exo/*endo* Preferences of Double Bonds in Three-Membered Ring Compounds − The Bias Toward Endocyclic Unsaturation in 3-Alkyl- and 3-Amino-2*H*-azirines: A Theoretical and Experimental Study[‡]

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Dedicated to Professor Manfred Christl on the occasion of his 60th birthday

Keywords: Ab initio calculations / Nitrogen heterocycles / Photolysis / Small ring systems / Tautomerism

Irradiation of the amino-4*H*-1,2,3-triazoles **7** ($\lambda \geq 280$ nm) affords molecular nitrogen and 3-amino-2*H*-azirines **8** in high yields. As shown on the basis of spectroscopic evidence, the photoproduct of **7a** exists exclusively as 3-amino-2*H*-azirine **8a** rather than in an equilibrium with the hypothetical iminoaziridine **10**. Ab initio quantum chemical calculations up to the Gaussian-3 level were performed for pairs of 3-substituted 2*H*-azirines (**1a**, **3a**, **5**)/aziridines (**2**, **4**, **6**) and 1-substituted cyclopropenes (**11**, **13**, **15**)/cyclopropanes with exocyclic double bonds (**12**, **14**, **16**). The G3 energies of acyclic pairs of tautomers **17**–**22** and other compounds were calculated for comparison. Ring strain was assessed with the help of two groups of homodesmotic reactions involving either hydrogen transfer (Equations 1–4) or exchange of carbon for nitrogen (Equations 5–7). In the cyclopropane series, relative ring strain and the stabilities of the functional groups both favour the *same* tautomer. The strain in aziridines – and in 2*H*-azirines in particular – is lower than in the corresponding cyclopropanes. This is the reason why the relative stabilities of the functional groups present in the N-heterocycles outweigh differences in strain that may be caused by the endo- or exocyclic location of the double bonds.
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Introduction

Most 1-alkylcyclopropenes may undergo base-catalysed isomerization to afford alkylidenecyclopropanes,[1,2] a reaction that is exothermic by 43.1 kJ/mol for the parent compounds **11** → **12**.[3] On the other hand, as demonstrated by many examples[4−6] including the parent 3-methyl-2*H*-azirine (**1a**),[7] the antibiotic azirinomycin (**1b**)[8] and related naturally occurring antibiotics,[9] 3-alkyl-2*H*-azirines do *not* rearrange into their isomers with the double bond in the *exo* position. This is evident from the formation and persistence of 3-alkyl-2*H*-azirines under the basic conditions of the Neber reaction.[5,6] The cause of the different behaviour of 1-alkylcyclopropenes and 3-alkyl-2*H*-azirines has not so far been addressed.

Three-membered heterocyclic compounds that may, in principle, exist as 3-amino-2*H*-azirines with a primary amino group and/or as iminoaziridines appear to prefer the tautomeric structure with the double bond in the *endo* position. They were obtained for the first time by Hyatt in the Neber rearrangement of *O*-sulfonyl amidoximes. He considered the available spectroscopic data as being compatible with the structure of either tautomer or with an equilibrium mixture of both, and drew the amino-2*H*-azirine formulae **3b** and **3c** merely as a convention.[10] Subsequently, Eremeev et al. synthesized some analogous compounds by Hyatt's method,[11] including the optically active diastereomers **3d**,[12] and concluded on the basis of spectroscopic evidence[13] and an X-ray diffraction analysis of (*R*,*R*)-**3d**[13] that they exist exclusively as the amino-2*H*-azirine tautomers. Similarly, adducts with chloral and with hexafluoro- and hexachloroacetone were reported to possess 3-amino-2*H*-azirine structures.[14,15] In view of the limited number of examples and, moreover, the restriction to strongly electron-withdrawing groups as ring substituents, compounds with other substitution patterns − and in particular, an explanation of the calculated relative stabilities of the parent compounds **3a** and **4** − appeared desirable.[16]

[‡] The experimental results are part of the Dissertation by T. Hergenröther, University of Würzburg, 1992.

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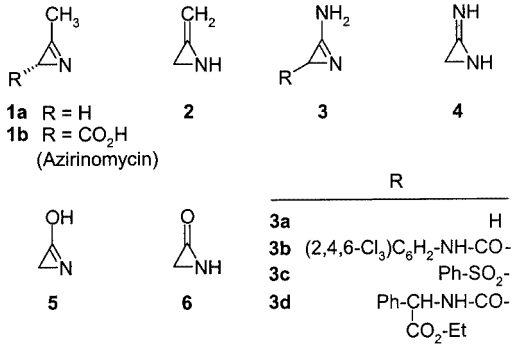
For these reasons, we report here on the synthesis and structure of 3-amino-2*H*-azirine **8a**, which may, in principle, equilibrate with its tautomer **10**, and we disclose the results of a Gaussian-3 computational study[17] of 3-methyl- (**1a**), 3-amino- (**3a**) and 3-hydroxy-2*H*-azirine (**5**) and their tautomers methylene- (**2a**) and iminoaziridine (**4**), and aziridinone (**6**) (Scheme 1). The analogous cyclopropene (**11**, **13**, **15**) and cyclopropane (**12**, **14**, **16**) derivatives are included for comparison. The results demonstrate that **1a** and **3a** are *more* stable than **2** and **4**, respectively, but **5** was calculated to be *less* stable than **6**.

