Synthesis of bis(glycosylamino)alkanes and bis(glycosylamino)arenes

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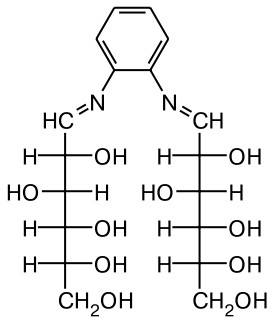
The condensation of D-mannose and D-galactose with aliphatic and aromatic diamines afforded a series of bis(glycosylamino)alkanes and -arenes. A possible mechanism was proposed for the formation of 1,2-bis(β-D-glycosylamino)benzenes.

Key words: bis(glycosylamino)alkanes, bis(glycosylamino)arenes, glycosylation, diamines, *N*-glycosylaminobenzenes, NMR spectroscopy, IR spectroscopy, X-ray diffraction analysis, chelation.

N-Glycosides are abundant in nature and perform various bioregulatory functions. Some of them have found use as drugs and ligands for the synthesis of metal complexes.[1—3] Bis(glycosylamino)ethanes, which were used as addends for coordination with salts of some transition metals,[3] were not isolated in the free state, and it was the condensation products of monosaccharides with ethylenediamine that were introduced into the complexation. Numerous glycosylamines with both aliphatic[4—10] and aromatic aglycones[11—16] have been synthesized by different methods. At the same time, despite a variety of the synthesized glycosylamines, many representatives of this class of carbohydrates are characterized incompletely. Probably, this is related to high lability of glycosylamines, which impedes their use and determination of their characteristics. The aforesaid concerns, in particular, bis(glycosylamino)alkanes and -arenes. It was assumed that the Schiff bases of type **1** can be the reaction products of monosaccharides with *o*-phenylenediamine (see Ref. 17).



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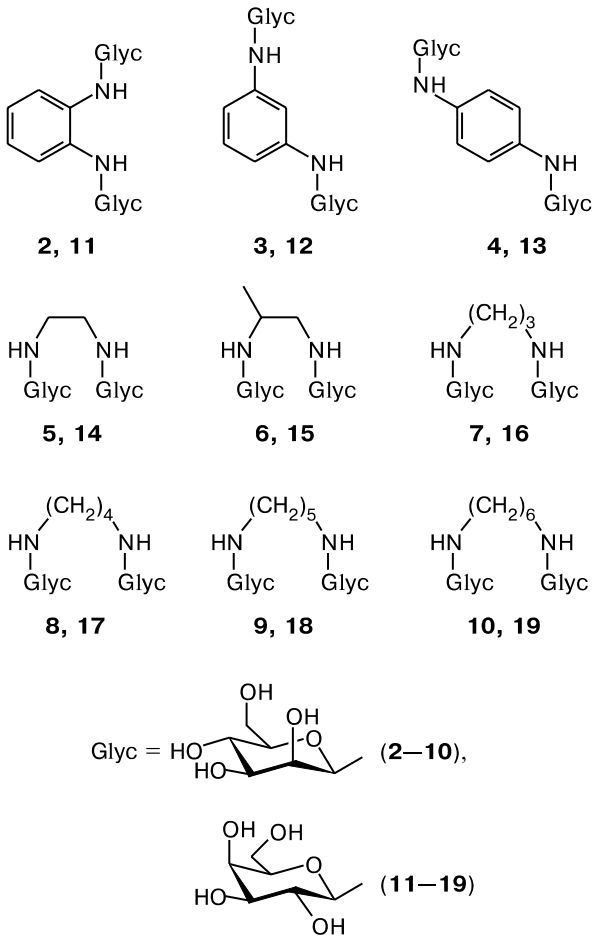
The problem of synthesis and study of the properties of bis(glycosylamino)alkanes and -arenes remains poorly explored. Therefore, it was of interest to study specific features of the synthesis of bis(glycosylamino)hydrocarbons, determine their structures, and characterize the resulting compounds. We have earlier[18] synthesized a series of bis(glycosylamino)benzenes, which are the disaccharide derivatives.

We performed condensation of D-mannose and D-galactose with 1,2-, 1,3-, and 1,4-diaminobenzenes, 1,2-diaminoethane, 1,2- and 1,3-diaminopropanes, 1,4-diaminobutane, 1,5-diaminopentane, and 1,6-diaminohexane. The following compounds were isolated as the reaction products: 1,2- (**2**), 1,3- (**3**), and 1,4-bis(β-D-mannopyranosylamino)benzene (**4**), 1,2-bis(β-D-mannopyranosylamino)ethane (**5**), 1,2- (**6**) and 1,3-bis(β-D-mannopyranosylamino)propane (**7**), 1,4-bis(β-D-mannopyranosylamino)butane (**8**), 1,5-bis(β-D-mannopyranosylamino)pentane (**9**), and 1,6-bis(β-D-mannopyranosylamino)hexane (**10**), respectively, and their galactose anologs, *viz.*, compounds **11—19**.

Compounds **2—19** were synthesized by the direct condensation of monosaccharides with 2 equiv. of diamine in 80% ethanol at room temperature in the absence of catalysts.

The reaction with aliphatic diamines is faster than that with aromatic diamines (except for that with *o*-phenylene-

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2793—2801, December, 2005.

