EurJOC
European Journal of Organic Chemistry

A Journal of ChemPubSoc Europe

Accepted Article

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201801112

Link to VoR: http://dx.doi.org/10.1002/ejoc.201801112

Supported by ACES Asian Chemical Editorial Society

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10.1002/ejoc.201801112

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Selective Catalytic Methylation of Phloroglucinol with Dimethyl Carbonate in the Presence of Heterogeneous Acids

Matthew Y. Lui,[a] Marco Noè,[a] Anthony F. Masters,[a] and Thomas Maschmeyer*[a]

Abstract: A facile process for the methylation of phloroglucinol using environmentally friendly dimethyl carbonate as methylating agent and solvent is described. Widely available and inexpensive solid acids have been used as catalysts to promote this transformation. H-Y zeolite proved particularly selective for monomethylation, hence it has been used for the convenient preparation of methoxyresorcinol (MR), with only limited co-production of dimethoxyphenol (DMP). Conversely, the use of tungstosilic acid on silica easily afforded DMP in excellent isolated yield.

Introduction

The transition towards a carbon neutral economy, based on the use of renewable resources is one of the major factors prompting research in many fields of science.[1] Specifically, the quest for new processes allowing the transformation and use of chemicals from renewables, such as biomass, represents one of the topics gaining considerable attention from both scientists and policy makers.[2] Several chemical solutions aimed at exploiting products from renewables have been investigated and many promising processes and products representing the foundation of the future biorefining industry have been described.[3] However, these processes do not easily generate cheap aromatic building blocks. Hence, a path for the exploitation of a bio-based source of aromatics is seen as one of the main challenges of Green Chemistry.[4] Methods to depolymerize lignin, the most abundant renewable source of aromatics, have been intensively researched in the past decade.[5]

Alternatively, brown algae are known to contain large amounts (up to 20 % dry weight) of a class of polyphenols, namely phlorotannins,[6] oligomers of phloroglucinol (1,3,5 trihydroxybenzene, PG) (Figure 1). PG is a very promising phenolic compound that is used in the pharmaceutical, cosmetic and dyeing industries.[7]

Yet, the depolymerization of phlorotannins has not been investigated extensively. Furthermore, phlorotannins are currently commercially far less readily available than is lignin. A promising route for the production of bio-derived phloroglucinol has been investigated by Frost and co-workers. In 2005 they described the biosynthesis of phloroglucinols encoded by the phlACBDE gene cluster found in Pseudomonas fluorescens Pf-5.[8] A decade later, Abdel-Ghany et al. reported the biosynthesis of phloroglucinols using a transgenic Arabidopsis plant with an enzyme encoded by phID gene.[9] These findings illustrate the possibility of producing bio-derived phloroglucinol at scale.

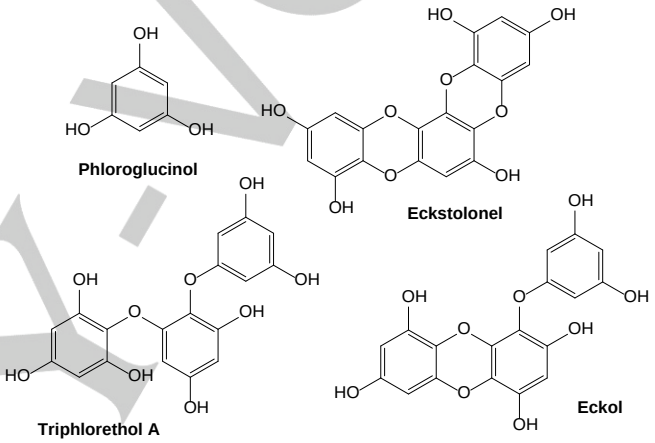

Figure 1. Phloroglucinol and three examples of phlorotannins (Eckstolonel, Triphlorethnol A and Eckol)

