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Spectral assignment and proton transfer studies of *N*-(*R*-salicylidene)-1-amino-1-deoxy-D-sorbitols

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Introduction

Schiff bases (**1–9**), derivatives of various *o*-hydroxyaldehydes and 1-amino-1-deoxy-D-sorbitol, are optically active compounds that can be studied as potential ligands for various metal complexes.[1,2] The properties of the Schiff base complexes and especially their use as enantioselective catalysts[3–6] are related to the structure of the ligands; therefore, the knowledge about factors crucial for structure of ligands like hydrogen bond and proton transfer processes can be important for the possible applications of studied compounds.

In this report, we present studies concerning intramolecular hydrogen bonding and tautomeric equilibrium as well as full assignment of ^{1}H and ^{13}C NMR spectra and ^{15}N NMR data of *N*-(*R*-salicylidene)-1-amino-1-deoxy-D-sorbitols, which can be useful in synthesis of various optically active metal complexes[1,2] or chiral *N*-acyloxazolines.[7] Schiff bases, derivatives of natural product like D-sorbitol, can be especially useful in synthesis of new chiral complexes because of the presence of carbon chain with several hydroxyl groups and possible formation of polydentate complexes. Additionally, recent studies concerning Schiff bases, derivatives of glucosamine, and their complexes deal usually with ring form of glucose moiety,[8,9] only few deal with chain form.[1,2]

Experimental

Materials

All salicyladehydes used and 1-amino-1-deoxy-D-sorbitol were purchased from Sigma-Aldrich Poznań, Poland, and the methanol was purchased from Chempur Piekary Śląskie, Poland.

Synthesis

Schiff bases (**1–9**) (Fig. 1) were prepared according to the procedure described in Ref. [7] in methanol solution. The crude products were recrystallized from methanol. Compounds (**1**) and (**6**) are already known and characterized[7]; the other studied Schiff bases have not been synthesized before. Melting point of these new compounds, elemental analysis, tables with FTIR-spectra description, UV-Vis bands as well as specific rotation are available in the Supporting information.

Measurements

The ^{1}H and ^{13}C NMR spectra were recorded on Bruker DPX-400 spectrometer (BRUKER BioSpin, Rheinstetten, Germany) at room temperature (25 °C) in DMSO-d_6 solution. The ^{15}N indirect correlation measurements have been performed on Bruker DRX-500 machine (BRUKER BioSpin, Rheinstetten, Germany) using triple-resonance inverse probehead. For single scan one-dimensional proton spectra, $\pi/2$ pulse was applied; for multi-pulse experiments, usually 30° flip angle was used. one-dimensional ^{13}C NMR spectra were obtained using 30° pulse with broadband proton decoupling. For proton spectra, the acquisition time of 4 s without additional relaxation delay was used. The carbon NMR spectra were recorded with acquisition time about 1.5 s and relaxation delay of 1 s. The typical spectral widths of 15, 220, and 400 ppm were used for proton, carbon, and nitrogen spectra, respectively. All two-dimensional spectra (gCOSY, gHSQC, and gHMBC) usually were acquired with 2048 data points for *t*2 and 256 for *t*1 increments. The long-range coupling correlation measurements (gHMBC) were optimized for $^{n}J = 8$ Hz for both carbon and nitrogen experiments. For all two-dimensional experiments, the linear prediction and zero filling procedures were applied. The following weighting functions were used: squared sine bell for f1 and f2 domains in gCOSY, Gaussian in f1 and squared sine bell in f2 for gHMBC, and Gaussian in f2 and f2 for gHSQC measurements. The ^{1}H and ^{13}C chemical shifts were referred to internal TMS, and ^{15}N chemical shifts were referred to external nitromethane as a standard according to Internation Union of Pure and Applied Chemistry (IUPAC) recommendation. The standard Bruker software was used for acquisition of spectra and data processing. Typical concentration of the samples was 0.1 M.

Results and discussion

The full assignments of ^{1}H signals of aromatic moiety as well as sugar moiety for studied compounds **1–9** in DMSO solutions are given in Table 1.

