Catal Lett (2015) 145:511–518
DOI 10.1007/s10562-014-1401-7

Hydrogenolysis of a γ-Acetylated Lignin Model Compound with a Ruthenium–Xantphos Catalyst

Adam Wu · Jean Michel Lauzon · Brian R. James

Received: 2 August 2014 / Accepted: 11 October 2014 / Published online: 30 October 2014

Abstract Catalytic hydrogenolysis of a γ-acetylated dimer lignin model compound is effected using a Ru–xantphos catalyst. Mechanistic investigations show monoaryl degradation products are generated from the β-O-4 substrate as well as a terminal alkene ketone dimer (bisaryl) that further dimerizes to a tetra-aryl product. Preliminary results using an acetylated kraft lignin as a substrate are also discussed.

Keywords Acetylated lignin · Hydrogenolysis · Ruthenium · Xantphos · Lignin degradation

1 Introduction

In the search for a renewable source of biofuel and other chemical building blocks currently derived from fossil fuels, lignocellulosic biomass is an attractive proposition. The intense surge in research in the past decade [1–9] is particularly significant within the pulp and paper industry, which generates large quantities that are currently treated as 'waste' [10]. This label is due in part to the irregular, complex structure of lignin: non-identical phenolic units interconnected by a series of C–C and C–O bonds [8, 9]. The predominant C–O bond, typically comprising 50–60 % of lignin structures, is the so-called β-O-4 linkage (Fig. 1). This bond has been identified as a target disconnection point for the depolymerisation of lignin using transition metal catalysts [11–13].

To this end, Bergman, Ellman, and co-workers showed that an in situ generated $Ru(H)_2(CO)(PPh_3)$(xantphos) complex could be used for the catalytic hydrogenolysis of the β-O-4 linkage in lignin model compounds (LMCs) [13]. This lead publication inspired our group to investigate the catalytic system in more detail, culminating in our own report [12]. During our study, it was discovered that LMCs containing γ-OH functional groups formed catalytically-inactive ruthenium complexes through a double-dehydrogenation mechanism. This revelation is of particular concern due to the prevalence of these γ-OH groups in lignin structures [9, 14–17], and this could be important in any industrial application of such Ru-based technology. Herein we report that the acetylation of the γ-OH groups to γ-OAc groups eliminates the double-dehydrogenation pathway and allows for hydrogenolysis of the β-O-4 linkage.

Acetylation of lignin in the γ-position is seen in several fibrous plants [18, 19], including a few hardwoods [20]; this results from the presence of acetylated monomers during biosynthesis [21]. Chemical acetylation of alcohol groups in lignin [22] has been used to characterize native lignins by NMR [23–26] and mass spectrometric [27] methods; similarly prepared samples, when compared to their unmodified precursors, have increased solubility in hydrophobic organic solvents [28, 29] and enhanced photostabilization [30]. Acetylated lignin has been incorporated into materials such as welded dowel joints [31], thin films [32], self-assembled spheres [33], and plastic blends [34].

Herein we report on our study of the catalytic hydrogenolysis of a γ-acetylated dimer LMC and preliminary results applying the strategy to acetylated lignin.

Electronic supplementary material The online version of this article (doi:10.1007/s10562-014-1401-7) contains supplementary material, which is available to authorized users.

A. Wu · J. M. Lauzon · B. R. James (✉)
Department of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, BC V6T 1Z1, Canada
e-mail: brj@chem.ubc.ca

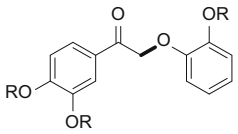


Fig. 1 Example of a generic, so-called dimeric lignin section (meaning two aromatic rings) with the β-O-4 bond highlighted

2 Experimental Methods

2.1 General Remarks

NMR spectra were recorded at room temperature (r.t., ~20 °C), unless otherwise noted, on Bruker spectrometers (300 or 400 MHz for ^{1}H, 75 or 100 MHz for ^{13}C{^{1}H}, and 122 MHz for ^{31}P{^{1}H}). Residual deuterated solvent proton ($\delta_H = 7.16$ s, for $CDCl_3$ or 2.08 qt, for toluene-d_8) and solvent carbon ($\delta_C = 77.16$, t, for $CDCl_3$) relative to external $SiMe_4$ were used as ^{1}H and ^{13}C references, respectively (s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, m = multiplet; coupling constants (*J*) are given in Hz) [35]. External 85 % H_3PO_4 ($\delta_P = 0.0$) was used as a ^{31}P reference. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. Gas chromatography/mass spectrometry (GC/MS) spectra were recorded on an Agilent 6890 N Network GC System with a 5975B inert MS detector. The GC column was an HP-5MS 5 % phenyl(methyl)siloxane capillary column (Agilent 19091 S-433) with 30.0 m × 250 µm × 0.25 µm nominal dimensions. The initial temperature was set at 50 °C and held for 1 min, then increased by 20 °C/min for 10 min to reach 250 °C, which was held for 9 min; a sample of ~0.5 µL was injected into the GC column by a 10 µL microsyringe. Electrospray ionization mass spectra in the positive ion mode (ESI/MS$^+$) were recorded on a Bruker Esquire-LC ion-trap instrument, with MeOH solution of samples being infused into the ion-source by a syringe pump at a flow rate of 200 µL/min. Elemental analyses were performed using a Carlo Erba EA1108 elemental analyzer. All solvents and reagents used in the syntheses were reagent grade and were used as supplied by Aldrich or Fisher Scientific. Silica gel (SiliaFlash® F60, 230–400 mesh) was purchased from Silicycle, and the Praxair gases H_2 (99.995 %, extra dry) and Ar (99.996 %) were used as received. $Ru(H)_2(CO)(PPh_3)$(xantphos) (**Ru***) was synthesised as reported [12]. Intermediates (**1**–**3**) were synthesised by modification of literature methods [36, 37]. The modifications involved the use of different solvents during reactions and modified work-up procedures; our corresponding ^{1}H and ^{13}C{^{1}H} NMR data for **1**–**3** (Figs S1-S3 respectively) are in good agreement with the literature [37]. ^{1}H and ^{13}C{^{1}H} NMR spectra for novel compounds **4**, **9**, and **10** are available in the ESI (Figs S4-S6). Compound **4** has been reported on briefly, but characterization involved only three ^{13}C{^{1}H} NMR shifts [22]. Acetylated kraft lignin was kindly donated by Weyerhaeuser Co (Seattle, WA, USA).

