DOI: 10.1002/ejoc.200600239

Stereochemistry of the Tetrabutylammonium Cyanide-Catalyzed Cyanosylilation of Cyclic α,β-Epoxyketones – Dependence of the Diastereoselectivity on the Ring Size

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Dedicated to the memory of Prof. Marcial Moreno Mañas

Keywords: Ab initio calculations / Diastereoselectivity / Cyanohydrins / Epoxyketones / Trimethylsilyl cyanide / Tetrabutylammonium cyanide

The diastereoselective Bu_4NCN-catalyzed addition of TMSCN to cyclic α,β-epoxyketones has been considered. Good diastereoselectivities were found, depending on the ring size of the starting material. Computational studies account for the observed diastereoselectivities.

Introduction

Cyanohydrins constitute versatile starting materials useful as intermediates for the synthesis of a variety of relevant targets such as α-hydroxyacids, β-amino alcohols, and their derivatives.[1] In particular, ketone cyanohydrins are of special interest as starting materials for the preparation of compounds with stereogenic quaternary centers.[2] The variety of synthetically useful transformations of the cyanohydrin moiety combined with those of other reactive functional groups in close proximity may give rise to new chemistry with no analogy in monofunctional systems. Considering that epoxides are important reactive intermediates,[3] we have envisaged the combination of an epoxide and a ketone cyanohydrin in the same molecule, focusing our attention on α,β-epoxycyanohydrins derived from α,β-epoxyketones. To the best of our knowledge, the stereocontrolled synthesis of these types of compounds has not been considered in previous literature.[4]

Among the various reagents available for the cyanosilylation of ketones,[2] the use of TMSCN has proven valuable from safety standpoints.[5] With few exceptions,[6] this reagent is only effective in the transfer of the CN group to the carbonyl moiety of aldehydes or ketones under the action of activators, which are mainly organometallic Lewis acids.[1] However, from the point of view of their environmentally benign nature, their ease of handling, and the cost of the reaction process, metal-free organocatalysts have recently attracted the attention of organic chemists. In this context, the use of different organocatalysts for the cyanosilylation of aldehydes and ketones has been reported.[7] Recently, we communicated the use of phosphonium[8] and ammonium[9] salts as a convenient catalytic reagent for the cyanosilylation of aldehydes and ketones. In this report, we wish to account for the application of tetrabutylammonium cyanide as the catalytic agent for the diastereoselective cyanosilylation of α,β-epoxyketones. As a matter of fact, an unprecedented dependence of the diastereoselectivity on the ring size in the case of cyclic epoxyketones has been observed. This behavior may be explained through appropriate theoretical calculations.

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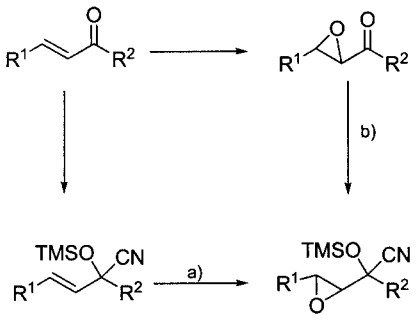
Results and Discussion

For the synthesis of α,β-epoxy-*O*-TMS cyanohydrins, two different strategies can be envisioned (Scheme 1): epoxidation of the cyanohydrins of α,β-unsaturated ketones (strategy *a*) or cyanohydrin formation from α,β-epoxyketones (strategy *b*).



Scheme 1.

At first, strategy *a* looks more appealing, because strategy *b* may suffer from competitive ring opening of the oxirane moiety under these reaction conditions.

Therefore, at the onset of our study, we considered the Bu_4NCN-catalyzed addition of TMSCN to ketone **1b** with subsequent epoxidation (mCPBA, CH_2Cl_2, Scheme 2) by using strategy *a*. The reaction took place only with low yield (10%, 2 h, room temperature), and diastereomers **8a** and **8b** were obtained in a 1:1 ratio.

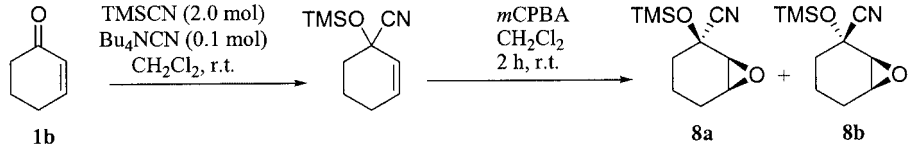
Discouraged by both low diastereoselectivity and yield,[10] we switched over to strategy *b* and considered the Bu_4NCN-catalyzed addition of TMSCN to the α,β-epoxyketone **3** (Scheme 3), obtained in turn by the epoxidation of the related α,β-unsaturated ketone **1b**. We observed that, in this case, diastereomers **8a** and **8b** were obtained in a 1:3 ratio and 90% isolated yield.

