



**Table 1** Products Composition (Molar Ratios in %) for the Reaction Mixtures of Benzylamines **3**, **7**, and **11** with DIAD

Reactant	Product		Imine	DIHD	Benzaldehyde		
<b>3</b>	13	<b>4</b>	17	<b>5</b>	43	22	4
<b>7</b>	17	<b>8</b>	<sup>a</sup>	<b>9</b>	43	27	13
<b>11</b> <sup>b</sup>	9	<b>12</b>	4	<b>13+14</b> <sup>c</sup>	<1	26	18

<sup>a</sup> Not detected.<sup>b</sup> In addition, three other unidentified compounds were found in approx. 1:1:1 ratio (43% overall yield).<sup>c</sup> Both compounds were detected in low amounts.

formations. If this moiety was not present in the molecule of a benzylamine, the reaction with DIAD clearly afforded N-debenzylated amine. For example, *trans*-(2-benzylamino)cyclohexanol **16** was transformed into *trans*-2-aminocyclohexanol hydrochloride **17** in 85% yield without difficulties.

GC-MS analysis did not show triazanes in the reaction mixtures, but triazanes **6** and **15** were detected by mass spectrometry. Having used ESI technique the molecular masses belonging to the triazanes were found in the spectra: for compound **6** {544 [M + H]<sup>+</sup> (C<sub>28</sub>H<sub>38</sub>N<sub>3</sub>O<sub>8</sub> requires 544)}, and for compound **10** {400 [M + H]<sup>+</sup> (C<sub>22</sub>H<sub>30</sub>N<sub>3</sub>O<sub>4</sub> requires 400)}.

The presence of triazanes as reaction intermediates was also proven by IR spectroscopy. Significant vibration bands belonging to triazanes **6**, **10**, and **15** are summarized in Table 2.

**Table 2** List of Selected Vibrations (Wavenumbers in cm<sup>-1</sup>) Found in IR Spectra of the Reaction Mixtures after N-Debenzylation of Benzylamines **3**, **7**, and **11**

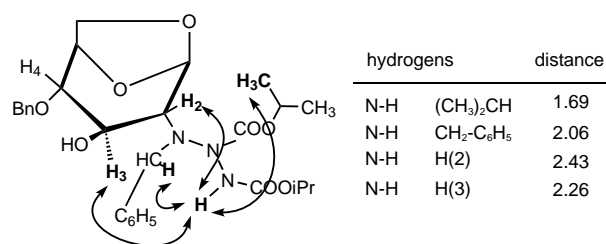
Group	Triazane		
	<b>6</b>	<b>10</b>	<b>15</b>
N-H	3296	<sup>a</sup>	3309
(C=O)1	1751	1753	1753
(C=O)2	1719	1721	1722
NHCO (amide)	1515	1514	1513

<sup>a</sup> Not estimated due to peaks overlap.

Recorded IR spectra exhibited bands for N-H bond, two C=O bonds and CONH amide bond which were assigned to the structures of triazanes **6**, **10**, and **15**. The assignment of the vibrations shown in Table 2 has been made by comparison with similar triazanes; lit.<sup>3</sup>: (NH) = 3390 cm<sup>-1</sup>, (CO)1 = 1746 cm<sup>-1</sup> and (CO)2 = 1721 cm<sup>-1</sup> in CHCl<sub>3</sub> solution, lit.<sup>4</sup>: (NH) = 3145–3265 cm<sup>-1</sup>, (CO)1 = 1742–1752 cm<sup>-1</sup>, (CO)2 = 1720–1752 cm<sup>-1</sup> and (amide) = 1500–1530 cm<sup>-1</sup> in KBr pellet, lit.<sup>5</sup>: (NH) = 3226 cm<sup>-1</sup>, (CO)1 = 1754

cm<sup>-1</sup>, (CO)2 = 1689 cm<sup>-1</sup> and (amide) = 1511–1520 cm<sup>-1</sup> in nujol suspension.

The ultimate proof for the reaction pathway involving imines and triazanes as reaction intermediates was done by the application of NMR spectroscopy to the reaction of benzylamine **3** with DIAD in perdeuterated THF. Imine **5** was detected as the main product after 14 days at room temperature together with triazane **6** and DIHD. The structure of compound **5** was deduced from the presence of only one benzyl group (O-CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>: δ<sub>1</sub> = 4.77 ppm and δ<sub>2</sub> = 4.72 ppm), -CH=N- moiety (δ = 8.29 ppm) and B<sub>3,0</sub> conformation of tetrahydropyran ring (benzylamine **3** exists in <sup>1</sup>C<sub>4</sub> conformation<sup>6</sup>) in <sup>1</sup>H NMR spectrum. The <sup>13</sup>C NMR spectrum also revealed the presence of a -CH=N- moiety with δ = 163.0 ppm. NMR spectral characteristics for triazane **6** could not be estimated completely due to its low concentration. However, the structure was evidenced by NOE couplings of N-H, N-CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>, (CH<sub>3</sub>)<sub>2</sub>CH, H(2) and H(3) hydrogens found in NOESY spectrum of the same sample (see Figure 2 for details). Simple molecular model of triazane **6** (based on MM2+ method) showed that observed NOE couplings were in agreement with the steric proximity of the mentioned hydrogens.

