Radical Cations of Trialkylamines: ESR Spectra and Structures

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Novel syntheses of cyclopropyldiisopropylamine (**15**), di-*tert*-butylcyclopropylamine (**16**), dicyclopropylisopropylamine (**17**), and tricyclopropylamine (**18**) are described. Hyperfine data were determined by ESR spectroscopy for the radical cations of these trialkylamines, as well as for those of ethyldiisopropylamine (**10**), diisopropyl-*n*-propylamine (**11**), dicyclohexylethylamine (**12**), diisopropyl-3-pentylamine (**14**), and 1-azabicyclo[3.3.3]undecane (manxine; **27**). The radical cation of triisopropylamine (**13**) was reexamined under conditions of improved spectral resolution. Coupling constants of the ^{14}N nucleus and the β-protons in the radical cations of 18 trialkylamines provide reliable information about the geometries of these species, which are confirmed by theoretical calculations. With the exception of a few oligocyclic amines, for which flattening is impaired by the rigid molecular framework, all of the radical cations should be planar. Correlation between the observed coupling constants of the β-protons and the calculated $<\cos^2\theta>$ values of the dihedral angle θ, defining the conformation of the alkyl substituent or the azacycloalkane, is verified. Upon oxidation, striking changes occur for those amines that have cyclopropyl substituents, because of the tendency of these groups to assume a perpendicular conformation in the neutral amines and a bisected orientation in the corresponding radical cations.

Introduction

Ammonia (**1**) is the simplest neutral molecule of pyramidal geometry and of C_{3v} symmetry.[1] Ionization of its N-lone pair requires an energy IE_v of 10.88 eV.[2,3] The radical cation $\mathbf{1}^{\bullet+}$ thus generated is planar and of D_{3h} symmetry, according to ESR-spectroscopic evidence[4,5] and theoretical calculations.[6] Because of the relatively high IE_v value of **1** and the poor persistence of $\mathbf{1}^{\bullet+}$, conversion of ammonia into its radical cation was performed in the solid state by γ-irradiation of a single crystal[4] or a polycrystalline powder[5] of NH_4ClO_4. Later on, an isotropic ESR spectrum of $\mathbf{1}^{\bullet+}$, generated by photoionization of **1** in a neon matrix at 4 K, was observed.[7]

Alkyl substitution on **1** and/or incorporation of ammonia into a cycle lowers the ionization energy of **1**[3,8−11] and enhances the persistence of the corresponding radical cation, so that the radical cations of diverse acyclic and oligocyclic amines could be studied by ESR spectroscopy in fluid solution or Freon matrices. In the following, a brief account of these studies is presented without claiming comprehensiveness.[12]

The majority of the radical cations in question were generated by UV-photolysis in strongly acidic solutions. This procedure was used for dimethylamine (**3**), diethylamine (**4**), di-*n*-propylamine (**5**), diisopropylamine (**6**), and *tert*-butylmethylamine (**7**) in 90% H_2SO_4,[13] for **3** and 2,2,6,6-tetramethylpiperidine (**22**) in CF_3COOH,[14] and for trimethylamine (**8**), 1-azabicyclo[2.2.1]heptane (1-azanorbornane, **24**), 1-azabicyclo[2.2.2]octane (quinuclidine, **25**), and 1-azatricyclo[3.3.1.1^{3,7}]decane (1-azaadamantane, **26**) in CF_3SO_3H.[15] Radical cations of **3** and **8** were also produced by steady-state radiolysis of the corresponding amines in aqueous $HClO_4$.[16] Generation of more persistent radical cations, such as those of triisopropylamine (**13**)[17] and 9-*tert*-butylazabicyclo[3.3.1]nonane (**23**),[18]

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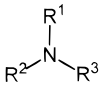
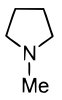
required less rigorous methods. These amines were oxidized in dichloromethane with SbF_5 and $(p\text{-}BrC_6H_4)_3N^{\bullet+}\text{-}SbCl_6^-$, respectively.

With the advent of γ-irradiation of organic compounds in Freon matrices at 77 K as a method of generating radical cations,[19] this treatment was applied to several amines in frozen $CFCl_3$, namely to methylamine (**2**),[20] **8**,[21] and triethylamine (**9**),[21] as well to azetidine (**19**),[22] *N*-methylpyrrolidine (**20**),[21] and *N*-methylpiperidine (**21**).[21] Recently, the radical cations were also produced from tricyclopropylamine (**18**)[23] and 10-azatricyclo[5.2.1.$0^{4,10}$]-decane (azatriquinane; **28**)[24] by γ-rays in a $CF_2ClCFCl_2$ matrix.



	R^1	R^2	R^3		R^1	R^2	R^3	
1	H	H	H	**10**	Et	*i*-Pr	*i*-Pr	
2	Me	H	H	**11**	*n*-Pr	*i*-Pr	*i*-Pr	*c*-Hx =
3	Me	Me	H	**12**	Et	*c*-Hx	*c*-Hx	cyclohexyl
4	Et	Et	H	**13**	*i*-Pr	*i*-Pr	*i*-Pr	
5	*n*-Pr	*n*-Pr	H	**14**	3Pn	*i*-Pr	*i*-Pr	3Pn =
6	*i*-Pr	*i*-Pr	H	**15**	*c*-Pr	*i*-Pr	*i*-Pr	3-pentyl
7	Me	*t*-Bu	H	**16**	*c*-Pr	*t*-Bu	*t*-Bu	
8	Me	Me	Me	**17**	*c*-Pr	*c*-Pr	*i*-Pr	*c*-Pr =
9	Et	Et	Et	**18**	*c*-Pr	*c*-Pr	*c*-Pr	cyclopropyl

19



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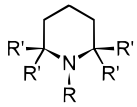
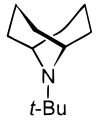


21 R = Me; R' = H
22 R = H; R' = Me



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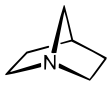

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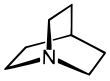

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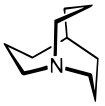

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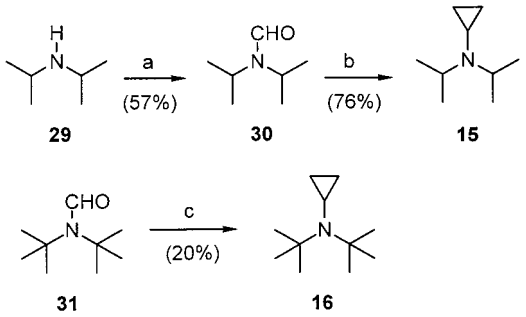
In the present work, we have extended the ESR studies to the radical cations of further acyclic and oligocyclic trialkylamines, i.e., those amines that contain three C−N single bonds. These compounds are ethyldiisopropylamine (**10**), diisopropyl-*n*-propylamine (**11**), dicyclohexylethylamine (**12**), diisopropyl-3-pentylamine (**14**), cyclopropyldiisopropylamine (**15**), di-*tert*-butylcyclopropylamine (**16**), dicyclopropylisopropylamine (**17**), and 1-azabicyclo[3.3.3]undecane (manxine, **27**). The ESR spectrum of the radical cation of triisopropylamine (**13**) has been reexamined. The interest is focused on the geometry of the radical cations, in particular on the planarity and on the conformation of alkyl substituents.

Scheme 1. Syntheses of Cyclopropyldiisopropylamine (15) and Di-*tert*-butylcyclopropylamine (16)[a]



[a]Key: (a) $CHCl_3$, 36% NaOH, cat. NBu_4Cl, CH_2Cl_2, reflux, 4 h; (b) 6 equiv of EtMgBr, 3 equiv of $Ti(O\text{-}i\text{-}Pr)_4$, THF, reflux, 3 d; (c) same as (b) but 10 d.

Results

Source of Compounds. The acyclic trialkylamines **10**−**12** and **14** are commercially available (Aldrich, Gold Label); they were purified before use. The tertiary amine **13**[17,25] and the bicyclic amine **27**[26] were prepared according to literature procedures.

The syntheses of the new tertiary cyclopropylamines **15**−**18** were achieved by appropriate adaptations of the previously developed,[27] titanium-mediated cyclopropanation of carboxylic acid dialkylamides. Diisopropylformamide (**30**), which is easily available from commercial diisopropylamine (**29**) by formylation with dichlorocarbene,[28] afforded cyclopropyldiisopropylamine (**15**) in good yield (76%) by treatment with the ethylmagnesium bromide/titanium tetraisopropoxide reagent at reflux temperature. On the other hand, the cyclopropanation of the more sterically congested di-*tert*-butylformamide (**31**)[29] with the same reagent was achieved only upon heating to give di-*tert*-butylcyclopropylamine (**16**), yet in low yield (20%) (Scheme 1). Thus, the success of this reaction, unlike any other one, demonstrates the high versatility of this titanium-mediated cyclopropanation of acid dialkylamides and its potential for the synthesis of even the most sterically congested and, not otherwise accessible, tertiary cyclopropylamines such as **16**.