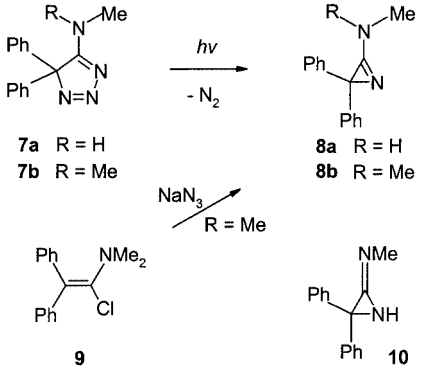


Scheme 1

Results and Discussion

Experimental Results

The Neber rearrangement of amidoxime *O*-sulfonates to afford 3-amino-2*H*-azirines, pioneered by Hyatt,[10] requires electron-withdrawing groups at the α-carbon atom and is thus confined to a particular class of 3-amino-2*H*-azirines, such as **3b**−**3d**. On the other hand, Ghosez's route to amino-2*H*-azirines by treatment of α-chloroenamines with sodium azide is restricted to *N*,*N*-substituted compounds,[18] such as **9** → **8b**.[14] Two examples of a third, photochemical synthesis have been reported by Bernard and Ghosez in a preliminary communication. Photolysis of 4,4-substituted 5-dimethylamino-4*H*-1,2,3-triazoles gave rise to the formation of molecular nitrogen and 3-dimethylamino-2*H*-azirines in excellent yields.[19] We employed this method for the synthesis of an amino-2*H*-azirine (**8a**) capable, in principle,



Scheme 2

of tautomerization to the iminoaziridine (**10**). Its *N*-methyl group served as a convenient diagnostic tool. The known *N*,*N*-dimethyl compound **8b**[14] was prepared in the same way and employed as reference for the structure of **8a** in solution (Scheme 2).

The methylamino-4*H*-1,2,3-triazole **7a** is by far the most stable of three possible tautomers.[20] When a degassed solution of **7a** in deuteroacetonitrile was irradiated at $\lambda \geq 280$ nm, a single product arose (as determined by ^{1}H NMR). After complete conversion, colourless crystals, m.p. 178−179 °C, were obtained on cooling of the clear, yellow solution. An X-ray diffraction analysis demonstrated that the photoproduct exist in the solid state as the 3-amino-2*H*-azirine tautomer **8a**, adopting the (*Z*) configuration as shown.[21] In fact, the very short bond between the 2*H*-azirine ring and the amino nitrogen atom (131.3 pm) is indicative of a high degree of double bond character. This is corroborated by the observation of two broadened ^{13}C signals for the methyl groups of **8b**, as a result of restricted rotation. The lengths of the ring bonds in (*Z*)-**8a** (N−C2 = 156.9, N−C3 = 127.8, C2−C3 = 143.7 pm) closely resemble those in *N*,*N*-substituted 3-amino-2*H*-azirines[14] and (*R*,*R*)-**3d**.[12] Of particular relevance to the solution structure of the photoproduct is the observation in the proton spectrum, recorded for a deuterodimethyl sulfoxide solution, of a 4.5 Hz coupling between the *N*-proton and the methyl group. The size of this coupling constant is not compatible with the iminoaziridine structure **10** and hence is indicative of a strong predominance of tautomer **8a** under these conditions. Further support for the virtually complete imbalance of the hypothetical tautomeric equilibrium **10** → **8a** was provided by the close similarity of chemical shifts in the proton and carbon-13 spectra of **8a** and **8b**, and the observation of the same value for the C=N frequencies (1785 cm^{-1}) in the IR spectra. In summary, there is no room for any doubt as to the structure **8a**, both in solution and in the solid state, for the photoproduct of **7a**.

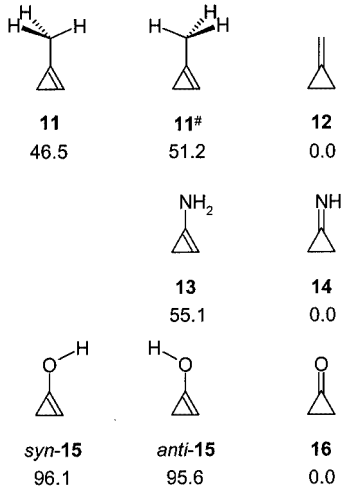
Computational Methods

Ab initio calculations were carried out for all compounds, including some transition structures for internal rotation, at various levels of theory (RHF/6-31+G**, MP2/6-31+G** optimization and MP4 single points), the highest being Gaussian-3, the most recent, efficient, and precise of the Gaussian high-accuracy energy models.[17] We performed a vibrational analysis at each stationary point in order to characterize it as a minimum (NIMAG = 0) or a transition structure (NIMAG = 1). Tables of total energies (E_0 [a.u.]), zero point energies (ZPE), heats of reaction of Equations (1)−(7), relative energies (E_{rel} [kJ/mol]) and the GAUSSIAN archive entries for the G3 calculations are available as Supporting Information. All calculations were carried out with the Gaussian 98 suite of programs.[22]

