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Base-catalysed cleavage of lignin β-O-4 model compounds in dimethyl carbonate

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A base-catalysed transformation and cleavage of lignin β-O-4 model compounds in dimethyl carbonate is reported. The reaction system consists of readily available bases and inexpensive dimethyl carbonate as a solvent and reagent, affording methoxy benzene or 2-aryloxyvinyl benzene derivatives in good to very good yields. The applicability of the system for the bond cleavage in an organosolv lignin sample was demonstrated.

1. Introduction

In recent years the importance of non-fossil-based feedstocks for the production of chemicals, fuels and energy has significantly increased due to world's depleting petroleum reserves.[1] One possible approach to these challenges involves the use of lignocellulosic biomass.[1] Lignocellulose consists of three main components: cellulose, hemicellulose and lignin.[2] Up until now the focus of investigations has primarily been on the conversion of cellulose and hemicellulose, leaving the transformation of lignin to value-added products mostly unexploited.[1,2] Lignin is an amorphous three dimensional polymer consisting of methoxylated aryl propane units.[3] Previous cleavage studies have mainly focused on the lignin β-O-4 linkage since it represents the predominant interconnecting bond (45% to 60%, depending on the wood type).[4-6] Due to the recalcitrant nature of lignin and the challenges that arise in its analytics, initial cleavage studies were often conducted with lignin model compounds.[7,8]

Along those lines we have recently reported the base-mediated cleavage of lignin and model compounds thereof through mechanical grinding.[9] Inspired by these findings, we explored analogous cleavage reactions of the lignin β-O-4 linkage in solution. Previous reports on the base-catalysed depolymerisation (BCD) of lignin have described harsh reaction conditions with temperatures of up to 340 °C and often high pressures.[10] Furthermore, the yields of monomer rich oils were limited to about 20 wt% of the original lignin mass due to the polymerisable nature of the phenolic products.[10g-10j] To minimise repolymerisation of lignin cleavage products, Lercher and co-workers have employed boric acid as capping agent.[10g] Recently, Toledano *et al.* have compared boric acid and phenol as capping agents and their influence on the formation of phenolic oils, char and the molecular weight of the residual lignin.[10j] They observed that both boric acid and phenol led to an increase in oil yield with the latter exhibiting higher monomer yields. Boric acid effectively reduced the repolymerisation of residual lignin but led to an increase in char formation.

In the light of these results we envisioned a reaction system that would be able to effectively cleave the β-O-4 linkage and at the same time, trap reactive phenol products preventing polymerisation. Hartwig and co-workers demonstrated that stoichiometric amounts of a strong base such as NaO*t*-Bu were able to cleave dilignol model compound **1a** at 100 °C after 2 h in *m*-xylene, yielding 2-methoxy phenol in 89%.[5b] Bearing in mind these findings our attention was caught by dimethyl carbonate, which is used in organic synthesis as non-toxic carboxymethylating and methylating reagent.[11,12] At temperatures >90 °C dimethyl carbonate generates methoxylates in the presence of catalytic amounts of base making it a potentially attractive reaction system for lignin cleavage studies. Here, we report on the selective transformation and cleavage of 1,3-dilignol model compounds affording methoxy benzene and 2-aryloxyvinyl benzene derivatives in the presence of Cs_2CO_3 and LiO*t*-Bu, respectively.

2. Results and discussion

The initial reactions were performed using *erythro* dilignol **1a** as starting material in the presence of 0.1 equivalents of NaOH as catalyst (see Table 1). After 24 h at 90 °C a conversion of 70% was observed with dicarbonate **6** as the main product (entry 1). Increasing the reaction temperature to 180 °C led to a complete conversion of dilignol **1a** (entry 2). To our delight the cleavage product veratrol (**4**) was obtained as the main product in 30% yield. Additionally, cis-alkene **2a** and methyl 3,4-dimethoxybenzoate (**5**) were obtained in 20% and 3% yield, respectively. Numerous bases were then screened to potentially enhance the product selectivities (see ESI). Interestingly, a clear trend in selectivity towards veratrol with an increasing cation radius of the base was observed. Cs_2CO_3

