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The intramolecular hydrogen bonds in some Schiff bases derived from cyclopropyl-, cyclobutyl- and cyclopentylamine

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Abstract

Eight Schiff bases (*N*-(R-salicylidene)–cycloalkilamines, R = H, 5-NO_2 and 5-Br) obtained from cyclopropyl, cyclobutyl- and cyclopentylamine were investigated in terms of intramolecular hydrogen bond formation in chloroform solution and in the solid state. The relationship between cycloalkyl ring size and proton position was discussed. For the compounds which exist as OH form (salicylaldehyde and 5-bromosalicylaldehyde derivatives), no correlation between ring size and proton position in hydrogen bond was found. For 5-nitro derivatives, the structure of hydrogen bridge strongly depends on the cycloaliphatic ring size.

Keywords: ^{1}H, ^{15}N, ^{13}C NMR; ^{13}C and ^{15}N CPMAS; Schiff base; Hydrogen bonds; Cyclopropyl; Cyclobutyl; Cyclopentyl rings

1. Introduction

The Schiff bases derived from substituted salicylaldehyde are very interesting and useful compounds in practical and theoretical considerations [1,2]. Many of the Schiff bases show tautomeric properties and have been studied by UV-VIS techniques [3–5], and X-ray [6–10], and DFT calculation [11], and both using NMR in the liquid and in solid state [12–16].

In the previous papers [12–16], we have investigated the influence of substituents in phenyl ring and amine used for condensation on the structure of intramolecular hydrogen bond formed in some Schiff bases. The first conclusion was as follows: all substituents in phenyl ring, which increase acidity of OH group in applied salicylaldehyde derivatives, promote the proton transfer from oxygen atom to nitrogen and vice versa. The second conclusion is, the imine derivatives of aliphatic amines can form intramolecular bridge in which proton is more effectively transferred to nitrogen atom comparing with aromatic amine derivatives. To obtain aromatic derivatives with proton transferred to the nitrogen atom, it is necessary to increase acidity of OH group by appropriate substitution of phenyl ring or by increasing basicity of imine moiety using specific substituted aniline derivatives for condensation (for example, *N*-diMe substituent in position 4) [17,18]. In the present paper, we would like to study the effect of presence of small aliphatic ring located on nitrogen atom on tautomeric equilibrium in some Schiff bases obtained from salicylaldehyde derivatives.

Generally for Schiff bases obtained from aliphatic amines, the nitro group in position 5 in benzene ring promotes the proton transfer from oxygen to nitrogen site leading to large upfield shift of nitrogen NMR imine atom signal to about −100.0 ppm at room temperature and to −180.2 ppm at 195 K [16]. In the solid state, we observed even stronger effect, the upfield shift to −200.9 ppm indicating even more effective proton transfer in this condition. After replacing ethyl substituent on nitrogen atom by cyclopropane ring, the structure of hydrogen bridge is completely different. In both phases, the nitrogen signals of imine moiety are in the same range: −70.9 ppm in chloroform solution at room temperature, −74.5 ppm at 223 K and −71.0 ppm in the solid state [15]. It means that in all applied conditions, the OH form with weak hydrogen bond is present. This is in contrast to ethyl derivative, where even at room temperature, the tautomeric equilibrium is

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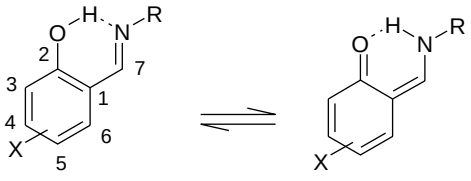

Fig. 1.

shifted to NH form, at low temperature and in the solid state the NH tautomeric form is a predominant one. To verify this observation, we extend now this investigations on eight new derivatives containing different substituents in phenyl ring and three different aliphatic small rings on nitrogen atom (Fig. 1).

2. Experimental

All investigated compounds have been synthesized by direct condensation of appropriate substituted salicylaldehydes with cycloalkyl amines in methanol solution. The mixtures of aldehyde and amine in proportion 1:1 were refluxed in methanol about 4 h and then after removing of the solvent were crystallized from ethanol. The yield of reactions were approximately 40–60% for oils (**1A**, **1B**, **1C** and **2B**) and 60–80% for solids (**2A**, **2C**, **3A**, **3B** and **3C**). Only in the case of reaction of 2-hydroxy-5-nitrobenzaldehyde, the product precipitates right after mixing of both substrates.