A similar formylation−cyclopropanation sequence as for **15** was used to convert cyclopropylisopropylamine (**33**) to dicyclopropylisopropylamine (**17**) (Scheme 2). The secondary amine **33** was prepared in excellent yield by reductive amination of acetone with cyclopropylamine (**32**), applying as reducing agent sodium cyanoborohy-

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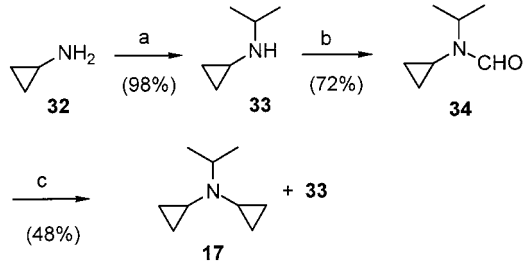
Scheme 2. Synthesis of Dicyclopropylisopropylamine (17)[a]



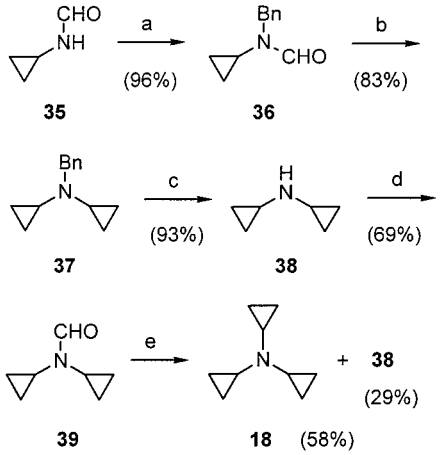
[a]Key: (a) Me_2CO, $NaBH_3CN$, HCl, CH_3OH, rt, 2 h; (b) $CHCl_3$, NaOH, H_2O, CH_2Cl_2, 40 °C, 4 h; (c) 2.3 equiv of EtMgBr, 1.3 equiv of Ti(O-*i*-Pr)$_4$, THF, rt, 3 d.

dride[30] rather than catalytic hydrogenation over platinum as previously reported (65% yield).[31] The crude hydrochloride of **33** was pure enough to be used for the formylation in the next step without purification. The cyclopropanation of the formyl group in **34** was achieved in 48% yield.

The preparation of tricyclopropylamine (**18**) required more steps, yet followed the same sequence of formylation of a secondary amine with dichlorocarbene and titanium-mediated cyclopropanation of the formyl group. A suitable starting material, benzylcyclopropylformamide (**36**), was prepared by benzylation of cyclopropylformamide (**35**)[32] with benzyl bromide after deprotonation with sodium hydride. Cyclopropanation of **36** by treatment with the ethylmagnesium bromide/titanium tetraisopropoxide reagent at ambient temperature produced the benzyldicyclopropylamine (**37**) (83%). Performing this reaction at elevated temperature led to the formation of significant quantities of the interesting byproduct, benzylcyclopropyl(3-pentyl)amine, apparently by transfer of two ethyl groups from the Grignard reagent onto the formyl group of **36** (probably mediated by the titanium tetraisopropoxide).[33] Removal of the benzyl group by catalytic hydrogenation over Pd/C gave dicyclopropylamine (**38**),[34] which was formylated again to dicyclopropylformamide (**39**); this compound, in turn, was cyclopropanated to give **18**[35] (overall yield from **35**: 28%) along with **38** (Scheme 3).

Generation of Radical Cations. The amines **10**−**16** and **27** were oxidized to their radical cations by SbF_5 in fluid dichloromethane solutions at 195 K, whereas for **17**, as for **18**[23] and **28**,[24] γ-irradiation with a ^{60}Co source in the "mobile" $CF_2ClCFCl_2$ matrix at 77 K was required to produce the corresponding radical cations. The slightly temperature-dependent ESR spectra of the fairly persistent radical cations **10**$^{\bullet+}$−**16**$^{\bullet+}$ and **27**$^{\bullet+}$ in dichloromethane were recorded in the range 200−300 K, with the resolution generally improving upon warming. The temperature dependence is mainly due to changes of the coupling constants of β-protons;[36] for example, that for **13**$^{\bullet+}$ increased from 0.13 to 0.16 mT on going from 230 to 300 K. For **17**$^{\bullet+}$ in a $CF_2ClCFCl_2$ matrix, as for **18**$^{\bullet+}$ [23] and **28**$^{\bullet+}$,[24] the resolution was strongly affected by the residual hyperfine anisotropy, but the spectra became quasi-isotropic at the softening point of the glass (ca. 125 K). Analyses of hyperfine patterns were carried out with the aid of a computer program.[37] An ^{1}H-ENDOR spectrum could be observed only for **13**$^{\bullet+}$. The *g* factors of the acyclic radical cations **10**$^{\bullet+}$−**18**$^{\bullet+}$ are all 2.0037 ± 0.0001; that of the bicyclic **27**$^{\bullet+}$ is slightly higher, 2.0041 ± 0.0001.

Scheme 3. Synthesis of the Tricyclopropylamine (18) via Dicyclopropylamine (38)[a]



[a]Key: (a) BnBr, NaH, benzene, 40 °C, 10 h; (b) 2.3 equiv of EtMgBr, 1.3 equiv of Ti(O-*i*-Pr)$_4$, THF, rt, 24 h; (c) Pd/C, H_2, MeOH; (d) $CHCl_3$, NaOH, cat. NBu_4Cl, CH_2Cl_2, 40 °C, 4 h; (e) same as (b) but 10 h.

Ethyldiisopropylamine (10), Diisopropyl-*n*-propylamine (11), and Dicyclohexylethylamine (12). Figure 1 shows the ESR spectra of the radical cations **11**$^{\bullet+}$ and **12**$^{\bullet+}$ at 300 K. As the major coupling constants are almost equal for **10**$^{\bullet+}$ and **11**$^{\bullet+}$, their spectra closely resemble each other; that of **10**$^{\bullet+}$ is, therefore, not reproduced here. With the values for **10**$^{\bullet+}$ preceding those for **11**$^{\bullet+}$, the ^{14}N-coupling constants amount to $|a_N| = 2.02 \pm 0.02$ and 2.00 ± 0.02 mT, while the two methylene β-protons[36] in the ethyl or *n*-propyl substituent give rise to the coupling constants $|a_H^{\beta}(\text{Et})| = 1.85 \pm 0.02$ and $|a_H^{\beta}(n\text{-Pr})| = 1.88 \pm 0.02$ mT. The corresponding values of the methine β-protons in the two isopropyl substituents are $|a_H^{\beta}(i\text{-Pr})| = 0.45 \pm 0.01$ and 0.44 ± 0.01 mT. The smallest resolved splittings in the spectra of both **10**$^{\bullet+}$ and **11**$^{\bullet+}$, $|a_H^{\gamma}(i\text{-Pr})| = 0.06 \pm 0.01$ mT, are due to the 12 methyl γ-protons in these substituents. Those from the three methyl γ-protons in the ethyl substituent of **10**$^{\bullet+}$

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(36) In ESR spectroscopy, protons separated from the spin-bearing π-center by 0, 1, 2, 3, and 4 sp^3-hybridized C atoms are denoted α, β, γ, δ, and ϵ. The π-center in amines is the N atom. Trialkylamines contain no α-protons. The following notation holds for the substituents at the N atom in **8**−**18**, **20**, **21**, and **23**: β-Protons are C*H*$_3$ in Me; C*H*$_2$ in Et and *n*-Pr; C*H* in *i*-Pr, 3Pn, *c*-Hx, and *c*-Pr. γ-Protons are C*H*$_3$ in Et, *i*-Pr, and *t*-Bu; C*H*$_2$ in *n*-Pr, 3Pn, *c*-Hx, and *c*-Pr. δ-Protons are C*H*$_3$ in 3Pn; C*H*$_2$ in *c*-Hx. ϵ-Protons are C*H*$_2$ in *c*-Hx. For the azacycles, the corresponding notation is as follows: β-Protons are C*H*$_2$ in **20**, **21**, and **24**−**27**; C*H* in **23** and **28**. γ-Protons are C*H*$_3$ in Me of **22**; C*H*$_2$ in **20**−**25**, **27**, and **28**; C*H* in **26**. δ-Protons are C*H*$_2$ in **21**−**23**, **26** and **27**; C*H* in **24** and **25**. ϵ-Proton is C*H* in **27**.