Often, during the processing of phloroglucinol in the preparation of fine and pharmaceutical chemicals, it is first methylated to block one or two of its hydroxylic functional groups prior to further transformations.[10] The mono-methylated derivative (flamenol, 5-methoxyresorcinol, MR) is particularly valuable, as reflected in its market price.[11]

Commonly reported methods for PG methylation require the use of methanol as methylating agent and a Brønsted acid such as H_2SO_4 or HCl as the catalyst.[12] This protocol suffers from low selectivity towards the desired MR derivative since dimethylated (3,5-dimethoxyphenol, DMP) or even trimethylated (1,3,5-trimethoxybenzene, TMB) products form well before the reaction reaches complete conversion. Another undesirable feature of this procedure is the use of toxic, volatile methanol. Furthermore, greater than stoichiometric amounts of Brønsted acid need to be quenched by neutralization with base, leading to the formation of large amounts of salts to be disposed of or extensive volumes of aqueous waste. The preparation of methoxyresorcinol via methylation of phloroglucinol clearly needs a better procedure that overcomes these issues.

The use of dimethyl carbonate (DMC) as a Green methylating agent is well established.[13] It compares favorably with methanol in terms of their relative toxicities. Methylation of phenols with DMC using heterogeneous (usually basic) catalysts was studied in detail and numerous studies can be found in the literature.[14]

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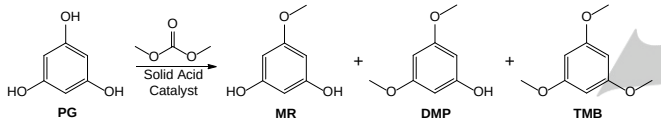
However, the reaction of DMC with phenols in the condensed phase at lower temperatures is often carried out using homogeneous catalysts. Indeed, our group and others have reported the use of base or nucleophilic catalysts for the methylation of phenols with DMC in condensed phases.[15] Nonetheless, separation and subsequent recycling of catalysts are difficult to achieve in these reaction systems.

To the best of our knowledge, no previous investigations on the methylation of phloroglucinol using heterogeneous catalysis, nor one using DMC as methylating agent have been reported. In the present work the methylation of phloroglucinol and other trihydroxy and dihydroxy benzenes have been investigated using easily separable, robust and inexpensive solid acid catalysts (Scheme 1). This work also demonstrates the use of focused microwave-mediated heating in a batch reactor set-up that allows accurate control of the reaction temperatures and times as well as real time monitoring of the reactor pressure. Modern microwave instruments also enable DMC to be superheated in a closed vessel, thereby reducing the reaction time. Using heterogeneous catalysts, in combination with an "industry-friendly" Green solvent/reactant such as DMC makes this investigation of interest for future industrial scale preparation of phloroglucinol derivatives as part of biorefinery strategies.



Scheme 1. Methylation of Phloroglucinol (PG) with dimethyl carbonate (DMC) using solid acid catalysts.

Results and Discussion

Our previous study[15b] on the DBU or NHC-catalyzed methylation of phenols demonstrate that DMC itself is not a reactive methylating agent and activation of DMC (e.g. by a nucleophilic catalyst) is desirable for effective methylation. A simple base is not able to activate DMC to render it more reactive. Nonetheless, the methylation of phloroglucinol has been reported to proceed under acidic conditions with methanol.[12] These considerations prompted us to consider acidic catalysis, with DMC as methylating agent. With the aim of developing a truly Green chemical process, solid or solid supported catalysts were considered the best alternative to H_2SO_4 and HCl. For the same reason no additional solvents were employed and DMC was used in excess as solvent/reagent.

A first screening using different catalysts was conducted to test the reactivity of PG dissolved in DMC at 155 °C and 165 °C in a catalyst to substrate ratio of 1:1 by weight. The results obtained for different catalysts are summarized in Table 1.

Table 1. Catalyst screening for methylation of PG with DMC.

