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

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(Received 18 April 1983)

ABSTRACT

X-ray analysis of 1-[(2S, 3S)-2-Af,./V-dibenzylamino-3-methyl-l-pentyl]pyridinium p-toluenesulphonate and 1-[(2S)-2-N,N-dibenzylamino-l-propyl]pyridinium p-toluenesulphonate 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⁻¹ 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<)ₙ [1, 2] we became interested in the structure and properties of N-(2-aminomethyl)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 1). The reaction probably 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 $^1$H NMR spectra of the salts showed unusually high field shifts of the ortho protons of the C$_6$H$_5$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 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-[(2S 3S)-2-N,N-dibenzylamino-3-methyl-1-pentyl]pyridinium p-toluenesulphonate.
atoms of the N\textsuperscript{1}—C—C—N\textsuperscript{2} moieties in 1\text{a} and 1\text{b} are in the ideal syn-clinal or gauche conformation (torsion angles 1\text{a}: −59.0(8)\degree, 1\text{b}: −60.8(4)\degree), 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\textsuperscript{1} from the ortho carbon atoms C\textsuperscript{25} is 0.32 nm and in both compounds the N\textsuperscript{1}-lone pair points approximately in the direction of this carbon atom (the angle between N\textsuperscript{1}-lone pair—C\textsuperscript{25} is 144\degree).

**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 1\text{c}. In these calculations atomic distances and angles for the carbon and nitrogen atoms of the structure observed for 1\text{b} 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 1\text{b}. 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 1\text{c} 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 kJ mol\textsuperscript{-1} relative to \phi = 60\degree) is calculated to occur for \phi = 58\degree, close to the observed angle. Compared to the conformation with \phi = 180\degree, in which no close contacts between the amino N and the pyridinium ring are possible, the \phi = 60\degree conformation is found to be 23.4 kJ mol\textsuperscript{-1} more stable, indicating a fairly strong NH\textsubscript{2}—pyridinium interaction in the \phi = 60\degree 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\textsubscript{2}-group and the positive ortho C\textsuperscript{25}—H group. However, from an inspection of the Mulliken overlap populations it appears that in the 60\degree-form there is in fact an incipient bond formation between N\textsuperscript{1} and C\textsuperscript{25}. This becomes apparent if one compares the \phi = 60\degree with the \phi = 180\degree-form. In the 60\degree-form the C\textsuperscript{25}—C\textsuperscript{26} and C\textsuperscript{25}—N\textsuperscript{2} populations are lower by 0.027 and 0.020, respectively, whereas the population between N\textsuperscript{1} and C\textsuperscript{25} reaches a value of 0.023. All other non-bonded

<table>
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<th>\phi(\degree)</th>
<th>0</th>
<th>60</th>
<th>120</th>
<th>180</th>
<th>240</th>
<th>300</th>
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</thead>
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<tr>
<td>E(kJ mol\textsuperscript{-1})</td>
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<td>0</td>
<td>34.7</td>
<td>23.4</td>
<td>43.1</td>
<td>15.9</td>
</tr>
</tbody>
</table>

\footnote{Relative to \phi = 60\degree. The total energy at this geometry was −379.081072 hartree.}
contacts have overlap populations which are negative or very slightly positive. Thus the ortho carbon atom C\textsuperscript{25} is approaching tetrahedral coordination.

Two other features in the populations are of interest. First, the N\textsuperscript{2}—C\textsuperscript{24} 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\textsuperscript{1}—C\textsuperscript{25} value, if $\phi$ is 60\degree. 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 1\textbf{a} and 1\textbf{b} are very similar suggesting that the conformation of the central fragment of these molecules is independent of the substituent R\textsuperscript{2}. The observed gauche conformation of this fragment is in line with our calculations on compound 1\textbf{c}. The calculated difference of 23.4 kJ mol\textsuperscript{-1} between the gauche and trans (anti-periplanar) form in compound 1\textbf{c} 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 N1 and the ortho carbon atoms C25 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 1H NMR spectra of 1a and 1b are at a higher δ -value than those of ordinary pyridinium salts.

