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Synthesis, Configuration, and ^{15}N NMR Spectra of Iminoaziridines. Synthons Equivalent to Three Components of the Ugi Reaction†

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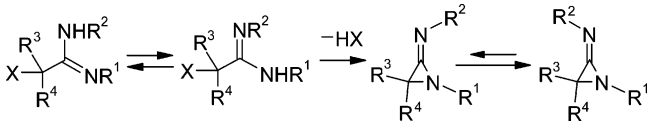
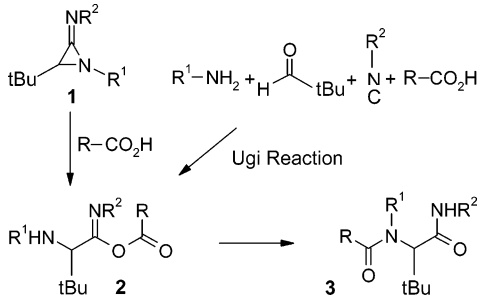


Monocyclic iminoaziridines and *exo*−*endo* diastereomers of spirocyclic iminoaziridines that are derived from norbornane are prepared in batches of up to 10 g to foster applications as building blocks in syntheses. *N*,*N*′-Disubstituted α-haloamidines, which are readily available in two steps from *N*-substituted α-halocarboxamides, are 1,3-dehydrohalogenated by strong bases such as alkali-metal hydrides or *tert*-butoxides to afford distillable oils or low-melting solids, which consist of slowly interconverting *E*−*Z* diastereomers of the title compounds. The scope and limitations are outlined for this reaction. The configurations *E* and *Z* that were assigned on the basis of homoallylic ^{1}H−^{1}H coupling and asymmetric solvent-induced shifts required that, in ^{13}C NMR spectra, the observed γ-effects of substitutents at the imino nitrogens were *deshielding*, contrary to the well-known shielding γ-effects in all other types of C═N compounds. However, an NOE NMR study demonstrated unequivocally that the previous assignments are correct and hence the observed γ-effects actually deshielding. The ranges of ^{15}N NMR chemical shifts span more than 60 ppm. Neither the β- nor the γ-effects of substituents on both types of nitrogen follow a uniform increment pattern.

Introduction

Iminoaziridines are synthetic equivalents for three of the four components of the Ugi reaction and related multicomponent reactions (MCRs),[1] viz., amine, carbonyl compound, and isocyanide (Scheme 1); in short, they are highly reactive α-amino acid synthons. By contrast to the Ugi reaction, where formation of the unstable "α-adducts" **2** is rate-limiting, the step leading to **2** is fast with iminoaziridines, even in cases of steric hindrance, due to their high reactivity resulting from relief of strain on addition to the imino group and subsequent ring-opening.[2] Nonracemic iminoaziridines **1**[3,4] and diastereomeric iminoaziridines *exo*- and *endo*-**6** provide the stereocenter

SCHEME 1



generated in the Ugi reaction and thus afford products of type **3** that are unavailable through the Ugi reaction without stereocontrol by (chiral) auxiliaries or catalysts.[1] 3,3-Disubstituted iminoaziridines **4**−**6** are potential synthons for derivatives of sterically constrained α-branched α-amino acids,[5a] viz.,

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(1) (a) Dömling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168. (b) Dömling, A. *Chem. Rev.* **2006**, *106*, 17. (c) *Multicomponent Reactions*; Zhu, J., Bienaymé, H., Eds.; Wiley-VCH: Weinheim, Germany, 2005.

(2) Quast, H.; Aldenkortt, S. *Chem.*−*Eur. J.* **1996**, *2*, 462.

(3) Quast, H.; Aldenkortt, S.; Heller, E.; Schäfer, P.; Schmitt, E. *Chem. Ber.* **1994**, *127*, 1699.

(4) Quast, H.; Aldenkortt, S.; Schäfer, P.; Schmitt, E.; Würthwein, E.-U. *Liebigs Ann.* **1995**, 2171.

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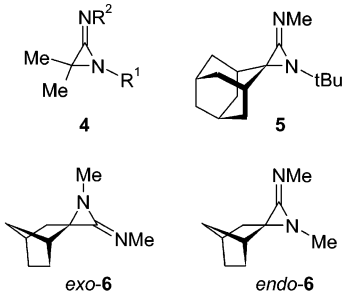
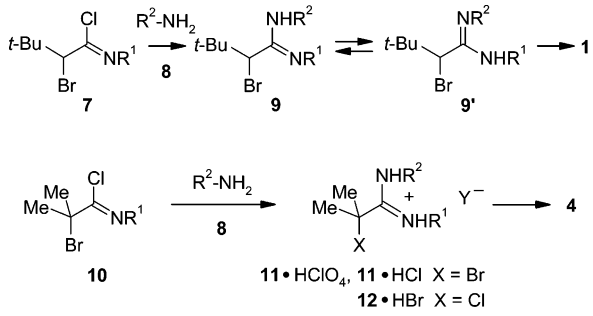
α-aminoisobutyric acid (Aib),[5b] 2-aminoadamantane-2-carboxylic acid,[6a] and *exo*- and *endo*-2-aminonorbornane-2-carboxylic acid,[6b] respectively.



1a, **4a**	$R^1 = R^2 = Me$	**1f**, **4f**	$R^1 = Me$; $R^2 = t$-Bu
4b	$R^1 = R^2 = CH_2Ph$	**1g**, **4g**	$R^1 = t$-Bu; $R^2 = Me$
1c, 4c	$R^1 = R^2 = i$-Pr	**1h**, **4h**	$R^1 = CH_2$-t-Bu; $R^2 = t$-Bu
1d	$R^1 = R^2 = CH(i\text{-Pr})_2$	**1i**	$R^1 = t$-Bu; $R^2 = CH_2$-t-Bu
4e	$R^1 = R^2 = CH_2$-t-Bu	**4j**	$R^1 = t$-Bu; $R^2 = CH_2Ph$
		1k	R^1 = Mes; $R^2 = t$-Bu
			(Mes = 2,4,6-$Me_3C_6H_2$)

Iminoaziridines have been invoked as intermediates on several occasions.[7] Irradiation of 5-alkylidene-4,5-dihydro-1*H*-tetrazoles[8] and 5-imino-4,5-dihydro-1*H*-1,2,3-triazoles[9] in small-scale experiments afforded iminoaziridines that were not isolated but characterized in solution by IR and NMR spectroscopy. The hitherto only route that leads to useful amounts of iminoaziridines involves base-induced 1,3-dehydrohalogenation of *N*,*N*′-disubstituted α-chloro- and α-bromoamidines. However, dehydrobromination of *N*-ethoxycarbonyl-, *N*-phosphoryl-, and *N*-sulfonyl-substituted α-bromoamidines did not yield iminoaziridines rather than five-membered heterocycles.[10] For physical organic chemistry studies, a few examples of types **1**[3,4] and **4**[4,9,11,12] and the spirocyclic iminoaziridine **5**[13] have been prepared in this way. To foster synthetic applications, we detail here the synthesis of **1** and **4** with various *N*-substituents and

SCHEME 2



10a	$R^1 = Me$	**8a**	$R^2 = Me$
10b	$R^1 = CH_2$• Ph	**8b**	$R^2 = CH_2Ph$
7c, **10c**	$R^1 = i$-Pr	**8c**	$R^2 = i$-Pr
7d	$R^1 = CH(i\text{-Pr})_2$	**8d**	$R^2 = CH(i\text{-Pr})_2$
7e	$R^1 = CH_2$-t-Bu	**8e**	$R^2 = t$-Bu
7f	R^1 = Mes		

11a•HCl, **12a**•HBr	$R^1 = R^2 = Me$
11b•HCl, **12b**•HBr	$R^1 = R^2 = CH_2Ph$
9c, **11c**•$HClO_4$	$R^1 = R^2 = i$-Pr
9d	$R^1 = R^2 = CH(i\text{-Pr})_2$
9e	$R^1 = CH_2$-t-Bu; $R^2 = t$-Bu
9f	R^1 = Mes; $R^2 = t$-Bu
11g	$R^1 = Me$; $R^2 = t$-Bu
11h•HCl, **12h**•HBr	$R^1 = CH_2Ph$; $R^2 = t$-Bu

of diastereomeric iminoaziridines *exo*- and *endo*-**6**. Because the Ugi reaction and related MCRs may suffer from steric hindrance, iminoaziridines with bulky substituents promise to become particularly useful and hence were included. To settle doubts about the configurations, we performed a detailed NOE NMR study. Finally, we report the first ^{15}N NMR spectra of iminoaziridines.

