



Synthesis of new cellulose ethers using Suzuki–Miyaura reactions



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ABSTRACT

Cellulose ethers are functionalized biopolymers that are industrially produced through drastic conditions employing gaseous reactants with a high risk of industrial accident. The cellulose ethers that are commercially available generally bear short carbon-chains. In this work, an alternative method using non-gaseous chemicals is proposed. It relies on the use of the Suzuki–Miyaura reaction employing mild, moisture- and air-stable conditions. Relatively innocuous reagents are used for this step, which allows the formation of a wide range of cellulose ethers bearing various functional groups with different chain-length.

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1. Introduction

Cellulose ethers are polymers derived from cellulose that display very interesting properties. Indeed, they can be used as thickeners, binders, films formers, water-retention agents, emulsifiers (Fukasawa et al., 2011; Thielking & Schmidt, 2000; Porter, 1989; Wang & Zhang, 2009), etc. Most of these derivatives are water-soluble and low concentrations are required to greatly modify the formulation rheology. The most commercially important cellulose ethers are carboxymethylcellulose (CMC; Thielking & Schmidt, 2000) and alkyl cellulose such as methyl cellulose (MC; Majewicz & Podlas, 2000) and ethyl cellulose (EC; Koch, 1937) but some derivatives bearing hydroxyl (hydroxyethylcellulose, HEC; Bert & Wagenknecht, 2008), carboxyl (Liebert & Heinze, 1998) or amino (Zhang et al., 2012) moieties have also been developed. These compounds are generally synthesized in two steps. The first step is a mercerization process, which results in a reduction in crys-

tallinity of cellulose. It is followed by a functionalization that often requires the use of gaseous substances such as methyl chloride, ethyl chloride, and ethylene oxide (Thielking & Schmidt, 2000). This step is generally realized in continuously stirred tank reactors, under pressure (around 3 MPa) at 50–120 °C or in the presence of solvents that solubilize gases. Faced to the small number of available cellulose ethers, their great potential and the drastic conditions used for their preparation, it is thus necessary to develop new processes that could easily provide a wide range of new ethers. These processes should use mild conditions and respect to the maximum the Twelve Principles of Green Chemistry (Anastas & Warner, 2000).

In this context, the Suzuki–Miyaura (SM) reaction was chosen as it matches most of these criteria and displays a great functional group tolerance (Bej, Srimania, & Sarkar, 2012; Bolliger & Frech, 2010). This pallado-catalyzed reaction involves the coupling of a boron reagent (boronic acid, esters or organotrifluoroborates) with a halide or a triflate. Most of these compounds do not require high-pressure equipment. In order to engage cellulose in a Suzuki–Miyaura reaction, a first step of functionalization was required to introduce a halide moiety on its scaffold. The SM reaction was then carried out on the halogenated cellulose to yield a series of new cellulose ethers. Noteworthy, to the best of our knowledge, this reaction has never been applied to cellulose derivatives.

Abbreviations: DS, degree of substitution; DG, degree of grafting; DMA, N,N-dimethylacetamide; GY, grafting yield; THF, tetrahydrofuran.

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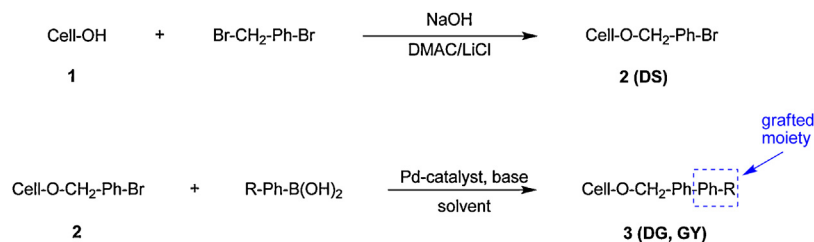


Fig. 1. Definition of the weight gain, DS, DG, GY, $M_{(3)}$ and m_{th} .

2. Experimental

2.1. Materials and equipment

4-Bromobenzyl bromide, anhydrous dimethylacetamide, lithium chloride, sodium hydroxide, sodium sulphate, potassium carbonate, tetrahydrofuran, isopropanol, toluene were purchased from Aldrich and used without further purification. Palladium-based catalysts were purchased from STREAM and used without further purification. All boron derivatives were purchased from Frontier Scientific and used without further purification. α -Cellulose (Aldrich) has been dried at 105 °C for 3 h prior to use.

NMR spectra were acquired with FOURIER300 (300 MHz) and AVANCE (500 MHz with cryoprobe) spectrometers from Bruker Corporation (Karlsruhe, Germany). The temperature probes were set at 300 K. Samples were dissolved in d_6 -DMSO or CDCl_3 . In that case, chemical shifts were referenced to tetramethylsilane at 0 ppm. Standard pulse sequences were used for ^1H -, ^{13}C -, DEPT135 and two-dimensional (COSY, HSQC, HMBC) NMR spectra. The DS and the DG were determined from the peak area obtained by integration of the ^1H NMR spectra.

2.2. Measurement

Two cellulose ethers **2** and **3** obtained through each step were characterized (Fig. 1).

The first compound (**2**) is the result of an etherification reaction introducing a bromide functionality on the hydroxyl groups of cellulose (**1**). The weight gain, the isolated product yield and the degree of substitution of the hydroxyl moieties of **2** (DS) were determined.

The second compound (**3**), obtained through the Suzuki–Miyaura cross-coupling reaction between **2** and a boron derivative, is characterized by its degree of grafting (DG). It represents the number of hydroxyl groups substituted by O-CH₂-Ph-Ph-R per anhydroglucose unit (AGU), after the SM reaction carried out on **2**. The grafting yield (GY) represents the yield of the SM reaction (ratio between the DG and the DS).