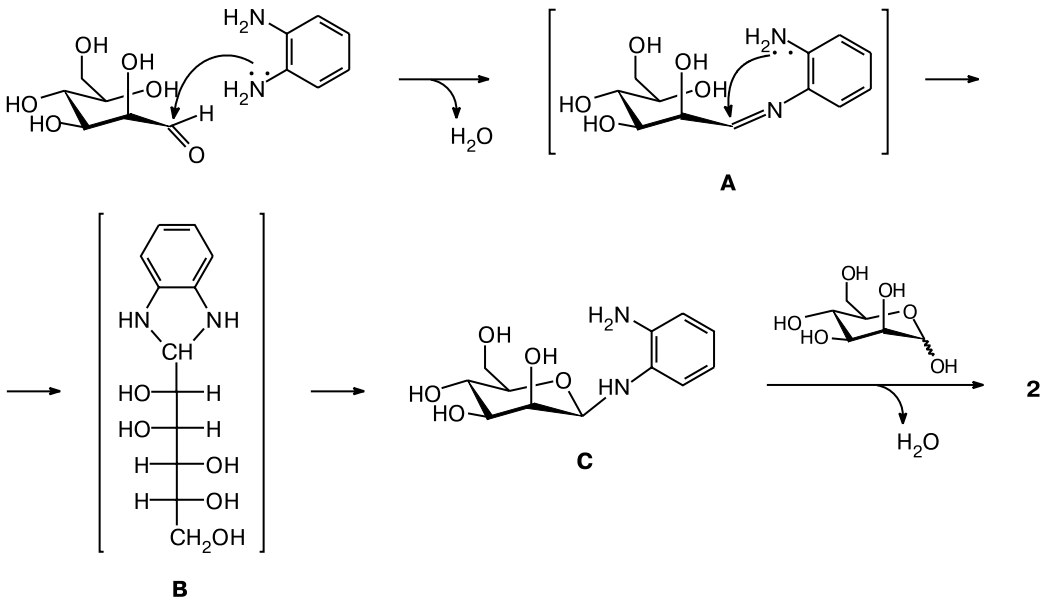


diamine). For instance, the glycosylation of diaminoalkanes completes within 1—6 h, while the reactions of *m*- and *p*-phenylenediamines with monosaccharides took 4—10 h. We believe that this difference is caused by a higher nucleophilicity of the nitrogen atoms of diamines of the aliphatic series. The duration of glycosylation of *o*-phenylenediamine is virtually comparable with that for aliphatic diamines: the process is over in 2—5 h. Probably, this fact is in favor of a special mechanism of formation of bisglycosides **2** and **11**. Perhaps, the reaction of *o*-phenylenediamine with monosaccharides affords the Schiff base (**A**), which gives intermediate **B** of the aminal nature due to the nucleophilic addition of the NH_2 group to the C=N multiple bond (Scheme 1). Subsequent transformations of aminal **B** involve the attack of the OH group at the C(5) atom, producing *N*-glycopyranoside **C**. The glycosylation of the liberated amino group gives, finally, bis(glycosylamino)benzene **2**.

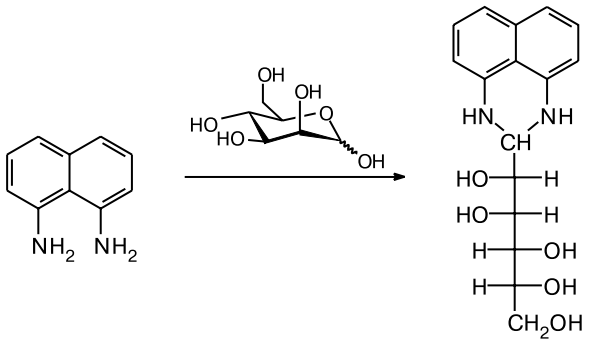
The fact that the reaction with 1,8-diaminonaphthalene affords only aminals **20** (D-mannose derivative) and **21** (D-galactose derivative), regardless of the amount of monosaccharide introduced into the reaction and the reaction temperature, can be regarded as an indirect proof of the proposed mechanism. The six-membered diaza rings are, most likely, more stable than the five-membered ring in intermediates **B**. Due to this, products **20** and **21** were isolated in the free state (Scheme 2).

The structure of aminal **20** was proved by ^{13}C and ^{1}H NMR spectroscopy using the C—H (HSQC) and H—H (COSY) correlations (Fig. 1). The signal for the C(1) atom of the saccharide fragment is observed at δ 66.7, and the chemical shift values of the C atoms of the carbohydrate moiety unambiguously indicate its open form. The high-field signal for C(5) (δ 71.3) seems to be the most indicative of the formation of the open form of the

Scheme 1



Scheme 2



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D-mannose fragment. In the ^{1}H NMR spectrum, the ratio of integral intensities of signals for the aromatic protons and protons of the carbohydrate fragment indicate the condensation of 1,8-diaminonaphthalene with one molecule of monosaccharide, which also agrees with the mass spectrometric data. Note that the protons bonded to the N atoms in compound **20** are magnetically nonequivalent, because they appear in the spectrum as two singlet signals (δ 5.95 and 6.27), the difference between which (Δδ) is 0.32 ppm. The NH protons are nonequivalent due to their diastereotopicity. In addition, the diastereotopicity is extended to the protons of the naphthylene fragment. For example, the ^{1}H NMR spectrum exhibits a divergence of signals for the C(2)H and C(7)H groups (δ 6.41 and 6.57) with Δδ = 0.16. The protons of C(4)H and C(5)H appear as two superimposed doublets, and the "diastereotopic" difference between the chemical shifts of these protons is 0.01 ppm. The protons of the C(3)H and C(6)H groups are also nonequivalent, and their triplet signals are also superimposed.

A substantial difference was revealed for the reaction rates of the monosaccharides under study with diamines. For instance, the mannosylation of diamines is over in 1—4 h, while galactose reacts completely in 5—10 h.

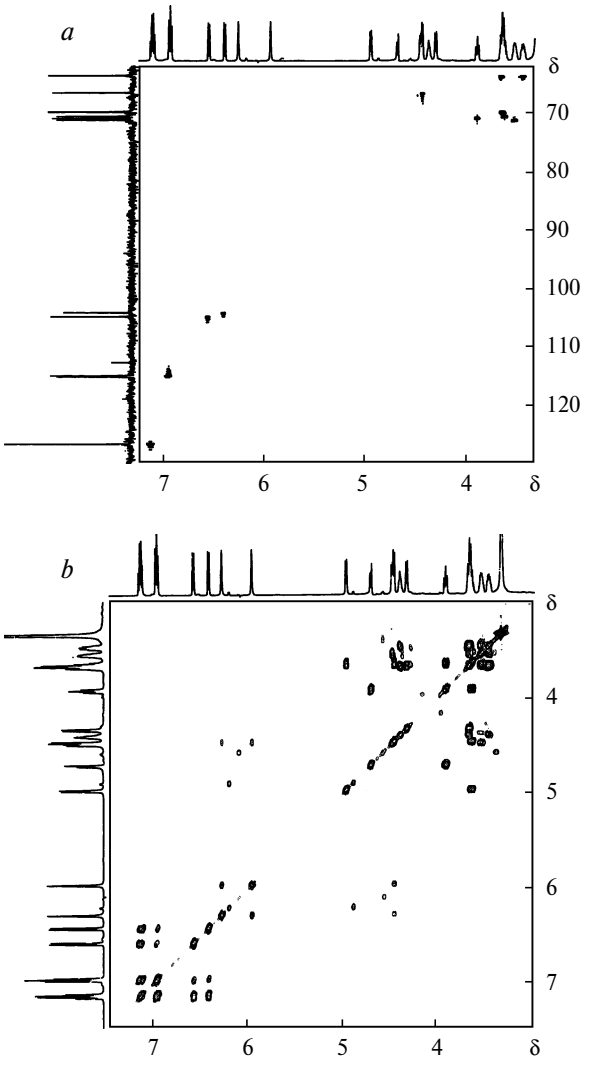

Fig. 1. HSQC (*a*) and COSY (*b*) spectra of compound **20**.