Results and Discussion

N,*N*′-Disubstituted α-haloamidines were prepared by the long-known[14] imidoylation of primary amines **8** using readily available α-bromoimidoyl chlorides **7** and **10** (Scheme 2)[15] and the bicyclic α-chloroimidoyl chlorides **14** (Scheme 3). The starting materials for the latter, viz., 2-chloronorbornane-2-carboxylic acids (*exo*- and *endo*-**13a**), were obtained with high diastereomeric purity, as described by Alder and co-workers,[16] by cycloaddition of cyclopentadiene and 2-chloroacrylic acid

(5) (a) For the significance of sterically constrained α-amino acids, see: Ellis, T. K.; Ueki, H.; Yamada, T.; Ohfune, Y.; Soloshonok, V. A. *J. Org. Chem.* **2006**, *71*, 8572 and references therein. (b) For *N*-(2,2-dimethyl-2*H*-azirin-3-yl) derivatives as Aib-pro synthons, see: Stamm, S.; Heimgartner, H. *Helv. Chim. Acta* **2006**, *89*, 1841.

(6) (a) Tager, H. S.; Christensen, H. N. *J. Am. Chem. Soc.* **1972**, *94*, 968. (b) Nagasawa, H. T.; Elberling, J. A.; Shirota, F. N. *J. Med. Chem.* **1973**, *16*, 823.

(7) (a) For a summary of early examples, see: L'abbé, G. In *Lectures in Heterocyclic Chemistry Vol. 9*; Castle, R. N., Neidlein, R., Eds. *J. Heterocycl. Chem.* **1987**, *24* (Suppl.), S-51. (b) Quast, H.; Bieber, L.; Regnat, D. *Chem. Ber.* **1990**, *123*, 1739. (c) Quast, H.; Balthasar, J.; Hergenröther, T.; Regnat, D. *Chem. Ber.* **1992**, *125*, 2749.

(8) (a) Quast, H.; Bieber. L.; Meichsner, G. *Chem. Ber.* **1988**, *121*, 2117. (b) Quast, H.; Hergenröther, T. *Chem. Ber.* **1992**, *125*, 2095. (c) Quast, H.; Fuss, A.; Nüdling, W. *Eur. J. Org. Chem.* **1998**, 317.

(9) Quast, H.; Regnat, D. *Chem. Ber.* **1990**, *123*, 2195.

(10) (a) L'abbé, G.; Verbruggen, A. *Tetrahedron Lett.* **1979**, 49. (b) L'abbé, G.; Verbruggen, A.; Toppet, S. *Bull. Soc. Chim. Belg.* **1981**, *90*, 99.

(11) Quast, H.; Aldenkortt, S.; Freudenreich, B.; Schäfer, P.; Peters, E.-M.; Peters, K.; von Schnering, H. G.; Würthwein, E.-U. *Liebigs Ann.* **1996**, 87.

(12) Schuchardt, U.; Ortellado G. Zelada, L. A. *J. Chem. Res., Synop.* **1983**, 270.

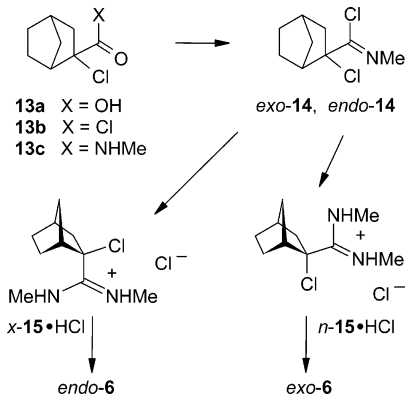
(13) Quast, H.; Schäfer, P.; Peters, K.; von Schnering, H. G. *Chem. Ber.* **1980**, *113*, 1921.

(14) (a) Tsatsas, G.; Delaby, R.; Quevauviller, A.; Damiens, R.; Blanpin, O. *Ann. Pharm. Fr.* **1956**, *4*, 607. (b) Tsatsas, G.; Delaby, R. *Ann. Pharm. Fr.* **1956**, *4*, 621. (c) Paul, H.; Weise, A.; Dettmer, R. *Chem. Ber.* **1965**, *98*, 1450. (c) Ostrowska, K.; Kolasa, A. In *Science of Synthesis*; Charette, A. B., Ed.; Thieme: Stuttgart, New York, 2005; Vol. 22, p 379.

(15) Quast, H.; Frank, R.; Freudenreich, B.; Schäfer, P.; Schmitt, E. *Liebigs Ann. Chem.* **1979**, 74.

(16) Alder, K.; Hartmann, R.; Roth, W. *Justus Liebigs Ann. Chem.* **1958**, *613*, 6.

SCHEME 3



followed by separation of the diastereomers using the iodolactonization protocol and subsequent hydrogenation. *N*-Methylamides **13c** resulted via the acid chlorides **13b**. The diastereomeric ratio *exo*-**13c**:*endo*-**13c** = 0.8:99.2 was determined by comparison of the downfield ^{13}C satellites of the 3-H_{exo} multiplet of *endo*-**13c** with the 3-H_{endo} multiplet of the traces of *exo*-**13c** present (600 MHz ^1H NMR, [$^2H_6$]benzene). Likewise, comparison of the upfield ^{13}C satellites of the 3-H_{endo} multiplet of *exo*-**13c** with the 3-H_{exo} multiplet of the traces of *endo*-**13c** gave the ratio *exo*-**13c**:*endo*-**13c** = 99.6:0.4. Treatment of **13c** with thionyl chloride furnished the α-chloroimidoyl chlorides **14** in high yields as colorless oils.

The α-bromoimidoyl chlorides **7** reacted smoothly with primary amines **8** to afford α-bromoamidines **9** with high yields as colorless oils or low-melting solids. In the case of **9c** and **9d**, crude α-bromoimidoyl chlorides, formed from α-bromoamides and thionyl chloride, were employed as starting materials. Small amounts of ketene imines were detected by IR spectroscopy in most crude α-bromoamidines **9**.[17] The presence of ketene imines is indicative of an elimination−addition mechanism of amidine formation. These impurities were separated by extracting **9** with dilute hydrochloric acid (→**9**·HCl) followed by regeneration of the free bases with concentrated sodium hydroxide solution. Free bases **9** were stable at low temperatures; the nicely crystallized perchlorates **9**·$HClO_4$ were shelf-stable (Table 1).

By contrast with α-bromoamidines **9**, which are derived from *tert*-butylacetic acid, many attempts to isolate pure α,α-disubstituted α-haloamidines **11** and **15** were frustrated by formation of products that contained mainly **11** and **15** but also iminoaziridines, as shown by their characteristic IR absorption around 1790 cm^{-1} (Table 2), and unknown products. The cause for the formation of the former is obviously the combination of the high basicity and high propensity of **11** and **15** to undergo base-induced 1,3-dehydrohalogenation. For example, neat α-bromoamidine **11c** slowly formed iminoaziridine **4c** and amidinium bromide **11c**·HBr. α-Bromoamidine **11g**, which was isolated after the reaction of **10a** with 3 mol of **8e**, was mixed with iminoaziridines **4f** and **4g**. To avoid premature 1,3-dehydrohalogenation during or after formation of **11** and **15**, the imidoyl chlorides **10** and **14** were allowed to react with only 1 equiv of **8** in a polar solvent, viz., acetonitrile. This method afforded amidinium salts in good yields (Table 1); however, partial or even complete exchange of the bromine atom of **11**·HCl for a chlorine atom (→**12**·HBr) was evident from ^1H and ^{13}C NMR spectra which showed the presence of two very similar compounds whose characteristic NMR signals differed just as those of *tert*-butyl bromide and *tert*-butyl chloride.[18,19] The observed halogen exchange results from the weaker solvation and hence stronger nucleophilicity in acetonitrile of the chloride compared with the bromide ion.[20] Fortunately, the isomerization does not detract from the value of the α-haloamidinium salts as starting materials for iminoaziridines.