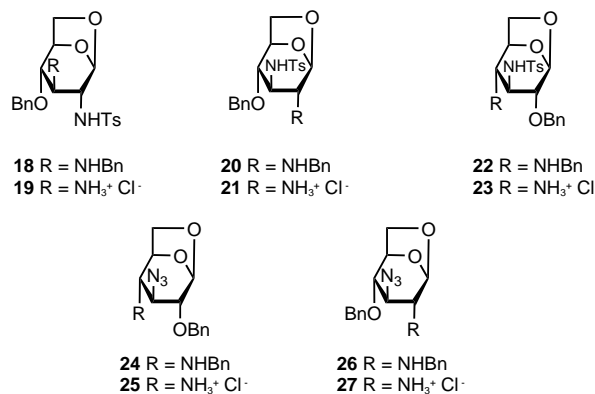
**Figure 2** Observed NOE couplings and estimated interatomic distances (Å) of selected couples of hydrogens in the molecule of triazane **6** based on NOESY spectrum and molecular modeling.

The usage of THF as reaction solvent was crucial since N-debenzylations in other solvents (toluene, pyridine, Et<sub>2</sub>O, and 1,2-dimethoxyethane) required longer reaction time to complete debenzylation or resulted either in decomposition of benzylamines or isolation of unreacted starting material.

As the second part of our study, we examined the possibility of N-debenzylation for benzylamines derived from 1,6-anhydro-β-D-glucopyranose skeleton (Figure 3).

Treatment of benzylamines **18**, **20**, **22**, **24**, and **26** with DIAD in THF followed by acidic hydrolysis gave amine hydrochlorides **19**, **21**, **23**, **25**, and **27** in 72–93% yield (see Table 3).

The course of debenzylation was not affected by the presence of azido, tosylamino, and O-benzyl groups in the molecule. It is interesting to note that reactions of these compounds with DIAD in toluene and in a mixture of pyridine-concd HCl resulted in complete decomposition of the benzylamines.



**Figure 3** Tosylamino and azido derivatives of 1,6-anhydro-β-D-glucopyranose used for *N*-debenzylation with DIAD and the corresponding products.

**Table 3** Reaction Details for *N*-Debenzylation of Benzylamines **18**, **20**, **22**, **24**, and **26**

Reactant	Product	Reaction in THF Time	Acidic hydrolysis Time	Yield (%)
<b>18</b>	<b>19</b>	19 h	4 d	93
<b>20</b>	<b>21</b>	10 h	2 d	85
<b>22</b>	<b>23</b>	27 h	3 d <sup>a</sup>	83
<b>24</b>	<b>25</b>	10 h	6 h	72
<b>26</b>	<b>27</b>	21 h	2 d	91

<sup>a</sup> Hydrolysis performed at r.t.

Melting points were determined on a Botius melting point microapparatus and are uncorrected. The optical rotations were measured on an Autopol III (Rudolph Research, Flanders, NJ) polarimeter at 23 °C. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured on a Varian INOVA-400 (<sup>1</sup>H at 400 MHz and <sup>13</sup>C at 100 MHz) instrument in C<sub>4</sub>D<sub>8</sub>O (referenced to TMS) or in CD<sub>3</sub>SOCD<sub>3</sub> at 25 °C. The <sup>1</sup>H-<sup>1</sup>H-COSY and NOESY and <sup>1</sup>H-<sup>13</sup>C-HMQC techniques were used for the structural assignments. The IR spectra were recorded on a Perkin-Elmer 490 spectrometer in CHCl<sub>3</sub> solutions at 23 °C. GC-MS analyses were carried out on a Hewlett-Packard HP 6890 gas chromatograph equipped with a HP5MS column (30 m long, inner diameter 250 μm, thickness of stationary phase 0.25 μm) and with Hewlett Packard HP 5973 mass selective detector (with EI ionization, 70 eV). MS-ESI spectra were recorded on a Bruker ESQUIRE 3000 instrument with the samples dissolved in MeOH. TLC was carried out on DC Alufolien with Kiesegel F<sub>254</sub>. TLC plates were developed with hexane-EtOAc (3:2) solvent system and visualized by UV detection at 254 nm or by an anisaldehyde detection reagent (composition: anisaldehyde: 10 mL, HOAc: 4 mL, concd H<sub>2</sub>SO<sub>4</sub>: 12.5 mL, EtOH: 340 mL). THF was distilled from LiAlH<sub>4</sub> prior use. DIAD (95% purity), 2-benzylamino ethanol and dibenzylamine were purchased from Sigma-Aldrich company. All reactions were carried under an Ar atmosphere. NMR spectral parameters are summarized in Tables 4 (<sup>1</sup>H) and 5 (<sup>13</sup>C).