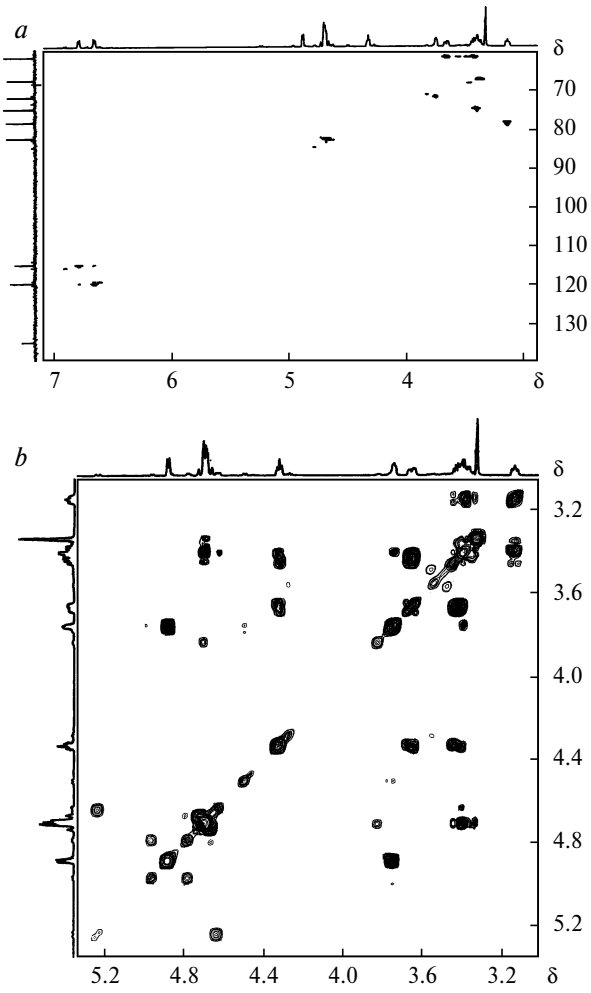

Fig. 2. HSQC (*a*) and COSY (*b*) spectra of compound **2**.

Table 1. Chemical shifts (δ) in the ^{13}C NMR spectra of compounds **2—19** (DMSO-d_6)

Compound	δ											
	Aglycone fragment						Carbohydrate fragments					
	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(1), C(1′)	C(2), C(2′)	C(3), C(3′)	C(4), C(4′)	C(5), C(5′)	C(6), C(6′)
2	134.4	134.4	114.5	119.3	119.3	114.5	81.9	71.4	74.4	67.1	77.8	61.3
3	146.9	99.3	146.9	104.0	129.2	104.0	81.6	71.3	74.6	67.2	77.8	61.3
4	138.1	114.9	114.9	138.1	114.9	114.9	82.4	71.4	74.6	67.2	77.8	61.3
5	45.3	45.3	—	—	—	—	87.6	71.6	74.8	67.6	78.0	61.8
6	51.5	46.9	20.3	—	—	—	86.6	71.6	74.8	67.7	77.9	61.8
7	43.4	30.7	43.4	—	—	—	87.4	71.5	74.8	67.6	77.9	61.7
8	44.8	27.8	27.8	44.8	—	—	87.3	71.4	74.7	67.6	77.9	61.7
9	44.8	29.9	24.6	29.9	44.8	—	87.3	71.4	74.7	67.6	77.8	61.7
10	44.9	30.0	26.9	26.9	30.0	44.9	87.3	71.5	74.7	67.6	77.9	61.7
11	135.4	135.4	113.0	118.6	118.6	113.0	86.1	70.4	73.8	68.4	75.6	60.6
12	149.8	98.2	149.8	104.6	132.8	104.6	86.4	70.3	73.8	68.5	75.7	60.5
13	139.4	115.3	115.3	139.4	115.3	115.3	86.4	70.3	73.6	68.8	75.5	60.8
14	45.5	45.5	—	—	—	—	82.4	71.4	74.6	67.2	77.8	61.3
15	51.9	47.9	20.6	—	—	—	82.5	71.6	74.8	67.2	77.7	61.3
16	43.9	30.5	43.9	—	—	—	82.3	71.5	74.5	67.3	77.8	61.3
17	44.9	27.8	27.8	44.9	—	—	82.7	71.6	74.5	67.2	77.8	61.3
18	45.2	30.2	24.6	30.2	45.2	—	82.1	71.6	74.8	67.4	78.0	61.2
19	45.0	30.1	26.9	26.9	30.1	45.0	82.7	71.5	74.9	67.3	77.9	61.4

Usually, glycosylation products **2—19** precipitated spontaneously from the reaction mixture as white powders and were isolated in the pure state in 70—80% yields.

The individual character and structures of glycosylamines **2—21** were proved by ^{13}C NMR and IR spectroscopy. The ^{13}C NMR spectra of the synthesized compounds contain signals for all the constituent C atoms. The signals for the anomeric C atoms are observed at δ 81—86 for the aromatic derivatives and at δ 82—89 in the case of bis(glycosylamino)alkanes (Table 1). This indicates the formation of the β,β′-isomers. The HSQC and COSY techniques were used to assign signals for the protons and carbon nuclei in compound **2** (Fig. 2).

