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Intermolecular Reactions of Foiled Carbenes with N−H Bonds: Evidence for an Ylidic Pathway[†,‡]

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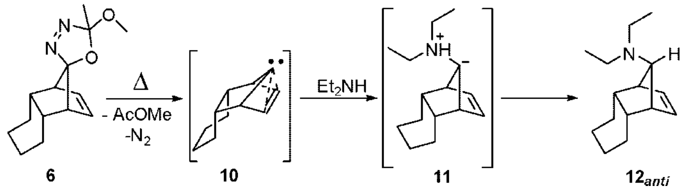

6 **10** **11** $\mathbf{12}_{anti}$

The chemistry of *endo*-tricyclo[6.2.1.0^{2,7}]undec-9-en-11-ylidene (**10**), an archetypal foiled carbene, has been investigated. The intermolecular reactions of **10** are most conveniently performed with oxadiazoline **6** because the corresponding diazirine can be obtained only in very low yield. Furthermore, the aziridinyl imine is difficult to decompose and the tosylhydrazone sodium salt poorly soluble in common organic solvents. Photolysis of **6** in diethylamine leads merely to a reduction of the diazo group and regeneration of acetyl hydrazone **5**, whereas thermolysis cleanly affords tertiary amine $\mathbf{12}_{anti}$ in 77% yield. Calculations show that even stabilized-nucleophilic carbenes react with amines through an ylidic pathway and not by a concerted insertion into the N−H bond. Nevertheless, in the gas phase, norbornen-7-ylidene (**13**) is predicted to be stabilized by one molecule of NH_3 more efficiently through a hydrogen bond than by ylide formation.

Introduction

In the last 10 years, the knowledge about the chemistry of foiled carbenes[1] has undergone a major revival.[2] This is due to the ready availability of computational methods which allow a better understanding of the reactive behavior of these intermediates. In a foiled carbene,[1,2] a functional group like a double bond that usually readily reacts with carbenes is located in close proximity to the divalent carbon atom leading to strong interactions between the two functionalities. Of course, the relative position of the two centers should be well designed in order to prevent the formation of the intramolecular addition product. Norbornen-7-ylidene (**13**), *the* classic example of a foiled carbene, was first generated by Moss some 35 years ago.[3] It has been shown that this type of carbene intramolecularly prefers to react through a vinyl shift.[3,4] However, the observation of this reaction is not a sufficient condition to prove that a carbene is foiled since, at any rate, a vinyl group is a good migrating group.[5,2f]

We expect a better understanding of the properties of foiled carbenes if their intermolecular reactions are studied. Calculations have established that a strong stabilization of the divalent carbon atom induces a substantial distortion in the geometry at

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[†] This paper is dedicated to Prof. Franz L. Dickert on the occasion of his 65th birthday.

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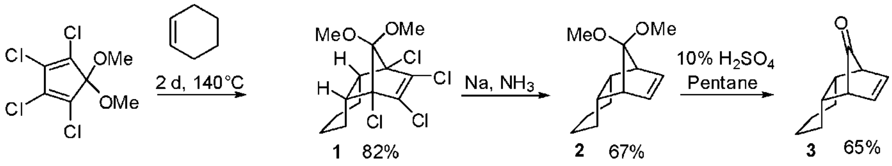
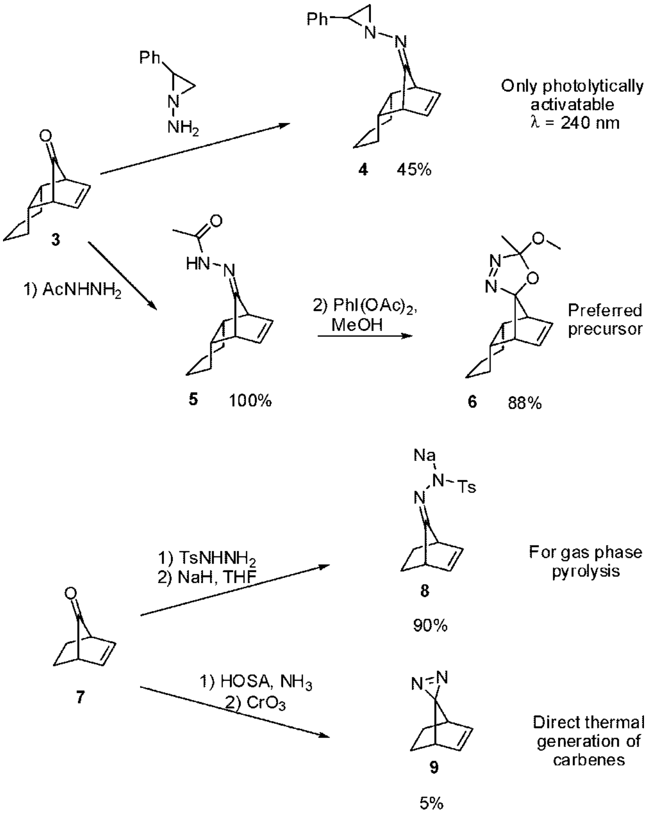
SCHEME 1. Synthesis of Tricyclo[6.2.1.0^{2,7}]undec-9-en-11-one (3)



the carbenic center leading to a bending of the carbene bridge toward the double bond.[1,2f,g] For example, in norbornen-7-ylidene (**13**), this interaction causes the divalent carbon bridge to lean toward the double bond by 37° when compared to norbornene.[2f] Thus, for intermolecular reactions at the side opposite to the double bond, more space is available. Therefore, real foiled carbenes are expected to react stereospecifically in intermolecular reactions. Moreover, the electron donation from the double bond to the carbenic center causes foiled carbenes to possess an increased nucleophilicity which leads to their classification as stabilized-nucleophilic carbenes.[6] Unfortunately, this strong stabilization makes foiled carbenes reluctant toward intermolecular reactions. Therefore, at present only few experimental results are available.[7] Thus, it is only known that norbornen-7-ylidene (**13**) can be trapped efficiently with methanol after protonation[7d] and that it adds in extremely low yield to *cis*-4-methylpent-2-ene (0.067%)[7a] and to *tert*-butylethylene (0.1%).[7c] In this study, we took tricyclo[6.2.1.0^{2,7}]undec-9-en-11-ylidene (**10**) as a model species and investigated its chemistry experimentally and theoretically (see Scheme 3). As a result, we demonstrate that the stabilized-nucleophilic carbene **10** reacts cleanly and stereoselectively with diethylamine. Moreover, this reaction provides evidence that even for a nucleophilic carbene, the ylidic pathway is preferred over a concerted insertion into the N−H bond. These results confirm the ambivalent behavior of carbenes which are still able to react as electrophiles with efficient electron donors even when their chemistry usually is dominated by their nucleophilic reactivity.