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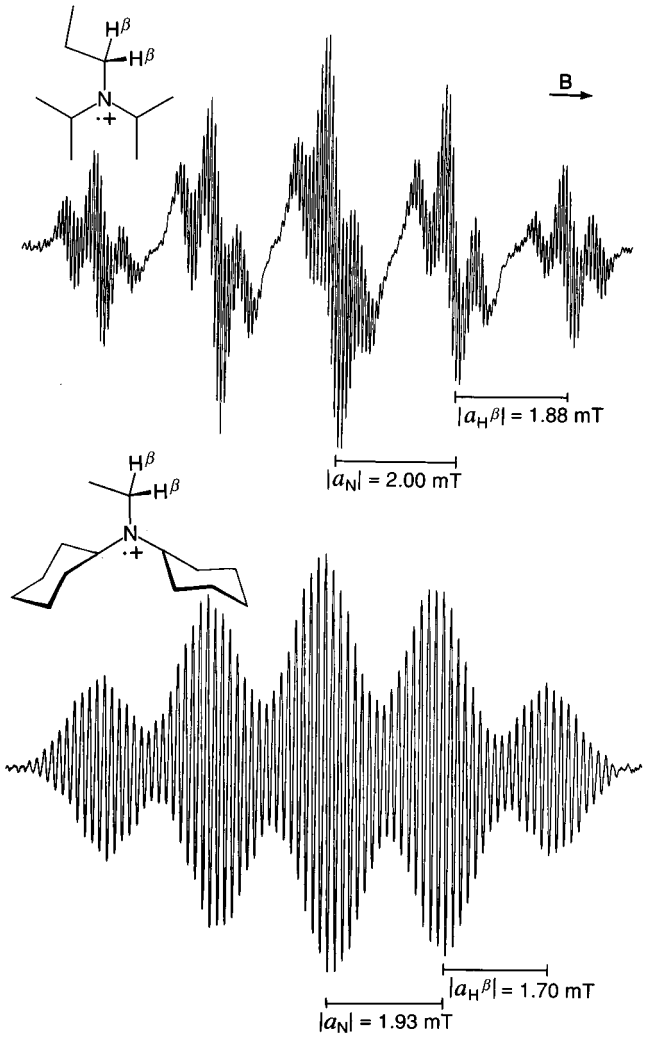

Figure 1. ESR spectra of **11**$^{\bullet+}$ (top) and **12**$^{\bullet+}$ (bottom). Solvent: CH_2Cl_2. Temperature: 300 K.

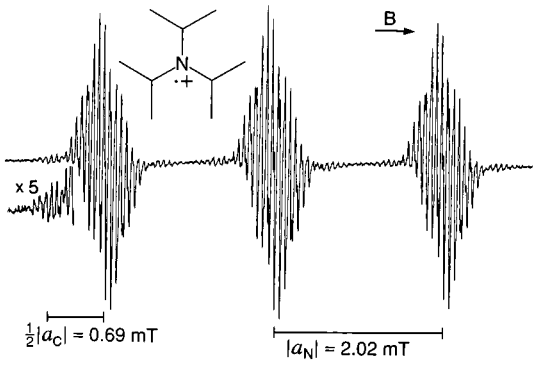

Figure 2. ESR spectrum of **13**$^{\bullet+}$. Solvent: CH_2Cl_2. Temperature: 270 K.

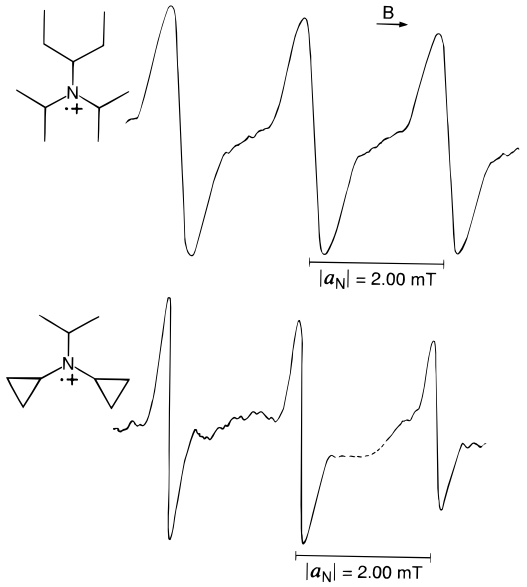

Figure 3. ESR spectra of **14**$^{\bullet+}$ (top) and **17**$^{\bullet+}$ (bottom). Solvent: CH_2Cl_2 (**14**$^{\bullet+}$) and $CF_2ClCFCl_2$ (**17**$^{\bullet+}$, matrix). Temperature: 300 K (**14**$^{\bullet+}$) and 125 K (**17**$^{\bullet+}$). The dashed part of the spectrum of **17**$^{\bullet+}$ is affected by an absorption from the γ-irradiated quartz sample tube.

and from the two methylene γ-protons and the three methyl δ-protons[36] in the propyl substituent of **11**$^{\bullet+}$ were unresolved, $|a_H^\gamma(\text{Et})|$, $|a_H^\gamma(n\text{-Pr})|$, $|a_H^\delta(n\text{-Pr})| < 0.03$ mT.

The two largest coupling constants for **12**$^{\bullet+}$, $|a_N| = 1.93 \pm 0.01$ mT and $|a_H^\beta(\text{Et})| = 1.70 \pm 0.01$ mT, of the two methylene β-protons in the ethyl substituent, do not greatly differ from the corresponding values in the spectrum of **10**$^{\bullet+}$ and **11**$^{\bullet+}$. Analysis of the remaining complex hyperfine pattern yielded 0.38 ± 0.01, 0.24 ± 0.01, and 0.12 ± 0.01 mT for two, eight, and eight protons, respectively, in the two cyclohexyl substituents. Guided by theoretical calculations (see Discussion), the largest value was assigned to the two methine β-protons, $|a_H^\beta(c\text{-Hx})|$, the middle-size one to the eight methylene δ-protons, $|a_H^\delta(c\text{-Hx})|$, and the smallest one to the eight methylene γ-protons, $|a_H^\gamma(c\text{-Hx})|$. The hyperfine splittings from the three methyl γ-protons in the ethyl substituent and the four methylene ϵ-protons[36] in the cyclohexyl rings were not resolved, $|a_H^\gamma(\text{Et})|$, $|a_H^\epsilon(c\text{-Hx})| < 0.03$ mT.

Triisopropylamine (13) and Diisopropyl-3-pentylamine (14). The radical cation **13**$^{\bullet+}$ enjoys an unusual thermodynamic and kinetic stability. In a previous study,[17] only the coupling constant $|a_N| = 1.95$ mT was derived from the ESR spectrum of **13**$^{\bullet+}$ consisting of three broad ^{14}N-hyperfine components. The splittings from the protons of the three isopropyl substituents were concealed by the large line width. In the ESR spectrum of **13**$^{\bullet+}$, taken at 270 K and presented in Figure 2, these splittings are fully resolved. Apart from $|a_N| = 2.02 \pm 0.01$ mT, the spectrum exhibits the coupling constants, $|a_H^\beta(i\text{-Pr})| = 0.148 \pm 0.002$ mT, of the three methine β-protons and, $|a_H^\gamma(i\text{-Pr})| = 0.060 \pm 0.002$ mT, of the 12 methyl γ-protons. Owing to the persistence and the high symmetry of **13**$^{\bullet+}$, ^{13}C satellites were also readily observable. Their relative intensities indicate that they arise from the ^{13}C isotopes in the six methyl groups with $|a_C| = 1.38 \pm 0.02$ mT.

The resolution of the ^{1}H-hyperfine splittings was lost in the ESR spectrum of **14**$^{\bullet+}$, as the replacement of the two γ-protons in one isopropyl substituent of **13**$^{\bullet+}$ by methyl groups lowers the symmetry of the radical cation. Disregarding the poor resolution, the spectrum of **14**$^{\bullet+}$, shown in Figure 3, is congruent with that of **13**$^{\bullet+}$, as the broad ^{14}N-hyperfine components in **14**$^{\bullet+}$ are spaced by $|a_N| = 2.00 \pm 0.02$ mT and their width is comparable to the sum of the ^{1}H-coupling constants for **13**$^{\bullet+}$. It is, therefore, reasonable to assume that these coupling constants are similar for both radical cations, in particular the $|a_H^\beta(i\text{-Pr})|$ values.

Cyclopropyldiisopropylamine (15) and Di-*tert*-butylcyclopropylamine (16). In contrast to **14**$^{\bullet+}$, replacement of one isopropyl by a cyclopropyl substituent did not substantially affect the resolution of the ESR spectrum on going from **13**$^{\bullet+}$ to **15**$^{\bullet+}$. The coupling constants for **15**$^{\bullet+}$ strongly resemble those for **13**$^{\bullet+}$; at 240 K, they are $|a_N| = 2.02 \pm 0.01$ mT, $|a_H^\beta(c\text{-Pr})| \approx |a_H^\beta(i\text{-Pr})| = 0.13 \pm 0.01$ mT, and $|a_H^\gamma(c\text{-Pr})| \approx |a_H^\gamma(i\text{-Pr})| = 0.06 \pm 0.01$ mT. Thus, within the limits of experimental resolution, the single methine β-proton in the cyclopropyl substituent has the same coupling constant as in its two isopropyl counterparts, and an analogous statement holds for the four methylene and the 12 methyl γ-protons in the cyclopropyl and the two isopropyl substituents, respectively.