In light of this result, we undertook the study of the Bu_4NCN-catalyzed addition of TMSCN to the cyclic α,β-epoxyketones **2**–**6**. The results of these reactions are gathered in Table 1.

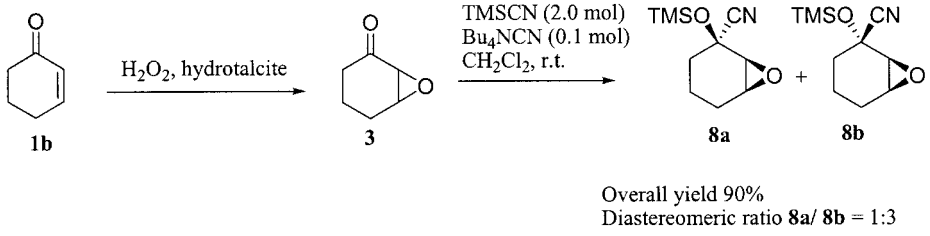
The inspection of these data puts forward that, for the epoxyketones **2**–**6**, good diastereoselectivities were obtained in all cases (Table 1, entries 1–5). However, the diastereoselectivity (i.e. the prevalence of isomer **a** or **b**) depended on the ring size of the starting cyclic epoxyketone. Thus, while the five-membered compounds **2** and **6** (Table 1, entries 1 and 5) afforded cyanohydrins **a** (arising from the *anti*-oxirane attack of the nucleophile on the carbonyl group) as major diastereomers, the six-, seven-, and eight-membered compounds **3**, **4**, and **5** (Table 1, entries 2, 3, and 4) afforded cyanohydrins **b** (arising from the *syn*-oxirane attack of the nucleophile on the carbonyl group) as major diastereomers.

The configurational assignment[11] was based on 1D gNOESY spectra. The ^1H NMR spectra of compounds **7**–**11** consisted of a series of complex multiplets, except for the methine protons of the oxirane ring and the methyl protons of the TMS group. The methylene protons adjacent to the CH group could be identified through 1D gCOSY and 1D gTOCSY experiments. Stereochemical assignments were mainly based on the observations of NOE effects between the methine protons of the oxirane moiety and the methyl protons of the TMS group in the **b** isomers (Table 1 and Figure 1).

The stereochemical outcome of the reaction (i.e. the dependence of the diastereomeric ratio on the ring size of the starting material) is an intriguing question. In order to get more insight into the factors responsible for the observed diastereoselectivity, computations were carried out on the cyclic systems **2**–**6**. Under kinetic control (see Table 2),[12] the observed diastereoselectivity may be explained in terms of free activation energy differences ($\Delta\Delta G^{\ddagger}_{298}$) of the *syn* or *anti* addition of the nucleophile to the corresponding epoxyketone. The picture of the reaction path for this cata-

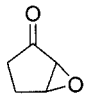
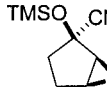
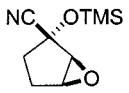
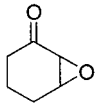
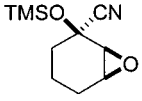
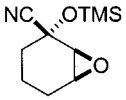
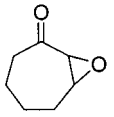
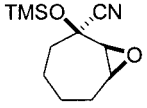
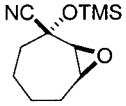
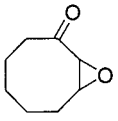
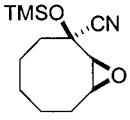
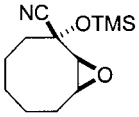
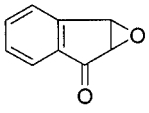
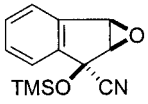
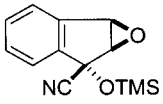


Scheme 2.



Scheme 3.

Table 1. Bu_4NCN-catalyzed cyanosilylation of epoxyketones **2**–**6**.

