Unconventional Cellulose Products by Fluorination of Tosyl Cellulose

*Andreas Koschella, Thomas Heinze**

Bergische Universität Wuppertal, FB9 (Chemie), Gauß Straße 20, D-42097 Wuppertal, Germany

Summary: The synthesis of novel deoxy-fluoro cellulose derivatives obtained by nucleophilic displacement reactions (SN) of p-toluenesulfonyl (tosyl) cellulose with tetrabutylammonium fluoride (TBAF) is described. Detailed studies concerning the influence of the reaction time and temperature as well as the water content of the TBAF on the composition of the products were carried out. The SN reaction occurs even at room temperature. The degree of substitution of deoxy-fluoro moieties (DSF) is in the range from 0.22 to 0.47. The polymers contain remaining tosyl groups. Preliminary 19F NMR measurements reveal the presence of the CH2F group. The degradation temperature of the deoxy-fluoro cellulose derivatives is increased compared to the starting tosyl cellulose, however, a distinct influence of the remaining tosyl groups appears.

Keywords: degradation; FT-IR; functionalization of polymers; thermogravimetric analysis (TGA)

Introduction

The majority of chemical modifications of cellulose have been directed towards the hydroxyl functions of the polymer chain. Consequently, various ethers, esters, and oxidation products are available which are even produced in a commercial scale.[1,2] In addition, regioselective functionalization using protective group technique represents an important goal in laboratory-scale cellulose chemistry, because it provides access to novel classes of cellulose derivatives and products with promising properties.[3] Major blocking groups of recent interest are the triphenylmethyl and bulky trialkylsilyl moieties.[3-5]

Another interesting synthesis path to new cellulosics is a nucleophilic displacement (S_N) of the hydroxyl group, i.e., a chemistry directed towards the C-atoms of the polymer. As a prerequisite of S_N reactions, a suitable change of reactivity is necessary because hydroxyl moieties are bad leaving groups.

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p-Toluenesulfonyl (tosyl) celluloses were found to be an excellent starting material for S_N reactions. Tosyl cellulose can be simply obtained by the homogeneous conversion of cellulose dissolved in *N,N*-dimethylacetamide/LiCl with tosyl chloride.[6,7] Tosyl cellulose had been already reacted with a variety of nucleophils including chloride, bromide, iodide[6], and different mono-, di-, tri- as well as chiral amines.[8-10] The conversion with, e.g., triethylamine yields 6-deoxy-6-triethylammonium cellulose[8] which is a water soluble polymer showing typical properties of polyelectrolytes. The S_N reaction with multifunctional amines yields water-soluble polymers useful as flocculation aid. It is worth to note that the mentioned S_N reactions are limited to the C-6-tosylate group, i.e., the reaction occurs with distinct regioselectivity. The remaining tosyl functions at position 2 and 3 may impart solubility to the products or can be removed by hydrolysis adding water to the reaction mixture. Moreover, they can be split-off by subsequent reactions.

Surprisingly, the promising synthetic path via S_N reaction was not applied to study deoxy-fluoro cellulose derivatives although deoxy-chloro, -bromo, and -iodo celluloses with degree of substitution (DS) of up to 0.94 were obtained starting from tosyl cellulose. However, this reaction pathway is not applicable for fluorination. One reason may be the poor solubility of alkali metal fluorides. In contrast, tetrabutylammonium fluoride (TBAF) trihydrate generates reactive fluoride ions in organic solvents. It is used as a versatile reagent for the deprotection of silylated organic compounds.[11]

In the course of our ongoing research on unconventional cellulose products, we were interested in deoxy-fluoro cellulose derivatives. In the present paper, S_N reactions of tosyl cellulose with fluoride ions generated from TBAF are discussed.