EXPERIMENTAL

1H and 13C NMR spectra were recorded on Varian EM390 and Bruker WH90 spectrometers, respectively. Chemical shifts, δ, are given in ppm down-field 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 LiAlH4 in THF [9]. The product was purified by distillation. Yield 95%. B.p. 160°C/0.001 mm Hg; [α]D = 86.9° (c 1.4, CHCl3); 1H NMR (CDCl3): δ 0.91 (J = 6.8, d, 3H, CH3), 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, CH2O), 3.31 and 3.79 (J(gem) = 13.2, 2 × d, 4H, NCH2), 7.3 (m, 10H, arom); 13C NMR (CDCl3): δ 9.08 (CH3), 63.07 (CH), 54.47 (CH2O), 53.25 (CH2N), 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 CHCl₃. The organic layer was washed and dried over Na₂SO₄. The amine was liberated from its HCl salt with NH₃ gas in CHCl₃. After column chromatography (silica, eluents CHCl₃—CH₂Cl₂ and CHCl₃—CH₃OH) and subsequent crystallization from CHCl₃—cyclohexane, 1a was obtained in 35% yield: m.p. 115°C; [α]D + 25.3° (c 1.6, CHCl₃); MS: no parent peak, 409 (M⁺—pyr); ¹H NMR (CDCl₃): δ 1.16 (J = 7.5, d, 3H, CH₃), 2.29 (s, 3H, CH₃ of tosyl), 2.8 (m, 1H, CH), 3.20 and 3.80 (J(gem) = 15, 2 X d, 4H, NCH₂Ph), 4.75 (m, 2H, CH₂—pyr), 7.1 (m, 14H, arom), 8.74, 7.65, 8.35 (m, 5H, o, p H's of pyr): ¹³C NMR (CDCl₃): δ 9.29 (CH₃), 20.52 (CH₃ of tosyl), 52.17 (NCH₂Ph), 54.29 (CH₂—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; [α]D + 45.0° (c 1.5, CHCl₃); ¹H NMR (CDCl₃): δ 0.84 (J = 6.6, d, 3H, CH₃), 0.86 (J = 7, t, 3H, CH₂—CH₃), 1.2 (m, 2H, CH₂—CH₃), 1.7 (m, 1H, CH—CH₃), 2.62 (J = 6.7, q, 1H, CH—N), 2.7 (s, 1H OH), 3.55 (J = 7, d, 2H, CH₂O), 3.61 and 3.89 (J(gem) = 13.2, 2 X d, 4H, CH₂—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; [α]D + 45.5° (c 0.6, CHCl₃); MS: no parent peak, 451 (M⁺—pyr); ¹H NMR (CDCl₃): δ 0.96 (m, 6H, 2 X CH₃), 1.40 (m, 2H, CH₂—CH₃), 1.95 (m, 1H, CH—CH₃), 2.27 (s, 3H, CH₃ of tosyl), 2.80 (m, 1H, CH—NBn), 3.34 and 3.92 (J(gem) = 12, 2 X d, 4H, CH₂—Ph), 4.7 (m, 2H, CH₂—pyr), 6.7 and 7.6 (J = 10, 2 X d, 4H, tosyl), 7.1 (m, arom), 8.70, 7.70, 8.35 (m, 5H, o, p H's of pyr); ¹³C NMR (CDCl₃): δ 11.89 (CH₂—CH₃), 16.00 (CH—CH₃), 21.00 (CH₃ of tosyl), 28.79 (CH₂—CH₃), 32.06 (CH—CH₂), 53.34 (N—CH₂—Ph), 59.41 (CH₂—pyr), 63.27 (CH—NBn), 125.71; 128.42; 138.57 (arom), 144.01 (>C—SO₃), 145.12, 144.52 (o, p C's of pyr).

ACKNOWLEDGEMENTS

We thank Mrs. Vera Kaats-Richters for experimental assistance and Dr. J. A. Vliegenthart and Dr. J. H. van Lenthe for their helpful cooperation in the calculations.
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