

Relative Basicities of Some *Endo* and *Exo* Norbornylamines

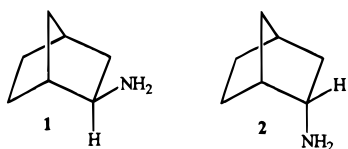
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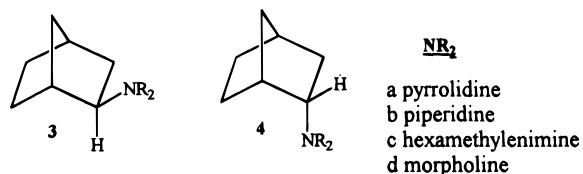
A series of *endo*- and *exo*-norbornylamines were synthesized and their relative basicities determined in acetonitrile and dimethylformamide solvents. The *exo* isomer is always more basic than the corresponding *endo* isomer in either solvent. All of the bicyclic amines studied have higher pK_a 's in acetonitrile solvent than in dimethylformamide except for the 2-morpholinonorbornanes which are just the reverse. This effect is explained by the ability of the morpholine group to disperse a positive charge and the relative polarizabilities of the solvents. Semiempirical AM1 and PM3 methods along with *ab initio* HF/STO-3G, HF/3-21G*, and HF/6-31G* methods were used to calculate proton affinities and dipole moments for each of the amines. The results of the theoretical calculations correspond well with the experimental observations.

The rigid norbornane bicyclic system holds 2-position substituents in fixed configurations of either *exo* or *endo* geometry. The reactions of substituted norbornanes can differ according to the substituent configurations. Protonation of an amine is one of the simplest possible chemical reactions. Proton affinity (PA) describes the extent of gas phase protonations.¹ The PA's of *exo*- (1) and *endo*-2-aminobicyclo[2.2.1]heptane (2) are identical with values of 221.7 kcal/mol¹. Therefore, *exo/endo* configurational changes 1 and 2 appear to have negligible effect on the basicity of these simple amines in the gas phase.



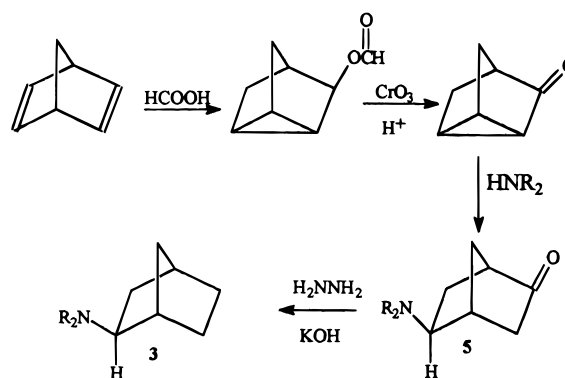
There are two additional factors that affect basicity of tertiary amines in solution as compared to primary bicyclic amines in the gas phase. These two factors are: (1) the nature of the substituents added to the central nitrogen atom to make it a tertiary amine; (2) the nature of the solvating solvent. We are reporting how the *exo/endo* configuration of the 2-aminonorbornane system interacts with these two additional effects.

The norbornane system studied is a series of 2-substituted norbornanes with tertiary amine substituents, these substituents having *exo* (3) and *endo* (4) configurations. The *endo* amines (4) were made by hydride



reduction of the corresponding iminium salts in a manner previously reported.² Syntheses of the *exo* amines (3)

Scheme 1



were carried out in a manner previously described³ as shown in Scheme 1.

The pK_a 's for these tertiary amines were determined in two different solvents, namely acetonitrile (AN) and N,N-dimethylformamide (DMF) (see Table 1). The substituent effect is demonstrated by the pK_a 's of the four different bicyclic amines. The pK_a 's of pyrrolidine, piperidine, and hexamethylenimine substituted norbornanes for a given configuration and solvent are of the same order of magnitude, whereas those for the morpholine-substituted norbornanes are substantially smaller. The configurational effect is demonstrated by the fact that the pK_a 's for all of the *exo* isomers are at least 0.3 pK_a units larger than the pK_a 's for the corresponding *endo* isomers. The solvation of the protonated 2-aminonorbornanes is more important than the solvation of the neutral amines.⁴ The chief reason for the difference in pK_a 's between the two configurations must be caused by a difference in the solvation energy between the conjugate bases since the intrinsic proton affinities (PA's) for the gas phase bases are very close to each other (see Table 3). Both semiempirical and *ab initio* calculations show differences in gas phase PA's between *exo* and *endo* configurations, but the semiempirical methods show the *endo* isomers with larger PA's than their corresponding *exo* isomers. On the other hand, all the *ab initio* methods show the *exo* isomers with larger PA's than their corresponding *endo* isomers which is the same direction as is

