

## PREFERRED *GAUCHE* CONFORMATION IN *N*-(2-AMINOETHYL)PYRIDINIUM IONS

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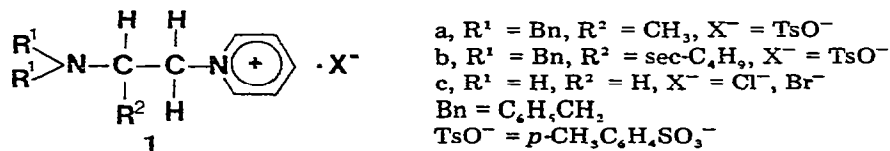
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### ABSTRACT

X-ray analysis of 1-[(2*S*, 3*S*)-2-*N,N*-dibenzylamino-3-methyl-1-pentyl]pyridinium *p*-toluenesulfonate and 1-[(2*S*)-2-*N,N*-dibenzylamino-1-propyl]pyridinium *p*-toluenesulfonate reveals that in both compounds the central N—C—C—N moiety is in the *syn*-clinal conformation. According to SCF-LCAO-MO calculations the *syn*-clinal conformation of the parent ion, *N*-(2-aminomethyl)pyridinium is 23.4 kJ mol<sup>-1</sup> lower in energy than the *anti*-periplanar conformation. The calculations suggest incipient bond formation between the amino nitrogen atom and the pyridinium ring in the *syn*-clinal conformation.

### INTRODUCTION

In the course of our studies on poly(iminomethylenes), (R—N=C<)<sub>*n*</sub> [1, 2] we became interested in the structure and properties of *N*-(2-aminoethyl)pyridinium ions 1.

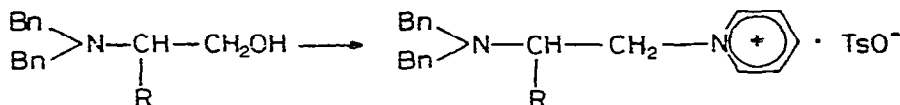


The parent compound 1c has been known since 1920, but is only stable in its double salt form [3]. In the present paper we report on the synthesis of compounds 1a and 1b and we discuss their molecular structures. These structures have been determined by X-ray analysis. Moreover, we performed SCF-LCAO-MO calculations on the cation of 1c.

## RESULTS

## Synthesis

Compounds **1a** and **1b** were synthesized from L-*N,N*-dibenzylalaninol (**2a**) and L-*N,N*-dibenzylisoleucinol (**2b**), respectively by treatment with *p*-toluenesulfonyl chloride in pyridine (Scheme I). The reaction probably



Scheme 1

proceeds via the intermediate tosylate which is subsequently attacked by a pyridine molecule. Compounds **1a** and **1b** are colourless solids which melt at 115 and 129°C, respectively. The  $^1\text{H}$  NMR spectra of the salts showed unusually high field shifts of the *ortho* protons of the  $\text{C}_6\text{H}_5\text{N}$  moiety. For instance, the *ortho* carbon atoms of compound **1a** are at approximately  $\delta$  8.70 ppm instead of in the  $\delta$  9.50–9.65 range found for 1-alkylpyridinium salts. This shift value would be more characteristic of a pyridine than of a pyridinium containing molecule.

## Crystal structure

Crystals of **1a** and **1b** were easily obtained from chloroform–cyclohexane mixtures. Single crystal X-ray analyses [4] were performed which unequivocally established the structure of the compounds to be that of pyridinium salts. With the exception of the alkyl groups  $\text{R}^2$  and of one of the phenyl rings, the structures of **1a** and **1b** are almost superimposable. In the observed structures the dibenzylamino nitrogen atoms are completely encapsulated. A PLUTO plot of compound **1b** is given in Fig. 1. The nitrogen

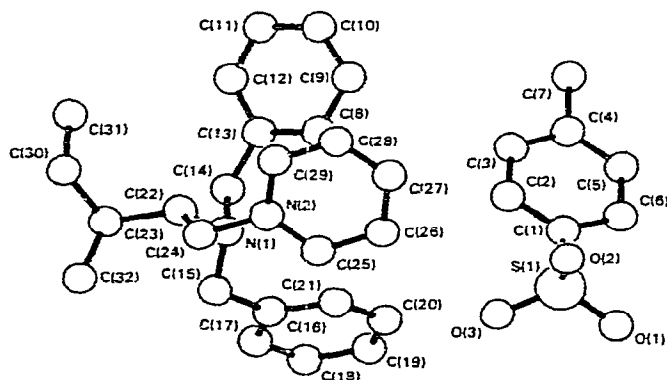


Fig. 1. Molecular structure and atomic labelling of 1-[(2*S*,3*S*)-2-*N,N*-dibenzylamino-3-methyl-1-pentyl]pyridinium *p*-toluenesulphonate.