Entry	Starting ketone	Isolated products	d.r.,[a] overall yield[b]
1	 **2**	 **7a**  **7b**	**7a/7b** = 4:1, 98%
2	 **3**	 **8a**  **8b**	**8a/8b** = 1:3, 90%
3	 **4**	 **9a**  **9b**	**9a/9b** = 1:8, 85%
4	 **5**	 **10a**  **10b**	**10a/10b** = 1:19, 98%
5	 **6**	 **11a**  **11b**	**11a/11b** = 3:1, 80%

[a] Diastereomeric ratios were determined by the integration of the corresponding signals in the ^1H NMR spectra ($CDCl_3$, 300 MHz) of the crude reaction mixtures. [b] Yield of the pure compound, isolated as a diastereomeric mixture.

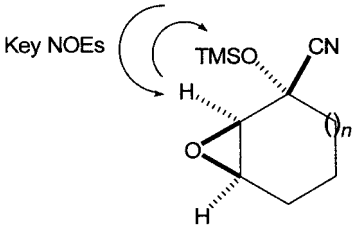
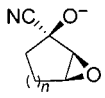
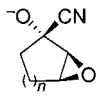


Figure 1. Representation of the NOE effects observed only in the **b** isomers.

lyzed addition is not a simple matter. The catalytic role of the ammonium salt may be explained by assuming a hypervalent silicon intermediate, thus increasing the efficiency of the cyanide ion transfer.[13] There is no doubt that, by analogy with many other reactions involving activated silicon species,[14] the mechanism of the process should involve an initial and a reversible attack of the nucleophilic catalyst to give a pentacoordinate silicon intermediate (Scheme 4). The

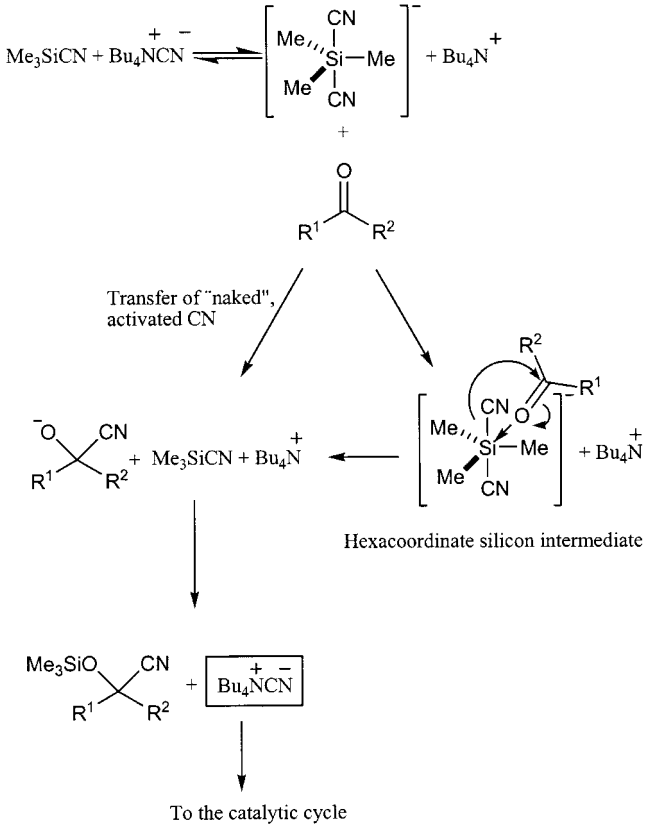
Table 2. Relative energies [ΔE][a] of the *syn* and *anti* isomers of compounds **7**–**10**.

 *syn*  *anti*

Entry	*n*	Compounds	ΔE(*anti*–*syn*) [kcal/mol]
1	1	**7a, 7b**	+2.73
2	2	**8a, 8b**	+4.20
3	3	**9a, 9b**	+3.05
4	4	**10a, 10b**	+2.90

[a] ΔE values in kcal/mol, computed as $\Delta E = E_{anti} - E_{syn}$. All values have been calculated at the B3LYP/6-31++G** + ΔZPVE level.

question is whether this first intermediate behaves as a source of "naked" reactive cyanide ion or undergoes coordination with the carbonyl group of the epoxyketone to give a hexacoordinate intermediate (or transition state), which evolves to the products by intramolecular transfer of the cyanide ion.[15] In these cases, however, all attempts to localize the transition state derived from a pentacoordinate silicon nucleophilic attack on an epoxyketone to give a hexacoordinate silicon intermediate met with no success. Thus, at least in these cases, the stereochemical result arises from the nucleophilic attack of an activated cyanide nucleophile on the carbonyl group. The intermediacy of this "hard" nucleophile can also explain the regioselectivity (i.e. attack only on the carbonyl group) of the reaction of some



Scheme 4.