The NMR measurements were run on a Bruker Avance DRX 500 spectrometer. For solutions, the triple resonance inverse 5 mm probehead with *Z*-gradient was applied. The solid state spectra were done using 4 mm CPMAS Bruker probehead. For solution experiments run at room temperature (303 K), about 5 mg of samples were dissolved in $CDCl_3$. The nitrogen and carbon chemical shifts were obtained and assigned by 2D GHMBC and GHSQC methods. In some cases to assign proton signals, the GCOSY homonuclear correlations were necessary. The nitrogen chemical shifts are reported with respect to external nitromethane. The typical spectral condition for natural abundance nitrogen CPMAS NMR spectra were: spectral width 28 kHz, acquisition time 40 ms, spin rate 6–12 kHz, contact time for spin-lock 5 ms, relaxation delay 10–120 s depending on relaxation condition for particular sample, estimated from carbon measurement. The typical experimental condition for carbon CPMAS were: spectral width 31 kHz, acquisition time 20 ms, contact time 2 ms, spin rate 12 kHz. To distinguish protonated and quaternary carbon atoms, the short contact time spectra with contact time 40 μs were done. In SCT experiments, only protonated carbon atom signals are displayed. Originally, the solid-state spectra were referenced to the solid glycine sample and then the obtained chemical shifts of appropriate signals were recalculated to TMS scale for carbon, and nitromethane for nitrogen measurements, respectively.

3. Results and discussion

All results of NMR measurements of eight new compounds and one taken from literature, in both phases, if possible, are collected in Tables 1–3. In contrast to the other compounds, the cyclobutyl and cyclopentyl derivative of 5-nitrosalicylaldehyde (**3B** and **3C**) were measured in chloroform solution only at 253 K. At lower temperatures, the severe broadening of signals appeared making any nitrogen NMR measurements impossible.

For the intramolecular hydrogen bond investigation, three spectral parameters have practical significance. The most important one is the nitrogen chemical shift of imine atom. This parameter provides quantitative estimation of

Table 1
Proton, carbon and nitrogen chemical shifts of cycloalkylamine derivatives of salicylaldehyde in chloroform solution

Atom position	Solution					
	N-salicylidene-cyclopropylamine, **1A**		*N*-salicylidene-cyclobutylamine. **1B**		*N*-salicylidene-cyclopentylamine, **1C**	
	^{1}H	$^{13}C/^{15}N$	^{1}H	$^{13}C/^{15}N$	^{1}H	$^{13}C/^{15}N$
1	–	119.1	–	118.7	–	118.9
2	–	160.4	–	161.7	–	161.2
3	6.91	116.8	6.93	117.2	6.98	117.0
4	7.25	131.6	7.27	132.2	7.26	131.9
5	6.85	118.6	6.83	118.4	6.83	118.4
6	7.20	130.7	7.20	131.4	7.20	131.1
7	8.46	161.9	8.20	162.0	8.30	162.3
OH	12.71	–	13.13	–	13.65	–
N 303 K	–	−72.9	–	–75.0	–	−70.0
N 223 K	–	−73.5[a]	–	−87.7	–	−72.3
1′	2.95	40.3	4.10	61.3	3.74	69.9
2′	0.97, 0.93	9.3	2.35, 2.18	30.6	1.21, 1.70	34.6
3′	–	–	1.85	15.7	1.83, 1.67	24.3

[a] Weak correlation with OH proton.

Table 2
Proton, carbon and nitrogen chemical shifts of cycloalkylamine derivatives of 5-bromosalicylaldehyde in chloroform solution and in solid state

Atom position	*N*-(5-bromosalicylidene)-cyclopropylamine, **2A**			*N*-(5-bromosalicylidene)-cyclobutylamine, **2B**		*N*-(5-bromosalicylidene)-cyclopentylamine, **2C**		
	Solution		CPMAS	Solution		Solution		CPMAS
	^{1}H	^{13}C/^{15}N	^{13}C/^{15}N	^{1}H	^{13}C/^{15}N	^{1}H	^{13}C/^{15}N	^{13}C/^{15}N
1	–	120.5	122.0	–	120.1	–	120.2	121.0
2	–	159.4	160.8	–	160.4	–	160.4	161.3
3	6.82	118.7	119.1	6.84	119.2	6.83	119.1	119.9
4	7.33	134.1	133.1[a]	7.34	135.0	7.35	134.7	133.7[a]
5	–	110.2	–[b]	–	109.8	–	109.8	–[b]
6	7.32	132.7	133.1[a]	7.31	133.4	7.33	133.2	133.7[a]
7	8.39	160.6	161.9	8.13	160.7	8.25	160.9	163.2
OH	12.7	–	–	13.65	–	13.65	–	–
N 303 K	–	−69.3	−66.2	–	−74.2	–	−68.4	−69.6
N 223 K	–	−70.3	–	–	−73.0	–	−69.1	–
1′	2.98	40.2	40.4	4.12	61.5	3.78	69.9	70.3
2′	1.01, 0.96	9.7	9.6	2.36, 2.18	30.4	1.95, 1.69	34.6	34.9
3′	–	–	–	1.86	15.7	1.87, 1.69	24.3	24.7

