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Interpretation of the Diastereoselectivity of the Cyclopropane Formation Involving π-Allyl Palladium Complexes Based on Molecular Mechanics Calculations

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Abstract—The diastereoselectivity of the base-induced cyclization of 2-amino-4-chlorobutyronitrile derivatives and of the palladium (0) catalyzed tandem alkylation and cyclization of (*E*)- and (*Z*)-1,4-dichlorobut-2-enes, providing suitable precursors of asymmetric 2,3-methanoamino acids, was interpreted by means of molecular mechanics calculations based on the MM2 force field. The dummy atom concept for the construction of η^3-allyl palladium complexes and a new parameter set for the calculation have been used. The observed diastereoselectivity which resulted from simple kinetic or thermodynamic control, can be however altered in some cases by the palladium-induced reversibility of the three-membered ring formation. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

1-Amino-1-cyclopropanecarboxylic acids (ACC) are widely and currently studied because they are endowed with a large spectrum of biological properties (enzyme inhibitions, antibacterial, antiviral, antitumor and neurochemical activities). They provide conformationally constrained peptidomimetics with enhanced biological activities and are used for the design of new drugs.[1] Their stereoselective synthesis presents a great deal of interest and many methods of cyclopropane formation have been reported to date.[2] We have recently published novel strategies for the stereoselective synthesis of highly functionalized cyclopropanes.[3a–k] The outcome of the reactions depends on the kinetic or thermodynamic controls and results probably from balanced steric and electronic interactions within either the intermediate reactive systems or in the formed three-membered rings. Therefore reliable explanations of the progress of the reactions require appropriate methods to calculate these interactions; molecular mechanics calculations have been proved to be useful for this purpose.

We report the molecular mechanics studies of systems leading to the functionalized cyclopropanes (*E*)-**1a**–**d**, convenient precursors of the (1*S*,2*S*)-norcoronamic, -coronamic, -dehydrocoronamic and -dehydrohomocoronamic acids **2a**–**d**, after simple acidic hydrolysis (6N HCl) and dehydrochlorination (ion exchange chromatography) and explain tentatively how calculations have guided our synthetic strategies (Scheme 1).

Our first approach was based on the base-induced cyclization of chiral non racemic 2-(*N*-benzylidene)amino- and 2-(*N*-diphenylmethylene)amino-4-chlorobutyronitrile derivatives (3*S*)-**3a-b′** (ee>88–95%) which provided in 80–100%

(*E*)-**1a-d** (R' = H, Ph)
(de: 30-100%; ee> 88-95%)

2a R = CH_3 (1*S*,2*S*)-*norcoronamic acid*
b C_2H_5 (1*S*,2*S*)-*coronamic acid*
c CH_2=CH (1*S*,2*S*)-*dehydrocoronamic acid*
d CH_3-CH=CH (1*S*,2*S*)-*dehydrohomocoronamic acid*

Scheme 1.

Keywords: molecular modelling mechanics; palladium and compounds; cyclopropanes; amino acids.
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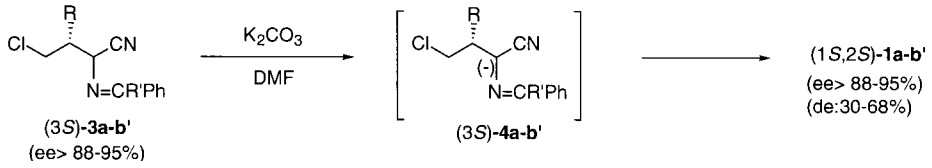


Scheme 2.

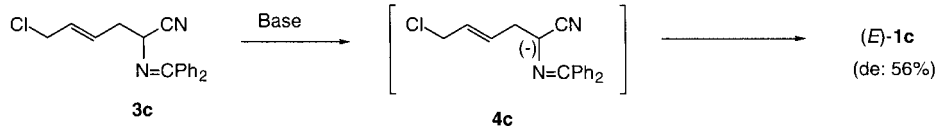
yields, via the anions (3*S*)-**4a-b′**, the (1*S*,2*S*) 1-aminocyclopropanecarbonitriles **1a-b′** with 68% (**1a**, R=Me, R′=H), 60% (**1b**, R=Et, R′=H) and 30% (**1b′**, R=Et, R′=Ph) diastereomeric excesses (Scheme 2).[3d]

Under the same basic conditions, the racemic 2-(*N*-diphenylmethylene)amino-6-chlorohex-4-enenitrile **3c** led, via the anion **4c**, to the 1-amino-2-vinylcyclopropane (*E*)-**1c** with only 56% of diastereoselectivity (Scheme 3).[3e]

