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Vitamin B1-Catalyzed Acetoin Formation from Acetaldehyde: A Key Step for Upgrading Bioethanol to Bulk C_4 Chemicals

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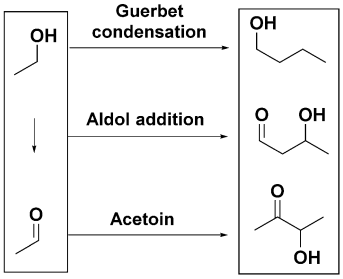
The production of bulk chemicals and fuels from renewable biobased feedstocks is of significant importance for the sustainability of human society. The production of ethanol from biomass has dramatically increased and bioethanol also holds considerable potential as a versatile building block for the chemical industry. Herein, we report a highly selective process for the conversion of ethanol to C_4 bulk chemicals, such as 2,3-butanediol and butene, via a vitamin B1 (thiamine)-derived *N*-heterocyclic carbene (NHC)-catalyzed acetoin condensation as the key step to assemble two C_2 acetaldehydes into a C_4 product. The environmentally benign and cheap natural catalyst vitamin B1 demonstrates high selectivity (99%), high efficiency (97% yield), and high tolerance toward ethanol and water impurities in the acetoin reaction. The results enable a novel and efficient process for ethanol upgrading.

The development of sustainable processes for the production of biobased commodity chemicals is one of the significant scientific challenges of today.[1] Utilizing renewable biobased chemicals as starting point for further transformations/products is highly desirable. This strategy not only offers benefits from an environment point of view—biobased chemical transformations are closely related to carbon-neutral cycles and biodegradable materials—but also important economic benefits.[2] The amount of ethanol produced from biomass has dramatically increased recently (reaching 105 billion liters in 2011), and hence ethanol has become one of the more prominent sources of biofuel.[3] In addition, bioethanol holds considerable potential as a versatile building block for chemical industries. Bioethanol is considered as one of the most profitable chemicals from renewable resources as compared to the fossil resources.[4,5] Therefore, the utilization of bioethanol for the production of value-added chemicals is more economically viable and could also help to reduce CO_2 emissions. A number of important processes for the conversion of ethanol to bulk chemicals have been established.[4] However, most of the successfully accessible products from bioethanol are still C_2 chemicals or related products (on a million-ton scale), such as ethylene, acetaldehyde, acetic acid, ethylacetate, and hydrogen.[4] There are also industrial processes available for the production of C_4 chemicals, such as butadiene[6] or 1-butanol.[7] However, these processes still suffer from poor selectivity and/or efficiency, which eliminates a significant part of their economic value.[4] It is highly desirable to develop a highly selective, green, and efficient process for the conversion of ethanol to C_4 bulk chemicals.

A major challenge for the conversion of ethanol to C_4 chemicals is the selectivity in the condensation or coupling of C_2 to C_4 (Scheme 1). The Guerbet reaction[8a] allows facile C–C bond formation from alcohols, which is described as "borrowed hydrogen" chemistry. However, ethanol is a specifically difficult substrate for these borrowed-hydrogen processes.[8] Very recently, Wass et al. reported a ruthenium-catalyzed system for the conversion of ethanol to *n*-butanol, in which the selectivity could be improved to 94%. However, this system still suffered from low conversion (20%).[9] The base-catalyzed aldol reaction of aldehydes is another well-studied protocol for C–C bond formation,[10a] However, from the reactive acetaldehyde (oxidized from ethanol), the selectivity for the aldol product 3-hydroxybutanal is always low, and is accompanied by undesired oligomeric and polymeric products.[10b] *N*-heterocyclic carbene (NHC)-catalyzed acyloin condensation usually provides a milder option for the C–C bond formation of two aldehydes.[11] However, the condensation of acetaldehyde to acetoin is rarely explored, probably due to low selectivity and poor tolerance to polar protic compounds.[12]



Scheme 1. Possible C_2 to C_4 reactions for ethanol upgrading processes.