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Table 1. pK_a Values of 2-Norbornylamines

| NR ₂ | acetonitrile | | | <i>N,N</i> -dimethylformamide | | | AN-DMF | |
|-----------------|--------------|-------------|---------------|-------------------------------|-------------|---------------|--------|-------|
| | exo | endo | ΔpK_a | exo | endo | ΔpK_a | exo | endo |
| pyrrolidino | 8.56 ± 0.04 | 8.24 ± 0.06 | 0.32 | 8.36 ± 0.02 | 8.06 ± 0.06 | 0.30 | 0.20 | 0.18 |
| piperidino | 8.48 ± 0.03 | 8.04 ± 0.04 | 0.44 | 8.09 ± 0.05 | 7.62 ± 0.01 | 0.47 | 0.39 | 0.42 |
| hexamethylene | 8.53 ± 0.09 | 8.15 ± 0.04 | 0.38 | 8.46 ± 0.09 | 7.82 ± 0.09 | 0.65 | 0.07 | 0.33 |
| morpholino | 5.75 ± 0.04 | 5.45 ± 0.09 | 0.30 | 6.26 ± 0.09 | 5.77 ± 0.08 | 0.49 | -0.51 | -0.32 |

Table 2. Dipole Moments (Debyes)

| NR ₂ | exo | | endo | |
|-------------------|-------------------|-------------------|-------------------|-------------------|
| | free amine | salt | free amine | salt |
| pyrrolidino | 0.56 ^a | 4.31 ^a | 0.66 ^a | 3.92 ^a |
| | 1.12 ^b | 4.50 ^b | 1.10 ^b | 3.99 ^b |
| piperidino | 0.52 ^a | 3.19 ^a | 0.56 ^a | 2.86 ^a |
| | 0.84 ^b | 3.31 ^b | 0.78 ^b | 2.99 ^b |
| hexamethylenimino | 0.64 ^c | | 0.82 ^c | |
| | 0.55 ^a | 1.99 ^a | 0.55 ^a | 2.25 ^a |
| morpholino | 0.85 ^b | 2.09 ^b | 0.72 ^b | 2.50 ^b |
| | 1.64 ^a | 1.55 ^a | 1.51 ^a | 0.99 ^a |
| | 1.43 ^b | 1.88 ^b | 1.37 ^b | 1.34 ^b |
| | 1.56 ^c | | 1.48 ^c | |

^a Determined using *ab initio* HF/6-31G* calculations. ^b Determined using semi empirical AM1 calculations. ^c Determined experimentally.