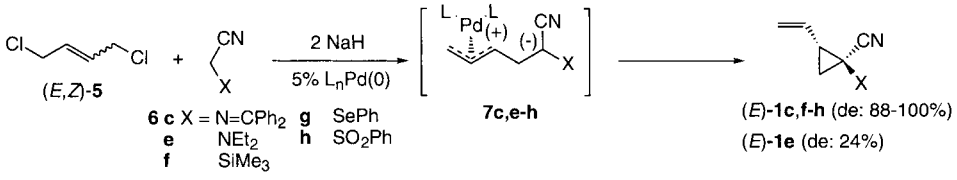
In order to improve the diastereoselectivity of the cyclopropane ring formation, we have then performed the one pot palladium (0) catalyzed tandem alkylation and cyclization of the (*E*)- and (*Z*)-1,4-dichlorobut-2-enes **5** by the anions of different a-substituted acetonitriles **6c**,**e**–**h** (X=N=CPh$_2$, NEt$_3$, SiMe$_3$, SePh, SO$_2$Ph) which provided, through the zwitterionic intermediate π-allylpalladium complexes **7c**,**e**–**h**, the 1-substituted-2-vinylcyclopropanecarbonitriles **1c**,**e**–**h**. The observed diastereoselectivity was in general excellent (de: 88–100%), apart for **6e** (X=NEt$_2$) for which under the same conditions, it decreased to 24% (Scheme 4).[3f]

Depending on the reaction conditions (temperature, base, cosolvent, reagent addition order, reaction time, etc.) a seven-membered heterocycle **9c** (R=H) could be formed from **6c** beside the expected cyclopropane (*E*)-**1c**. This by-product arose probably from a subsequent $C_3 \rightarrow C_7$ aza-Cope ring expansion of the diastereomer (*Z*)-**1c** into the enamine **8c**, which then underwent a 1,3-hydrogen shift to provide the conjugated azacycloheptadiene **9c** (Scheme 5).[3g,k]

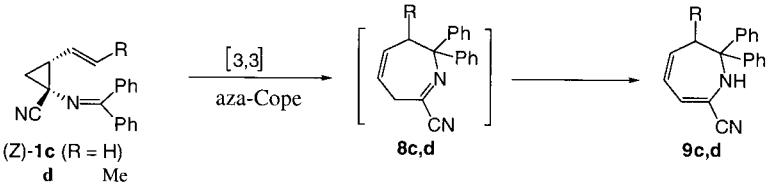
This one pot palladium (0) catalyzed tandem alkylation and cyclization attempted from the asymmetric (*E*)-1-chloropent-2-en-4-ol derivatives (4*S*)-**10j**–**l** (X=OAc, OCO$_2$*t*-Bu, O-2,4-diClBz; ee>94%) failed to provide the expected cyclopropanes (*E*)-**1d**. However, palladium (0) catalyzed alkylation of (4*S*)-**10i** (X=OH), gave the



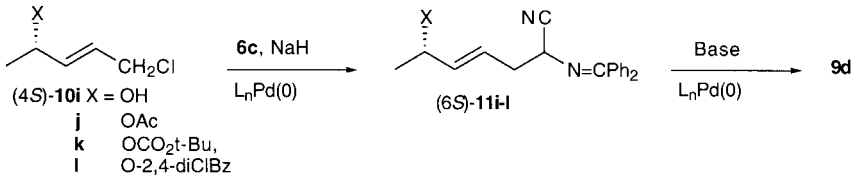
Scheme 3.



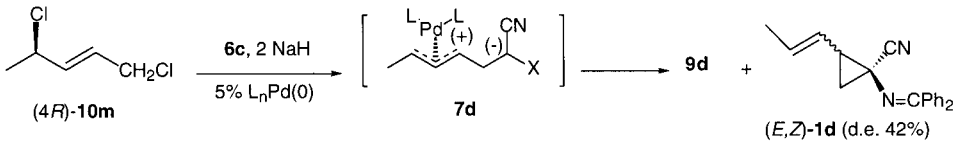
Scheme 4.



Scheme 5.



Scheme 6.



Scheme 7.

2-amino-6-hydroxyhept-4-enenitrile (6*S*)-**11i** (X=OH); $S_{N'}$ cyclization of the corresponding carbonate and esters (6*S*)-**11j**–**l**, under various basic conditions (NaH, DBU, *n*-BuLi), led always to the seven-membered ring **9d** (R=Me), arising also from subsequent $C_3 \rightarrow C_7$ aza-Cope ring expansion. It must be underlined that in the absence of Pd(0) no reaction occurred (Scheme 6).