Experimental

Materials

p-Toluenesulfonyl (tosyl) cellulose (sample **2a** and **2b**, degree of substitution 1.22 and 1.74) was synthesized by reacting microcrystalline cellulose (Avicel PH-101) with tosyl chloride and triethylamine in *N,N*-dimethylacetamide/LiCl under homogeneous conditions as described

elsewhere.[12] Tetrabutylammonium fluoride (TBAF) trihydrate and a 1 M solution of TBAF in tetrahydrofuran containing 4.5-5% water was purchased from Fluka.

Methods

FTIR spectra were recorded with a Nicolet Protegé 460 FTIR spectrometer using the KBr technique. NMR spectra were measured in DMSO-d_6 solution (5%, w/v) at 60°C on a Bruker ARX 400 NMR spectrometer (16 scans for ^{1}H, 20000 for ^{13}C, and 2000 for ^{19}F). Thermogravimetric analysis were carried out using a Mettler Toledo TC 15 Mettler TG 50 thermobalance with a temperature increase of 10 K/min from ambient temperature up to 600°C under air (200 ml/min).

Deoxy-fluoro cellulose ***3c***

In a typical procedure, 5.0 g (14.3 mmole) tosyl cellulose **2a** (DS 1.22) was dissolved in 100 ml *N,N*-dimethylformamide. 22.6 g (71.5 mmole, 5 equivalents) TBAF trihydrate were added and the solution was stirred for 16 h at room temperature. The polymer was precipitated in ethanol, filtered off, washed carefully with ethanol and dried in vacuum at 50°C.

Yield: 2.22 g

Dewatering of tetrabutylammonium fluoride (TBAF) trihydrate

30 g TBAF trihydrate were placed in a roundbottom flask equipped with a magnetic stirrer. The flask was evacuated to oil-pump vacuum and heated at 45°C for at least 48 h. While heating, the TBAF becomes liquid and looses the crystal water. The amount of residual water was estimated from the mass loss.

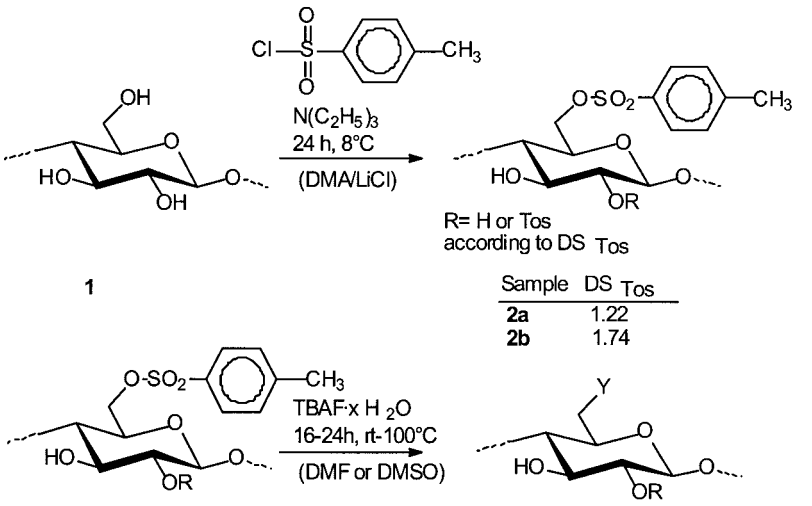
Results and Discussion

p-Toluenesulfonyl (tosyl) cellulose is a valuable intermediate in cellulose chemistry. Tosyl cellulose can be prepared under homogeneous conditions by reacting the cellulose with tosyl chloride and triethylamine in *N,N*-dimethylacetamide (DMA)/LiCl, Fig. 1. It is known that the

tosylation reaction occurs faster at the primary OH group compared to the secondary ones under these reaction conditions. Thus, the degree of substitution of tosyl groups (DS_{Tos}), controlled by the molar ratio of anhydroglucose unit (AGU) and tosyl chloride, was adjusted in order to obtain a polymer with DS_{Tos} 1.22 (sample **2a**) and 1.74 (**2b**), i.e., a preferred and complete functionalization of *O*-6. **2a** and **2b** are well soluble in aprotic-dipolar solvents like *N,N*-dimethylformamide (DMF). In addition, **2b** can be dissolved in tetrahydrofuran (THF).