The 1,3-dehydrohalogenation of α-haloamidines to afford iminoaziridines results in a shift of the strong C=N absorptions by about 150 cm^{-1} toward higher wavenumbers, cf. Tables 1 and 2, which permitted convenient monitoring of the progress of reaction by IR spectroscopy. Best results were achieved, in ether or tetrahydrofuran, with an excess of strong bases such as sodium or potassium hydride, potassium *tert*-butoxide, or

TABLE 1. Yields, Physical Data, and Wavenumbers of IR absorptions $\tilde{\nu}$ (KBr) (cm^{-1}) of α-Bromoamidines and α-Haloamidinium Salts and Solvents Used for Recrystallization

compd	yield (%)	mp (°C) (bp (°C)/ pressure (Torr))	[a]	$\tilde{\nu}$(C=N)	$\tilde{\nu}$(NH)
9c	61	(56−57/0.04)		1636	3430[b]
9c·$HClO_4$	89	171−172	I		
9d	66	41−42	P	1632	3430[b]
9d·$HClO_4$	59	142−143	C	1631	3240, 3300, 3415
9e	73	(70−72/0.1)		1645	3435[b]
9e·$HClO_4$	85	163−164	E	1640	3380
9f	64	85−86	P	1622	3445[b]
9f·$HClO_4$	78	186−187	F	1626	3280, 3420
11a·HCl[c]	87	163−164	I	1644	3200
11b·HCl[d]	55	164−165[e]	I	1631	3150, 3415
11c·$HClO_4$	72	179−180	I	1631	3325, 3405
12h·HBr	43	159−160[e]	I		
exo-**15**·HCl	84	198−202		1640	
endo-**15**·HCl	94	212−213		1645	

[a] Solvent: C = chloroform; E = ethanol; F = ethanol/ethyl acetate; I = isopropyl alcohol; P = pentane. [b] Neat liquid. [c] Contained 6% **12a**·HBr. [d] Contained 12% **12b**·HBr. [e] With decomposition.

TABLE 2. Experimental Conditions and Yields of 1,3-Dehydrohalogenations of α-Haloamidines and Wavenumbers $\tilde{\nu}$ (cm^{-1}) of C=N IR Absorptions of Iminoaziridines

product	starting material	base	solvent	temp (°C)	yield (%)	$\tilde{\nu}$[a]
1c	**9c**	*t*-BuOK	Et_2O	rt	85	1790
		NaH	THF	66	75	
1d	**9d**	*t*-BuOK	THF	rt	79	1792
1h	**9e**	*t*-BuOK	THF	0	81	1775[b]
1h, **1i**[c]	**9e**	NaH	THF	66	57	
1k	**9f**	*t*-BuOK	Et_2O	−15	82	1783
4a	**11a**·HCl	Et_3COK	pentane	rt	32	1795[d]
4b	**11b**·HCl	*t*-BuOK	THF	−25	44	1785
4c	**11c**·$HClO_4$	*t*-BuOK	Et_2O	rt	85	1781
		NaH	THF	rt	86	
4f, **4g**[e]	**10a**	*t*-$BuNH_2$	*t*-$BuNH_2$	0	71	1791
4j	**11h**·HCl, **12h**·HBr	*t*-BuOK	THF	−25	28	1771
exo-**6**	*n*-**15**·HCl	KH[f]	Et_2O	rt	60	1795
endo-**6**	*x*-**15**·HCl	KH[f]	Et_2O	rt	58	1795

[a] Neat liquid. [b] In carbon tetrachloride. [c] **1h**:**1i** = 85:15. [d] In benzene. [e] **4f**:**4g** = 8:92. [f] In the presence of 18-crown-6.

(17) (a) Stevens, C. L.; French, J. C. *J. Am. Chem. Soc.* **1954**, *76*, 4398. (b) Hünig, S.; Rehder, W. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 304. (c) Perst, H. In *Science of Synthesis*; Danheiser, R. L., Ed.; Thieme: Stuttgart, New York, 2006; Vol. 23, p 781.

(18) Wilk, W. D.; Allred, A. L.; Koven, B. A.; Marshall, J. A. *J. Chem. Soc. B* **1969**, 565.

(19) Kalinowski, H.-O.; Berger, S.; Braun, S. *^{13}C-NMR-Spektroskopie*; Thieme: Stuttgart, New York, 1984.

(20) Yamdagni, R.; Kebarle, P. *J. Am. Chem. Soc.* **1972**, *94*, 2940.

potassium hydride−18-crown-6.[3,4] 1,2-Dehydrohalogenation of **11** and **15** to yield unsaturated amidines, which is a conceivable competitive reaction, was not observed.[21] 1,3-Dehydrohalogenation of **11** and **12** occurred much more readily than that of **9**. While the former reacted with sodium hydride at ambient temperatures, prolonged heating in boiling tetrahydrofuran was required for the latter. Even *tert*-butylamine (**8e**), employed as a solvent, sufficed for complete 1,3-dehydrobromination of **11g** to produce a mixture of **4f** and **4g**.

Iminoaziridines are colorless oils or low-melting solids of characteristic odor. They can be distilled or sublimed under high vacuum and kept under an inert atmosphere at low temperatures. The purity and structures were based on spectroscopic evidence and, for **1c**, **1d**, **1h**, and **1k**, furthermore on thermal decomposition into isocyanides and imines, which were identified by comparison of ^{1}H NMR spectra with those of authentic samples.[22−26] The *exo*- and *endo*-configurations of the spirocyclic iminoaziridines **6** were inferred from the observation that 1,3-dehydrohalogenations furnishing iminoaziridines **1a**[3] and **1g**[4] and aziridinones (α-lactames)[27] involve inversion at the carbon bearing the leaving group. We note that *exo*- and *endo*-**6** are the first spirocycles that consist of the norbornane skeleton and a three-membered heterocyclic ring with an exocyclic double bond. Spirocyclic iminooxiranes similar to **6** have been invoked as labile intermediates in the reaction of 2-chloronorbornene-2-carboxamides with potassium hydroxide, yielding cyanide and norbornenone.[28] Carbocyclic systems of this type arose by the addition of unsaturated carbenes at camphene[29] and the reaction of diazomethane with 2-(oxomethylene)norbornane.[30]

When iminoaziridines are to be applied as building blocks in synthesis, the isomeric purity and hence regioselectivity of ring closure are crucial for α-haloamidines that possess two different nitrogen substituents, viz., **9e**, **9f**, **11g**, **11h**, and **12h**. The aryl groups of *N*-aryl-α-haloamidines appear exclusively at the ring nitrogen of the resulting iminoaziridines, e.g., **9f** → **1k**, not at the exocyclic nitrogen.[12] In the case of **1f** and **1g**, ring closure could be shifted almost completely in either direction with the help of the reaction temperature and the base−solvent combination.[4] Similarly, potassium *tert*-butoxide converted **9e** exclusively into **1h**, while sodium hydride in boiling tetrahydrofuran resulted in the formation of an 85:15 mixture of **1h** and **1i**. Because **1h** decomposes into isocyanide and imine at much lower temperatures (≥40 °C) than **1i**, partial thermolysis at 80 °C depleted **1h** and gave mixtures enriched in **1i**, after the thermolysis products of **1h** had been separated by distillation.

TABLE 3. Differences in the Chemical Shifts $\Delta_{sa} = \delta_{syn}(E) - \delta_{anti}(Z)$ (ppm) of the Ring Carbons C-3 of Diastereomeric Iminoaziridines[a]

compd	>NR^1	=NR^2	Δ_{sa}	[b]
1a	Me	Me	0.9	B[c]
1f	Me	*t*-Bu	8.1	C[d]
1g	*t*-Bu	Me	2.4	C[d]
			2.54	B[e]
4a	Me	Me	0.39	B[f]
			0.47	cH[f]
4e	CH_2-*t*-Bu	CH_2-*t*-Bu	0.12	C[g]
4l	Me	CH_2-*t*-Bu	0.63	T[f]
4m	CH_2-*t*-Bu	Me	0.0	C[f]
			0.0	cH[f]
4n	Me	Ph	4.5	cH[h]
4o	Ph	Me	1.6	cH[h]
16	Me	Me	0.5	cH[h]
exo-**6**	Me	Me	1.6	B[e]
endo-**6**	Me	Me	0.5	B[e]

[a] The configurations are based on homoallylic ^{1}H−^{1}H coupling constants (for **1a**, **1g**, and **16**) and ASIS experiments. [b] Solvents: B = [$^2H_6$]benzene; C = [^{2}H]chloroform; cH = [$^2H_{12}$]cyclohexane; T = [$^2H_8$]toluene. [c] Reference 8a. [d] Reference 4. [e] This work. [f] Reference 9. [g] Reference 11. [h] Reference 8b.

The mixture of **11h**·HCl and **12h**·HBr gave a low yield of only a single iminoaziridine (**4j**), which bears the *tert*-butyl group at the ring nitrogen. Likewise, iminoaziridine **4g** with the *tert*-butyl group at the ring was preferred over isomer **4f**. The experimental conditions and results are summarized in Table 2.