On the other hand, from the (*E*)-1,4-dichloropent-2-ene (4*R*)-**10m** was obtained in 49% yield, through the zwitterion **7d**, a diastereomeric mixture of (*E*)- and (*Z*)-**1d** (de: 42%), beside **9d** (24%, Scheme 7).[3k]

Considering these experimental results, we have then tried to interpret and if possible to predict the diastereoselectivity of the base-induced cyclization of the chloronitriles **3a**–**c** and of the palladium (0) catalyzed cyclization of the allylic chlorides (*E*,*Z*)-**5** and (4*R*)-**10m** by the anions of the α-aminoacetonitriles **6c**,**e**. In our molecular mechanics approach, parameters such as solvents, bases and counterions, were not taken into account. As it has recently been clearly demonstrated, the steric effect in the nucleophilic attack can be considered as the most important;[4] then, we have chosen for probe model, the conformations of the intermediate anions **4a**–**c** and of the zwitterions **7c**–**e** corresponding to the possible transition states. Such models could appeared simplistic, but they have previously been proved sufficient to predict such kind of relative stereoselectivities.[4] To complete this analysis, we have moreover studied the relative stabilities of the cyclopropanes (*E*)- and (*Z*)-**1a**–**e**. The aim of this work was to determine the factors responsible for the stereoselectivity of these cyclizations and to demonstrate that the reactions pathways were controlled either by the geometry of the transition states or by the relative stabilities of the cyclization products: i.e. that the reactions were either under kinetic or thermodynamic control?

Results

Molecular mechanics calculations of the intermediate anions 4a–c

The calculations were performed with the Chem 3D system using a Allinger's MM2 type force field.[5] In order to build each atom of the structures with the suitable geometry, we have first performed PM3 calculations on the anions **4a-b′**.[6] In every case, the anions adopted a planar geometry at C_1 ($\Sigma\alpha$=358°); therefore, C(sp2) and C(sp) types for the C_1 and the $C_{1'}$ carbon atoms must be imposed in the MM2 calculations, respectively.

These semi-empirical calculations showed moreover that the two (a) and (b) phenyl groups of the (*N*-diphenylmethylene)amino moiety of **4b′** adopted the relative positions previously reported from crystallographic data,[7,8] thus confirming the minimized structure obtained from MM2 calculations (the $N_{1''}C_{2''}C_{1a}C_{2a}$ and $N_{1''}C_{2''}C_{1b}C_{2b}$ dihedral angles values were +10 and −75°, respectively). We have then considered that the Chem 3D force field took into account the important non-bonded interactions. In the base-induced cyclization of the chloronitriles **3a**–**c** (Schemes 2 and 3), the cyclopropane ring formation can be considered as intramolecular nucleophilic reactions.[9] The constrained conformations (I) and (II) of the anions **4a**–**c** which led to the (*Z*)- or (*E*)-cyclopropanes **1a**–**c** respectively, have been minimized. A value of 180° was

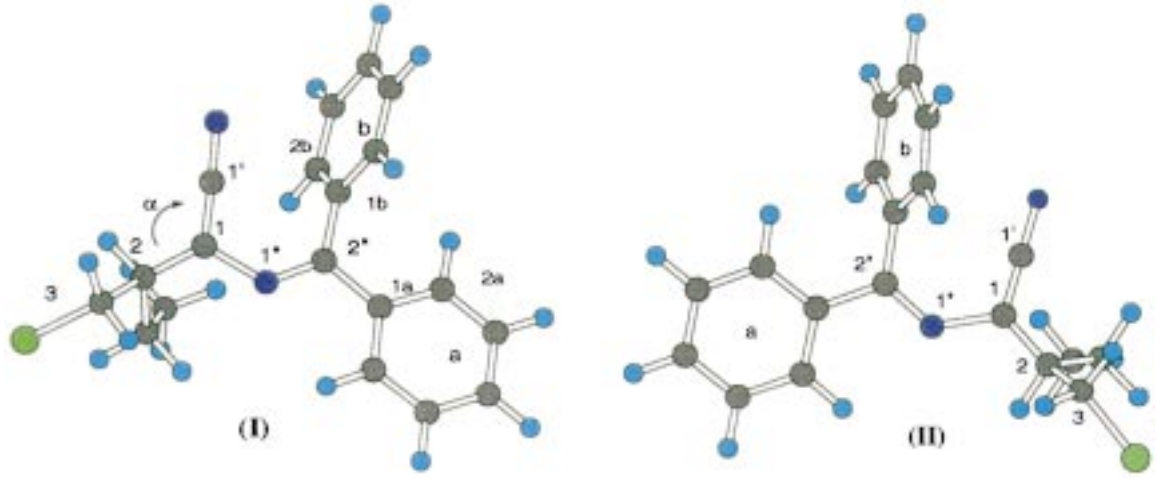


Figure 1. MM2 minimized geometries of (I) and (II) conformations of **4b′**.