The weight gain, DS, DG, GY, $M_{(3)}$ and m_{th} were calculated by Eqs. (1)–(6).

$$\text{Weight gain (WG, \%)} = \frac{m_{\text{exp}} - m_{\text{starting material}}}{m_{\text{starting material}}} \quad (1)$$

$$\text{Degree of substitution (DS)} = \frac{7}{4 \times (I_{\text{AGU}}/I_{\text{phenyl}} - 1/2)} \quad (2)$$

I_{AGU} is the peak area of the protons on the AGU scaffold and CH₂ of the benzyl moiety from 5.25 ppm to 2.88 ppm. I_{phenyl} is the peak area corresponding to the phenyl group of the benzyl moiety from 6.60 ppm to 7.88 ppm.

$$\text{Degree of grafting (DG)} = \frac{7 + 2 \times \text{DS}}{2} \times \frac{I_{\text{CH}_2}}{I_{\text{AGU}}} \quad (3)$$

I_{CH_2} is the peak area of the CH₂ moiety of the ethyl group.

$$\text{Grafting yield (GY, \%)} = \frac{\text{DG}}{\text{DS}} \times 100 \quad (4)$$

$$M_{(3)} (\text{g mol}^{-1}) = M_{\text{AGU}} + \text{DS} \times M_{\text{CH}_2\text{PhBr}} + \text{DG} \times (M_{\text{PhCH}_2\text{H}_5} - M_{\text{Br}}) \quad (5)$$

$$m_{th} (\text{g}) = n_{\text{starting material}} \times M_{(3)} \quad (6)$$

$M_{(x)}$, m_x and n_x are respectively the molar mass, the experimental weight and the number of moles of compound or group x .

2.3. Synthesis of 4-bromobenzyl cellulose **2c**

α -Cellulose (1.0 g, 6.170 mmol) were stirred in 30 mL of DMA at 160 °C for 2 h then cooled down to 100 °C. Lithium chloride (3.4 g, 0.080 mol) was added and the mixture was allowed to cool to room temperature overnight. Mixture was heated to 65 °C and powdered NaOH (9.4 g, 0.235 mol) was added followed by a solution of 4-bromobenzyl bromide (25.4 g, 0.102 mol) in DMA (30 mL) dropwise. The resulting mixture was stirred for 24 h at 65 °C and then cooled to room temperature. 100 mL of distilled water and 100 mL of chloroform were then added. The aqueous layer was extracted with chloroform. The combined organic layers were collected and washed with distilled water and concentrated. Ethanol was added and the resulting mixture was stirred for 24 h and then filtered. The obtained solid was washed with distilled water, ethanol and cyclohexane and then dried under vacuum to give 2.60 g of the desired compound as a white powder (DS = 2.78, 60%).

^1H NMR (500 MHz, CDCl_3): δ = 3.13 (H-5), 3.23 (H-2), 3.29 (H-3), 3.38 (H-7'), 3.60 (H-6), 3.84 (H-4), 4.34 (H-1), 4.14 (H-7), 4.60 (H-7''a), 4.99 (H-7''b), 6.78–7.68 (H-Ar).

^{13}C NMR (125 MHz, CDCl_3): δ = 68.1 (C-6), 72.2 (C-7), 74.3 (C-7''), 74.7 (C-7'), 75.0 (C-5), 77.0 (C-4), 81.8 (C-2), 83.5 (C-3), 102.7 (C-1), 121.1, 121.5, 121.7 (C-11/11'/11''), 129.1, 129.2, 129.4 (C-9/9'/9''), 131.3, 131.5, 131.6 (C-10/10'/10''), 137.0, 137.1, 138.3 (C-8/8'/8'').

FT-IR (KBr, cm^{-1}): 3452 ν_{OH} (weak), 2960, 2865 $\nu_{\text{C-H}}$, 1595, 1487 $\nu_{\text{C=C}}$, 1404, 1358, $\nu_{\text{C-H}}$, 1152–1037 $\nu_{\text{C-O-C}}$, 802 $\nu_{\text{C-Br}}$.

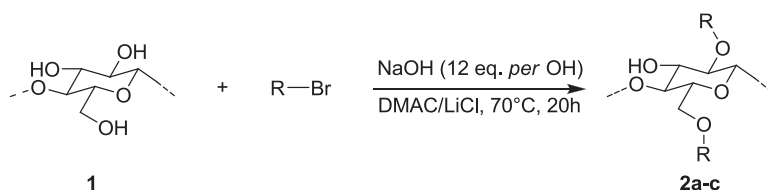
2c soluble in THF, DMSO and chloroform.

2.4. General procedure for Suzuki reactions: synthesis of compounds **3**

4-Bromobenzylcellulose **2c** (300 mg, DS = 2.78), the corresponding boronic acid (1.471 mmol), sodium sulfate (15 mg, 0.106 mmol), palladium chloride (7 mg, 0.049 mmol) and potassium carbonate (550 mg, 4.4 mmol) were added to a mixture of 9 mL of THF and 1 mL of water. The resulting mixture was stirred at 45 °C for 8 h. Solvents were evaporated and the resulting grey powder was washed with 3 $\times$ 100 mL of cold water, 3 $\times$ 100 mL of ethanol and then dried under vacuum.

Table 1

Results for the preparation of halogenated cellulose derivatives.



Entry	Reagent	Number of eq., addition mode	Sample	DS	Weight gain	Yield (isolated product)	Comments
1	1,3-Dibromopropane	12 eq., one portion	2a	–	–	–	Elimination reaction
2	1-Bromo-4-(2-bromoethyl)benzene	12 eq., one portion	2b	–	–	–	Elimination reaction
3	1-Bromo-4-(bromomethyl)benzene	12 eq., one portion	2c	–	–63%	10%	Insoluble
4	1-Bromo-4-(bromomethyl)benzene	12 eq., three portions	2c	2.76	38%	35%	Soluble in THF/CDCl ₃
5	1-Bromo-4-(bromomethyl)benzene ^a	12 eq., dropwise	2c	2.78	130%	60%	Soluble in THF/CDCl ₃

^a Reaction time: 24 h.

Compound **3a** was obtained as a grey powder (330 mg, DG = 2.18), using (4-ethylphenyl)boronic acid.

¹H NMR (500 MHz, CDCl₃): δ = 1.25 (–CH₂–CH₃), 2.68 (–CH₂–CH₃), 3.15 (H-5), 3.24 (H-2), 3.36 (H-3), 3.63 (H-6), 3.90 (H-4), 4.13, 4.36 (H-7/7''), 4.38 (H-1), 4.59, 5.00 (H-7/7''), 6.88–7.69 (H-Ar).