Ab initio Quantum Chemical Results

In Schemes 3−7 we confine the discussion to relative energies calculated at the highest level of theory (Gaussian-

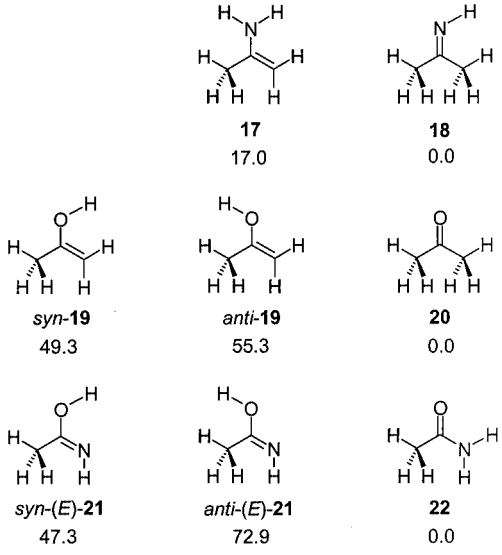
3). Their rounded values in kJ/mol are listed below each formula. Likewise, the energies of homodesmotic reactions are given in kJ/mol along with the Equations (1)−(7).



Scheme 3

In view of the strong preference for exocyclic over endocyclic unsaturation in cyclopropane derivatives [compare methylcyclopropene (**11**) and methylenecyclopropane (**12**)[3]], the surprising notion that emerges from all experimental studies is that the contrary is true for some, but not all, 3-substituted 2*H*-azirine derivatives. Compounds **1a** and **3**, for example, are more stable than their tautomers **2** and **4** with exocyclic double bonds. On the other hand, the order of stabilities of 3-hydroxy-2*H*-azirine (**5**) and aziridinone (**6**) is the same as that of **11** and **12**.

According to common textbook knowledge, ketimines are more stable than their tautomeric enamines, as once again demonstrated by the calculated 17 kJ/mol difference between enamine **17** and ketimine **18** (Scheme 4). Nevertheless, it is surprising that the energetic preference for the ketimine functionality present in **1a** should override a difference in ring strain if it were as high as that between methylcyclopropene (**11**) and methylenecyclopropane (**12**).[3] Below, we assume that the interplay of ring strain and the stabilities of the functional groups present tips the balance in favour of a particular tautomer, and we interpret the calculated relative energies in terms of either "cooperation" or "competition" between the former and the latter concept. Functional group stabilities are quantified with the help of the acyclic reference compounds **17**−**22**.



Scheme 4

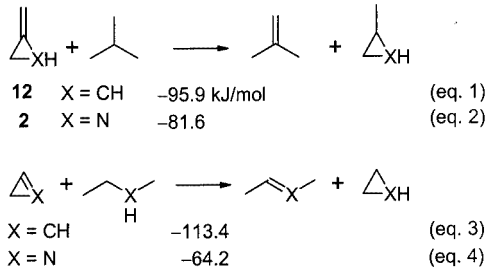
For comparison, we begin with an analysis of this interplay in the cyclopropane derivatives **13**−**16**. Because we are considering only strain arising from endocyclic and exocyclic double bonds, we adopt P. von R. Schleyer's concept of olefinic strain, which is defined as the difference between the strain energies of a cycloalkene and a cycloalkane.[23] We extend this concept to 2*H*-azirines although these possess a carbon-nitrogen rather than a carbon-carbon double bond.

Since A. von Baeyer's fundamental work,[24] strain in cyclopropanes has been the topic of a host of experimental and theoretical studies.[2,25] An impressive number of calculations have focused on cyclopropanone (**16**).[26] Iminocyclopropane (**14**) has been investigated by photoelectron spectroscopy and by MNDO[27] and ab initio calculations.[28] The carbocyclic analogues **13**−**16** of the heterocycles **3**−**6** provide examples of cooperation between strain and the relative stabilities of functional groups. The calculated energy difference between the parent hydrocarbons **11** and **12**, which is a measure of their difference in olefinic strain, is in excellent agreement with the experimentally determined value.[3] The relative stabilities of the tautomer pairs **13/14**, *syn*-**15/16**, and *anti*-**15/16** may be interpreted on the basis of this difference and of the energy differences between the corresponding pairs of acyclic tautomers **17/18**, *syn*-**19/20**, and *anti*-**19/20**, respectively. In fact, the relative stabilities of **13/14** (55 kJ/mol) and *anti*-**15/16** (96 kJ/mol) are only 6−8 kJ/mol smaller than the sums of the energy difference between **11** and **12** (47 kJ/mol) plus that between the tautomers **17/18** (17 kJ/mol) and *anti*-**19/20** (55 kJ/mol), respectively. The deviation from additivity is even less than 0.5 kJ/mol in case of the tautomer pair *syn*-**15/16**.