Synthesis and characterization of deoxy-fluoro celluloses

In a first series of experiments, commercially available tetrabutylammonium fluoride trihydrate (TBAF·3 H_2O) was allowed to react with tosyl cellulose while varying the reaction time (16 and 24 h) and temperature in the range from room temperature up to 100°C (Fig. 1). All polymers were isolated as fine powders by precipitation in ethanol. The color of the products is light brown if the reaction is carried out at room temperature and becomes dark brown at a reaction temperature of 100°C. Elemental analysis revealed the presence of both sulfur and fluorine in the samples indicating that a partial displacement of the tosyl groups took place. The calculation of the degree of substitution of deoxy-fluoro moieties (DS_F) and tosyl groups (DS_{Tos}) was carried out by computer supported correlation of the fluorine and sulfur content.



DMA = *N,N*-dimethylacetamide
DMF = *N,N*-dimethylformamide
TBAF = Tetrabutylammonium fluoride
DS = degree of substitution
rt = room temperature
Tos = *p*-toluenesulfonyl

Y = F, OTos, or OH according to DS_F and DS_{Tos} respectively

Sample	DS_F	DS_{Tos}
3a-h	see Tab. 1	

Figure 1. Reaction scheme for the preparation of *p*-toluenesulfonyl (tosyl) cellulose and subsequent conversion to deoxy-fluoro cellulose derivatives.

The results show that the displacement reaction even occurs at room temperature. This is, in fact, interesting because conversion of tosyl cellulose with other halides needs to be carried out at a temperature above 100°C. By reacting tosyl cellulose **2a** and 5 equivalents TBAF·3 H_2O, the highest DS_F of 0.41 and the lowest DS_{Tos} of 0.07 were obtained after a reaction time of 24 h at 100°C (**3a**). Decrease of the reaction time to 16 h at 50°C yields sample **3d** with DS_F 0.30 and DS_{Tos} 0.12. **3c** (16 h at room temperature) shows the lowest DS_F of 0.22 and the highest DS_{Tos} of 0.36, i.e., the increase of reaction temperature yields products with higher DS_F values. Moreover, the content of remaining tosyl groups is decreased with increasing temperature. This can be explained by the presence of water which also acts as nucleophile especially at elevated temperatures leading to hydroxyl groups in a side reaction.

Table 1. Conditions and results of the conversion of *p*-toluenesulfonyl (tosyl) cellulose with 5 equivalents tetrabutylammoniumfluoride (TBAF) in dependence on the water content of the TBAF as well as time and temperature.

Reaction conditions					Sample								
Tosyl cellulose. (g)	Solv.[a] (ml)	TBAF hydrate (g)	Time (h)	θ (°C)	No.	Yield (g)	DS_F[b]	DS_{Tos}[b]	Elemental analysis (%)				
									C	H	N	S	F
2a 5.0	DMF 90	3 H_2O 22.6	24	100	**3a**	1.01	0.41	0.07	45.59	5.32	0.27	1.35	4.52
2a 6.65	DMSO 135	0.25 H_2O 25.3	15	50	**3b**	0.89	0.34	0.10	47.39	5.68	0.15	1.81	3.62
2a 5.0	DMF 100	3 H_2O 22.6	16	rt[c]	**3c**	2.22	0.22	0.36	48.07	5.36	0	5.33	1.88
2a 5.0	DMF 100	3 H_2O 22.6	16	50	**3d**	1.39	0.30	0.12	47.07	5.53	0	2.08	3.14
2a 6.10	DMF 122	0.25 H_2O 23.26	16	rt[c]	**3e**	1.85	0.24	0.21	47.6	5.23	0	3.44	2.33
2a 6.69	DMF 133.8	0.64 H_2O 26.11	16	50	**3f**	1.65	0.28	0.09	46.27	5.14	0	1.58	3.01
2b 3.87	THF 32.5	45 ml 1M in THF	16	rt[c]	**3g**	2.7	0.32	0.64	49.34	4.97	0	7.87	2.34
2b 3.87	THF 32.5	45 ml 1M in THF	16	50	**3h**	0.85	0.47	0.28	49.47	5.14	0	4.39	4.3