atoms of the  $N^1-C-C-N^2$  moieties in 1a and 1b are in the ideal *syn-clinal* or *gauche* conformation (torsion angles 1a:  $-59.0(8)^\circ$ , 1b:  $-60.8(4)^\circ$ ), and are at the very short distance of 0.29 nm. This distance is smaller than the sum of the Van der Waals radii, which is 0.32 nm. In both compounds the distance of the dibenzylamino nitrogen  $N^1$  from the *ortho* carbon atoms  $C^{25}$  is 0.32 nm and in both compounds the  $N^1$ -lone pair points approximately in the direction of this carbon atom (the angle between  $N^1$ -lone pair- $C^{25}$  is  $144^\circ$ ).

### Electronic structure

More information about the stability of the observed *gauche* conformation was obtained from SCF-LCAO-MO calculations on the cation of the parent compound 1c. In these calculations atomic distances and angles for the carbon and nitrogen atoms of the structure observed for 1b were used. The hydrogen atoms were placed at standard distances and angles given for carbon-hydrogen. The amino hydrogen atoms were placed at a standard distance for amino-hydrogen in the direction of the benzyl groups of compound 1b. A standard split-valence Gaussian basis was used for the N and C atoms [5], together with a minimal basis for all H atoms [5]. The total energy of 1c was calculated as a function of the torsion angle ( $\phi$ ) around the NC-CN bond, keeping all other structural parameters fixed (Table 1). Since the structure is not symmetric, there is no symmetry of the calculated energy around  $\phi = 0$ . The minimum energy ( $-0.4 \text{ kJ mol}^{-1}$  relative to  $\phi = 60^\circ$ ) is calculated to occur for  $\phi = 58^\circ$ , close to the observed angle. Compared to the conformation with  $\phi = 180^\circ$ , in which no close contacts between the amino N and the pyridinium ring are possible, the  $\phi = 60^\circ$  conformation is found to be  $23.4 \text{ kJ mol}^{-1}$  more stable, indicating a fairly strong  $NH_2$ -pyridinium interaction in the  $\phi = 60^\circ$  form. The Mulliken net atomic populations (Figs. 2 and 3) suggest that this interaction is at least in part an electrostatic one, involving the negative  $NH_2$ -group and the positive *ortho*  $C^{25}$ -H group. However, from an inspection of the Mulliken overlap populations it appears that in the  $60^\circ$ -form there is in fact an incipient bond formation between  $N^1$  and  $C^{25}$ . This becomes apparent if one compares the  $\phi = 60^\circ$ -with the  $\phi = 180^\circ$ -form. In the  $60^\circ$ -form the  $C^{25}-C^{26}$  and  $C^{25}-N^2$  populations are lower by 0.027 and 0.020, respectively, whereas the population between  $N^1$  and  $C^{25}$  reaches a value of 0.023. All other non-bonded

TABLE 1

Relative energy ( $E$ ) of compound 1c as a function of the torsion angle  $\phi^a$

$\phi(^\circ)$	0	60	120	180	240	300
$E(\text{kJ mol}^{-1})$	24.2	0	34.7	23.4	43.1	15.9

<sup>a</sup>Relative to  $\phi = 60^\circ$ . The total energy at this geometry was  $-379.081072$  hartree.

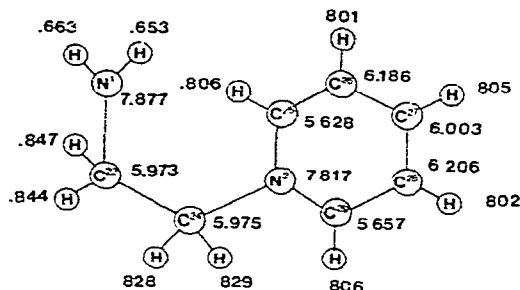


Fig. 2. The Mulliken net atomic population of compound 1c for  $\phi = 60^\circ$ .