SCHEME 2. Preparation of Carbene Precursors



Results and Discussion

Synthesis of Precursors. Carbene **10** (Scheme 3) was generated from two different precursors that were prepared from *endo*-tricyclo[6.2.1.0^{2,7}]undec-9-en-11-one (**3**); see Scheme 1. Ketone **3** was synthesized in three steps starting from a [4 + 2]-cycloaddition between 6,6-dimethoxy-2,3,4,5-tetrachlorocyclopentadiene and cyclohexene.[8,9] In contrast to the methodology described in the literature,[8] a 3−4-fold excess of cyclohexene was applied. Therefore, an autoclave was used in order to reach the reaction temperature of 140 °C. These conditions gave better yields because less dimer of 6,6-dimethoxy-2,3,4,5-tetrachlorocyclopentadiene was formed. In addition, the subsequent dechlorination was carried out in liquid ammonia[10] instead of refluxing THF/*t*-BuOH[9] to get a cleaner crude product. Dechlorination in presence of an alcohol to some extent leads to hydrogenation of the double bond. Most of the experimental work has been performed with oxadiazoline **6** which is readily available from the condensation of ketone **3** with acetyl hydrazide followed by oxidation in methanol.[11] A mixture of two diastereomers (ratio 1:1)[12] was obtained that can be activated thermally as well as photochemically under mild conditions (λ_{max} = ca. 330 nm).[13] 2-Methoxy-2-methyl-Δ^3-1,3,4-oxadiazolines are versatile precursors that are known to decompose through a variety of pathways and finally generate the carbenes, especially under photochemical conditions.[13]

Alternatively, some attempts have been made with phenylaziridinyl imine **4**,[14] which proved to be not as convenient as **6** (Scheme 2). In particular, the thermal decomposition did not lead to carbene formation and the photolysis had to be carried out at λ = 240 nm. Since many compounds absorb light of this wavelength and, therefore, may also be activated, this fact significantly reduces the scope of the reaction. Here, a diazo species is formed prior to carbene generation. Our first experiments have been performed starting from norbornen-7-one (**7**) with which two further precursors were tested. Sodium salts of

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[11] Yang, R.-Y.; Dai, L.-X. *J. Org. Chem.* **1993**, *58*, 3381.

[12] The oxygen atom but also the azo function of the oxadiazoline ring can be positioned above the double bond of **6**.

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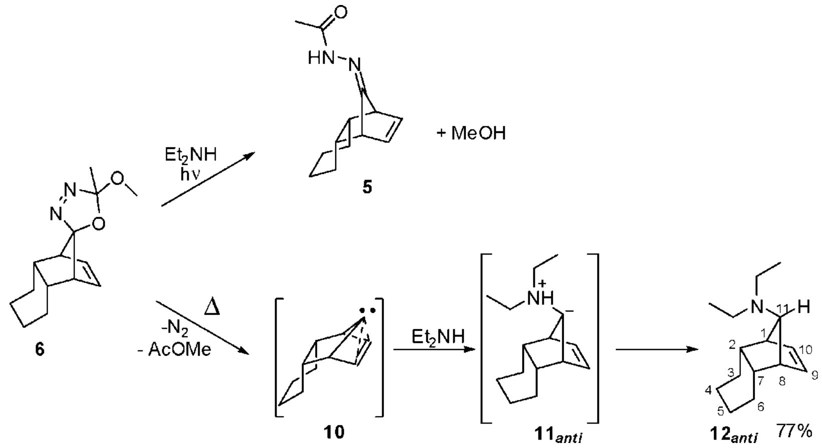
[14] (a) Kirmse, W. *Eur. J. Org. Chem.* **1998**, 201. (b) Hashmi, A. S. K. *J. Prakt. Chem.* **1999**, *341*, 600. (c) May, J. A.; Stoltz, B. M. *J. Am. Chem. Soc.* **2002**, *124*, 12426.

SCHEME 3. Reaction of Oxadiazoline 6 with Diethylamine



tosylhydrazones traditionally were one of the most popular sources of carbenes. However, it was not really convenient to work with **8**[7d] neither by photolysis nor by thermolysis, since under apolar conditions low yields of products were obtained because of the poor solubility of the carbene precursor. But the sodium salts of tosylhydrazones are still our preferred source of carbenes for gas phase pyrolyses. From a mechanistic point of view, diazirine **9** represents the best carbene precursor, since it is recognized that under photolytic conditions **9** directly generates the carbene and only small amounts of the corresponding diazo species. The product distributions obtained from the irradiation of spiro[bicyclo[2.2.1]heptene-7,3′diazirine] (**9**) in methanol suggest the intervention of only 4−6% of the diazo compound.[7d] However, the synthesis of **9** with a satisfactory yield remains a challenging task.[7d]