Resolution of ^{1}H-hyperfine splittings is retained in the ESR spectrum of **16**$^{\bullet+}$ when the two isopropyl substituents in **15**$^{\bullet+}$ are replaced by *tert*-butyl groups. The coupling constants observed for **16**$^{\bullet+}$ at 210 K are $|a_N| = 2.01 \pm 0.02$ and $|a_H^\beta(c\text{-Pr})| = 0.11 \pm 0.01$ of the single β-proton in the cyclopropyl substituent, and $|a_H^\gamma(c\text{-Pr})| \approx |a_H^\gamma(t\text{-Bu})| = 0.07 \pm 0.01$ of the four methylene γ-protons in the cyclopropyl substituent and the 18 methyl γ-protons in the two *tert*-butyl groups.

Dicyclopropylisopropylamine (17) and Tricyclopropylamine (18). As stated in the section on generation of radical cations, the ESR spectrum of **17**$^{\bullet+}$, like that of **18**$^{\bullet+}$,[23] was taken in a $CF_2ClCFCl_2$ matrix at 125 K. The resolution was greatly affected by the residual hyperfine anisotropy, so that the splittings from the protons remained unresolved in both spectra. The coupling constants, $|a_N| = 2.00 \pm 0.01$ mT for **17**$^{\bullet+}$ and $|a_N| = 2.01 \pm 0.01$ mT for **18**$^{\bullet+}$, are close to the corresponding values for **10**$^{\bullet+}$−**16**$^{\bullet+}$. A striking characteristic is the narrowing of the ^{14}N-hyperfine components, as illustrated in Figure 3 by comparison of the ESR spectra of **14**$^{\bullet+}$ and **17**$^{\bullet+}$; on going from the former to the latter, the peak-to-peak distance diminishes from 0.45 to 0.15 mT. This finding points to a strong reduction in the coupling constant of the methine β-protons. As stated above, such $|a_H^\beta|$ values decrease on lowering the temperature, which is the case when using Freon matrices. In addition, with the successive replacement of isopropyl or 3-pentyl by cyclopropyl substituents, the coupling constants of the methine β-protons may be reduced, because the "bisected" orientation of cyclopropyl groups becomes increasingly favored (see below). For the three methine β-protons in the radical cation **18**$^{\bullet+}$, an $|a_H^\beta(c\text{-Pr})|$ value of 0.06−0.08 mT was estimated in the previous communication.[23]

1-Azabicyclo[3.3.3]undecane (Manxine, 27). A prominent feature of the ESR spectrum of **27**$^{\bullet+}$, displayed in Figure 4, is the large coupling constant of the three methylene β-protons, which are equatorial with respect to the ring and in a favorable position for hyperconjugation with the p-orbital at the spin-bearing N atom (see below); the value, $|a_H^\beta(\text{eq})| = 3.85 \pm 0.03$ mT, of this coupling constant is twice $|a_N| = 1.92 \pm 0.02$ mT. Analysis of the smaller hyperfine splittings reveals a coupling constant $|a_H^\epsilon| = 0.60 \pm 0.01$ mT, due to the single methine ϵ-proton[36] in the bridgehead position (through-space, long-range interaction[15]), as well as three smaller $|a_H|$ values, 0.23, 0.18, and 0.16, each arising from three protons. Candidates therefore are the sets of the axial methylene β-protons, $|a_H^\beta(\text{ax})|$, and those of the axial and/or equatorial methylene γ- and δ-protons.

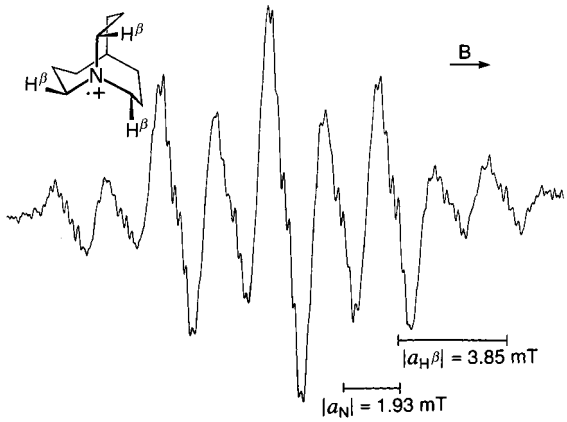

Figure 4. ESR spectrum of **27**$^{\bullet+}$. Solvent: CH_2Cl_2. Temperature: 240 K.

Discussion

Ionization Energies. Table 1 lists the vertical ionization energies, IE_v, determined by photoelectron spectroscopy for those trialkylamines, of which radical cations were characterized by their hyperfine data (see Introduction). A relation exists between these gas-phase values and the method required for generation of the radical cations. In our present and recent work,[23,24] the borderline ionization energy IE_v appears to be about 8 eV. Thus, the acyclic trialkylamines **10**−**16**, with none or one cyclopropyl substituents could be oxidized to persistent radical cations by SbF_5 in fluid solution, whereas for **17** and **18** with two or three cyclopropyl substituents, as for azatriquinane (**28**),[24] γ-irradiation in a Freon matrix had to be used to this aim. The tricyclic amine **28** represents an exception insofar, as its IE_v value is somewhat lower than 8 eV.

Planarity. In general, alkyl-substituted amines are expected to share the pyramidal structure of the parent ammonia (**1**).[1] The geometry at the N atom is reflected by the sum, $\Sigma\varphi$, of the three CNC angles, φ, and by the distance, d, of this atom from the plane of its C neighbors. Such $\Sigma\varphi$ and d values, listed in Table 1, were calculated by AM1[38] and, in part, by other quantum theoretical methods[39−41] (see footnotes to Table 1). Planarity implies $\Sigma\varphi = 360°$ and $d = 0$, while a decrease in the former and an increase in the latter indicate a progressive pyramidalization. The predicted pyramidal geometry at the N atom was experimentally confirmed for trimethylamine (**8**)[42] and triethylamine (**9**).[43] Trialkylamines with at least

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(39) For SCF−STO-G calculations on **8** and **13**, see: Kölmel, C.; Ochsenfeld, C.; Ahlrichs, R. *Theor. Chim. Acta* **1991**, *82*, 271.

(40) 3-21G* and DFT calculations were performed with GAUSSIAN 94.[41] The latter involve B3LYP hybrid functionals: Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098; *J. Chem. Phys.* **1993**, *98*, 1372.

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(42) Blake, A. J.; Ebsworth, E. A. V.; Welch, A. J. *Acta Crystallogr., Sect. C* **1984**, *40*, 413.

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Table 1. Observed and Calculated Data for Trialkylamines and Their Radical Cation[a]

