2-Azido-2-deoxycellulose: Synthesis and 1,3-Dipolar Cycloaddition

by **Fuyi Zhang**, **Bruno Bernet**, **Véronique Bonnet**, **Olivier Dangles**, **Francisco Sarabia**, and **Andrea Vasella***

Laboratory of Organic Chemistry, Department of Chemistry and Applied Biosciences, ETH Zürich, Wolfgang-Pauli-Strasse 10, CH-8093 Zürich (e-mail: vasella@org.chem.ethz.ch)

Chitosan (**1**) was prepared by basic hydrolysis of chitin of an average molecular weight of 70000 Da, ^{1}H-NMR spectra indicating almost complete deacetylation. *N*-Phthaloylation of **1** yielded the known *N*-phthaloylchitosan (**2**), which was tritylated to provide **3a** and methoxytritylated to **3b**. Dephthaloylation of **3a** with $NH_2NH_2 \cdot H_2O$ gave the 6-*O*-tritylated chitosan **4a**. Similarly, **3b** gave the 6-*O*-methoxytritylated **4b**. $CuSO_4$-Catalyzed diazo transfer to **4a** yielded 95% of the azide **5a**, and uncatalyzed diazo transfer to **4b** gave 82% of azide **5b**. Further treatment of **5a** with $CuSO_4$ produced 2-azido-2-deoxycellulose (**7**). Demethoxytritylation of **5b** in HCOOH gave 2-azido-2-deoxy-3,6-di-*O*-formylcellulose (**6**), which was deformylated to **7**. The 1,3-dipolar cycloaddition of **7** to a range of phenyl-, (phenyl)alkyl-, and alkyl-monosubstituted alkynes in DMSO in the presence of CuI gave the 1,2,3-triazoles **8**–**15** in high yields.

Introduction. – Chitin, an abundant polysaccharide of 1,4-linked 2-acetamido-2-deoxy-β-D-glucopyranose (β-D-GlcNAc), is found in animals, fungi, and some bacteria [1], and readily isolated by deproteinization and demineralization of crustacean shells [2]. Chitosans, fully or partially deacetylated chitin derivatives, and their modifications [3] possess antiviral and antimicrobial properties [4], and know a number of applications, being useful in enzyme inhibition and immobilization [5], in grafts copolymerization [6], as carriers for drugs [7] and genes [8], and for biomedical purposes such as wound healing and immunostimulation [9]. Further applications include their use as food supplements or preservatives [10], as adsorbents of metals [11], for treatment of waste waters [12], as support for heterogeneous catalysis [13], and as packaging material [14]. The NH_2 group at C(2) of chitosan was modified in many ways, mostly by *N*-alkylation [15], *N*-acylation [16], *N*-phosphorylation [17], *N*-sulfation [18], and by condensation with thiolated reagents [19].

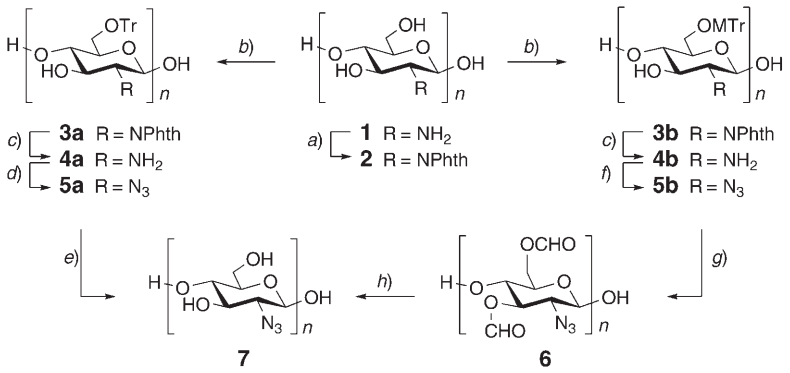
2-Azido-2-deoxycellulose should be available from chitosan by diazo transfer. 1,3-Cycloadditions of 2-azido-2-deoxycellulose to alkynes should introduce 1,2,3-triazolyl side chains into chitosan and formally into cellulose, similarly as it is known for 6-azido-6-deoxypolysaccharides [20][21][1]). In the following, we describe the synthesis of 2-azido-2-deoxycellulose and its reactivity in the 1,3-dipolar cycloaddition to alkynes, leading to new chitin/cellulose derivatives.