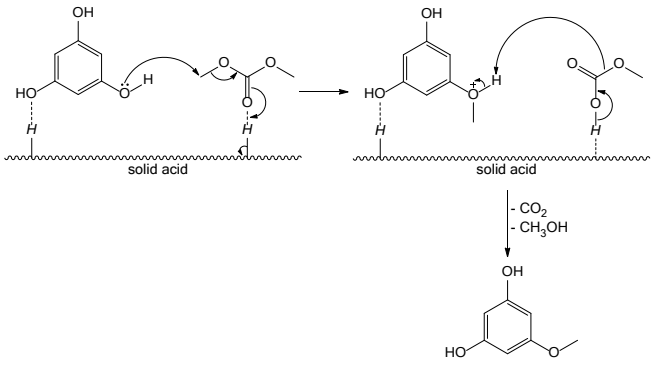
Entry	Time (min)	Catalyst[a]	Conv. (%)[b]	MR (%)[b]	DMP (%)[b]	TMB (%)[b]	MR Sel (%)[b]
1	40	Acidic Al_2O_3	-	-	-	-	-
2	40	γ-Al_2O_3	-	-	-	-	-
3	40	Na-Y Zeolite	-	-	-	-	-
4	40	H-Y Zeolite	6	6	-	-	100
5	240	H-Y Zeolite	70	68	2	-	98
6[c]	40	H-Y Zeolite	11	11	-	-	100
7[c]	240	H-Y Zeolite	80	71	8	-	89
8[d]	40	H-Y Zeolite	-	-	-	-	-
9	40	H-ZSM-5	1	1	-	-	-
10	40	TS/SiO_2	100	-	91	-	-
11	10	TS/SiO_2	84	57	21	-	68
12	40	Nafion SAC13	52	48	3	-	92
13	40	Nafion NR50	100	11	77	4	11
14	20	Nafion NR50	85	37	40	1	44

[a] 200 mg of catalyst was mixed with 200 mg of phloroglucinol and 3 mL of DMC in a 10 mL glass tube. The tube was heated in an Anton Paar Monowave 300 microwave synthesis reactor with a stirring rate of 600 rpm. [b] conversion carried out at 155 °C unless stated otherwise; data determined by GC-FID (on derivatized product). [c] conversion carried out at 165 °C. [d] MeOH was used in place of DMC.

Slightly acidic materials such as acidic alumina, γ-Alumina, Na-Y zeolite were not able to catalyze the methylation reaction and not even traces of the desired products were detected (entries 1–3). Only the use of stronger acidic materials like H-Y zeolite (entries 4–7), tungstosilicic acid (entries 10 and 11) or sulfonated fluoroethylene polymers (entries 12–14) promoted the reaction.

Both the silica-supported tungstosilicic acid (TS/SiO_2) and the two forms of Nafion tested proved to be very efficient, leading to very high conversions in short times. Using H-Y as the catalyst and conducting the reaction over a longer time (240 min, entry 5 and 7) also afforded high conversions of up to 98 %.

It is proposed that DMC is activated by the acidic site through its carbonyl oxygen, a process which renders the methyl group of DMC more electrophilic.[16] Moreover, PG could be absorbed onto an adjacent site of the solid acid by hydrogen bonding (Scheme 2).[17] Alkylation occurs when the oxygen atoms of PG nucleophilically attacks the methyl group of the activated DMC. The methylcarbonate moiety, formed as a result of alkylation, then decomposes[18] to form carbon dioxide and methanol as byproducts via proton transfers (Scheme 2).



Scheme 2. Proposed mechanism for the methylation of phloroglucinol with DMC over solid acid catalysts; "*H*"s in italics indicate acid sites on solid acid.

As discussed in the introduction, a process for the selective monomethylation of PG to obtain MR would be very valuable. Selectivity towards MR was still very high (98%) when H-Y zeolite was used as the catalyst, even at 70% conversion, while, in the case of TS/SiO_2, when 84% conversion was achieved, selectivity had already dropped to 68%. SAC13 is even less selective, i.e. at 85% conversion, the selectivity dropped to 44%. Methanol was found to be less reactive than DMC for the acid-catalyzed methylation of PG (entry 8).