Chemistry of *endo*-Tricyclo[6.2.1.0^{2,7}]undec-9-en-11-ylidene (10). It has been shown previously that foiled carbenes react efficiently with methanol[7d] and that they possess a predominantly nucleophilic behavior[6] combined with a high proton affinity.[2f] These results motivated us to try to intercept **10** with slightly acidic compounds and with polar substances. Moreover, it has been shown that a secondary amine like piperidine can capture alkyl carbenes,[15] and many other examples are known for the insertion of carbenes into N−H bonds.[16] In fact, despite the relatively low acidity of amines (pK_a of pyrrolidine in DMSO = 44),[17] during this work diethylamine has been revealed to be one of the most efficient traps for **10**. Thus, thermolysis of oxadiazoline **6** in Et$_2$NH afforded tertiary amine **12**$_{anti}$[18] in an isolated yield of 77% (Scheme 2).[19] The configuration of the product was established by NMR spectroscopy, the most characteristic signal being the cross peak between H(2), H(7), and the CH$_2$ of the ethyl group in the NOESY spectrum. However, the stereoselectivity observed is in contradiction with the prediction obtained from calculations with norbornen-7-ylidene (**13**) and NH$_3$ (Figure 1).

Computational Results. If a concerted insertion into the N−H bond is assumed, the *syn* product **14**$_{syn}$ (TS(**13**/**14**$_{syn}$): 11.2 kcal/mol) is expected to be formed in a substantial excess over **14**$_{anti}$ (TS(**13**/**14**$_{anti}$): 11.8 kcal/mol). The stereochemical preference is related to the high activation energy needed for this conversion: at the respective transition structures, the carbenic centers do not interact anymore with the double bond, a fact which is reflected in the large C(2)−C(7) distance of 2.271 and 2.401 Å, respectively. Thereafter, the outcome of the reaction is dominated by steric considerations which lead to a favored approach above the double bond and a preferred formation of the *syn* product. The same *syn* selectivity is observed for example by the reduction of norbornen-7-one (**7**) with NaBH$_4$.[21] Since *syn* amine **12**$_{syn}$ is not found experimentally in the reaction of **6** and diethylamine and because the calculated barriers (more than 15 kcal/mol from complex **13a** for both TS(**13**/**14**), see Figure 2) are prohibitively high for an alkyl carbene, the product formation should occur through another pathway. It is well-known that electrophilic and reactive carbenes form readily ylides in the presence of efficient electron donors like nitrogen- and sulfur-containing compounds. And indeed, even for the nucleophilic **13**, ylide formation is predicted to be strongly preferred over the concerted insertion into the N−H bond (Figure 2A).

With ammonia, carbene **13** specifically forms the *anti* ylide **15**$_{anti}$ and the conversion occurs by overcoming a low barrier (TS(**13**/**15**$_{anti}$)) which is only 1.3 kcal/mol higher in energy than the reactants (6.5 kcal/mol if complex **13a** is taken as reference). In the gas phase, as a polar species, ylide **15**$_{anti}$ is predicted to be higher in energy than the complex in which the carbene and the ammonia molecule are held together by a hydrogen bridge. Still, in the gas phase, product formation by rearrangement of

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[15] Fernamberg, K.; Snoonian, J. R.; Platz, M. S. *Tetrahedron Lett.* **2001**, *42*, 8761.

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[18] In this study, the description *anti* is given if the substituent is oriented away from the alkenic bridge in order to facilitate the comparison between the bicyclo[2.2.1]hept-2-ene and the tricyclo[6.2.1.02,7]undec-9-ene systems. According to the IUPAC Gold Book, the description *anti* should be used when the group is oriented away from the lowest numbered bridge.

[19] It is worth noticing that this reaction does not give satisfactory results under photochemical conditions. First of all, the photolysis of oxadiazoline **6** in diethylamine is significantly slower than in other solvents. Moreover, only 12% of **12**$_{anti}$ are formed. Instead, acetylhydrazone **5** is isolated, a compound resulting from reduction of the azo group followed by tautomerization and ring opening. It has already been observed that amines are able to photoreduce azoalkanes; see, for example: Adam, W.; Moorthy, J. N.; Nau, W. M.; Scaiano, J. C. *J. Am. Chem. Soc.* **1997**, *119*, 6749.

[20] Calculations at this level of theory could only be performed for the structures having C_s symmetry.

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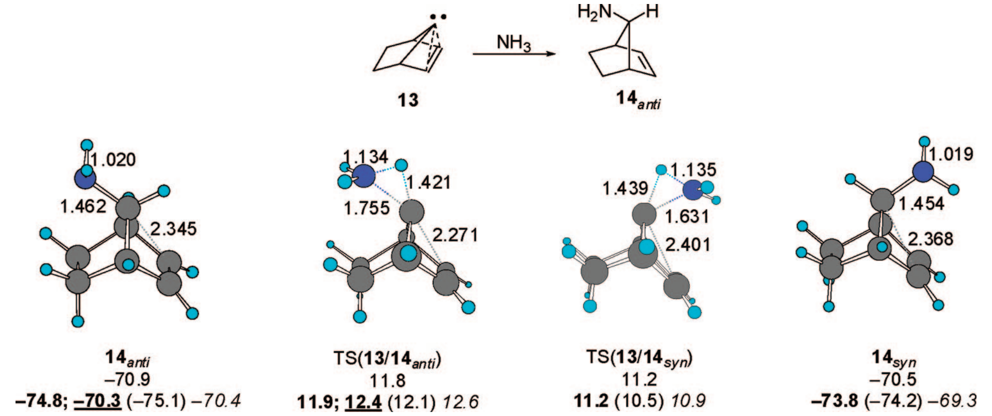

FIGURE 1. Geometries and relative energies of the transition structures for the concerted insertion of carbene **13** into ammonia and for the most stable conformer of bicyclo[2.2.1]hept-2-en-7-amines **14**$_{anti}$ and **14**$_{syn}$ according to B3LYP/6-31G(d) calculations. Values in bold: CCSD(T)/6-31G(d)//B3LYP/6-31G(d), underlined and bold: CCSD(T)/6-31+G(d,p)//B3LYP/6-31G(d), in parentheses: MP2(FC)/6-31G(d), in italics: MP2(FC)/6-31+G(d,p). Distances in Å and energies in kcal/mol.