Results and Discussion. – *A priori*, the desired 2-azido-2-deoxycellulose should be available from chitosan (**1**) by diazo transfer from trifluoromethanesulfonyl azide,

[1]) For the preparation of 6-azido-6-deoxycellulose, -chitin, and -chitosan, see [22–25].

which is readily prepared *in situ* from NaN_3 and trifluoromethanesulfonic anhydride (Tf_2O) [26][27]. We prepared chitosan according to an improved protocol of *Kurita et al.* [28] by boiling low-molecular-mass chitin (average molecular weight: 70000 Da) under reflux in 10M NaOH for 5 days (*Scheme 1*). The determination of high degrees of deacetylation (DD) on the basis of the relative intensity of the NAc, H–C(1), and H–C(2–6) signals [29] in the ^{1}H-NMR spectrum of **1** proved convenient and more precise than using CD and IR spectroscopy, or other methods [30]. A high DD (> 99.5%; as compared to 91–92% for commercial chitosans) of the product was evidenced by the almost complete disappearance of the NAc signal of **1**. However, although the $CuSO_4$-catalyzed diazo transfer from TfN_3[2]) is known to tolerate H_2O, it did not provide more that 10–15% of the desired azide **7** from **1**, on account of the low solubility of **1** in MeOH (*Scheme 1*). The poor solubility of chitosan (**1**) in organic solvents is indeed a frequently encountered problem in regioselective chemical modifications of chitosan, resulting in unsatisfactory yields, low selectivities, and an irregular structure of the product. For this reason, we transformed chitosan (**1**) into the known phthalimide **2** [32]. Stirring a suspension of chitosan and 3 equiv. of phthalic anhydride in DMF at 130° for 15 h led to a clear, viscous solution that was treated with H_2O and then purified by *Soxhlet* extraction with EtOH to give **2** in 85% yield [32]. Tritylation and monomethoxytritylation of **2** provided the ethers **3a** [32] and **3b**, respectively, in high yields[3]). The IR spectra of **2**, **3a**, and **3b** show the expected weak and strong absorptions of the phthalimido group at 1776–1777 and 1709–1716 cm^{-1}, respectively. Dephthaloylation of **3a** and **3b** by treatment with $NH_2NH_2 \cdot H_2O$ yielded 6-*O*-trityl chitosan **4a** (65%) [32] and the 6-*O*-methoxytrityl chitosan **4b** (62%), respectively.

Scheme 1



Phth = Phthaloyl; Tf = trifluoromethylsulfonyl; Tr = trityl (= triphenylmethyl); MTr = monomethoxytrityl (= (4-methoxyphenyl)diphenylmethyl). *a*) Phthaloyl anhydride, DMF, 130°, 15 h; 85%. *b*) TrCl or MTrCl, pyridine, 90–100°, 30 h; > 98% of **3a**; 90% of **3b**. *c*) $NH_2NH_2 \cdot H_2O$, H_2O, 100–110°, 15–17 h; 65% of **4a**; 62% of **4b**. *d*) TfN_3 in CH_2Cl_2, $CuSO_4$, Et_3N, H_2O/MeOH, r.t., 15 d; 95%. *e*) $CuSO_4$, toluene, 110°, 6 h; 95%. *f*) MeONa, TfN_3 in CH_2Cl_2, 4-(dimethylamino)pyridine (DMAP), MeOH, r.t., 20 d; 82%. *g*) HCOOH, Et_2O, r.t., 30 h; 88%. *h*) MeONa, MeOH, r.t., 12 h; 95%.

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[2]) *WARNING:* neat TfN_3 has been reported to be explosive [31]!

[3]) For a regioselective silylation of **2**, see [33].

As expected, the C(6)-*O*-tritylated chitosans **4a** and **4b** are far more soluble in MeOH than **1**. The $CuSO_4$-catalyzed diazo transfer from TfN_3 to **4a** required 15 days at room temperature, until a negative *Kaiser* test [34] evidenced less than 0.5% of free NH_2 groups. The azide **5a** (95%) was obtained in a high yield, but the Cu salts could not be completely removed by washing with H_2O, or by treatment with $NaCS_2NEt_2 \cdot 3\ H_2O$ [35]. The uncatalyzed diazo transfer [26] of Tf_2O to the monomethoxytrityl ether **4b** in the presence of MeONa and 4-(dimethylamino)pyridine in MeOH at room temperature also proceeded slowly, and was continued until the *Kaiser* test was negative (17 days), to provide 82% of **5b**[4]). The introduction of the N_3 group was evidenced by a strong IR absorption of **5a** and **5b** at 2116 and 2109 cm^{-1}, respectively. Detritylation by treating **5a** with $CuSO_4$ in boiling toluene afforded 95% of the desired azide **7**, which was, however, contaminated with Cu salts. Treatment of the monomethoxytrityl ether **5b** with HCOOH gave 2-azido-2-deoxy-3,6-di-*O*-formylcellulose (**6**) in 88% yield. The CHO groups of **6** are evidenced by the C=O band at 1720 cm^{-1}. The formate **6** was deacylated by treating a suspension of **6** in DMSO with MeONa, to generate **7** in 95% yield. The IR spectrum of **7** shows a sharp and strong N_3 band at 2112 cm^{-1}. A negative *Kaiser* test and a negative fluorescence test[5]) evidenced the absence of amino groups in **7**.