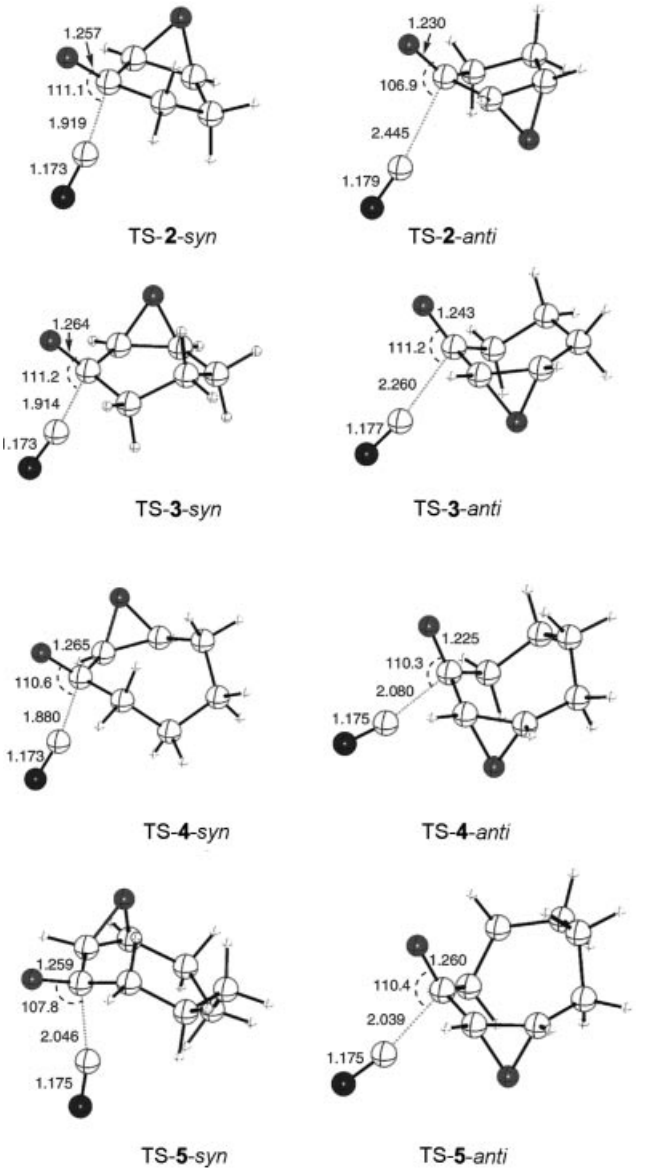
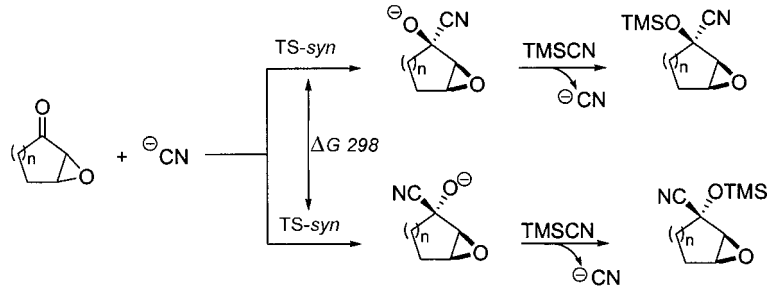


Figure 2. Ball and stick representations of transition states for the nucleophilic addition of the cyanide ion to compounds **2**–**5**. All structures correspond to fully optimized B3LYP/6-31++G(d,p) geometries. Bond lengths are given in Å and angles in degrees. Unless otherwise stated, white (small), white (big), gray, and black colors denote hydrogen, carbon, oxygen, and nitrogen atoms, respectively.



Scheme 5.

spiroepoxycyclohexadienones with TMSCN in the presence of Bu_4NCN.[9b,16]

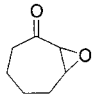
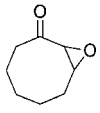
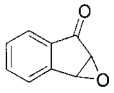
Thus, the observed diastereoselectivity may be explained in terms of free activation energy differences ($\Delta\Delta G^{\ddagger}_{298}$) of the *syn* or *anti* addition of the cyanide ion (which is rapidly formed from the hypervalent silicon species) to the corresponding epoxyketones (Scheme 5).