TABLE 1. Comparison of the Reactivity of Ammonia and Diethylamine (16) with Norbornen-7-ylidene (13)[a]

entry	reaction with NH_3[b]		reaction with **16**[c]	
a	**13a**	−5.2	**19**	−5.3
b	TS(**13/14**$_{anti}$)	11.8	TS(**13/18**$_{anti}$)	13.0
			TS(**13/18**$_{anti}$)*	12.9
c	TS(**13/14**$_{syn}$)	11.2	TS(**13/18**$_{syn}$)	13.7
			TS(**13/18**$_{dyn}$)*	12.5
d	TS(**13/15**$_{anti}$)	1.3	TS(**13/17**$_{anti}$)	3.4
			TS(**13/17**$_{anti}$)*	3.2
e	TS(**13/15**$_{syn}$)	10.4	TS(**13/17**$_{syn}$)	10.8
f	**14**$_{anti}$	−70.9	**18**$_{anti}$*	−68.7
g	**14**$_{syn}$	−70.5	**18**$_{syn}$*	−66.1
h	**15**$_{anti}$	−1.0	**17**$_{anti}$*	−2.9
			17$_{anti}$#	4.1
i	**15**$_{syn}$	−5.8	**17**$_{syn}$*	−7.7
			17$_{syn}$#	−1.7
j	**13′**$_{anti}$	−7.3	**19′**$_{anti}$	−4.2
k	**13′**$_{syn}$	−10.5	**10′**	−6.1
l	**15′**$_{anti}$	−11.9	**17′**$_{anti}$*:**Cx1**	−6.7
			17′$_{anti}$*:**Cx2**	−2.4
m	**15′**$_{syn}$	−15.9	**17′**$_{syn}$*:**Cx1**	−10.8
			17′$_{syn}$*:**Cx2**	−7.5
n	TS(**15′**$_{anti}$/**14′**$_{anti}$)	−9.3	TS(**17′**$_{anti}$/**18′**$_{anti}$)*	5.1
			TS1$_{anti}$	5.2
o	TS(**15′**$_{syn}$/**14′**$_{syn}$)	−11.4	TS(**17′**$_{syn}$/**18′**$_{syn}$)*	−0.3
			TS1$_{syn}$	0.5

[a] The computations were performed at the B3LYP/6-31G(d) level of theory. [b] Norbornenylidene and ammonia were taken as reference for entries a−i. Norbornenylidene and the ammonia dimer were taken as reference for entries j−o (0 kcal/mol). [c] Norbornenylidene and diethylamine were taken as reference for entries a−i. Norbornenylidene and the diethylamine dimer were taken as reference for entries j−o (0 kcal/mol).

the ylide remains difficult to model, probably because a concerted process requires an antarafacial reaction mode.[22] However, the decomposition of an ylide displays retention of configuration in the majority of cases and is usually described by occurring through a radical pair confined in a solvent cage.[22] In our case, because the ylidic bond is very weak and only 2.3 kcal/mol are needed to cleave it, the most probable pathway for this rearrangement would correspond to the same transition structure described before for the concerted insertion of carbene **13** into a N−H bond (See Figure 1, TS(**13/14**$_{anti}$)). Indeed, only small changes in the geometry are required, i.e., elongation of the C−N bond from 1.586 to 1.755 Å and rotation of the NH_3 group by 60°. However, since the requirements in the electron distribution are different, with 12.8 kcal/mol, the energy difference is relatively high and this process is not very likely to take place.

In fact, the reaction of **13** in ammonia is not well modeled until two nitrogen-containing molecules are explicitly taken into consideration (Figure 2B). Thereby, a pathway is found in which no barrier is higher than 3 kcal/mol. Low barriers are a precondition for the intermolecular trapping of alkyl carbenes because they can easily rearrange intramolecularly. The second ammonia molecule first helps to stabilize the polar reactive intermediates **13** and **15** and, finally, catalyzes very efficiently the rearrangement of the ylide by accepting a proton from the amino group and concomitantly donating another proton to the former carbenic center (TS(**15′/14′**)). A similar approach has already been described for the insertion of carbenes into an O−H bond.[23]

Is it acceptable to replace in the calculations diethylamine with ammonia? What are the differences between these two reactions? To answer these questions, we repeated the calculations with diethylamine instead of ammonia. Overall, similar results were obtained, and the same preference for formation of the product with an *anti* configuration via the intermediacy of an ylide is predicted. The main divergences arise from steric hindrance between the ethyl groups and the norbornenyl moiety causing higher activation barriers. In fact, the most stable conformation of diethylamine is its linear form **16**. However, because of steric repulsion, this arrangement is impossible in the products, i.e., tertiary amines **18***. Therefore, the terminal methyl groups are pushed away from the bicyclic skeleton. The energetic costs for this partial rotation can be estimated at 2.4 kcal/mol because conformer **16*** is 2.4 kcal/mol higher in energy than **16**. A second value of 2.2 kcal/mol can be obtained from a comparison of the exothermicity of the insertion reaction of norbornenylidene **13** into ammonia and diethylamine, respectively (Table 1, entry f). Formation of **18**$_{syn}$* is even less favorable because of adverse interactions between the lone pair on the nitrogen atom and the double bond (4.4 kcal/mol, entry g).

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(23) Pliego, J. R.; De Almeida, W. B. *J. Phys. Chem. A* **1999**, *103*, 3904.