¹³C NMR (125 MHz, CDCl₃): δ = 15.6 (–CH₂–CH₃), 28.5 (–CH₂–CH₃), 68.0 (C-6), 72.1, 72.8, 74.5 (C-7/7''), 75.0 (C-5), 77.1 (C-4), 81.6 (C-2), 83.5 (C-3), 102.7 (C-1), 121.5 (C_q-Ar), 126.8, 126.9, 128.2, 129.0, 129.3, 131.1, 131.4 (C-Ar), 136.4, 137.7, 138.4, 140.1, 140.6, 143.1, 143.6 (C_q-Ar).

FT-IR (KBr, cm^{–1}): 3434 ν OH (weak), 3024, 2961, 2926, 2868 ν C–H, 1498 ν C=C, 1458, 1400 ν C–H, 1152–1037 ν C–O–C, 810 ν C–Br.

3a is soluble in THF and chloroform.

Compound **3b** was obtained as a grey powder (326 mg, DG = 1.76), using (4-butylphenyl)boronic acid.

¹H NMR (500 MHz, CDCl₃): δ = 0.89 (–CH₂–CH₂–CH₂–CH₃), 1.41 (–CH₂–CH₂–CH₂–CH₃), 1.61 (–CH₂–CH₂–CH₂–CH₃), 2.64 (–CH₂–CH₂–CH₂–CH₃), 3.11 (H-5), 3.21 (H-2), 3.30 (H-3), 3.60 (H-6), 3.88 (H-4), 4.12 (H-7), 4.33 (H-1), 4.55 (H-7''a), 4.63 (H-7'), 4.99 (H-7''b), 6.77–7.70 (H-Ar).

¹³C NMR (125 MHz, CDCl₃): δ = 14.3 (–CH₂–CH₂–CH₂–CH₃), 22.8 (–CH₂–CH₂–CH₂–CH₃), 32.0 (–CH₂–CH₂–CH₂–CH₃), 37.3 (–CH₂–CH₂–CH₂–CH₃), 68.2 (C-6), 72.3 (C-7), 74.3 (C-7'), 74.7 (C-7''), 75.1 (C-5), 76.9 (C-4), 81.8 (C-2), 83.6 (C-3), 102.7 (C-1), 121.2, 121.5 (C_q-Ar), 129.1, 129.2, 129.3, 129.4, 129.7, 131.3, 131.4, 131.5, 131.6, 131.7, 131.8 (C-Ar), 136.8, 137.0, 137.1, 138.3 (C_q-Ar).

FT-IR (KBr, cm^{–1}): 3424 ν OH (weak), 2924, 2867 ν C–H, 1488 ν C=C, 1458, 1358 ν C–H, 1174–970 ν C–O–C, 802 ν C–Br.

3b is soluble in THF and chloroform.

Compound **3c** was obtained as a grey powder (330 mg, DG = 1.20), using (4-(ethoxycarbonyl)phenyl)boronic acid.

¹H NMR (500 MHz, CDCl₃): δ = 1.34 (–CH₂–CH₃), 3.06 (H-5), 3.17 (H-2), 3.49 (H-3), 3.51 (H-6), 3.77 (H-4), 4.05 (H-7/7''), 4.27 (H-1), 4.33 (–CH₂–CH₃), 4.43 (H-7/7''), 4.64 (H-7/7''), 6.71–8.15 (H-Ar).

¹³C NMR (125 MHz, CDCl₃): δ = 14.4 (–CH₂–CH₃), 61.1 (–CH–CH₃), 69.9 (C-6), 72.2, 74.3, 74.6 (C-7/7''), 75.2 (C-5), 76.9 (C-4), 81.8 (C-2), 83.6 (C-3), 102.7 (C-1), 121.8 (C_q-Ar), 126.9, 127.2, 128.3, 129.0, 129.1, 129.3, 130.0, 130.2, 131.2, 131.4, 131.5 (C-Ar), 143.9, 144.3, 144.9, 166.6 (C_q-Ar).

FT-IR (KBr, cm^{–1}): 3435 ν OH (weak), 2867 ν C–H, 1710 ν C=O, 1487 ν C=C, 1397, 1365 ν C–H, 1183–950 ν C–O–C, 803 ν C–Br.

3c is soluble in THF and chloroform.

3. Results and discussion

3.1. Preparation of the halogenated cellulose derivatives

The first step of this study was the preparation of a halogenated cellulose derivative. Cellulose was thus solubilized in *N,N*-dimethyl acetamide (DMA)/LiCl in the presence of sodium hydroxide and 1,3-dibromopropane was added (Table 1, entry 1) (Sachinvala et al., 2000). Even after 20 h at 70 °C, we could not observe the formation of the desired halogenated cellulose **2a**, but the presence of allyl-cellulose, issued from an elimination reaction of a HBr molecule in this basic medium, was detected. The same behaviour was observed on 1-bromo-4-(2-bromoethyl)benzene, leading to the formation of 1-allyl-4-bromobenzene (Table 1, entry 2). 1-Bromo-4-(bromomethyl)benzene was then chosen (Table 1, entry 3) as no elimination can occur on this reagent. Indeed, the desired halogenated cellulose **2c** was obtained but with a DS too low to be soluble in common solvents, such as CDCl₃ (which prevented the DS to be determined by NMR). It seems highly likely that cellulose ethers that have even lower DS are soluble in the aqueous phase and are thus lost during the extraction process, accounting for the negative weight gain.

The brominated reagent was then added in three portions instead of one at the beginning of the reaction, which led to the formation of **2c** in 10% yield. Noteworthy, **2c** is soluble in THF, DMSO and CDCl₃. It was thus dissolved in DMSO-*d*₆ in order to be analyzed by NMR spectroscopy (Fig. 2). A DS of 2.76 was determined thanks to the addition of a few drops of *d*₁-TFA in the NMR tube in order to displace downfield the NMR signals of exchangeable protons and water (Ross & Lowe, 2000). An excellent yield of 60% was then obtained when 1-bromo-4-(bromomethyl)benzene was added dropwise over the course of 24 h (Table 1, entry 5), which seems to show the poor stability of this reactant in our reaction conditions. Full structure characterization of **2c** was carried out at 500 MHz using one-, two-dimensional homo- and ¹H–¹³C hetero-correlated techniques. Experiments were run in CDCl₃ as *d*₆-DMSO caused spectral line broadening and required long accumulation time because of the poor solubility of **2c** in this solvent. Thanks to the ¹H/¹H COSY and ¹H/¹³C HSQC NMR analyses (Fig. 4), the ¹H and ¹³C signals of the modified AGU can be respectively assigned as follows (Fig. 3): 3.13 ppm (H-5), 3.23 ppm (H-2), 3.29 ppm (H-3), 3.60 ppm (H-6), 3.84 ppm (H-4), 4.34 ppm (H-1) and 68.1 ppm (C-6), 75.0 ppm (C-5), 77.0 ppm (C-4), 81.8 ppm (C-2), 83.5 ppm (C-3), 102.7 ppm (C-1). The signals for H-7 and H-7' were respectively found at 4.14 and 3.38 ppm, while the protons in position 7'' are