As readily seen in Figure 2, in the reactive approximation the nucleophile follows a typical nonperpendicular Bürgi–Dunitz trajectory[17] with angles ca. 110–111° and N≡C···C(=O) distances ranging from 1.9–2.2 Å. In general, the latter geometrical feature is always shorter in the *syn* transition states than that in the corresponding *anti* analogues.

The calculated $\Delta\Delta G^{\ddagger}_{298}$ values measured as $\Delta G^{\ddagger}_{298}$(TS-*syn*) – $\Delta G^{\ddagger}_{298}$(TS-*anti*) are compiled in Table 3. It is clear that for small ring sizes (i.e. five-membered epoxyketone **2** and its aromatic analogue **6**), the free activation energies of the *syn* addition are smaller. In sharp contrast, the corresponding transition states for the *anti* addition in six- to eight-membered epoxyketones **3**–**5** are more stable than the *syn* attack transition states, and therefore, the reactions involving compounds **3**–**5** lead to *anti* products predominantly. In consequence, the diastereoselectivity of this process strongly depends on the ring size. These results are in good agreement with the experimental findings.

The stereochemical outcome of the process may be explained in terms of Felkin–Anh's model,[18] which means that cyanide addition takes place preferentially from the less hindered side of the carbonyl group to afford the observed *anti* isomer for epoxyketones **3**–**5**. However, the epoxyketones **2** and **6** (five-membered ring compounds) do not follow this trend based on steric considerations. Thus, electronic factors should play an important role in these cases, and the stereochemical result must be the consequence of a delicate balance between both contributions.[19] Second-order perturbation theory reveals the origins of this stereocontrol. In both transition states TS-**2***syn* and TS-**6***syn* (Figure 3), there are two two-electron donations that stabilize both species, and therefore, render the *syn* addition more favorable than the *anti* addition. As readily seen in Figure 3, the electronic donations occur from the $\sigma_{1,2}$ localized orbital to the $\sigma^{*}_{3,5}$ orbital and from the $\sigma_{3,4}$ orbital to $\sigma^{*}_{2,6}$ orbital. We found the highest values of the stabilizing perturbation energy [$\Delta E(2)$] in the TS-**2***syn* and TS-**6***syn* transition states (7.1 kcal/mol and 3.7 kcal/mol, respectively, for TS-**6***syn* and 6.9 kcal/mol and 3.4 kcal/mol, respectively, for TS-**2***syn*). These large stabilizing energies override the steric interactions associated with these transition states. On the other hand, in the transition states de-

Table 3. Calculated $\Delta\Delta G^{\ddagger}_{298}$ (*syn–anti*) vaules for cyanide addition to epoxyketones **2**–**6**.

Entry	Epoxyketone	$\Delta\Delta G^{\ddagger}_{298}$(*syn–anti*)[a]	Exp. ratio *syn*/*anti*[b]
1	 **2**	–3.55	4:1
2	 **3**	+0.14	1:3
3	 **4**	+3.46	1:8
4	 **5**	+5.40	1:19
5	 **6**	–5.31	3:1

[a] Relative free activation energy difference [$\Delta\Delta G^{\ddagger}_{298}$ (*syn–anti*)] values in kcal/mol computed as $\Delta\Delta G^{\ddagger}_{298} = \Delta G^{\ddagger}_{298}(syn) - \Delta G^{\ddagger}_{298}(anti)$. All values have been calculated at the B3LYP/6-31++G(d,p) level. [b] Experimental diastereomeric ratio determined by integration of the appropriate signals in the ^1H NMR ($CDCl_3$, 250 MHz) spectra of the crude reaction mixtures.