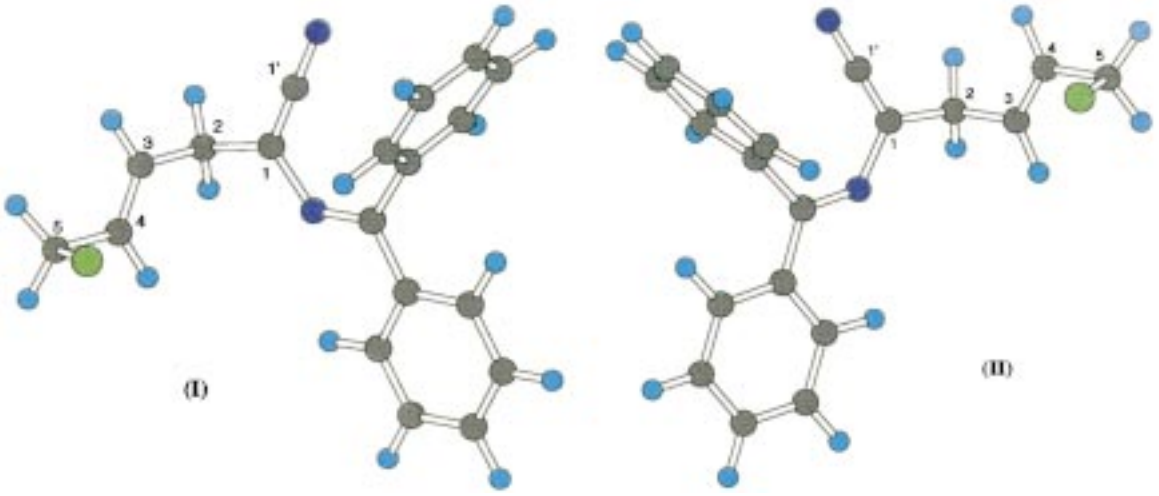


Figure 2. MM2 minimized geometries of (I) and (II) conformations of **4c**.

imposed on the $C_1C_2C_3Cl$ dihedral angle and values of -90 and $+90°$ on the $C_{1'}C_1C_2C_3$ dihedral angles for the conformations (I) and (II) of the anions **4a-b′**, respectively (Fig. 1).

For the anion **4c**, after to have determined the suitable position of the chlorine atom relatively to the iminonitrile moiety, values of $-90°$ were assigned to the $C_1C_2C_3C_4$ and $C_3C_4C_5Cl$, and 180° to the $C_2C_3C_4C_5$ dihedral angles, while -90 and $+90°$ values to the $C_{1'}C_1C_2C_3$ angles for the conformations (I) and (II), respectively (Fig. 2).

The relative stabilities of the cyclized products (*E*)- and (*Z*)-**1a–c** were calculated also from their minimized structures obtained after an extensive grid search. The results are summarized in the Table 1. It should be noted that for all the minimized conformations (I) and (II) of **4a–c**, the iminonitrile anion system adopted a *s-cis* conformation (Figs. 1 and 2).

Molecular mechanics calculation of the zwitterionic η^3-allyl palladium complexes 7c–e

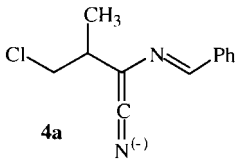
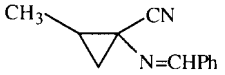
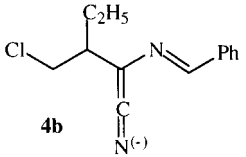
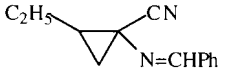
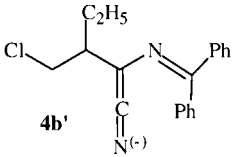
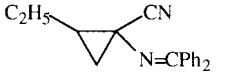
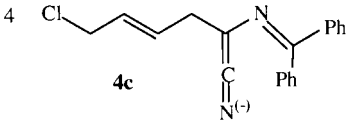
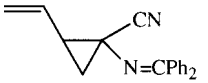
Such calculations for a rational design of metal catalysts and the development of molecular mechanics parameter sets for the η^3-allyl palladium complexes using Allinger force fields have been recently reported.[10–12] Using the MM2 force field we had to adopt the dummy atom concept of Norrby and Akermark for the construction of normal square-planar complexes, and used their parameter set for the η^3-allyl palladium moiety. For the modelling of phosphine ligands, the geometry parameters (bond lengths and bond angles), and the stretching and bending force constants were deduced from the parameters adjusted by Landis for the square-planar rhodium complexes.[13] Effectively, it has been considered that the force constants for Pd(II), Rh(I) and Ni(II) complexes were in the same order of magnitude; calculations performed with these parameters led to a good fit between calculated and experimental structures.[13,14] For the torsional parameters, we have used the values reported for the amine ligands.[12]