The proton signals with the highest frequencies, assigned to the proton donor group, are observed in the range $\delta = 13.33$–14.58 (Table 1) and indicate the presence of a medium strong hydrogen bond.[10] The most deshielded signals are of low intensity and mostly broad. For all compounds studied, imine signals at room temperature were in the range from 8.25 to 8.69 ppm. The proton chemical shifts of sugar moiety have changed only slightly with

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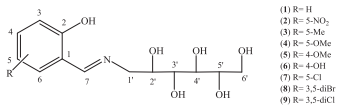

Figure 1. Studied *N*-(*R*-salicylidene)-1-amino-1-deoxy-D-sorbitols (**1–9**).

the change of substituents on aromatic ring (DELTA δ_H up to ~0.1 ppm). Larger change of the chemical shifts (up to 0.4 ppm) was observed for OH signals at position 2′.

The full assignments of ^{13}C signals for studied compounds **1–9** in DMSO solutions are given in Table 2. The values of ^{13}C chemical shifts of aromatic moiety for compounds (**1**), (**8**), and (**9**) were similar to those observed for glucosamine Schiff bases in DMSO.[9]

The chemical shift of the C-2 carbons, the most sensitive for the position of the proton transfer equilibrium, was in the range from $\delta = 154.70$ ppm for *N*-(5-methoxysalicylidene)-1-amino-1-deoxy-D-sorbitol (**4**) to 178.60 ppm for *N*-(5-nitrosalicylidene)-1-amino-1-deoxy-D-sorbitol (**2**) and was similar to those observed for other Schiff bases, derivatives of various aromatic *o*-hydroxyaldehydes.[11–13] For compounds (**1**), (**3**), (**4**), and (**7**), values of δC-2 about 160 ppm suggested localization of the hydrogen at oxygen atom of OH group, while for compounds (**2**), (**5–6**), and (**8–9**), values above ~165 ppm might indicate the presence of proton transfer equilibrium (Fig. 2).

To estimate the equilibrium constants for the proton transfer process in the Schiff base and hence mole fraction of the NH form, the equation proposed in Ref. [14] has been used:

$$K = \frac{\delta - \delta_{OH}}{\delta_{NH} - \delta}$$

where δ is the observed chemical shift and δ_{OH} and δ_{NH} are chemical shifts for the pure OH and NH forms, respectively. As a reference, values of δ_{OH} and of δ_{NH}, 152.2[11] and 180.4 ppm,[12] respectively, have been used. Detailed description of calculation of the χ_{NH} values is available in the Supporting information. The estimated mole fractions of the NH form (χ_{NH}) on the basis of the δC-2 chemical shift are given in Table 3.

The established χ_{NH} values suggested the presence of proton transfer equilibrium for almost all the compounds studied (except **4**). For compounds **2**, **5**, **6**, **8**, and **9**, χ_{NH} values were equal to or even larger than 0.5. The strongest influences on the position of the proton transfer equilibrium have shown to be electron-withdrawing nitro group at position 5, methoxy or hydroxyl group at position 4, and presence of the halogen atoms at positions 3 and 5. Similar effect of substituent at position 5 was observed for Schiff bases, derivatives of benzylamine.[13]

In the glucose moiety, the largest variation of the chemical shifts was observed for C-1′ and C-2′ carbons. Smaller values at δC-1′ and δC-2′ were found for these compounds, where proton transfer equilibrium has been suggested, for example, (**2**), (**5–6**), and (**8–9**).