2.2 Synthesis of γ-Acetylated β-O-4 Ketone Dimer Substrate (**4**)

2.2.1 3,4-Dimethoxybromoacetylbenzene (1)

3,4-Dimethoxyacetophenone (10 g, 55 mmol) in $CHCl_3$ (100 mL) was stirred in a round-bottom flask, while Br_2 (10.6 g, 66 mmol) was added drop-wise over 1 h; the mixture was then stirred then for 16 h at r.t. The solvent was then removed in vacuo to give an oil; addition of EtOH (40 mL) and cooling to −15 °C gave a cream-white precipitate that was filtered off, washed with EtOH (2 × 20 mL), and dried in vacuo. Yield = 7.0 g (49 %). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta_H = 3.95$, 3.97 (OC*H*$_3$, s, 3H each), 4.42 (C*H*$_2$Br, s, 2H), 6.92 (Ar–*H*, d, 1H, $^{3}J_{HH} = 8.7$), 7.56 (Ar–*H*, s, 1H), 7.62 (Ar–*H*, d, 1H, $^{3}J_{HH} = 8.4$). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): $\delta_C = 30.5$ (*C*H$_2$Br), 56.1, 56.2 (O*C*H$_3$), 110.2, 110.9, 123.9 (*C*$_{Ar}$–H), 127.1 (*C*$_{Ar}$*C*=O), 149.4, 154.1 (*C*$_{Ar}$–OCH$_3$), 190.1 (*C*=O). ESI/MS$^+$: 283 [M + Na]$^+$. Anal. Calcd (Found) for $C_{10}H_{11}O_3Br$: C, 46.36 (46.37); H, 4.28 (4.25).

2.2.2 1-(3,4-Dimethoxyphenyl)-2-(2-Methoxyphenoxy)Ethanone (2)

Compound **1** (6.5 g, 25 mmol) and K_2CO_3 (5.2 g, 38 mmol) were stirred in acetone (150 mL) in a round-bottom flask while guaiacol (3.7 g, 30 mmol) was added drop-wise, and the reaction mixture was then stirred for 16 h at r.t. Remaining solid was filtered off, and the filtrate was concentrated in vacuo to give an oil; addition of EtOH (40 mL) and cooling to −15 °C gave a cream-coloured precipitate that was filtered off, washed with EtOH (2 × 20 mL), and dried in vacuo. Yield = 6.0 g (79 %). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta_H = 3.89$, 3.93, 3.95 (OC*H*$_3$, s, 3H each), 5.29 (C*H*$_2$, s, 2H), 6.75–7.05 (Ar–*H*, m, 5H), 7.60 (Ar–*H*, s, 1H), 7.68 (Ar–*H*, d, 1H, $^{3}J_{HH} = 8.4$). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): $\delta_C = 56.0$, 56.1, 56.2 (O*C*H$_3$), 72.1 (*C*H$_2$), 110.2, 110.5, 112.2, 114.8, 120.9, 122.4, 122.9 (*C*$_{Ar}$–H), 127.9 (*C*$_{Ar}$*C*=O), 147.7 (*C*$_{Ar}$–OCH$_2$), 149.3, 149.8, 153.9 (*C*$_{Ar}$–OCH$_3$), 193.4 (*C*=O). ESI/MS$^+$: 325 [M + Na]$^+$. Anal. Calcd (Found) for $C_{17}H_{18}O_5$: C, 67.54 (67.69); H, 6.00 (5.90).

2.2.3 3-Hydroxy-2-(2-Methoxyphenoxy)-1-(3,4-Dimethoxyphenyl)-1-Propanone (3)

In a round-bottom flask, **2** (2.2 g, 7.3 mmol), K_2CO_3 (1.2 g, 8.7 mmol), and 37 wt% formaldehyde (0.89 g, 11 mmol) were stirred in a 1:1 EtOH/acetone solution (60 mL) for 2 h at r.t. The filtrate from this was concentrated in vacuo to

give an oil that was subsequently purified by silica gel chromatography (1:1–1:2 hexanes/EtOAc). The appropriate fractions were collected and concentrated in vacuo to give an oil. Addition of CH_2Cl_2/hexanes (10 mL/50 mL) precipitated a white powder that was filtered off, and dried in vacuo. Yield = 1.2 g (49 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H = 3.21 (O*H*, t, 1H, $^3J_{HH}$ = 6.5), 3.85, 3.91, 3.94 (OCH_3, s, 3H each), 4.07 (HOCH_2, d, 2H, $^3J_{HH}$ = 5.9), 5.40 (C*H*CH$_2$, t, 1H, $^3J_{HH}$ = 5.3), 6.70–7.10 (Ar–*H*, m, 5H), 7.61 (Ar–*H*, d, 1H, $^3J_{HH}$ = 1.5), 7.75 (Ar–*H*, dd, 1H, $^2J_{HH}$ = 8.3, $^3J_{HH}$ = 1.7). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ_C = 55.9, 56.1, 56.2 (O*C*H$_3$), 63.9 (CH*C*H-$_2$), 84.6 (*C*HCH$_2$), 110.2, 111.1, 112.4, 118.4, 121.3, 123.7, 123.8 (C_{Ar}–H), 128.2 (C_{Ar}*C*=O), 147.1 (C_{Ar}–OCH$_2$), 149.3, 150.5, 154.0 (C_{Ar}–OCH$_3$), 195.1 (*C*=O). ESI/MS-$^+$: 333 [M + H]$^+$. Anal Calcd (Found) for $C_{18}H_{20}O_6{\cdot}H_2O$: C, 61.71 (61.56); H, 6.33 (6.20). The H_2O was detected qualitatively in ^{1}H NMR spectrum (Fig S3).