Table 3. Calculated Heats of Formation (kcal/mol) and Proton Affinity

| NR ₂ , ^a NHR ₂ ⁺ | AM1 | | PM3 | | STO-3G | | 3-21G* | | 6-31G* | |
|---|--------------|-------|--------------|-------|--------------|-------|--------------|-------|--------------|-------|
| | ΔH_f | PA | ΔH_f | PA | total energy | PA | total energy | PA | total energy | PA |
| exo 1 ^b | -11.3 | 218.5 | -9.5 | 215.5 | -323.20572 | 270.1 | -325.28045 | 237.8 | -327.08207 | 229.5 |
| exo 1' | 137.4 | | 142.2 | | -323.64874 | | -325.67192 | | -327.46045 | |
| endo 2 ^c | -8.2 | 220.8 | -6.5 | 218.1 | -323.20516 | 269.1 | -325.28040 | 236.2 | -327.08184 | 228.5 |
| endo 2' | 138.2 | | 142.6 | | -323.64666 | | -325.66940 | | -327.45857 | |
| exo 3a | -6.1 | 225.8 | -14.8 | 216.5 | -476.37469 | 284.3 | -479.38577 | 250.5 | -482.04505 | 242.4 |
| exo 3a' | 135.3 | | 135.9 | | -476.84029 | | -479.79764 | | -482.44398 | |
| endo 4a | -5.4 | 225.6 | -13.9 | 217.0 | -476.37531 | 283.3 | -479.38660 | 249.5 | -482.04580 | 241.7 |
| endo 4a' | 136.2 | | 136.3 | | -476.83941 | | -479.79673 | | -482.44359 | |
| exo 3b | -15.2 | 226.9 | -20.7 | 218.2 | -514.95578 | 286.9 | -518.20804 | 252.9 | -521.08090 | 245.2 |
| exo 3b' | 125.1 | | 128.3 | | -515.42566 | | -518.62366 | | -521.48420 | |
| endo 4b | -13.7 | 228.4 | -18.5 | 219.9 | -514.95928 | 285.0 | -518.21188 | 250.6 | -521.08509 | 243.1 |
| endo 4b' | 125.1 | | 128.8 | | -515.42605 | | -518.62384 | | -521.48509 | |
| exo 3c | -18.0 | 226.5 | -21.4 | 217.7 | -553.52250 | 287.2 | -557.01628 | 251.1 | -560.10263 | 245.0 |
| exo 3c' | 122.7 | | 128.1 | | -553.99282 | | -557.42906 | | -560.50571 | |
| endo 4c | -15.4 | 230.2 | -17.7 | 221.0 | -553.52495 | 285.9 | -557.01558 | 252.1 | -560.10445 | 244.5 |
| endo 4c' | 121.6 | | 128.5 | | -553.99314 | | -557.42987 | | -560.50668 | |
| exo 3d ^d | -44.3 | 220.8 | -47.5 | 211.9 | -550.21004 | 280.1 | -553.81624 | 245.7 | -556.89112 | 239.1 |
| exo 3d' | 102.1 | | 107.8 | | -550.66903 | | -554.22042 | | -557.28472 | |
| endo 4d | -43.0 | 221.9 | -45.5 | 213.5 | -550.21367 | 277.9 | -553.82014 | 243.2 | -556.89541 | 236.8 |
| endo 4d' | 102.3 | | 108.2 | | -550.66908 | | -554.22035 | | -557.28530 | |

^a 1,2 = Amino, 1',2' = aminium, 3a,4a = pyrrolidino, 3a',4a' = pyrrolidinium, 3b,4b = piperidino, 3b',4b' = piperidinium, 3c,4c = hexamethylenimino, 3c',4c' = hexamethylenimino, 3d,4d = morpholino, 3d',4d' = morpholinium. ^b The reported experimental PA is 221.7¹. ^c The reported experimental PA is 221.7¹. This was also run using BLYP/6-31G* method, and the PA was determined as 228.5 kcal/mol. ^d The lowest energy when using AM1 and PM3 is an axial attachment on the morpholine ring system. The lowest energy using the *ab initio* method has an equatorial attachment.

found in solution. A significant factor in the solution differences in pK_a 's between these isomers is probably the greater ease of solvation of the less sterically hindered protonated *exo* isomer.

Another interesting observation concerns the change in pK_a 's with changing solvents. In all of the bicyclic systems except for morpholine, the pK_a of the 2-aminonorborene in DMF is at least 0.2 pK_a units lower than in AN. However, the pK_a of 2-morpholinonorborene is significantly larger in DMF than in AN. In order to test this "morpholine effect", the basicity of another morpholine amine, *N*-methylmorpholine, was measured both in AN and DMF. Again the pK_a of the morpholino compound is higher in DMF (6.30 ± 0.01) than in AN (5.85 ± 0.02). This suggests that the oxygen in the morpholine ring affects this bicyclic amine in DMF and AN in such a way as to reverse the solvent effects that are observed with the pyrrolidine, piperidine, and hexamethylenimine systems.