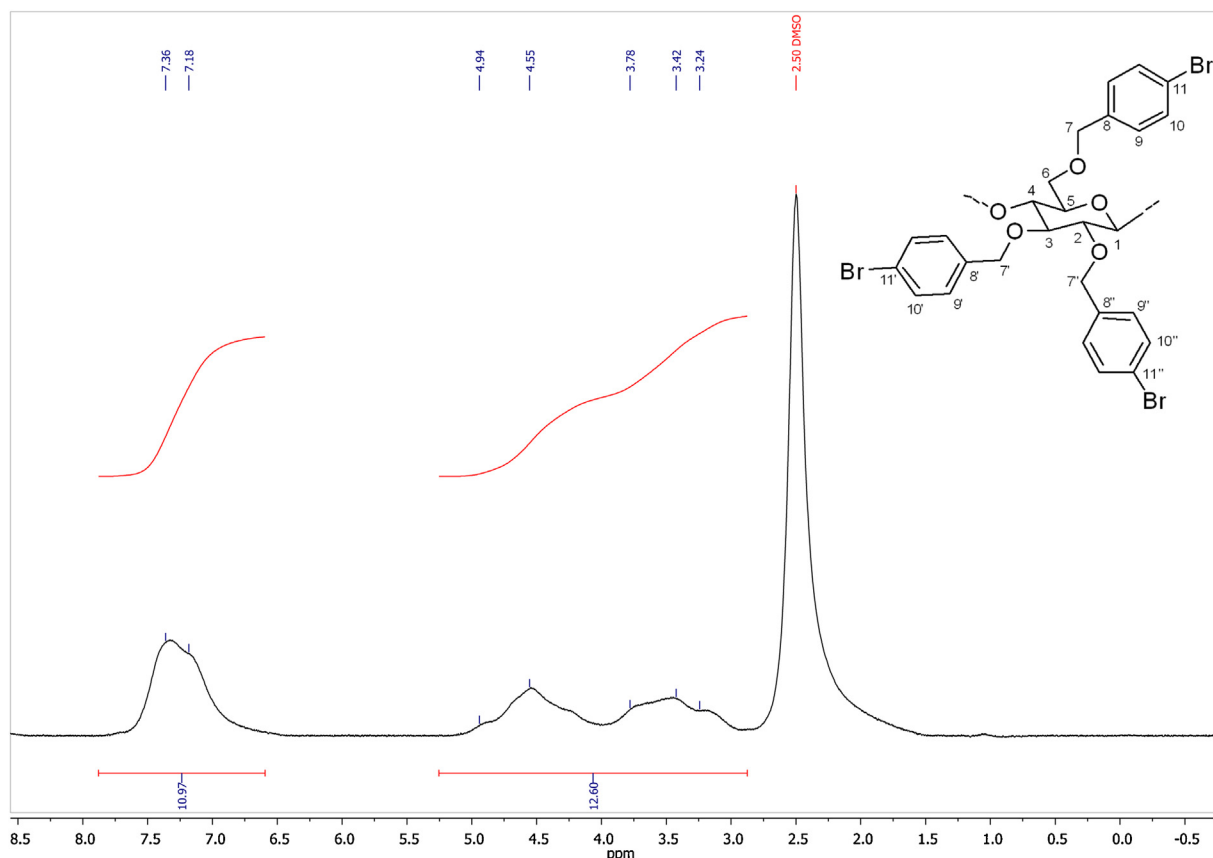


Fig. 2. ^1H NMR spectrum of cellulose ether **2c** in $\text{DMSO}-d_6$ (with addition of a few drops of d_1 -TFA).

split and give peaks at 4.60 and 4.99 ppm. The corresponding carbons appear at 72.2 ppm (C-7), 74.3 ppm (C-7'), 74.7 ppm (C-7''). Further confirmation of the structure of **2c** was then obtained from the HMBC correlation peaks between H-2 and C-7'', H-3 and C-7' and H-7 and C-6 (Fig. 4).

3.2. Preparation of new cellulose ethers using Suzuki–Miyaura reactions

The brominated cellulose **2c** was then engaged in the key step of this synthesis: the Suzuki–Miyaura reaction. Based on the reaction conditions described by Bora's team (Mondal and Bora, 2012), a solution of **2c** and 4-ethylphenylboronic acid (1 equiv.) in *i*-PrOH was stirred in the presence of PdCl_2 (4 mol%), Na_2SO_3 (8 mol%) and K_2CO_3 (3 equiv.) at 45 °C for 8 h. These mild, moisture- and air-compatible conditions led to the formation of the cellulose ether **3a** (Table 2, entry 1).

A degree of grafting of 1.09 was determined thanks to the ^1H NMR spectra analyses. A typical ^1H NMR of **3a** is shown in Fig. 5. Noteworthy, the chemical shift of the ethyl group is not in the region of cellulose scaffold, which allows to obtain reliable integrations of the different signals. The DG determination thus indicated that only a part of the brominated ether moieties have been chemically modified by the SM reaction.

For subsequent assays (Table 2, entries 2–4), *i*-PrOH was replaced by toluene, water or a mixture of THF/water (9/1). The latest conditions gave the best results with a grafting yield of 79% (Table 2, entry 4). THF/water was thus used for the rest of this work.

The influence of the amount of boronic acid was then investigated. The number of equivalents of 4-ethylphenylboronic acid was doubled (Table 2, entry 5), yielding **3a** in 84% yield. However,

compared to the cost of boronic acids, this yield improvement was not significant enough and the subsequent assays were carried out with only one equivalent of boron species.

In order to study the influence of the temperature on the grafting yield, the SM reaction was then carried out at room temperature and 78 °C (Table 2, entries 6 and 7). A drop of the grafting yields was observed, indicating that it is better to run this cross-coupling reaction at 45 °C.