2.2.4 3-Acetoxy-2-(2-Methoxyphenoxy)-1-(3,4-Dimethoxyphenyl)-1-Propanone (4)

Pyridine (0.29 g, 3.7 mmol) and acetyl bromide (1.5 g, 12 mmol) were added step-wise to **3** (1.0 g, 3.0 mmol) dissolved in THF (10 mL), and the reaction mixture was stirred for 30 min at r.t.; this was filtered, and the filtrate was concentrated in vacuo to give an oil which was purified by silica gel chromatography (1:1 EtOAc/hexanes). The appropriate fractions were collected and concentrated in vacuo to give an oil. The white powder that precipitated upon addition of CH_2Cl_2/hexanes (5 mL/50 mL) was filtered off, and dried in vacuo. Yield = 0.90 g (80 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H = 2.04 (C(O)CH_3, s, 3H), 3.77, 3.92, 3.94 (OCH_3, s, 3H each), 4.51 (CHC*H*H, dd, 1H, $^2J_{HH}$ = 11.6, $^3J_{HH}$ = 7.2), 4.66 (CHCH*H*, dd, 1H, $^2J_{HH}$ = 12.4, $^3J_{HH}$ = 3.6), 5.61 (C*H*CH$_2$, dd, 1H, $^2J_{HH}$ = 7.0, $^3J_{HH}$ = 3.8), 6.76–7.20 (Ar–*H*, m, 5H), 7.67 (Ar–*H*, d, 1H, $^3J_{HH}$ = 2.0), 7.84 (Ar–*H*, dd, 1H, $^2J_{HH}$ = 8.2, $^3J_{HH}$ = 2.2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C = 20.9 (C(O)*C*H$_3$), 55.9, 56.1, 56.2 (O*C*H$_3$), 64.8 (CH*C*H-$_2$), 80.4 (*C*HCH$_2$), 110.3, 111.2, 112.7, 118.1, 121.1, 123.5, 123.9 (C_{Ar}–H), 128.1 (C_{Ar}*C*=O), 147.0 (C_{Ar}–OCH$_2$), 149.2, 150.4, 154.0 (C_{Ar}–OCH$_3$), 171.1 (*C*(O)CH$_3$), 194.2 (*C*(O)CH). ESI/MS-$^+$: 397 [M + Na]$^+$, 413 [M + K]$^+$. Anal Calcd (Found) for $C_{20}H_{22}O_7$: C, 64.16 (63.92); H, 5.92 (5.92).

2.3 Synthesis of Catalysis By-products

2.3.1 2-(2-Methoxyphenoxy)-1-(3,4-Dimethoxyphenyl)-1-Oxo-2-Propene (9)

Method 1: A THF solution (20 mL) of **3** (1.0 g, 3.0 mmol) and KOH (0.34 g, 6.1 mmol) was stirred for 1 h at r.t.; concentration in vacuo gave an oil that was purified by silica gel chromatography (1:1 EtOAc/hexanes). The appropriate fractions were collected and concentrated in vacuo to give an oil, which when scratched with a spatula in a glass vial yielded a white solid that was collected and dried in vacuo. Yield = 0.25 g (26 %).

Method 2: A CH_2Cl_2 solution (15 mL) of **3** (0.50 g, 1.5 mmol) and Et_3N (441 μL, 3.16 mmol) was stirred at 30 °C for 10 min. After addition of tosyl chloride (0.34 mg, 1.81 mmol), the mixture was stirred overnight, and then diluted with 10 mL CH_2Cl_2, washed with 15 mL of H_2O, dried with $MgSO_4$, and concentrated in vacuo to give a yellow oil that was purified by silica gel chromatography (1:5 EtOAc/hexanes). The appropriate fractions were collected and concentrated in vacuo to give an oil, from which a white solid was precipitated with hexanes. The solid was filtered off and dried in vacuo. Yield = 0.38 g (80 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ_H = 3.86, 3.936, 3.942 (OCH_3, s, 3H each), 4.70 (C=C*H*H, d, 1H, $^2J_{HH}$ = 2.4), 5.20 (C=CH*H*, d, 1H, $^2J_{HH}$ = 2.4), 6.87–7.00 (Ar–*H*, m, 3H), 7.05–7.17 (Ar–*H*, m, 2H), 7.64 (Ar–*H*, d, 1H, $^3J_{HH}$ = 2.4), 7.83 (Ar–*H*, dd, 1H, $^2J_{HH}$ = 8.4, $^3J_{HH}$ = 2.0). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C = 56.0, 56.1, 56.2 (O*C*H$_3$), 100.0 (C=*C*H$_2$), 110.0, 112.4, 113.0, 121.3, 121.8, 125.2, 125.9 (C_{Ar}–H), 129.2 (C_{Ar}*C*=O), 143.4 (C_{Ar}–OC), 148.8, 151.1, 153.5 (C_{Ar}–OCH$_3$), 158.1 (*C*=CH$_2$), 189.2 (*C*=O). ESI/MS$^+$: 315 [M + H]$^+$, 337 [M + Na]$^+$, 353 [M + K]$^+$. Anal. Calcd (Found) for $C_{18}H_{18}O_5$: C, 68.78 (68.57); H, 5.77 (5.78).

2.3.2 A Cyclobutyl(diketo)tetramer (10)

Compound **9** (0.20 g, 0.32 mmol) was dissolved in toluene (5 mL) in a Schlenk flask which, after three freeze–pump–thaw cycles, was filled with Ar to 1 atm. The mixture was heated with stirring at 135 °C for 20 h, and then cooled to r.t. The solvent was removed in vacuo and the residue was purified by silica gel chromatography (1:1 hexanes/EtOAc). The first set of fractions was simply reactant **9** (0.072 g, 36 %). The second set of fractions when concentrated in vacuo gave an oil, which on being scratched yielded **10** as a white solid that was collected and dried in vacuo. Yield = 0.10 g (50 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H = 2.32–2.48 (C*H*H, C′*H*H, m, 2H), 2.58–2.71 (C′H*H*, m, 1H), 2.80–2.95 (CH*H*, m, 1H), 3.63, 3.73, 3.80, 3.83, 3.87, 3.91 (OCH_3, s, 3H each), 6.66–7.00 (Ar–*H*, m, 9H), 7.16–7.22 (Ar–*H*, m, 3H), 7.78 (Ar–*H*, d, 1H, $^3J_{HH}$ = 2.0), 8.05 (Ar–*H*, dd, 1H, $^2J_{HH}$ = 8.8, $^3J_{HH}$ = 2.0). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C = 20.7 (*C*H$_2$), 29.5 (*C*′H$_2$), 55.6, 55.7, 55.8, 56.0, 56.0, 56.1 (O*C*H$_3$), 101.9, 110.1 (*CC*=O), 110.5, 110.6, 112.2, 112.4, 112.9, 115.1, 119.9, 120.6, 120.7, 121.0, 122.4, 123.9, 125.5, 127.0 (C_{Ar}–H), 131.3, 140.3 (C_{Ar}*C*=O), 143.0, 145.8 (C_{Ar}–OC), 148.2, 148.6, 148.7, 149.6, 151.2, 153.5 (C_{Ar}–OCH$_3$), 192.7