The factors that determine the magnitude of solvation energy in these systems are hydrogen bond acceptance ability of the solvent, dipole-dipole interactions, and dipole-induced dipole interactions.⁵⁻⁸ Acetonitrile is an aprotic, dipolar protophobic solvent while DMF is an aprotic dipolar protophilic solvent.⁹ A solvent basicity scale (SB) has been proposed⁷ which measures the hydrogen bond basicity for a solvent. This scale has a good linear correlation with the Kamlet and Taft β basicity scale.⁵ The SB value for acetonitrile is 0.44, and the value for DMF is 0.71.⁷ Since DMF is more basic than AN, amines will normally be less basic in DMF solvent than in AN solvent. Therefore, based on the

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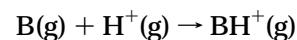
hydrogen bond basicity factor alone, the pK_a values of the 2-aminonorbornanes should be lower in DMF solvent. This is true in the cases of all of the amines studied except that of 2-morpholinonorbornane and *N*-methylmorpholine.

The reason for this "morpholine effect" can be ascertained by observing the dipole moments of the amine salts (see Table 2). The calculated dipole moments of these amines correspond very closely to the experimental values in four test cases including those of the morpholines. So it is assumed that all of the *ab initio* (HF/6-31G*) and semiempirical (AM1) calculated dipole moments are close to the actual values. The large dipole moments of the salts of pyrrolidino-, hexamethylenimino-, and piperidinonorbornane show that they possess very localized charges. So they require much greater solvation than the 2-morpholinonorbornane salts which have much smaller dipole moments and hence a much more diffuse charge. This more diffuse charge distribution is due to the presence of the ring oxygen atom which causes the 2-morpholinium norbornane salt to be more polarizable than the other salts. This is shown by its much smaller dipole moment than would be anticipated if the positive charge were more localized. Solvents with high polarizability are good solvators for highly polarizable cations.¹⁰ The polarizability of DMF and AN can be determined through the Lorenz-Lorentz equation from refractive indexes. Solvents with a large refractive index have strong dispersion forces. The refractive index at 20 °C for DMF and AN are 1.4305 and 1.3441, respectively.¹⁰ These values correspond to polarizabilities (α_0) of 1.06×10^{-23} and 4.39×10^{-24} , respectively.¹⁰ This difference in solvents is shown also by the fact that the solvent polarity-polarizability scale of DMF is 0.954 whereas that of AN is 0.895.¹¹ The 2-morpholinonorbornane aminium cations are more solvated in more polarizable solvents like DMF than in a less polarizable solvent like AN. Hence this cation is more stable in DMF than in AN, and the acid/base equilibrium for 2-morpholinonorbornane is shifted more toward the conjugate acid side in DMF, resulting in its being a stronger base in this solvent. A similar effect has been reported in comparing the relative basicities of both morpholine and DABCO (1,4-diazabicyclo[2.2.2]octane) with those of triethylamine, pyrrolidine, and piperidine in different solvents.¹² These are both 1,4-bifunctional molecules. The solvents used were water and DMSO. The former is a polar protic solvent, and the latter is an aprotic, dipolar protophilic solvent^{5,9} like DMF.

This "morpholine effect" was further demonstrated by using another aprotic dipolar protophilic solvent for some pK_a determinations of *exo*-2-morpholinonorbornane (**3d**) and *endo*-2-pyrrolidinonorbornane (**4a**). This additional solvent was 1-methyl-2-pyrrolidone with a refractive index¹⁰ at 20 °C of 1.4700, and a polarizability of 1.06×10^{-23} . The pK_a of **3d** in this solvent is 6.03 ± 0.08 , a pK_a increase of 0.28 units over AN solvent. The pK_a of **4a** in this solvent is 7.02 ± 0.04 , a pK_a decrease of 1.22 units over AN.

Theoretical proton affinities (PA) for each of the bicyclic amines were determined using both semiempirical and *ab initio* methods. Proton affinity of a base, B, is defined

as the negative of the gas phase heat of reaction of



that is,

$$PA = -[\Delta H_f(BH^+) - \Delta H_f(B) - \Delta H_f(H^+)]$$

The experimental value for the heat of formation for the proton, $\Delta H_f(H^+) = 367.2$ kcal/mol,¹³ was used in the semiempirical calculations.