We then focused our study on the screening of different palladium-based catalysts. Classical Suzuki–Miyaura catalysts, such as palladium(II) acetate or [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) were used (Table 2, entries 8 and 9) and palladium chloride appeared to give the best results. The amount of this catalyst was then optimized (Table 2, entries 10–12) with loading varying from 1 to 10 mol%. Similar yields were obtained with 4 and 10 mol% (Table 2, entries 4 and 12). For economical reasons, a catalyst loading of 4 mol% was chosen for the rest of the study.

In order to broaden the scope of the synthesized products, we next proposed to modify the nature of the boronic acid using our optimized conditions. Boronic acids were chosen so that a part of the grafted moiety NMR signals do not superimpose itself on the AGU peaks in order to obtain accurate integrations and so accurate degrees of grafting. Cellulose ether **3b**, bearing a longer alkyl chain, was obtained in good yield (Table 2, entry 13) with the use of 4-butylphenylboronic acid. Furthermore, electron-poor boronic acids appeared to be compatible with these reaction conditions as **3c** was obtained in 43% yield, when 4-(ethoxycarbonyl)phenylboronic acid was engaged in the reaction (Table 2, entry 14). This lower yield can be explained by the low nucleophilicity of electron-deficient aryl boronic acids that decreases the transmetalation rate. These boron

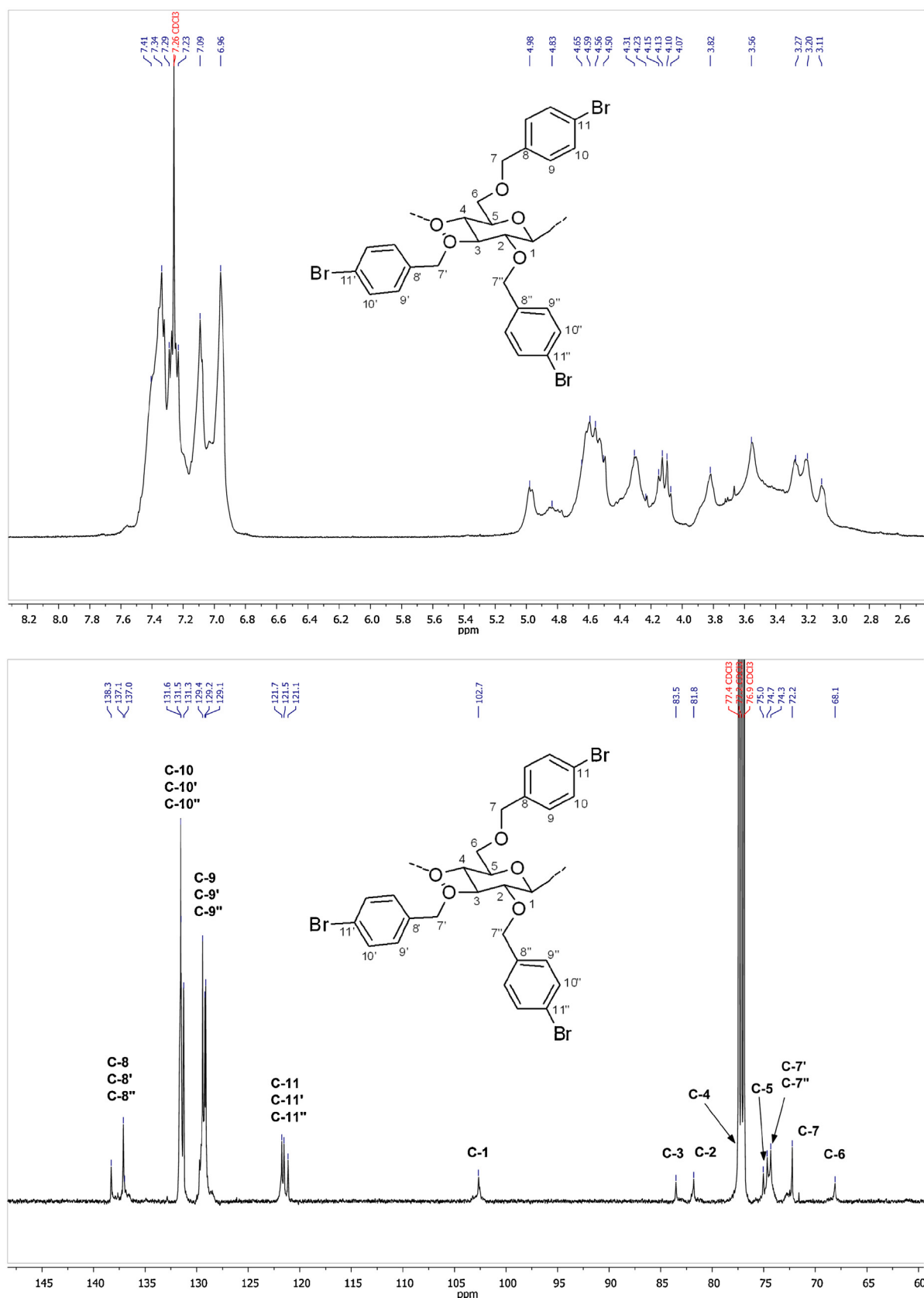


Fig. 3. ^1H - and ^{13}C NMR spectra of cellulose ether **2c** in CDCl_3 .

