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Probing the Nature and Extent of Stabilization within Foiled Carbenes: Homoallylic Participation by a Neighboring Cyclopropane Ring

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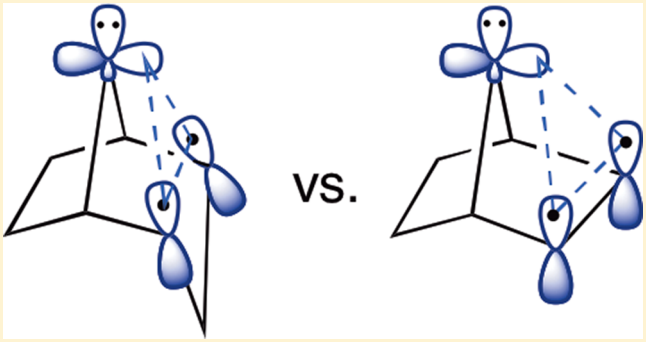
Supporting Information

ABSTRACT: Oxadiazoline **6** was synthesized to generate *endo*-tricyclo[3.2.1.0^{2,4}]octan-8-ylidene (**3**) by either photolysis or thermolysis. Diastereomer **6a** thermally decomposed twice as fast as **6b**. Carbene **3** was trapped stereoselectively by acrylonitrile and diethylamine in high yields. It behaved as a nucleophilic carbene with electron-poor alkenes, like acrylonitrile, but as an electrophile with very electron-rich species, such as diethylamine. However, when the reactions were performed in cyclohexane and cyclohexene, isomerization of **3** was favored. Replacement of the double bond in 7-norbornenylidene (**1**) by the single bond in the *endo*-fused cyclopropane unit of carbene **3** led to similar outcomes. Carbene **3** rightfully belongs to the family of foiled carbenes.



INTRODUCTION

In 1968, Gleiter and Hoffmann coined the term "foiled carbenes" for a special class of singlet carbenes.[1,2] These reactive species are stabilized to some degree by electron donation from an intramolecular π-bond into the empty p-orbital of the divalent carbon atom (Figure 1). This results in the formation of a two-electron, three-center bond, a charge-delocalized arrangement found in certain analogous (non-classical) carbonium ions.[3] Addition of the divalent carbon to the double bond is foiled because it would lead to an impossibly strained product featuring an inverted carbon atom with all four bonds pointed in one hemisphere.

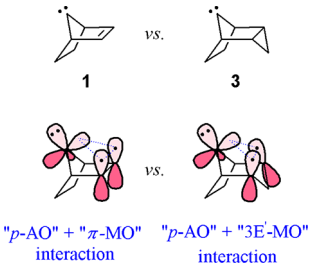
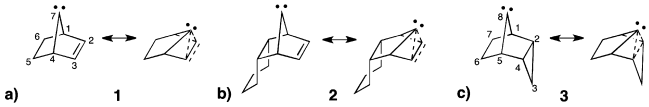


Figure 1. Interaction of the single bond Walsh orbital in carbene **3** mimics that of the double bond π-MO in carbene **1**, thereby establishing a two-electron, three-center bond with each carbene's p-AO.

The classic example of a foiled carbene is norbornen-7-ylidene (**1**) (Scheme 1a).[4] Computations indicate that the bridge containing the divalent carbon leans toward the double bond by ω = 37° when compared with norbornene.[5] Early on, it was suggested that such bending should be reflected in the stereoselectivity of intermolecular reactions; a reactant should approach the divalent carbon more easily from the face *anti* to the double bond because more space is available.[1] Indeed, a substantial bias was observed for the addition of **1** with 3,3-dimethylbutene.[6] Pyrolysis of the corresponding tosylhydrazone carbene precursor (i.e., Bamford–Stevens reagent) in the presence of the alkene gave two adducts wherein the *tert*-butyl group was oriented *syn* or *anti* to the double bond in a ratio of 7:1. However, the combined yield of the two products amounted to only 0.1%. The stereoselectivity was also investigated using density functional theory (DFT).[7] The most stable transition state was obtained when 3,3-dimethylbutene approached the divalent carbon of **1** *anti* to the double bond with the bulky *tert*-butyl group directed head-on to avoid a steric interaction with the *exo* hydrogens at C-5 and C-6 of **1**. This course would lead to the *syn* product, which was indeed the "major" product obtained experimentally.[6]

Scheme 1. Stabilization of Foiled Carbenes by Electron Donation to the Divalent Carbon Atom



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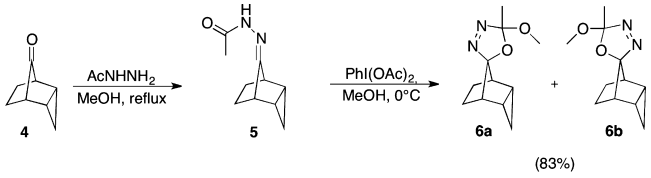
In order to achieve reasonable yields of intermolecular products from foiled carbenes, one must recognize their predominantly nucleophilic behavior.[8,9] The introduction of reactants that can behave as electron-pair acceptors is warranted. For example, tricyclo[6.2.1.0^{2,7}]undec-9-en-11-ylidene (**2**) comprises **1** as a subunit (Scheme 1b). It was generated by thermal decomposition of an oxadiazoline precursor. Carbene **2** reacted stereoselectively, via *anti* approach, with each of the following reactants: diethylamine (77% yield),[10] acrylonitrile (42% yield),[7] and malononitrile (29% yield).[11]

Cyclopropanes sometimes demonstrate a reactivity resembling that of alkenes. DFT calculations indicate that the three-membered ring of *endo*-tricyclo[3.2.1.0^{2,4}]octan-8-ylidene (**3**) stabilizes the divalent carbon in a way similar to that of a double bond (Figure 1 and Scheme 1c).[12] Computations also suggest the singlet electronic state of **3** to be lower in energy than the triplet.[12] Thus far, few experiments have been conducted to support the existence of an interaction between the divalent carbon atom and the cyclopropane ring.[13] Although rearrangements of **3** have been studied,[13] its potential classification as a foiled carbene could be more thoroughly assessed by examining its intermolecular reactions. Herein, the results of such experiments are presented. For these studies, oxadiazolines were employed as carbene precursors. Their syntheses and kinetics of decomposition are described as well.