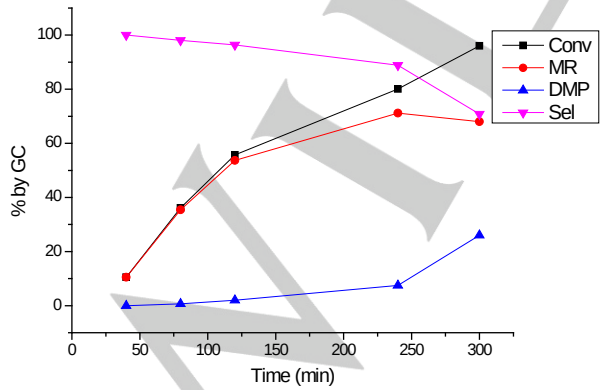


Figure 2. Reaction profile for the reaction of phloroglucinol with DMC catalysed by H-Y zeolite at 165 °C. "Sel" indicates selectivity to MR.

A time-course study with H-Y as catalyst at 165 °C (Figure 2) reveals that approximately 100% conversion is reached after 300 min. with selectivity remaining well above 80% until 80% conversion is reached after about 250 min. This observation is consistent with the relative lack of substrate allowing the more difficult follow-on methylation to become more prominent.

We also investigated the dependence of MR yield on temperature and, as expected, the conversion rate of substrate increased with temperature, peaking at around 70% irrespective of the temperature employed (Figure S1, Supporting Information).

This yield limit is further consistent with the previous interpretation of competing substrate concentrations. To further investigate the effect of the temperature on selectivity, the same reaction was carried out for 40 minutes at temperatures of 150, 160, 170, 180 and 190 °C. Conversions of phloroglucinol and selectivities for MR and DMP are illustrated in Figure 3.

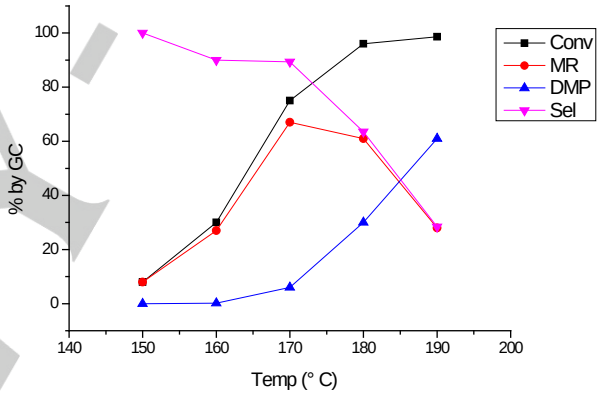


Figure 3. Reactions of phloroglucinol with DMC in the presence of H-Y zeolite at different temperatures after 40 minutes. "Sel" indicates selectivity to MR.

As expected, at higher temperatures H-Y promoted the second methylation step and, hence, the formation of DMP. At 190 °C the GC yield for DMP was approximately 60% after only 40 minutes.

To establish if other active but "less selective" catalysts like TS/SiO_2, Nafion SAC13 and NR50 could be made more selective toward MR under optimized conditions, similar tests at different temperatures were conducted using both TS/SiO_2 and Nafion SAC13 (Figures 4 and S2, Supporting Information).

As indicated in Table 1 both NR50 and TS/SiO_2 catalysts were far more active than was H-Y, and high conversions could be achieved at relatively low temperatures. TS/SiO_2 in particular was so active that the reaction time was reduced to 10 minutes.

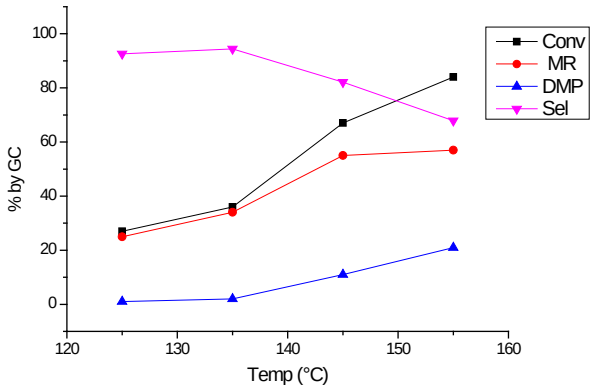


Figure 4. Reactions of phloroglucinol with DMC in the presence of TS/SiO_2 at different temperatures after 10 minutes. "Sel" indicates selectivity to MR.