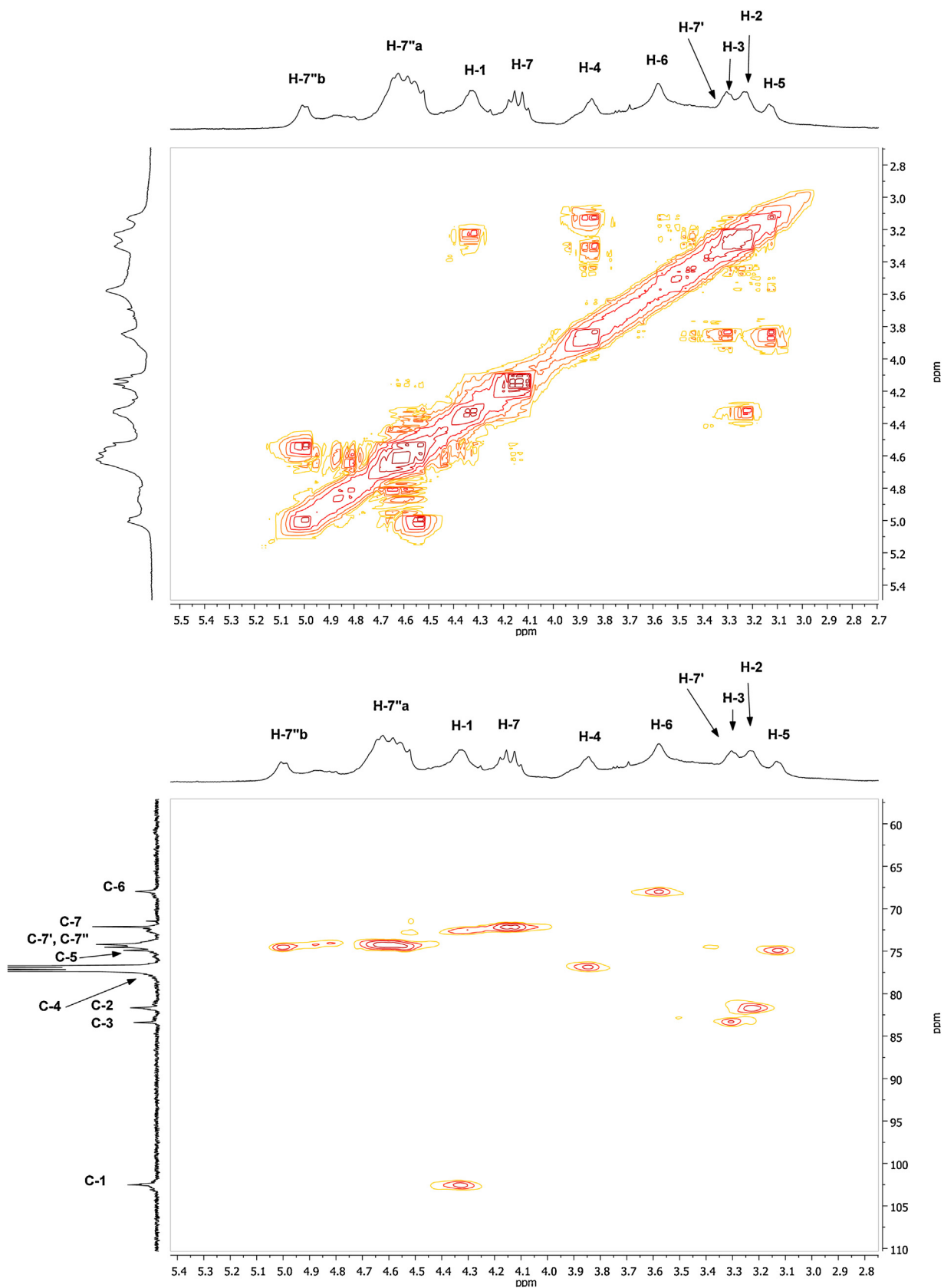


Fig. 4. ¹H/¹H-COSY NMR, ¹H/¹³C-HSQC and ¹H/¹³C-HMBC NMR spectra of cellulose ether **2c** in CDCl₃.

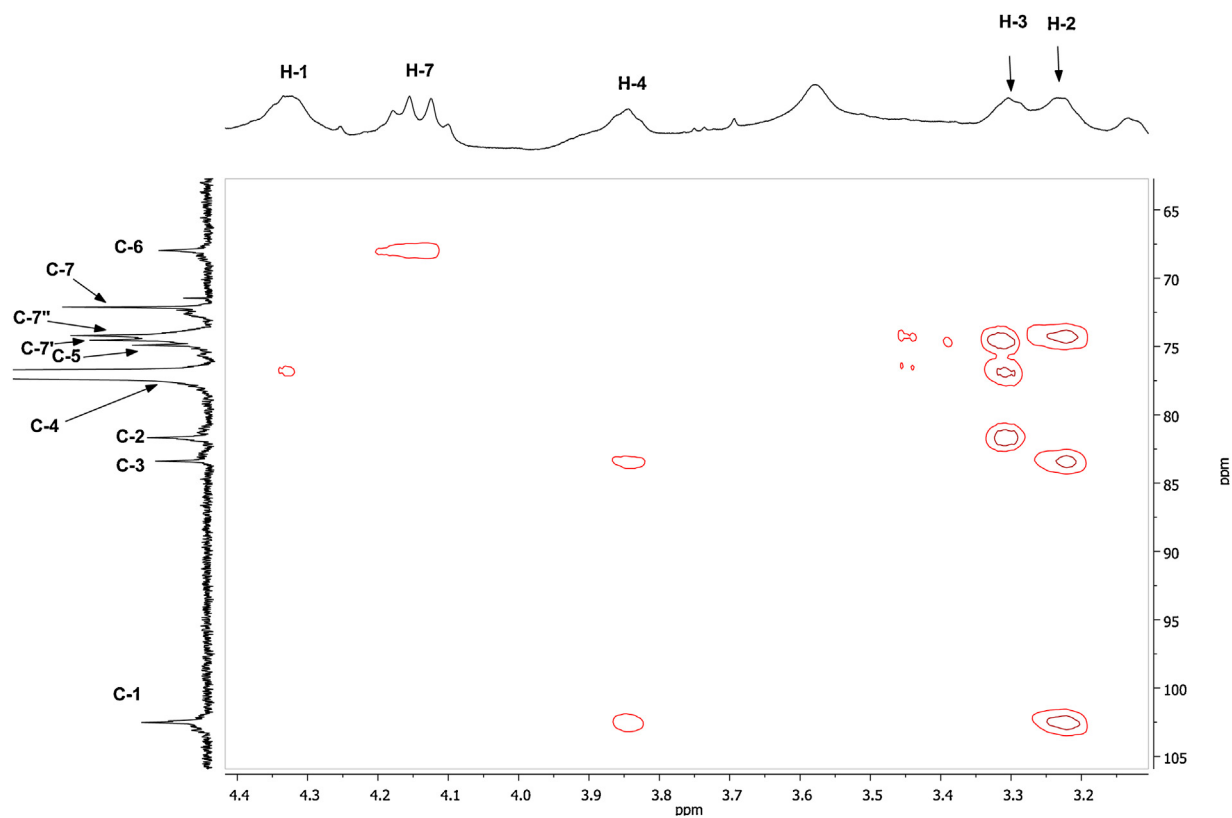


Fig. 4. (Continued).