The semiempirical methods used were AM1^{14,15} and PM3.¹⁶ These methods were used to calculate the heats of formation of the free amines and their aminium salts along with their dipole moments. Full geometric optimizations were carried out for these molecules including the use of the lowest energy conformation about the bicyclic-C to N bond. The results of these calculations are shown in Table 3. All of the PA's tend to be smaller with PM3 calculations than with AM1 calculations, and the two experimental PA's that have been reported (*endo*- and *exo*-2-aminonorbornane¹) have values closer to those of AM1. This is consistent with the comparison of these two methods for calculating PA's made by Burk and co-workers.¹⁷

Using *ab initio* methods, the proton affinity is determined by with ΔE_0^{el} the electronic energy difference of

$$PA = -\Delta E_0^{el} - \Delta ZPE + 5/2RT$$

$E(BH^+) - E(B)$, ΔZPE the zero point energy difference, and $5/2RT$ the H^+ contribution to C_p .

The *ab initio* calculations were made on HF level using STO-3G, 3-21G*, and 6-31G* basis sets. Two calculations were made at the BLYP level which includes some estimate of correlation energy. These methods were used to calculate the total electronic energies as well as dipole moments. Again full geometric optimizations were carried out for these molecules. The lowest energy conformation about the bicyclic-C to N bond was used in these calculations. The change in zero point energy between the free amines and the corresponding salts (from STO-3G calculations on *exo*- and *endo*-2-aminonorbornane) was determined to be 9.5 kcal/mol, so this number was used throughout the calculations. The results of these calculations are shown in Table 3. The *ab initio* calculated gas phase PA's show the same trends as those observed in the experimental solution pK_a 's; namely, the *exo* isomers have larger PA's than the corresponding *endo* isomers. However, the semiempirical calculations have these reversed. Both methods show the morpholine bicyclic amines have smaller PA's than the other three tertiary bicyclic amines. The agreement between the measured proton affinity and the *ab initio* calculations improved dramatically as we went to larger basis sets.

The calculated hybridization for the lone electron pair on the nitrogen atoms show greater p character for the *exo* isomers than for the corresponding *endo* isomers (87 to 99% p character). This also leads to the prediction

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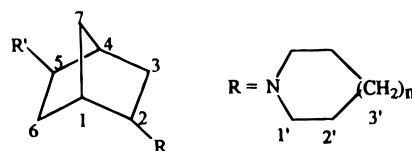
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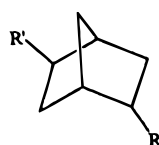
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Table 4. ^{13}C NMR Chemical Shifts (ppm)^a

| Amine ^b | R' | C ₁ | C ₂ | C ₃ | C ₄ | C ₅ | C ₆ | C ₇ | C _{1'} | C _{2'} | C _{3'} |
|-------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|-----------------|-----------------|-----------------|
| 5a , <i>exo</i> | =O | 39.4 | 67.6 | 34.3 | 49.7 | 217.5 | 43.0 | 23.2 | 52.7 | 31.8 | — |
| 5b , <i>exo</i> | =O | 36.6 | 67.9 | 34.4 | 49.6 | 217.5 | 43.5 | 24.4 | 52.2 | 30.9 | 25.8 |
| 5c , <i>exo</i> | =O | 37.9 | 65.3 | 33.9 | 49.8 | 217.5 | 43.1 | 26.8 | 52.5 | 31.7 | 28.2 |
| 5d , <i>exo</i> | =O | 35.9 | 67.1 | 33.6 | 49.8 | 216.3 | 42.4 | 30.1 | 51.3 | 66.3 | — |
| 4a , <i>endo</i> | H ₂ | 40.7 | 68.0 | 38.0 | 36.9 | 30.4 | 21.4 | 36.4 | 53.8 | 23.2 | — |
| 3a , <i>exo</i> | H ₂ | 40.2 | 70.1 | 38.0 | 35.9 | 28.4 | 27.6 | 35.0 | 52.4 | 23.0 | — |
| 4b , <i>endo</i> | H ₂ | 39.0 | 68.3 | 38.0 | 36.7 | 30.5 | 21.0 | 36.2 | 53.9 | 25.7 | 24.6 |
| 3b , <i>exo</i> | H ₂ | 37.4 | 70.1 | 37.0 | 35.9 | 28.5 | 28.2 | 35.4 | 52.0 | 25.9 | 24.7 |
| 4c , <i>endo</i> | H ₂ | 39.8 | 65.6 | 37.8 | 36.8 | 30.5 | 20.8 | 36.6 | 53.8 | 28.1 | 27.1 |
| 3c , <i>exo</i> | H ₂ | 38.8 | 67.4 | 38.0 | 36.1 | 28.2 | 27.9 | 34.8 | 52.4 | 28.4 | 26.9 |
| 4d , <i>endo</i> | H ₂ | 38.4 | 66.7 | 37.8 | 36.6 | 30.4 | 20.8 | 35.2 | 53.1 | 67.8 | — |
| 3d , <i>exo</i> | H ₂ | 37.1 | 69.8 | 36.7 | 35.8 | 28.2 | 27.8 | 35.0 | 51.6 | 66.9 | — |