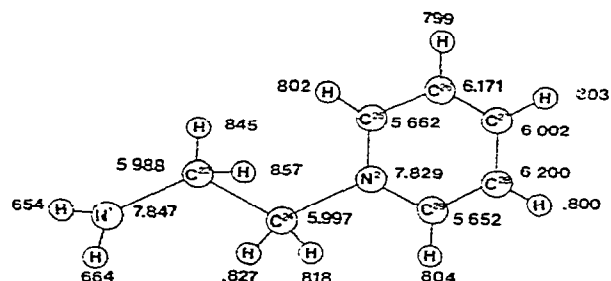


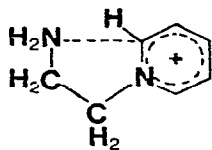
Fig. 3. The Mulliken net atomic population of compound 1c for  $\phi = 180^\circ$ .

contacts have overlap populations which are negative or very slightly positive. Thus the *ortho* carbon atom C<sup>25</sup> is approaching tetrahedral coordination.

Two other features in the populations are of interest. First, the N<sup>2</sup>-C<sup>24</sup> overlap population is very low, both in the  $\phi = 60^\circ$  (0.10) and in the  $\phi = 180^\circ$  (0.07) form. Note that these values are only 3 to 4 times larger than the N<sup>1</sup>-C<sup>25</sup> value, if  $\phi$  is  $60^\circ$ . Secondly, the positive charge of the ion is about equally divided between the pyridinium ring (+0.48) and the C-C-N fragment (+0.52).

## DISCUSSION

The X-ray structures of 1a and 1b are very similar suggesting that the conformation of the central fragment of these molecules is independent of the substituent R<sup>2</sup>. The observed *gauche* conformation of this fragment is in line with our calculations on compound 1c. The calculated difference of 23.4 kJ mol<sup>-1</sup> between the *gauche* and *trans* (*anti*-periplanar) form in compound 1c is larger than usually observed for compounds stabilized by the so-called *gauche* effect. In fact we are dealing with a transition-state like situation of bond formation between the amino function and the pyridinium ring, 3. The situation can be compared to neighbouring group participation by nitrogen in solvolysis reactions, where the lone pair of nitrogen interacts with an incipient carbocation [6].



This result fits into the reactivity pattern of compound 1c. When we tried to synthesize 1c, the reaction mixtures after work-up always yielded black oils from which no well-defined products could be isolated. Compound 1c probably polymerizes after initial intra- or intermolecular nucleophilic attack of the amino function on the pyridinium *ortho* carbon atoms. The short distances between the amino nitrogen N<sup>1</sup> and the *ortho* carbon atoms C<sup>25</sup> of the pyridinium rings in the crystal structures of 1a and 1b are in line with this. However, in these compounds the amino-benzyl groups prevent the nucleophilic attack. Our calculations on molecule 1c suggest that there is a considerable redistribution of charge in compounds 1. As a result of this redistribution the pyridinium rings are only partly positive. This explains why the pyridinium proton shifts in the <sup>1</sup>H NMR spectra of 1a and 1b are at a higher  $\delta$ -value than those of ordinary pyridinium salts.

## EXPERIMENTAL

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Varian EM390 and Bruker WH90 spectrometers, respectively. Chemical shifts,  $\delta$ , are given in ppm downfield from internal tetramethylsilane. The coupling constants, *J*, are given in Hz; abbreviations used are: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, dist = distorted. IR spectra were recorded on a Perkin-Elmer type 283 spectrometer and mass spectra on an AEI MS-902 mass spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter at 20°C. Melting points were determined on a Mettler FP5/FP51 melting point apparatus.

### *L*-N,N-Dibenzylalaninol (2a)

This compound was prepared from *L*-N,N-dibenzylalanine [7] by esterification with methanol and HCl gas [8] and subsequent reduction with LiAlH<sub>4</sub> in THF [9]. The product was purified by distillation. Yield 95%. B.p. 160°C/0.001 mm Hg;  $[\alpha]_D + 86.9^\circ$  (c 1.4, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.91 (*J* = 6.8, d, 3H, CH<sub>3</sub>), 3.0 (m, 1H, CH), 3.1 (s, 1H, OH), 3.25 and 3.48 (*J* = 5.1 and 9.1, *J*(gem) = 13.5, 2H, CH<sub>2</sub>O), 3.31 and 3.79 (*J*(gem) = 13.2, 2 × d, 4H, NCH<sub>2</sub>), 7.3 (m, 10H, arom); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  9.08 (CH<sub>3</sub>), 63.07 (CH), 54.47 (CH<sub>2</sub>O), 53.25 (CH<sub>2</sub>N), 127.41; 128.69; 129.17; 139.63 (arom).