The minimization of the η^3-allyl palladium moiety **7** built according to the dummy atom bonding model with the new parameter set,[10,11] retained the square-planar geometry of the palladium complex (the torsional angles values $C_1C_3PdP_2$ and $C_3C_1PdP_1$ were -171 and $+175°$, respectively). In both the phosphine ligands, the phenyl groups adopted positions with non-bonded interactions; this geometry was validated by comparison with the related X-ray structure data of a η^3-allylpalladium complex containing triphenylphosphine ligands (Fig. 3).[15]

For the palladium (0) catalyzed tandem alkylation and cyclization of the allylic chlorides (*E*)- and (*Z*)-**5** and (4*R*)-**10m** by the anions of the α-aminonitrile **6c**,**e**, the ring closure can be considered as an internal S_N2 substitution of the π-coordinated palladium by the nucleophilic carbanion (Schemes 4 and 7). From the MM2-minimized complex **7**, the possible structures of the η^3-allyl palladium zwitterionic complex **7c–e** were built according to the transition state model, recently described by Norrby.[4,16] A suitable position for the nucleophilic carbon C_1 required a *syn* position for the anionic group relatively to the allylic system, which imposed a value of $+90°$ for the $C_1C_2C_3C_4$ dihedral angle. The $C_{11}P_1PdC_4$ and $C_3C_4PdP_1$ dihedral angles have been constrained to a suitable distortion, in order to bring the resulting olefinic moiety into the P–Pd–P coordination plane. Thus, this distortion led to a geometry corresponding to the Norrby's transition state model (with C_3C_1 distances=2.44–2.45 Å, bond angles PdC_1C_3= 152–159°, $C_4C_3C_1$=+113–115° and dihedral angles $PdC_4C_3C_1$=+150–157°) (Fig. 4).

Likewise, the minimized conformations (I) and (II) of the zwitterions **7c–e** leading to the cyclopropanes (*Z*)- and (*E*)-**1c–e**, imposed $C_{1'}C_1C_2C_3$ dihedral angle values of -90 and $+90°$, respectively. The relative steric energies of the cyclopropanes (*Z*)- and (*E*)-**1c–e** have been also minimized. The results are reported in the Table 2. The favoured conformation of the iminonitrile moiety for the zwitterionic π-allyl palladium systems **7c**,**d** was *s-cis*. For **7d**, the two minimized conformations (I) and (II) which led to **1d** bearing a (*E*)-2-(1-propenyl) group were *syn*, *syn*.

Table 1. Calculated relative energies of intermediate anions **4a–c** and cyclopropanes **1a–c** and experimental data of the ring closure

Entry	Intermediate Anions **4a–c** (I) and (II)	Products (*E*,*Z*)-**1a–c**	Calculations		Experimental data		
			Relative anion stabilities $E(I)-E(II)$ kcal mol^{-1}	Relative product stabilities $E(Z)-E(E)$ kcal mol^{-1}	Reaction conditions[a] *t* (h)	*E*/*Z* ratio[b]	Yield
1	 **4a**	 **1a**	0.3	0.3	(0.5)	84/16	80
2	 **4b**	 **1b**	0.4	0.2	(0.5)	80/20	70
3	 **4b'**	 **1b'**	0.9	1.3	(3)	65/35	92
4	 **4c**	 **1c**	0.5	0.3	(24)	78/22	84

[a] Reaction conditions were optimized to obtain the best yields (K_2CO_3, DMF, rt).
[b] Ratios were determined from NMR data.

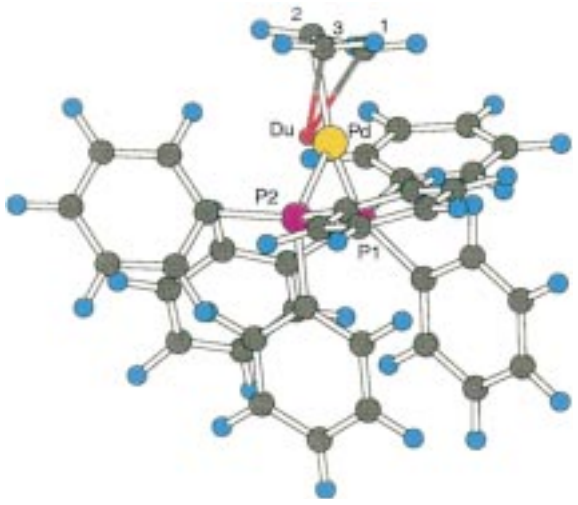


Figure 3. MM2 minimized square-plane geometry of **7** (Du=dummy atom).