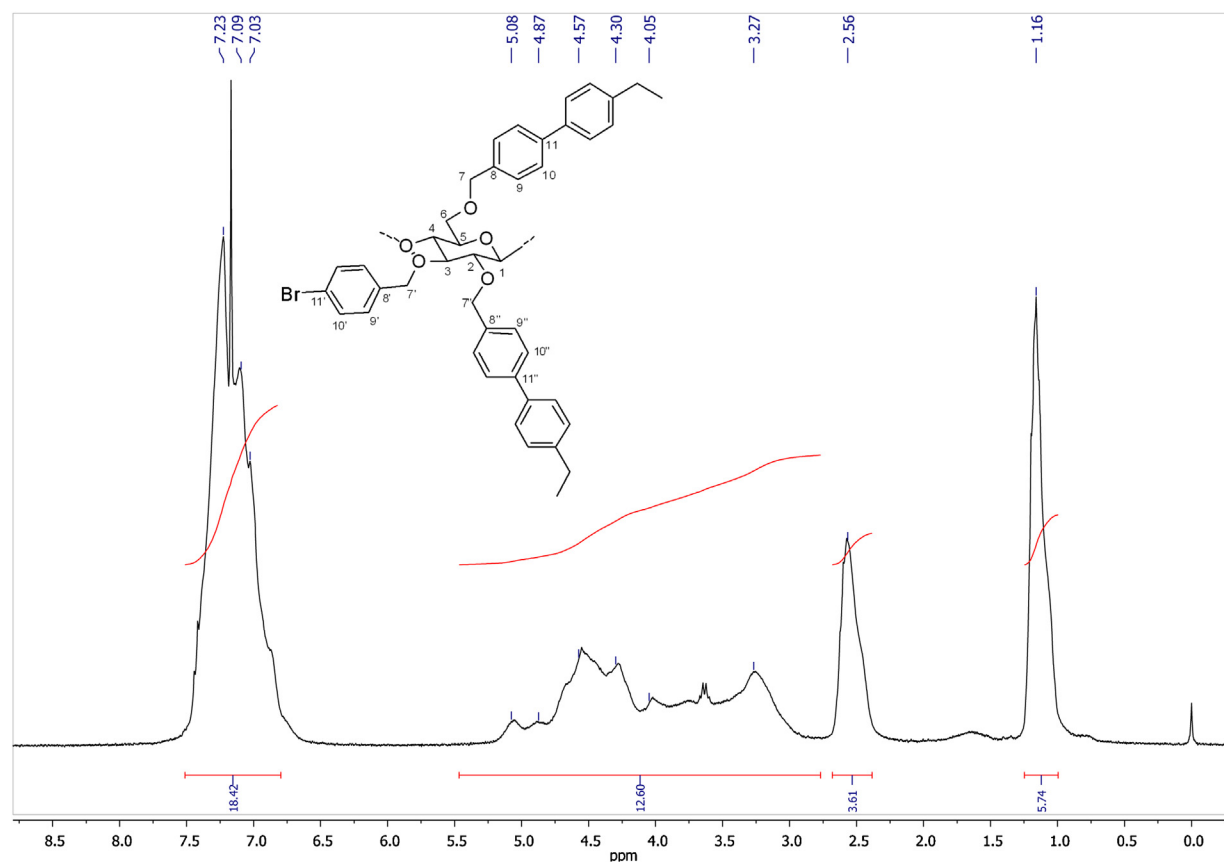
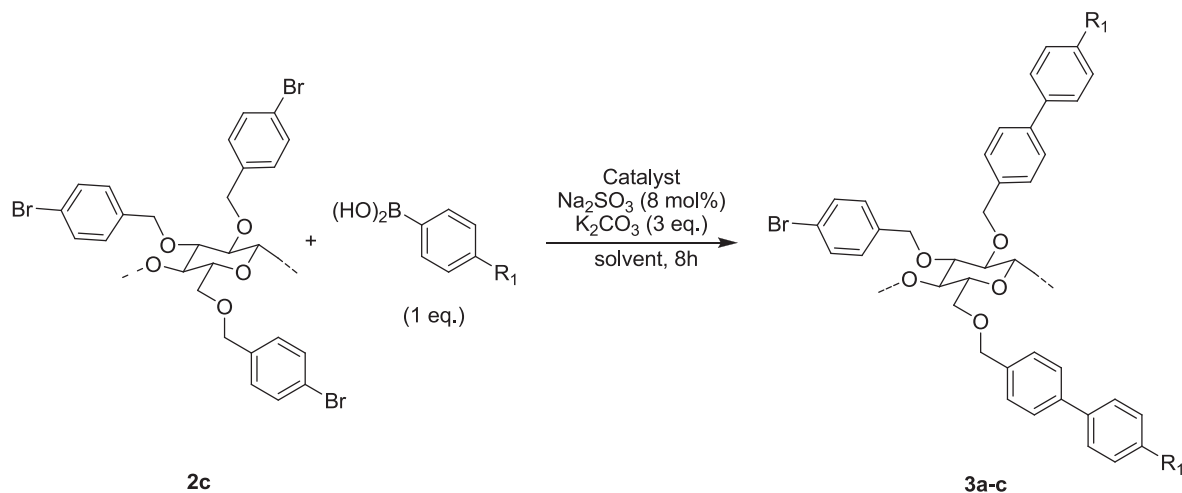
Fig. 5. ^1H NMR spectrum of cellulose ether **3a** in CDCl_3 .

Table 2
Results for the preparation of various cellulose ethers.