[a]Solvent: DMF= *N,N*-dimethylformamide, DMSO= dimethylsulfoxide, THF= tetrahydrofuran
[b]DS= degree of substitution, index F= deoxy-fluoro and index Tos= *p*-toluenesulfonyl
[c]Room temperature

A partly dewatered TBAF was used for further experiments. The conversion of the TBAF trihydrate into the anhydrous material is rather difficult very likely due to decomposition reactions.[13,14] TBAF·0.64 H_2O and TBAF·0.25 H_2O were prepared and subsequently allowed to react with tosyl cellulose **2a** under the conditions described for TBAF·3 H_2O. For instance, TBAF·0.25 H_2O was reacted with **2a** for 16 h at room temperature yielding sample **3e** with DS_F 0.24 and DS_{Tos} 0.21. The conversion of TBAF·0.64 H_2O for 16 h at 50°C yields polymer **3f** with DS_F 0.28 and DS_{Tos} 0.09. There is no influence of the water content of the TBAF on the DS_F. Applying comparable reaction conditions, a difference in DS_F of 0.02 appears only. In contrast, there is a distinct influence of the water content on the DS_{Tos} values. As these results show, the partly dried TBAF yields polymers with lower DS_{Tos} compared with the conversions of the TBAF·3 H_2O, like sample **3e** (DS_{Tos} 0.21, starting from TBAF·0.25 H_2O) and sample **3d** (DS_{Tos}

0.36, starting from TBAF·3 H_2O). The reason for this finding is probably a special solvent polymer interaction (supramolecular microstructure) in the solution containing DMF, TBAF, and water. Detailed studies of the solution complex are under progress using light scattering techniques. Polymers **3a-f** are soluble in dipolar-aprotic solvents like DMA, DMF and dimethylsulfoxide (DMSO), i.e., they possess the same solubility like the starting tosyl cellulose **2a**.

Samples **3g** and **3h** were prepared starting from tosyl cellulose **2b** (DS_{Tos} 1.74) and a commercially available solution of TBAF in THF within a reaction time of 16 h. Products of a DS_F of 0.32 and DS_{Tos} of 0.64 (room temperature, **3g**) and of a DS_F of 0.47 and DS_{Tos} of 0.28 (50°C, **3h**) were obtained. The synthesized deoxy-fluoro celluloses are soluble in aprotic-dipolar solvents.

The FTIR spectrum of the tosyl cellulose **2a** shows all typical bands like ν(OH) at 3550 cm^{-1}, ν(=CH) at 3074 cm^{-1}, ν(CH) at 2930 cm^{-1}, ν(C=C) at 1600 cm^{-1}, δ(CH) and $\nu_{as}(SO_2)$ at 1367 cm^{-1}, ν(C-O-C) at 1118 cm^{-1}, and δ(=CH) at 810 cm^{-1} (Fig. 2). After the fluorination, a decrease of the intensity of the tosyl bands was observed in the FTIR spectra, e.g., of sample **3a** with DS_F 0.41 and DS_{Tos} 0.07. Unfortunately, the C-F vibration could not be clearly determined. The ^{13}C NMR spectrum of **3d** shows the typical peaks of the tosyl moieties at 20 ppm (methyl group) and 125-145 ppm (aromatic carbons) indicating that tosyl groups are still present in the polymer (Fig. 3). The carbon atom of position 6 (CH_2OH) appears at 60 ppm. The signals of C-2,3,4, and 5 are found in the range from 68 to 78 ppm as broad peaks.