Discussion

The molecular mechanics data reported in the Table 1 pointed out that the conformations of lowest energy for the anions **4a**–**c**, were always of type II and that the (*E*)-configuration of the resulting cyclopropanes **1a**–**c** was the most stable. However, the difference of energies between the (I) and (II) conformations for **4a**–**c** being always lower than 1 kcal mol^{-1}, and the difference of stabilities of (*E*)- and (*Z*)-**1a**–**c** ranging from 0.2 to 1.3 kcal mol^{-1} (Table 1, entries 1–4), the increase of the sizes of the R group (entries 1 and 2) and of the imine moiety (entries 2 and 3) or furthermore the modification of the electrophilic site (entry 4) could not induce any significant effects on the base-induced cyclization of the chloronitriles **3a**–**c**. This fact was effectively observed experimentally; therefore, no useful conclusions concerning the factors determining the diastereoselectivity of the reaction could be drawn from these low energy differences.[17]

In order to overcome this problem, the leaving groups in **3a**–**c**, i.e. the chlorine and the allylic chlorine, were then replaced by a π-allyl palladium complex for which, metal–allyl, metal–ligand and nucleophile interactions could be considered as major factors for the diastereoselectivity of the cyclization step.[4,16] Thus, the zwitterionic palladium complexes **7c**,**d** were investigated by molecular mechanics calculations, comparatively to the complex **7e** to test the steric effect of the (*N*-diphenylmethylene)amino group (Table 2).

The two minimized conformations (I) and (II) of **7c** exhibited then an energy difference of 3.2 kcal mol^{-1} predicting the exclusive formation of the cyclopropane (*E*)-**1c**. This expectation was really in good agreement with the experimental result, which disclosed a (*E*)/(*Z*) ratio value of 100/0 (entry 1, Table 2). Therefore in this case, the one pot palladium (0) catalyzed tandem alkylation and cyclization can be considered under total kinetic control. Comparatively to the results obtained from the base-induced cyclization reaction of **4c** (Table 1, entry 4), it appeared clearly that the bulky *p*-allyl palladium complex which enhanced the steric effects within the zwitterionic intermediate **7c**, improved accordingly the diastereoselectivity of this cyclization.

On the other hand, the calculated energy difference of 1.7 kcal mol^{-1} for the two minimized conformations (I) and (II) of **7d**, should have provided also the cyclopropane (*E*)-**1d** with a good stereoselectivity (entry 2). But the

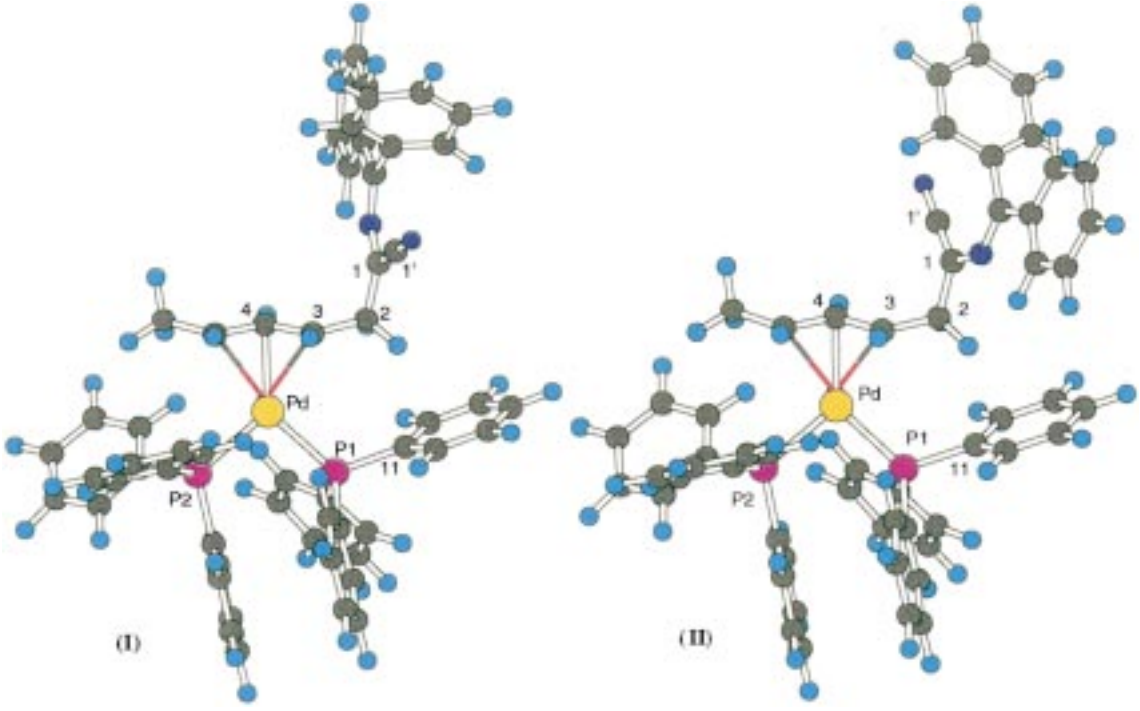
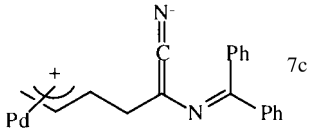
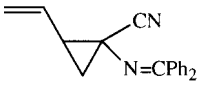
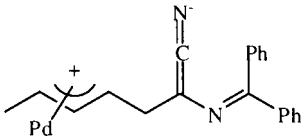
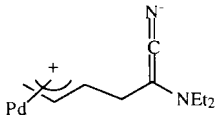