(*C*=O). ESI/MS$^+$: 651 $[M + Na]^+$, 667 $[M + K]^+$. Anal. Calcd (Found) for $C_{36}H_{36}O_{10}{\cdot}0.5H_2O$: C, 67.81 (67.97); H, 5.85 (5.71). The H_2O was detected qualitatively in the ^1H NMR spectrum (Fig S6). **10** (20 mg) was also dissolved in C_6D_6 (0.6 mL) in a J-Young NMR tube, and the ^1H NMR spectra recorded from 25–90 °C, and then again at 25 °C (Fig S7, Table S1).

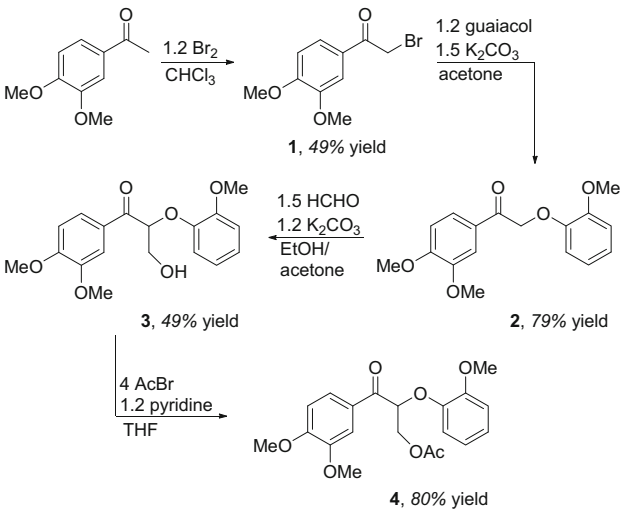
2.4 Procedure for Catalytic Hydrogenolysis

The lignin model substrate **4** (0.10 mmol), **9** (0.10 mmol), or acetylated kraft lignin (15 mg) and the catalyst (5 mol % of **Ru***) were dissolved in toluene-d_8 (0.5 mL) and transferred to a J-Young NMR tube. After three freeze–pump–thaw cycles, the tube was filled with 1 atm of H_2 or Ar. The ^1H NMR spectrum was recorded at r.t., and the tube was then placed in a 135 °C oil-bath for 20 h. The reaction mixture was then cooled to r.t., and pivalic acid (5–15 mg, 0.05–0.15 mmol) was added as an external standard for determination of product yields and substrate conversions. The relevant δ_H values used in toluene-d_8 solutions are: for **4** (5.67, C*H*CH_2, dd), **5** (1.15, CH_3, t), **6** (3.19, OCH_3, s), **7** (2.22, CH_3, s), **8** (1.91, CH_3C(O), s), **9** (5.26, C=CH*H*, d), **10** (2.70–2.88, CH*H*, m), and pivalic acid (1.07, $(CH_3)_3$, s). To confirm the presences of all species, ~0.5 µL of the reaction mixture (prior to the addition of pivalic acid) was injected into the GC/MS instrument, and their *m/z* values observed: for **5** (194), **6** (124), **7** (180), **8** (166), **9** (314), and PPh_3 (262).

3 Results and Discussion

3.1 Synthesis and Catalytic Hydrogenolysis of 4

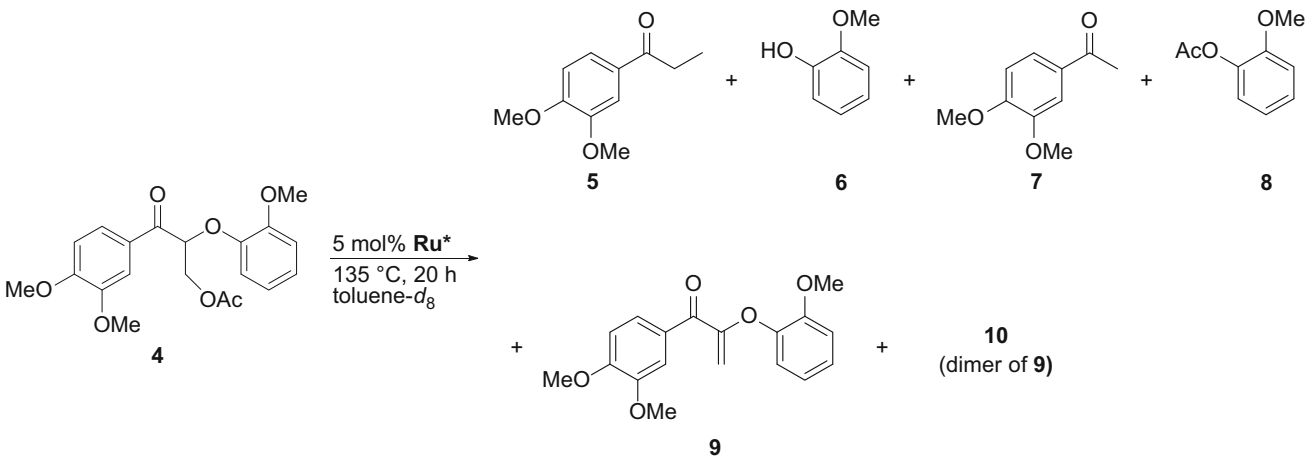
The synthesis of γ-acetylated β-O-4 ketone dimer lignin model compound 3-acetoxy-2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)-1-propanone (**4**) is outlined in Scheme 1. First, 3,4-(dimethoxy)acetophenone is reacted with Br_2 in $CHCl_3$ to produce 3,4-dimethoxy(bromoacetyl)benzene (**1**) in moderate yield (49 %). Reaction of **1** with K_2CO_3 and guaiacol in acetone gives the β-O-4 ketone dimer 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanone (**2**, 79 %). The γ-OH moiety is then incorporated using K_2CO_3 and HCHO in acetone/EtOH to give 3-hydroxy-2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)-1-propanone (**3**, 49 %). The syntheses of intermediates **1**–**3** described in the experimental section involve modifications of literature methods [36, 37]. Production of **4** (in 80 % yield) from **3** was accomplished using AcBr and pyridine for the acetylation; on previous smaller scale syntheses (0.05–0.2 mmol) in the absence of pyridine, the yield was only 21 % [22]. The pyridine neutralizes the HBr byproduct and prevents its reaction with **4**.