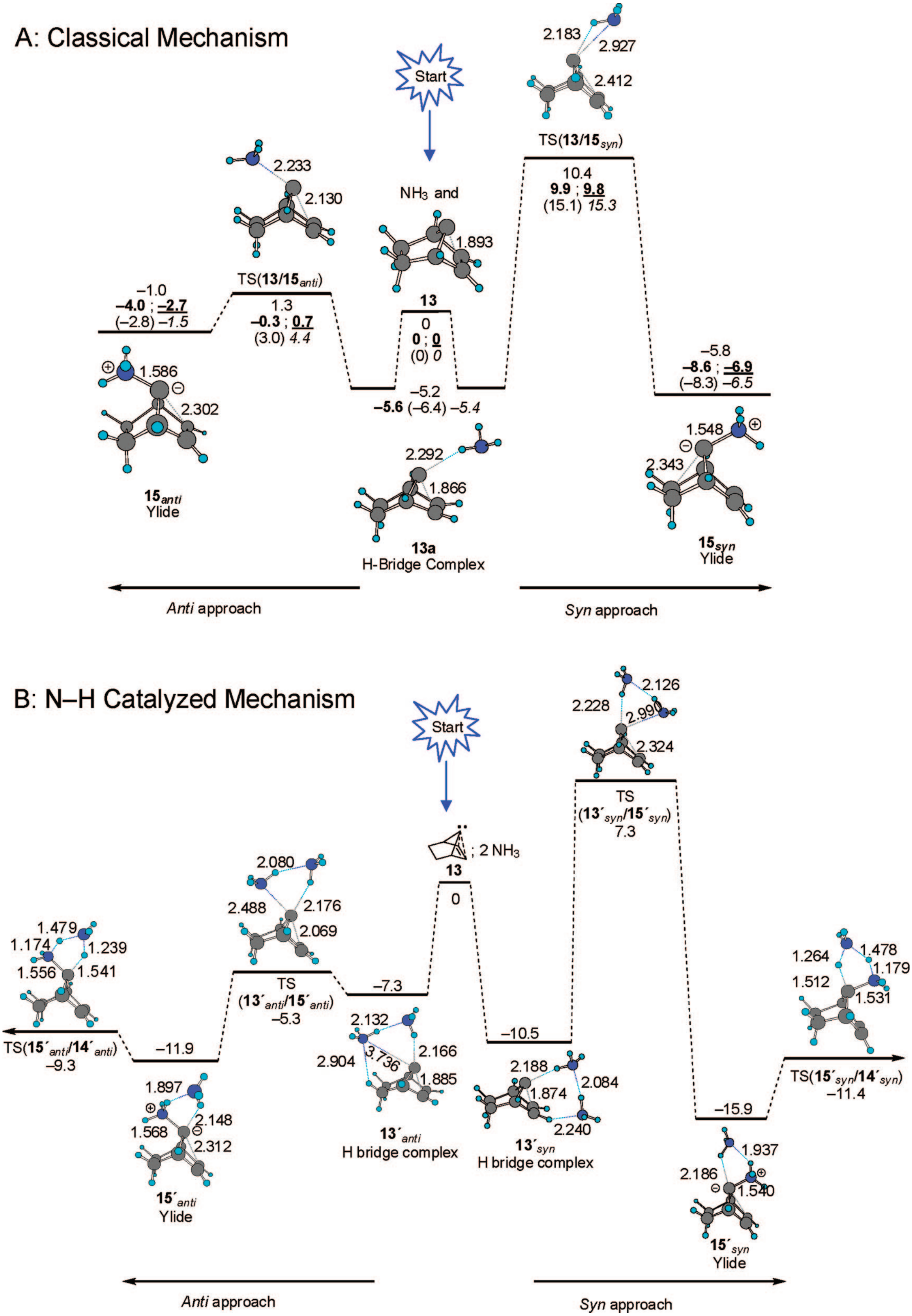

FIGURE 2. Energy diagram, geometries, and relative energies of the most relevant stationery points of the reaction between norbornen-7-ylidene (**13**) and ammonia according to B3LYP/6-31G(d) calculations. Values in bold: CCSD(T)/6-31G(d)//B3LYP/6-31G(d), underlined and bold: CCSD(T)/6-31+G(d,p)//B3LYP/6-31G(d),[1] in parentheses: MP2(FC)/6-31G(d), in italics: MP2(FC)/6-31+G(d,p). Distances in Å and energies in kcal/mol.

This discrepancy is found again in the transition structures modeling the concerted insertion into the N−H bond which are 1.2 kcal/mol (entry b) and 1.3 kcal/mol (entry c) higher in energy when diethylamine is attacked instead of ammonia. Moreover, the corresponding geometries of these transition structures have changed. For example, by insertion into diethylamine the N−H