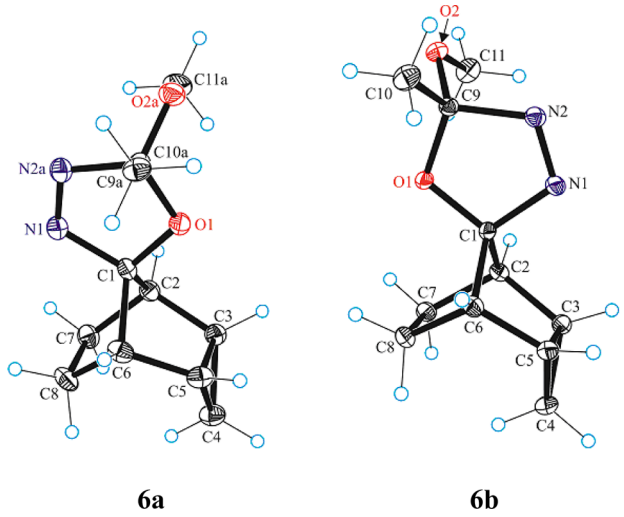
RESULTS AND DISCUSSION

Synthesis of Oxadiazolines as Carbene Precursors. Oxadiazolines are quite versatile compounds and popular carbene precursors.[10,14] Depending on their substituents, they decompose by different pathways to give a variety of products. (1′*R*,2′*R*,4′*S*,5′*S*)-5-Methoxy-5-methylspiro[2,5-dihydro-1,3,4-oxadiazole-2,8′-tricyclo[3.2.1.0^{2,4}]octane] (**6**) is expected to generate the requisite carbene **3** by either photolysis or thermolysis. Carbene **3**, however, is not produced directly from **6**, but through either a carbonyl ylide or a diazo intermediate (vide infra). The necessary oxadiazoline **6** was synthesized from ketone **4** (Scheme 2).[15] Two diastereomers were produced (dr = 1:1.7) in a combined yield of 83%. Isomers **6a** and **6b** were separated by column chromatography, and the absolute configuration of each pseudoasymmetric spirocyclic C atom (i.e., *r*/*syn* vs *s*/*anti*) was determined by X-ray crystallography (Figure 2).

Scheme 2. Synthesis of the Oxadiazoline (6) Used To Generate Carbene 3



Kinetics Measurements. The rate of thermolysis of **6a** and **6b** was measured at 116 °C (1 mg/mL in decane) by monitoring the decay of the UV absorption maxima of their oxadiazoline groups at λ_{max} = 338 and 333 nm, respectively. The decay of both **6a** and **6b** follows a first-order rate law with rate constants $k = 2.3 \times 10^{-5}$ s^{-1} and $k = 1.2 \times 10^{-5}$ s^{-1}, respectively. These values are typical for the decomposition of oxadiazolines (Figure 3),[14e,k] which normally thermolyze by first expelling molecular nitrogen.[14b,c] Diastereomer **6a** decomposes about twice as fast as **6b**, ostensibly because its configuration allows the cyclopropane ring to anchimerically assist with the expulsion of N_2. Such an interpretation is supported by results from solvolysis experiments with tricyclo[3.2.1.0^{2,4}]octan-8-ol derivatives, which have shown that the relative orientation of the cyclopropyl subunit and the leaving group at C-8 are decisive when considering the rates of solvolysis.[16] The order of observed reactivity is *endo,anti* ≫ *exo,syn* > *endo,syn* > *exo,anti*.[17] Thus, it is not surprising that the *endo,anti* relationship between the nitrogen and cyclopropyl group of **6a** accelerates its decomposition when compared with that of **6b**, which exhibits an *endo,syn* relationship. Among other factors, the modest 2-fold rate increase may arise from anchimeric assistance by the filled Walsh orbital of the cyclopropane moiety of **6a** into an antibonding MO, resulting in the loss of N_2.



6a **6b**

Figure 2. Single-crystal X-ray diffraction was used to elucidate the structures of the *rel*-(1′*R*,2*r*,2′*R*,4′*S*,5*R*,5′*S*)-5-methoxy-5-methylspiro-[2,5-dihydro-1,3,4-oxadiazole-2,8′-tricyclo[3.2.1.0^{2,4}]octane] (**6a**) and *rel*-(1′*R*,2*s*,2′*R*,4′*S*,5*R*,5′*S*)-5-methoxy-5-methylspiro[2,5-dihydro-1,3,4-oxadiazole-2,8′-tricyclo[3.2.1.0^{2,4}]octane] (**6b**).

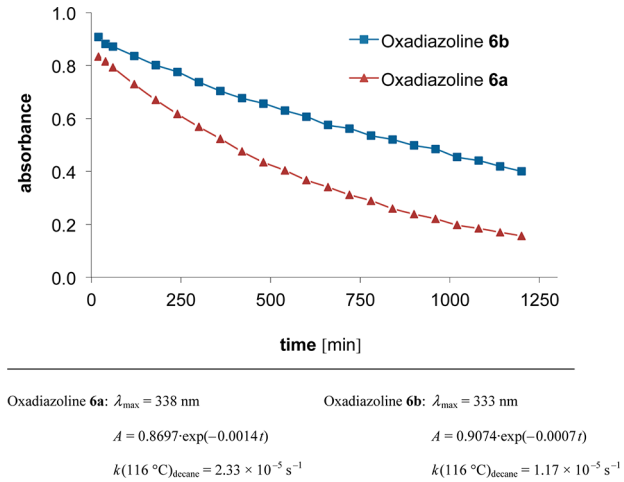


Figure 3. Decay of oxadiazolines **6a** and **6b** at 116 °C monitored using their UV absorbance maxima and found to be first-order.