Scheme 1 Synthesis of the γ-acetylated β-O-4 ketone dimer lignin model compound **4**

Compound **4** (0.20 M), on treatment with 5 mol % $Ru(H)_2(CO)(PPh_3)$(xantphos) (**Ru***) in toluene-d_8 at 135 °C for 20 h under Ar or H_2 is converted completely to hydrogenolysis products: 3,4-dimethoxypropiophenone (**5**), guaiacol (**6**), 3,4-dimethoxyacetophenone (**7**), 2-methoxyphenyl acetate (**8**), 2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)-1-oxo-2-propene (**9**), and the cyclobutyl(diketo)tetramer (**10**) (Scheme 2); mono-aryl product yields up to 42 % were observed (Table 1: Entry II). All of the products except **10** were identified (as well as PPh_3) using GC/MS; presumably, the larger molecular size of **10** prevents its elution through the GC column. The findings contrast sharply with our previous results using non-acetylated substrates where the γ-hydroxyl group interacted to form catalytically inactive Ru complexes that were fully characterized [12]. Of note, just prior to the submission of our paper, Li and co-workers, who had followed up studies by our group [12] and those of Bergman and Ellman [13], reported that a 'dimer' (bis-aryl) LMC containing a γ-OH group could be degraded in toluene at 125 °C over 12–48 h under Ar using $RuHCl(CO)(PPh_3)_3$ and KOH ***in the absence*** of xantphos [38]. As with our acetylated substrate (Table 1), consumption of the dimer LMC approached 100 %, with one mono-aryl product being formed in 26 % over 24 h (others were present in <10 %), and the fate of most of the substrate was unaccounted for; dimerized products akin to **10** were not mentioned. Although not discussed, the conditions suggest a heterogeneously catalyzed system, and deeper insight into the mechanism of this KOH promoted method is needed.

The yields of **5** and **6** are significantly higher under H_2 (vs. under Ar), a consequence of the two equivalents of H_2 necessary for their formation from **9** (vide infra). Yields of **7** and **8** are comparable under either atmosphere. The yields of **10** could not be determined because of



Scheme 2 Products of the catalytic hydrogenolysis of **4**. See Scheme 5 for a representation of **10**

Table 1 Catalytic hydrogenolysis of **4** (Scheme 2) and 9 (Scheme 5) after 20 h

Entry	Substrate[a]	Catalyst	Gas[b]	Consumpn.[c]	**5**[c]	**6**[c]	**7**[c]	**8**[c]	**9**[c]	**10**[c]
I	**4**	**Ru***	Ar	100	9	20	25	24	17	≤39[d]
II	**4**	**Ru***	H_2	100	27	42	19	18	9	≤31[d]
III	**9**	**Ru***	Ar	85	8	13	0	0	–	72
IV	**9**	**Ru***	H_2	86	15	23	0	0	–	≤63[d]
V	**9**	None	Ar	81	0	<2	0	0	–	75
VI	**9**	None	H_2	82	0	<2	0	0	–	77

[a] 0.20 M

[b] 1 atm

[c] Average consumption and yield (average of duplicate experiments) determined by ^{1}H NMR integration

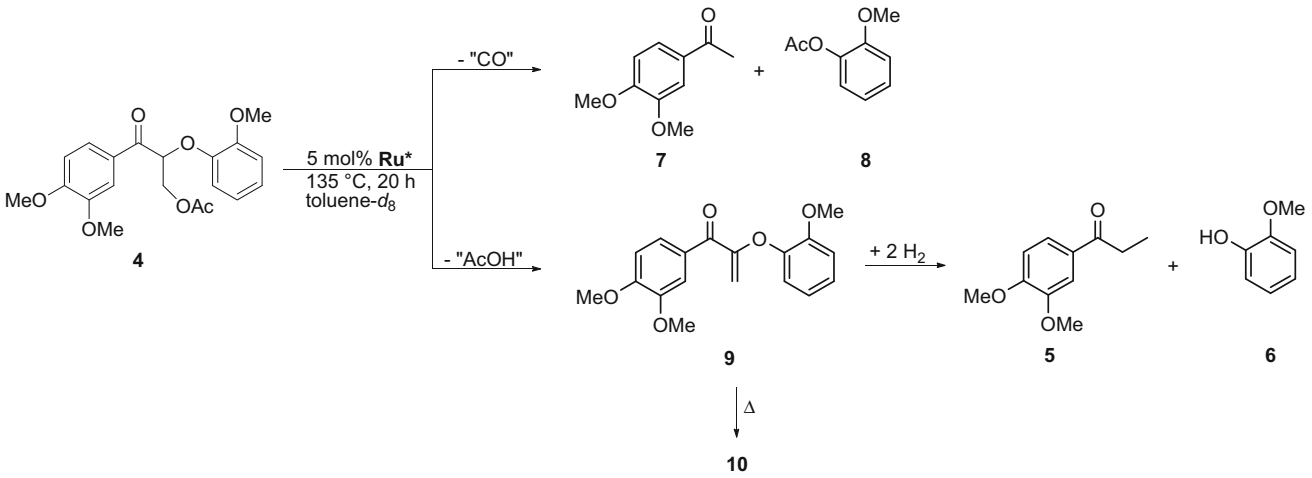
[d] Overlapping signals prevent determination of yield; the upper limit is given, based on mass balance

overlapping ^{1}H NMR signals for the 'bridging' cylcobutyl protons but, based on mass balance, the upper limits are 39 % under Ar and 31 % under H_2. In the absence of the Ru–xantphos catalyst, no reaction of **4** is observed under H_2 or Ar.