Entry	Reagent	Solvent	Temperature (°C)	Catalyst	Catalyst amount (mol%)	Sample	Weight gain (%)	DG	GY (%)	$m_{\text{exp}}/m_{\text{th}}^a$ (100×, %)
1	4-Ethylphenylboronic acid	i-PrOH	45	PdCl ₂	4	3a	5.0	1.09	39	100.5
2	4-Ethylphenylboronic acid	Toluene	45	PdCl ₂	4	3a	7.2	1.71	61	100.1
3	4-Ethylphenylboronic acid	H ₂ O	45	PdCl ₂	4	3a	3.2	ND	ND	ND
4	4-Ethylphenylboronic acid	THF/H ₂ O (9/1)	45	PdCl ₂	4	3a	10.0	2.18	78	101.0
5	4-Ethylphenylboronic acid ^b	THF/H ₂ O (9/1)	45	PdCl ₂	4	3a	9.0	2.34	84	88.0
6	4-Ethylphenylboronic acid	THF/H ₂ O (9/1)	RT	PdCl ₂	4	3a	5.7	1.57	56	99.3
7	4-Ethylphenylboronic acid	THF/H ₂ O (9/1)	78	PdCl ₂	4	3a	5.8	1.04	37	101.5
8	4-Ethylphenylboronic acid	THF/H ₂ O (9/1)	45	Pd(OAc) ₂	4	3a	7.2	1.71	61	100.1
9	4-Ethylphenylboronic acid	THF/H ₂ O (9/1)	45	Pd(dppf)Cl ₂	4	3a	5.5	1.40	50	99.7
10	4-Ethylphenylboronic acid	THF/H ₂ O (9/1)	45	PdCl ₂	1	3a	1.0	ND	ND	ND
11	4-Ethylphenylboronic acid	THF/H ₂ O (9/1)	45	PdCl ₂	2	3a	8.6	1.40	50	102.7
12	4-Ethylphenylboronic acid	THF/H ₂ O (9/1)	45	PdCl ₂	10	3a	10.0	2.24	80	100.7
13	4-Butylphenylboronic acid	THF/H ₂ O (9/1)	45	PdCl ₂	4	3b	14.1	1.76	63	99.3
14	4-(Ethoxycarbonyl)phenylboronic acid	THF/H ₂ O (9/1)	45	PdCl ₂	4	3c	10.1	1.20	43	99.6

^a m_{th} was calculated using the DG that was determined with the NMR analysis.

^b Two equivalents of 4-ethylphenylboronic acid were used.

species are also prone to react in homo-coupling side reactions (Wong & Zhang, 2001) and more susceptible to metal-catalyzed protodeboronation (Kuivila, Reuwer, & Mangravite, 1964).

Noteworthy, in all cases, the experimental and theoretical masses were very close to each other, indicating that the mass balance is in agreement with the NMR analysis and that no degradation occurred during the SM reaction.

4. Conclusion and perspectives

New cellulose ethers can be easily synthesized through the use of a Suzuki–Miyaura cross-coupling reaction. This new process is carried out in mild, moisture- and air-stable conditions. Thanks to its great functional group tolerance, cellulose ethers bearing various alkyl chains and different functionalities can be obtained in good to excellent yields. Detailed investigation of the physico-chemical properties of these new cellulose ethers will be published in due course. This synthetic route might also be interesting for the grafting of sensitive functional groups to the cellulose backbones under mild conditions.

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References

- Anastas, P. T., & Warner, J. C. (2000). *Green chemistry: Theory and practice*. New York, USA: Oxford University Press.
- Bej, A., Srimania, D., & Sarkar, A. (2012). Palladium nanoparticle catalysis: Borylation of aryl and benzyl halides and one-pot biaryl synthesis via sequential borylation–Suzuki–Miyaura coupling. *Green Chemistry*, 14(3), 661–667.
- Bert, V., & Wagenknecht, W. (2008). Substitution patterns of cellulose ethers – influence of the synthetic pathway. *Macromolecular Symposia*, 262, 97–118.
- Bolliger, J., & Frech, C. (2010). Dichloro-bis(aminophosphine) complexes of palladium: Highly convenient, reliable and extremely active Suzuki–Miyaura catalysts with excellent functional group tolerance. *Chemistry – A European Journal*, 16, 4075–4081.
- Fukasawa, M., Hayakawa, K., & Kuribayashi, D. (2011). Meat additive, pickling liquid and processed meat product. Patent, US20110091632 A1.
- Koch, W. (1937). Properties and uses of ethylcellulose. *Industrial & Engineering Chemistry*, 29, 687–690.
- Kuivila, H. G., Reuwer, J. F., Jr., & Mangravite, J. A. (1964). Metal ion catalysis in the protodeboronation of areneboronic acids. *Journal of the American Chemical Society*, 86, 2666–2670.
- Liebert, T., & Heinze, T. (1998). Synthesis path versus distribution of functional groups in cellulose ethers. *Macromolecular Symposia*, 130, 271–283.
- Majewicz, T. G., & Podlas, T. J. (2000). Cellulose ethers. In *Kirk–Othmer encyclopedia of chemical technology*. New York: John Wiley & Sons, Inc.
- Mondal, M., & Bora, U. (2012). An efficient protocol for palladium-catalyzed ligand-free Suzuki–Miyaura coupling in water. *Green Chemistry*, 14, 1873–1876.
- Porter, S. C. (1989). Controlled-release film coatings based on ethylcellulose. *Drug Development and Industrial Pharmacy*, 15, 1495–1521.
- Ross, S. A., & Lowe, G. (2000). Downfield displacement of the NMR signal of water in deuterated dimethylsulfoxide by the addition of deuterated trifluoroacetic acid. *Tetrahedron Letters*, 41, 3225–3227.
- Sachinvala, N. D., Winsor, D. L., Hamed, O. A., Maskos, K., Niemczura, W. P., Tregre, G. J., et al. (2000). The physical and NMR characterizations of

- allyl- and crotylcelluloses. *Journal of Polymer Science Part A: Polymer Chemistry*, 38, 1889–1902.
- Thielking, H., & Schmidt, M. (2000). Cellulose Ethers. In *Ullmann's encyclopedia of industrial chemistry*. Wiley-VCH Verlag GmbH & Co. KGaA.
- Wang, Y., & Zhang, L. (2009). Blends and composites based on cellulose and natural polymers. In L. Yu (Ed.), *Biodegradable polymer blends and composites from renewable resources* (pp. 129–161). John Wiley & Sons, Inc.
- Wong, M. S., & Zhang, X. L. (2001). Ligand promoted palladium-catalyzed homo-coupling of arylboronic acids. *Tetrahedron Letters*, 42, 4087–4089.
- Zhang, D., Xie, J., Yu, P., Huang, X., Yang, M., & Liu, H. (2012). Antifungal activity and humidity sensitivity of quaternized cellulose synthesized in NaOH/urea aqueous solution. *Cellulose*, 19, 189–198.