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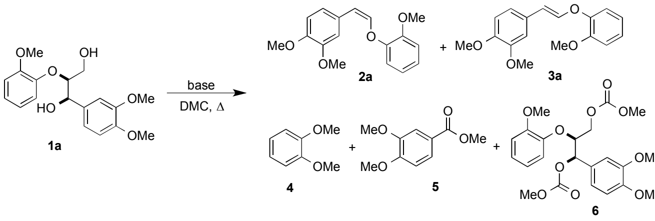
gave the highest yield for veratrol with 57%, and concomitantly methyl 3,4-dimethoxybenzoate was formed in 15% (entry 3). A shorter reaction time of 8 h improved the yield of veratrol to 60%, and the catalyst loading could be decreased to 0.05 eq. without loss in yield (entries 5 and 6). However, a lowering of the reaction temperature to 150 °C or utilising a reflux condenser was not beneficial (entries 8 and 9). Reports in the literature indicated that treatment of lignin in alkaline solution at elevated temperatures and under oxygen atmosphere led to the formation of aromatic aldehyde cleavage products.[13] Here, however, changing the reaction atmosphere to oxygen or argon had a negligible influence on the yields affording **4** in 58% and 61%, respectively (entries 11 and 12). Furthermore, we were able to demonstrate that the good yield of veratrol was maintained when the reaction was performed on a 2 mmol scale (entry 10). When the cation-radius of the employed base was decreased, the selectivity shifted towards alkene **2a**. LiO*t*-Bu afforded cis-alkene **2a** in 70% yield with trans-alkene **3a** being formed as a side product in 11% yield (entry 4). Once more the reaction time could be shortened and the catalyst loading reduced (12 h and 0.05 eq.), furnishing **2a** in 75% and **3a** in 9% yield (entries 13 and 14). As previously observed for Cs_2CO_3, performing the reaction with a reflux condenser was not beneficial for the yields. A control reaction without the catalyst revealed that veratrol (**4**) and **2a** were only present in trace amounts after 24 h at 180 °C and dicarbonate **6** was isolated as the main product (entry 17). Despite the fact that Cs_2CO_3 and LiO*t*-Bu displayed distinctly different product selectivities both reaction systems initially formed dicarbonate **6** as a reaction intermediate (entries 7 and 15).

Table 1: Catalyst screening for the basic cleavage of dilignol **1**.[a]

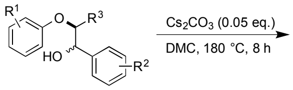


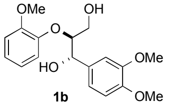
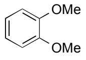
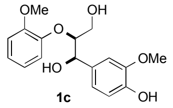
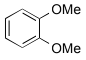
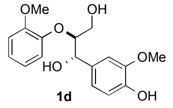
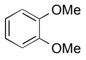
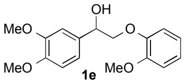
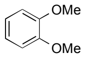
Entry	Base	T [°C]	*t* [h]	Yields [%][b]				
				2a	**3a**	**4**	**5**	**6**
1	NaOH	90	24	-	-	-	-	45
2	NaOH	180	24	20	-	30	3	-
3	Cs_2CO_3	180	24	-	-	57	15	-
4	LiO*t*-Bu	180	24	70	11	-	-	-
5	Cs_2CO_3	180	8	-	-	60	14	-
6[c]	Cs_2CO_3	180	8	-	-	60	14	-
7[c]	Cs_2CO_3	180	0.2	-	-	-	-	55
8[c]	Cs_2CO_3	150	8	-	-	23	2	-
9[c,d]	Cs_2CO_3	180	8	-	-	24	3	-
10[c,e]	Cs_2CO_3	180	8	-	-	60[f]	15[f]	-
11[c,g]	Cs_2CO_3	180	8	-	-	58	11	-
12[c,h]	Cs_2CO_3	180	8	-	-	61	13	-
13	LiO*t*-Bu	180	12	75	9	-	-	-
14[c]	LiO*t*-Bu	180	12	75	9	-	-	-
15[c]	LiO*t*-Bu	180	0.5	-	-	-	-	90
16[c]	LiO*t*-Bu	150	12	64	4	-	-	-
16[c,d]	LiO*t*-Bu	180	12	23	1	-	-	-
17	-	180	24	trace	-	trace	-	35

[a] Reaction conditions: **1** (0.25 mmol); base (0.025 mmol, 0.1 eq.), dimethyl carbonate (1.25 mL); [b] as determined by HPLC using diphenyl ether or 3,4-dimethoxybenzyl alcohol as internal standard; [c] use of 0.05 eq. of base; [d] reaction performed under reflux; [e] reaction performed on a 2 mmol scale; [f] yield after column chromatography; [g] under argon atmosphere; [h] under oxygen atmosphere.