### Reaction of Benzylamines **3**, **7**, and **11** with DIAD

To a solution of benzylamine **3** (102 mg, 0.3 mmol), **7** (177 mg, 1 mmol) or **11** (181 mg, 1.2 mmol) in THF (1 mL), DIAD was added (67 μL, 0.34 mmol, 223 μL, 1.13 mmol, or 268 μL, 1.36 mmol, respectively). Reaction mixtures were kept at r.t. until the yellow color of DIAD disappeared. After 14 d, the mixtures were evaporated and analyzed by the techniques mentioned above in the text. For NMR measurement, the same mixture of benzylamine **3** with DIAD was prepared using deuterated THF.

### Debenzylation of *Trans*-(2-benzyl amino)cyclohexanol (**16**)

Racemic *trans*-(2-benzyl amino)cyclohexanol (**16**) (205 mg, 1 mmol), DIAD (217 μL, 1.1 mmol), and THF (2 mL) were mixed and stirred at r.t. until the starting benzylamine disappeared (15 d). To the solution, 5% aq HCl (2 mL) was added and the mixture was stirred at r.t. for 7 d. After hydrolysis of the imine, the mixture was evaporated under reduced pressure and the residue was triturated by CHCl<sub>3</sub> (3 mL) yielding solid *trans*-2-aminocyclohexanol hydrochloride (**17**) (129 mg, 85%). Its identity was confirmed by comparison with an authentic specimen on the basis of NMR spectra.

### Debenzylation of Benzylamine **18**

1,6-Anhydro-4-*O*-benzyl-3-(benzylamino)-2,3-dideoxy-2-(tosylamino)-β-D-glucopyranose (**18**)<sup>7</sup> (83 mg, 0.167 mmol) was dissolved in THF (1 mL) and DIAD (38 μL, 0.183 mmol) was added. The solution was heated under reflux for 19 h. TLC revealed the presence of imine (R<sub>f</sub> ca. 0.5) and DIHD (R<sub>f</sub> ca. 0.6) which were visualized as colored spots by anisaldehyde detection reagent (grey and yellow color, respectively). To the solution, THF (2 mL) and 5% aq HCl (0.5 mL) were added and the mixture was refluxed for 4 d. During this time, imine had gradually disappeared and amine hydrochloride **19** was formed. The mixture was evaporated under reduced pressure and the residue was partitioned between CHCl<sub>3</sub> (30 mL) and 5% aq HCl (3 × 30 mL). The combined aqueous layers were evaporated in vacuo yielding a white powder. Its crystallization (EtOH-Et<sub>2</sub>O) afforded pure 3-amino-1,6-anhydro-4-*O*-benzyl-2,3-dideoxy-2-(tosylamino)-β-D-glucopyranose hydrochloride (**19**). Yield: 69 mg (93%); mp 163–166 °C (dec.); [α]<sub>D</sub> = -89 (c 0.11 in H<sub>2</sub>O).

Anal. Calcd for C<sub>20</sub>H<sub>25</sub>ClN<sub>2</sub>O<sub>5</sub>S (440.94): C, 54.48; H, 5.71; N, 6.35; Cl, 8.04. Found: C, 54.68; H, 5.85; N, 6.32; Cl, 8.44.

### Debenzylation of Benzylamine **20**

1,6-Anhydro-4-*O*-benzyl-2-(benzylamino)-2,3-dideoxy-3-(tosylamino)-β-D-glucopyranose (**20**)<sup>7</sup> (60 mg, 0.121 mmol) was dissolved in THF (1 mL) and DIAD (28 μL, 0.135 mmol) was added. The solution was heated under reflux for 10 h. Reaction was monitored by TLC and stopped after consumption of benzylamine **20**. To the mixture, THF (5 mL) and 5% aq HCl (5 mL) were added and the mixture was refluxed for 2 d. During this time, imine had gradually disappeared and amine hydrochloride **21** was formed. The mixture was worked up as described above for the preparation of amine **19** and afforded 2-amino-1,6-anhydro-4-*O*-benzyl-2,3-dideoxy-3-(tosylamino)-β-D-glucopyranose hydrochloride (**21**). Yield: 45 mg (85%); mp 169–173 °C (dec.); [α]<sub>D</sub> = -10 (c 0.15, H<sub>2</sub>O).