Extension of the explanation provided above for the aziridine derivatives **1**−**6** requires an assessment of the strain in aziridines and 2*H*-azirines. The parent cyclopropane and aziridine have been reported to possess virtually the same strain energies (115 and 113 kJ/mol, respectively), calculated on the basis of experimentally determined and estimated enthalpies of formation.[29] The high strain in 2*H*-azirines, as evidenced by high C=N stretching frequencies and ^{13}C-H coupling constant values,[29] has been estimated only occasionally. On the basis of the reported almost equal strain in cyclopropane and aziridine, Heimgartner assumed close similarity for the strain energies of cyclopropene and 2*H*-azirine.[14] More recently, Sordo et al. computed the MP2/6-31G* and B3LYP/6-31G* strain energies of 2*H*-azirine (186.6 and 195.4 kJ/mol) with the help of a homodesmotic reaction involving six acyclic molecules. Without disclosing any details, they mentioned that the correspond-

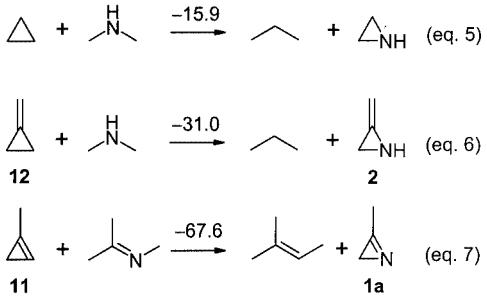
ing values for cyclopropene were higher by as much as about 42 kJ/mol at the same levels of theory.[30]

We calculate the olefinic strain of carbocyclic and heterocyclic three-membered rings by means of homodesmotic reactions.[31] Similar reactions (“homoisodesmic reactions”) have been employed by Wiberg for the thermochemical characterization of aromaticity and antiaromaticity.[32] In the first four Equations (Scheme 5), hydrogen is transferred from strain-free acyclic compounds to methylenecyclopropane [**12**, Equation (1)], methyleneaziridine [**2**, Equation (2)], cyclopropene [Equation (3)] and 2*H*-azirine [Equation (4)]. The olefinic strain of **2** is lower than that of **12** by only 14 kJ/mol. Stabilization of **2** by conjugation is probably small, since the nitrogen atom adopts a pyramidal conformation, while the planar structure **2#**, in which conjugation is at its maximum, is calculated to be higher in energy by 44.6 kJ/mol.[33] Incidentally, this value is in excellent agreement with the experimentally determined and MINDO barriers to nitrogen inversion in *N*-alkylmethyleneaziridines.[34] In contrast to that in the *exo* methylene compounds **2** and **12** the value for the olefinic strain of 2*H*-azirine is smaller than that of cyclopropene by 49 kJ/mol. Thus, the preference for the endocyclic carbon-nitrogen double bond in **1a** relative to the exocyclic carbon-carbon double bond in **2** is a consequence not only of the relative stability of the functional groups (compare **17** and **18**), but also of the relatively small value of the “olefinic” strain in 2*H*-azirine.

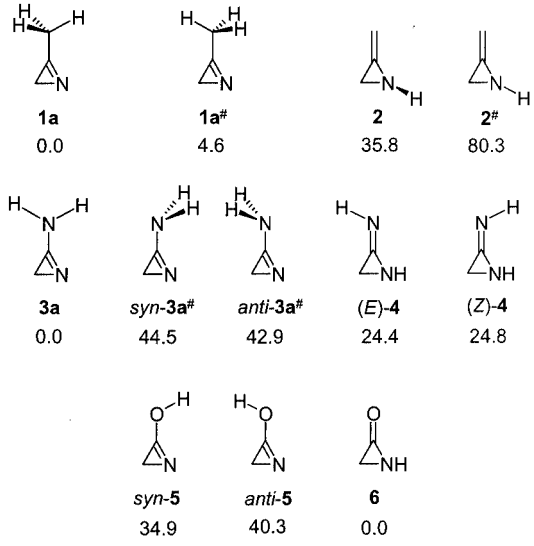


Scheme 5. Homodesmotic reactions transferring hydrogen from acyclic molecules to methyleneaziridine (**2**), methylenecyclopropane (**12**), cyclopropene and 2*H*-azirine