With the optimised reaction conditions in hand we investigated the substrate scope with model compounds that exhibited different stereochemistry, greater steric hindrance, contained a phenolic hydroxyl group or lacked the primary OH. Using Cs_2CO_3 as catalyst (Table 2), the corresponding *threo* diastereomer **1b** of dilignol **1a** afforded veratrol (**4**) in 61%. Cleavage of *erythro* dilignol **1c**, containing a phenolic hydroxyl group, gave **4** in a slightly lower yield (45%). Likewise, *threo* dilignol **1d** furnished veratrol in a similar yield of 42% as the corresponding *erythro* diastereomer **1c**. For monolignol **1e** lacking the primary hydroxyl group a strong decrease in yield of **4** was observed (18%, Table 2, entry 4). Bearing in mind that dilignol **1a** was converted to dicarbonate **6** before the cleavage this result indicated that the second carbonate functionality had an impact on the progression of the reaction. Thus, the decrease in yield for monolignol **1e** should not be regarded as a limitation for any applications in the natural polymer because this structural motif without an aliphatic hydroxyl is absent in native lignin. An increased steric hindrance on the arene adjacent to the benzylic hydroxyl group resulted in the formation of cis-alkene **2b** in 80% and 82% yield for both the *erythro* and *threo* diastereomer **1f** and **1g**, respectively. This alteration in selectivity has to be taken into account when employing lignin sources that have a high content of synapyl-alcohol derived building blocks. The same trend was not observed when the steric hindrance was increased at the second aryl ring. 1,3,5-Trimethoxybenzene (**7**) and 1,2,3-trimethoxybenzene (**8**) were obtained as the main products in 57% and 62% yield, respectively, for the cleavage of **1h** and **1i** (Table 2, entries 7 and 8) in which the steric hindrance was increased in either the *meta*- or the *ortho*-position.

***Table 2:* Cleavage of lignin model compounds with Cs_2CO_3 as catalyst.**[a]



Entry	Model Compound	Product	Yield [%]
1[b]	 **1b**	 **4**	61
2[b]	 **1c**	 **4**	45
3[b]	 **1d**	 **4**	42
4[b]	 **1e**	 **4**	18

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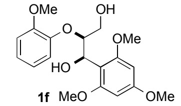
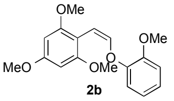
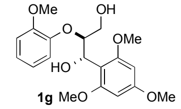
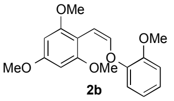
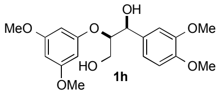
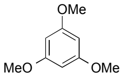
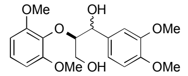
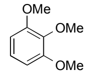
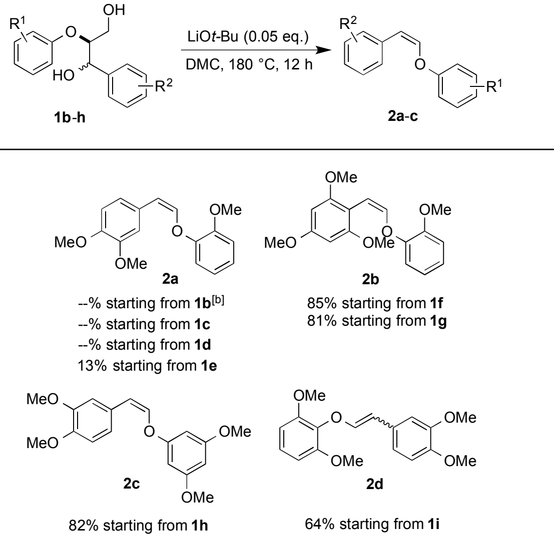
5	 **1f**	 **2b**	80
6	 **1g**	 **2b**	82
7	 **1h**	 **7**	57
8	 **1i**	 **8**	62

[a] Reaction conditions: **1** (0.25 mmol), Cs_2CO_3 (0.013 mmol, 0.05 eq.), dimethyl carbonate (1.25 mL), 180 °C, 8 h. Yields after column chromatography; [b] as determined by HPLC with 3,4-dimethoxybenzyl alcohol as internal standard.