Anal. Calcd for C<sub>20</sub>H<sub>25</sub>ClN<sub>2</sub>O<sub>5</sub>S (440.94): C, 54.48; H, 5.71; N, 6.35. Found: C, 54.55; H, 5.72; N, 6.42.

### Debenzylation of Benzylamine **22**

1,6-Anhydro-2-*O*-benzyl-4-(benzylamino)-3,4-dideoxy-3-(tosylamino)-β-D-glucopyranose (**22**)<sup>7</sup> (121 mg, 0.245 mmol) was dissolved in THF (3 mL) and DIAD (56 μL, 0.27 mmol) was added. The solution was heated under reflux for 27 h. Reaction was monitored by TLC and stopped after consumption of benzylamine **22**. During this time, imine and DIHD were formed in the reaction mixture. To the mixture, 5% aq HCl (1 mL) was added and the mixture was stirred for 3 d at r.t. During this time, imine had gradually dis-

**Table 4** Proton NMR Data (400 MHz) for Imine **5** (in C<sub>4</sub>D<sub>8</sub>O) and for Amine Hydrochlorides **19**, **21**, **23**, **25**, and **27** in CD<sub>3</sub>SOCD<sub>3</sub>

Com- pound	Chemical shifts (ppm)/Signal multiplicity												
	H-1	H-2	H-3	H-4	H-5	H-6 <sub>exo</sub>	H-6 <sub>endo</sub>	OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	NH <sub>3</sub> <sup>+</sup>	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>4</sub> (5)	CH <sub>3</sub>	
<b>5</b> <sup>a</sup>	5.27	3.06	3.67	3.41	4.59	3.63	3.74	4.77	4.72	–	7.21–7.80	–	
<b>19</b>	4.77	3.61	2.90	3.24	4.69	3.50	3.75	4.65	4.53	8.40	7.44–7.31	7.77, 7.75	2.40
<b>21</b>	5.51	3.33	3.40	2.99	4.68	3.69	4.30	3.92	4.20	8.50	7.10–7.43	7.98, 7.82	2.40
<b>23</b>	5.46	3.25	3.39	3.17	4.66	3.69	4.25	3.94	4.18	8.45	7.00–7.42	8.00, 7.85	2.40
<b>25</b>	5.57	3.36	3.99	3.21	4.72	3.65	3.99	4.67	4.72	8.75	7.42–7.32	–	–
<b>27</b>	5.62	3.56	4.02	2.97	4.81	3.62	3.93	4.64	4.72	8.80	7.42–7.31	–	–
	Coupling constants <i>J</i> (Hz)												
	1,2	2,3	3,4	4,5	5,6 <sub>exo</sub>	5,6 <sub>endo</sub>	6,6	1,3	2,4	3,5	O-CH <sub>2</sub>		
<b>5</b>	< 1	7.2	6.6	< 1	0.9	5.5	7.3	ca. 0	ca. 0	ca. 0	12.2		
<b>19</b>	< 1	6.8	7.85	< 1	1.1	5.6	8.2	ca. 0	ca. 0	ca. 0	11.3		
<b>21</b>	< 1	5.5	6.2	< 1	1.0	5.5	8.1	ca. 0	ca. 0	ca. 0	12.1		
<b>23</b>	< 1	5.8	6.4	< 1	< 1	5.5	8.0	ca. 0	ca. 0	ca. 0	12.2		
<b>25</b>	1.1	4.3	5.2	1.4	1.0	5.5	7.8	ca. 0	ca. 0	ca. 0	11.75		
<b>27</b>	0.9	4.6	5.3	1.4	0.9	5.5	7.9	ca. 0	ca. 0	ca. 0	11.75		

<sup>a</sup> δ (–CH=N–) = 8.29 ppm.

appeared and amine hydrochloride **23** was formed. The mixture was worked up as described above for the preparation of amine **19** and afforded 4-amino-1,6-anhydro-2-*O*-benzyl-3,4-dideoxy-3-(tosylamino)-β-D-glucopyranose hydrochloride (**23**). Yield: 90 mg (83%); mp 157–160 °C (dec.); [α]<sub>D</sub> = +5 (c 0.19, H<sub>2</sub>O).