We had no difficulty preparing iminoaziridines in batches as large as 5−10 g. The scope of the synthesis is broad, as shown by the wide variety of substituents (Scheme 2). Limitations due to the volatility and lack of stability of the products came not unexpected. Thus, high volatility frustrated attempts to separate **4a** from the solvent. The neat *N*-benzyl compounds **4b** and **4j** remained unchanged at low temperatures but turned yellow at room temperature. Thermal stability was lowest for **1k**, which decomposed into *tert*-butyl isocyanide and *N*-(2,2-dimethylpropylidene)mesitylamine[22] at a temperature as low as 0 °C.

Configuration of Iminoaziridines. In principle, iminoaziridines may exist in the *E*- and *Z*-configurations. For a number of iminoaziridines, two slowly interconverting diastereomers of different stabilities were observed by ^{1}H NMR spectroscopy and, in most cases, also by ^{13}C NMR spectroscopy (Table 3). In contrast, the signals of the less stable diastereomers of **1c**, **1d**, **1h**, **1i**, **4c**, **4f**,[31] **4h**,[4] and **4j**[31] did not emerge from the noise. At low temperatures, the members of the former group are formed with diastereomeric ratios that differ from those at room temperature. The less stable diastereomers make up a larger fraction in freshly prepared than in equilibrated samples. Monitoring thermal equilibration by ^{1}H and ^{13}C NMR spectroscopy allows the assignment of NMR signals to a particular diastereomer when similar amounts of both diastereomers are present in equilibrated solutions at room temperature.

So far, the configuration of only a single iminoaziridine was established unequivocally, viz., that of (*E*)-**5** in the solid state by X-ray crystallography.[13] The assignment of *E*- and *Z*-configurations to the major and minor diastereomers of **1a**,[3] **1g**,[4] and **16**[8b] was based on the relative size of the homoallylic ^{1}H−^{1}H coupling between the ring proton and the imino methyl group, i.e., $^5J_{trans} > {}^5J_{cis}$,[32] and relative asymmetric solvent-

(21) This is at variance with the reported 1,2-dehydrobromination by potassium *tert*-butoxide of α-bromo-*N*-phenylamidines of type **11** to afford *N*-phenylmethacrylamidines.[12]

(22) (a) Russel, G. A.; Rajaratnam, R.; Chen, P. *Acta Chem. Scand.* **1998**, *52*, 528. (b) Nanni, D.; Pareschi, P.; Walton, J. C. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1098.

(23) (a) Mosher, H. S.; Blanz, E. J., Jr. *J. Org. Chem.* **1957**, *22*, 445. (b) Blanz, E., Jr.; Mosher, H. S. *J. Org. Chem.* **1958**, *23*, 492.

(24) Lavallo, V.; Mafhouz, J.; Canac, Y.; Donnadieu, B.; Schoeller, W.; Bertrand, G. *J. Am. Chem. Soc.* **2004**, *126*, 8670.

(25) Kuntz, I. D., Jr.; Schleyer, P. von Rague; Allerhand, A. *J. Chem. Phys.* **1961**, *35*, 1533.

(26) Meier, M.; Müller, B.; Rüchardt, C. *J. Org. Chem.* **1987**, *52*, 648.

(27) (a) Quast, H.; Leybach, H. *Chem. Ber.* **1991**, *124*, 2105. (b) Maran, F. *J. Am. Chem. Soc.* **1993**, *115*, 6557.

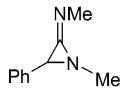
(28) Shiner, C. S.; Fisher, A. M.; Yacoby, F. *Tetrahedron Lett.* **1983**, *24*, 5687.

(29) (a) Sasaki, T.; Eguchi, S.; Ogawa, T. *J. Org. Chem.* **1974**, *39*, 1927. (b) Sasaki, T.; Eguchi, S.; Tanida, M.; Nakata, F.; Esaki, T. *J. Org. Chem.* **1983**, *48*, 1579. (c) Eguchi, S.; Arasaki, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1047.

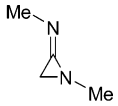
(30) Cordes, M. H. J.; Berson, J. A. *J. Am. Chem. Soc.* **1992**, *114*, 11010.

(31) This work.

induced shifts (ASISs):[33] asymmetric solvation of the imine moiety by benzene shifts resonances of protons that reside at the side of the imino alkyl group stronger to high field than protons at the side of the lone pair. Configurational assignments for other iminoaziridines rest on analogy with **1a**, **1g**, **16**, and ASIS experiments, or lack any support.[12] Homoallylic coupling and ASISs are useful stereochemical indicators for imines, imidates, and thioimidates,[32,33] and their applicability to iminoaziridines seems reasonable, but cannot be taken for granted, however. Obviously, these criteria cannot be applied when only a single diastereomer is observable.



16



17

High-field shifts of ^{13}C NMR signals by atoms in the γ-position are extremely valuable and diagnostically the most useful of all substituent effects in ^{13}C NMR spectroscopy.[34] In ^{13}C NMR spectra recorded for *N*-alkylketimines, Fraser et al. observed very pronounced upfield shifts of -6 to -12 ppm for α-carbons *syn* to the *N*-alkyl groups in comparison with the same carbon when *anti*.[35] These differences of chemical shifts are hereafter referred to as $\Delta_{sa} = \delta_{syn} - \delta_{anti}$. Jackman and Jen reported upfield shifts of $\Delta_{sa} = -2.0$ and -3.9 ppm for *E*/*Z* diastereomeric amidines, viz., 2-[*N*-(2,6-dichlorophenyl)imino]-pyrrolidine and -piperidine, respectively.[36] Similar observations in other classes of C=N compounds[37] nurtured hope that shift differences Δ_{sa} in *E*/*Z* pairs of iminoaziridines would support the stereochemical assignments based on homoallylic coupling and ASISs. However, scrutiny of the ^{13}C NMR spectra recorded for such pairs frustrated this expectation as shown by the Δ_{sa} values in Table 3, which indicate *downfield* shifts for the *syn*-carbons compared to the same carbons in *anti*-position to the group at the imino nitrogen.

The values of Δ_{sa} span a range of 8 ppm and show that the γ-effects of the groups at the imino nitrogens are *deshielding* in almost all cases provided that the configurations have been assigned correctly. However, if this condition is not met, the γ-effects would be normal and shielding as expected by analogy with imines,[35] amidines,[36] and other C=N compounds.[34,37] In view of this disturbing situation and the recent revival of interest in *syn*−*anti* isomerizations of imines,[38] we embarked on an NOE NMR study, which also allows unequivocal stereochemical assignment when only a single diastereomer is observable. We included the known iminoaziridines **1f**, **1g**,[4] **4e**,[11] **4h**,[4] and **5**.[13]

The ^1H NMR signals were assigned with the help of $^1H-^1H$ decoupling experiments and one-bond and long-range $^{13}C-^1H$ shift correlations. 1D NOESY experiments were performed after the relaxation times T_1 had been determined. The 1D NOESY experiment using **1g** was carried out at a temperature of -60 °C, because, at room temperature, irradiation with the resonance frequency of the *N*-methyl group enhanced the 3-H signal only negligibly although the observed NOE effect for the *tert*-butyl group at C-3 was indicative of the *E*-configuration. All 1D NOESY results confirmed that *the predominant diastereomers do possess the E-configuration in accordance with the homoallylic coupling and ASIS criteria*. In addition, the signal enhancements that were observed for the minor diastereomer of **4e** proved its *Z*-configuration. It is gratifying that these results lend credence to the experimentally very simple relative ASIS method. Therefore, only this method was used for the assignment of *E* and *Z* to the diastereomers of *exo*- and *endo*-**6**.

A literature search uncovered an unexpected dearth of data that parallel or may explain the unusual shift differences Δ_{sa} in Table 3.[32a,34,37,39] An early ^{13}C NMR and ASIS study of α/β-unsaturated *N*,*N*-disubstituted *N*′-phenylamidines reported small *deshielding* γ-effects (ca. 1 ppm) of the phenyl group.[40] ^{13}C NMR spectra of ethylidenecyclopropanes suggest that γ-effects in these three-membered ring compounds may become deshielding. Not only are the shielding γ-effects caused by the methyl group of ethylidenecyclopropanes much smaller than in comparable five-membered ring compounds, they even approach zero with increasing substitution of the ring carbons.[41] Indeed, the methyl groups of the (*E*)- and (*Z*)-ethylidenecyclopropanes that bear a hydroxymethyl and a *tert*-butyl group in *trans*-position at the ring fail to cause γ-effects; i.e., the value of Δ_{sa} is zero for both ring carbons.[42] It is in line with this admittedly scant data that the *N*-*tert*-butyl group in **1f** and the *N*-phenyl ring in **4n** give rise to the by far strongest deshielding effects.