The HSQC spectrum of compound **2** shows that the signal for the anomeric protons lies at δ 4.70—4.73 and the nuclei of the anomeric atoms resonate at δ 81.9. An analysis of the cross-peaks suggests that the highest-field signal in the ^1H NMR spectrum of compound **2** belongs to the H(5) protons (H(5)/H(6′) correlation is observed) and the multiplet with δ 3.36—3.46 is the superposition of signals for the H(4) (cross-peak H(4)/H(5)), H(3) (cross-peak H(3)/H(4)), and H(6′) atoms (cross-peaks H(6′)/H(5) and H(6′)/H(6)). The low intensity of the H(3)/H(2) cross-peak ($\delta_{H(2)}$ 3.75) indicates a weak coupling of the equatorial (H(2)) and axial (H(3)) protons. Note that the cross-peaks H(5)/H(6) and H(1)/H(2) are absent. Thus, in the ^1H and ^{13}C NMR spectra of 1,2-bis(β-D-mannopyranosylamino)benzene, the positions (but not the chemical shifts) of signals for the protons and carbon nuclei are similar to those for β-D-mannopyranose.[19] Most likely, the signals in the ^{13}C NMR spectra of mannopyranosylamines **3—10** can be attributed to certain carbon nuclei similarly to compound **2**, while for derivatives **11—19** they are similar to those for β-D-galactopyranose (see Table 1). A comparison of the ^1H NMR spectra of bisglycosides **2** and **11** shows a substantial difference in the chemical shifts of the protons of the NH groups (δ 3.32 and 5.18, respectively). In addition, the ^1H NMR spectrum of glycoside **11** exhibits the spin-spin coupling with $J = 8.8$ Hz between the H(1) and H(2) protons, which indicates the β-structure of galactosylamines **11—19**.

The IR spectra of the synthesized compounds exhibit a broad intense band in the region of 3550—3000 cm^{-1}, which is characteristic of stretching vibrations of the OH and NH groups and the CH fragments of the aromatic system of compounds **2—4** and **11—13**. This band remains almost unchanged on going from the aromatic to aliphatic derivatives, and its position is independent of the nature of monosaccharide. The same concerns the intense characteristic bands at 1500—1400 and 1400—1310 cm^{-1} corresponding to bending vibrations of the OH groups of the monosaccharides. Some changes are observed for frequencies corresponding to stretching vibrations of C—O of the alcohol groups and to vibrations of the deformational character of the NH fragments. On going from bis(glycosylamino)benzenes to bis(glycosylamino)alkanes, the position and width of bands corresponding to the C—O groups change from 1120—950 cm^{-1} (s) to 1140—835 cm^{-1} (m). The intensity

of the band at 1640—1550 cm^{-1} (s) corresponding to stretching vibrations of the NH fragment of the aromatic derivatives increases in comparison with the intensity of a similar band in the spectra of the derivatives of aliphatic diamines (1600—1540 cm^{-1} (w)), which is, most likely, a consequence of superposition of variable-intensity bands corresponding to the vibrations of the benzene ring on the band of stretching vibrations of the NH groups of bis(glycosylamino)arenes. The IR spectra of compounds **5—10** and **14—19** also contain bands at 750—700 cm^{-1} (s). Rocking vibrations of the CH_2 groups are responsible for the bands at 750—700 cm^{-1}.

The structure of product **2** was also proved by X-ray diffraction analysis. The general view of a molecule of 1,2-bis(β-D-mannopyranosylamino)benzene **2** is shown in Fig. 3.

It seemed of interest to compare the geometric parameters of a molecule of the synthesized "cross-linked" *N*-glycoside and *N*-glycosides of the chosen monosaccharides with the phenyl substituent as the aglycone. For this purpose, we obtained and characterized for the first time by X-ray diffraction analysis *N*-β-D-mannopyranosylaniline (**22**) and *N*-β-D-galactopyranosylaniline (**23**). The general views of molecules of *N*-glycosides **22** and **23** are shown in Figs 4 and 5. Selected structural parameters and crystallographic data for compounds **2**, **22**, and **23** are presented in Tables 2 and 3.

The bond lengths and bond angles in compounds **2**, **22**, and **23** are similar to the values characteristic of substances of this class. In all compounds under study, the carbohydrate fragments correspond to the β-form and

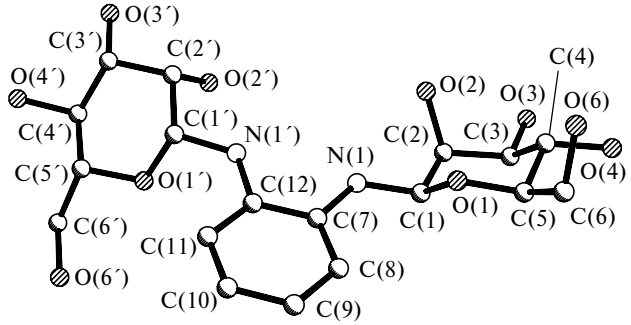

Fig. 3. Structure of 1,2-bis(β-D-mannopyranosylamino)benzene (**2**).

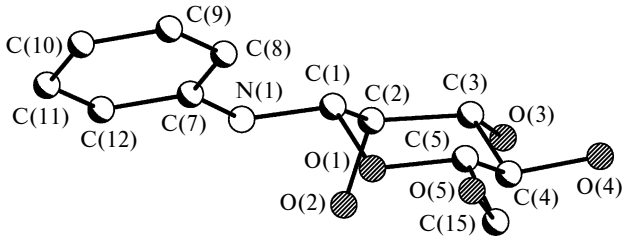

Fig. 4. Structure of *N*-β-D-mannopyranosylaniline (**22**).

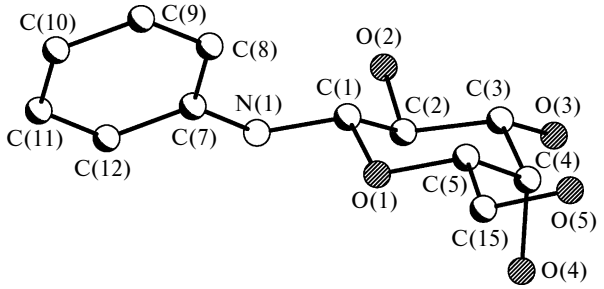

Fig. 5. Structure of *N*-β-D-galactopyranosylaniline (**23**).

have a chair conformation with deviations of the C(1) and C(4) atoms from the C(2)C(3)C(5)O(1) plane of 0.68 and 0.66 Å on the average (for the Δ_1 and Δ_4 parameters, see Table 2). The angle between the C(2)C(3)C(5)O(1) and C(2′)C(3′)C(5′)O(1′) planes of two carbohydrate fragments in the molecule of **2** is 69.7°. The angles between the C(2)C(3)C(5)O(1) planes of the carbohydrate fragments and phenyl substituents in molecules **22** and **23** are 42.2 and 39.3°, respectively.