Reactions of *endo*-Tricyclo[3.2.1.0^{2,4}]octan-8-ylidene (3). All thermolysis (165 °C) and photolysis (λ > 200 nm,

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Table 1. GC−MS Analysis of Product Distribution Obtained from Thermolysis and Photolysis of Oxadiazolines 6a and 6b in Cyclohexane and Cyclohexene

precursor	substrate	concn (mg/mL)	conditions	intermol. product yield (%)	intramol. product **8** yield (%)	intramol. product **9** yield (%)	azine **11** yield (%)
6a	cyclohexane	10	Δ	3	55	3	—
6b		10	Δ	4	17	1	31
6a		10	*hν*	—	27	2	47
6a		6	*hν*	—	23	2	31
6b		11	*hν*	—	44	3	31
6b		5	*hν*	—	20	1	38
6a	cyclohexene	10	Δ	5	71	10	—
6b		10	Δ	4	71	10	—
6a		10	*hν*	6	15	1	40
6a		6	*hν*	8	20	2	35
6b		12	*hν*	2	12	1	25
6b		5	*hν*	3	25	2	17

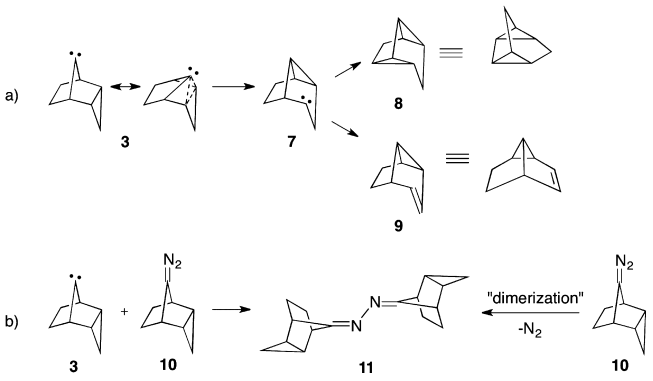
water bath, room temperature) experiments were conducted by dissolving precursors **6a** and **6b**, respectively, in the solvent under investigation. First, the chemistry of **3** in cyclohexane and cyclohexene was studied under the conditions listed in Table 1. The resulting solutions were subjected to GC−MS analysis, and yields were determined using camphor as an internal standard.

As presented in Table 1, there were some cases in which small peaks were detected in the chromatograms that might derive from compounds formed by intermolecular reactions of carbene **3** with cyclohexane (M^+; m/z = 190) or cyclohexene (M^+; m/z = 188). However, the estimated yields were low (ca. 2−8%). This lack of reactivity indicates a stabilization of carbene **3**, but it could also mean that intramolecular reactions are faster. Moreover, the *slow* addition to the electron-rich double bond of cyclohexene suggests that **3** acts as a nucleophilic carbene as gauged by the "philicity" scale of carbenes in carbene−alkene addition reactions.[18]

In all experiments, significant formation of a product (M^+; m/z = 106) was observed. This presumably results from an isomerization of **3**. In order to identify this compound, thermolysis of **6b** was carried out in cyclohexane-d_{12}, and the reaction mixture was analyzed by NMR spectroscopy. Additionally, **6b** was thermolyzed in pentane, and after concentration, the resulting product mixture was subjected to diffusion-edited NMR.[19] Two spectra with attenuated signals were obtained after conducting two pulsed-field gradient spin echo experiments in which one had a very low gradient amplitude and the other had a much higher one. A pure trace for compound **8** was computed by subtracting these spectra from each other after the vertical scale was adjusted to the peak of the undesired background (Figure S13 in the Supporting Information). The ^{1}H NMR and ^{13}C NMR signals were in accordance with tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octane (**8**) (Scheme 3a).[20] In addition, a minor product with the same mass was formed. It is thought to be tricyclo[3.3.0.0^{4,6}]oct-2-ene (dihydrosemibullvalene) (**9**) (Scheme 3a), based on characteristic ^{1}H NMR patterns of the alkenyl hydrogens.[14k,21] Compounds **8** and **9** have also been obtained from carbene **3** under different conditions (vide infra).[13a,b] A mechanism for the formation of **8** and **9** was proposed involving a conversion of **3** into **7**,[13b,22] as shown in Scheme 3a.

Under nearly all reaction conditions (Table 1), *endo*-tricyclo[3.2.1.0^{2,4}]octan-8-one azine (**11**) (Scheme 3b) was formed. The compound was identified by scaling up the reaction of the thermolysis of **6b** in pentane, which gave **11** in

Scheme 3. Products Formed by Thermolysis or Photolysis of Oxadiazoline 6a or 6b in Cyclohexane or Cyclohexene



an isolated yield of 11%. The azine can derive either from the reaction of carbene **3** with diazo compound **10**, which is formed by the loss of methyl acetate from oxadiazoline **6**, or from a bimolecular reaction of **10** with itself followed by the loss of N_2 (Scheme 3b).[23] These processes can occur simultaneously wherein the dominating one depends on the solution's concentration. As an additional possibility, carbene **3** might attack the remote N atom of precursor **6**, which would subsequently lose methyl acetate to afford **11**. The GC−MS results indicate that **11** is formed more frequently during photolysis than thermolysis. Alternatively, oxadiazolines **6a** and **6b** can decompose by an initial loss of N_2, yielding a carbonyl ylide, which further collapses to carbene **3**.[14] The ^{13}C NMR spectrum of **11** revealed two sets of signals in a 1:1 ratio. After evaporation of the solvent, the sample was redissolved and allowed to stand for 3 h before another analysis. Subsequently, the spectrum revealed one major and one minor set of signals. However, the 1:1 ratio was reestablished over time as the two species equilibrated (Figure S25 in the Supporting Information).