^{15}N NMR Spectra of Iminoaziridines. So far, only ^{14}N NMR data of a single iminoaziridine[12] but no ^{15}N NMR spectra have been reported. The results of the first ^{15}N NMR study of iminoaziridines are listed in Table 4. Amino nitrogens N(sp^3) resonate by 100 ppm at higher field than double-bonded nitrogen atoms N(sp^2).[43] This allows the assignment of the two observed signals to the exocyclic (=NR^2) and ring nitrogens (>NR^1). The ranges of chemical shifts span more than 60 ppm and are found where they are to be expected by comparison with the few data reported for amidines.[44,45]

Resonance frequencies of ^{15}N NMR signals are shifted downfield by carbons in the β-position. These β-effects are particularly large for both types of nitrogen when an *N*-methyl group is exchanged for an *N*-isopropyl group; cf. (*E*)-**1c** vs (*E*)-**1f**, $\Delta\delta(NR^1) = 28$, and (*E*)-**4c** vs (*E*)-**4g**, $\Delta\delta(NR^2) = 49$ ppm. In contrast, replacement of an *N*-isopropyl with an *N*-*tert*-butyl

(32) (a) Martin, G. L.; Martin, M. L. *Prog. NMR Spectrosc.* **1972**, *8* (3), 163. (b) Nelson, D. A.; Atkins, R. L. *Tetrahedron Lett.* **1967**, 5197. (c) Kyba, E. P. *Tetrahedron Lett.* **1973**, 5117. (d) Meese, C. O.; Walter, W.; Berger, M. *J. Am. Chem. Soc.* **1974**, *96*, 2259. (e) Satterthwait, A. C.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 7045. (f) Walter, W.; Meese, C. O. *Chem. Ber.* **1976**, *109*, 922.

(33) (a) Karabatsos, G. J.; Lande, S. S. *Tetrahedron* **1968**, *24*, 3907. (b) Karabatsos, G. J.; Taller, R. A. *Tetrahedron* **1968**, *24*, 3923. (c) Rummens, F. H. A.; Krystynak, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 6914.

(34) Duddeck, H. *Top. Stereochem.* **1986**, *16*, 219.

(35) Fraser, R. R.; Banville, J.; Akiyama, F.; Chuaqui-Offermanns, N. *Can. J. Chem.* **1981**, *59*, 705.

(36) Jackman, L. M.; Jen, T. *J. Am. Chem. Soc.* **1975**, *97*, 2811.

(37) Perrin, C. L. In *The Chemistry of Amidines and Imidates*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, U.K., New York, 1991; Chapter 3.

(38) (a) Lehn, J.-M. *Chem.*−*Eur. J.* **2006**, *12*, 5910. (b) Amati, M.; Bonini, C.; D'Auria, M.; Funicello, M.; Lelj, F.; Racioppi, R. *J. Org. Chem.* **2006**, *71*, 7165. (c) Ammal, S. C.; Yamataka, H. *Eur. J. Org. Chem.* **2006**, 4327.

(39) (a) Eliel, E. L.; Pietrusiewicz, K. M. *Top. Carbon-13 Spectrosc.* **1979**, *3*, 171. (b) Hansen, P. E. In *Supplement A: The Chemistry of Double-Bonded Functional Groups*; Patai, S., Ed.; Wiley: New York, 1989; Vol. 2, Part 1, Chapter 3.

(40) Naulet, N.; Filleux, M. L.; Martin, G. J.; Pornet, J. *Org. Magn. Reson.* **1975**, *7*, 326.

(41) Crawford, R. J.; Tokunaga, H.; Schrijver, L. M. H. C.; Godard, J. C.; Nakashima, T. *Can. J. Chem.* **1978**, *56*, 992.

(42) Vincens, M.; Dumont, C., Vidal, M. *Tetrahedron* **1981**, *37*, 2683.

(43) Witanowski, M.; Stefaniak, L.; Webb, G. A. In *Annual Reports on NMR Spectroscopy*; Webb, G. A., Ed.; Academic Press: London, 1993; Vol. 25.

(44) Wawer, I. *Magn. Reson. Chem.* **1989**, *27*, 1031.

(45) Wiench, J. W.; Stefaniak, L.; Grech, E.; Bednarek, E. *J. Chem. Soc., Perkin Trans. 2* **1999**, 885.

TABLE 4. Chemical Shifts δ (ppm) (Relative to the Peak for Nitromethane as an External Standard) in 40.5 MHz ^{15}N NMR Spectra Recorded for Solutions of Iminoaziridines in [$^2H_6$]Benzene at a Temperature of 22 °C and Numbers of β- and γ-Effects That Exceed Those in (Hypothetical) (*E*)-(1-Methylaziridin-2-ylidene)-methylamine (17)

compd	$\delta(>NR^1)$	β	γ	$\delta(=R^2)$	β	γ
(*E*)-**1c**	−308.9	3	3	−132.1	2	1
(*E*)-**1d**	−309.5	3	7	−146.9	2	5
(*E*)-**1f**	−337.0	1	3	−123.5	3	1
(*E*)-**1g**	−300.5	4	3	−167.4	0	1
(*E*)-**1h**	−327.6	2	6	−126.4	3	1
(*E*)-**1i**	−300.2	4	3	−156.9	1	4
(*E*)-**4c**	−293.7	4	0	−142.9	2	2
(*E*)-**4e**	−306.2	3	3	−164.6	1	5
(*E*)-**4g**	−282.2	5	0	−191.9	0	2
(*E*)-**4h**	−311.2	3	3	−136.6	3	2
(*E*)-**5**	−273.8	5	4	−189.7	0	2

group results in only moderate downfield shifts; cf. (*E*)-**1g** vs (*E*)-**1c**, $\Delta\delta(NR^1) = 8.4$, (*E*)-**1i** vs (*E*)-**1c**, $\Delta\delta(NR^1) = 8.7$, (*E*)-**4g** vs (*E*)-**4c**, $\Delta\delta(NR^1) = 11.5$, (*E*)-**1h** vs (*E*)-**1c**, $\Delta\delta(NR^2) = 5.7$, (*E*)-**1f** vs (*E*)-**1c**, $\Delta\delta(NR^2) = 8.6$, and (*E*)-**4h** vs (*E*)-**4c**, $\Delta\delta(NR^2) = 6.3$ ppm. Obviously, the β-effects on both types of nitrogen in iminoaziridines cannot be represented by uniform increments as is true for amines.[46]

The upfield shifts by carbons in the γ-position vary even more strongly than the β-effects as is indicated by the effects of four γ-carbons when an *N*-isopropyl group is exchanged for an *N*-3-(2,4-dimethyl)pentyl group; cf. (*E*)-**1d** vs (*E*)-**1c**, $\Delta\delta(NR^1) = -0.6$, but $\Delta\delta(NR^2) = -14.8$ ppm. Four γ-carbons, together with the rest of the adamantane skeleton, may even result in a downfield shift; cf. (*E*)-**5** vs (*E*)-**4g**, $\Delta\delta(NR^1) = 8.4$ ppm. By contrast with other classes of compounds, neither generally applicable β- nor such γ-increments are conceivable that might permit estimates of ^{15}N NMR chemical shifts of iminoaziridines.

Conclusion

Iminoaziridines with a broad range of substituents at the ring carbon C-3 are readily available in three steps from α-halocarboxamides and in quantities useful for syntheses. Nevertheless, their preparation requires too great an effort to make them competitive in cases where commercially available components of the Ugi and related MCRs suffice; however, steric hindrance in the four-component systems or the need for stereochemically defined products may render iminoaziridines the building blocks of choice due to their high reactivity and the stereocenter C-3, which is untouched in the formation of Ugi and similar MCR products.[2] NMR evidence unequivocally demonstrates the *E*-configuration for the major diastereomers, in contradiction to the assignments based on normal γ-effects. Therefore, caution is recommended when γ-effects are to be employed as stereochemical indicators for three-membered rings with an exocyclic double bond. The observed effects of carbons in β- and γ-positions on the ^{15}N NMR chemical shifts of iminoaziridines do not follow a uniform increment pattern, neither for the ring nitrogen nor for the exocyclic nitrogen atom.

Experimental Section

α-Bromoimidoyl chlorides **7**[15] and **10**[15] and iminoaziridines **1f**, **1g**,[4] **4e**,[11] **4h**,[4] and **5**[13] were prepared as described in the literature. Synthetic procedures for α-bromoamidines and α-haloamidinium salts, elemental analyses, ^{1}H and ^{13}C NMR chemical shifts, ^{1}H NMR spectra (**6**, **13c**, **15**·HCl), and ^{13}C−^{1}H one-bond shift correlation diagrams (*endo*-**13a**, **13c**, **15**·HCl) are given in the Supporting Information.