The ^{15}N chemical shifts were in the range from −83.9 ppm for *N*-(5-methoxysalicylidene)-1-amino-1-deoxy-D-sorbitol (**4**) to −141.9 ppm for *N*-(4-methoxysalicylidene)-1-amino-1-deoxy-D-sorbitol (**5**) (Table 4). Almost all δN values are typical for Schiff bases with OH···N intramolecular hydrogen bond where proton transfer exists,[15] similar to those observed for glucosamine Schiff bases[9] as well as for derivatives of benzylamine.[13] Using the equation proposed by Ref. [14], the position of the proton transfer equilibrium has been also estimated taking into account the values of ^{15}N chemical shifts (Table 3). The value −83.1 ppm has been taken as a reference value for pure OH form while −243.9 ppm for the pure NH form.[16]

Table 1. ^{1}H chemical shifts (ppm) of *N*-(*R*-salicylidene)-1-amino-1-deoxy-D-sorbitols (**1–9**) in DMSO-d_6 solution (in parenthesis *J*-values in Hz)

Comp.	R	Position											
		2	3	4	5	6	7	1′	2′	3′	4′	5′	6′
(**1**)	H	13.67[b] (s)	~6.84[a] (d)	7.30 (dt, 7.6,1.7)	~6.86[a] (t)	7.42 (dd, 7.5, 1.6)	8.48 (s)	~3.83[a] 3.53[a]	3.83[a] 4.84 (d, 4.8)	3.67 (t, 4.7) 4.40(d, 6.4)	3.49[a] 4.50 (d, 5.1)	3.50[a] 4.36 (t, 5.6)	3.59[a] ~3.37[a] ~4.4[b]
(**2**)	5-NO_2	14.11[b] (s)	6.55 (d, 9.7)	8.00 (dd, 9.7, 3.1)	—	8.43 (d, 3.1)	8.69 (s)	3.85[a] ~3.63[a]	3.88 5.24 (d, 5.1)	3.65 (m) 4.54 (d, 4.7)	3.48[a] 4.61 (d, 6.2)	~3.48[a] 4.40 (t, 5.3)	~3.60[a] 3.42 (m) ~4.4[b]
(**3**)	5-Me	13.33[b] (s)	6.76 (d, 8.3)	7.12 (dd, 8.4, 1.9)	—(2.23) (s)	7.21 (d, 1.7)	8.42 (s)	3.82[a] 3.52 (m)	3.80[a] 4.82 (d, 4.8)	3.66(t, 4.6) 4.39 (d, 6.5)	~3.50[a] 4.49 (d, 4.8)	~3.50[a] 4.37(t, 5.5)	~3.60[a] 3.38[a] (m) ~4.4[b]
(**4**)	5-OMe	12.99[b] (s)	6.80 (d, 8.9)	6.93 (dd, 9, 3.2)	—(3.71)	7.04 (d, 3.1)	8.45 (s)	~3.80[a] ~3.50[a]	3.80[a] 4.82 (d, 3.9)	3.66 (m) 4.39[a]	~3.50[a] 4.50 (d, 4.1)	~3.50[a] 4.35[a]	3.58 (m) 3.39[a] ~4.4[b]
(**5**)	4-OMe	14.01[b] (s)	6.29 (d, 2.4)	—(~3.80)	6.34 (dd, 8.7, 2.4)	7.28 (d, 8.7)	8.35 (s)	~3.80[a] ~3.50[a]	~3.80[a] 4.97 (d, 4.8)	3.70 (t, 4.6) 4.49 (d, 6.4)	~3.50[a] 4.57 (d, 5.1)	~3.50[a] 4.43 (m)	~3.64 (m) 3.40[a] br.
(**6**)	4-OH	13.86[b] (s)	6.10 (d, 2.1)	—(9.85)[b]	6.20 (dd, 8.5, 2.2)	7.15 (d, 8.5)	8.25 (s)	~3.74[a] ~3.42[a]	3.74 4.87[b]	3.64 (m) ~4.50[a,b]	~3.50[a] ~4.50[a,b]	~3.50[a] ~4.41[a]	3.40[a] 3.58 (m) ~4.4[a,b]
(**7**)	5-Cl	13.77[b] (s)	6.83 (d, 8.9)	7.33 (dd, 8.8, 2.7)	—	7.55 (d, 2.7)	8.48 (s)	~3.84[a] ~3.54[a]	~3.85 4.88 (d, 5.0)	3.61 (t, 4.7) 4.50 (d, 5.1)	~3.50[a] 4.42 (d, 6.4)	~3.50[a] 4.37 (t, 5.7)	3.40[a] 3.60 (m) ~4.4[a,b]
(**8**)	3,5-diBr	14.58[b] (s)	—	7.76 (d, 2.5)	—	7.55 (d, 2.5)	8.46 (s)	~3.87[a] ~3.62[a]	~3.81[a] 5.16 (d, 4.7)	3.68 ~4.50[a]	~3.50[a] 4.42[a]	~3.50[a] 4.58[a]	3.40[a] 3.60 (m) ~4.45[a,b]
(**9**)	3,5-diCl	14.58[b] (s)	—	7.55 (s)	—	7.41 (d, 1.6)	8.50 (s)	3.84[a] ~3.62[a]	3.80[a] 5.15 (s)	3.67[a] ~4.55[a]	3.48[a] 4.55[a]	3.48[a] ~4.40[a]	~3.40[a] ~3.60[a] ~4.45[a,b]