The Cu^I-catalysed 1,3-dipolar cycloaddition of azides to monosubstituted alkynes was used in a few cases to modify 6-azido-6-deoxypolysaccharides [37]. It leads selectively to 4-substituted 1,2,3-triazoles, while *ca.* 1:1 mixtures of 4- and 5-substituted 1,2,3-triazoles are obtained in the absence of Cu^I catalysis [38][39], as we had experienced in an early application of the 'click reaction' to the synthesis of modified cyclodextrins [40]. The reactivity of 2-azido-2-deoxycellulose (**7**) in this cycloaddition was evaluated by treating **7** with monosubstituted alkynes in DMSO in the presence of CuI [41] (*Scheme 2*). Phenyl-, (phenyl)alkyl-, and alkylacetylenes were transformed in high yields at 60–100° within 48–72 h into the 4-substituted 1,2,3-triazoles **8**–**15** (*Table 1*). A complete cycloaddition was evidenced by the absence of an azido band in the IR spectra of the products. The 1,2,3-triazolyl group of **8**–**15** is evidenced by a weak, broad IR band at 1640–1668 cm^{-1}. Two bands appearing at 694–702 and 720–763 cm^{-1} are assigned to the monosubstituted Ph group of **8**–**11**[6]).

The solubility of **6**, **7**, and **12** was determined for solutions in DMSO, pyridine, and MeOH (*Table 2*). The three compounds are sparingly soluble, DMSO proving the best solvent. As expected, the diformate **6** is more highly soluble than the unprotected azide **7**.

Attempts to obtain well-resolved ^1H- and ^{13}C-NMR spectra of **6**–**15** in (D_6)DMSO failed. Strong line broadening prevented an assignment of the signals, especially for the glycosyl H- and C-atoms. However, the structures of **5b**, **6**–**9**, and **13** were

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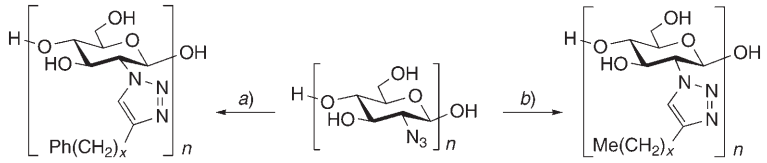
4) When the reaction was performed at 50–60°, TfN_3 was consumed within 6 h (reaction of TfN_3 with MeONa?), but the *Kaiser* test was still positive.

5) The reaction with fluorescamine allows detection of 0.1% of unreacted amino groups [36].

6) The attempted 1,3-dipolar cycloaddition of **7** to nitriles in DMSO at $\leq 100°$ failed even for nitriles activated by electron-withdrawing substituents, such as 3-hydroxypropanenitrile, 4-nitrobenzonitrile, and toluenesulfonyl and benzoyl cyanide, while heating **7** to 130–150° for more than 2 days in the presence of 4–6 equiv. of the nitriles resulted in only a partial transformation.

Scheme 2



8 $x = 0$
9 $x = 1$
10 $x = 2$
11 $x = 3$

7

12 $x = 2$
13 $x = 3$
14 $x = 4$
15 $x = 5$

a) 4.0 equiv. of $Ph(CH_2)_xC \equiv CH$ ($x = 0$, 1, 2, or 3), CuI, DMSO, 80–100°, 48–60 h; 86–90%. *b*) 4.0–10.0 equiv. of $Me(CH_2)_xC \equiv CH$ ($x = 2$, 3, 4, or 5), CuI, DMSO, 60–100°, 50–72 h; 85–93%.