Anal. Calcd for C<sub>20</sub>H<sub>25</sub>ClN<sub>2</sub>O<sub>5</sub>S (440.94): C, 54.48; H, 5.71; N, 6.35; Cl, 8.04. Found: C, 54.57; H, 5.80; N, 6.38; Cl, 8.23.

#### Debenzylation of Benzylamine **24**

1,6-Anhydro-3-azido-2-*O*-benzyl-4-(benzylamino)-3,4-dideoxy-β-D-glucopyranose (**24**)<sup>8</sup> (297 mg, 0.81 mmol) was dissolved in THF (10 mL) and DIAD (190 μL, 0.965 mmol) was added. The solution was heated under reflux for 10 h. Reaction was monitored by TLC and stopped after consumption of benzylamine **24**. To the mixture, 5% aq HCl (2.5 mL) was added and the mixture was refluxed for 6 h. The mixture was worked up as described above for the preparation of amine **19** and afforded 4-amino-1,6-anhydro-3-azido-2-*O*-

**Table 5** <sup>13</sup>C (100 MHz) Chemical Shifts (in ppm) of Imine **5** (in C<sub>4</sub>D<sub>8</sub>O) and of Amine Hydrochlorides **19**, **21**, **23**, **25** and **27** in CD<sub>3</sub>SOCD<sub>3</sub>

Com- pound	C-1	C-2	C-3	C-4	C-5	C-6	OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub> (4)	CH <sub>3</sub>
<b>5</b> <sup>a</sup>	104.6	72.4	68.8	77.3	78.0	68.2	72.5	140.1, 137.6, 131.3, 129.1 (2), 129.1 (2), 128.8 (2), 128.3 (2), 128.0	–
<b>19</b>	100.7	51.1	55.8	74.0	77.3	66.3	70.6	143.3, 138.0, 137.6, 129.9, 128.2 (2), 128.1 (2), 127.7 (2), 126.7 (2)	21.0
<b>21</b>	99.4	50.7	50.2	73.4	74.9	66.0	70.7	143.3, 137.0, 128.3 (2), 128.2 (2), 128.0 (2), 127.8, 127.4 (20)	21.0
<b>23</b>	99.6	70.4	50.2	50.9	73.9	65.2	72.2	143.2, 137.0, 136.2, 129.5(2), 128.2 (2), 127.7, 127.5 (2), 127.4 (2)	21.0
<b>25</b>	99.8	71.2	57.5	50.7	77.0	66.3	72.2	137.3, 128.3 (2), 128.1 (2), 127.9	–
<b>27</b>	98.2	51.6	57.9	74.2	77.7	65.9	70.7	137.4, 128.3 (2), 128.0 (2), 127.8	–

<sup>a</sup> δ (–CH=N–) = 163.0 ppm.

benzyl-3,4-dideoxy- $\beta$ -D-glucopyranose hydrochloride (**25**). Yield: 181 mg (71.5%); mp 213–217 °C (dec.);  $[\alpha]_D = -39$  (*c* 0.20, H<sub>2</sub>O).

Anal. Calcd for C<sub>13</sub>H<sub>17</sub>ClN<sub>4</sub>O<sub>3</sub> (312.76): C, 49.92; H, 5.48; N, 17.91; Cl, 11.34. Found: C, 50.27; H, 5.20; N, 18.02; Cl, 11.43.

#### Debenzylation of Benzylamine **26**

1,6-Anhydro-3-azido-4-*O*-benzyl-2-(benzylamino)-2,3-dideoxy- $\beta$ -D-glucopyranose (**26**)<sup>8</sup> (500 mg, 1.365 mmol) was dissolved in THF (10 mL) and DIAD (340  $\mu$ L, 1.64 mmol) was added. The solution was heated under reflux for 21 h. Reaction was monitored by TLC and stopped after consumption of benzylamine **26**. To the mixture, 5% aq HCl (5 mL) was added and the mixture was refluxed for 2 d. The mixture was worked up as described above for the preparation of amine **19** and afforded 2-amino-1,6-anhydro-3-azido-4-*O*-benzyl-2,3-dideoxy- $\beta$ -D-glucopyranose hydrochloride (**27**). Yield: 388 mg (91%); mp 155–158 °C (dec.);  $[\alpha]_D = -17$  (*c* 0.26, H<sub>2</sub>O).

Anal. Calcd for C<sub>13</sub>H<sub>17</sub>ClN<sub>4</sub>O<sub>3</sub> (312.76): C, 49.92; H, 5.48; N, 17.91; Cl, 11.34. Found: C, 50.11; H, 5.49; N, 17.99; Cl, 11.43.

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