^a DEPT was used as a help in making signal assignments. ^b R: a = pyrrolidino, b = piperidino, c = hexamethylenimino, d = morpholino.

Table 5. Bicyclic Amine Physical and Analytical Data

| amine ^a | R' | yield (%) | bp, °C (mm) | <i>n</i> _D ²⁰ | IR (cm ⁻¹) C=O | <i>m/e</i> parent | formula | C, % | | H, % | |
|--------------------------------------|----------------|-----------|----------------|-------------------------------------|-------------------------------|----------------------|---|-------|-------|-------|-------|
| | | | | | | | | calcd | found | calcd | found |
| 5a , <i>exo</i> | =O | 62 | 101–2(0.9) | — | 1750 | 179 | C ₁₁ H ₁₇ NO | 73.69 | 73.35 | 9.56 | 9.53 |
| 5b , <i>exo</i> | =O | 71 | 123 (1.7) | — | 1750 | — | C ₁₂ H ₁₉ NO | 74.57 | 74.53 | 9.91 | 10.16 |
| 5c , ^b <i>exo</i> | =O | 58 | 135–6(1.2) | — | 1750 | 207 | C ₁₃ H ₂₁ NO | 75.32 | 75.33 | 10.21 | 10.31 |
| 5d , ^b <i>exo</i> | =O | 74 | 111 (0.5) | 1.5130 | 1750 | 195 | C ₁₁ H ₁₇ NO ₂ | — | — | — | — |
| 4a , ^c <i>endo</i> | H ₂ | 52 | 62 (0.5) | 1.4956 | — | 165 | C ₁₁ H ₁₉ N | — | — | — | — |
| 3a , <i>exo</i> | H ₂ | 37 | 51–2 (0.2) | 1.4981 | — | 165 | C ₁₁ H ₁₉ N | 79.94 | 79.26 | 11.59 | 11.65 |
| 4b , ^c <i>endo</i> | H ₂ | 51 | 57–60(0.2) | 1.4989 | — | 179 | C ₁₂ H ₂₁ N | — | — | — | — |
| 3b , <i>exo</i> | H ₂ | 40 | 55 (0.2) | 1.5001 | — | 179 | C ₁₂ H ₂₁ N | 80.38 | 79.96 | 11.80 | 11.96 |
| 4c , ^b <i>endo</i> | H ₂ | 79 | 75 (0.4) | 1.4996 | — | 193 | C ₁₃ H ₂₃ N | — | — | — | — |
| 3c , <i>exo</i> | H ₂ | 37 | 77–8 (0.3) | 1.5030 | — | 193 | C ₁₃ H ₂₃ N | 80.76 | 80.87 | 11.99 | 11.90 |
| 4d , ^d <i>endo</i> | H ₂ | 71 | 76 (0.6) | 1.4966 | — | 181 | C ₁₁ H ₁₉ NO | — | — | — | — |
| 3d , <i>exo</i> | H ₂ | 56 | 80 (0.6) | 1.4993 | — | 181 | C ₁₁ H ₁₉ NO | — | — | — | — |

^a R: a = pyrrolidino, b = piperidino, c = hexamethylenimino, d = morpholino. ^b Reported in Reference 2. ^c Reported in Stephen, J. F.; Marcus, E. *J. Org. Chem.* **1969**, *34*, 2535. ^d Reported in reference 3 and in Cook, A. G.; Kosman, W. M. *Tetrahedron Lett.* **1966**, 5847.

for the *exo* isomers to be more basic than the *endo* isomers^{18,19} which is what our experimental results show.