In crystal, the molecules of **2**, **22**, and **23** form three-dimensional frameworks linked through hydrogen bonds between the OH and NH groups. The O...O interatomic distances range from 2.75 to 3.07 Å, and the O—H—O angles are 146—171°. Thus, the intermolecular hydrogen bonds O—H...O correspond to weak bonds of this type. The N—H—O bonds can also be characterized as weak: the N...O distances and N—H—O bond angles in molecules **22** and **23** are equal to 3.061 and 3.139 Å, 176 and 130°, respectively.

Bis(glycosylamino)hydrocarbons were isolated from the reaction mixture as stable hydrates. In our opinion,

Table 2. Selected bond lengths and bond angles in molecules of glycosylamines **2**, **22**, and **23**

Parameter	**2**	**22**	**23**
Bond		*d*/Å	
O(1)—C(5)	1.429(6)	1.438(5)	1.423(3)
O(1)—C(1)	1.445(5)	1.470(5)	1.450(3)
O(2)—C(2)	1.443(7)	1.436(5)	1.425(3)
O(3)—C(3)	1.430(6)	1.435(5)	1.439(3)
O(4)—C(4)	1.432(7)	1.436(4)	1.442(3)
O(6)—C(6)	1.412(7)	—	—
N(1)—C(1)	1.411(7)	1.412(5)	1.417(3)
N(1)—C(7)	1.407(3)	1.394(5)	1.404(3)
O(5)—C(15)	—	1.432(5)	1.428(3)
Δ_1[a]	0.65	0.68	0.68
Δ_4[b]	0.69	0.64	0.71
Angle		ω/deg	
C(5)—O(1)—C(1)	111.4(5)	113.3(3)	112.2(2)
C(1)—N(1)—C(7)	124.2(4)	122.2(4)	120.3(2)
N(1)—C(1)—O(1)	110.1(4)	108.1(3)	109.3(2)

[a] Shift of the C(1) atom from the plane.
[b] Shift of the C(4) atom from the plane.

Table 3. Selected parameters of X-ray diffraction experiment and crystallographic data for compounds **2**, **22**, and **23**

Parameter	**2**	**22**	**23**
Molecular formula	$C_{18}H_{30}N_2O_{11}$	$C_{12}H_{17}NO_5$	$C_{12}H_{16}NO_5$
Molecular weight	450.44	255.27	254.26
T/K	293	110	110
Space group	$P2_1$	$P2_12_12_1$	$P2_1$
a/Å	28.518(6)	6.4402(13)	4.7541(4)
b/Å	5.2740(10)	6.7366(13)	8.6869(9)
c/Å	13.708(3)	28.002(6)	13.9719(14)
β/deg	93.94(3)		96.219(2)
V/Å^3	2056.9(7)	1214.9(4)	573.62(10)
d_{calc}/g cm^{-3}	1.455	1.396	1.472
Z	2	4	2
$2\theta_{max}$/deg	64.94	60.12	60.08
F(000)	960	544	270
Scan mode	θ/2θ	ω	ω
Number of collected reflections	2046	10116	5534
Number of independent reflections (R_{int})	1958 (0.122)	3540 (0.0995)	3027 (0.0324)
Number of observed reflections with $I > 2\sigma(I)$	1292	1247	2435
Number of refined parameters	281	163	227
Absorption coefficient/cm^{-1}	1.04	1.09	1.15
R_1 ($I > 2\sigma(I)$)	0.0497	0.0521	0.0602
wR_2	0.1313	0.1612	0.1531

water of crystallization often serves as a causative agent for the destruction of *N*-glycosides on their heating and prolong storage. These compounds can be transformed into anhydrous forms by dissolution of *N*-glycosides in anhydrous DMF containing 20—25% (v/v) benzene followed by vacuum azeotropic distillation of water of crystallization together with benzene.

All the compounds synthesized are soluble in the same solvents in which free monosaccharides pass into solution. Note that solutions of the synthesized bisglycosides in DMF and especially in pyridine rapidly solidify. This can be related to the chelation of these solvents with *N*-glycosides to form inclusion complexes. A complex of 1,2-bis(β-D-mannopyranosylamino)benzene (**2**) with pyridine was isolated in the individual state and characterized by ^{1}H NMR. An analysis of the integral intensity of signals for the protons of pyridine and bisglycoside suggests the ratio of the constituents of the complex to be 1 : 3, respectively. According to the ^{1}H NMR data, coordination with pyridine involves protons of the C(2)OH and C(6)OH groups and, most likely, of the NH group. This conclusion is based on the fact that the signals for protons of the C(2)OH and C(6)OH groups in the ^{1}H NMR spectrum of the isolated complex differ by 0.07—0.08 ppm from the signals of the same groups in the spectrum of compound **2**. The signals for the H(1) protons exhibit an upfield shift by 0.09 ppm, which can be caused by the participation of the NH groups in coordination (the signal for the protons of the NH group in the complex is also shifted toward a multiplet with δ 3.39—3.47). The chemical shifts of other protons in compound **2** are the same as those in the complex of **2** with pyridine. The melting point of the complex differs substantially from that for compound **2** and equals 161—164 °C (decomp.). It is most likely that DMF is also coordinated with bisglycosides to form inclusion compounds. Interestingly, the "cross-linked" saccharides favor the solubilization of alkali metal halides (*e.g.,* NaCl, NaBr, KCl, and KBr) in methanol and ethanol. We found that these salts are much more rapidly dissolved in alcoholic solutions of bis(β-D-mannopyranosylamino)alkanes **5—10** than in alcohols containing no compounds **5—10**.

Prolong storage of solutions of bisglycosides results in anomerization, whose rate decreases in the following order of solvents: water, pyridine, DMSO. The formation of α-anomers (exemplifed by glycosides **2—4**) is distinctly observed in the ^{13}C NMR spectra containing signals with chemical shifts at δ 84—86. The dissolution of compounds **2—19** in water is accompanied by their gradual destruction to free carbohydrates and the corresponding diamines. The destruction is especially fast in the presence of acids. Glycosides of the aromatic series are most stable toward hydrolysis. Bis(galactosylamino)hydrocarbons are somewhat more stable than the mannose analogs. Attempts to determine the optical rotation values of the synthesized compounds were unsuccessful, because the glycosylamines are hydrolyzed in water, which is often used as the solvent for these purposes. Complexation occurs in DMF and pyridine. Solutions of compounds **2—19** in DMSO (at concentrations higher than 0.5 g mL^{-1}) are highly viscous, which impedes strongly the determination of $[\alpha]_D$.