Using either TS/SiO_2 or Nafion as catalysts, acceptable yields of MR could be achieved (57 and 66 % respectively). However, the selectivity towards MR dropped much more quickly than when H-Y zeolite was used as the catalyst.

The use of TS/SiO_2 at lower temperature for longer reaction times did not improve the outcome of the reaction. Thus, for example, carrying out the reaction at 130 °C for 40 minutes, the selectivity remained around 70 % at 81 % conversion.

The formation of the bis-methylated product, DMP, is more rapid with TS/SiO_2 as catalyst than when using HY zeolite as catalyst. H-Y zeolite not only is inexpensive and readily available, but it also promotes very high selectivities toward the desired product.

Conversely Nafion NR50 showed the lowest selectivity towards the desired mono-methylated product. In fact, not only was DMP produced at relatively low conversion, but also appreciable amounts of TMB could be detected (Table 1, entries 11–12), in contrast to the products obtained with the other catalysts tested.

Since TS and Nafion both exhibit extremely strong acidic behavior: TS being more acidic than p-toluenesulfonic acid[19] and Nafion being a superacid, the results suggested that conversion rates of both PG and MR were significantly dependent on the acidity of the catalysts.

It is well known that Si/Al ratios affect the abundance of active sites and the acid/base properties of zeolites.[20] To verify that acidity has the major influence on the outcome of the reactions, several zeolite of different Si/Ai ratios were prepared and tested as catalysts.

First, the behavior of a highly acidic zeolite such as H beta zeolite (Si/Al: 15) was investigated (Figure S3, Supporting Information).

Unsurprisingly, excellent conversions were achieved at relatively low temperatures and low selectivities toward MR were observed. DMP was obtained as the major product (50 %). Remarkably, temperatures above 170 °C could not be explored, since the pressure reached the maximum allowed for our system, *i.e.* 32 Bar.

The pressure reached by the vessel furnishes significant information on the reaction outcome. Faujasites/zeolites are reported to promote the decomposition of DMC into dimethyl ether and CO_2 under the conditions used in our investigation.[21] The more acidic the catalyst, the higher the rate of this decomposition pathway. Hence, high-pressures are produced by activation and decomposition of DMC by the acidic zeolite catalyst.

Then, conversions of PG were carried out using X and Y zeolites under similar conditions. Although, the two catalysts possess the identical solid structures and similar pore sizes, their behaviors were vastly different for this process. For instance, using a poorly acidic zeolite like X zeolite (Si/Al: 1.5), the reaction was so slow that no product formation could be observed at 170 °C after 40 minutes, while the pressure remained around 12 bar (Table 2). Conversely, zeolite Y, which has moderate acidity with Si/Ai ratio (2.6) in between of that of β and X zeolites, gave a good yield of MR (67 %) but a small amount of DMP (6 %). Overall, our results demonstrated that the pore size and number of acid sites of catalysts have neligible effects on the performance of the process. Acidity of the catalyst has a major influence on the rate of the process and the yields of MR and DMP.

Table 2. Methylation of PG with DMC using different H form zeolites.

Catalyst	Si/Ai Ratio	Pressure (bar)	Conv. (%)[a]	MR (%)[a]	DMP (%)[a]	MR Sel (%)
H-X Zeolite	1.5	12	-	-	-	-
H-Y Zeolite	2.6	14	75	67	6	89
H-β Zeolite	15	32	96	44	50	46

[a] determined by GC-FID (on derivatized product) after 40 min at 170 °C.