The *exo*-2-norbornylamines had larger ^{13}C NMR C-2 and C-6 chemical shifts than the shifts for the corresponding *endo*-2-norbornylamines (see Table 4). This helps confirm the configurations of these amines.²⁰

Experimental Section

Both ^1H and ^{13}C NMR spectra were recorded on a Bruker Model AC-200 FT-NMR spectrometer. The general method used to determine dipole moments was that of Guggenheim.²¹ Dielectric constants were measured with a Wissenschaftlich-Technische Werkstätten Model DM-01 dipolmeter fitted with

(18) *Progress in Physical Organic Chemistry*; Taft, R. W., Gal, J.-F.; Maria, P.-C., Eds.; Wiley-Interscience: New York, 1990; Vol. 17, p 159.

(19) Ijjaali, F.; Mo, O.; Yanez, M.; Abboud, J.-L. M. *THEOCHEM* **1995**, *338*, 225.

(20) *Stereochemical Analysis of Alicyclic Compounds by C-13 NMR Spectroscopy*; Whitesell, J. K., Minton, M. A., Eds.; Chapman and Hall: New York, 1987.

(21) (a) Guggenheim, E. A. *Trans. Faraday Soc.* **1949**, *45*, 714. (b) Guggenheim, E. A. *Trans. Faraday Soc.* **1951**, *47*, 573. (c) Smith, J. W. *Trans. Faraday Soc.* **1950**, *46*, 394.

a DFL-1 sample holding cell. Measurements were made in benzene solution at 25.0 ± 0.1 °C with a range 0.00050 to 0.00350 weight fraction of the solute. Refractive indices of the solutions were measured with an Abbe refractometer. Infrared spectra were obtained with a Bomem Michelson 120 FT-infrared spectrophotometer. The mass spectra were determined on a Hewlett Packard GCD Plus GC-MS system. The $\text{p}K_a$'s were determined by titrating a 0.01 M solution of amine in acetonitrile with a 0.1 M solution of 70% perchloric acid in acetonitrile delivered by an automatic pump and measured potentiometrically with glass and calomel electrodes. The determination of the $\text{p}K_a$'s in *N,N*-dimethylformamide and 1-methyl-2-pyrrolidinone involved use of 0.25 M perchloric acid solutions in the respective solvent. The millivolt potential was analyzed using Grans plot to obtain the $\text{p}K_a$'s. The analyses were carried out by Schwarzkopf Microanalytical Laboratory, Woodside, NY.

Synthesis of *endo*-2-Aminonorbornanes (4).² These amines were produced by the reduction of their corresponding iminium perchlorate salts (produced by the reaction of the amine perchlorate salt and norcamphor with the azeotropic removal of water) by one of two methods: (1) use of an excess of lithium aluminum hydride in ether solvent;² (2) use of an excess of sodium borohydride in 2-propanol solvent. The yields

from these reactions and the physical properties of the resultant amines are given in Table 5.

Synthesis of *exo*-5-Aminonorbornan-2-ones (5).² These amino ketones were synthesized by treating 5.4 g (0.05 mol) of tricyclo[2.2.1.0]heptan-3-one and a catalytic amount of TsOH with 0.10 mol of the corresponding secondary amine. This mixture was refluxed in 75 mL of xylene for 2 h to produce, after solvent removal and distillation, the corresponding *exo*-5-aminonorbornan-2-one. The yields from these reactions and the physical properties of the resultant amino ketones are given in Table 5.

Synthesis of *exo*-2-Aminonorbornanes (3).³ These amines were produced by heating a mixture of 0.05 mol of the amino ketone, 45 mL of diethylene glycol, 11 g of potassium

hydroxide, and 8 mL of 85% hydrazine hydrate at 110 °C for 6 h. The product mixture was steam distilled, the distillate extracted with diethyl ether, and the combined ether extract dried with MgSO₄. The extract was filtered, solvent removed, and the residual oil distilled. The yields from these reactions and the physical properties of the resultant amines are given in Table 5.

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