		observed		AM1-calculated			observed		
		IE_v [eV]	ref	$\Sigma\varphi$ (deg)	d (pm)	θ (deg)	a_N (mT)	a_{H^β} (mT)	ref
NMe_3	**8**	8.53	3	339[b]	39[b]	45			
	8$^{\bullet+}$			360	0	45	+2.07	+2.85	16
NEt_3	**9**	8.08	3	337[c]	41[c]	52/68			
	9$^{\bullet+}$			360	0	57/57	+2.08[d]	+1.9	21
NEt(*i*-Pr)$_2$	**10**	7.7	11	349[e]	29[e]	41/74(Et)/82(*i*-Pr)			
	10$^{\bullet+}$			360	<1	36/84(Et)/82(*i*-Pr)	+2.02	+1.85(Et)/+0.45(*i*-Pr)	this work
N(*n*-Pr)(*i*-Pr)$_2$	**11**	*f*		349	28	41/74(*n*-Pr)/86(*i*-Pr)			
	11$^{\bullet+}$			360	<1	41/80(*n*-Pr)/83(*i*-Pr)	+2.00	+1.88(*n*-Pr)/+0.44(*i*-Pr)	this work
NEt(*c*-Hx)$_2$	**12**	7.35	11	349[g]	28[g]	39/84(Et)/83(*c*-Hx)			
	12$^{\bullet+}$			360	<1	40/80(Et)/85(*c*-Hx)	+1.93	+1.70(Et)/+0.38(*c*-Hx)	this work
N(*i*-Pr)$_3$	**13**	7.18	17	349[h]	28[h]	88(*i*-Pr)			
	13$^{\bullet+}$			360	<1	89(*i*-Pr)	+2.02	+0.15	this work
N(3Pn)(*i*-Pr)$_2$	**14**	7.2	11	350[i]	27[i]	80(3Pn)/88(*i*-Pr)			
	14$^{\bullet+}$			360	0	85(3Pn)/84(*i*-Pr)	+2.00	<0.2[j]	this work
N(*c*-Pr)(*i*-Pr)$_2$	**15**	7.79	23	343[k]	36[k]	174(*c*-Pr)/80(*i*-Pr)			
	15$^{\bullet+}$			360	<1	90(*c*-Pr)/89(*i*-Pr)	+2.02	+0.13(*c*-Pr)/+0.13(*i*-Pr)	this work
N(*c*-Pr)(*t*-Bu)$_2$	**16**	7.76	49	342[l]	36[l]	174			
	16$^{\bullet+}$			360	0	84	+2.01	+0.11(*c*-Pr)	this work
N(*c*-Pr)$_2$(*i*-Pr)	**17**	8.14	23	338[m]	40[m]	177(*c*-Pr)/68(*i*-Pr)			
	17$^{\bullet+}$			360	<1	90(*c*-Pr)/90(*i*-Pr)	+2.00	<0.1[j]	this work
N(*c*-Pr)$_3$	**18**	8.44	23	335[n]	43[n]	179			
	18$^{\bullet+}$			360[o]	0[o]	90	+2.01	+0.06 to +0.08	23
NMe-pyrrolidine	**20**	8.41	9	336	42	178(ax)/64(eq)/45(Me)			
	20$^{\bullet+}$			360	<1	151/34("ax/eq")/45(Me)	*p*	+5.7(ax)/+2.8(eq;Me)	21
NMe-piperidine	**21**	8.29	9	338	40	178(ax)/64(eq)/45(Me)			
	21$^{\bullet+}$			360	2	178(ax)/66(eq)/45(Me)	*p*	+3.8(ax)/+2.9(Me)	21
N(*t*-Bu)bicyclononane	**23**	*f*		360	0	0			
	23$^{\bullet+}$			360	0	0	+1.95	*f*	18
azanorbornane	**24**	*f*		308	65	44(exo)/75(endo)			
	24$^{\bullet+}$			325	52	47(exo)/75(endo)	+3.02	+1.51(exo)/+0.30(endo)	15
quinuclidine	**25**	8.05	3	325	52	58			
	25$^{\bullet+}$			340	39	60	+2.51	+0.94	15
azaadamantane	**26**	7.94	50	327	50	59			
	26$^{\bullet+}$			342	36	61	+2.16	+0.87	15
manxine	**27**	7.13	11	349	28	32(ax)/83(eq)			
	27$^{\bullet+}$			359[q]	5[q]	34(eq)/84(ax)	+1.92	+3.85(eq)	this work
azatriquinane	**28**	7.80	45	326[r]	52[r]	0			
	28$^{\bullet+}$			343[s]	36[s]	0	+2.50	+4.00	24

[a] See text for the meaning of $\Sigma\varphi$, d, and θ. [b] SCF-STO-G: $\Sigma\varphi = 335°$, $d = 42$ pm (ref 39); exptl: $\Sigma\varphi = 331°$, $d = 46$ pm (ref 42). [c] Exptl: $\Sigma\varphi = 330°$, $d = 47$ pm (ref 43). [d] This more reliable value is taken from ref 48. [e] 3-21G*: $\Sigma\varphi = 353°$, $d = 23$ pm. [f] Not reported. [g] 3-21G*: $\Sigma\varphi = 354°$, $d = 20$ pm. [h] SCF-STO-G: $\Sigma\varphi = 357°$, $d = 15$ pm (ref 39); exptl: $\Sigma\varphi = 350°$, $d = 28$ pm (ref 43). [i] 3-21G*: $\Sigma\varphi = 360°$, $d = 0$ pm. [j] Not resolved. [k] 3-21G*: $\Sigma\varphi = 349°$, $d = 29$ pm; exptl: $\Sigma\varphi = 340°$, $d = 39$ (ref 44). [l] 3-21G*: $\Sigma\varphi = 346°$, $d = 33$ pm. [m] 3-21G*: $\Sigma\varphi = 342°$, $d = 37$ pm. [n] RB3LYP/6-31G**: $\Sigma\varphi = 333°$, $d = 44$ pm (ref 23); exptl: $\Sigma\varphi = 330°$, $d = 47$ pm (ref 23). [o] UB3LYP/6-31G**: $\Sigma\varphi = 360°$, $d = 0$ pm (ref 23). [p] Only a rough estimate is reported. [q] UB3LYP/6-31G**: $\Sigma\varphi = 360°$, $d = 0$ pm. [r] 6-31G*: $\Sigma\varphi = 326°$, $d = 51$ pm (ref 45). [s] UB3LYP/6-31G**: $\Sigma\varphi = 346°$, $d = 24$ pm (ref 24).

two isopropyl substituents, such as **10**, **11**, and **13**−**15**, should be closer to planarity. On the other hand, introduction of cyclopropyl groups, to yield successively **15** (or **16**), **17**, and **18**, is expected to increase pyramidalization. These predictions were confirmed by X-ray crystal-structure analyses for **13**,[43] **15**,[44] and **18**[23] with $\Sigma\varphi = 350$, 340, and 330°, respectively. The monocyclic *N*-methylpyrrolidine (**20**) and *N*-methylpiperidine (**21**) are predicted to be pyramidal as are certainly the bicyclic 1-azanorbornane (**24**) and quinuclidine (**25**), as well as the tricyclic 1-azaadamantane (**26**) and azatriquinane (**28**),[45] while the bicyclic *N*-*tert*-butylbicyclononane (**23**) and manxine (**27**) should be planar or nearly planar.

On passing to their radical cations, all alkyl-substituted amines tend to flatten at the N atom, as does ammonia (**1**) on its conversion to **1**$^{\bullet+}$. However, planarity cannot be achieved for the radical cations of the oligocyclic amines **24**−**26** and **28**, because it is impaired by their rigid molecular frameworks. Inspection of the observed ^{14}N-coupling constants with a positive sign, required by theory[46] (see Table 1), reveals that those a_N values that markedly exceed +2.0 mT belong to these four radical cations. The sequence of increasing a_N, **26**$^{\bullet+}$ < **25**$^{\bullet+}$ ≈ **28**$^{\bullet+}$ < **24**$^{\bullet+}$, indicates that the pyramidalization becomes more pronounced in this order, as expected from the $\Sigma\varphi$ and d values. On the other hand, the ^{14}N-coupling constants of the radical cations of the remaining acyclic and bicyclic amines are +2.0 mT with a deviation of less than 0.1 mT; this finding is also in accord with the prediction.

The increase in the a_N values upon pyramidalization is due to a growing s-contribution by the spin-bearing orbital at the N atom. Such an s-contribution arises from p,s-spin delocalization, while in planar radical cations this orbital has a "pure p-character" with the ^{14}N-coupling constants brought about solely by p,s-spin polarization.[46]

Conformations. Apart from $\Sigma\varphi$ and d values, calculations by the AM1 procedure yielded the dihedral angles, θ, between the axis of the spin-bearing p-orbital at the N atom and the direction of the C−H$^\beta$ bond. These angles are also listed in Table 1 for the trialkylamines and their

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(45) Galasso, V.; Hansen, J.; Jones, D.; Mascal, M. *THEOCHEM* **1997**, *392*, 21.
(46) See, e.g.: Gerson, F. *High-Resolution ESR Spectroscopy*; Wiley and Verlag Chemie: New York and Weinheim, Germany, 1970; Chapter 1.5.

radical cations, along with the observed coupling constants a_H^β, for which theory requires a positive sign.[46] In general, the θ values vary only slightly on going from the neutral amines to their radical cations. Striking exceptions are those with cyclopropyl substituents, in which θ changes from ca. 180° in **15**−**18** to ca. 90° in **15**$^{\bullet+}$−**18**$^{\bullet+}$. Such a change occurs because these rings assume a "bisected" orientation with $\theta = 90°$ in the radical cations instead of a "perpendicular" conformation in the corresponding neutral compounds where they are vertical to the orbital axis at the N atom, i.e., have $\theta = 180°$.[23]

The coupling constants a_H^β should be proportional to $\langle\cos^2\theta\rangle$,[47]

$$a_H^\beta = B\langle\cos^2\theta\rangle \quad (1)$$

as they are due to p,s-spin delocalization from the p-orbital at the N atom to a pseudo-p-MO formed by the 1s-AO's of the H$^\beta$ atoms (hyperconjugation). Thus, $\theta = 0°$ or 180° and $\langle\cos^2\theta\rangle = 1$ imply eclipsing of the p-axis at the N atom by the C−H$^\beta$ bond (hyperconjugation at its optimum), while $\theta = 90°$ and $\langle\cos^2\theta\rangle = 0$ point to a position of this bond in the nodal plane of the p-orbital (no hyperconjugation). For a freely rotating methyl substituent, $\langle\cos^2\theta\rangle = 0.5$, which corresponds to $\theta = 45°$, so that the proportionality factor B in eq 1 should be equal to $2a_H^\beta$. With $a_H^\beta = +2.85$ mT for the nine methyl β-protons in the radical cation, **8**$^{\bullet+}$, of trimethylamine,[16] B thus becomes +5.7 mT. It is evident from Figure 5, in which the observed coupling constants a_H^β are plotted vs the AM1-calculated angles θ, that eq 1 with $B = 5.7$ mT holds for planar radical cations, such as **8**$^{\bullet+}$−**15**$^{\bullet+}$, **17**$^{\bullet+}$, **18**$^{\bullet+}$, and **27**$^{\bullet+}$. However, for the nonplanar **24**$^{\bullet+}$−**26**$^{\bullet+}$ and **28**$^{\bullet+}$, eq 1 with a much smaller B value of ca. 4 mT appears to be more appropriate.