In parenthesis are *J* values in Hz.
[a]Overlapped.
[b]Broad.

Table 2. ^{13}C chemical shifts (ppm) of *N*-(*R*-salicylidene)-1-amino-1-deoxy-D-sorbitols (**1–9**) in DMSO-d_6 solution

Compound	Position												
	1	2	3	4	5	6	7	1′	2′	3′	4′	5′	6′
(**1**)	118.68	161.23	116.62	132.21	118.18	131.63	166.64	61.37	72.26	70.06	71.64	71.50	63.43
(**2**)	113.36	178.60	123.11	129.34	132.92	133.25	167.82	54.82	70.88	70.20	71.14	71.40	63.37
(**3**)	118.42	158.66	116.29	132.81	126.80 (19.95)	131.44	166.51	61.63	72.30	70.03	71.68	71.50	63.43
(**4**)	119.08	154.70	117.16	118.55	151.43 (55.56)	114.85	166.29	61.81	72.29	70.05	71.67	71.50	63.43
(**5**)	111.63	168.67	101.33	163.84 (55.15)	105.40	133.45	165.13	58.29	72.22	70.02	71.52	71.47	63.42
(**6**)	111.09	167.16	102.96	162.20	106.45	133.61	165.29	58.98	72.31	69.98	71.61	71.48	63.42
(**7**)	119.50	160.75	118.93	132.00	121.18	130.55	165.56	61.00	72.09	70.10	71.48[a]	71.48[a]	63.43
(**8**)	116.73[a]	166.35	116.73[a]	138.39	102.65	134.37	166.09	55.72	71.45	70.15	71.42	71.01	63.39
(**9**)	116.25	166.12	115.77	133.09	125.29	130.51	166.17	56.00	71.49	70.16	71.42	71.02	63.40

[a]Overlapped.

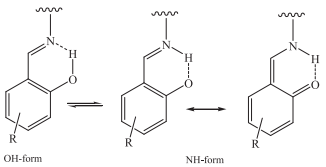

Figure 2. Proton transfer equilibrium in Schiff bases.

Table 3. Estimated mole fraction of the NH form (χ_{NH}) of compounds studied

Compound	(χ_{NH})		
	^{13}C NMR	^{15}N NMR	UV-Vis
1	0.3	0	0.2
2	0.9	0.2	0.6
3	0.2	0	0.1
4	0	0	0.1
5	0.6	0.4	0.3
6	0.5	0.3	0.3
7	0.3	0	0.2
8	0.5	0	0.8
9	0.5	—	0.8

Table 4. ^{15}N chemical shifts (ppm) of *N*-(*R*-salicylidene)-1-amino-1-deoxy-D-sorbitols (**1–8**) in DMSO-d_6 solution

Compound	δ
(**1**)	−90.4
(**2**)	−110.2
(**3**)	−87.6
(**4**)	−83.9
(**5**)	−141.9
(**6**)	−132.9
(**7**)	−92.2
(**8**)	−94.4