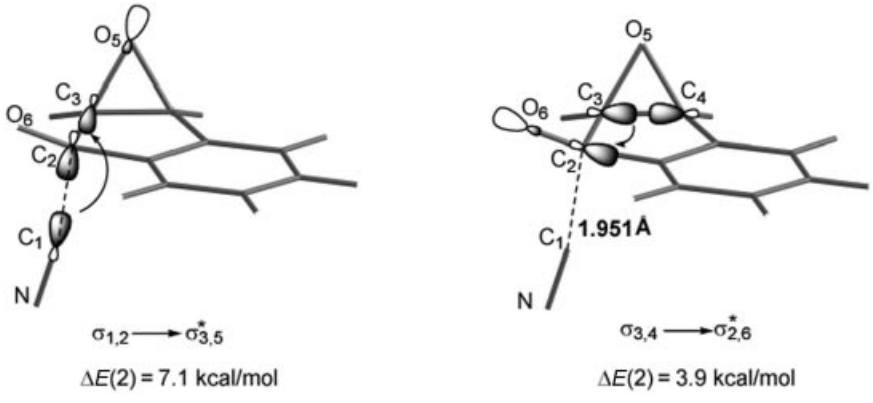


Figure 3. Two-electron interactions and associated second-order perturbation energies, $\Delta E(2)$, in transition state TS-**6***syn*.

rived from epoxyketones **3**–**5**, the stabilization associated with these two-electron donations is much smaller than the corresponding $\Delta E(2)$ values for the TS-**2***syn* and TS-**6***syn* transition states. For instance, the $\Delta E(2)$ values for TS-**5***syn* are 3.9 kcal/mol and 0.7 kcal/mol, respectively. Therefore, compounds **3**–**5** follow the general trend and produce the *anti* isomer.

Conclusions

In conclusion, we have described the chemo- and diastereoselective formation of cyanohydrins derived from cyclic α,β-epoxyketones using TMSCN as the cyanide source and Bu_4NCN as the catalyst. Under these reactions conditions, good diastereoselectivities were obtained. In the case of the cyanohydrins derived from five-membered cyclic epoxyketones, the reaction leads mainly to the *syn* diastereomer arising from the *anti*-epoxide attack of the incoming nucleophile, whereas in the case of cyanohydrins derived from six-, seven-, and eight-membered cyclic ketones, the *anti* diastereoisomer (*syn* nucleophilic attack with respect to the epoxide moiety) was the major one. These results may be explained by considering the stereoelectronic effects associated with both competitive transition states, which can be accurately reproduced by computational experiments.

It should be pointed out that, from the synthetic point of view, the combination of functional groups present in these molecules may promote their use as building blocks for the synthesis of more complicated scaffolds.

Experimental Section

Computational Details: All the calculations reported in this paper were obtained with the GAUSSIAN 03 suite of programs.[20] Electron correlation has been partially taken into account by using the hybrid functional usually denoted as B3LYP,[21] and the standard 6-31++G(d,p) basis set[22] was selected in order to obtain accurate energies. Zero point vibrational energy (ZPVE) corrections have been computed at the B3LYP/6-31++G(d,p) level and have not been corrected. Stationary points were characterized by frequency calculations[23] and have positive defined Hessian matrices. Transition structures (TSs) show only one negative eigenvalue in their diagonalized force constant matrices, and their associated eigenvectors were confirmed to correspond to the motion along the reaction coordinate under consideration by using the Intrinsic Reaction Coordinate (IRC)[24] method. Donor–acceptor interactions have been computed with the Natural Bond Order (NBO)[25] method. The energies associated with these two-electron interactions have been computed according to the following Equation (1):

$$\Delta E^{(2)}_{\phi\phi^*} = -n_\phi \frac{\langle \phi^* | \hat{F} | \phi \rangle^2}{\epsilon_{\phi^*} - \epsilon_\phi} \quad (1)$$

where *Fblabla* is the density functional theory (DFT) equivalent of the Fock operator and φ and $\varphi*$ are two filled and unfilled natural bond orbitals having $\in_\varphi$ and $\in_{\varphi*}$energies, respectively; n_φ stands for the occupation number of the filled orbital.

Cyanosilylation of Epoxyketones

Starting Materials: The experimental procedures for the synthesis of starting epoxyketones **2**–**6** obtained by epoxidation reactions of the related α,β-unsaturated ketones **1a**–**e** are described in the Supporting Information.

General Procedure: To a solution of the epoxyketone (100 mg, 1.02 mmol) in dry CH_2Cl_2 (5 mL) was added, under argon and at room temperature, TMSCN (0.25 mL, 2.04 mmol) followed by a solution of Bu_4NCN (27 mg, 0.10 mmol) in dry CH_2Cl_2 (5 mL). The mixture was stirred at room temperature for 1 h. The solvent was evaporated under vacuum. The crude reaction mixture was diluted with Et_2O (10 mL) and washed with H_2O (2 × 10 mL). Drying of the organic phase with $MgSO_4$ was followed by evaporation of the solvent under vacuum. The product was purified by chromatography on silica gel (ethyl acetate/hexane, 1:5).