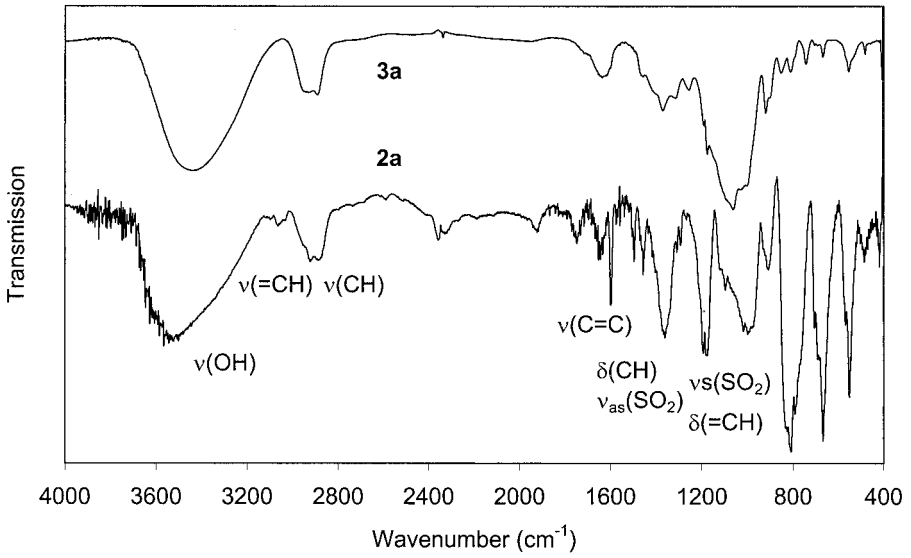


Figure 2. FTIR spectra of *p*-toluenesulfonyl cellulose **2a** and deoxy-fluoro cellulose **3a**. For details of composition see Tab. 1.

Two further peaks were detected at 81.4 and 82.9 ppm. According to Kasuya *et al.*, they are assigned to 6-deoxy-6-fluoro moieties.[15] The C-1 signal is observed at 100 ppm. Moreover, further signals appear which are caused by a tosyl respectively deoxy-fluoro substituent at position 2. It is not clearly obvious if the peaks are caused by a deoxy-fluoro substituent at position 2 or 3.

The ^{19}F NMR spectra of the deoxy-fluoro celluloses show a peak in the range of -230 to -233 ppm which is characteristic of a CH_2F group (Fig. 4). Further peaks below -230 ppm are found in the spectrum of **3a** as well. These peaks seems to be caused by a polymeric substance due to the broad line width. Therefore, it is possible that the S_N reaction also took place partly at position 2 and 3 of the repeating units. Samples **3c** and **3d** were prepared under mild reaction conditions. No signals below -230 ppm appear in the spectra of these substances. This leads to the conclusion that the fluorination of the secondary positions can be omitted applying comparable mild conditions.