Catalyst recycling. The recyclability of H-Y zeolite as a catalyst for the selective mono-methylation of phloroglucinol was tested. After the reaction was conducted under the best conditions for the highest methoxyresorcinol yield (*i. e.* 170 °C for 40 minutes), the zeolite was separated by centrifugation of the mixture and successively washed with portions of ethyl acetate (3 x 2 mL). The zeolite was then washed with DMC (3 x 2 mL) to remove ethyl acetate and the resulting zeolite impregnated by DMC was used in the following cycle. The procedure was repeated several times and the results thus obtained are reported in Figure 5.

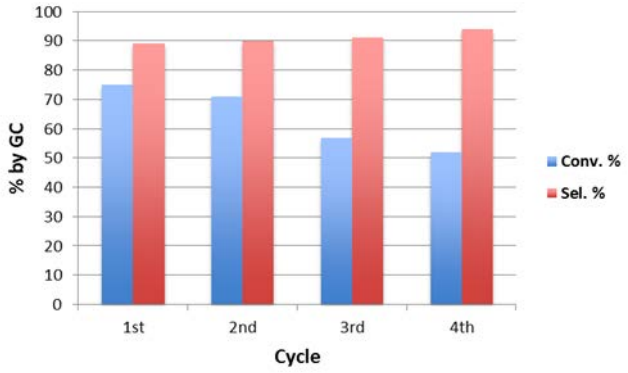


Figure 5. H-Y zeolite recycling for monomethylation of phloroglucinol with DMC (170 °C, 40 min).

The conversion of phloroglucinol dropped from 75 to 52% after the H-Y catalyst was reused 3 times. The selectivity towards the desired mono-methylated product, however, remained remarkably high after recycling of the catalyst (≥90%).

Preparation of 3,5-dimethoxyphenol. Optimized conditions for the preparation of DMP were also investigated. Not only were the most active TS/SiO_2 and Nafion based catalysts used, but H-Y Zeolite was also considered in order to evaluate its ability in promoting the formation of the dimethylated compound (DMP) at higher temperature and by performing the reaction for longer times. The results are summarized in Table 3.

Table 3. Conditions for dimethoxyphenol preparation using different catalysts.

Entry	T (°C)	Catalyst	Conv. (%)[a]	MR (%)[a]	DMP (%)[a]	TMB (%)[a]	Others (%)[a]
1	150	TS/SiO_2	100	-	93	-	7
2	190	H-Y Zeolite	100	10	77	-	13
3	190	Nafion SAC13	100	6	88	-	6
4	150	Nafion NR50	100	11	77	4	7

[a] determined by GC-FID (on derivatized product) after 40 min.

TS/SiO_2 was, as expected, the best performing catalyst. After 40 minutes at a relatively low temperature (150 °C, entry 1), the desired compound was obtained with excellent selectivity (93% yield).

The selectivity was good but lower when using a polymeric material like Nafion NR50 (entry 4). When Nafion was supported on silica (entry 3), a very good selectivity was observed (88% yield), even if a higher temperature (190 °C) was required. Good selectivity for DMP was also achieved using H-Y zeolite at 190 °C (entry 2). To the best of our knowledge, the yield of DMP obtained using TS/SiO_2 as catalyst is the highest among all the reported examples of conversion of phloroglucinol. Overall, none of the catalysts tested was as good as TS/SiO_2 for the preparation of DMP.

To demonstrate the applicability of this protocol for preparative purposes, the optimized procedures for MR and DMP preparation were carried out using 1 g of reactant. The products were purified by column chromatography. As shown in Table 4, the two target compounds, MR and DMP, could be isolated in good yields (62 and 85 % respectively).

Table 4. Preparative experiments.

Entry	T (°C)	Catalyst[a]	MR (%)[c]	DMP (%)[c]
1	170	H-Y Zeolite	62	2
2	150	TS/SiO_2	5	85

[a] 1.00 g of catalyst was mixed with 1.00 g of PG and 15 mL of DMC in a 30 mL glass tube. The tube was heated for 40 min in an Anton Paar Monowave 300 microwave synthesis reactor with a stirring rate of 600 rpm. [b] isolated yield.