Figure 4. MM2 minimized geometries of (I) and (II) conformations of **7d**.

Table 2. Calculated relative energies of zwitterionic palladium allyl complexes **7c–e** and cyclopropanes **1c–e** and experimental data of the ring closure

Entry	Intermediate Zwitterions **7c–e** (I) and (II)	Products (*E*,*Z*)-**1c–e**	Calculations		Experimental data		
			Relative stabilities zwitterion *E*(I)−*E*(II) kcal mol^{-1}	Relative stabilities product *E*(*Z*)−*E*(*E*) kcal mol^{-1}	Reaction Conditions[a] *t* (h)	*E*/*Z* Ratio[b]	Yield
1	 7c	 **1c**	3.2	0.3	(0.25)	100/0	74
2	 **7d**	 **1d**	1.7	0.1	(5)	71/29	49[c]
3	 **7e**	 **1e**	0.4	1.2	(6)	62/38	76

[a] Reaction conditions were optimized to obtain the best yields [2NaH, Pd(0) 5%].
[b] Ratios were determined from NMR data.
[c] (*Z*,*E*)-**1d** mixture was accompanied by 24% of **9d** (*E*/*Z*/**9d** ratio=48/19/33).

obtention in 49% yield, of a 71/29 diastereomeric mixture of (*E*)- and (*Z*)-**1d** (de: 42%), beside **9d** as by-product, proved that in this case the reaction was not under kinetic control. The energy stability difference of 0.1 kcal mol^{-1} between the cyclopropanes (*Z*)- and (*E*)-**1d**, also could not explain the result. However, the difference of reactivity pointed out by the required reaction times to complete the reaction, 0.25 and 5 h for **1c** and **1d**, respectively, (Table 2, entries 1 and 2) can be held responsible for the lower yield and diastereoselectivity obtained from **7d**. As a matter of fact, vinylcyclopropanes undergo palladium(0) induced ring opening,[18] consequently longer reaction time resulting from the methyl introduction on the π-allyl palladium moiety of **7d**, entailed the ring opening of **1d**, i.e. the reversibility of the cyclization. Then (*Z*)-**1d** was formed and its further ring expansion into **9d** provoked the equilibrium shift. This fact was chemically verified; thus, when treated under the same reaction conditions, i.e. in the presence of the palladium(0) catalysis, a 92/8 diastereomeric mixture of (*E*)- and (*Z*)-**1d** underwent complete rearrangement into the heterocycle **9d**, while an enantiomerically enriched derivative of (*E*)-**1c** (ee>32%) underwent racemization and even epimerization (ee>−9%).[3k]

From **7e**, the energy difference of 0.4 kcal mol^{-1} between the (I) and (II) complexes and of 1.2 kcal mol^{-1} between the cyclopropanes (*Z*)- and (*E*)-**1e** stabilities (entry 3), could predict the low (*E*) selectivity observed (*E*/*Z*=62/38). Comparatively to the calculations performed on **7c**, these results showed that weaker steric hindrance of the amino group induced lower stereoselectivity. It appeared then clearly that to obtain the cyclopropanes (*E*)-**1** with a useful stereoselectivity, the intramolecular $S_{N'}$ reaction required a bulky nucleophile such as the (*N*-diphenylmethylene)-aminonitrile anion. Moreover, to avoid the possible subsequent ring expansion the use of palladium catalyst must be precluded when the cyclization step was too slow. A solution to this problem was found, when the cyclization was performed under the Mitsunobu reaction conditions. Thus for instance, a 94/6 mixture of (*E*)- and (*Z*)-**1d** (de: 88%) could be obtained readily on simple addition of a 1:1 mixture of diethyl azodicarboxylate and of trimethylphosphine to (6*S*)-**11i**.[3h,k]

Conclusion

The MM2 minimized geometries arising from these molecular mechanics calculations allowed a rational interpretation of the experimental results. The diastereoselectivities observed in these three-membered ring formations resulted essentially from steric and electronic effects within the anionic **4a–c** and the zwitterionic intermediaries **7c–e**; therefore it appeared not necessary to take into account others reactivity factors. These calculations, which have also evidenced the palladium-induced reversibility of the ring closure, provided a useful and convenient tool for the understanding and for the search of the improvement of the stereoselectivity in such reactions. Finally, we expect to have contributed with this study to widen the scope of application, both in organic and organometallic chemistry, of the available parameter sets for the force field modelling of reactive intermediaries and products.