Table 1. *1,3-Dipolar Cycloadditions of* **7** *to Monosubstituted Alkynes: Conditions, Products, and Yields*

Alkyne	Conditions	Product (Yield [%])
$PhC \equiv CH$	60 h, 80°	**8** (87)
$PhCH_2C \equiv CH$	50 h, 80°	**9** (90)
$Ph(CH_2)_2C \equiv CH$	48 h, 100°	**10** (88)
$Ph(CH_2)_3C \equiv CH$	40 h, 100°	**11** (86)
Pent-1-yne	72 h, 60°	**12** (93)
Hex-1-yne	60 h, 80°	**13** (90)
Hept-1-yne	50 h, 100°	**14** (88)
Oct-1-yne	72 h, 100°	**15** (85)

Table 2. *Solubility* [g/l] *of* **6**, **7**, *and* **12** *in DMSO, Pyridine, and MeOH*

	6	**7**	**12**
DMSO	4.6	2.8	1.2
Pyridine	1.2	0.8	0.8
MeOH	1.0	1.4	0.2

corroborated by solid state CP/MAS ^{13}C-NMR spectroscopy. Their chemical shifts are listed together with those of β-chitin [42], chitosan [43], and cellulose II [44] in *Table 3*, and the spectra of **6**, **7**, and **9** are depicted in the *Figure*.

The CP/MAS ^{13}C-NMR spectra of **5b**, **6**–**9**, and **13** show the presence of a single compound. The spectra, and especially the chemical shifts of C(1), C(4), and C(2)/C(3), resemble those of β-chitin and chitosan. C(2) and C(6) of **5b** and **6** resonate as a broad signal at *ca*. 65.5 ppm, whereas the spectra of **7**–**9** and **13** show two signals at 65.3–66.1 and 61.0–62.1 ppm. A comparison with β-chitin and chitosan suggests that the former signal corresponds to C(2) and the latter one to C(6). As expected, the CP/MAS ^{13}C-NMR spectra of **5b**, **6**–**9**, and **13** differ significantly from the spectrum of cellulose II, which is strongly influenced by the intra- and intermolecular H-bonding network of HO–C(2) and HO–C(6) (see [45] and refs. cit. therein).

The chemical shifts for C(4) and C(5) of the 1,2,3-triazolyl unit of **8**, **9**, and **10** (146.1–147.9 and 125.1–126 ppm) confirm the formation of 4-substituted 1,2,3-

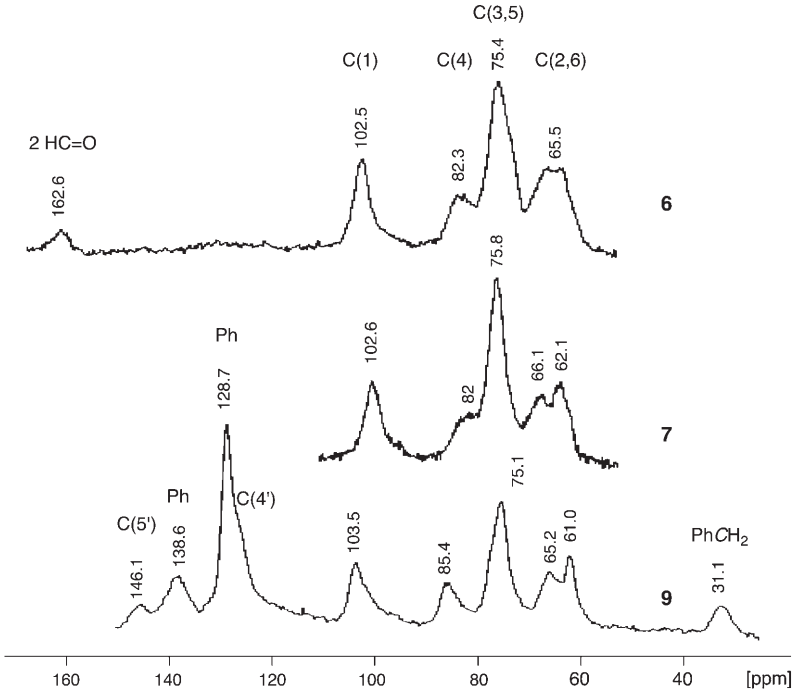


Figure. *CP/MAS ^{13}C-NMR Spectra of* **6**, **7**, *and* **9**

Table 3. *CP/MAS ^{13}C-NMR Chemical Shifts* [ppm] *of* **5b**, **6**–**9**, **13**, *β-Chitin* [42], *Chitosan* [43], *and Cellulose II* [44]