Although Breslow disclosed the mechanism of thiazolylidene-catalyzed benzoin condensation as early as 1958,[11] the successful preparation of acyloins with thiazolylidene or triazolylidene catalysts was mostly limited to aromatic aldehydes or aldehydes with alkyl chain longer than a methyl group.[12b,13] A thiazole-based, enzyme-catalyzed acetoin reaction was also re-

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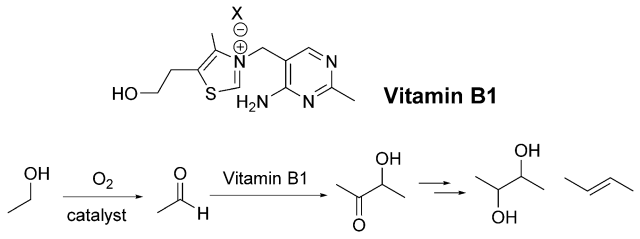
ported.[14] However, the reaction efficiency was rather low. Recently, a patent disclosed that structural modifications of thiazolium precatalysts can generate NHCs by thermolysis, and that these NHCs can efficiently catalyze the formation of acetoin from acetaldehyde.[15] In this system, a series of costly precatalysts synthesized in multiple steps were applied and the catalytic process was very sensitive toward impurities. Hence, to the best of our knowledge, there exists no catalytic system suitable for bioethanol-based acetaldehyde (with small amounts of ethanol and water impurities) condensation reactions.

Herein, we demonstrate an efficient catalytic system for the formation of acetoin, using simple, cheap, environmentally benign, and readily available natural vitamin B1 salts (also called VB1 or thiamine; Scheme 2) as precatalysts. Excellent



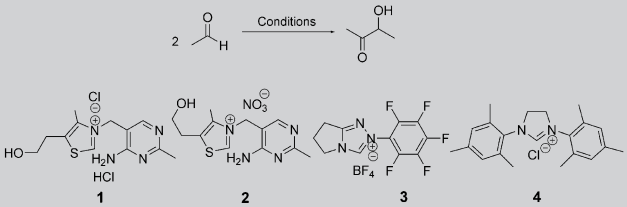
Scheme 2. Ethanol upgrading to C_4 bulk chemicals via the thiamine (VB1)-catalyzed acetoin condensation.

acetoin yields (up to 97%) could be achieved from acetaldehyde. More importantly, this catalytic system tolerates ethanol and water impurities, rendering it suitable for bioethanol upgrading process. Hence, a combined process, from ethanol to C_4 bulk chemicals, with acetoin as key intermediate is also reported here.

We started by screening various precatalysts, looking for high selectivity in the reaction. A first preliminary screening round for the acetoin reaction was conducted to condense neat acetaldehyde at room temperature with an NHC catalyst loading of 0.1 mol% [assuming in situ generation from 0.1 mol% precatalyst in the presence of a slight excess (1.3 equiv) of sodium carbonate or potassium carbonate as the base; Supporting Information, Table S1]. To our surprise, we did not observe any acetoin with most of precatalysts used in our screening, probably due to the poor solubility of the precatalysts and inorganic bases in acetaldehyde. The precatalysts with imidazolium and imidazolinium[16] skeletons [other than 1,3-bis(2,4,6-trimethylphenyl)imidazolinium (SIMes); entry 4] were generally inert towards the reaction (entries 5–13). In contrast, thiamine-based precatalysts (entries 1–2) and triazolium (entry 3) precatalyst demonstrated potential for the acetoin reaction. Therefore, precatalysts **1**–**4** (Table 1) were selected for further screening at elevated temperatures and/or higher catalyst loadings.