Experimental

Computational analysis

Structure minimization was carried out with the Chem 3D system using a modified Allinger's MM2 force field.[5] Semi-empiral calculations were carried out using the PM3 programme provided in the Hyperchem 51 system.[6]

The description of (*E*)-**1a-b**′, synthesized from the base-induced cyclization of (3*S*)-**4a-b**′,[3b] and the description of (*E*)-**1c**,**d** prepared from the palladium(0)-catalyzed tandem alkylation and $S_{N'}$ cyclization of (*E*,*Z*)-**5** and (4*S*)-**10**, respectively,[3k] have been recently reported.

(*E*)- and (*Z*)-1-(Diethylamino)-2-ethenylcyclopropanecarbonitrile 1e. *General procedure*. A solution of 29 mg (0.05 mmol) of $Pd(dba)_2$ and 26.3 mg (0.1 mmol) of PPh_3 in 4 ml of THF was stirred under argon stream for 10 min. Then was added a solution of 125 mg (1 mmol) of a 85:15 mixture of (*E*,*Z*)-1,4-dichlorobut-2-ene **5** in 2 ml of THF, and the mixture was stirred at room temperature until its color turned from deep red to orange-yellow. The mixture was cooled to −78°C and then were added a solution of 112 mg (1 mmol) of (diethylamino)acetonitrile **6e** in 2 ml of THF, 0.7 ml (4 mmol) of HMPA and 3.2 ml (2 mmol) of a 1.6 M solution of *n*-BuLi in THF, at −78°C. The mixture was stirred for 15 h at room temperature. After addition of 4 ml of saturated ammonium chloride aqueous solution and 20 ml of diethyl ether, followed by filtration through celite, the organic phase was acidifed by 2 ml of 0.25N HCl, washed with satured sodium chloride (twice) and with water and finally dried (Na_2SO_4) and evaporated in vacuo. The residue was purified by column chromatography over silica gel eluting with hexane/diethyl ether (9/1) to give 124.6 mg (76%) of a 62/38 mixture of (*E*)- and (*Z*)-**1c** which were separated by gas chromatography (Cpsil, 25m, 80+10°C/min).

*Major diastereomer (E)-**1e**:* (Retention time: 2.15 min) IR ($CDCl_3$) 2220 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.98–1.0 (m, 1H), 1.0–1.20 (m, 6H), 1.60 (dd, *J*=5.4 and 9.3 Hz, 1H), 2.07 (dq, *J*=7.3 and 2.0 Hz, 1H), 2.60–2.80 (m, 4H), 5.23 (ddd, *J*=17.3, 10.20 and 1.7 Hz, 2H), 5.56 (ddd, *J*=17.3, 10.20 and 9.1 Hz, 1H); ^{13}C NMR (62 MHz, $CDCl_3$) δ (ppm): 12.72, 22.63, 34.95, 39.13, 46.81, 117.34, 119.7 (n_{CN}), 133.96; MS (EI) *m/e* (rel. intensity) 164 (M^+, 2); 149 (100), 135 (7), 123 (33), 107 (28), 94 (18), 80 (32), 68 (42), 56 (38), 39 (23); MS (CI, NH_3) *m/e* (rel. intensity) 165 (M+1, 100), 164 (M, 3). Anal. calcd for $C_{10}H_{16}N_2$: C, 73.13; H, 982. Found: C, 73.23, H, 9.72.

*Minor diastereomer (Z)-**1e**:* (Retention time: 2.11 min) IR ($CDCl_3$) 2220 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.05–1.15 (m, 6H), 1.25–1.45 (m, 2H), 1.95 (dd, *J*=16.3 and 8.6 Hz, 1H), 2.60–2.80 (m, 4H), 5.23 (m, 2H), 5.63 (ddd, *J*=17, 10.1 and 8.5 Hz, 1H); ^{13}C NMR (62 MHz, $CDCl_3$) δ (ppm): 13.13, 22.16, 32.31, 40.85, 47.55, 117.85, 118.05, 133.93; MS (EI) *m/e* (rel. intensity) 164 (M^+, 1.7); 149 (100), 135 (6), 123 (31), 107 (26), 94 (16), 80 (27), 68 (33), 56 (32), 39 (18); MS (CI, NH_3) *m/e* (rel. intensity) 165 (M+1, 100), 164 (M, 2.5). Exact mass M^+ 164.1313 (calcd for $C_{10}H_{16}N_2$ 164.13134).

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