Thus, in the present work, we showed a possibility to synthesize bis(glycosylamino)hydrocarbons of different chemical nature by direct condensation in the absence of catalysts, suggested the formation of an aminal intermediate in the synthesis of the *o*-phenylenediamine derivatives, and described some physicochemical properties of the synthesized compounds.

Experimental

^{13}C NMR spectra were recorded on a Bruker AC-200 spectrometer with an operating frequency of 50 MHz in DMSO-d_6 as the solvent with Me_4Si as the internal standard. ^{1}H NMR spectra of compounds **2** and **20** were obtained on a Bruker DRX-500 spectrometer with an operating frequency of 500 MHz. ^{1}H NMR spectra of compound **11**, the complex of **2** with pyridine, and compound **2** (for comparison with the ^{1}H NMR spectrum of the complex of **2** with pyridine) were measured on a Bruker H-250 spectrometer with an operating frequency of 250 MHz in DMSO-d_6 as the solvent with Me_4Si as the internal standard.

IR spectra were obtained on a Specord IR-75 instrument using NaCl lenses. Mass spectra were measured on a Finnigan LCQ (electrospray, (ESI)) instrument.

Synthesis of bis(β-D-glycopyranosylamino)benzenes 2—4 and 11—13 (general procedure). A suspension of the corresponding anhydrous monosaccharide (10 g, 55.55 mmol) in 80% ethanol (250 mL) was stirred at room temperature with the corresponding phenylenediamine (3 g, 27.75 mmol). After the end of the reaction, precipitates that formed were filtered off, washed three times with 95.5% ethanol preheated to 50 °C, and dried *in vacuo*. The glycosylation products were white powders with a very bitter taste, soluble in pyridine, DMF, DMSO, and water (hydrolysis), and poorly soluble in methanol and ethanol. The duration of reactions, yields, melting points, and elemental analysis data are given in Table 4. The spectral characteristics of the products are presented in Tables 1 and 5.

1,2-Bis(β-D-mannopyranosylamino)benzene (2). ^{1}H NMR (500 MHz), δ, carbohydrate fragment: 3.15 (dd, 2 H, 2 H(5)); 3.32 (s, 2 H, NH); 3.37 (m, 2 H, 2 H(4)); 3.41 (m, 2 H, 2 H(3)); 3.44 (m, 2 H, 2 H(6′)); 3.66 (dd, 2 H, 2 H(6)); 3.75 (dd, 2 H, 2 H(2)); 4.33 (t, 2 H, 2 C(6)OH, ^3J = 5.5 Hz); 4.66—4.73 (m, 6 H, 2 C(4)OH, 2 C(3)OH, 2 H(1)); 4.88 (d, 2 H, 2 C(2)OH, ^3J = 5.5 Hz); aglycone fragment: 6.64 (m, 2 H, C(3)H, C(6)H); 6.78 (m, 2 H, C(4)H, C(5)H). ^{1}H NMR (250 MHz), δ, carbohydrate fragment: 3.14 (dd, 2 H, 2 H(5)); 3.29 (s, 2 H, NH); 3.38—3.45 (m, 6 H, 2 H(4), 2 H(3), 2 H(6′)); 3.67 (dd, 2 H, 2 H(6)); 3.75 (dd, 2 H, 2 H(2)); 4.33 (t, 2 H, 2 C(6)OH, ^3J = 5.8 Hz); 4.62 (m, 2 H, 2 C(4)OH); 4.70 (m, 2 H, 2 C(3)OH); 4.81 (d, 2 H, 2 H(1)); 4.88 (d, 2 H, 2 C(2)OH, ^3J = 5.5 Hz); aglycone fragment: 6.65 (m, 2 H, C(3)H, $^3J_{H(3),H(4)}$ = 5.8 Hz, $^3J_{H(3),H(5)}$ = 3.6 Hz, C(6)H); 6.80 (m, 2 H, C(4)H, C(5)H).

Complex of 2 with pyridine. Compound **2** (1 g) was dissolved in pyridine (10 mL) at 25 °C. After 5—7 min, the solution transformed into a gel, which was filtered off, triply washed with ethanol, and dried *in vacuo* to a constant weight. The yield was 0.68 g (66.8%); white powder with a bitter taste; m.p. 161—164 °C (decomp.). ^{1}H NMR, δ, carbohydrate fragment: 3.15 (dd, 2 H, 2 H(5)); 3.39—3.47 (m, 8 H, 2 NH, 2 H(4), 2 H(3), 2 H(6′)); 3.64 (dd, 2 H, 2 H(6)); 3.76 (dd, 2 H, 2 H(2)); 4.25 (m, 2 H, 2 C(6)OH); 4.65 (m, 2 H, 2 C(4)OH); 4.69 (m, 2 H, 2 C(3)OH); 4.72 (m, 2 H, 2 H(1)); 4.81 (m, 2 H, 2 C(2)OH); aglycone fragment: 6.65 (m, 2 H, C(3)H, C(6)H); 6.79 (m, 2 H, C(4)H, C(5)H); pyridine: 7.36 (dd, 2 H, C(3)H, C(5)); 7.77 (m, 1 H, C(4)H); 8.57 (d, 2 H, C(2)H, C(6)H).

1,2-Bis(β-D-galactopyranosylamino)benzene (11). ^{1}H NMR, δ, carbohydrate fragment: 3.41—3.57 (m, 10 H, 2 H(2), 2 H(3), 2 H(4), 2 H(5), 2 H(6)); 3.74 (m, 2 H, 2 H(6′)); 4.23 (t, 2 H, 2 C(6)OH, $^3J_{OH,H(6)}$ = 3.6); 4.29 (dd, 2 H, 2 H(1), $^3J_{H(1),H(2)}$ = 8.8 Hz); 4.48 (m, 2 H, 2 C(4)OH)*; 4.69 (d, 2 H, 2 C(2)OH, ^3J = 5.2 Hz)*; 4.79 (d, 2 H, 2 C(3)OH, ^3J = 3.4 Hz)*; 5.18 (d, 1 H, NH, $^3J_{NH,H(1)}$ = 9.1 Hz); aglycone fragment: 6.59 (m, 2 H, C(3)H, C(6)H); 6.70 (m, 2 H, C(4)H, C(5)H).