In the second group of homodesmotic reactions (Scheme 6), a carbon atom in each of cyclopropane [Equation (5)], methylenecyclopropane [**12**, Equation (6)] and 1-methylcyclopropene [**11**, Equation (7)] is exchanged for a nitrogen atom. These equations offer the most direct comparison between the carbocyclic and the heterocyclic systems. Nitrogen can reduce angle strain by the adoption of s character for the lone pair[29] and can thus accommodate itself in a three-membered ring more easily than carbon. The energies of Equation (5)−(7) represent the thermochemical consequences of this capability and provide the basis for a second but equivalent explanation of the bias toward endocyclic unsaturation. The fact that Equation (5) is exothermic by 16 kJ/mol is at variance with the reported virtually equal strain of the parent compounds cyclopropane and aziridine.[29] A single planar (sp^2) carbon atom renders the formal exchange more exothermic by only 15 kJ/mol [Equation (6)]. This small effect from the exocyclic double bonds in **2** and **12** is due to comparable olefinic strain in both molecules and a minor contribution from conjugation in methyleneaziridine (**2**). Ring strain and conjugation in **2** are opposing each other, resulting in a balance with the structural consequence of a pyramidal conformation of the nitrogen atom. The most important factor for the higher stability of **1a**, compared to **2**, becomes obvious from the high exothermicity of Equation (7), which measures the difference in strain between **1a** and **11**. Thus, this is more than 50% larger than the value (42 kJ/mol) reported by Sordo et al. for the parent compounds.[30] The much higher strain in **11**, relative to **12**, is drastically reduced in **1a** by the capability of nitrogen to employ its p orbitals for bonding and its s orbital for the lone pair.[29]



Scheme 6. Homodesmotic reactions exchanging a carbon and nitrogen atom between acyclic molecules and cyclopropane, methylenecyclopropane (**12**) and methylcyclopropene (**11**)



Scheme 7

The geometry,[16,35] energy[16] and protonation[36] of amino-2*H*-azirine **3a** have been calculated. The iminoaziridines **4** have been investigated by computational methods in the context of thermal isomerization and [2+1] cycloreversion,[16,28,37] and of protonation.[36,37] Several quantum chemical calculations of aziridinone (**6**) have been reported in various contexts.[38,39] The 3-hydroxy-2*H*-azirine tautomers **5** have not yet been studied.

The very short amino group bond in 3-amino-2*H*-azirines, as calculated[16] and also as found by X-ray diffraction

analyses,[12,14,21] and the high barrier toward bond rotation through **3a#**, as calculated for **3a** and observed by means of the ^{13}C NMR spectra of *N*,*N*-dimethylamino-2*H*-azirines such as **8b**, confirm extensive delocalization of the 4π system of **3a**.[14] An X-ray diffraction analysis of a substituted iminoaziridine[40] and the computed geometries for (*E*)- and (*Z*)-**4**[16] agree that the ring nitrogen atom adopts a pyramidal conformation. While all three tautomers **3a** and (*E*)/(*Z*)-**4** possess amidine moieties, the planar amino group of **3a** is a much better donor than the pyramidal ring nitrogen atom of (*E*)- and (*Z*)-**4**. The energetic consequence of this difference overcomes any strain differences and tips the balance in favour of tautomer **3a**.

The opposite is true for the hypothetical tautomeric equilibria between the 3-hydroxy-2*H*-azirines *syn*/*anti*-**5** and the aziridinone **6**. Like iminoaziridines, aziridinones possess a pyramidal ring nitrogen atom, as shown by X-ray studies[41] and by calculation of **6**.[39] Unlike 3-amino-2*H*-azirines and iminoaziridines, which are both characterised by an amidine system, however, the functionalities of *syn*/*anti*-**5** and **6**, as represented by s*yn*/*anti*-(*E*)-**21** and acetamide (**22**),[42] differ in energy by 47 (*syn*) and 73 kJ/mol (*anti*). The energy gain from even the imperfect amide resonance in **6** outweighs any differences in ring strain. In fact, the enthalpy differences between the heterocycles *syn*/*anti*-**5** and **6** are smaller than those between the acyclic reference compounds *syn*/*anti*-(*E*)-**21** and **22** by only 12 (*syn*) and 33 kJ/mol (*anti*).

Conclusion

Methylamino-2*H*-azirine **8a**, which is substituted with phenyl moieties rather than the electron-withdrawing groups present as substituents in all existing 3-amino-2*H*-azirines with a primary amino group, does *not* tautomerize to (*N*-methylimino)aziridine **10**, thus indicating that the higher stability of the 3-amino-2*H*-azirine tautomers does not depend on a particular substitution pattern. The ubiquitous preference for *exo* versus *endo* unsaturation in the cyclopropane series is interpreted in terms of a quasi-*additive* combination of relative ring strain and stability of the functionalities present. The puzzling bias towards endocyclic unsaturation in 3-alkyl- and 3-amino-2*H*-azirines, in contrast with aziridinones, is primarily due to the small size of the olefinic strain relative to that in cyclopropanes, and the balance between that strain and the relative stabilities of the functional groups characteristic for the tautomer pairs.