Next, we explored reactions with LiO*t*-Bu as base. Surprisingly, *threo* dilignol **1b** did not yield alkene **2a** but veratrol (**4**) in 20% as the main product. Alkene **2a** remained undetected. Furthermore, it was noted that the reaction conditions with LiO*t*-Bu were unsuitable for model compounds **1c** and **1d** which both contained a phenolic hydroxyl group. Instead of the formation of alkene **2a** or veratrol a glue being insoluble in any standard organic solvents, sticking to the reaction vessel, was formed. The reaction with monolignol **1e** afforded, similar to the observation made with Cs_2CO_3, **2a** in significantly lower yield of 13%, indicating once more that the second aliphatic hydroxyl is crucial for both the formation of veratrol and alkene **2a**. The sterically more hindered dilignol diastereomers **1f** and **1g** both furnished cis-alkene **2b** in 85% and 81% yield, respectively. Likewise, starting from **1h** and **1i** having a greater steric hindrance at the second aryl ring led to cis-alkene **2c** in 82% yield and a mixture of cis- and trans-alkene **2d** in 64% yield (44 % cis and 20 % trans alkene).

Scheme 1: Transformation of lignin model compounds with LiO*t*-Bu.[a]



[a] Reaction conditions: **1** (0.25 mmol), LiO*t*-Bu (0.013 mmol, 0.05 eq.), dimethyl carbonate (1.25 mL), 180 °C, 12 h. Yields after column chromatography. [b] Instead of alkene **2a**, veratrol (**4**) was formed in 20% yield.

Encouraged by the success of the reaction system in the cleavage of the model compounds, the applicability of both Cs_2CO_3 and LiO*t*-Bu in a degradation of a more complex lignin polymer was studied. For this purpose beech wood lignin, which had been extracted in an ethanol-based organosolv process, was employed as starting material (for additional information on the lignin source see ESI). To monitor the bond cleavage of prominent linkages such as the *β*-O-4, 2D-NMR (HSQC) experiments were conducted. Figure 1 shows the results for the degradation studies with 5 wt% (0.0153 mmol) of Cs_2CO_3 (Figure 1, b) and 1.2 wt% (0.0153 mmol) of LiO*t*-Bu (Figure 1, c) at 180 °C after a reaction time of 8 h and 12 h, respectively. The interpretation of the structural changes within the lignin samples (with Figure 1, a as starting point) followed those outlined by Sun and coworkers.[14] To our delight both bases were able to completely degrade the *β*-O-4 linkages **A, A'** and phenylcoumaran substructures **C**, as their characteristic signals in the HSQC disappeared entirely. In contrast, the resinol units **B** remained unaffected in both cases. This observation was not surprising considering that the resinol structures did not contain any aliphatic hydroxyl groups, which proved to have a strong influence on the degradation of the lignin model compounds.

3. Conclusions

We have developed a base-catalysed system for the cleavage of lignin model compounds containing *β*-O-4 linkages. Employing Cs_2CO_3 as catalyst, we obtained methoxy benzene derivatives as main products in good yields. An increase in steric hindrance at the aryl ring adjacent to the benzylic hydroxyl group resulted in a selectivity change, affording the corresponding 2-aryloxyvinyl benzene derivatives in very good yields. Furthermore, we established a base-catalysed transformation with LiO*t*-Bu for non-phenolic model compounds to 2-aryloxyvinyl benzene derivatives in very good yields. For both reaction systems the presence of a primary hydroxyl group on the model compound was important. The reaction scope was further expanded by applying an organosolv lignin extracted from beech wood. 2D-NMR (HSQC) experiments revealed that both protected and unprotected *β*-O-4 linkages as well as phenylcoumaran substructures were degraded by both systems. Further investigations focusing on mechanistic studies and degradations of differently extracted lignins are currently being conducted in our laboratories.