As shown in Table 1, precatalysts vitamin B1 (**1** and **2**) proved to be outstanding for the acetaldehyde self-condensation reaction. Excellent yields were obtained in a clean manner by elevating the temperature to 80 °C with 1 mol% catalyst

Table 1. Screening of precatalysts in acetoin formation via NHC-catalyzed condensations.[a]



1 **2** **3** **4**

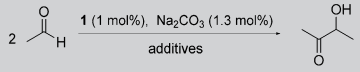
Entry	Catalyst	Amount [mol%]	Base	Amount [mol%]	Yield [%]
1	**1**	0.1	Na_2CO_3	0.13	24
2	**1**	0.2	Na_2CO_3	0.27	30
3	**1**	0.5	Na_2CO_3	0.65	54
4	**1**	1	Na_2CO_3	1.3	96
5	**1**	1	Na_2CO_3	1.3	97[b]
6	**1**	1	Et_3N	1.3	n.d.[c]
7	**1**	1	DBU	1.3	n.d.
8	**1**	1	DIPEA	1.3	n.d.
9	**1**	1	NaOH	1.3	80[d]
10	**1**	1	K_2CO_3	1.3	86[d]
11	**2**	0.1	K_2CO_3	0.13	12
12	**2**	1	K_2CO_3	1.3	97
13	**3**	0.2	K_2CO_3	0.27	13
14	**3**	0.5	K_2CO_3	0.65	56
15	**3**	1	K_2CO_3	1.3	96
16	**4**	1	Na_2CO_3	1.3	63[d]

[a] Reaction conditions: A mixture of precatalyst, base and 2 mL acetaldehyde (35.5 mmol) were stirred in a sealed tube at 80 °C for 4 h. Yields were measured by ^{1}H NMR. [b] Reaction scale was enlarged to 20 mL (355 mmol). [c] n.d. = not determined. [d] Small amounts of byproducts were observed.

1 or **2** (entries 4, 5, and 12). The expensive triazolium precatalyst **3** also demonstrated comparable activity and selectivity in this reaction (entry 15). However, compared to precatalyst **1**–**3**, the imidazolinium precatalyst **4** offered inferior selectivity and activity (entry 16) at 80 °C. Therefore, vitamin B1 salt (**1**) was chosen for further investigation. The effect of bases for acetoin formation based on precatalyst **1** was then studied. Although some works have reported that acetoin can be obtained in moderate yield with thiazolium precatalyst and Et_3N in absolute ethanol,[12] the results of our control experiment indicate that no reaction occurs for vitamin B1 precatalyst and organobase systems under these neat conditions (entries 6–8). The weak inorganic base Na_2CO_3 worked well for this reaction (entry 4), while with the stronger bases K_2CO_3 or NaOH, the reaction became less selective (entries 9 and 10). In addition, a larger-scale reaction (20 mL acetaldehyde) achieved an acetoin yield of 97% (entry 5).

Using treatment methods such as distillation and dehydration, the purity of bioethanol can reach as high as 99.5%. The major impurities in bioethanol are water (ca. 0.2%), methanol (< 0.1%), and small amounts of other alcohols. In the process of upgrading bioethanol to C_4 chemicals, ethanol is first dehydrogenated to acetaldehyde in the gas phase. Owing to the limited conversion, the presence of ethanol (5 to 30%) in the acetaldehyde feedstock is inevitable. Herein, the tolerance to

Table 2. Water and alcohol tolerances for acetoin condensations.[a]

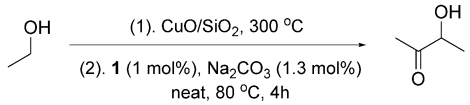


Entry	Additive	Amount [mol%]	Time [h]	Yield [%]
1	–	–	4	96
2	ethanol	28	4	96
3	ethanol	56	4	96
4	methanol	5	4	96
5	water	1.1	4	82[b]
6	water	0.5	16	93

[a] Reaction conditions: A mixture of precatalyst (0.35 mmol), sodium carbonate (0.47 mmol), ethanol or water and 2 mL acetaldehyde (35.5 mmol) was stirred in a sealed tube at 80 °C. [b] Trace amounts of byproducts were observed.