Different Substrates. To verify the scope of the reaction protocol, all isomers of mono- di- and trihydroxybenzenes were tested under the optimized conditions for mono and dimethylation of phloroglucinol (Table S1, Supporting Information). Surprisingly, the conversion was much lower when compared to that of PG in all cases, except for hydroxyquinol (1,2,4 trihydroxybenezene, entries 3 and 9). Under the conditions for mono and dimethylation of PG, high conversions (100 and 89% respectively), but low selectivities toward O-methylation (less than 40%) of hydroxyquinol were observed.

This behavior further confirms the particular features of phloroglucinol as a reactant and therefore justifies the study of dedicated processes for its chemical upgrading.

Conclusions

We unveil an environmentally friendly process for the selective methylation of phloroglucinol as a strategy to obtain valuable fine chemicals from a bio-derived aromatic compound. In this study, phloroglucinol was methylated with environmentally friendly DMC, which also acted as the solvent, using easily accessible heterogeneous catalysts such as zeolites, tungstosilic acid and Nafion based materials in short reaction times.

The results indicated that monomethylation of phloroglucinol to yield methylresorcinol can be easily achieved with very high selectivity (up to 98%) using H-Y zeolite in a straightforward process of short reaction time, in which the substrate is treated with DMC as solvent/reagent and the catalyst can be easily removed once the reaction is completed.

Using other catalysts, conversions were higher, allowing the conduct of the reaction at lower temperature and even shorter times. Unfortunately, this led to a drop in selectivities toward the desired MR. However, the most active catalyst, i.e. tungstosilic acid supported on silica, proved highly suitable as catalyst for the preparation of the dimethylated analogue DMP. Therefore, two procedures were optimized for the preparation of MR and DMP using H-Y zeolite and TS/SiO_2 respectively. The DMP yield (93%) obtained using TS/SiO_2 is the highest among all the reported examples of methylation of phloroglucinol. Overall, the performance of this methylation process is governed largely by the acidity of the catalysts.

In order to verify the preparative scope of the procedures, the protocols were also performed on the gram scale, affording the respective target compounds in good isolated yields.

The interest in a dedicated procedure for the methylation of PG is demonstrated by its peculiar reactivity. Under similar conditions, methylation of other phenolic derivatives was considerably more difficult than phloroglucinol. Poor conversions were observed for the methylation of mono-, di and other trihydroxybenzenes under the best conditions for the preparation of MR and DMP.

Experimental Section

Materials. Phloroglucinol ($C_6H_3(OH)_3.2H_2O$) was purchased from Fluka and recrystallised with distilled water before use. DMC was supplied from Aldrich. Acidic Al_2O_3 (Condea Vista Co.), γ-Al_2O_3 (Condea Vista Co.), Nafion® SAC-13 (Aldrich), Nafion® NR50 (Aldrich), Faujasite Na-Y (Zeolyst), H-ZSM-5 (Zeolyst) tungstosilicic acid hydrate (Fluka) silica gel (Grace) and methanol (Redox Chemicals) were used as received. H-beta was synthesized using a modification of the method reported by Klomp and co-workers:[22] $NaAlO_2$ (3.316 g) and a 35% TEAOH solution in water (16 mL) were mixed and stirred for 15 min. To this mixture, LUDOX HS-40 (30 mL) was added. The thick gel formed was transferred to Teflon-lined autoclaves and the gel was heated at 170 °C for 4 days. The autoclaves were quenched with water to room temperature, and the white powder obtained was centrifuged, washed with water 3 times and then dried in air overnight. The white powder was calcined at 550 °C for 15 h. After cooling, Na^+ was exchanged by H^+ by stirring the zeolite for 48 h with a 0.1 M solution of NH_4NO_3 (500 mL). The zeolite was calcined at 450 °C for 15 h to yield a white powder.