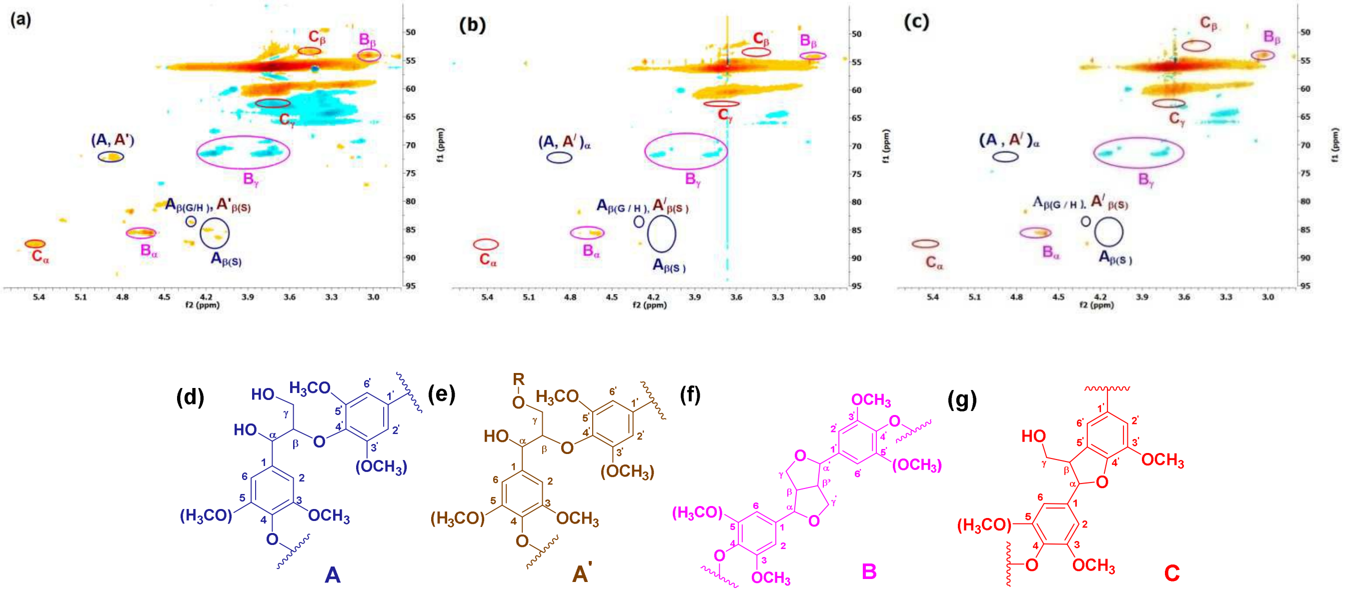


Figure 1. 2D HSQC NMR spectra (in DMSO-d_6) of organosolv beech lignin; a) before the reaction; b) after the reaction with Cs_2CO_3; c) after the reaction with LiO*t*-Bu; d) β-O-4' aryl ether linkages with a free -OH at the γ-carbon; e) β-O-4' aryl ether linkages with acetylated and/or *p*-hydroxybenzoated -OH at γ-carbon; f) resinol substructures formed by β-β', α-O-γ', and γ-O-α' linkages; g) phenylcoumaran substructures formed by β-5' and α-O-4' linkages; For additional information on the reaction conditions see ESI.†

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Notes and references

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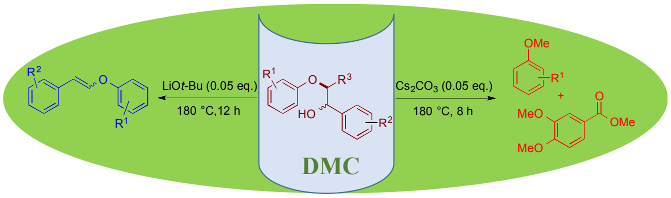
TOC



Dimethyl carbonate (DMC) was used as solvent and non-toxic capping agent in a base-catalysed selective cleavage of lignin model compounds.