Synthesis of bis(β-D-glycopyranosylamino)alkanes 5—10 and 14—19 (general procedure). A suspension of anhydrous monosaccharide (10 g, 55.55 mmol) in 80% ethanol (250 mL) was stirred at room temperature with a twofold excess of the corresponding diamine. After the end of glycosylation, precipitates that formed were filtered off, washed three times with 95.5% ethanol preheated to 50 °C, and dried *in vacuo*. The resulting products were white powders with a taste from burning to bitter-sweet, soluble in pyridine, DMF, DMSO, methanol, and water (hydrolysis), and poorly soluble in ethanol. The duration of reactions, yields, melting points, and elemental analysis data are given in Table 4. The spectral characteristics of the products are presented in Tables 1 and 5.

1-(2,3-Dihydro-1*H*-perimidin-2-yl)pentane-1(*S*),2(*S*),3(*R*),4(*R*),5-pentol (20). A suspension of anhydrous D-mannose (5 g, 27.77 mmol) in 80% ethanol (100 mL) was stirred at room temperature with 1,8-diaminonaphthalene (4.4 g, 27.85 mmol). After the end of the reaction, the precipitate was filtered off, washed three times with 95.5% ethanol preheated to 40 °C, and dried. A white powder soluble in pyridine, DMSO, DMF, and water (slow hydrolysis) was obtained. ^{13}C NMR, δ, carbohydrate fragment: 63.8 (C(6)); 66.7 (C(1)); 69.8 (C(4)); 70.6 (C(2)); 71.0 (C(3)); 71.3 (C(5)); naphthalene fragment: 104.3 (C(2)); 104.9 (C(7)); 112.8 (C(10)); 115.1 (C(4)); 115.2 (C(5)); 126.9 (C(3), C(6)); 134.4 (C(9)); 142.6 (C(8)); 142.8 (C(1)). ^{1}H NMR, δ, carbohydrate fragment: 3.43 (m, 1 H, H(6′), $^2J_{H(6′),H(6)}$ = 10.3 Hz); 3.53 (m, 1 H, H(5), $^3J_{H(5),H(4)}$ = 8.2 Hz); 3.60—3.66 (m, 3 H, H(2), H(4), H(6)); 3.89 (t, 1 H, H(3), $^3J_{H(3),H(2)}$ = 7.8 Hz); 4.30 (d, 1 H, C(4)OH, ^3J = 7.5 Hz); 4.38 (m, 1 H, C(6)OH); 4.44 (d, 1 H, H(1), $^3J_{H(1),H(2)}$ = 5.8 Hz); 4.46 (d, 1 H, C(5)OH, ^3J = 5.4 Hz); 4. 86 (d, 1 H, C(3)OH, ^3J = 7.2 Hz); 4.95 (d, 1 H, C(2)OH, ^3J = 6.6 Hz); naphthalene fragment: 5.95 (s, 1 H, H(8), NH); 6.27 (s, 1 H, H(1), NH); 6.41 (d, 1 H, H(2), $^3J_{H(2),H(3)}$ = 7.3 Hz)**; 6.57 (d, 1 H, H(7), $^3J_{H(7),H(6)}$ = 7.3 Hz)**; 6.94 (d, H, H(4), $^3J_{H(4),H(3)}$ = 7.3 Hz)**; 6.96 (d, H, H(5), $^3J_{H(5),H(6)}$ = 7.3 Hz)**; 7.12 (t, H, H(3))**; 7.13 (t, H, H(6))**. Mass spectrum, *m/z* (I_{rel} (%)): 320.2 (14) $[M]^+$, 319.1 (100) $[M - H]^+$, 259.1 (5), 211.1 (6), 202.1 (15), 169.3 (88), 168.2 (36), 115.1 (2).

1-(2,3-Dihydro-1*H*-perimidin-2-yl)pentane-1(*R*),2(*S*),3(*S*),4(*R*),5-pentol (21). 1,8-Diaminonaphthalene (4.4 g, 27.85 mmol) was added to a suspension of anhydrous

* The assignment of signals of the protons of the OH groups can be opposite.

** The assignment of signals can be opposite.

Table 4. Duration of reactions (τ), yields, melting points, and elemental analysis data for compounds **2—21**

Compound	τ/h	Yield (%)	M.p./°C (decomp.)	Found / Calculated (%)			Molecular formula
				C	H	N	
2	2—2.5	79	195—197	46.84	7.01	5.62	$C_{18}H_{28}N_2O_{10}\cdot 2H_2O$
				46.15	6.89	5.98	
3	3.5—4	73	203—205	48.08	6.76	6.24	$C_{18}H_{28}N_2O_{10}\cdot H_2O$
				48.00	6.71	6.22	
4	3.5—4	78	188—190	48.12	6.76	6.25	$C_{18}H_{28}N_2O_{10}\cdot H_2O$
				48.00	6.71	6.22	
5	2—3	85	143—145	41.82	7.60	6.70	$C_{14}H_{28}N_2O_{10}\cdot H_2O$
				41.79	7.51	6.96	
6	2—3	82	152—154	43.31	7.80	6.75	$C_{15}H_{30}N_2O_{10}\cdot H_2O$
				43.26	7.75	6.73	
7	2—3	86	149—151	44.56	7.99	6.81	$C_{15}H_{30}N_2O_{10}\cdot H_2O$
				43.26	7.75	6.73	
8	2—2.5	86	130—132	44.70	7.95	6.53	$C_{16}H_{32}N_2O_{10}\cdot H_2O$
				44.64	7.96	6.51	
9	2.5—3	83	140—142	45.80	7.98	6.23	$C_{17}H_{34}N_2O_{10}\cdot H_2O$
				45.94	8.16	6.30	
10	2.5—3	86	110—112	47.21	8.39	6.13	$C_{18}H_{36}N_2O_{10}\cdot H_2O$
				47.15	8.35	6.11	
11	5—5.5	73	185—186	46.82	7.09	5.77	$C_{18}H_{28}N_2O_{10}\cdot 2H_2O$
				46.15	6.89	5.98	
12	8—10	75	197—200	48.84	6.81	6.33	$C_{18}H_{28}N_2O_{10}\cdot H_2O$
				48.00	6.71	6.22	
13	8—10	76	205—207	46.93	6.95	6.40	$C_{18}H_{28}N_2O_{10}\cdot H_2O$
				48.0	6.71	6.22	
14	6.5—6	85	158—160	41.89	7.66	6.69	$C_{14}H_{28}N_2O_{10}\cdot H_2O$
				41.79	7.51	6.96	
15	6.5—6	73	156—158	43.42	7.86	6.76	$C_{15}H_{30}N_2O_{10}\cdot H_2O$
				43.26	7.75	6.73	
16	5—6	76	148—150	43.35	7.84	6.78	$C_{15}H_{30}N_2O_{10}\cdot H_2O$
				43.26	7.75	6.73	
17	5—6	86	135—137	44.76	7.98	6.60	$C_{16}H_{32}N_2O_{10}\cdot H_2O$
				44.64	7.96	6.51	
18	5—6	86	132—133	45.78	7.95	6.25	$C_{17}H_{34}N_2O_{10}\cdot H_2O$
				45.94	8.16	6.30	
19	5—6	86	130—131	47.30	8.41	6.14	$C_{18}H_{36}N_2O_{10}\cdot H_2O$
				47.15	8.35	6.11	
20	2—3	68	214—216	59.87	6.24	8.70	$C_{16}H_{20}N_2O_5$
				59.99	6.29	8.74	
21	6—7	60	232—235	59.92	6.21	8.71	$C_{16}H_{20}N_2O_5$
				59.99	6.29	8.74	