Tungstosilic acid on SiO_2, TS/SiO_2 catalyst was prepared using a modification of the method reported by Nasr-Esfahani and co-workers:[23] silica gel (1.4 g) was mixed with a solution of tungstosilicic acid hydrate (0.6 g) in distilled water (20 mL). After removal of water in a rotary evaporator, the resulting solid was dried and calcined in air at 300 °C for 3 h.

Zeolite Na-X was prepared using the method reported by Balkus and Ly.[24] Zeolites H-X and H-Y were prepared from Na-X and Na-Y using the procedure described by Carà and co-workers.[25]

Instrumentation. The Anton Paar Monowave 300 microwave synthesis reactor has the following specifications: magnetron frequency, 2455 MHz; power consumption, 1600 VA; and an AC 230 V ± 10% 50 Hz/60 Hz power supply.

Quantification of the reaction products was performed on a Shimadzu GC-2010 Plus gas chromatograph equipped with Rtx-5MS 0.25 µm × 30 m × 0.25 mm column under the following conditions. The temperature program had an isothermal period of 5 min at 100 °C, then the temperature was increased by 15 °C/min to another isothermal period of 15 min at 300 °C.

Compound identification by GC-MS was performed on a Shimadzu GCMS-QP2010 equipped with Rtx-5MS 0.25 µm × 30 m × 0.25 mm column under the following conditions. The temperature program had an isothermal period of 5 min at 100 °C. Then the temperature was increased by 15 °C/min to another isothermal period of 15 min at 330 °C. Compounds were identified by comparing the EI-MS spectrum with the MS library NIST05.

^{1}H NMR spectra were recorded at 300 MHz at ambient temperature with $(CD_3)_2CO$.^{13}C NMR spectra were recorded at 75 MHz at ambient temperature with $(CD_3)_2CO$.

Conversion of phloroglucinol. A typical procedure for the conversion of phloroglucinol with DMC using solid acid catalysts is as follows: Phloroglucinol (200 mg), catalyst (200 mg) and DMC (3 mL, 29 eqv.) were heated in a 10 mL glass tube, fitted with a pressure cap in an Anton Paar Monowave 300 microwave synthesis reactor with a stirring rate of 600 rpm. After heating, the reaction tube was removed from the microwave reactor and cooled to room temperature. The resulting mixtures were centrifuged to remove the solid catalyst. GC analysis of the product mixture was carried out after derivatization of the hydroxyl groups with Ac_2O:pyridine (6:1) for better quality of separation.[26] For isolation of products, the product mixtures were concentrated *in vacuo* and separated by column chromatography (eluent: hexane/ethyl acetate (gradient)). MR: ^{1}H NMR (300MHz, $(CD_3)_2CO$) δ 3.67 (3H, s), 5.94 (2H, m), 5.98 (1H, m). 8.17 (2H, br); ^{13}C NMR (75MHz, $(CD_3)_2CO$) δ 55.25 (1C), 93.95 (2C), 96.85 (1C), 159.98 (2C), 162.69 (1C). DMP: ^{1}H NMR (300MHz, $(CD_3)_2CO$) δ 3.71 (6H, s), 6.00 (1H, m), 6.03 (2H, m); ^{13}C NMR (75MHz, $(CD_3)_2CO$) δ 55.38 (2C), 92.69 (1C), 94.89 (2C), 160.00 (1C), 162.67 (2C).

Acknowledgements

The authors thank the Australian Research Council, Science and Industry Endowment Fund (SIEF, RP03-028) (M.Y.L.) and the Australia Awards Endeavour Scholarships and Fellowships (M.N.) for financial support.

Keywords: alkylation • biomass • dimethyl carbonate • green solvent • solid acids

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10.1002/ejoc.201801112

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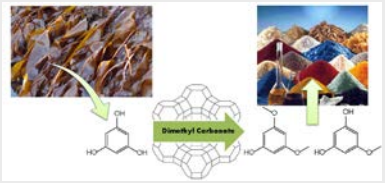

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