	C(1)	C(4)	C(3), C(5)	C(2), C(6)	C(4′)	C(5′)	other C
5b	101.1 (br.)	82 (br.)	75.3	65.4 (br.)	–	–	MTrO: 159.0, 148.2 (br.) 141.9 (br.), 128.4, 112.8 (br.), 87.0, 54.9
6	102.5	82.3 (br.)	75.4	65.5 (br.)	–	–	2 CH=O: 162.6
7	102.6	82 (br.)	75.8	66.1, 62.1	–	–	–
8	102.4 (br.)	84.7	74.8	65.3, 61.2	147.9	125.8	Ph: 141.2, 128.9
9	103.5	85.4	75.1	65.2, 61.0	146.1	[a])	$PhCH_2$: 138.6, 128.7, 31.1
13	103.3 (br.)	85.1 (br.)	75.3	65.9, 61.4	147.5	125.1	Bu: 31.9, 25.9, 23.0, 14.1
β-Chitin	104.1	83.4	73.9	55.2, 60.8	–	–	NHAc: 173.6, 22.8
Chitosan	104.8	81 (sh)	75.9	58.9 (br.)	–	–	–
Cellulose II	108.3, 106.2	89.9, 88.7	[b])	[b])	–	–	–

[a]) Shoulder of Ph signal (*ca.* 126 ppm). [b]) C(2), C(3), and C(5): 77.8, 75.9, and 73.8 ppm; C(6): 64.2 and 63.6 ppm.

triazoles (compare with 143–148 and 117–126 ppm for monomeric 4-substituted 1,2,3-triazoles [46] in solution, differing clearly from the chemical shifts (131 and 139 ppm) of 5-substituted 1,2,3-triazoles [47]).

We thank the ETH Zürich and the *Swiss National Science Foundation* for generous support, Dr. *Anu Koivula*, Espoo, for a generous gift of cellulases, Mr. *Nicolas Bogliotti* for the solubility measurements, and Prof. Dr. *Beat Meier* and Mr. *Thomas Westfeld* for the CP/MAS ^{13}C-NMR spectra.

Experimental Part

Chitosan (**1**) [28]. A suspension of chitin (6.0 g, average molecular weight: 70 kDa) in 10N NaOH soln. (360 ml) was kept under reflux for 5 d. After filtration, the solid was washed with water until pH 7.0 and dried (P_2O_5) to give **1** (4.70 g, 98%). For ^{1}H-NMR spectroscopy, a suspension of **1** (10 mg) in D_2O/10.8N DCl 98 : 2 (2 ml) was stirred at 60° until a clear soln. was formed. IR (ATR): 3358*m* (br.), 2866*w* (br.), 1590*w*, 1419*w*, 1374*m*, 1194*w*, 1147*m*, 1057*s*, 1015*s*, 988*s*, 889*s*, 804*m*, 734*m*, 661*s*. ^{1}H-NMR (300 MHz, D_2O, 70°; *cf.* [29]): 5.05 (br. *s*, H–C(1)); 4.06, 3.90 (2 br. *s*, H–C(3), H–C(4), H–C(5), 2 H–C(6)); 3.36 (br. *s*, H–C(2)); 2.20 (*s*, < 0.5%, NAc). Anal. calc. for $C_6H_{11}NO_4$ (161.16): C 44.72, H 6.88, N 8.69; found: C 44.31, H 6.95, N 8.16.

N-*Phthaloylchitosan* (**2**). According to [32], a mixture of **1** (4.73 g, 29.02 mmol amino-group equiv.) and phthalic anhydride (13.0 g, 87.74 mmol) in anh. DMF (95.0 ml) was stirred at 130° for 7 h and diluted with DMF (100 ml), affording a clear soln. The mixture was stirred at 130° for 15 h, cooled to r.t., and poured into ice-water. The precipitate was collected by filtration, washed completely by *Soxhlet* extraction with EtOH for *ca.* 9 h and dried (P_2O_5) to give **2** (7.3 g, 85%). IR (ATR) : 3474*w* (br.), 2942*w* (br.), 1776*w*, 1709*s*, 1611*w*, 1468*w*, 1384*s*, 1286*m*, 1255*m*, 1196*w*, 1111*m*, 1062*s*, 1035*s*, 1011*s*, 968*m*, 873*m*, 792*m*, 741*m*, 718*s*, 666*m*.

N-*Phthaloyl-6*-O-*(triphenylmethyl)chitosan* (**3a**). According to [32], a soln. of **2** (170 mg, 590 μmol amino-group equiv.) in pyridine (8 ml) was treated with TrCl (2.10 g, 7.52 mmol), stirred for 24 h at 90° under Ar, cooled to r.t., and poured into EtOH. The precipitate was filtered off, and washed with EtOH and Et_2O. Drying gave **3a** (310 mg, quant.). IR (KBr): 3438*m*, 2922*w*, 1777*m*, 1716*s*, 1489*w*, 1469*w*, 1388*s*, 1110*m*, 1020*m*, 719*m*.