[a] Specific assignment impossible because of signals overlapping.
[b] Missing signal probably due to large broadening.

proton position. The typical value of this parameter for pure imine structure is about −50 ppm [19]. Intramolecular hydrogen bond or proton transfer shift this signal upfield to −240 ppm [13]. The one bond coupling constants are even better for such estimation but only for the compounds where the tautomeric equilibrium is shifted to NH form [16]. For the tautomeric systems where the equilibrium is shifted to OH form, measurement of this coupling is impossible. For the tautomeric equilibrium estimations, but only on qualitative level, the carbon chemical shifts of atoms in position 2 can be applied. In this case, the downfield shift of C-2 signal to about 170–180 ppm is typical for the structure with proton transfer from oxygen to nitrogen atom [16].

The analysis of nitrogen chemical shifts collected in Tables 1 and 2 leads to the conclusion that both series of compounds have a very similar structure in both solvent and solid state. The δ_N values in the range from −66 to −87 ppm show that in all cases the OH form with hydrogen bond is present. At low temperature, usually the tautomeric equilibrium position is shifted slightly more to NH form, but this effect for the investigated compounds is very weak, except for the compound **1B**, where observed difference suggests some higher contribution of form NH. However, the differences between nitrogen chemical shifts for compounds **1A–1C**, **2A–2C** and **3A** are small to make some reliable conclusion in terms of hydrogen bond strengths. We have to

Table 3
Proton, carbon and nitrogen chemical shifts of cycloalkylamine derivatives of 5-nitrosalicylaldehyde in chloroform solution and in solid state

Atom position	*N*-(5-nitrosalicylidene)-cyclopropylamine, **3A**			*N*-(5-nitrosalicylidene)-cyclobutylamine, **3B**			*N*-(5-nitrosalicylidene)-cyclopentylamine, **3C**		
	Solution		CPMAS	Solution		CPMAS	Solution		CPMAS
	^{1}H	^{13}C/^{15}N	^{13}C/^{15}N	^{1}H	^{13}C/^{15}N	^{13}C/^{15}N	^{1}H	^{13}C/^{15}N	^{13}C/^{15}N
1	–	118.1	118.6	–	116.3	112.9	–	116.3	113.0
2	–	166.4	166.2[a]	–	170.4	180.4	–	170.7	180.4
3	6.98	118.2	117.5	6.95	119.5	122.7	6.98	119.5	123.0
4	8.17	126.8	126.7	8.18	128.5	130.4	8.18	128.2	130.2
5	–	139.7	138.9	–	138.5	132.3	–	138.4	132.2
6	8.21	126.7	126.7	8.23	128.6	135.9	8.24	128.3	135.0
7	8.54	160.5	160.6	8.25	161.2	164.5	8.36	161.8	163.7
OH	13.85	–	–	14.4	–		14.4	–	–
N 303 K	–	−70.9[a]	−71.0[a]	–	−100.8	−198.4	–	−101.7	−197.2
N 223 K	–	−74.5[a]	–	–	−130.7[b]	–	–	−129.6[b]	–
1′	3.07	40.1	40.2	4.23	59.8	54.2	3.54	68.0	62.3[c]
2′	1.02, 1.09	9.9	9.8	2.45, 2.25	30.3	31.9, 25.0	2.05, 1.75	34.2	33.1, 28.0
3′	–	–	–	1.90	15.6	14.5	1.85, 1.70	24.1	22.9, 21.9

[a] Data taken from literature [15].
[b] 253 K.
[c] Two close overlapped signals.