Experimental Section

General Remarks: Ref.[20]

3-(Methylamino)-2,2-diphenyl-2*H*-azirine (8a): A solution of **7a**[20] (25.0 mg, 0.10 mmol) in dry (CaH_2) CD_3CN (0.5 mL) was degassed by several freeze-thaw cycles (10^{-5} Torr) and sealed under vacuum in an NMR sample tube. The solution was irradiated at 20 °C and at λ ≥ 280 nm with a focussed 500-W high-pressure mercury lamp [Osram HBO 500 W/2, quartz optics, 10-cm water filter, 5-mm WG 280 Schott & Gen. (Mainz) cut-off filter] while the degree of conversion was monitored by ^1H NMR spectroscopy (200 MHz). The yield was ≥ 95% after complete conversion of **7a**. Cooling of the irradiated solution at −30 °C yielded colourless crystals, m.p. 178−179 °C. IR (CD_3CN): $\tilde{\nu}$ = 1785 cm^{-1}. ^1H NMR ([D$_6$]DMSO): δ = 2.90 (d, *J* = 4.5 Hz, 3 H), 7.2−7.4 (m, 10 H), 7.8 (br., 1 H). ^{13}C NMR (CD_3CN): δ = 29.6 (CH_3), 49.0 (quat. C, C2), 127.7 (*p*-CH), 128.9, 129.2 (*o*-, *m*-CH), 143.8 (*ipso*-C), 158.0 (quat. C, C=N). EI-MS (70 eV): *m*/*z* (%) = 222 (84) [M^+], 207 (60) [$M^+ - CH_3$], 193 (26), 180 (18), 165 (100), 152 (13), 139 (9), 131 (17), 119 (21), 104 (45). HR-MS: calcd. for $C_{15}H_{14}N_2$ 222.1157; found 222.1166.

3-Dimethylamino-2,2-diphenyl-2*H*-azirine (8b): A degassed solution of **7b**[20] (26.4 mg, 0.10 mmol) in dry CD_3CN (0.5 mL) was irradiated for 6.3 h according to the preceding procedure. The yield was ≥ 95% (^1H NMR). Distillation of the solvent i. vac. afforded yellow crystals. IR (CD_3CN): $\tilde{\nu}$ = 1785 cm^{-1}. ^1H NMR (CD_3CN): δ = 3.03 (s, 6 H), 7.2−7.3 (m, 10 H). ^{13}C NMR (CD_3CN): δ = 36.5 (br., CH_3), 39.7 (br., CH_3), 51.0 (quat. C, C2), 127.9 (*p*-CH), 128.8, 129.3 (*o*-, *m*-CH), 143.7 (*ipso*-C), 159.2 (quat. C, C=N). EI-MS (70 eV): *m*/*z* (%) = 236 (36) [M^+], 221 (40) [$M^+ - CH_3$], 193 (34), 165 (100), 152 (7), 139 (8), 133 (19), 118 (86). HR-MS: calcd. for $C_{16}H_{16}N_2$ 236.1313; found 236.1312.

Acknowledgments

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[1] [1a] G. Schröder, *Chem. Ber.* **1963**, *96*, 3178−3183. [1b] M. A. Battiste, J. M. Coxon, in *The chemistry of the cyclopropyl group* (Ed.: Z. Rappoport), 1st ed., Wiley, Chichester, U. K., **1987**, vol. 1, part 1, chapter 6, p. 269. [1c] A. Brandi, A. Goti, *Chem. Rev.* **1998**, *98*, 589−635.
[2] B. Halton, M. G. Banwell, in *The chemistry of the cyclopropyl group* (Ed.: Z. Rappoport), 1st ed., Wiley, Chichester, U. K., **1987**, vol. 1, part 2, chapter 21, p. 1223−1339.
[3] K. B. Wiberg, R. A. Fenoglio, *J. Am. Chem. Soc.* **1968**, *90*, 3395−3397.
[4] [4a] G. Smolinsky, *J. Org. Chem.* **1962**, *27*, 3557−3559. [4b] K. Banert, M. Hagedorn, *Angew. Chem.* **1989**, *101*, 1710−1711; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1675−1676. [4c] K. Banert, M. Hagedorn, *Angew. Chem.* **1990**, *102*, 90−92; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 103−105.
[5] F. Palacios, A. M. Ochoa de Retana, J. I. Gil, J. M. Ezpeleta, *J. Org. Chem.* **2000**, *65*, 3213−3217.
[6] For reviews on 2*H*-azirines see: F. Palacios, A. M. Ochoa de Retana, E. M. de Marigorta, J. M. de los Santos, *Eur. J. Org. Chem.* **2001**, 2401−2414, and references cited therein.
[7] M. Sugie, H. Takeo, C. Matsumura, *J. Mol. Struct.* **1997**, *413*−*414*, 387−394.
[8] T. M. Miller, E. W. Tristram, F. J. Wolf, *J. Antibiotics* **1971**, *24*, 48−50.
[9] [9a] T. F. Molinski, C. M. Ireland, *J. Org. Chem.* **1988**, *53*, 2103−2105. [9b] C. E. Salomon, D. H. Williams, D. J. Faulkner, *J. Nat. Prod.* **1995**, *58*, 1463−1466.
[10] J. A. Hyatt, *J. Org. Chem.* **1981**, *46*, 3953−3955.
[11] A. V. Eremeev, I. P. Piskunova, R. S. Él'kinson, *Khim. Geterotsikl. Soedin.* **1985**, 1202−1206; *Chem. Abstr.* **1987**, *107*, 7016w.
[12] I. P. Piskunova, A. V. Eremeev, A. F. Mishnev, I. A. Vosekalna, *Tetrahedron* **1993**, *49*, 4671−4676.
[13] [13a] É. É. Liepin'sh, R. S. Él'kinson, I. P. Piskunova, A. V.