In previous experiments,[13a,b] the corresponding tosylhydrazone precursor of carbene **3** was thermolyzed in diglyme (i.e., 2,5,8-trioxanonane) in the presence of 5.74 equiv of sodium methoxide. In addition to products **8** and **9**, three methyl ethers were obtained, resulting from intermolecular reactions of carbene **3** with methanol. These compounds are believed to form through a carbenium ion pathway in which the carbene is protonated. Either the carbenium ion or the carbene route can be favored by varying the reaction conditions. Here, a different

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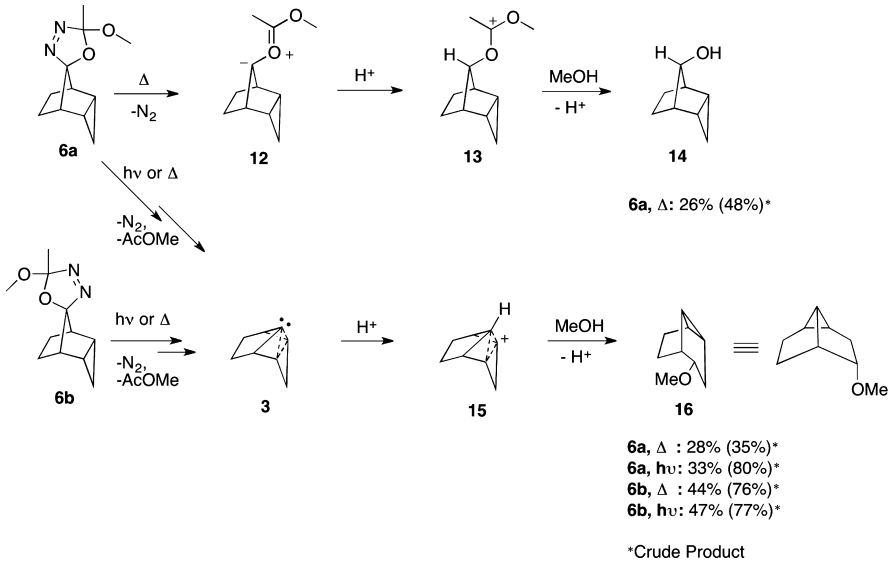
Scheme 4. Thermolysis and Photolysis of Oxadiazolines 6a and 6b in the Presence of Methanol



carbene precursor was used (i.e., an oxadiazoline) that was directly dissolved in methanol. This could lead to a different outcome. In addition, the reactions were carried out under both thermolytic and photolytic conditions.

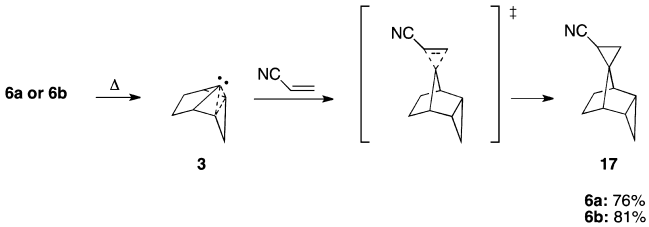
In all experiments, only methyl ethers were formed. In each case, GC–MS of the crude sample showed one main product, which was isolated by column chromatography and identified as *rac*-(1*R*,2*S*,4*S*,5*R*,6*R*)-2-methoxytricyclo[3.3.0.0^{4,6}]octane (**16**) (Scheme 4). Compound **16** is identical to the main methyl ether obtained by the reported Bamford–Stevens reaction.[13a,b] The isolated yields were considerably lower after chromatography (Scheme 4). It is possible that **16** decomposes on silica adsorbent because the crude products were quite pure according to ^{1}H NMR analysis.

In addition to **16**, *endo,syn*-tricyclo[3.2.1.0^{2,4}]octan-8-ol (**14**) was formed in 26% yield during the thermolysis of **6a** in methanol (Scheme 4). The production of alcohol **14** is best explained by protonation of the proximal ylide intermediate **12** with methanol to afford **13**, which locks in the stereoconfiguration at C-8. Subsequent methanolysis of **13** gives **14**. A similar reaction sequence was observed for the oxadiazoline precursor of **2**.[24] In contrast, the distal ylide intermediate formed from **6b** (not shown) might be destabilized by electron donation from the three-membered ring because of the aforementioned *endo,anti* relationship. This may lead to its collapse before being trapped by a proton. However, proton transfer rates to a negatively charged C atom are extremely fast. The experiments with methanol therefore stand as the single example where **6a** and **6b** reacted differently. Because **14** is not formed during photolysis, it can be assumed that the oxadiazoline decomposes through diazo intermediate **10** rather than ylide **12**.

The formal insertion reaction of foiled carbenes into methanol has been shown to occur through initial protonation of the carbene to give a carbenium ion.[25] The positive charge in **15** is delocalized among C-2, C-4, and C-8. Product **16** is formed by an attack of methanol at C-2 or C-4. This indicates that the charge is concentrated largely at these identical carbon atoms. In addition, the delocalized charge in **15** shields it from an attack by methanol at the *exo* positions of C-4 and C-2. Thus, formation of the corresponding *exo*-methyl ether of **16** is prevented.[16b,c] The stereochemistry of product **16** is determined by **15** originating from protonation of carbene **3**.[26]

Next, conditions were needed where carbene **3** would react directly with an added substrate. Because foiled carbenes in general are nucleophilic, trapping them with an electron-deficient alkene has proven to be successful.[7] Thus, when **6a** or **6b** was thermolyzed in acrylonitrile, *rel*-(1*s*,1′*R*,2*R*,2′*R*,4′*S*,5′*S*)-spiro[cyclopropane-1,8′-tricyclo[3.2.1.0^{2,4}]octane]-2-carbonitrile (**17**) (Scheme 5) was formed exclusively in a yield of 76%