6-O-*[(4-Methoxyphenyl)diphenylmethyl]*-N-*phthaloylchitosan* (**3b**). A soln. of **2** (6.00 g, 20.6 mmol amino-group equiv.) in pyridine (120 ml) was treated with MTrCl (60.0 g, 177.1 mmol). The soln. was stirred at 100° for 30 h under Ar, cooled to r.t., and poured into EtOH. The precipitate was filtered off and washed with EtOH to give **5** (10.40 g, 90%). A small sample was dissolved in CH_2Cl_2, treated with MeOH, and resulting precipitate of **3b** was filtered off. This procedure was repeated eight times to obtain pure **3b** for analysis. IR (ATR): 3477*w* (br.), 2933*w* (br.), 1777*w*, 1714*s*, 1608*w*, 1509*m*, 1491*w*, 1467*w*, 1447*w*, 1385*s*, 1300*w*, 1250*m*, 1176*m*, 1031*s*, 874*w*, 830*m*, 795*w*, 767*m*, 740*m*, 719*s*, 700*s*, 670*m*, 631*m*.

6-O-*(Triphenylmethyl)chitosan* (**4a**). According to [32], a suspension of **3a** (220 mg, 420 μmol amino-group equiv.) and $NH_2NH_2 \cdot H_2O$ (5 ml) in H_2O (10 ml) was stirred at 100° for 15 h, cooled to r.t., and evaporated. The residue was three times suspended in H_2O (15 ml) and evaporated. The colourless precipitate in H_2O was filtered off, and washed with EtOH and Et_2O. Drying gave **4a** (109 mg, 65%). IR (KBr): 3455*s*, 2865*m*, 1602*w*, 1383*w*, 1091*s*, 607*w*.

6-O-*[(4-Methoxyphenyl)diphenylmethyl]chitosan* (**4b**). A suspension of **3b** (7.30 g, 12.9 mmol amino-group equiv.) and $NH_2NH_2 \cdot H_2O$ (155 ml) in H_2O (300 ml) was stirred at 110° for 17 h and cooled to r.t. After concentration to 100 ml, the precipitate was filtered off and washed with EtOH. The solid was suspended in fresh $NH_2NH_2 \cdot H_2O$ (100 ml), and the treatment was repeated until disappearance of the C=O band in the IR spectrum. The mixture was cooled to r.t. and evaporated. The residue was suspended in H_2O (150 ml), and the precipitate was filtered off and washed with EtOH to give **4b** (3.5 g, 62%). A small sample was dissolved in CH_2Cl_2 and treated with MeOH. The resulting precipitate of **4b** was filtered off. This procedure was repeated seven times to obtain pure **4b** for analysis. IR (ATR): 3451*w* (br.), 2876*w* (br.), 1655*w*, 1607*w*, 1583*w*, 1509*m*, 1495*w*, 1446*w*, 1300*w*, 1249*m*, 1178*m*, 1154*m*, 1031*s*, 901*m*, 830*m*, 796*m*, 756*m*, 727*m*, 700*s*, 631*m*.

2-Azido-2-deoxy-6-O-*(triphenylmethyl)cellulose* (**5a**). A vigorously stirred suspension of **4a** (100 mg, *ca.* 270 μmol amino-group equiv.) in H_2O (3.8 ml) was treated with $CuSO_4$ (2.6 mg, 14.5 μmol), a soln. of TfN_3 (8.068 mmol) in CH_2Cl_2 (3.2 ml), and Et_3N (604 μl, 4.36 mmol), diluted dropwise with MeOH (16.6 ml), and stirred at r.t. for 15 days. After concentration to *ca.* 5 ml, the precipitate was

filtered off and washed with EtOH and Et_2O. Drying gave **5a** (100 mg, 95%) contaminated with Cu salts. IR (KBr): 3453*s*, 2920*w*, 2116*s*, 1630*w*, 1374*w*, 1314*w*, 1154*m*, 1074*s*, 608*w*.