The solution ^{1}H NMR spectrum at the end of a Ru-catalyzed reaction of **4** under Ar or H_2 shows no high-field Ru-hydride signals, and, consistent with this, the ^{31}P NMR spectrum shows no P–H coupling patterns. Free PPh_3 ($\delta_P = -4.7$) is seen in the $^{31}P\{^1H\}$ NMR spectrum, in agreement with the GC/MS data; seen also are unassigned diamagnetic signals at $\delta_P = 22.1$, 26.9, 33.5, 39.8, 42.8, and 49.4, presumably of new Ru–xantphos non-hydride species.

3.2 Proposed Pathway for the Hydrogenolysis

The catalyzed hydrogenolysis of **4** yields multiple products, implying complex mechanistic pathways. Cleavage of **4** to give mono-aryl products **7** and **8** occurs in the presence of **Ru*** (Scheme 3). The yields of **7** and **8** under H_2 or Ar (Table 1) suggest they are formed from one molecule in an H_2-free process; the mass balance by-product for such a process is CO, via a net catalytic decarbonylation. This is a well-known Ru-catalyzed reaction [39–41] that has been reported for acetic acid [41], but to our knowledge not for an acetyl group. A reviewer suggested other pathways, both involving formation of **3** as an intermediate: one involved acetyl transfer from **4** to **6** to give **8** and **3**, which then undergoes a retro-aldehyde reaction to form **2** and HCHO (Scheme 1); the aldehyde could decompose into CO and H_2, the latter reacting with **2** to give **7** and **6**, which then picks up the acetyl again to form **8**; the second suggestion hinged on an initial dehydrogenation of the CH_2OH group of **3**, followed by decarbonylation of the aldehyde product. We thus exposed equimolar amounts of **6** and **4** to the 'standard' catalysis conditions, and found that **3** was not formed, while **4** was totally consumed according to the observed catalysis profile (Table 1, Entry I); pathways involving **3** thus look unlikely, and indeed we have established that such γ-OH functional groups lead to formation of catalytically inactive



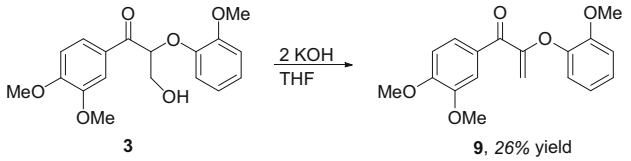
Scheme 3 Proposed mechanistic pathways for hydrogenolysis of **4**

Ru species (see Introduction). Some key mechanistic details of Scheme 3 thus remain unclear.

Control experiments also showed that **6** does not react with AcOH to yield **8** (under the catalytic conditions with Ar or H_2), but does react quantitatively with AcBr to give **8**. Thus, the formation of **8** requires C–O cleavage and intramolecular transfer of the acetyl group to the guaiacol oxygen; the formation of **7** requires the cleavage of the C_β−C_γ bond.

Formation of **9** was surprising (Scheme 3). A mono-aryl species featuring a terminal alkene group has been formed as a final product in the degradation of a dimer LMC using a vanadium catalyst, and a radical mechanism was suggested [36]. In our system, **9** is an intermediate, as evidenced by the higher 4 h yields (40 and 50 % for H_2 and Ar, respectively) compared to the 20 h yields (9 and 17 %, respectively; Table 1). The mass balance by-product of the **4**–**9** conversion is AcOH, but this could not be confirmed by ^{1}H NMR spectroscopy because of overlapping signals for the CH_3 groups of both species ($\delta_H = 1.6$ in toluene-d_8). Hydrogenolysis of **9** via C–O cleavage at the β-O-4 linkage, involving two equivalents of H_2, would generate **5** and **6**; indirect support for this mechanism is the higher yields of **5** and **6** observed when the reaction is performed under H_2. In addition, **9** can dimerize to give **10**.

These mechanistic pathways have been supported by an independent synthesis of **9** from **3** (Scheme 4), followed by its exposure to catalytic conditions. The ^{1}H NMR spectrum of **9** in $CDCl_3$ shows coupled doublets for the two inequivalent C=CH_2 protons ($\delta_H = 4.70$ and 5.20, $^2J_{HH} = 2.4$ Hz). This type of dehydration reaction has been reported for the synthesis of an analogous compound, 1-(4-ethoxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-1-oxo-2-propene, by treatment of the corresponding γ-OH species with $POCl_3$ in pyridine [42]. However, the synthesis of **9** using this



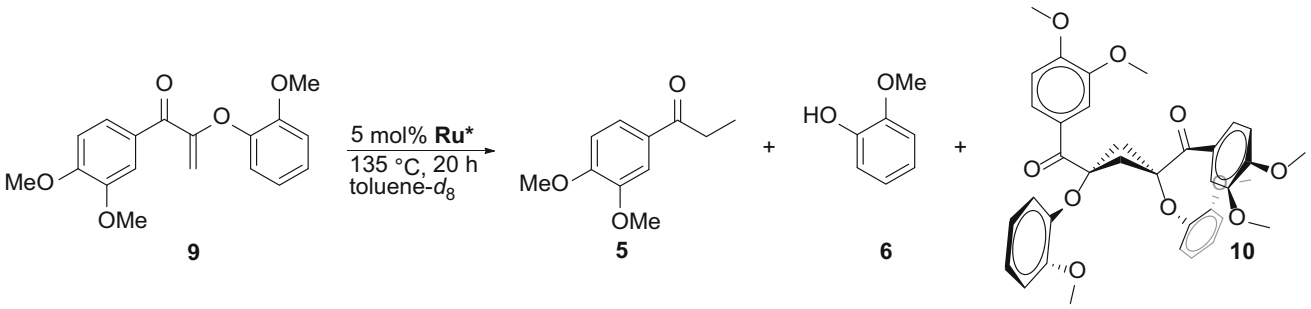
Scheme 4 Synthesis of **9** (26 % yield) from intermediate **3**

procedure was unsuccessful because isolation via silica gel chromatography could not be effected.