In the case of methylene β-protons of ethyl or *n*-propyl substituents in **9**$^{\bullet+}$−**12**$^{\bullet+}$, the coupling constants a_H^β(Et) and a_H^β(*n*-Pr) cluster at about +1.7 to +1.9 mT. The value for **9**$^{\bullet+}$ correlates with $\langle\cos^2\theta\rangle = 0.30$, where $\theta = 57°$, and those for **10**$^{\bullet+}$−**12**$^{\bullet+}$ with an average $^1/_2(\langle\cos^2\theta_1\rangle + \langle\cos^2\theta_2\rangle) \approx 0.30$, where $\theta_1 \approx 40$ and $\theta_2 \approx 80°$ stand for two interchanging conformations. Clustering also occurs for methine β-protons of isopropyl or cyclohexyl substituents in **10**$^{\bullet+}$−**12**$^{\bullet+}$ with a_H^β(*i*-Pr), a_H^β(*c*-Hx) ≈ +0.4 mT, and for those of isopropyl or cyclopropyl substituents in **13**$^{\bullet+}$, **15**$^{\bullet+}$, **17**$^{\bullet+}$, and **18**$^{\bullet+}$ with a_H^β(*i*-Pr), a_H^β(*c*-Pr) ≈ +0.1 mT; the corresponding $\langle\cos^2\theta\rangle$ values are 0−0.03 where $\theta = 90-80°$. Not included in Figure 5 are the pertinent points for the radical cations, **20**$^{\bullet+}$ and **21**$^{\bullet+}$, of the monocyclic *N*-methylamines, because the AM1 calculations failed to yield results compatible with the reported coupling constants of the methylene β-protons in the ring.

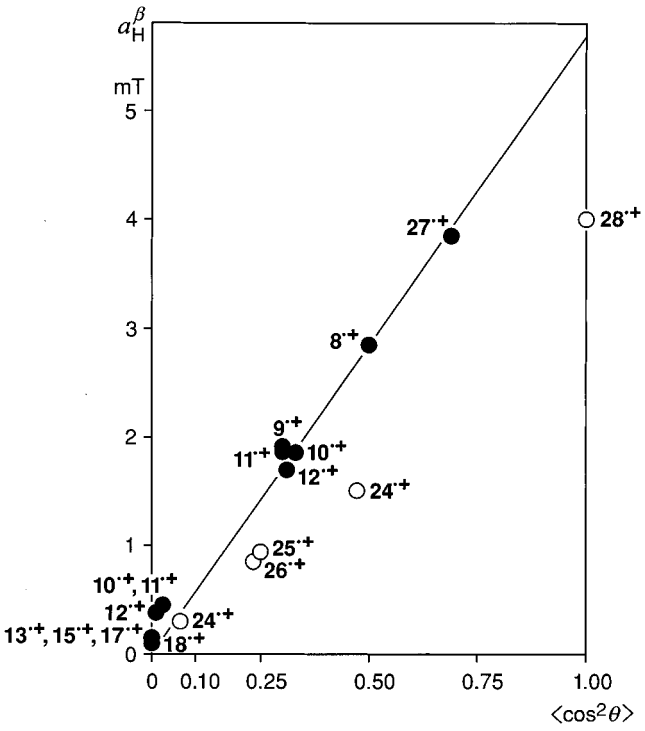

Figure 5. Observed coupling constants of β-protons, a_H^β in mT, vs $\langle\cos^2\theta\rangle$ values of AM1-calculated dihedral angles θ for radical cations of trialkylamines. Filled and open circles refer to planar and nonplanar species, respectively.

Experimental Section

General Methods. Melting points are uncorrected. IR spectra were recorded for neat films. ^{1}H NMR and ^{13}C NMR spectra were taken at 250 and 62.9 MHz. Chemical shifts are expressed in ppm downfield from tetramethylsilane used as an internal standard (δ value). Coupling constants J are given in Hz. Assignments of ^{13}C signals were made with the aid of DEPT (distortionless enhancement by polarization transfer) experiments, and multiplicities are indicated by the usual symbols, i.e., + for primary and tertiary, − for secondary, and C_{quat} for quaternary carbons (no signal in the DEPT spectrum). Mass spectra were measured with Varian MAT CH 7, MAT 731 mass spectrometers. Silica gel TLC was performed on 60F-254 precoated sheets (E. Merck), and column chromatography was carried out using Merck Kieselgel 60 (200−400 mesh). Elemental analyses were performed in the Microanalytical Laboratory of the Institut für Organische Chemie, Universität Göttingen.

General Procedure (GP 1) for the Formylation of Dialkylamines with Dichlorocarbene. To a mixture of 30 mL of dichloromethane, 7.0 mL (87 mmol) of chloroform, 10.0 mmol of dialkylamine or its hydrochloride, and 23 mL of 36% NaOH solution was added 0.5 g of Et_3BnNCl (TEBACl), and the mixture was heated under reflux for 4 h. After being cooled, the mixture was diluted with 30 mL of water, the organic phase was separated, and the water phase was extracted with three portions of 20 mL each of dichloromethane. The combined organic extracts were washed with 20 mL of 0.5 N HCl solution and then with 20 mL of saturated sodium bicarbonate solution, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was then purified by column chromatography on silica gel (**34** and **39**) or by distillation (**30**).

Diisopropylformamide (**30**). The large-scale formylation of 14.0 mL (0.10 mol) of diisopropylamine according to GP 1 gave a brown mixture of crude products. The distillation afforded 7.35 g (57%) of **30** as a colorless liquid.

General Procedure (GP 2) for the Cyclopropanation of Dialkylformamides. A solution of ethylmagnesium bromide in diethyl ether was added via cannula to 200 mL of anhydrous THF kept in a dry ice bath to form a suspension, to which was added at −78 °C a solution of titanium tetraisopropoxide in 20 mL of anhydrous THF via cannula over 2 min. After the mixture had been stirred for an additional 2

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min, a solution of the respective dialkylformamide in 10 mL of anhydrous THF was added during 1 min via cannula. Stirring was continued at −78 °C for 5 min, the cooling was stopped, and the mixture was allowed to warm to room temperature and stirred at this temperature or heated under reflux for the stated time. The mixture was then hydrolyzed by addition of 150 mL of concentrated NH_4Cl solution, followed by 50 mL of water and stirring for 1−3 h until it became colorless (yellow). The precipitate was filtered off and washed twice with 30 mL of diethyl ether. The filtrate was made alkaline (pH > 11) by addition of 15% NaOH until $Mg(OH)_2$ started to precipitate, and extracted with three portions of 50 mL each of diethyl ether. The combined organic extracts were washed with brine, dried over K_2CO_3, and filtered. The high-boiling amine **37** was then purified by distillation after evaporation of the solvent. Low-boiling amines were converted into hydrochlorides by addition of ethereal HCl to the extracts. The solvent was then evaporated under reduced pressure at 0 °C, the residue was taken up with 50 mL of chloroform, and the solvent was evaporated again. This procedure was repeated two more times to remove traces of 2-propanol and water. Most of the amines were released from hydrochlorides by addition of a 40% aqueous solution of K_2CO_3 and subsequent extraction with three portions of 10 mL each of pentane. The combined pentane solutions were dried over K_2CO_3, the solvent was removed under reduced pressure, and the products were purified by means of preparative GC (Intersmat 131, 2 m 15% SE 30) after "bulb-to-bulb" distillation in vacuo.

