_3CH_2-), 1.44-1.90 (4H, m, CH_3CH_2- and -CH_2CH_2O-), 2.21 (1H, br s, -O-H), 3.18 (1H, ddd, *J*=6.5, 4.6, 2.0, C_4-H pyrazoline), 3.55-3.69 (2H, m, -CH_2O-), 3.83 (3H, s, CH_3OCO-), 4.50 (1H, ddd, *J*=6.7, 4.6, 3.3, C_5-H pyrazoline), 7.0-7.2 (5H, m, aromatics); MS: 276 *m/z* (M^+). *Anal.* Calcd for $C_{15}H_{20}N_2O_3$: C, 65.20; H, 7.30; N, 10.14. Found: C, 65.24; H, 7.32; N, 10.20.

1-(4-Methoxyphenyl)-3-methoxycarbonyl-4-(*S**)-(1-hydroxy)ethyl-5-(*R**)-ethyl-4,5-dihydropyrazole (**9b**) (0.28 g, 90%) as white needles having mp 65-67°C; IR (Nujol): 3435, 1740 (cm^{-1}); ^{1}H-NMR: 0.88 (3H, t, *J*=7.3, CH_3CH_2-), 1.40-1.80 (4H, m, CH_3CH_2- and -CH_2CH_2O-), 2.08 (1H, br s, -O-H), 3.33 (1H, ddd, *J*=6.4, 4.4, 2.3, C_4-H pyrazoline), 3.50-3.70 (2H, m, -CH_2O-), 3.66 (3H, s, CH_3O-), 3.92 (3H, s,

C$\underline{H}_3$OCO-), 4.44 (1H, ddd, *J*=6.7, 4.4, 3.0, C_5-$\underline{H}$ pyrazoline), 6.8-7.2 (4H, m, aromatics); MS: 306 *m/z* (M^+). *Anal.* Calcd for $C_{16}H_{22}N_2O_4$: C, 62.73; H, 7.24; N, 9.14. Found: C, 60.33; H, 8.04; N, 7.48.

1-Phenyl-3-methoxycarbonyl-4-(*R**)-(1-hydroxy)ethyl-5-(*R**)-ethyl-4,5-dihydropyrazole (**10a**) (0.23 g, 85%) as white powder having mp 66-68°C; IR (Nujol): 3430, 1740 (cm^{-1}); ^{1}H-NMR: 0.92 (3H, t, *J*=7.2, C$\underline{H}_3$CH_2-), 1.44-1.90 (4H, m, CH_3C$\underline{H}_2$- and -C$\underline{H}_2$CH_2O-), 2.21 (1H, br s, -O-$\underline{H}$), 3.18 (1H, ddd, *J*=6.7, 5.6, 2.0, C_4-$\underline{H}$ pyrazoline), 3.55-3.69 (2H, m, -C$\underline{H}_2$O-), 3.83 (3H, s, C$\underline{H}_3$OCO-), 4.50 (1H, ddd, *J*=6.7, 5.4, 3.3, C_5-$\underline{H}$ pyrazoline), 7.0-7.2 (5H, m, aromatics); MS: 276 *m/z* (M^+). *Anal.* Calcd for $C_{15}H_{20}N_2O_3$: C, 65.20; H, 7.30; N, 10.14. Found: C, 65.16; H, 7.26; N, 10.18.

1-(4-Methoxyphenyl)-3-methoxycarbonyl-4-(*R**)-(1-hydroxy)ethyl-5-(*R**)-ethyl-4,5-dihydropyrazole (**10b**) (0.25 g, 83%) as white needles having mp 65-67°C; IR (Nujol): 3435, 1740 (cm^{-1}); ^{1}H-NMR: 0.88 (3H, t, *J*=7.3, C$\underline{H}_3$CH_2-), 1.40-1.80 (4H, m, CH_3C$\underline{H}_2$- and -C$\underline{H}_2$CH_2O-), 2.08 (1H, br s, -O-$\underline{H}$), 3.33 (1H, ddd, *J*=7.0, 6.3, 2.3, C_4-$\underline{H}$ pyrazoline), 3.50-3.70 (2H, m, -C$\underline{H}_2$O-), 3.66 (3H, s, C$\underline{H}_3$O-), 3.92 (3H, s, C$\underline{H}_3$OCO-), 4.44 (1H, ddd, *J*=7.0, 6.1, 3.0, C_5-$\underline{H}$ pyrazoline), 6.8-7.2 (4H, m, aromatics); MS: 306 *m/z* (M^+). *Anal.* Calcd for $C_{16}H_{22}N_2O_4$: C, 62.73; H, 7.24; N, 9.14. Found: C, 60.33; H, 8.04; N, 7.48.

Computational Details

The geometry of all the studied systems (**D**, **TS1**, **E**; **2b**, **B**, **TS2**, **5**) was fully optimized at the B3LYP/cc-pVDZ level; when silver was part of the system, it was described by a small-core pseudo-potential[25] and the cc-pVDZ-pp basis set.[26] Transition states **TS1** and **TS2** was confirmed by harmonic analysis. The solvent effect on the energetics of these systems was studied by the PCM model[27] with the following parameters for ethyl acetate (EPS=6.02, RSOLV=2.6 (estimated), VMOL=163., DENSITY=6.13E-03, EPSINF=1.17). All computations were carried out by the Gaussian 03 suite.[28]

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