Reactions were carried out in flame-dried glassware under an atmosphere of argon or nitrogen. Potassium *tert*-butoxide was sublimed twice at 10^{-2} Torr and handled under argon. Diethyl ether and THF were distilled from a sodium−potassium alloy. KH was purified as described in the literature.[47] Petroleum (pet) ether had a boiling range of 50−70 °C. Iminoaziridines were distilled under high vacuum (10^{-2} to 10^{-6} Torr) in a short-path distillation apparatus (condensor and receiver at −20 to −70 °C) or in a sublimation apparatus equipped with a magnetic stirring bar and a cold finger whose temperature was sufficiently low to render the distilled product highly viscous. Fractionating distillations were carried out on a 20 cm Spaltrohr column (Fischer, D-53340 Meckenheim, Germany). Iminoaziridines were stored at −20 °C in sealed glass tubes or under argon. ^{1}H NMR data of new iminoaziridines **1** and **4** are found in Table 5. ^{13}C NMR chemical shifts of the spirocyclic iminoaziridines **6** are listed in Table 6.

Iminoaziridine 1c. Method A. α-Bromoamidine **9c** (13.9 g, 50 mmol) was added dropwise within 0.5 h to a stirred solution of potassium *tert*-butoxide (11.2 g, 0.10 mol) in diethyl ether (250 mL). Stirring was continued for 1 h followed by addition of pentane (100 mL) and distillation of the solvent under vacuum The residue was suspended in pentane (120 mL). The solvent was distilled under vacuum and the residue suspended again in pentane (100 mL). The solid material was removed by filtration and washed with pentane. The cooled (0 °C) filtrate was washed with ice−water (4 × 30 mL) and dried with K_2CO_3. Distillation of the solvent under vacuum and the remaining liquid (bath temperature 15−20 °C) afforded a colorless oil (bp 15−18 °C/5 × 10^{-3} Torr, 8.34 g, 85%). MS (EI 70 eV): *m*/*z* (rel intens) = 196 (1.4) [M^+], 181 (1.0), 153 (1.8), 140 (0.7), 127 (40) [M^+ − *i*-PrNC], 112 (58), 111 (40), 84 (10) 70 (100). ^{13}C NMR [(*E*)-**1c**] ([$^2H_6$]benzene, 100 MHz): δ = 21.97 (CH_3), 22.30 (CH_3), 24.99 (CH_3), 25.70 (CH_3), 27.64 (3 CH_3, *t*-Bu), 30.76 (quat C), 54.40 (CH), 56.18 (CH), 56.54 (CH), 151.90 (quat C).

Method B. A stirred suspension of NaH (4.8 g, 0.20 mol) in a solution of **9c** (5.55 g, 20 mmol) in THF (100 mL) was heated under reflux for 24 h. The solvent was distilled under vacuum followed by workup as described (method A) to afford a colorless oil (2.94 g, 75%).

Iminoaziridine 1d. α-Bromoamidine **9d** (11.7 g, 30 mmol) was added dropwise to a stirred solution of potassium *tert*-butoxide (6.7 g, 60 mmol) in THF (200 mL). Stirring was continued for 15 h followed by distillation of the solvent under vacuum The suspension of the residue in pet ether (150 mL) was stirred for 5 h. Workup as described for **1c** yielded a yellow oil which was distilled (bath temperature 95−100 °C) to afford a colorless oil (bp 76−80 °C/10^{-4} Torr, 7.83 g, 79%). The analytical sample was distilled again (bp 68−70 °C/8 × 10^{-5} Torr). MS (EI 70 eV): *m*/*z* (rel intens) = 308 (0.1) [M^+], 293 (0.1), 265 (1.0), 209 (0.4), 195 (0.2), 183 (1.5) [$M^+ - C_7H_{15}NC$], 168 (1.0), 167 (1.4), 140 (100). ^{13}C NMR [(*E*)-**1d**] ([$^2H_6$]benzene, 100 MHz): δ = 17.36 (CH_3), 17.81 (CH_3), 19.86 (CH_3), 19.91 (CH_3), 20.04 (CH_3), 20.70 (CH_3), 21.64 (CH_3), 23.97 (CH_3), 27.28 (CH), 27.92 (3 CH_3, *t*-Bu), 30.13 (CH), 30.96 (CH), 31.80 (quat C), 31.86 (CH), 56.81 (CH), 75.25 (CH), 76.37 (CH), 151.96 (quat C).

Iminoaziridine 1h. α-Bromoamidine **9e** (6.39 g, 20 mmol) was added dropwise to a stirred solution of potassium *tert*-butoxide (6.72 g, 60 mmol) in THF (120 mL) kept at 0 °C followed by stirring for 0.5 h at that temperature, addition of pentane (200 mL), and workup as described for **1c**. Distillation of the remaining liquid (bath temperature 30−35 °C) afforded a colorless oil (3.88 g, 81%, bp 20−25 °C/10^{-3} Torr) which contained small amounts of *tert*-butyl isocyanide and *N*-(2,2-dimethylpropylidene)-2,2-dimethyl-

(46) Duthaler, R. O.; Roberts, J. D. *J. Am. Chem. Soc.* **1978**, *100*, 3889.

(47) Macdonald, T. L.; Natalie, K. J., Jr.; Prasad, G.; Sawyer, J. S. *J. Org. Chem.* **1986**, *51*, 1124.

TABLE 5. Chemical Shifts (ppm) (Relative to the Peak for TMS) and $^1H-^1H$ Coupling Constants *J* (Hz) (in Italics) in 400 MHz ^1H NMR Spectra Recorded for Solutions of Iminoaziridines in [$^2H_6$]Benzene[a]

compd	*t*-Bu	CH	>NR[1]	=NR[2]
(*E*)-**1c**	0.88	1.64	*i*-Pr: 0.93 (d, 6.3, Me), 1.31 (d, *6.4*, Me), 2.23 (sept, *6.4*, 1 H)	*i*-Pr: 1.22 (d, *6.4*, Me), 1.24 (d, *6.3*, Me), 3.44 (sept, *6.3*, 1 H)
(*E*)-**1d**	0.96	1.86	CH(*i*-Pr)$_2$: 0.87 (d, *6.6*), 0.99 (d, *6.9*), 1.26 (d, *7.0*), 1.29 (d, *6.8*) (4 Me), 1.81 (sept d, *3.2*, *6.9*, 1 H), 1.91−2.02 (m, 2 H)	CH(*i*-Pr)$_2$: 0.85 (d, *6.6*), 0.93 (d, *6.8*), 1.01 (d, *6.9*), 1.07 (d, *6.6*) (4 Me), 1.96 (m, 1 H), 2.06 (oct, *6.8*, 1 H), 2.64 (dd, *4.9*, *7.0*, 1 H)
(*E*)-**1f**	0.91	1.51	Me: 2.35	*t*-Bu: 1.29
(*E*)-**1g**[b]	0.88	2.03	*t*-Bu: 1.06	Me: 3.14
(*Z*)-**1g**[b]	0.93	2.07	*t*-Bu: 0.95	Me: 3.16
(*E*)-**1h**	0.94	1.70	CH$_2$-*t*-Bu: 1.05 (*t*-Bu), 2.25, 2.35 (2 d, *11.3*, CH$_2$)	*t*-Bu: 1.30
(*E*)-**1i**[c]	0.90	2.04	*t*-Bu: 1.08	CH$_2$-*t*-Bu: 1.02 (*t*-Bu), 3.04, 3.23 (2 d, *11.6*, CH$_2$)