Cyclopropyldiisopropylamine (**15**). According to GP 2, 1.29 g (10.0 mmol) of diisopropylformamide (**30**) was treated with 8.53 g (30.0 mmol) of titanium tetraisopropoxide and 60.0 mmol of ethylmagnesium bromide. The reaction mixture was heated under reflux for 3 d, after which time **30** could not be found any more in a hydrolyzed aliquot of the reaction mixture. The product was purified by preparative GC (Intersmat 131, 2 m 15% SE 30, 95 °C), which afforded 1.07 g (76%) of **15** as a colorless oil (t_R 12.3 min): ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.42 (d, 4 H, ^3J 5.6, *c*-Pr-H), 1.08 [d, 12 H, ^3J 6.5, $(CH_3)_2CH$], 1.92 [quint, 1 H, ^3J 5.6, $(CH_2)_2CH$], 3.05 [sept, 2 H, ^3J 6.5, $(CH_3)_2CH$]; ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 6.67 (−, C-2 and C-3), 21.21 [+, $CH(CH_3)_2$], 28.64 (+, C-1), 50.49 [+, $CH(CH_3)_2$]. Anal. Calcd for $C_9H_{20}ClN$: C, 60.83; H, 11.34. Found: C, 60.63; H, 11.26. Hydrochloride **15·HCl**: mp 154 °C ($CHCl_3$/Et_2O).

Di-*tert*-butylcyclopropylamine (**16**)**.** The title compound was prepared according to GP 2 from 19.2 mmol of ethylmagnesium bromide, 2.85 mL (9.6 mmol) of titanium tetraisopropoxide, and 0.50 g (3.2 mmol) of di-*tert*-butylformamide[28] (**31**) in 100 mL of anhydrous THF. The reaction mixture was heated under reflux for 10 d, after which time the crude hydrochloride, containing large quantities of side products, was obtained as a brown oil. Column chromatography of the residue after workup on 50 g of silica gel with dichloromethane−methanol (10:1) gave fraction I: 73 mg (23%) of *tert*-butylformamide (mixture of syn and anti isomers) as a colorless oil (R_f 0.71).

Fraction II: **16·HCl** (R_f 0.60), pale brown oil (135 mg, 20%), most of which slowly crystallized as colorless needles which decomposed with gas evolution (isobutene?) at 104 °C to leave a solid which melted at 195 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.68−0.79 (m, 2 H, *c*-Pr-H), 1.52−1.65 (m, 2 H, *c*-Pr-H), 1.45 [s, 18 H, $C(CH_3)_3$], 2.23−2.36 (m, 1 H, *c*-Pr-H), 9.56 (bs, 1 H, NH^+); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 8.11 (−, C-2 and C-3), 29.88 [+, $C(CH_3)_3$], 33.71 [C_{quat}, $C(CH_3)_3$], 72.00 (+, C-1). Anal. Calcd for $C_{11}H_{24}ClN$: C, 64.21; H, 11.76. Found: C, 64.61; H, 11.89.

Fraction III: 50 mg of mixture of di-*tert*-butylamine hydrochloride (**29·HCl**) and *tert*-butylcyclopropylamine hydrochloride (1:1) as a colorless, slowly crystallizing oil (R_f 0.42).

Fraction IV: 108 mg (31%) of *tert*-butylamine hydrochloride (R_f 0.14).

The experiment was repeated on a larger scale, starting from 14.50 g (92.2 mmol) of **31**, to give the hydrochloride **16·HCl** after column chromatography. The latter was treated under cooling (ice−water) with 10 mL of saturated K_2CO_3 solution, and the amine was extracted with three portions of 5 mL each of pentane. The extracts were dried over K_2CO_3 and filtered, and the solvent was removed under reduced pressure with cooling. Purification by means of preparative GC (Intersmat 131, 2 m 15% SE 30, 150 °C) gave 1.24 g (8%) of **16** as a colorless oil (t_R 11.2 min): IR (film) 2970 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.52−0.75 (m, 4 H, *c*-Pr-H), 1.32 [s, 18 H, $C(CH_3)_3$], 1.89 (m_c, 1 H, *c*-Pr-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 11.11 (−, C-2 and C-3), 31.16 (+, C-1), 32.59 [+, $C(CH_3)_3$], 59.44 [C_{quat}, $C(CH_3)_3$]; MS *m*/*z* 169 [M^+] (1); HRMS calcd for $C_{11}H_{23}N$ 169.1830, found 169.1830.

Cyclopropylisopropylamine Hydrochloride (**33·HCl**).[31] To a solution of 1.0 mL (14.2 mmol) of cyclopropylamine in 10 mL of anhydrous methanol were successively added 12.5 mL (50 mmol) of a 0.4 N methanolic solution of HCl and 2.2 mL (30 mmol) of anhydrous acetone. The solution was allowed to cool to room temperature, and 1.15 g (18 mmol) of $NaBH_3CN$ was added at a rate so as to keep the gas evolution from becoming too fast. After 2 h of stirring at room temperature, the solvent was removed under reduced pressure (50 °C), and the solid residue was dissolved with cooling in 30 mL of a 10% NaOH solution. The product was extracted with three portions of 20 mL each of diethyl ether, and the combined extracts were dried over K_2CO_3, filtered, and acidified with ethereal HCl. Evaporation of the solvent in vacuo gave 1.89 g (98%) of the colorless hydrochloride **33·HCl**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.74 (m_c, 2 H, *c*-Pr-H), 1.19 (m_c, 2 H, *c*-Pr-H), 1.43 [d, 6 H, ^3J 6.5, $(CH_3)_2CH$], 2.46 (m_c, 1 H, *c*-Pr-H), 3.33 [sept, 1 H, ^3J 6.4, $(CH_3)_2CH$], 9.33 (bs, 2 H, NH_2^+); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 3.40 (−, C-2 and C-3), 19.03 (+, CH_3), 27.57 (+, C-1), 51.87 (+, CH).

Cyclopropylisopropylformamide (**34**). The title compound was prepared from 1.35 g (10.0 mmol) of cyclopropylisopropylamine hydrochloride (**33·HCl**) according to GP 1. Column chromatography on 20 g of silica gel with diethyl ether gave 1.00 g of **34** as a pale brown oil (R_f 0.59), which was almost pure according to its ^{1}H NMR spectrum. Additional purification via "bulb-to-bulb" distillation afforded 914 mg (72%) of **34** as a colorless oil: IR (film) 3030, 2872 (HCO), 1674 (C═O) cm^{-1}. The ^{1}H and ^{13}C NMR spectra indicated a mixture of syn and anti diastereomers in a ratio of 1:9: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.52−0.65 (m, 2 H, *c*-Pr-H), 0.65−0.78 (m, 2 H, *c*-Pr-H), 1.15 [d, 5.4 H, ^3J = 8.4, $(CH_3)_2CH$ anti], 1.21 [d, 0.6 H, ^3J 8.4, $(CH_3)_2CH$ syn], 2.31 [m_c, 0.1 H, $(CH_2)_2CH$ syn], 2.41 [m_c, 0.9 H, $(CH_2)_2CH$ anti], 3.57 [sept, 0.1 H, $(CH_3)_2CH$ syn], 4.38 [sept, 0.9 H, $(CH_3)_2CH$ anti], 8.14 (s, 1 H, HC═O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 5.03 (−, C-2 and C-3), 20.10 (+, CH_3), 25.75 (+, C-1), 45.21 (+, CH), 163.88 (+, CH═O) [anti]; 6.07 (−, C-2 and C-3), 22.43 (+, CH_3), 24.66 (+, C-1), 50.95 (+, CH), 163.28 (+, CH═O) [syn]; MS *m*/*z* 127 [M^+] (18); HRMS calcd for $C_7H_{13}NO$ 127.0997, found 127.0997.

Dicyclopropylisopropylamine (**17**). The title compound was prepared according to GP 2 from 1.40 g (11.0 mmol) of cyclopropylisopropylformamide (**34**), 4.05 g (14.3 mmol) of titanium tetraisopropoxide, and 25.4 mmol of ethylmagnesium bromide. The reaction mixture was stirred for 3 d at room temperature and worked up as normal, which afforded 1.16 g of a mixture of hydrochlorides of **17** and cyclopropylisopropylamine (**33**) in a ratio of 7:1 (according to ^{1}H NMR analysis). The free amines obtained from these hydrochlorides were separated by means of preparative GC (Intersmat 131, 2 m 15% SE 30, 111 °C) to give pure 730 mg (48%) of **17** as a colorless liquid (t_R 12.4 min): ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.35−0.51 (m, 8 H, *c*-Pr-H), 1.11 [d, 6 H, ^3J 6.4, $(CH_3)_2CH$], 1.95 (m_c, 2 H, *c*-Pr-H), 3.08 [sept, 1 H, ^3J 6.4, $(CH_3)_2CH$]; ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 5.86 (−, *c*-Pr-C), 19.04 (+, CH_3), 33.14 (+, C-1), 54.61 (+, CH). Anal. Calcd for $C_9H_{18}ClN$: C, 61.53; H, 10.33. Found: C, 60.68; H, 10.42. Hydrochloride **17·HCl**: mp 166 °C (MeOH/Et_2O).

