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Direct vinylation of natural alcohols and derivatives with calcium carbide Siew Ping Teong, Ariel Yi Hui Chua, Shiyun Deng, Xiukai Li and Yugen Zhang^{*}

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Vinyl ethers are essential synthetic building blocks for organic synthesis, especially for polymer synthesis and highly vinylated polyol substrates. Herein, a transition metal-free, mild and safe protocol for the direct vinylation of natural alcohols with calcium carbide has been developed. Various sugar alcohols, phenol and its derivatives were tested and proved to work using this green methodology. Selectivity of full vinylated products of the reaction decreases with increasing hydroxyl groups due to side reactions occurring under the basic medium. Electron-donating substituted phenols works more efficiently as compared to electron-withdrawing substituted phenols in general. This methodology may provide new insights on selective vinylation of electron-rich biomass-derived materials.

Vinyl ethers are no doubt essential synthetic building blocks for general organic synthesis,¹ particularly used as precursors in polymeric formulations.² Highly vinylated products obtained from the polyol substrates are specifically attractive as they may provide opportunities for developing new biodegradable polymeric materials due to the additional possibilities for modification with the multiple reactive vinyloxy groups. Over the years, various methods have been developed to prepare vinyl ethers³ such as the metal-catalyzed coupling reactions⁴ and elimination reactions⁵. The most simple and convenient method is the direct vinylation of alcohols with acetylene gas, namely, Favorskii-Reppe reaction, which has been used as the industrial process for vinyl ethers since 1960s.⁶ Methods for the direct vinylation of various alcohols using acetylene gas have been reported⁷, while, in general, harsh conditions were employed with dedicated laboratory set-up for the gaseous reagent and high pressure conditions. Polyols and phenol are derivatives from sustainable nature carbohydrates, such as cellulose, hemicellulose and lignin.⁸ The direct full vinylation of polyols and phenol is still a great challenge (Scheme 1).^{7, 9, 10} In recent years, calcium carbide has been used increasingly by our group¹¹ and others¹² as a sustainable, easy-to-handle, and low-cost feedstock in organic synthesis. Particularly, vinylation reactions of benzylic alcohols¹³, thiols¹⁴ and indoles¹⁰ with calcium carbide as acetylene source have been reported very recently. During the preparation of this manuscript, vinylation of substituted electronrich phenol substrates (4 examples) was also reported¹⁰. The direct vinylation of glycerol and phenol with calcium carbide was investigated, however, it was reported that no reaction was

observed¹¹⁻¹³. Herein, we developed a transition metal-free, mild and simple methodology for the direct vinylation of natural alcohols (polyols and phenols) with calcium carbide (Scheme 1).





We first begin our study using a simple diol, 1,5-pentanediol which is commonly synthesized by hydrogenation of glutaric acid, furfural and their derivatives.¹⁵ Various bases and solvents were screened with the reaction conditions optimized (Table 1). DMSO was the best solvent for this reaction as it forms superbase system with even catalytic amount of Cs_2CO_3 . In contrast, no desired product was observed for the polar aprotic DMF. The reaction proceeded efficiently in DMSO/H₂O with calcium carbide (3 mmol) in the presence of Cs_2CO_3 (0.3 mmol) at 120 °C for 8h, yielding 99% of the desired product (Table S1, Entry 8). High yield and selectivity of 98% was also obtained for the shorter chain diol, ethylene glycol,¹⁶ at shorter reaction time of 3h (Scheme 2).



S. P. Teong, A. Y. H. Chua, S. Deng, Dr. X. Li and Dr. Y.G. Zhang. Institute of Bioengineering and Nanotechnology, 31 Biopolis Way, The Nanos, Singapore 138669, Singapore. E-mail: ygzhang@ibn.a-star.edu.sg Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See

Scheme 2. Vinylated products: 1,5-bis(vinyloxy)pentane 3b and 1,2-bis(vinyloxy)ethane 4

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Table 1 Base and Solvent Screening⁴



Entry	Base	Solvent	Yield ^b (%) 3a:3b	
1	-	DMSO + 4 vol% H $_{2}^{\circ}$	NR	
2	CsOH	DMSO + 4 vol% H_{2}^{0}	11:88	
3	Cs ₂ CO ₃	DMSO + 4 vol% H_{2}^{0}	12:87	
4	ĸŢĊŎŢ	DMSO + 4 vol% H_{2}^{0}	13:0	
5	NaCO	DMSO + 4 vol% H_{2}^{0}	NR	
6	NaHCO	DMSO + 4 vol% H_{2}^{0}	NR	
7	DBU	DMSO + 4 vol% H_{2}^{0}	NR	
8	TEA	DMSO + 4 vol% H_{2}^{0}	NR	
9	Cs _c Co ₃	Anhydrous DMSO	trace : 0	
10	Cs_CO_	DMF + 4 vol% H ₂ O	NR	
11	Cs [°] CO [°]	CH ₂ CN + 4 vol% H ₂ O	NR	
12	Cs¯CO	THF + 4 vol% H ₂ O	NR	
13	Cs [°] CO [°]	Dioxane + 4 vol ⁵ H ₂ O	NR	
^a Reaction conditions: Diol (1 mmol), CaC ₂ (4 mmol), solvent (5 mL),				

base (0.3 mmol), 120 °C, 3 h. ^b NMR yield.