Scheme 5. Thermolysis of Oxadiazolines 6a and 6b in the Presence of Acrylonitrile



or 81%, respectively. These values are considerably higher than those obtained for carbene **2**. The stereochemistry of **17** was assigned with the help of two-dimensional NMR experiments. Because the reaction occurs stereoselectively (i.e., the cyano group is always found to be *anti* to the cyclopropane), it can be assumed that the product is formed through a concerted mechanism, which is expected for a singlet carbene.[2c] The assumed transition state is shown in Scheme 5. Previous DFT calculations suggest that the *anti* product is formed with electron-poor alkenes, whereas the *syn* product is preferred with electron-rich alkenes.[7] In both cases, the alkene approaches the divalent carbon *anti* to the stabilizing moiety (i.e., double bond or cyclopropane ring), but subsequent stereoelectronic effects determine how the alkene's substituents are orientated in the product. Both the nucleophilic behavior and the diastereoselectivity in this reaction provide strong evidence for a foiled carbene **3**.

Foiled carbenes can also exhibit ambiphilicity. For example, carbene **2** was successfully trapped by highly nucleophilic diethylamine.[10] Therefore, thermolyses were carried out for

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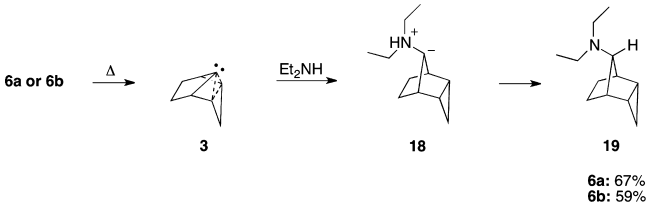
both **6a** and **6b** in the neat amine. One main product was obtained from both reactions: *endo,anti-N,N*-diethyltricyclo-[3.2.1.$0^{2,4}$]octan-8-amine (**19**) (Scheme 6), in yields of 67%

Scheme 6. Thermolysis of Oxadiazolines 6a and 6b in the Presence of Diethylamine



and 59% from **6a** and **6b**, respectively. The GC−MS chromatograms showed a small amount of an additional compound with the same molar mass as **19** in ratios of 30:1 and 58:1, respectively. This minor product could be the *syn* analog of **19**, or it could result from a reaction of diethylamine with carbene **7**. The reaction **6** → **19** is assumed to proceed through ylide intermediate **18** (Scheme 6),[10,27] thereby preserving the diastereoselectivity of step **3** → **18**.[28] The stereochemistry of product **19** suggests an *anti* approach of diethylamine. In any case, however, an *anti* approach is necessary to obtain **19** even if the mechanism involves a concerted insertion of carbene **3** into the N−H bond. Thus, this reaction also suggests a foiled carbene **3** as an intermediate.

CONCLUSION

The experiments described above support that *endo*-tricyclo-[3.2.1.$0^{2,4}$]octan-8-ylidene (**3**) is a stabilized carbene. The occupied Walsh orbitals of the three-membered ring donate electron density into the empty p-orbital of the divalent carbon (Figure 1), causing the main bridge to bend toward the cyclopropane ring as is the case with alkenylidene **1**. This is reflected in intermolecular reactions with acrylonitrile and diethylamine, which both approach the divalent carbon *anti* to the cyclopropane unit. Oxadiazolines **6a** and **6b** are useful precursors of **3**. The two diastereomers show almost identical reactivities, although **6a** thermally decomposes about twice as fast as **6b**. Azine **11** was isolated in nearly all reactions (Table 1). It is formed more frequently during photolysis than thermolysis. In the thermolysis of **6a**, ylide intermediate **12** was trapped with methanol to give the tricyclic alcohol **14**. Carbene **3** is added as a nucleophile to acrylonitrile and as an electrophile to diethylamine in high yields. The reactions are stereoselective. Replacing the CH═CH unit in 7-norbornenylidene (**1**) with an *endo*-fused cyclopropane ring, as in carbene **3**, leads to comparable reactive behavior. Thus, on the basis of the experiments outlined in this study, carbene **3** rightfully belongs to the family of foiled carbenes.

EXPERIMENTAL SECTION

Equipment. Melting points were measured on a melting point microscope and are uncorrected. The NMR spectra were obtained on either a DRX 400 WB instrument, operating at a frequency of 400.13 MHz for ^{1}H and 100.62 MHz for ^{13}C, or a DRX 600 at a frequency of 600.13 MHz for ^{1}H and 150.95 MHz for ^{13}C. The chemical shifts are given in parts per million with respect to TMS. For the ^{1}H NMR spectra, the residual peak of $CDCl_3$ (δ_H = 7.26 ppm) or cyclohexane-d_{12} (δ_H = 1.38 ppm) was used as an internal standard. For the ^{13}C NMR spectra, the central peak of the $CDCl_3$ triplet (δ_C = 77.16 ppm) was used as an internal standard. Conventional gradient-enhanced two-dimensional COSY, NOESY, HMBC, and HMQC spectra were used to derive proton and carbon assignments. The diffusion edited NMR experiments were done on the DRX 600, where a longitudinal eddy current delay sequence with 1 ms smoothened square bipolar gradient pulse pairs[29] was used, with a diffusion delay set to 100 ms. Two spectra were recorded, one with 3% and the second with 73% gradient amplitude. The resulting ^{1}H NMR spectra were subtracted by scaling the signal intensity of the background signals to equal heights, giving a trace with only compound **8** (Figure S13 in the Supporting Information). Infrared spectra were measured with an ATR attachment, and the absorptions are given in wavenumbers (cm^{-1}). HRMS was performed on a mass spectrometer outfitted with a TOF analyzer using ESI techniques, or a double-focusing sector field analyzer using EI (70 eV) techniques. Single-crystal X-ray analyses were performed on a diffractometer. Photolysis experiments were carried out using a medium pressure mercury lamp doped with FeI_2 (λ_{max} = 370 nm), which was placed in a water-cooled jacket made of quartz. GC−MS data were obtained using an instrument equipped with a mass selective detector (70 eV) on a 30 m × 0.25 mm HP-5MS poly(methylphenylsiloxane) (95% dimethyl and 5% diphenyl, 0.25 μm film thickness) capillary column using helium as the carrier gas.