2-[(Trimethylsilyl)oxy]-6-oxabicyclo[3.1.0]hexane-2-carbonitrile (7): Colorless oil (195 mg, 0.99 mmol). Yield: 98%. Diastereomeric mixture (**7a/7b** = 4:1). **7a:** ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.29 (s, 9 H), 1.75 (dd, J = 11.7, 8.5 Hz, 1 H), 1.83 (dd, J = 11.7, 9.0 Hz, 1 H), 2.12 (dd, J = 13.3, 9.0 Hz, 1 H), 2.21 (dd, J = 13.3, 8.5 Hz, 1 H), 3.56 (d, J = 2.6 Hz, 1 H), 3.66 (d, J = 2.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 24.91, 32.62, 55.17, 59.64, 74.91, 119.61 ppm. MS (70 eV): *m/z* (%) = 182 (49) $[M - CH_3]^+$, 155 (34) $[M - CH_3 - HCN]^+$, 127 (81), 84 (28), 81 (33), 75 (55) $[(CH_3)_2SiOH]^+$, 73 (100) $[(CH_3)_3Si]^+$, 45 (44), 43 (22), 41 (75). **7b:** ^{1}H NMR ([D$_6$]DMSO, 500 MHz): δ = 0.22 (s, 9 H), 1.50–2.10 (m, 4 H), 3.73 (d, J = 2.5 Hz, 1 H), 3.82 (d, J = 2.5 Hz, 1 H). MS (70 eV): *m/z* (%) = 182 (21) $[M - CH_3]^+$, 155 (69) $[M - CH_3 - HCN]^+$, 126 (12), 113 (14), 101 (13), 84 (16), 81 (35), 75 (28) $[(CH_3)_2SiOH]^+$, 73 (100) $[(CH_3)_3Si]^+$, 47 (13), 45 (35), 43 (16). $C_9H_{15}NO_2Si$ (197.31): calcd. C 54.79, H 7.66, N 7.10; found C 54.95, H 7.80, N 7.00.

2-[(Trimethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptane-2-carbonitrile (8): Orange oil (255 mg, 1.21 mmol). Yield: 90%. Diastereomeric mixture (**8a/8b** = 1:3). **8a:** ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.32 (s, 9 H), 1.40–2.10 (m, 6 H), 3.20 (d, J = 3.5 Hz, 1 H), 3.34 (t, J = 3.5 Hz, 1 H) ppm. **8b:** ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.30 (s, 9 H), 1.40–2.10 (m, 6 H), 3.38 (t, J = 4.0 Hz, 1 H), 3.40 (d, J = 4.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 18.82, 21.16, 32.03, 55.09, 56.71, 70.65, 119.72 ppm. $C_{10}H_{17}NO_2Si$ (211.33): calcd. C 56.83, H 8.11, N 6.63; found C 56.60, H 8.20, N 6.41.

2-[(Trimethylsilyl)oxy]-8-oxabicyclo[5.1.0]octane-2-carbonitrile (9): Colorless oil (40 mg, 0.20 mmol). Yield: 85%. Diastereomeric mixture (**9a/9b** = 1:8). **9a:** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.28 (s, 9 H), 1.30–2.20 (m, 8 H), 3.14–3.24 (m, 1 H), 3.35 (d, J = 4.4 Hz, 1 H) ppm. MS (70 eV): *m/z* (%) = 210 (27) $[M - CH_3]^+$, 183 (66) $[M - CH_3 - HCN]^+$, 180 (42), 181 (6), 168 (31), 155 (29), 154(24), 129 (23), 92 (27), 84 (23), 81 (46), 75 (100) $[(CH_3)_2SiOH]^+$, 73 (76) $[(CH_3)_3Si]^+$, 67 (22), 55 (21). **9b:** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.30 (s, 9 H), 1.30–1.70 (m, 4 H), 1.80–2.00 (m, 2 H, CH_2), 2.02–2.20(m, 2 H), 3.18 (m, 1 H), 3.27 (d, J = 4.4 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 23.20, 23.53, 28.11, 38.94, 56.90, 61.16, 73.69, 121.26 ppm. MS (70 eV): *m/z* (%) = 210 (6) $[M - CH_3]^+$, 184 (7), 183 (53) $[M - CH_3 - HCN]^+$, 182 (8), 181 (6), 174 (9), 173 (18), 172 (100), 168 (6), 155 (9), 129 (9), 109 (6), 81 (20), 75 (5) $[(CH_3)_2SiOH]^+$, 73 (8) $[(CH_3)_3Si]^+$, 67 (6). $C_{11}H_{19}NO_2Si$ (225.36): calcd. C 58.63, H 8.50, N 6.22; found C 58.47, H 8.29, N 6.31.