remember that nitrogen chemical shift depends not only on hydrogen bond structure but also on substitution effects on nitrogen atom. In our case we should expect few long-range substitution effects whose values are difficult to estimate because in literature there are no data concerning this type of interaction in small aliphatic rings. Usually such substitution increments are about a few parts per million upfield or downfield which makes any estimation very difficult. Taking into account these facts, we can state that in all discussing cases the hydrogen bonds are weak and similar to each other. Examination of ^{13}C NMR data for compounds **1A**, **1B**, **1C** and **2A**, **2B**, **2C** leads to the same conclusion. It is known that only carbon chemical shift of atom 2 provides valuable structural information. The signals of those atoms for the discussed compounds are located very close to 160 ppm which is typical for OH weakly hydrogen bonded structure and they do not change at low temperature or in solid state. The number of ^{13}C CPMAS signals for **3B** and **3C** in aliphatic region suggests that in the solid state, the four and five membered rings are non-planar and in this condition two non-equivalent forms are present (two signals for C-2′ and two for C-3′ positions). This differentiation also leads to two overlapped signals of C-1′ atoms.

Quite different situation was found for 5-nitro derivatives. Previously, three *N*-(5-nitrosalicylidene)-alkylamines [16] have been investigated: N–Et, N–iPr and N–*t*Bu. All of those compounds, at room temperature, show a large upfield shift of nitrogen signal indicating a strong intramolecular hydrogen bond (for 5-nitrosalicylaldehyde derivative with $EtNH_2$ at 254 K $\delta_N = -131.3$ ppm). The lowering of temperature causes further proton transfer from oxygen to nitrogen site. As a result of this, the nitrogen signals are shifted to −180 ppm region at 195 K. In the solid state, this process is even stronger, shifting nitrogen signals from −180 to −200 ppm range. The cyclobutyl **3B** and cyclopentyl **3C** derivatives provide very similar spectral picture, which allow to conclude that there are no significant differences between the structure in intramolecular hydrogen bonds of derivatives with four and five membered cycloaliphatic rings. In contrast to this, cyclopropyl derivative **3A** in all applied conditions exists as OH structure with relatively weak hydrogen bond. This effect was observed previously for cyclopropyl derivative of 5-nitrosalicylaldehyde [15]. Since in all 5-nitro derivatives, acidity of OH group determined by nitro substituent should be very similar, then the difference in molecular structure between **3A** and **3B**, **3C** must be caused by property of aliphatic rings bonded to nitrogen atom. Comparing the data in Table 3 with the other aliphatic derivatives available, we can state that the cyclobutyl and cyclopentyl rings have very similar proton donating properties as the chain aliphatic groups. In contrast to this, the electron donating properties of cyclopropyl ring must be much weaker and it means that cyclopropylamine must be significantly weaker base than cyclobutyl- and cyclopentylamine. The low value of $pK_a = 9.10$ of cyclopropylamine [20] comparing with cyclobutylamine ($pK = 10.04$) and cyclopentylamine ($pK = 10.65$) can be explained by the partially olefinic character of cyclopropane ring and by the differences in stability of the cycloalkanes with respect of ring size [21]. These differences are not big enough to change structure of hydrogen bonds in salicylaldehyde and 5-bromosalicylaldehyde derivatives (Tables 1 and 2). The proton positions in those compounds are determined by relatively low acidity of OH group. The nitro group in position 5 increases the acidity of OH and makes possible the proton transfer to nitrogen atom. The electron donating character of chain alkyls and cyclobutyl and cyclopentyl rings, which increases basicity of imine group, make this transfer very effective.

Cyclopropyl ring does not possess such property and as a consequence, the imine group is not enough basic to allow such transfer. From this point of view, the cyclopropane ring reacts very similar to substituted benzene ring (for example, p*K* value for aniline is 9.42).

4. Conclusion

The proton position in intramolecular hydrogen bridge formed by Schiff bases obtained from salicylaldehyde derivatives is very sensitive to both substituents present in phenyl ring and amine used for condensation. The nitro substituent in position 5 in phenyl ring increases acidity of OH group so effectively that, for aliphatic derivatives the proton transfer to nitrogen atom becomes possible, especially at low temperature and in the solid state [16]. Similar effect was found for cyclobutyl and cyclopentyl derivatives. The cyclopropyl derivative behaves completely differently. In all experimental conditions, chloroform solution and in the solid state, only a OH structure with a weak hydrogen bond was observed. It means that electron-donating effect created by four and five membered aliphatic ring is strong enough to increase basicity of imine nitrogen atom to make proton transfer effective. For derivative with cyclopropane ring, this effect is much smaller or even absent.

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