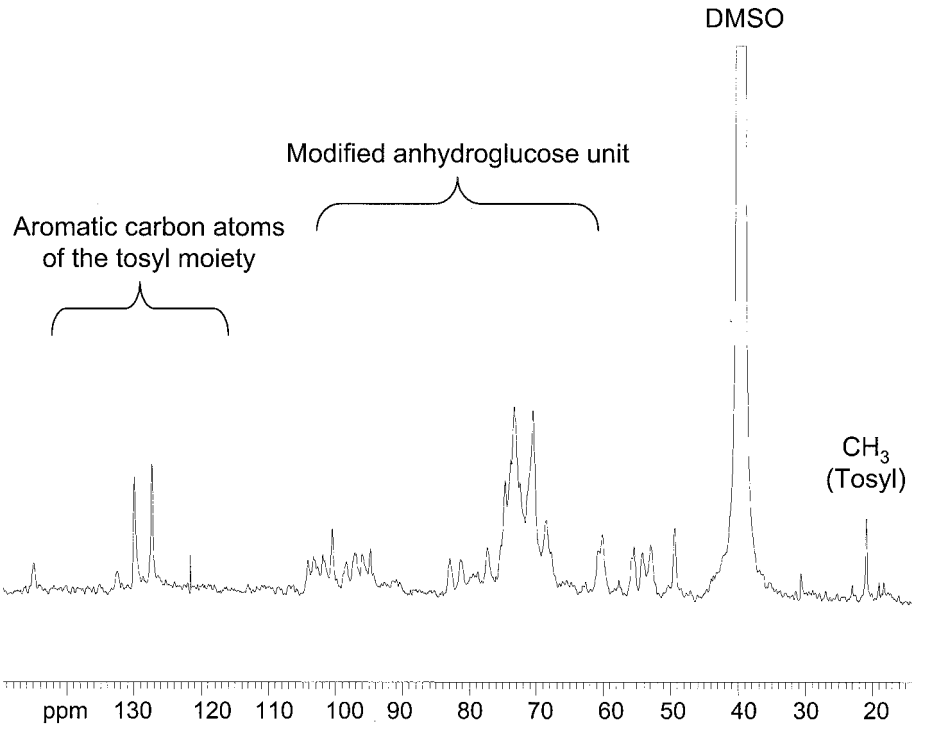


Figure 3. ^{13}C NMR spectrum of deoxy-fluoro cellulose **3d** recorded in dimethylsulfoxide-d_6 (29,000 scans, 60°C).

Thermogravimetric analysis (TG)

Interesting results appear from the thermal analysis of the polymers which were investigated by thermogravimetry in the temperature range from 35°C up to 600°C under air (Fig. 5). The TG curve of tosyl cellulose **2a** is characterized by a clearly visible first decomposition at an onset temperature of 174°C followed by a second broad decomposition beginning at 216°C as already shown by a detailed study of the thermal behavior of tosyl cellulose by Heinze *et al.*[16]. The introduction of fluorine in the polymer (samples **3a-h**) shifts the start of the decomposition to higher temperature in the range of 204°C (**3c**) to 247°C (**3a**).

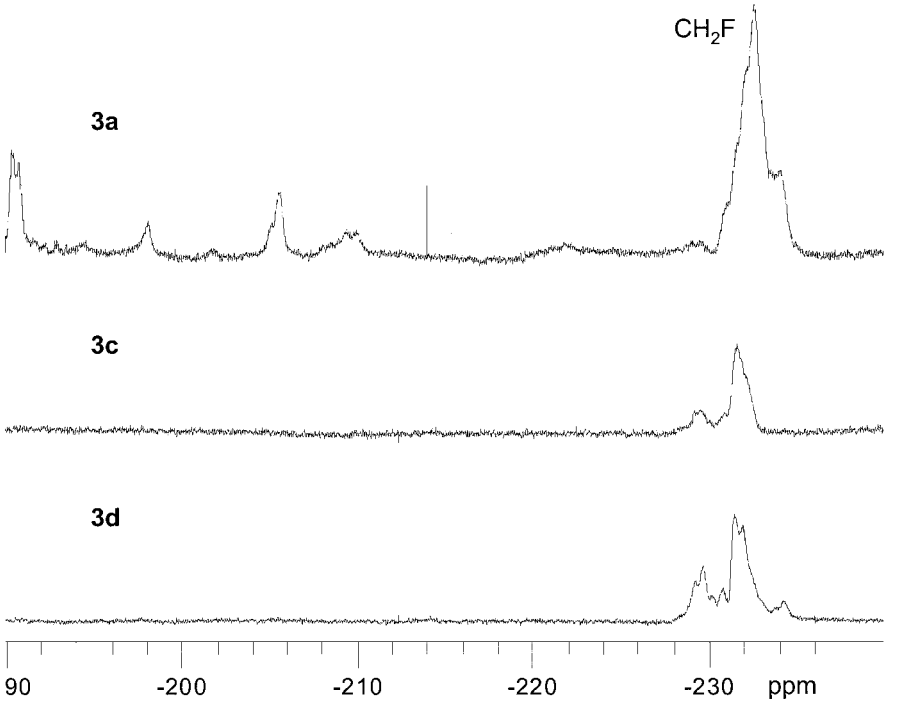


Figure 4. ^{19}F NMR spectra of the deoxy-fluoro celluloses **3a**, **3c**, and **3d** (see Tab. 1).