Under the catalysis conditions for 20 h under Ar or H_2, **9** is 85–86 % consumed to give hydrogenolysis products **5** and **6**, and **10** (abbreviated as the 'tetramer'); see Scheme 5 and Table 1: Entries III and IV. The **5** and **6** yields are low (<25 %), being best under the H_2 conditions. No **7** and **8** products (*cf.* Scheme 3, top) were observed by ^{1}H NMR or GC/MS. Most of **9** was converted into **10** under either Ar or H_2 (72 and 63 % yield respectively) but, even in the absence of catalyst under otherwise identical conditions, similar conversion is seen, and with no hydrogenolysis products (**5** and **6**, Table 1: Entries V and VI). Thus, **9** mainly dimerizes to give **10**.

The ^{1}H NMR spectrum for the reaction of **9** (like that of **4**) under catalytic conditions shows no Ru-hydride signals, and is similar to that observed for the reaction of **4**, while the ^{31}P{^{1}H} NMR spectrum again shows free PPh_3 and a similar set of unidentified resonances (at $\delta_P = 14.7$, 31.9, 44.7, and 47.4).

Compound **10** was isolated in 50 % yield by heating **9** in toluene at 135 °C for 20 h under Ar, with unconverted **9** being recovered in 36 % yield. The ^{1}H NMR spectrum of **10** in $CDCl_3$ shows multiplets at $\delta_H = 2.32$–2.48 (2H), 2.58–2.71 (1H), and 2.80–2.95 (1H) for four coupled protons, and these signals are assigned to the two 'bridging' cylcobutyl CH_2/CH_2 groups. The OCH_3 protons appear as



Scheme 5 Products of the catalytic hydrogenolysis of **9**

six singlets (δ_H = 3.63, 3.73, 3.80, 3.83, 3.87, and 3.91), and there are twice as many $^{13}C\{^1H\}$ NMR signals than are present in the monomer unit **9**. These data support a structure such as that proposed in Scheme 5—any dimer structure allows for the calculated yields of **10** (Table 1). Despite numerous attempts, no X-ray quality crystals of **10** could be grown to confirm this structure. A variable temperature ^1H NMR study (25–90 °C) was undertaken to see if the six OCH_3 signals would coalesce to three due to symmetry at elevated temperatures (Fig S7, Table S1). Repeat 25 °C data showed that no decomposition occurred up to 90 °C. In contrast to the six OCH_3 signals observed in $CDCl_3$, only five signals were seen at 25 °C, but one of them (δ_H = 3.40) had a double integration value for six protons, due to two overlapping signals. The signals shift downfield with increasing temperature, but at different rates, causing two signals to appear as one at 70 °C; however, above this temperature, these revert to two signals. The non-coalescence is consistent with a non-symmetrical structure, as exemplified in Scheme 5. Preliminary calculations were also performed to explore the lack of symmetry in **10**. Two geometries possessing C2 symmetry, and two with no symmetry, were optimized using density functional theory (B3LYP/6-31G*); optimization to local energy minima revealed that none of the structures contained symmetry elements, the lowest relative energy structure (3.3–5.8 kcal/mol lower than the other minima) being shown in Scheme 5 (see also Fig S8). This structure is one of many orientations that do not possess C2 symmetry, and is consistent with six OCH_3 signals in the ^1H NMR spectrum. The mechanism of the net dimerization of **9** → **10** is unclear but, because 2 + 2 cycloadditions are thermally forbidden, reaction between two molecules of **9** behaving differently, for example, one more nucleophilic and one more electrophilic, must be involved; this is indirectly consistent with **10** having no C2 symmetry.

3.3 Catalytic Hydrogenolysis of Acetylated Lignin

Having established the successful hydrogenolysis of **4**, we subjected an acetylated kraft lignin to the catalytic conditions noted above. Despite the increased solubility of lignins upon acetylation [28, 29], 15 mg of acetylated lignin was not totally dissolved in 0.5 mL of toluene-d_8 even at elevated temperatures (135 °C). However, a significant change is observed in the ^1H NMR spectrum with an increase in the number of signals observed from δ_H = 3.2–3.6 (Fig S9), suggesting that more species with OCH_3 groups are in solution, presumably from a degradation process. Other qualitative differences appear in the aromatic region (δ_H = 6.5–9.0); however, the identities of these new species are impossible to discern due to overlapping NMR signals. A control experiment performed in the absence of the Ru catalyst did not show an increase of signals in this region (Fig S10). While ^1H NMR does not identify reaction products, the qualitative data in concert with GC/MS fragmentation patterns assist in determining the types of degradation products. Figure 2 outlines major fragments present in the chromatogram (Fig S11, Table S2), and in addition there are two higher mass fragments (*m/z* 171, 295) that may correspond to a highly substituted mono-aryl species and a dimeric (bis-aryl) compound.

To increase the solubility of the acetylated lignin, varying amounts of *N*,*N*-dimethylformamide (DMF) were added to the J-Young tube as a co-solvent with the toluene-d_8. A previous screening of non-protic, high-boiling, polar solvents, all of which are capable of dissolving a range of lignins, has shown that neat DMF promoted the highest substrate conversion of dimer LMCs [43]. Unfortunately, this conversion is typically 50 % lower than when toluene-d_8 is used as the solvent [43]. This decrease in activity, perhaps due to competitive binding of the amide to the Ru, is mirrored in the current study: with increasing percent of DMF, catalytic reactivity decreases. This decline is evidenced by almost identical ^1H NMR spectra before and after the reaction when neat DMF is used with further qualitative data from GC/MS experiments.

Though preliminary, these initial studies with acetylated lignin seem promising. When native lignin is exposed to these reaction conditions, no change in the ^1H NMR spectrum is observed, probably due to the complete lack of solubility in toluene-d_8. Current research is focused on the

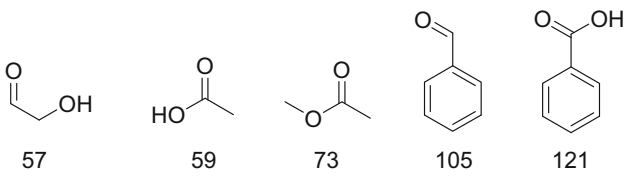


Fig. 2 Mass fragments corresponding to signals observed in GC/MS chromatogram

separation and characterization of the degradation products formed during catalysis.