General Settings for GC−MS Analysis. Pressure: 0.416 bar. Flow: 0.7 mL/min. Average velocity: 32 cm/s. Injection volume: 1.0 μL. Split ratio: 1:25. Injection temperature: 270 °C. Starting temperature: 80 °C for 2 min. Ramp: 5 °C/min up to 145 °C. Ramp: 15 °C/min up to 220 °C. Isotherm: 220 °C for 3 min. Ramp: 15 °C/min up to 270 °C. Isotherm: 270 °C for 3 min.

Materials. Dry pentane was obtained by distillation from calcium hydride. Cyclohexane, cyclohexene, acrylonitrile, diethylamine, and methanol were distilled and dried over molecular sieves (3 Å or 4 Å) before use. Commercially available compounds were used without further purification. Ketone **4** was synthesized according to the literature.[16b,30] Analytical TLC was performed on aluminum plates with silica gel 60 F_{254}, and detection was obtained with an iodine chamber or a UV lamp at λ = 254 nm. Flash chromatography was conducted using silica gel 60 (230−400 mesh) as the stationary phase with hexane, ethyl acetate, and dichloromethane in different ratios as the mobile phase.

*rac-(1′R,2′R,4′S,5′S)-5-Methoxy-5-methylspiro[2,5-dihydro-1,3,4-oxadiazole-2,8′-tricyclo[3.2.1.$0^{2,4}$]octane] (**6**).* Ketone **4** (1.830 g, 14.98 mmol) and acetyl hydrazide (1.225 g, 16.54 mmol) were dissolved in methanol (100 mL) and refluxed for 3 h. The reaction mixture was cooled to 0 °C, and $PhI(OAc)_2$ (5.308 g, 16.48 mmol) was added over a period of 5 min. The mixture was stirred overnight as the ice bath melted. The solvent was removed on a rotary evaporator, and the product was isolated as a diastereomeric mixture (**6a**:**6b** = 1:1.7) by column chromatography using hexane/ethyl acetate (4:1) as eluant to give **6** (2.594 g, 83%). The two diastereomers were separated by column chromatography using hexane/dichloromethane (2:3) as eluant, affording **6a** and **6b** as white solids.

*rel-(1′R,2r,2′R,4′S,5R,5′S)-5-Methoxy-5-methylspiro[2,5-dihydro-1,3,4-oxadiazole-2,8′-tricyclo[3.2.1.$0^{2,4}$]octane] (**6a**).* mp: 35−39 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 3.09 (s, 3H), 2.38−2.16 (m, 3H), 2.03−1.97 (m, 1H), 1.68−1.59 (m, 2H), 1.63 (s, 3H), 1.44−1.34 (m, 3H), 1.06−1.01 (dt, *J* = 7.4 Hz (t), 6.5 Hz (d), 1H). ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 142.3 (C), 130.2 (C), 50.2 (CH_3), 45.0 (CH), 43.7 (CH), 24.3 (CH_2), 24.1 (CH_2), 23.1 (CH_3), 20.7 (CH), 20.6 (CH), 16.7 (CH_2). IR: ν 3069 (w), 2964 (m), 2880 (w), 1568 (w), 1477 (w), 1446 (w), 1377 (m), 1309 (w), 1240 (m), 1203 (s), 1131 (s), 1081 (m), 1045 (s), 987 (w), 927 (s), 907 (s), 872 (s), 787 (w), 760 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* 208 $[M]^+$ (<1), 177 (7), 153 (4), 115 (6), 105 (38), 91 (100), 78 (48), 65 (10), 51 (7). HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{17}N_2O_2$ 209.1290; found 209.1289. Anal. Calcd for $C_{11}H_{16}N_2O_2$: C, 63.44; H, 7.74; N, 13.45; O, 15.37. Found: C, 63.76; H, 7.61; N, 13.34; O, 15.21.

*rel-(1′R,2s,2′R,4′S,5R,5′S)-5-Methoxy-5-methylspiro[2,5-dihydro-1,3,4-oxadiazole-2,8′-tricyclo[3.2.1.$0^{2,4}$]octane] (**6b**).* mp: 54−58 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 3.05 (s, 3H), 2.26−2.21 (m, 1H), 2.05−1.99 (m, 1H), 1.83−1.73 (m, 3H), 1.72−1.64 (m, 1H), 1.58 (s, 3H), 1.39−1.24 (m, 2H), 1.17−1.11 (m, 1H), 0.95−0.88 (m, 1H). ^{13}C

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NMR (100.62 MHz, $CDCl_3$): δ 141.1 (C), 131.8 (C), 50.1 (CH_3), 44.7 (CH), 43.4 (CH), 25.8 (CH_2), 25.7 (CH_2), 23.0 (CH_3), 16.9 (CH), 16.6 (CH), 12.2 (CH_2). IR: ν 3042 (w), 2966 (m), 2877 (w), 1560 (w), 1472 (w), 1448 (w), 1376 (m), 1313 (w), 1238 (m), 1201 (s), 1138 (s), 1083 (m), 1051 (s), 977 (w), 913 (s), 869 (m), 791 (m), 761 (m) cm^{-1}. MS (EI, 70 eV): m/z 208 $[M]^+$ (<1), 177 (9), 153 (5), 115 (6), 105 (38), 91 (100), 78 (45), 65 (8), 51 (6). HRMS (EI, 70 eV): m/z $[M]^+$ calcd for $C_{11}H_{16}N_2O_2$ 208.1212; found 208.1215. Anal. Calcd for $C_{11}H_{16}N_2O_2$: C, 63.44; H, 7.74; N, 13.45; O, 15.37. Found: C, 63.65; H, 7.63; N, 13.31; O, 14.93.