It is worth mentioning that the balance between DS_F and DS_{Tos} influences the degradation. For instance, the first mass loss of sample **3a** (DS_F 0.41, DS_{Tos} 0.07) was observed at 247°C while polymer **3c** (DS_F 0.22, DS_{Tos} 0.36) is decomposed already at 206°C. A similar behavior was found for polymers **3e-h**. This indicates that the content of remaining tosyl groups is an important factor influencing the thermal degradation, i.e., the lower DS_{Tos} leads to a higher thermal stability. The effect of the DS_F on the decomposition temperature can not be clearly seen.

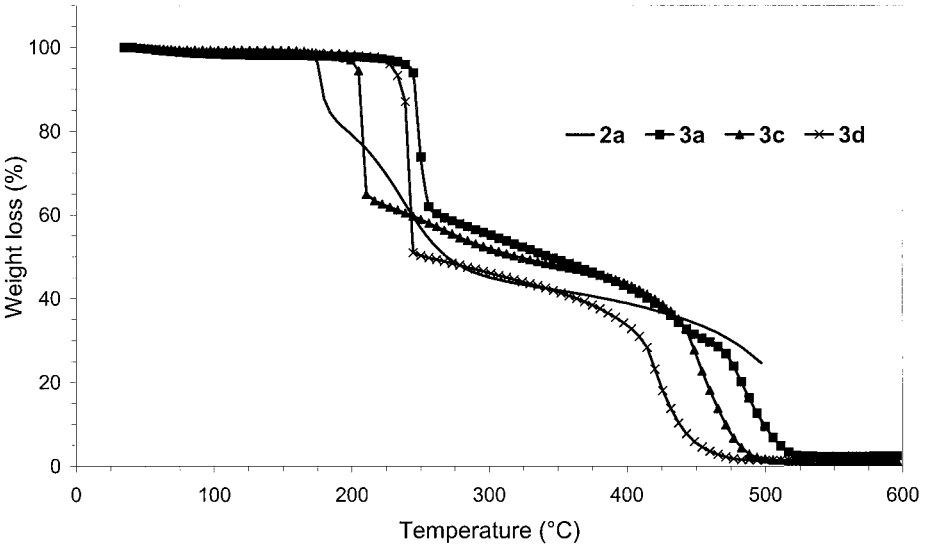


Figure 5. Thermogravimetric analysis of *p*-toluenesulfonyl cellulose **2a** and deoxy-fluoro celluloses **3a**, **3c**, and **3d**.

Conclusion

This study demonstrates that the synthesis of deoxy-fluoro cellulose derivatives by nucleophilic displacement reactions (S_N) of *p*-toluenesulfonyl (tosyl) cellulose is an interesting path for unconventional cellulose derivatives. In contrast to the synthesis of other deoxy-halo celluloses, the S_N reaction can be carried out under comparatively mild conditions. It is worth to note that the reaction occurs even at room temperature. A further advantage of this synthesis is the use of activated cellulose while Kasuya *et al.*[15] synthesized 6-deoxy-6-fluoro cellulose starting from 2,3-di-*O*-protected cellulose derivatives and diethylamino sulfur trifluoride. The products are thermally more stable than the starting tosyl cellulose, however, it seems to be that a distinct influence of the tosyl groups on the degradation temperature exists. In further studies, deoxy-fluoro cellulose derivatives without tosyl groups will be synthesized and investigated.

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