D-galactose (5 g, 27.77 mmol) in 80% ethanol (100 mL). The mixture was stirred for 6 h, and then the precipitate was filtered off, triply washed with warm ethanol, and dried. Compound **21**, which is soluble in pyridine, DMSO, DMF, and water (slow hydrolysis), was obtained. ^{13}C NMR, δ, carbohydrate fragment: 60.8 (C(6)); 66.6 (C(1)); 67.3 (C(4)); 71.4 (C(2)); 70.8 (C(3)); 71.4 (C(5)); naphthalene fragment: 104.5 (C(2)); 104.8 (C(7)); 112.6 (C(10)); 115.5 (C(4)); 115.4 (C(5)); 126.5 (C(3), C(6)); 133.7 (C(9)); 142.8 (C(8)); 142.9 (C(1)).

***N*-β-D-Mannopyranosylaniline (22).** A mixture of anhydrous D-mannose (5 g) and aniline (2.6 g) was homogenized in water (3 mL). Then water was slowly distilled off with weak heating *in vacuo* of a water-jet pump. The mixture was kept *in vacuo* for 2 h. The product formed upon glycosylation was recrystallized from hot ethanol. The resulting white precipitate was filtered off, washed with ethanol, and dried *in vacuo*. The yield was 5.6 g (79%), m.p. 219—220 °C (*cf.* Ref. 21: m.p. 181 °C (decomp.)). ^{13}C NMR, δ, carbohydrate fragment: 61.4 (C(6)); 67.2 (C(4)); 71.3 (C(2)); 74.6 (C(3)); 77.9 (C(5)); 81.5 (C(1)); aglycone fragment: 113.8 (C(2), C(6)); 117.5 (C(4)); 128.9 (C(3), C(5)); 146.4 (C(1)).

***N*-β-D-Galactopyranosylaniline (23)** was synthesized similarly to **22** from anhydrous D-galactose (5 g) and aniline (2.6 g). The yield was 85%, white powder, m.p. 176—178 °C (*cf.* Ref. 11: m.p. 159 °C (decomp.)). ^{13}C NMR, δ, carbohydrate fragment: 60.6 (C(6)); 68.5 (C(4)); 70.3 (C(2)); 74.3 (C(3)); 75.6 (C(5));

Table 5. IR spectroscopic data for compounds **2—19**

Compound	ν/cm^{-1}						
	ν(OH), ν(NH), ν(CH arom.)	ν(C=C)	δ(NH)	δ(C=C)	δ(OH)	ν(C—O)	ν(CH_2)
2	3250	1650	1560	1470	1415, 1335	1020	—
3	3400	1650	1615	1515	1455, 1375	1060	—
4	3400	1650	1615	1510	1450, 1370	1060	—
5	3300	—	1555	—	1415, 1340	1050	790, 680
6	3300	—	1550	—	1415, 1330	1055	795, 685
7	3300	—	1550	—	1415, 1330	1050	790, 680
8	3300	—	1550	—	1410, 1330	1055	790, 685
9	3300	—	1550	—	1410, 1335	1050	790, 680
10	3300	—	1555	—	1410, 1335	1050	795, 680
11	3400	1655	1620	1515	1450, 1370	1065	—
12	3400	1650	1610	1510	1455, 1370	1065	—
13	3400	1655	1615	1510	1450, 1375	1060	—
14	3300	—	1555	—	1410, 1330	1050	790, 685
15	3300	—	1550	—	1415, 1335	1050	790, 680
16	3300	—	1550	—	1410, 1335	1050	795, 685
17	3300	—	1550	—	1410, 1330	1055	790, 680
18	3300	—	1555	—	1410, 1335	1050	790, 685
19	3300	—	1550	—	1415, 1330	1050	790, 680

85.7 (C(1)); aglycone fragment: 113.3 (C(2), C(6)); 117.0 (C(4)); 128.8 (C(3), C(5)); 147.4 (C(1)).

X-ray diffraction study of crystals of 2, 22, and 23. Experiments were carried out on Bruker Smart CCD 1000 (for **22** and **23**) and Enraf—Nonius CAD-4 (for glycosylamine **2**) diffractometers. The structures were solved by a direct method and refined by the full-matrix least-squares method for F^2 in the anisotropic approximation for non-hydrogen atoms. Hydrogen atoms of hydroxyl groups were localized from the difference Fourier syntheses imposing additional constraints in terms of the riding model. Attempts to localize the hydrogen atoms of the solvate water molecule in structure **2** were unsuccessful. All calculations were performed using the SHELXTL PLUS program complex (version 5.10).[20] The crystallographic parameters and selected details of X-ray diffraction experiments are presented in Table 3. The coordinates of atoms were deposited with the Cambridge Structure Database.

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Received February 14, 2005;
in revised form December 8, 2005