*2-Azido-2-deoxy-6-*O*-[(4-methoxyphenyl)diphenylmethyl]cellulose* (**5b**). A mixture of **4b** (4.40 g, *ca.* 10.15 mmol amino-group equiv.) and MeONa (2.57 g, 47.59 mmol) in MeOH (198 ml) was treated with a soln. of TfN_3 (110 mmol) in CH_2Cl_2 (160 ml) and 4-(dimethylamino)pyridine (5.20 g, 42.46 mmol) and stirred at r.t. under Ar for 7 d. After the addition of additional TfN_3 (110 mmol) in CH_2Cl_2 (160 ml), stirring at r.t. was continued for 10 d; after that time, a negative *Kaiser* test was obtained. The mixture was concentrated, and the precipitate was filtered off, washed with CH_2Cl_2 and MeOH, and dried to give **5b** (3.82 g, 82%). IR (ATR): 3460*w* (br.), 2878*w* (br.), 2109*m*, 1655*w*, 1607*w*, 1581*w*, 1509*m*, 1446*w*, 1299*w*, 1249*m*, 1217*m*, 1177*m*, 1152*m*, 1030*s*, 830*m*, 796*w*, 756*m*, 726*w*, 699*s*, 631*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.41, 7.25 (2 br. *s*, 12 arom. H); 6.85 (br. *s*, 2 arom. H); 4.20–3.80 (br. *s*, 2 H); 3.73 (br. *s*, MeO); 3.49, 3.34 (2 br. *s*, 5 H).

Kaiser *Test* [34]. A few milligrams of **5a** or **5b** was treated with 3 drops of soln. *A* (20 g of phenol in 5 ml of abs. EtOH), 3 drops of soln. *B* (2 ml of 10^{-2} M aq. KCN in 100 ml of pyridine), and 3 drops of soln. *C* (0.5 g of ninhydrin in 10 ml of abs. EtOH). The yellow soln. was heated to 100° for 3 min. A persisting yellow colour indicates the absence of amino groups.

*2-Azido-2-deoxy-3,6-di-*O*-formylcellulose* (**6**). A suspension of **5b** (5.00 g, *ca.* 10.88 mmol amino-group equiv.) in Et_2O (75 ml) was treated with HCOOH (75 ml), stirred at r.t. for 30 h and poured into acetone. The precipitate was filtered off, washed with CH_2Cl_2 and MeOH, and dried to give **6** (2.32 g, 88%). IR (ATR): 3418*w* (br.), 2918*w*, 2112*m*, 1720*m*, 1484*w*, 1435*w*, 1404*w*, 1373*w*, 1313*w*, 1152*m*, 1014*s*, 950*s*, 821*m*, 767*m*, 698*m*.

2-Azido-2-deoxycellulose (**7**). a) *From* **5a**. A suspension of **5a** (100 mg, *ca.* 270 µmol amino-group equiv.) in toluene (4 ml) was treated with $CuSO_4$ (100 mg, 557 µmol) and stirred at reflux for 6 h. The solid was filtered off and washed with acetone. Drying gave **7** (44 mg, 95%) contaminated with Cu salts.

b) *From* **6**. A suspension of **6** (100 mg, 0.411 mmol) in MeOH (15 ml) was treated with MeONa (55 mg, 1.02 mmol), stirred at r.t. for 12 h, and filtered. The solid was washed with CH_2Cl_2 and MeOH, and dried to give **7** (73.1 mg, 95%). IR (ATR): 3362*m* (br.), 2931*w*, 2887*w*, 2112*s*, 1371*w*, 1311*w*, 1276*w*, 1254*w*, 1197*m*, 1149*m*, 1059*s*, 1027*s*, 949*m*, 896*m*.

Quant. Fluorescence Test for Measuring Residual Amino Group of **7** [36]. Solns. of **7** (1 mg) and glucosamine (6.5 mg and 6 dilutions) in deionized H_2O (5 ml, pH adjusted to 8 with Et_3N) were treated with a fluorescamine soln. (333 µl of 3 mg of fluorescamine soln. in 1 ml of MeCN). The excitation wavelength was 405 nm, and the emission of fluorescence was measured at 535 nm and 24°. A comparison of the curve of **7** with that of glucosamine indicated a negligible presence of amino groups in **7**.

General Procedure for the 1,3-Dipolar Cycloadditions of **7** *to Alkynes.* A suspension of **7** (50 mg, *ca.* 0.267 mmol saccharide units) and CuI (2.0 mg) in DMSO (1 ml) was treated with the alkyne (4 equiv.) and heated to 60–100° until complete disappearance of the IR band at 2112 cm^{-1}. The mixture was cooled to r.t., and dialysed against H_2O. The solid was filtered off, washed with CH_2Cl_2 and MeOH, and dried to give the triazoles **8**–**15**.

*2-Deoxy-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)cellulose* (**8**). The mixture was heated to 80° for 60 h. Yield: 87%. IR (ATR): 3416*w* (br.), 2884*w*, 1640*w* (br.), 1484*w*, 1458*w*, 1362*w* (br.), 1205*m*, 1150*m*, 1066*s*, 1029*s*, 818*m*, 763*m*, 694*m*.