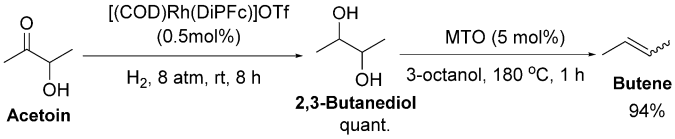
ethanol and other impurities was measured in acetoin reactions with vitamin B1 precatalyst **1**. As shown in Table 2, with precatalyst **1**, the reaction could tolerate at least 56% of ethanol without compromising the reactivity (entries 1–3). There was almost no effect on acetoin selectivity when 5% of methanol was added into the reaction mixture (entry 4). These remarkable results indicate the excellent selectivity of the reaction toward acetoin condensation. In addition, there was only a minor influence on the reaction in the case of a small amount of water impurity (0.5%; entry 5). These good tolerances render this VB1-catalyzed acetoin condensation very suitable for ethanol upgrading.

To achieve this application, ethanol upgrading, precatalyst **1** was tested with fresh acetaldehyde from ethanol by oxidation: a CuO/SiO_2 catalyst was used for ethanol oxidization in a fixed-bed reaction system (see Supporting Information).[17] Acetaldehyde (4 g, purity: 77%, with unreacted ethanol as the major impurity) was collected and used as feedstock for the acetoin condensation reaction. To our delight, a 95% conversion of as-prepared acetaldehyde, exclusively to acetoin, was achieved with 1 mol% of precatalyst **1** in the presence of Na_2CO_3 (Scheme 3). This result demonstrates that the VB1 precatalyst investigated herein is suitable for upgrading bioethanol to C_4 chemicals.



Scheme 3. A two-step conversion of ethanol to acetoin.

To further illustrate the use of acetoin as a flexible intermediate towards various C_4 bulk chemicals, the highly selective transformations of acetoin to 2,3-butanediol and butene were also demonstrated. Firstly, an acetoin hydrogenation reaction was conducted using a rhodium catalyst under an atmosphere of H_2 (8 atm; 1 atm = 1.01325×10^5 Pa).[18] 2,3-Butanediol was obtained in quantitative yield in 8 h at room temperature. Subsequently, a deoxydehydration (DODH)[19,20] process converted



Scheme 4. From acetoin to other C_4 industrial chemicals.

2,3-butanediol to butene. The reaction was conducted in 3-octanol at 180 °C using methyltrioxorhenium (MTO) (5 mol%) as catalyst. Butene was obtained in a yield of 94% in 1 h (Scheme 4).

In conclusion, a sustainable process for upgrading ethanol to C_4 chemicals with a thiamine-catalyzed acetoin condensation reaction as the key step is achieved. A cheap, green, and commercially available thiamine [vitamin B1 (VB1)] is the precatalyst for the organo-*N*-heterocyclic carbene (NHC)-catalyzed acetoin reaction, and is highly efficient and tolerant towards ethanol and moisture impurities. Excellent yields and selectivities are achieved using low precatalyst loadings. The VB1 precatalyst also demonstrates its suitability for the acetoin condensation of acetaldehyde generated in situ from ethanol. In addition, the entire process of upgrading ethanol towards C_4 chemicals (2,3-butanediol and butene) is successfully demonstrated. Further investigations and applications to processes from bioethanol to C_4 chemicals via acetoin intermediates are ongoing in our laboratory.

Experimental Section

General procedure for acetion formation via condensation of acetaldehyde: To a 4 mL thick wall glass tube with stirring bar was added the precatalyst, the base, and acetaldehyde (2 mL, 35.5 mmol). The tube was sealed. After the reaction mixture was stirred at the indicated temperature and the indicated time, the mixture was cooled to room temperature and subjected to ^{1}H NMR analysis. Yield were measured via ^{1}H NMR using mesitylene or 1,10-phenanthroline as the internal standard. The spectra were consistent with the analytical standard purchased (Sigma–Aldrich): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.25$ (q, $J = 7.2$ Hz, 1H), 3.48 (br, 1H), 2.21 (s, 3H), 1.40 ppm (d, $J = 7.2$ Hz, 3H).

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