Delighted with the results, we expanded the methodology on other polyols (Scheme 3 - 5). The increase in hydroxyl groups resulted in more calcium carbide to be added and hence, the amount of water has to be adjusted. An optimized yield of 69% was obtained for the vinylation of glycerol¹⁷ with the starting material fully converted (Scheme 3). Heating the reaction at 120 °C for glycerol resulted in lower yield (Table S2, Entries 9 - 11), with possible acetal formation while a longer reaction time (16 h) was required for the reaction to reach the optimum yield (68%) at 80 °C (Table S2, Entry 13). Additives like TBAB, KBr and 18-crown-6 were added and proved to have no enhanced effect on the yield.



Scheme 3. Vinylation of glycerol with calcium carbide: Glycerol (1 mmol), CaC_2 (6 mmol), Cs_2CO_3 (1.2 mmol), DMSO + 7 vol% H₂O, 100 °C, 3 h.

This simple methodology also works for polyols like erythritol¹⁸ and xylitol,^{18, 19} albeit lower selectivity due to side reactions that occurred in this basic medium. 43% yield was obtained for erythritol (Scheme 4) whereas only trace amount (<5%) was detected for xylitol (Scheme 5). Side products isolated for both reactions were attributed to the well-known side process of base-catalyzed vinylation resulting in the formation of cyclic acetals^{7c}. Interestingly, as the reaction time was prolonged to 18 h for erythritol reaction, we observed elimination of the terminal vinyl ethers, resulting in the formation of product **8b** in 49% yield and

other uncharacterized volatile products. Herein, **8b** is generated by elimination of vinyl alcohol from **8a**.²⁰ DOI: 10.1039/C6GC03579E



Scheme 4. Vinylation of erythritol with calcium carbide: Erythritol (1 mmol), CaC_2 (9 mmol), Cs_2CO_3 (1.2 mmol), DMSO + 9 vol% H₂O, 100 °C.



Scheme 5. Vinylation of xylitol with calcium carbide: Xylitol (1 mmol), CaC_2 (10 mmol), Cs_2CO_3 (1.2 mmol), DMSO + 12 vol% H₂O, 100 °C, 3 h.

In contrast with the literatures that no vinylation product was observed¹⁰⁻¹², phenol works in our methodology. The amount of water plays an important role in this reaction with the yield improved from 78% to 93% by addition of water from 4 vol% to 7 vol% (Table 2, Entries 2 - 5).

Table 2 Optimization of Reaction Conditions for Phenol^a

ſ	OH Ca	Cs ₂ CO ₃ (0.5 eq.)	~~ ° ~⁄		
Ľ,	∠ C C C C	DMSO + H₂O 140 °C, 16 h	12a		
Entry	CaC ₂ (mmol)	vol% H ₂ O	Yield ^b (%)		
1	2	4	33		
2 ^c	4	4	78		
3 ^c	4	6	84		
4 ^c	4	7	93		
5 ^c	4	8	76		
^a Reaction conditions: Phenol (1 mmol), DMSO + vol% H_2O (5 mL),					
$C_{\rm s}$ CO (0.5 mmol) 140 °C 16 h ^D NIMR yield ^C Average of 2 runs					

Other substrates were tested and in general, the electron-rich phenols (**12b**, **12d-j**, Scheme 6) worked exceptionally well while the halide substituted and weak electron-withdrawing group substituted phenols gave low to moderate yield (**12k-n**, **12o-q**). No products were observed for strong electron-withdrawing group substituted phenols (**12r-t**). It is noted that while **12b** resulted in high yield, catechol **12c** gave only trace amount of product, leaving a hardened gel after reaction. This could possibly due to some polymerization side reaction that may have taken place. *O*- and *m*-substituted bromophenols proceeded slower compared to *p*-

bromophenol, with over 50% yield obtained only after reacting for 3 days. Electron donating groups **12d** to **12j** proceeded smoothly with excellent yields obtained. 2-naphthol **11p** proceeded more efficiently with 56% yield than 1-naphthol **11o** with 30% yield after reaction for 3 days.



Scheme 6. Substrate Scope of Phenols Derivatives with CaC₂: Reaction conditions: Alcohol (1.0 mmol), CaC₂ (4.0 mmol), Cs₂CO₃ (0.5 mmol), DMSO + 7 vol% H₂O (5mL), 140 °C, 16 h. NMR yield. Isolated yield is in parentheses. ^a CaC₂ (8 mmol), 14 vol% H₂O. ^b 9 vol% H₂O. ^c 3 days.

Diphenyl carbonate **13** as the key functional group in polycarbonate plastics could undergo C-O bond cleavage through basic hydrolysis, readily forming phenol **11a** as the major product under the optimized condition. As reaction prolonged to 3 days, the resulting phenol then formed vinyloxy(benzene) **12a**. (Scheme **7**)



Scheme 7. Vinylation of Diphenyl Carbonate with CaC₂: Reaction conditions: Diphenyl carbonate (1.0 mmol), CaC₂ (4.0 mmol), Cs₂CO₃ (0.5 mmol), DMSO + 7 vol% H₂O (5mL), 140 °C.

Although base-catalyzed alcohol vinylation with acetylene is well known,⁶ the current calcium carbide with control amount of water system demonstrated much high activity for this reaction. It is believed that the small amount of water promotes the reaction by breaking down the polymeric structure of calcium carbide to form calcium acetylide which is much more active than acetylene.¹¹ In addition, the presence of base could also stabilize the acetylide intermediate.

Conclusions

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We have developed a transition metal-free, mild and safe protocol for the direct vinylation of natural alcohols with calcium carbide. Various sugar alcohols, phenol and its derivatives were tested and proved to work using this green methodology. Selectivity of the reaction decreases with increasing hydroxyl groups due to side reactions occurring under the basic medium. Electron-donating substituted phenols works more efficiently as compared to electron-withdrawing substituted phenols in general. This methodology may provide new insights on selective vinylation of electron-rich biomass-derived materials.

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