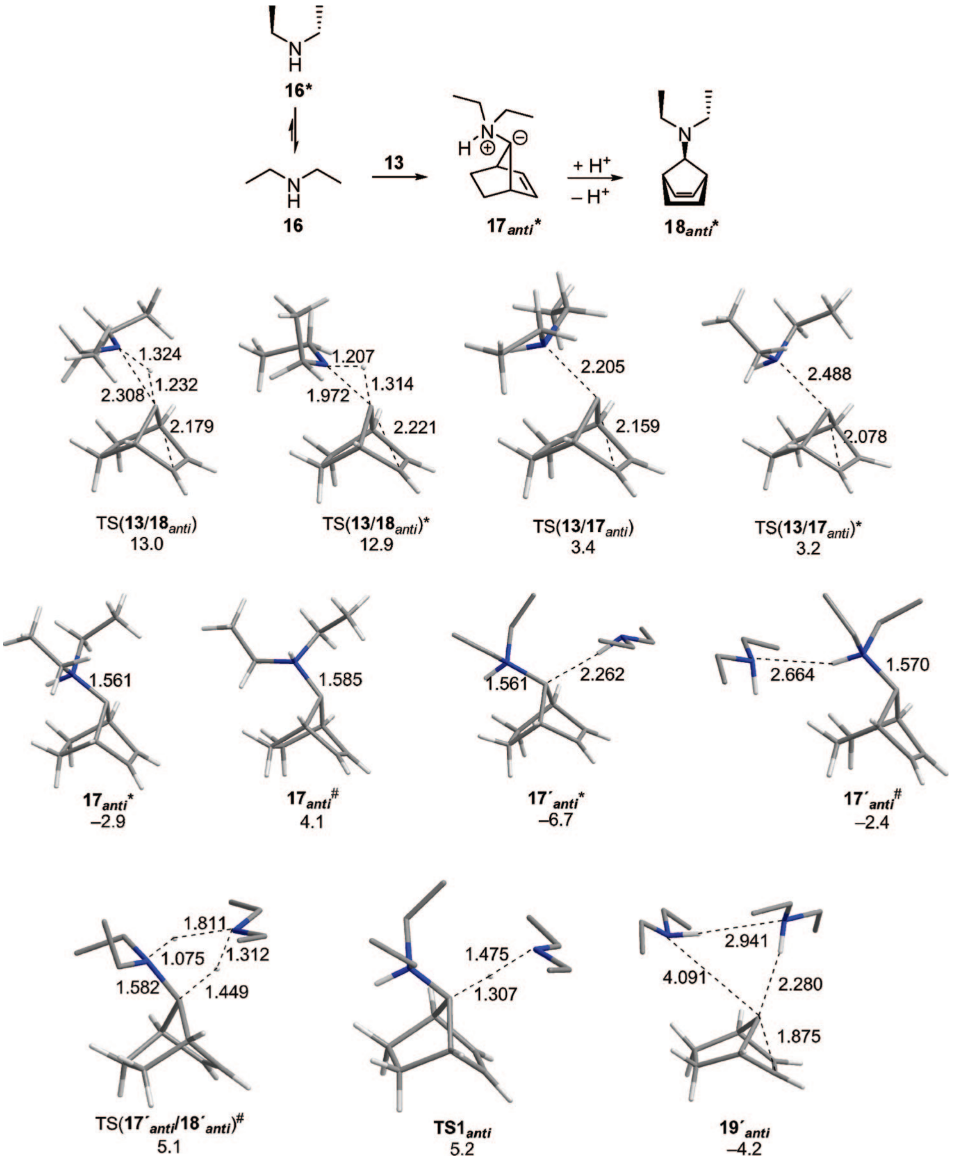

FIGURE 3. Geometries and relative energies of the most relevant stationery points of the reaction between norbornen-7-ylidene (**13**) and diethylamine (**16**) according to B3LYP/6-31G(d) calculations. For clarity, the hydrogen atoms of the ethyl groups are not shown in structures **17′**$_{anti}$*, **17′**$_{anti}$#, TS(**17′**$_{anti}$/**18′**$_{anti}$)*, **TS1**$_{anti}$, and **19′**$_{anti}$.

bond is more broken (1.207 Å for TS(**13/18**$_{anti}$)*, Figure 3 instead of 1.134 Å in TS(**13/14**$_{anti}$), Figure 1) whereas the distance between the carbon and the nitrogen atom of the incipient C−N bond is getting larger (1.972 Å in TS(**13/18**$_{anti}$)* vs 1.755 Å in TS(**13/14**$_{anti}$)).

Accordingly, ylide formation requires 1.9 and 0.4 kcal/mol more energy with diethylamine than with ammonia (entries d and e). However, these transition structures lead to the slightly more stabilized ylides **17**$_{anti}$***** and **17**$_{syn}$***** (gain of 1.9 kcal/mol, respectively, entries h and i). This increase in stability is probably due to a better spreading of the positive charge through the ethyl groups. Again, due to the steric requirements of the alkyl chains, the N−H bond is virtually blocked above the C_2H_4 bridge: the alternative conformation **17**$_{anti}$**#** is 7.0 kcal/mol higher in energy than **17**$_{anti}$*****. This explains that a single diethylamine molecule cannot efficiently catalyze the rearrangement of **17**$_{anti}$***** to **18**$_{anti}$***** (11.8 kcal/mol are required, compare TS(**17′**$_{anti}$/**18′**$_{anti}$)* (entry n) with **17′**$_{anti}$*****:**Cx1** (entry l)). The transformation of **17** to **18** most probably occurs through protonation of the ylide; for this reaction a transition structure could be located with a similar energy barrier (**TS1**$_{anti}$: 5.2 kcal/mol, 11.9 kcal/mol from the reactant, entry n) although solvation effects have not been taken into account. On the whole, ylides **17** generated from diethylamine are predicted to have a better kinetic stability than ylides **15** generated from ammonia.

Generally, steric hindrance is the reason why the N−H bond catalyzed mechanism is not effective in the case of diethylamine. Indeed, norbornenylidene **13** can interact efficiently only with one diethylamine molecule as can be seen for example in structure **19′**$_{anti}$, the second diethylamine molecule remaining far away from the carbenic center (4.091 Å) and the other nitrogen atom (2.941 Å, see Figure 3).

Conclusion

This study provides further arguments in favor of the validity of the B3LYP/6-31G(d) methodology for the modeling of carbene reactions. Indeed, the results obtained are in good agreement with the experimental results and with calculations made with methods requiring more computational efforts like

MP2 and CCSD(T). It has been revealed that even stabilized-nucleophilic carbenes react with amines through an ylidic pathway and not by a concerted insertion into the N−H bonds. Nevertheless, in the gas phase, norbornen-7-ylidene (**13**) is predicted to be stabilized by one molecule of NH_3 or amine more efficiently through a hydrogen bond than by ylide formation. This study also shows that a carbene reaction which proceeds through highly polar intermediates and transition structures can be satisfactorily modeled by an explicit consideration of two molecules of the substrate. In this case, ammonia, especially if this substrate is small. Finally, foiled carbene **10** has been shown to react stereospecifically to form exclusively amine $\mathbf{12}_{anti}$.