Eremeev, *Khim. Geterotsikl. Soedin.* **1986**, 1181−1183; *Chem. Abstr.* **1987**, *106*, 175677k. [13b] A. V. Eremeev, I. P. Piskunova, R. S. Él'kinson, I. B. Mazheika, I. V. Dipan, *Khim. Geterotsikl. Soedin.* **1987**, 1202−1206; *Chem. Abstr.* **1988**, *108*, 130873w.

[14] H. Heimgartner, *Angew. Chem.* **1991**, *103*, 271−297; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 238−264.

[15] [15a] A. V. Eremeev, I. P. Piskunova, R. S. Él'kinson, *Izv. Akad. Nauk. Latv. SSR, Ser. Khim.* **1986**, 244−245; *Chem. Abstr.* **1987**, *106*, 4772h. [15b] A. V. Eremeev, I. P. Piskunova, *Khim. Geterotsikl. Soedin.* **1990**, 867−887; *Chem. Abstr.* **1991**, *114*, 228644w.

[16] H. Quast, S. Aldenkortt, P. Schäfer, E. Schmitt, E.-U. Würthwein, *Liebigs Ann.* **1995**, 2171−2188.

[17] L. A. Curtiss, K. Raghavachari, P. C. Redfern, V. Rassolov, J. A. Pople, *J. Chem. Phys.* **1998**, *109*, 7764−7776.

[18] M. Rens, L. Ghosez, *Tetrahedron Lett.* **1970**, 3765−3768.

[19] C. Bernard, L. Ghosez, *J. Chem. Soc., Chem. Commun.* **1980**, 940−941.

[20] H. Quast, T. Hergenröther, K. Banert, E.-M. Peters, K. Peters, H. G. von Schnering, *Chem. Ber.* **1993**, *126*, 103−108.

[21] K. Peters, E.-M. Peters, T. Hergenröther, H. Quast, *Z. Kristallogr. − New Cryst. Struct.* **2000**, *215*, 303−304.

[22] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, P. Salvador, J. J. Dannenberg, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, J. A. Pople, *Gaussian 98*, Revision A.11, Gaussian, Inc., Pittsburgh PA, **2001**, and earlier versions of this program.

[23] W. F. Maier, P. von R. Schleyer, *J. Am. Chem. Soc.* **1981**, *103*, 1891−1900.

[24] R. Huisgen, *Angew. Chem.* **1986**, *98*, 297−311; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 297−311.

[25] [25a] K. B. Wiberg, *Angew. Chem.* **1986**, *98*, 312−322; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 312−322. [25b] K. B. Wiberg, in *The chemistry of the cyclopropyl group* (Ed.: Z. Rappoport), 1st ed., Wiley: Chichester, U. K., **1987**, vol. 1, part 1, chapter 1. [25c] D. Cremer, E. Kraka, K. J. Szabo, in *The chemistry of the cyclopropyl group* (Ed.: Z. Rappoport), 1st ed., Wiley, Chichester, U. K., **1995**, vol. 2, chapter 2, p. 43−137. [25d] J. F. Liebman, in *The chemistry of the cyclopropyl group* (Ed.: Z. Rappoport), 1st ed., Wiley, Chichester, U. K., **1995**, vol. 2, chapter 4, p. 223−260. [25e] E. L. Eliel, S. H. Wilen, L. N. Mander, *Stereochemistry of Organic Compounds*, 1st ed., Wiley-Interscience, New York, **1994**.

[26] [26a] H. H. Wasserman, G. M. Clark, P. C. Turley, *Top. Curr. Chem.* **1974**, *47*, 73−156. [26b] H. H. Wasserman, D. R. Berdahl, T.-J. Lu, in *The chemistry of the cyclopropyl group* (Ed.: Z. Rappoport), 1st ed., Wiley, Chichester, U. K., **1987**, vol. 1, part 2, chapter 23, p. 1455−1532. [26c] K. B. Wiberg, K. M. Morgan, H. Maltz, *J. Am. Chem. Soc.* **1994**, *116*, 11067−11077. [26d] D. C. Lim, D. A. Hrovat, W. T. Borden, W. L. Jorgensen, *J. Am. Chem. Soc.* **1994**, *116*, 3494−3499. [26e] C. F. Rodriquez, I. H. Williams, *J. Chem. Soc., Perkin Trans. 2* **1997**, 953−957. [26f] B. A. Hess, U. Eckart, J. Fabian, *J. Am. Chem. Soc.* **1998**, *120*, 12310−12315. [26g] B. A. Hess, L. Smentek, *Eur. J. Org. Chem.* **1999**, 3363−3367. [26h] N. Balcioglu, F. Sevin, *J. Mol. Model.* **2000**, *6*, 48−54. [26i] W. Sander, R. Wrobel, P. Komnick, P. Rademacher, H. M. Muchall, H. Quast, *Eur. J. Org. Chem.* **2000**, 91−98.