*1-[2(S)-2-N,N-Dibenzylamino-1-propyl]pyridinium p-toluenesulfonate (1a)*

This compound was synthesized by stirring 2a with 1.3 equivalents of *p*-toluenesulfonyl chloride in pyridine at 0–25°C for 2 days. The product was isolated by pouring the mixture in aqueous HCl at 0°C and extracting the resulting solution with CHCl<sub>3</sub>. The organic layer was washed and dried over Na<sub>2</sub>SO<sub>4</sub>. The amine was liberated from its HCl salt with NH<sub>3</sub> gas in CHCl<sub>3</sub>. After column chromatography (silica, eluents CHCl<sub>3</sub>–CH<sub>2</sub>Cl<sub>2</sub> and CHCl<sub>3</sub>–CH<sub>3</sub>OH) and subsequent crystallization from CHCl<sub>3</sub>–cyclohexane, 1a was obtained in 35% yield: m.p. 115°C;  $[\alpha]_D + 25.3^\circ$  (c 1.6, CHCl<sub>3</sub>); MS: no parent peak, 409 (M<sup>+</sup>–pyr); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.16 (*J* = 7.5, d, 3H, CH<sub>3</sub>), 2.29 (s, 3H, CH<sub>3</sub> of tosyl), 2.8 (m, 1H, CH), 3.20 and 3.80 (*J*(gem) = 15, 2 × d, 4H, NCH<sub>2</sub>Ph), 4.75 (m, 2H, CH<sub>2</sub>–pyr), 7.1 (m, 14H, arom), 8.74, 7.65, 8.35 (m, 5H, *o*, *m*, *p* H's of pyr): <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 9.29 (CH<sub>3</sub>), 20.52 (CH<sub>3</sub> of tosyl), 52.17 (NCH<sub>2</sub>Ph), 54.29 (CH<sub>2</sub>–pyr), 61.89 (CH), 125.13; 128.67; 138.53 (benzyl), 144.23, 143.15 (*o*, *p*, C's of pyr).

*L-N,N-Dibenzylisoleucinol (2b)*

This compound was prepared from *L-N,N*-dibenzylisoleucine [7] as described for 2a. Yield 95%; b.p. 170–180°C/0.005 mm Hg;  $[\alpha]_D + 45.0^\circ$  (c 1.5, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.84 (*J* = 6.6, d, 3H, CH<sub>3</sub>), 0.86 (*J* = 7, t, 3H, CH<sub>2</sub>–CH<sub>3</sub>), 1.2 (m, 2H, CH<sub>2</sub>–CH<sub>3</sub>), 1.7 (m, 1H, CH–CH<sub>3</sub>), 2.62 (*J* = 6.7, q, 1H, CH–N), 2.7 (s, 1H OH), 3.55 (*J* = 7, d, 2H, CH<sub>2</sub>O), 3.61 and 3.89 (*J*(gem) = 13.2, 2 × d, 4H, CH<sub>2</sub>–N), 7.3 (m, 10H, arom).

*1-[2(S),3(S)-N,N-Dibenzylamino-3-methyl-1-pentyl]pyridinium p-toluenesulfonate (1b)*

This compound was prepared as described for 1a. M.p. 129°C;  $[\alpha]_D + 45.5^\circ$  (c 0.6, CHCl<sub>3</sub>); MS: no parent peak, 451 (M<sup>+</sup>–pyr); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.96 (m, 6H, 2 × CH<sub>3</sub>), 1.40 (m, 2H, CH<sub>2</sub>–CH<sub>3</sub>), 1.95 (m, 1H, CH–CH<sub>3</sub>), 2.27 (s, 3H, CH<sub>3</sub> of tosyl), 2.80 (m, 1H, CH–NBn), 3.34 and 3.92 (*J*(gem) = 12, 2 × d, 4H, CH<sub>2</sub>–Ph), 4.7 (m, 2H, CH<sub>2</sub>–pyr), 6.7 and 7.6 (*J* = 10, 2 × d, 4H, tosyl), 7.1 (m, arom), 8.70, 7.70, 8.35 (m, 5H, *o*, *m*, *p* H's of pyr); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 11.89 (CH<sub>2</sub>–CH<sub>3</sub>), 16.00 (CH–CH<sub>3</sub>), 21.00 (CH<sub>3</sub> of tosyl), 28.79 (CH<sub>2</sub>–CH<sub>3</sub>), 32.06 (CH–CH<sub>3</sub>), 53.34 (N–CH<sub>2</sub>–Ph), 59.41 (CH<sub>2</sub>–pyr), 63.27 (CH–NBn), 125.71; 128.42; 138.57 (arom), 144.01 (>C–SO<sub>3</sub>), 145.12, 144.52 (*o*, *p* C's of pyr).

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