Computational Methods. The Gaussian 03 program[24] was used for density functional theory calculations, employing Becke's[25] three-parameter hybrid method, and the exchange functional of Lee, Yang, and Parr (B3LYP)[26] and also for MP2 and CCSD(T) computations. Geometries were optimized at the B3LYP/6-31G(d) and, for the smaller structures, at the MP2(FC)/6-31G(d) and at MP2(FC)/6-31+G(d,p) levels of theory. These results were confirmed using single-point calculations at the CCSD(T)/6-31G(d) and at the CCSD(T)/6-31+G(d,p) level of theory. This method represents a coupled cluster calculation using single and double substitutions augmented by a noniterative treatment of triple excitations.[27] The stationary points were characterized by vibrational analysis. All reported energies include zero-point corrections. For the CCSD(T) calculations, the zero-point vibrational energies were taken from the B3LYP calculations. Unless otherwise stated, all values in the text refer to B3LYP/6-31G(d) calculations. A good agreement was obtained with the other computational methods, especially with CCSD(T)/6-31+G(d,p)//B3LYP/6-31G(d). Norbornen-7-ylidene (**13**) and ammonia were taken as model compounds for carbene **10** and diethylamine in order to minimize the number of conformations to be analyzed and to reduce calculation time (see Figures 1 and 2). The B3LYP method is known to slightly underestimate the strength of dative bonds whereas the MP2 methodology tends to overestimate this interaction.[28] Moreover, for normal reactions, predicted activation barriers are usually slightly too high at the B3LYP/6-31G(d) level of theory and too low with MP2/6-31G(d);[29] for carbene rearrangements, the opposite is true.[30]

Experimental Section

General Experimental Methods. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer. The chemical shifts at $\delta = 7.26$ ppm and 77.0 ppm of $CHCl_3$ were used as internal standards for ^{1}H and ^{13}C spectra. Conventional 2D COSY, NOESY, HMBC, and HMQC spectra were used to derive proton and carbon assignments.

***endo*-11,11-Dimethoxytricyclo[6.2.1.0^{2,7}]undec-9-ene (2).**[9] In a 1 L three-necked flask fitted with a 250 mL dropping funnel and a cooling finger filled with dry ice/acetone, dry ammonia (500 mL) was liquefied at −78 °C. Afterward, sodium (35.51 g, 1.544 mol) was added, accompanied by a blue coloring of the mixture. Then a solution of 48.46 g (140 mmol) of *endo*-11,11-dimethoxy-1,8,9,10-tetrachlorotricyclo[6.2.1.0^{2,7}]undec-9-ene (**1**) in 200 mL of THF was added dropwise at −78 °C under stirring and argon over 1.5 h. Afterward, the mixture was kept stirring for an additional 30 min at the same temperature. The solution was then treated with ammonium chloride until the blue color disappeared and the ammonia was allowed to evaporate overnight. The obtained mixture was taken up in water and saturated with sodium chloride and then extracted six times with dichloromethane. The collected organic phases were washed with brine, dried over magnesium sulfate, and filtered through Celite, and the solvent was removed in vacuum. Yield: 19.60 g (67%), oil.

***endo*-Tricyclo[6.2.1.0^{2,7}]undec-9-en-11-one (3).**[8,31] Dimethyl ketal **2**(19.55 g, 93.8 mmol) was stirred vigorously overnight with 100 mL of an aqueous 10% sulfuric acid solution. After extraction with hexane, the crude product was washed with $NaHCO_3$ and dried over magnesium sulfate. The product was crystallized as white needles at −78 °C from hexane. Yield: 9.06 g (60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.46 (t, $J = 2.3$ Hz, 2H), 2.80 (p, $J = 2.0$ Hz, 2H), 2.25−2.19 (m, 2H), 1.64−1.58 (m, 2H), 1.41−1.33 (m, 4H), 1.08−0.96 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.5, 131.8, 52.0, 34.6, 21.2, 19.3 ppm. MS (70 eV): m/z 162 (M^+, 0.1), 134 (56), 119 (16), 105 (23), 91 (100), 78 (23).

(*endo*-Tricyclo[6.2.1.0^{2,7}]undec-9-en-11-ylidene)(2-phenylaziridin-1-yl)amine (4). Ketone **3** (540 mg, 3.333 mmol) was dissolved in 10 mL of benzene. To this solution was added 1-amino-2-phenylaziridine[32] (470 mg, 3.51 mmol). After 2 h at room temperature, the solvent was rotary evaporated. The crude product consists of a mixture of two diastereomers in a 56/44 ratio. The major diastereomer was crystallized from methanol. Yield: 420 mg (1.51 mmol, 45%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26−7.14 (m, 5H), 6.27 (dd, $J = 6.3$, 3.2 Hz, 1H), 6.17 (dd, $J = 6.4$, 3.2 Hz, 1H), 3.54−3.52 (m, 1H), 2.88−2.85 (m, 1H), 2.70 (dd, $J = 7.7$, 4.8 Hz, 1H), 2.27 (d, $J = 7.7$ Hz, 1H), 2.15 (d, $J = 4.8$ Hz, 1H), 2.15−2.09 (m, 2H), 1.56−1.52 (m, 2H), 1.39−1.26 (4H), 0.95−0.84 (2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.4, 138.9, 134.4, 132.9, 128.3, 127.0, 126.4, 48.9, 45.2, 43.4, 40.2, 37.3, 36.0, 22.0, 21.7, 19.6 ppm. MS (70 eV): m/z 278 (M^+, 0.3), 250 (1), 193 (1), 174 (5), 168 (8), 146 (17), 131 (39), 117 (70), 104 (56), 92 (100), 78 (40), 64 (27). Mp: 112−114 °C. Anal. Calcd for $C_{19}H_{22}N_2$: C, 81.97; H, 7.97; N, 10.06. Found: C, 81.64; H, 8.11; N, 9.85.