[27] H. Bock, R. Dammel, *Chem. Ber.* **1987**, *120*, 1961−1970.

[28] M. T. Nguyen, A. Van Keer, L. G. Vanquickenborne, *Chem. Ber./Recueil* **1997**, *130*, 69−75.

[29] T. L. Gilchrist, *Heterocyclic Chemistry*, 2nd ed., Longman Scientific & Technical, Harlow, Essex, England, **1992**.

[30] S. Calvo-Losada, J. J. Quirante, D. Suárez, T. L. Sordo, *J. Comput. Chem.* **1998**, *19*, 912−922.

[31] P. George, M. Trachtman, C. W. Bock, A. M. Brett, *Tetrahedron* **1976**, *32*, 317−323.

[32] K. B. Wiberg, *Chem. Rev.* **2001**, *101*, 1317−1331.

[33] Stabilization of **2**$^{\#}$ by conjugation may be inferred from the observation that the barriers toward nitrogen inversion are significantly lower for methyleneaziridines than for aziridines: W. B. Jennings, D. R. Boyd, "*Strained Rings*", in *Cyclic Organonitrogen Stereodynamics* (Eds.: J. B. Lambert, Y. Takeuchi), 1st ed., VCH Publishers, New York, **1992**, p. 105−158.

[34] The early data for the barrier toward inversion of *N*-methylmethyleneaziridine (E_a = 26.8 kJ/mol, $A = 1 \times 10^9$ s^{-1}: A. Loewenstein, J. F. Neumer, J. D. Roberts, *J. Am. Chem. Soc.* **1960**, *82*, 3599−3601) are probably too low. A line-shape analysis of the AB spin system of 3,3-[D_2]-*N*-neopentylmethyleneaziridine in the temperature range 153−269 K (dichloromethane/chlorotrifluoromethane solution) gave $\Delta H^{\ddagger}$ = (47.7 ± 0.4) kJ/mol, $\Delta S^{\ddagger}$ = (37.2 ± 2.9) J/mol K: W. Risler, Dissertation, University of Würzburg, **1977**. The $\Delta H^{\ddagger}$ value is close to the MINDO barrier of *N*-methylmethyleneaziridine (43.9 kJ/mol): M. J. S. Dewar, M. Shanshal, *J. Am. Chem. Soc.* **1969**, *91*, 3654−3655.

[35] J. Galloy, J.-P. Putzeys, G. Germain, J.-P. Declercq, M. Van Meerssche, *Acta Crystallogr., Sect. B* **1974**, *30*, 2462−2464.

[36] H. Quast, S. Aldenkortt, B. Freudenreich, P. Schäfer, E.-M. Peters, K. Peters, H. G. von Schnering, E.-U. Würthwein, *Liebigs Ann.* **1996**, 87−98.

[37] M. T. Nguyen, A. Van Keer, L. G. Vanquickenborne, *J. Chem. Soc., Perkin Trans. 2* **1996**, 299−305.

[38] [38a] E. R. Talaty, M. E. Zandler, *J. Heterocycl. Chem.* **1975**, *12*, 151−154. [38b] L. Treschanke, P. Rademacher, *J. Mol. Struct.* **1985**, *122*, 35−45, 47−57. [38c] P. V. Sudhakar, J. Chandrasekhar, *J. Mol. Struct.(Theochem)* **1989**, *194*, 135−147. [38d] A. Greenberg, Y.-Y. Chiu, J. L. Johnson, J. F. Liebman, *Struct. Chem.* **1991**, *2*, 117−126. [38e] A. Greenberg, H.-J. Hsing, J. F. Liebman, *J. Mol. Struct. (Theochem)* **1995**, *338*, 83−100. [38f] D. J. Tantillo, K. N. Houk, R. V. Hoffman, J. Tao, *J. Org. Chem.* **1999**, *64*, 3830−3837.

[39] H. Quast, H. Leybach, E.-U. Würthwein, *Chem. Ber.* **1992**, *125*, 1249−1262.

[40] H. Quast, P. Schäfer, K. Peters, H. G. von Schnering, *Chem. Ber.* **1980**, *113*, 1921−1930.

[41] [41a] E. R. Talaty, A. E. Dupuy, Jr., A. E. Cancienne, Jr., *J. Heterocycl. Chem.* **1967**, *4*, 657−658. [41b] A. H.-J. Wang, I. C. Paul, *J. Chem. Soc., Chem. Commun.* **1972**, 43−44.

[42] For a recent computational study of amides see: M. Avalos, R. Babiano, J. L. Barneto, J. L. Bravo, P. Cintas, J. L. Jiménez, J. C. Palacios, *J. Org. Chem.* **2001**, *66*, 7275−7282.

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