4 Conclusions

Reported here is the first catalytic hydrogenolysis of a γ-acetylated lignin model compound (**4**) with a Ru–xantphos catalyst; this contrasts with the noted non-acetylated (γ-OH) models that form catalytically inactive Ru species [12]. The catalysis products include a β-O-4 dimer with a terminal alkene group (**9**) that can undergo further catalysis to yield two mono-aryl products (**5** and **6**) and a dimerization product (**10**). The formation of **5**, **6**, and **10** from **9** was confirmed by using an independently synthesised **9** as a substrate. This finding also proved that **7** and **8** are catalytic hydrogenolysis products formed directly from the γ-OAc substrate **4**. The catalytic methodology was also applied to an acetylated kraft lignin with promising preliminary results, including detection of mono-aryl fragments using GC/MS.

Acknowledgments We thank the NSERC Lignoworks Network for funding, Weyerhaeuser Co (Seattle, WA, USA) for supplying the acetylated lignin, and a reviewer for constructive comments.

References

1. Thilakaratne R, Brown T, Li YH, Hu GP, Brown R (2014) Green Chem 16:627
2. Saha B, Abu-Omar MM (2014) Green Chem 16:24
3. Osatiashtiani A, Lee AF, Brown DR, Melero JA, Morales G, Wilson K (2014) Catal Sci Technol 4:333
4. Rahimi A, Azarpira A, Kim H, Ralph J, Stahl SS (2013) J Am Chem Soc 135:6415
5. Heracleous E, Lemonidou A (2013) Platinum Met Rev 57:101
6. Hanson SK, Wu R, Silks LAP (2012) Angew Chem. Int Ed 51:3410
7. Azadi P, Carrasquillo-Flores R, Pagan-Torres YJ, Gurbuz EI, Farnood R, Dumesic JA (2012) Green Chem 14:1573
8. Collinson SR, Thielemans W (2010) Coord Chem Rev 254:1854
9. Zakzeski J, Bruijnincx PCA, Jongerius AL, Weckhuysen BM (2010) Chem Rev 110:3552
10. Saito T, Brown RH, Hunt MA, Pickel DL, Pickel JM, Messman JM, Baker FS, Keller M, Naskar AK (2012) Green Chem 14:3295
11. Sergeev AG, Hartwig JF (2011) Science 332:439
12. Wu A, Patrick BO, Chung E, James BR (2012) Dalton Trans 41:11093
13. Nichols JM, Bishop LM, Bergman RG, Ellman JA (2010) J Am Chem Soc 132:12554
14. Yang Q, Shi J, Lin L, Peng L, Zhuang J (2012) Bioresour Technol 123:49
15. Shimizu S, Yokoyama T, Akiyama T, Matsumoto Y (2012) J Agric Food Chem 60:6471
16. El-Zawawy WK, Ibrahim MM, Belgacem MN, Dufresne A (2011) Mater Chem Phys 131:348
17. Kim YS, Chang H-M, Kadla JF (2008) Holzforschung 62:38
18. Del Río JC, Gutiérrez A, Martínez ÁT (2004) Rapid Commun Mass Spectrom 18:1181
19. Ralph J (1996) J Nat Prod 59:341
20. Del Río JC, Marques G, Rencoret J, Martínez ÁT, Gutiérrez A (2007) J Agric Food Chem 55:5461
21. Lu F, Ralph J (2002) Chem Commun 1:90–91
22. Lu F, Ralph J (1996) Holzforschung 50:360
23. Zhang L, Gellerstedt G (2007) Magn Reson Chem 45:37
24. Capanema EA, Balakshin MY, Kadla JF (2005) J Agric Food Chem 53:9639
25. Qu C, Kishimoto T, Kishino M, Hamada M, Nakajima N (2011) J Agric Food Chem 59:5382
26. Nimz HH, Lüdemann HD (1976) Holzforschung 30:33
27. Sonoda T, Ona T, Yokoi H, Ishida Y, Ohtani H, Tsuge S (2001) Anal Chem 73:5429
28. Obataya E, Shibutani S, Minato K (2007) J Wood Sci 53:408
29. Mörck R, Kringstad Knut P (1985) Holzforschung 39:109.
30. Pu Y, Ragauskas AJ (2005) Can J Chem 83:2132
31. Pizzi A, Zhou X, Navarrete P, Segovia C, Mansouri HR, Placentia Pena MI, Pichelin F (2013) J Adhes Sci Technol 27:252.
32. Hoeger IC, Filpponen I, Martin-Sampedro R, Johansson L-S, Österberg M, Laine J, Kelley S, Rojas OJ (2012) Biomacromolecules 13:3228
33. Qian Y, Deng Y, Qiu X, Li H, Yang D (2014) Green Chem 16:2156
34. Ghosh I, Jain RK, Glasser WG (1999) J Appl Polym Sci 74:448
35. Fulmer GR, Miller AJM, Sherden NH, Gottlieb HE, Nudelman A, Stoltz BM, Bercaw JE, Goldberg KI (2010) Organometallics 29:2176
36. Son S, Toste FD (2010) Angew Chem. Int Ed 49:3791
37. Cho DW, Parthasarathi R, Pimentel AS, Maestas GD, Park HJ, Yoon UC, Dunaway-Mariano D, Gnanakaran S, Langan P, Mariano PS (2010) J Org Chem 75:6549
38. Huo W, Li W, Zhang M, Fan W, Chang H-M, Jameel H (2014) Catal Lett 144:1159
39. Baird IR, Rettig SJ, James BR, Skov KA (1998) Can J Chem 76:1379
40. James BR, Addison AW, Cairns M, Dolphin D, Farrell NP, Paulson DR, Walker S (1979) In: Tsutsui M (ed) Fundamental research in homogeneous catalysis, ch. 50. Springer, New York
41. Chow BC, Cohen IA (1971) Bioinorg Chem 1:57
42. Enoki A, Goldsby G, Gold M (1981) Arch Microbiol 129:141
43. Lauzon JMP, James BR Unpublished results. A summary of the findings is available in Table S3 in the ESI