compd	Me$_2$C	>NR[1]	=NR[2]
4b[d]	1.27	CH$_2$Ph: 4.04 (CH$_2$), 7.2−7.4 (m, Ph)	CH$_2$Ph: 4.56 (CH$_2$), 7.2−7.4 (m, Ph)
	1.42	CH$_2$Ph: 4.10 (CH$_2$)	CH$_2$Ph: 4.51 (CH$_2$)
(*E*)-**4c**	1.12	*i*-Pr: 1.16 (d, *6.4*, 2 Me), 2.61 (sept, *6.3*, 1 H)	*i*-Pr: 1.21 (d, *6.4*, 2 Me), 3.49 (sept, *6.4*, 1 H)
(*E*)-**4e**	1.09	CH$_2$-*t*-Bu: 0.92 (*t*-Bu), 2.45 (CH$_2$)	CH$_2$-*t*-Bu: 1.06 (*t*-Bu), 3.19 (CH$_2$)
(*Z*)-**4e**	1.10	CH$_2$-*t*-Bu: 0.87 (t-Bu), 2.54 (CH$_2$)	CH$_2$-*t*-Bu: 1.11 (*t*-Bu), 3.32 (CH$_2$)
4f[e]	1.35	Me: 2.44	*t*-Bu: 1.28
(*E*)-**4g**[e]	1.41	*t*-Bu: 1.21	Me: 2.99
(*Z*)-**4g**[e]		*t*-Bu: 1.13	Me: 3.04
4f[f]	1.03	Me: 2.35	*t*-Bu: 1.20
(*E*)-**4g**[f]	1.19	*t*-Bu: 1.16	Me: 3.10
(*Z*)-**4g**[f]	1.22	*t*-Bu: 1.07	Me: 3.15
(*E*)-**4h**	1.06	CH$_2$-*t*-Bu: 0.87 (*t*-Bu), 2.34 (CH$_2$)	*t*-Bu: 1.17
4j[g]	1.31	*t*-Bu: 1.27	CH$_2$Ph: 4.40 (CH$_2$), 7.22 (m, Ph)
(*E*)-**5**[h]		t-Bu: 1.31	Me: 3.26
(*Z*)-**5**[h]		*t*-Bu: 1.18	Me: 3.21

[a] Signals are singlets unless described otherwise. [b] (*E*)-**1g**:(*Z*)-**1g** = 10:1; the *tert*-butyl signals of (*Z*)-**1g** may be exchanged. [c] **1h**:**1i** = 11:9. [d] Solution in [^{2}H]chloroform, 90 MHz; first row, major diastereomer; second row, minor diastereomer; ratio 3:2. [e] Neat liquid, 90 MHz; **4f**:**4g** = 1:9; (*E*)-**4g**:(*Z*)-**4g** = 7:3. [f] **4f**:**4g** = 1:4; (*E*)-**4g**:(*Z*)-**4g** = 3:1. [g] Solution in CCl_4, 60 MHz. [h] (*E*)-**5**:(*Z*)-**5** = 10:1. Adamantane protons of (*E*)-**5**: 1.60−1.64 (m, 4 H), 1.69 (br d, *12.0*, 2 H), 1.72−1.78 (m, 3 H), 1.83 (br m, 1 H), 1.93 (br d, *12.0*, 2 H), 2.00 (br d, *12.0*, 2 H). Adamantane protons of (*Z*)-**5**: 1.84 (br m), 2.00 (d), further signals hidden under those of (*E*)-**5**.

TABLE 6. Chemical Shifts (ppm) (Relative to the Peak for TMS) in ^{13}C NMR Spectra Recorded for Solutions of Iminoaziridines 6 in [$^2H_6$]Benzene

compd	C=N	NMe	C-1	C-2	C-3	C-4	C-5	C-6	C-7
(*E*)-*exo*-**6**[a]	158.8	32.8, 40.8	44.4	57.8	33.4	36.5	28.60	26.7	37.4
(*Z*)-*exo*-**6**[a]	158.3	33.1, 37.8	43.2	56.2	34.8	36.9	28.39	25.4	38.1
(*E*)-*endo*-**6**[b]	160.0	34.90, 40.5	42.5	57.1	31.35	36.85	28.77	24.70	38.91
(*Z*)-*endo*-**6**[b]	159.4	35.08, 38.0	42.9	56.6	31.58	36.60	28.77	24.75	38.54

[a] 50 MHz. [b] 151 MHz; (*E*)-*endo*-**6**:(*Z*)-*endo*-**6** = 5:4.

propylamine[23] (^1H NMR). These decomposition products of **1h** were removed by distillation through a 20 cm Spaltrohr column at a pressure of 10^{-3} Torr. ^{13}C NMR [(*E*)-**1h**] ([$^2H_6$]benzene, 100 MHz): δ = 27.09 (3 CH_3, CH-*t*-Bu), 28.28 (3 CH_3, CH_2-*t*-Bu), 31.55 (3 CH_3, *N*-*t*-Bu), 32.27 (quat C, CH_2-*t*-Bu), 32.35 (quat C, CH-*t*-Bu), 54.19 (quat C, *N*-*t*-Bu), 57.56 (CH), 69.54 (CH_2), 150.29 (quat C).

Iminoaziridines 1h and 1i. A stirred suspension of NaH (4.8 g, 0.20 mol) in a solution of **9e** (12.8 g, 40 mmol) in THF (200 mL) was heated under reflux for 9 h. The solvent was distilled under vacuum followed by workup as described for **1c** to afford a pale yellow oil which was distilled (bath temperature 40 °C) through a 20 cm Spaltrohr column to give a colorless oil (5.42 g, 57%, bp 20−25 °C/10^{-3} Torr) which contained **1h** and **1i** (85:15) and small amounts of *tert*-butyl isocyanide and *N*-(2,2-dimethylpropylidene)-2,2-dimethylpropylamine[23] (^1H NMR). A second distillation through a 20 cm Spaltrohr column at a pressure of 10^{-3} Torr yielded pure **1h**. The amount of **1i** in the 85:15 mixture was enriched by partial thermolysis of **1h** at 80 °C followed by fractionating distillation to afford a mixture with **1h**:**1i** = 55:45. ^{13}C NMR [(*E*)-**1i**] ([$^2H_6$]benzene, 100 MHz): δ = 27.05 (3 CH_3, *N*-*t*-Bu), 27.82 (3 CH_3, CH-*t*-Bu), 28.23 (3 CH_3, CH_2-*t*-Bu), 30.84 (quat C, CH-*t*-Bu), 32.57 (quat C, CH_2-*t*-Bu), 49.47 (CH), 54.76 (quat C, *N*-*t*-Bu), 68.29 (CH_2), 150.12 (quat C).

Iminoaziridine 1k. α-Bromoamidine **9f** (14.7 g, 40 mmol) was added to a stirred solution of potassium *tert*-butoxide (5.6 g, 50 mmol) in diethyl ether (200 mL) kept at −50 °C. The mixture was allowed to warm to −15 °C within 10 h and stirred at that temperature for 0.5 h. Addition of cold pet ether (−70 °C, 100 mL) was followed by washing with a strongly cooled aqueous solution of K_2CO_3 (0.5 m, 3 × 100 mL) and drying of the cold (−30 °C) organic layer with K_2CO_3. The solvent was distilled at −20 °C/10^{-2} Torr (receiver cooled with liquid N_2) and the solid residue recrystallized from pentane at −20 °C to afford colorless crystals (9.4 g, 82%) which decomposed above 0 °C into *tert*-butyl isocyanide and *N*-(2,2-dimethylpropylidene)mesitylamine[22] (^1H NMR).

Iminoaziridine 4a. 3-Ethylpentan-3-ol (2.65 g, 25 mmol) was added dropwise to a stirred suspension of KH (4.0 g, 0.10 mol) in pentane (100 mL). Stirring was continued for 20 min followed by addition of **11a**·HCl (4.59 g, 20 mmol) in small portions. After stirring of the mixture for 2 h, the solid material was removed by filtration and washed with pentane. Most of the solvent was removed by distillation through a 50 cm Vigreux column at a pressure of 150 Torr. Benzene (5 mL) was added to the concentrated solution. Distillation at a pressure of 10^{-2} Torr (bath temperature 20 °C) afforded a colorless liquid (1.81 g) which consisted of **4a** and benzene (3:7, ^1H NMR), yield 32%. The product was identical with thermally equilibrated samples prepared via two different photochemical routes (IR, ^1H and ^{13}C NMR).[8a,9]

Iminoaziridine 4b. A solution of potassium *tert*-butoxide (2.69 g, 24 mmol) in THF (20 mL) was added dropwise to a stirred

mixture of **11b**·HCl (3.82 g, 10 mmol) in THF (40 mL) cooled at −25 °C. Stirring was continued for 4 h followed by the addition of pentane (100 mL). The solid was removed by filtration and the filtrate washed twice with ice−water and dried with K_2CO_3. Distillation of the solvent under vacuum and the residue in a sublimation apparatus at 4×10^{-6} Torr/bath temperature 45 °C afforded a colorless, viscous oil (1.16 g, 44%).