General Procedure for GC–MS Analysis of Thermolysis and Photolysis of Oxadiazolines 6a and 6b in Cyclohexane and Cyclohexene. For thermolysis, the oxadiazoline was dissolved in either cyclohexane or cyclohexene and stirred in a pressure tube at 165 °C for 3–6 h. For photolysis, the oxadiazoline was dissolved in either cyclohexane or cyclohexene in a round-bottomed flask equipped with a rubber septum. The solution was degassed with argon and subjected to photolysis for 6–15 h. The temperature was controlled with a water bath. Camphor was added as an internal standard to the resultant reaction mixtures before GC–MS analysis.

*Tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octane (**8**).* A solution of oxadiazoline **6b** (0.319 g, 1.53 mmol) in pentane (20 mL) was stirred in a pressure tube for 4 h at 165 °C. Pentane was carefully removed by Kugelrohr distillation, and the residue was subjected to gradient NMR analysis. Spectroscopic data were in agreement with the literature.[20]

^{1}H NMR (600.13 MHz, $CDCl_3$): δ 1.74–1.69 (m, 2H), 1.65–1.55 (m, 4H), 1.29–1.25 (m, 4H). ^{13}C NMR (150.95 MHz, $CDCl_3$): δ 25.7 (CH), 24.0 (CH_2), 21.8 (CH).

*Thermolysis of **6b** in Cyclohexane-d_{12}.* A solution of oxadiazoline **6b** (0.030 g, 0.14 mmol) in cyclohexane-d_{12} (1 mL) was stirred in a pressure tube for 3 h at 165 °C. The reaction mixture was subjected to NMR analysis (see Figure S18 in the Supporting Information for ^{1}H NMR spectrum of the mixture).

*endo-Tricyclo[3.2.1.0^{2,4}]octan-8-one Azine (**11**).* A solution of oxadiazoline **6b** (0.254 g, 1.22 mmol) in pentane (3 mL) was stirred in a pressure tube for 4 h at 165 °C. The reaction mixture was filtered and concentrated. The product was isolated by column chromatography using hexane/ethyl acetate (1:1) as eluant, giving **11** (0.016 g, 11%) as a sticky white solid.

mp: 130–143 °C. ^{1}H NMR (600.13 MHz, $CDCl_3$): δ 3.21–3.14 (m, 2H), 2.54–2.46 (m, 2H), 1.69–1.51 (m, 4H), 1.47–1.36 (m, 4H), 1.28–1.16 (m, 4H), 1.03–0.97 (m, 2H), 0.97–0.90 (m, 2H). ^{13}C NMR (150.95 MHz, $CDCl_3$): δ 180.88 and 180.79 (C), 37.62 and 37.61 (CH), 32.44 and 32.42 (CH), 24.04 and 24.00 (CH_2), 23.44 and 23.42 (CH_2), 15.29 and 15.28 (CH), 14.79 and 14.76 (CH), 11.48 and 11.44 (CH_2). IR: ν 3029 (m), 2950 (m), 2873 (m), 1682 (s), 1523 (m), 1473 (m), 1311 (m), 1301 (m), 1180 (w), 1147 (m), 1108 (m), 1047 (m), 1030 (m), 928 (m), 789 (m), 757 (s), 719 (m) cm^{-1}. MS (EI, 70 eV): m/z 240 $[M]^+$ (12), 174 (3), 120 (36), 93 (100), 77 (27), 65 (13), 54 (7). HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{16}H_{21}N_2$ 241.1705; found 241.1696.

*endo,syn-Tricyclo[3.2.1.0^{2,4}]octan-8-ol (**14**).* See the procedure below for thermolysis of **6a** in methanol. **14** was isolated (0.022 g, 26%) as a white solid. Spectroscopic data were in agreement with the literature.[16b,31]

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 4.27–4.16 (m, 1H), 2.32–2.24 (m, 1H), 2.07–1.99 (m, 2H), 1.61–1.51 (m, 2H), 1.50–1.40 (m, 2H), 1.31–1.23 (m, 1H), 1.10–0.97 (m, 3H). ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 93.8 (CH), 41.0 (CH), 24.2 (CH_2), 19.8 (CH), 18.7 (CH_2).

*rac-(1R,2S,4S,5R,6R)-2-Methoxytricyclo[3.3.0.0^{4,6}]octane (**16**).* From thermolysis of **6a**: A solution of oxadiazoline **6a** (0.141 g, 0.677 mmol) in methanol (7.5 mL) was stirred in a pressure tube for 4 h at 165 °C. The reaction mixture was filtered and concentrated in vacuo. The crude product was subjected to column chromatography using hexane/ethyl acetate (9:1) as eluant, giving **16** (0.026 g, 28%) as a yellow liquid.

From thermolysis of **6b**: A solution of oxadiazoline **6b** (0.143 g, 0.687 mmol) in methanol (7.5 mL) was stirred in a pressure tube for 4 h at 165 °C. The reaction mixture was filtered and concentrated in vacuo. The crude product was subjected to column chromatography using hexane/ethyl acetate (9:1) as eluant, giving **16** (0.042 g, 44%) as a yellow liquid.

From photolysis of **6a**: A solution of oxadiazoline **6a** (0.100 g, 0.480 mmol) in methanol (5 mL) was degassed with argon and photolyzed for 7 h, using a water bath for cooling. The reaction mixture was filtered and concentrated in vacuo. The crude product was subjected to column chromatography using hexane/ethyl acetate (9:1) as eluant, giving **16** (0.022 g, 33%) as a yellow liquid.