(*endo*-Tricyclo[6.2.1.0^{2,7}]undec-9-en-11-ylidene)acetohydrazide (5). Ketone **3** (3.3 g, 20.3 mmol) and acetyl hydrazine (1.65 g) were dissolved in methanol (150 mL) and refluxed during 4 h. After removal of the solvent, the resulting hydrazone was submitted directly to the following step without further purification Yield: 4.44 g (100%). The NMR spectra reveal two set of peaks with a ratio of 81/19. ^{1}H NMR (400 MHz, $CDCl_3$): major conformer: δ 8.67 (s, 1H), 6.41 (dd, $J = 6.3$; 3.2 Hz, 1H), 6.25 (dd, $J = 6.3$; 3.2 Hz, 1H), 3.51−3.46 (m, 1H), 3.02−2.98 (m, 1H), 2.26−2.04 (m,

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2H), 2.18 (s, 3H), 1.64−1.58 (m, 2H), 1.47−1.31 (m, 4H), 1.03−0.90 (m, 2H) ppm. Minor conformer, characteristic peaks: δ 8.17 (s, 1H), 6.22 (dd, *J* = 6.3; 3.2 Hz, 1H), 3.38−3.35 (m, 1H), 3.16−3.13 (m, 1H), 2.01 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): major conformer: δ 173.2, 166.5, 135.2, 132.3, 48.8, 42.5, 37.3, 36.42, 21.9, 21.7, 20.1, 19.54, 19.48 ppm. Minor conformer, characteristic peaks: δ 135.7, 131.5, 48.9, 42.8, 36.9, 36.35 ppm. MS (70 eV): *m*/*z* 218 (M^+, 69), 194 (34), 179 (10), 161 (15), 136 (29), 116 (26), 105 (23), 94 (64), 91 (71), 74 (100). HRMS (70 eV): calcd for $C_{13}H_{18}ON_2$ 218.1419, found 218.1424. Mp: 172−174 °C.

***rac*-5-Methoxy-5-methylspiro[5*H*-[1,3,4]oxadiazole-2,11′-endotricyclo[6.2.1.0^{2,7}]undec-9-ene] (6).** Hydrazone **5** (4.44 g, 20.3 mmol) was dissolved in 150 mL of methanol and stirred in an ice bath. $PhI(OAc)_2$ (8.52 g, 26.5 mmol) was added within 5 min. After an additional 15 min, the solvent was rotary evaporated. The two diastereoisomers (ratio 1:1) were separated by column chromatography with hexane/dichloromethane (2:3) as eluent. Yield: 5.05 g (88%). Diastereoisomer A: R_f = 0.37. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.30 (s, 2H), 3.03 (s, 3H), 2.73−2.92 (m, 3H), 2.65−2.64 (m, 1H), 1.73−1.62 (m, 2H), 1.57 (s, 3H), 1.51−1.40 (m, 4H), 1.09−0.99 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 133.2, 132.9, 120.0, 54.8, 53.7, 50.0, 36.2, 36.9, 22.9, 21.8, 21.7, 19.7 ppm. MS (70 eV): *m*/*z* 247 (M^+ − 1, 0.5), 188 (3), 163 (9), 147 (29), 138 (56), 131 (44), 117 (76), 104 (41), 91 (100), 81 (42), 78 (54), 67 (28), 51 (27). HRMS (70 eV): calcd for $C_{14}H_{19}O_2N_2$ (M^+ − 1) 247.1447, found 247.1443. Mp: 77−78 °C. Anal. Calcd for $C_{14}H_{20}O_2N_2$: C, 67.71; H, 8.12; N, 11.28. Found: C, 68.11; H, 8.04; N, 11.22. Diastereoisomer B, R_f = 0.18. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.36 (ddd, *J* = 6.4, 3.2, 0.6 Hz, 1H), 6.32 (ddd, *J* = 6.4, 3.2, 0.6 Hz, 1H), 3.03 (s, 3H), 2.72−2.70 (m, 1H), 2.50−2.48 (m, 1H), 2.38−2.27 (m, 2H), 1.68−1.63 (m, 2H), 1.59 (s, 3H), 1.48−1.37 (m, 4H), 1.09−1.04 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.6, 133.0, 132.7, 132.2, 53.6, 52.7, 50.0, 37.8, 37.5, 23.4, 21.8, 21.6, 19.9 ppm. MS (70 eV): *m*/*z* 247 (M^+ − 1, 1.5), 220 (3), 188 (5), 163 (15), 147 (35), 138 (81), 131 (64), 117 (93), 104 (61), 91 (100), 81 (62), 78 (58), 67 (31), 51 (29). HRMS (70 eV): calcd for $C_{14}H_{19}O_2N_2$ (M^+ − 1) 247.1447, found 247.1443. Mp: 99−100 °C. See also the crystallographic data in the Supporting Information.

***N*,*N*-Diethyl-11-*anti*,*endo*-tricyclo[6.2.1.0^{2,7}]undec-9-en-11-amine (12).** Oxadiazoline **6** (250 mg, 1.008 mmol) was dissolved in 13 mL of diethylamine and stirred for 4 h at 160 °C in a pressure tube. After removal of the solvent, the crude product was submitted to column chromatography with ethyl acetate as eluent. Yield: 168 mg (77%) oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.04 (t, *J* = 2.2 Hz, 2H), 2.64−2.61 (m, 2H), 2.53 (q, *J* = 7.1 Hz, 4H), 2.36−2.34 (m, 1H), 2.17−2.11 (m, 2H), 1.61−1.53 (m, 2H), 1.40−1.33 (m, 4H), 0.96−0.82 (m, 2H), 0.93 (t, *J* = 7.1 Hz, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.2, 77.5, 48.7, 42.5, 36.1, 23.1, 20.4, 10.4 ppm. MS (70 eV): *m*/*z* 219 (M^+, 94), 204 (55), 190 (35), 176 (30), 162 (44), 147 (30), 122 (34), 110 (39), 99 (76), 91 (100), 86 (80), 79 (62), 67 (59). HRMS (70 eV): calcd for $C_{15}H_{25}N$ 219.1987, found 219.1983.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for all new compounds. Cartesian coordinates and energies for all relevant stationary points, CIF (Crystallographic Information File) for crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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