Benzylcyclopropylformamide (**36**)**.** A 9.0 g (0.22 mol) portion of a 60% sodium hydride suspension in mineral oil was washed with three portions of 40 mL of anhydrous toluene each and the residue suspended in 200 mL of anhydrous benzene. The suspension was warmed to 70 °C, and 15.2 g (0.18 mol) of cyclopropylformamide (**35**) was added over 20 min. After being heated under reflux for 10 min, the mixture was allowed to cool to 40 °C, and 29.7 mL (0.25 mol) of benzyl

bromide in 30 mL of anhydrous benzene was added. The mixture was stirred at this temperature for 10 h and then allowed to cool to room temperature. Sodium bromide was removed by filtration and the filtrate distilled through a 20 cm Vigreux column to give 30.1 g (96%) of **36** as a colorless oil: bp 104 °C (0.2 mbar); IR (film) 2977, 2878 (HCO), 1675 (C=O) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.65−0.80 (m, 4 H, *c*-Pr-H), 2.50 (m_c, 1 H, *c*-Pr-H), 5.00 (s, 2 H, CH_2Ph), 7.22−7.40 (m, 5 H, Ph-H), 8.39 (s, 1 H, HC=O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 5.51 (−, C-2 and C-3), 28.78 (+, C-1), 47.79 (−, CH_2-Ph), 127.19 (+, Ph-C), 128.11 (+, Ph-C), 128.30 (+, Ph-C), 136.75 (C_{quat}, Ph-C), 163.99 (+, CH=O); MS *m*/*z* 175 [M^+] (36); HRMS calcd for $C_{11}H_{13}NO$ 175.0997, found 175.0997.

Benzyldicyclopropylamine (37). The title compound was prepared according to GP 2 from 5.0 g (28.5 mmol) of benzylcyclopropylformamide (**36**), 10.5 g (36.9 mmol) of titanium tetraisopropoxide, and 65.6 mmol of ethylmagnesium bromide. The reaction mixture was stirred for 24 h at room temperature and hydrolyzed and the product distilled in vacuo to give 4.43 g (83%) of **37** as a colorless oil: bp 48 °C (0.2 mbar); IR (film) 3087, 3063, 3011, 2922, 2851 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.40−0.57 (m, 8 H, *c*-Pr-H), 1.84−1.96 (m_c, 2 H, *c*-Pr-H), 3.91 (s, 2 H, CH_2Ph), 7.27−7.42 (m, 5 H, Ph-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 6.22 (−, *c*-Pr-C), 35.92 (+, *c*-Pr-C), 60.57 (−, CH_2Ph), 126.80 (+, Ph-C), 127.82 (+, Ph-C), 129.93 (+, Ph-C), 137.82 (C_{quat}, Ph-C); MS *m*/*z* 187 [M^+] (21); HRMS calcd for $C_{13}H_{17}N$ 187.1360, found 187.1360. Hydrochloride: mp 166 °C dec ($MeOH/Et_2O$).

In another run, the reaction mixture was heated under reflux for 3 h. The usual workup gave a crude product containing considerable amounts of the side product benzylcyclopropyl(3-pentyl)amine, which could not be separated from **37** by distillation. Column chromatography on 150 g of silica gel eluting with pentane−diethyl ether (40:1) gave fraction I, 2.20 g (35%) of benzylcyclopropyl(3-pentyl)amine as a colorless oil (R_f 0.92): ^1H NMR (250 MHz, $CDCl_3$) δ 0.33−0.42 (m, 2 H, *c*-Pr-H), 0.42−0.54 (m, 2 H, *c*-Pr-H), 1.08 (t, 6 H, ^3J 7.4, CH_3-CH_2), 1.52 (m, 2 H, CH_3CHH), 1.76 (m, 2 H, CH_3CHH), 2.19 (m_c, 1 H, *c*-Pr-H), 2.56 [m_c, 1 H, $(CH_3CH_2)_2CH$], 3.87 (s, 2 H, CH_2Ph), 7.28−7.49 (m, 5 H, Ph-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 7.17 (−, *c*-Pr-C), 12.20 (+, CH_3), 23.30 (−, CH_2), 33.81 (+, C-1), 55.83 (−, CH_2Ph), 65.56 (+, CH), 126.37 (+, Ph-C), 128.36 (+, Ph-C), 129.07 (+, Ph-C), 141.76 (C_{quat}, Ph-C).

Fraction II: 2.72 g (51%) of **37** (R_f 0.38).

Dicyclopropylamine Hydrochloride (38·HCl). A solution of 1.73 g (9.2 mmol) of benzyldicyclopropylamine (**37**) in 40 mL of anhydrous methanol was hydrogenated over 100 mg of 10% Pd on charcoal at atmospheric pressure. After the calculated volume of hydrogen (210 mL) had been consumed, the mixture was flushed with nitrogen to remove dissolved hydrogen, and filtered from the catalyst through a 1 cm layer of silica gel. The catalyst was washed with 20 mL of methanol and the combined methanolic solutions were acidified with ethereal HCl. The solvent was removed under reduced pressure, and the solid residue was treated with 20 mL of chloroform, the solvent evaporated to dryness, and this treatment with 20 mL of chloroform and evaporation was repeated two more times to remove traces of 2-propanol and water. The crude hydrochloride **38·HCl** (1.15 g, 93%) thus obtained was formylated according to GP 1 without further purification to give dicyclopropylformamide (**39**).

Dicyclopropylamine (**38**).[34] The free base **38** was obtained from 1.00 g (7.5 mmol) of crude hydrochloride **38·HCl** as described for amine **17**. Purification by preparative GC (Intersmat 131, 2 m 15% SE 30, 110 °C) gave 630 mg (87%) based on crude hydrochloride) of **38** as a colorless oil (t_R 4.0 min) with cyclopropylamine smell: ^1H NMR (250 MHz, $CDCl_3$) δ 0.28−0.39 (m, 4 H, *c*-Pr-H), 0.39−0.51 (m, 4 H, *c*-Pr-H), 1.75−1.98 (bs, 1 H, NH), 2.24 (m_c, 2 H, *c*-Pr-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 5.78 (−, C-2 and C-3), 30.30 (+, C-1); MS *m*/*z* 97 [M^+] (23). Hydrochloride **38·HCl**: Anal. Calcd for $C_6H_{12}ClN$: C, 53.93; H, 9.05. Found: C, 54.08; H, 8.96.

Dicyclopropylformamide (**39**). The title compound was prepared from 1.33 g (10.0 mmol) of dicyclopropylamine hydrochloride (**38·HCl**) according to GP 1. Column chromatography on 20 g of silica gel eluting with diethyl ether gave 922 mg of **39** as a pale brown oil (R_f 0.31) that was almost pure according to its ^1H NMR spectrum. Additional purification via "bulb-to-bulb" distillation afforded 860 mg (69%) of pure **39** as a colorless oil: IR (film) 3093, 3014, 2875 (HCO), 1680 (C=O) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.48−0.59 (m, 2 H, *c*-Pr-H), 0.59−0.78 (m, 6 H, *c*-Pr-H), 2.37 (m_c, 1 H, *c*-Pr-H), 2.50 (m_c, 1 H, *c*-Pr-H), 8.11 (s, 1 H, HC=O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 5.03 (−, *c*-Pr-C), 5.58 (−, *c*-Pr-C), 27.14 (+, *c*-Pr-C), 28.64 (+, *c*-Pr-C), 165.44 (+, CH=O); MS *m*/*z* 125 [M^+] (4); HRMS calcd for $C_7H_{11}NO$ 125.0840, found 125.0840.

Tricyclopropylamine (**18**).[23] The title compound was prepared according to GP 2 from 4.00 g (32.0 mmol) of dicyclopropylformamide (**39**), 11.8 g (41.5 mmol) of titanium tetraisopropoxide, and 73.6 mmol of ethylmagnesium bromide. The reaction mixture was stirred for 10 h at room temperature and worked up as usual to afford 5.11 g of a mixture of the hydrochlorides of **18** and **38** in a ratio of 2:1 (according to ^1H NMR analysis). The free amines obtained from this hydrochloride mixture were separated by means of preparative GC (Intersmat 131, 2 m 15% SE 30, 111 °C) to give 2.54 g (58%) of pure **18** as a colorless oil (t_R 16.1 min): IR (film) 3093, 3014, 2925, 2865 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.39−0.42 (m, 6 H, *c*-Pr-H), 0.42−0.45 (m, 6 H, *c*-Pr-H), 1.92−2.03 (m_c, 3 H, *c*-Pr-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 4.55 (−, C-2 and C-3), 37.90 (+, C-1); Hydrochloride **18·HCl**: mp (dec and sublimation) 181 °C ($MeOH/Et_2O$).

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