From photolysis of **6b**: A solution of oxadiazoline **6b** (0.100 g, 0.480 mmol) in methanol (5 mL) was degassed with argon and photolyzed for 7 h, using a water bath for cooling. The reaction mixture was filtered and concentrated in vacuo. The crude product was subjected to column chromatography using hexane/ethyl acetate (9:1), giving **16** (0.031 g, 47%) as a yellow liquid. Spectroscopic data were in agreement with the literature.[13b]

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 3.80–3.72 (m, 1H), 3.22 (s, 3H), 2.60–2.51 (m, 1H), 2.25–2.12 (m, 1H), 1.99–1.88 (m, 1H), 1.83–1.69 (m, 2H), 1.69–1.57 (m, 1H), 1.49–1.39 (m, 2H), 1.16–1.05 (m, 2H). ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 88.1 (CH), 56.8 (CH_3), 43.6 (CH), 30.3 (CH_2), 27.3 (CH_2), 27.2 (CH), 26.0 (CH), 24.1 (CH_2), 19.2 (CH). IR: ν 3029 (m), 2943 (m), 2867 (m), 1736 (m), 1471 (m), 1450 (m), 1367 (m), 1349 (m), 1212 (m), 1177 (m), 1117 (s), 1098 (s), 975 (m) cm^{-1}. MS (EI, 70 eV): m/z 138 $[M]^+$ (4), 123 (3), 106 (28), 91 (21), 84 (10), 79 (45), 71 (100), 67 (17), 53 (5). HRMS (EI, 70 eV): m/z $[M]^+$ calcd for $C_9H_{14}O$ 138.1045; found 138.1044.

*rel-(1s,1′R,2R,2′R,4′S,5′S)-Spiro[cyclopropane-1,8′-tricyclo-[3.2.1.0^{2,4}]octane]-2-carbonitrile (**17**).* From thermolysis of **6a**: A solution of oxadiazoline **6a** (0.122 g, 0.586 mmol) in acrylonitrile (6 mL) was stirred in a pressure tube for 4 h at 165 °C. The reaction mixture was filtered and concentrated in vacuo. The product was isolated by column chromatography using hexane/ethyl acetate (4:1) as eluant, giving **17** (0.071 g, 76%) as a white solid.

From thermolysis of **6b**: A solution of oxadiazoline **6b** (0.125 g, 0.600 mmol) in acrylonitrile (6 mL) was stirred in a pressure tube for 4 h at 165 °C. The reaction mixture was filtered and concentrated in vacuo. The product was isolated by column chromatography using hexane/ethyl acetate (4:1) as eluant, giving **17** (0.077 g, 81%) as a white solid.

mp: 34–36 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 2.02–1.94 (m, 1H), 1.84–1.70 (m, 1H), 1.68–1.48 (m, 4H), 1.42–1.19 (m, 5H), 1.14–1.08 (m, 1H), 0.88–0.83 (dt, J = 7.4 Hz (t), 6.3 Hz (d), 1H). ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 121.0 (C), 54.4 (C), 41.7 (CH), 40.7 (CH), 26.8 (CH_2), 26.4 (CH_2), 21.7 (CH), 21.2 (CH), 16.1 (CH_2), 14.6 (CH_2), 3.9 (CH). IR: ν 3028 (m), 2959 (s), 2877 (m), 2228 (s), 1474 (m), 1442 (m), 1386 (w), 1317 (m), 1302 (m), 1205 (w), 1173 (m), 1113 (m), 1097 (m), 1037 (m), 1010 (s), 963 (m), 928 (s), 837 (m), 786 (s), 732 (s) cm^{-1}. MS (EI, 70 eV): m/z 159 $[M]^+$ (<1), 144 (4), 130 (15), 117 (15), 104 (21), 91 (50), 78 (100), 65 (10), 51 (9). HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{11}H_{13}NNa$ 182.0946; found 182.0947.

*endo,anti-N,N-Diethyltricyclo[3.2.1.0^{2,4}]octan-8-amine (**19**).* From thermolysis of **6a**: A solution of oxadiazoline **6a** (0.122 g, 0.586 mmol) in diethylamine (6 mL) was stirred in a pressure tube for 4 h at 165 °C. The reaction mixture was filtered and concentrated in vacuo. The product was isolated by column chromatography using ethyl acetate as eluant, giving **19** (0.070 g, 67%) as a yellow liquid.

From thermolysis of **6b**: A solution of oxadiazoline **6b** (0.120 g, 0.576 mmol) in diethylamine (6 mL) was stirred in a pressure tube for 4 h at 165 °C. The reaction mixture was filtered and concentrated in vacuo. The product was isolated by column chromatography using ethyl acetate as eluant, giving **19** (0.061 g, 59%) as a yellow liquid.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 2.94–2.91 (m, 1H), 2.59–2.50 (q, J = 7.1 Hz, 4H), 2.20–2.14 (m, 2H), 1.68–1.58 (m, 2H), 1.28–1.19 (m, 2H), 0.97–0.92 (t, J = 7.1 Hz, 6H), 0.92–0.85 (m, 3H), 0.56–0.49 (dt, J = 7.4 Hz (t), 6.0 Hz (d), 1H). ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 83.2 (CH), 43.6 (CH_2), 38.4 (CH), 25.1 (CH_2), 19.1 (CH), 12.2 (CH_2), 10.8 (CH_3). IR: ν 3022 (m), 2964 (s), 2816 (m), 1469 (m), 1369 (m), 1209 (m), 1180 (m), 1121 (m), 1070 (m), 1038

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(m), 988 (w), 791 (m), 740 (m) cm^{-1}. MS (EI, 70 eV): *m/z* 179 $[M]^+$ (2), 164 (4), 125 (5), 112 (100), 99 (13), 79 (11), 56 (15). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{12}H_{22}N$ 180.1752; found 180.1746.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra for all new compounds and CIFs for crystallographic data of **6a** and **6b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(28) One reviewer's calculations (B3LYP/6-31G(d)) found ylide **18** to be 9 kcal/mol more stable than the separated reactants. Moreover, solvation should further increase its stability.

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