*2-(4-Benzyl-1*H*-1,2,3-triazol-1-yl)-2-deoxycellulose* (**9**). The mixture was heated to 80° for 50 h. Yield: 90%. IR (ATR): 3439*w* (br.), 2905*w*, 1658*w* (br.), 1547*w*, 1496*w*, 1454*w*, 1347*w*, 1207*m*, 1151*m*, 1066*s*, 1050*s*, 1026*s*, 1000*s*, 897*w*, 829*m*, 771*w*, 720*m*, 702*m*.

*2-Deoxy-2-[4-(2-phenylethyl)-1*H*-1,2,3-triazol-1-yl]cellulose* (**10**). The mixture was heated to 100° for 48 h. Yield: 88%. IR (ATR): 3417*w* (br.), 2929*w*, 1640*w* (br.), 1603*w*, 1548*w*, 1496*w*, 1453*w*, 1372*w*, 1215*m*, 1151*m*, 1065*s*, 1031*s*, 897*w*, 821*m*, 749*m*, 699*m*.

*2-Deoxy-2-[4-(3-phenylpropyl)-1*H*-1,2,3-triazol-1-yl]cellulose* (**11**). The mixture was heated to 100° for 40 h. Yield: 90%. IR (ATR): 3438*w* (br.), 2931*w*, 2861*w*, 1654*w* (br.), 1601*w*, 1549*w*, 1496*w*, 1453*w*, 1350*w*, 1298*w*, 1207*m*, 1151*s*, 1058*s*, 1029*s*, 901*w*, 821*m*, 745*m*, 699*m*.

*2-Deoxy-2-(4-propyl-1*H*-1,2,3-triazol-1-yl)cellulose* (**12**). The mixture (10 equiv. of pent-1-yne) was heated to 60° for 72 h. Yield: 93%. IR (ATR): 3393*w* (br.), 2958*w*, 2934*w*, 2870*w*, 1646*w* (br.), 1548*w*, 1456*w*, 1374*w*, 1316*w*, 1207*m*, 1149*m*, 1058*s*, 1033*s*, 932*w*, 898*w*, 824*m*.

*2-(4-Butyl-1*H*-1,2,3-triazol-1-yl)-2-deoxycellulose* (**13**). The mixture was heated to 80° for 60 h. Yield: 90%. IR (ATR): 3416*w* (br.), 2953*w*, 2932*w*, 2870*w*, 1666*w* (br.), 1548*w*, 1456*w*, 1376*w*, 1303*w*, 1204*m*, 1149*m*, 1064*s*, 998*m*, 897*w*, 823*m*.

*2-Deoxy-2-(4-pentyl-1*H*-1,2,3-triazol-1-yl)cellulose* (**14**). The mixture was heated to 100° for 50 h. Yield: 88%. IR (ATR): 3438*w* (br.), 2930*w*, 2861*w*, 1658*w* (br.), 1550*w*, 1376*w*, 1303*w*, 1205*m*, 1149*s*, 1066*s*, 998*m*, 898*w*, 823*m*.

*2-Deoxy-2-(4-hexyl-1*H*-1,2,3-triazol-1-yl)cellulose* (**15**). The mixture was heated to 100° for 72 h. Yield: 85%. IR (ATR): 3417*w* (br.), 2931*w*, 2870*w*, 1668*w* (br.), 1531*w*, 1458*w*, 1366*w*, 1206*s*, 1150*s*, 1063*s*, 1033*s*, 811*m*.

Solubility of **6**, **7**, *and* **12** *in DMSO, Pyridine, and MeOH*. A suspension of a dried sample (14 h at high vacuum over P_2O_5) of the substrate (10 mg) in the given solvent (0.85 ml) was sonicated at 50° for 5 h. After centrifugation (14,000 rpm) for 10 min, 0.5 ml of the supernatant were evaporated and dried for 4 h at high vacuum. The data are listed in *Table 2*.

CP/MAS ^{13}*C-NMR Spectra of* **5b**, **6**–**9**, *and* **13**. The CP/MAS ^{13}C-NMR spectra were recorded at 25° on a 600-MHz (for **6** and **7**) or a 300-MHz apparatus (for **5b**, **8**, **9**, and **13**) with adamantane as external reference. Conditions: 2048 scans, MAS frequence: 15 kHz, 100 kHz SPINAL64 decoupling during acquisition, CP variance for 3 ms: 65 kHz for H and 50 kHz for C. The chemical shifts are listed in *Table 3*, and the spectra of **6**, **7**, and **9** are depicted in the *Figure*.

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Received January 30, 2008