For compounds (**1**), (**3–4**), and (**7–8**), the ^{15}N NMR chemical shifts have suggested position of the equilibrium strongly shifted towards the OH form and the mole fraction of the NH form was equal to 0 or close to 0, while for (**2**), (**5**), and (**6**), χ_{NH} values are between 0.2 and 0.4. However, these values were much smaller than calculated based on ^{13}C chemical shifts. Because of discrepancy of the χ_{NH} values estimated based on ^{13}C and ^{15}N chemical shifts, the position of the proton transfer equilibrium was also evaluated based on UV-Vis results (Table 3). The presence of two bands, low-energy band at ~400 nm and high-energy band ~300 nm, for all *N*-(*R*-salicylidene)-1-amino-1-deoxy-D-sorbitols indicated the existence of the proton transfer equilibrium[17,18] (Table S1 in the Supporting information) and allowed calculating the mole fractions of the NH form (Table 3). The description of the equilibrium constants calculation and χ_{NH} values of the studied *N*-(*R*-salicylidene)-1-amino-1-deoxy-D-sorbitols is available in the Supporting information.

Comparison of the data from Table 3 has shown better agreement between χ values estimated based on ^{13}C chemical shift and evaluated by UV-Vis spectroscopy than estimated based on ^{15}N chemical shift values for almost all compounds studied. The extremely large variation of the χ values for **8** and **2** has shown the sensitivity of the $\delta^{15}N$ not only to position of the proton transfer equilibrium but also to substituent effects. Hence, δC-2 values were a better tool in preliminary estimation of position of the proton transfer equilibrium than δN values. Larger differences between both values (χ up to 0.3) were observed for compounds where mole fraction of the NH form was larger or equal to 0.5. Different values of χ calculated based on δC-2, δN, and UV-Vis data clearly have shown that chemical shifts can be useful only for preliminary estimation of the mole fraction of the NH form.

Taking into account the χ values estimated by UV-Vis spectroscopy, the nitro group at position 5 or halogens at positions 3 and 5 have the strongest influence on proton transfer equilibrium. Substituents at position 5 or at 3 and 5 have influence on acidity of the phenolic group through mesomeric and steric effects. Smaller effect was observed for compounds with substituents at position 4 where both effects caused a change in the basicity of the nitrogen atom. Similar influence of the substituents on position of the proton transfer equilibrium was observed for *N*-(*R*-salicylidene)-glucamines[9] and *N*-(*R*-salicylidene)-methylamines[11] or *N*-(5-*R*-salicylidene)-benzylamines.[13]

All studied compounds were optically active, so their optical properties, especially stability of the molar rotation, are also important. The specific and molar rotations [α] of compounds studied in DMSO are summarized in Table S2 and available in the Supporting information. Molar rotation was stable in time, and no signs of racemisation were observed. The values of [α] were in the range from −62.7 for compound (**9**) to −1.98 for compound (**1**).

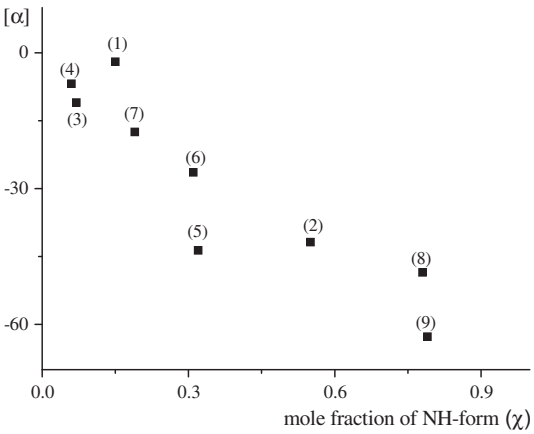

Figure 3. Dependence of the molar rotation on position of the proton transfer equilibrium for Schiff bases (**1–9**).

Taking into account estimated χ_{NH} values established from UV-Vis measurements, relationship between position of the proton transfer equilibrium and molar rotation was observed for the compounds studied (Fig. 3). Compounds where mole fraction of the NH form was larger (e.g., compounds **2**, **8**, and **9**) have shown higher negative values of [α] in comparison to those where OH form prevails, for example, compounds **1**, **4**, and **7**.

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Supporting information

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