2-[(Trimethylsilyl)oxy]-9-oxabicyclo[6.1.0]nonane-2-carbonitrile (10): Yellow oil (40 mg, 0.29 mmol). Yield: 98%. Diastereomeric

mixture (**10a/10b** = 1:19). **10b:** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.29 (s, 9 H), 1.20–1.76 (m, 6 H), 1.80–2.15 (m, 5 H), 2.27(ddd, J = 14.6, 6.8, 2.2 Hz, 1 H), 2.87 (dt, J = 10.7, 4.2 Hz, 1 H), 3.27 (d, J = 4.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.79, 23.36, 24.59, 26.08, 41.61, 56.77, 58.65, 70.10, 122.06 ppm. MS (70 eV): *m/z* (%) = 224 (18) $[M - CH_3]^+$, 206 (22), 197 (52) $[M - CH_3 - HCN]^+$, 172 (41), 129 (26), 105 (27), 95 (100), 75 (32) $[(CH_3)_2SiOH]^+$, 73 (38) $[(CH_3)_3Si]^+$, 55 (17). **10a:** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.30 (s, 9 H), 1.20–2.35 (m, 10 H), 2.92–2.97 (m, 2 H) ppm. MS (70 eV): *m/z* (%) = 224 (43) $[M - CH_3]^+$, 197 (96) $[M - CH_3 - HCN]^+$, 169 (29), 155 (30), 154 (36), 129 (48), 95 (74), 84 (29), 75 (85) $[(CH_3)_2SiOH]^+$, 73 (100) $[(CH_3)_3Si]^+$, 55 (31). $C_{12}H_{21}NO_2Si$ (239.39): calcd. C 60.21, H 8.84, N 5.85; found C 60.34, H 9.09, N 5.76.

6-[Trimethylsilyloxy]-6,6a-dihydro-1a*H*-indene[1,2-b]oxirene-6-carbonitrile (11): Colorless oil (21 mg, 0.14 mmol). Yield: 80%. Diastereomeric mixture (**11a/11b** = 3:1). **11a:** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.27 (s, 9 H), 4.23 (d, J = 2,6 Hz, 1 H), 4.32 (d, J = 2.6 Hz, 1 H), 7.32–7.62 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 56.91, 57.65, 74.17, 118.66, 125.58, 126.03, 129.80, 130.27, 138.24, 141.81 ppm. MS (70 eV): *m/z* (%) = 245 (18) $[M^{+\cdot}]$, 230 (100) $[M - CH_3]^+$, 217 (48), 203 (47) $[M - CH_3 - HCN]^+$, 202 (28), 186 (27), 156 (27), 118 (47), 90 (27), 89 (31), 75 (24) $[(CH_3)_2SiOH]^+$, 73 (95) $[(CH_3)_3Si]^+$. **11b:** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.17 (s, 9 H), 4.24 (d, J = 2.4 Hz, 1 H), 4.39 (d, J = 2.4 Hz, 1 H), 7.32–7.62 (m, 4 H) ppm. MS (70 eV): *m/z* (%) = 245 (6) $[M^{+\cdot}]$, 230 (89) $[M - CH_3]^+$, 203 (33) $[M - CH_3 - HCN]^+$, 202 (28), 186 (83), 156 (41), 146 (26), 118 (100), 101 (25), 90 (28), 89 (35), 84 (24), 75 (26) $[(CH_3)_2SiOH]^+$, 73 (26) $[(CH_3)_3Si]^+$. $C_{13}H_{15}NO_2Si$ (245.35): calcd. C 63.64, H 6.16, N 5.71; found C 63.87, H 6.29, N 5.66.

Supporting Information (see footnote on the first page of this article): Experimental procedures for the synthesis of the starting epoxyketones, stereochemical assignments of new compounds, and Cartesian coordinates (in Å) and free energies (in a.u.) of all transition states discussed in the text.

Acknowledgments

Ministerio de Educación, Cultura y Deporte, Project BQU2003-04967 is gratefully thanked for financial support.

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Received: March 17, 2006
Published Online: July 3, 2006