Iminoaziridine 4c. Method A. α-Bromoamidinium perchlorate **11c**·$HClO_4$ (14.0 g, 40 mmol) was added to a stirred solution of potassium *tert*-butoxide (22.4 g, 0.20 mol) in diethyl ether (250 mL). The suspension was stirred for 2 d followed by addition of pentane (200 mL) and workup as described for **1c.** Distillation of the remaining liquid afforded a colorless oil (bath temperature 8−12 °C, receiver −78 °C, bp < 10 °C/10^{-3} Torr, 5.7 g, 85%). MS (EI 70 eV): *m*/*z* (rel intens) = 168 (1.1) [M^+], 153 (0.4), 132 (0.5), 125 (1.9), 112 (0.5), 100 (4.4), 99 (2.1) [M^+ − *i*-PrNC], 84 (100), 83 (66). ^{13}C NMR [(*E*)-**4c**] ([$^2H_6$]benzene, 100 MHz): δ = 20.88 (2 CH_3), 23.17 (2 CH_3), 25.32 (2 CH_3), 44.56 (quat C), 50.41 (CH), 54.72 (CH), 155.82 (quat C).

Method B. α-Bromoamidinium perchlorate **11c**·$HClO_4$ (14.0 g, 40 mmol) was added in small portions to a stirred suspension of NaH (4.8 g, 0.20 mol) in THF (100 mL). Stirring was continued for 1 h followed by addition of pet ether (100 mL) and workup as described for **1c** to afford a colorless oil (5.8 g, 86%).

Iminoaziridines 4f and 4g.[48] α-Bromoimidoyl chloride **10a** (19.9 g, 0.10 mol) was added dropwise within 1 h to stirred dry **8e** (300 mL) cooled at 0 °C. Stirring at 0 °C was continued for 3 d and the mixture allowed to attain rt. The solid material (*tert*-butylammonium halides, 38.4 g) was removed by filtration and washed with *tert*-butylamine. The solvent was distilled under vacuum followed by addition of pet ether (200 mL) and removal of the solid material by filtration. Distillation of the solvent under vacuum and the residue through a 20 cm Spaltrohr column (bath temperature 15−20 °C, condensor and receiver −30 °C, bp < 15 °C/10^{-2} Torr) afforded a colorless liquid (11.0 g, 71%) which consisted of **4f** and **4g** (8:92, ^{1}H NMR). ^{13}C NMR [(*E*)-**4g**] ([$^2H_6$]benzene, 100 MHz): δ = 22.74 (2 CH_3), 29.02 (3 CH_3, *t*-Bu), 40.24 (CH_3), 46.03 (quat C), 56.20 (quat C), 152.61 (quat C).

Iminoaziridine 4j was prepared from a mixture of **11h**·HCl and **12h**·HBr according to the procedure given for **4b**. Sublimation at 10^{-5} Torr/bath temperature 20 °C afforded pale yellow crystals (0.65 g, 28%). Recrystallization from pentane gave colorless crystals, mp 29−30 °C.

Spirocyclic Iminoaziridine *exo*-6. A suspension of *endo*-**15**·HCl (2.37 g, 10 mmol) and KH (2.0 g, 50 mmol) in diethyl ether (160 mL) was stirred in a 250 mL round-bottom flask equipped with an argon inlet, a magnetic stirring bar, and a glass sinter funnel. Deprotonation of *endo*-**15**·HCl to yield *endo*-**15** was shown by the emerging IR band at 1634 cm^{-1}. Addition of 18-crown-6 (80 mg, 0.3 mmol) after 2 h triggered gas evolution (H_2) with concomitant formation of *exo*-**6** (IR: 1795 cm^{-1}). Stirring was continued until the IR band at 1634 cm^{-1} had disappeared (ca. 2 h). The solid material was allowed to settle, removed by filtration, and washed with pentane. The cooled (0 °C) filtrate was washed with ice−water and dried with K_2CO_3. The solvent was distilled under vacuum to afford a pale yellow oil. Distillation yielded a colorless oil (bath temperature 38−40 °C, bp 34−35 °C/10^{-3} Torr, 985 mg, 60%), *E*:*Z* = 48:52 (^{1}H NMR). Redistillation afforded the analytical sample. ^{1}H NMR (600 MHz, [$^2H_6$]benzene): δ = 0.90−1.03 (dm, 1 H, 7-H_{anti}), 1.04−1.10 (m, 1 H), 1.10−1.17 (m, ca. 0.5 H), 1.22−1.39 (m, 4 H), 1.45−1.50 (m, ca. 0.5 H, 3-H_{exo} of *E*-isomer), 1.57−1.62 (m, ca. 0.5 H, 3-H_{exo} of *Z*-isomer), 1.68−1.74 (m, ca. 0.5 H, 6-H_{endo}), 2.04−2.09 (m, ca. 1.5 H), 2.105 (br d, *J* = 4.1 Hz, ca. 0.5 H), 2.23 (s, >NCH_3 of *Z*-isomer), 2.26 (s, >NCH_3 of *E*-isomer), 3.20 (s, =NCH_3 of *Z*-isomer), 3.21 (s, =NCH_3 of *E*-isomer). ^{1}H NMR (200 MHz, [^{2}H]chloroform): δ = 1.25−1.9 (m, 8 H), 2.19 (m, 1 H, 4-H), 2.42−2.54 (m, 1-H, 1-H), 2.47 (s, >NCH_3 of *E*-isomer), 2.58 (s, >NCH_3 of *Z*-isomer), 3.17 (s, =NCH_3 of *Z*-isomer), 3.19 (s, =NCH_3 of *E*-isomer).

Spirocyclic Iminoaziridine *endo*-6. According to the procedure described for *exo*-**6**, a colorless oil was obtained (bp 35 °C/10^{-3} Torr, 936 mg, 57%), *E*:*Z* = 55:44. ^{1}H NMR (600 MHz, [$^2H_6$]benzene): δ = 1.03−1.14 (m, ca. 3 H, 3-H of *E*-isomer, 3-H_{endo} of *Z*-isomer, 5-H, 7-H_{anti}), 1.29−1.39 (m, ca. 2.5 H, 3-H of *E*-isomer, 5-H, 6-H_{exo}), 1.39−1.44 (m, ca. 0.5 H, 7-H_{syn} of *E*-isomer), 1.50−1.54 (m, ca. 0.5 H, 7-H_{syn} of *Z*-isomer), 1.59−1.64 (m, ca. 0.5 H, 3-H_{exo} of *Z*-isomer), 1.70−1.75 (m, 1 H, 6-H_{endo}), 1.93−1.95 (m, ca. 0.5 H, 1-H of *E*-isomer), 1.99−2.03 (m, 1 H, 4-H), 2.04−2.08 (m, ca. 0.5 H, 1-H of *Z*-isomer), 2.265 (s, ca. 1.5 H, >NCH_3 of *Z*-isomer), 2.335 (s, ca. 1.5 H, >NCH_3 of *E*-isomer), 3.164 (s, ca. 1.5 H, =NCH_3 of *E*-isomer), 3.166 (s, ca. 1.5 H, =NCH_3 of *Z*-isomer). ^{1}H NMR (200 MHz, [^{2}H]chloroform): δ = 1.3−1.9 (m, 8 H), 2.11 (br s) 2.35−2.47 (m) ($\sum$ = 2 H, 1-H, 4-H), 2.57 (s, >NCH_3 of *E*-isomer), 2.66 (s, >NCH_3 of *Z*-isomer), 3.154 (s, =NCH_3 of *E*-isomer), 3.159 (s, =NCH_3 of *Z*-isomer).

Thermal Stability. Neat iminoaziridines **1c** and **1d** contained in degassed sealed NMR sample tubes were heated while thermolysis into isocyanide and imine was monitored by ^{1}H NMR spectroscopy. Decomposition was complete after 12 h at 100 °C and 20 h at 120 °C. Heating of a neat mixture of **1h** and **1i** (85:15) for 21 h at 80 °C resulted in complete thermolysis of **1h** into *tert*-butyl isocyanide and *N*-(2,2-dimethylpropylidene)-2,2-dimethylpropyl)amine,[23] whereas **1i** remained unchanged. A solution of *endo*-**6** in [$^2H_6$]benzene did not change during 0.5 h at a temperature of 83 °C.

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Supporting Information Available: General experimental procedure, experimental procedures and ^{1}H and ^{13}C NMR data for α-bromoamidines, α-haloamidinium salts, and 2-chloronorbornane derivatives **13**−**15**·HCl, ^{13}C NMR chemical shifts of **1f**, **1g**, **4e**, **4h**, and **5**, elemental analyses, and 14 figures showing ^{1}H NMR spectra of **6** and ^{1}H NMR spectra and ^{13}C−^{1}H correlation diagrams of *endo*-**13a**, **13c**, and **15**·HCl. This material is available free of charge via the Internet at http://pubs.acs.org.

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