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Continuous isomerisation of 2,5-dimethylfuran to 2,4-dimethylfuran over Ga-silicate

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2,4-dimethylfuran has a rare disubstitution pattern in the five-membered heterocyclic furan ring that is highly interesting chemically but challenging to access synthetically. We present a heterogeneously catalysed route to synthesise 2,4-dimethylfuran from commonly available 2,5-dimethylfuran using a zeolite packed-bed flow reactor. As supported by DFT calculations, the reaction occurs inside the zeolite channels, where the acid sites catalyse proton transfer followed by migration of a methyl group. The zeotype Ga-silicate (MFI type) appears superior to an aluminium-containing ZSM-5 by demonstrating higher selectivities and slower catalyst deactivation. This work provides new opportunities for the continuous valorisation of bio-feedstock molecules in the perspective of the emerging biorefinery era.

2,4-dimethylfuran (2,4-dmf) possesses a disubstitution pattern of the five-membered heterocyclic furan ring that is interesting to utilise chemically but challenging to achieve synthetically. In fact it has been recognized that 2,4-disubstitutions are "difficult to access synthetically, and the most common routes to such compounds rely on intramolecular rearrangements of complex motifs."[1] Accessing this rare substitution pattern is of interest not only because it is synthetically challenging, but also since 2,4-dmf has been used several times for the total synthesis of complex organic molecules in which specific stereoselectivity is required.[2,3] It has further been found to be a flavour component, for example in olive oil.[4] In a broader perspective the "importance of furans has attained a new dimension with its ever-increasing use in materials science for a variety of vital applications such as conducting polymers, photovoltaics, self-healing materials, etc. This importance has motivated chemists to constantly research new ways of synthesising furan derivatives with defined substitution patterns."[5] Looking forward, furans are among the platform molecules considered for emerging biorefineries.[6] A readily available commercial technology for the transformation of furans is thus desirable. This becomes especially important in the perspective of a global shift towards increased utilisation of biomass and its bio-derived molecules, a key interest to forest-rich countries like Sweden.

Contrary to burning biomass or converting it into fuel, a more sustainable approach is to build on the already existing natural chemical complexity by making further molecular modifications, as to meet our needs for green chemical production and materials manufacture. The growing interest to use bio-based polymers such as polyethylene furanoate (PEF),[7] or furan dicarboxylic acid as an alternative to (iso)terephtalic acid for the modification of PET,[8] or other polymer plastics directly from furan based rings constitute good examples. Hitherto, a few successful attempts using (catalytic) organic chemistry approaches for the synthesis of 2,4-disubstituted furans have been presented.[1,5,9–12] The gold-catalysed carbene transfer to alkynes[1] and annulation-based β-bromoenol phosphate route,[5] as summarised in Scheme 1a) and b), respectively, provide access to a wide range of 2,4-disubstituted furans.

From a green chemistry perspective, however, new routes are highly desirable because established routes are based on batch operation using expensive precious metal catalysts, potentially hazardous bromine and/or need protecting groups, which may be acceptable only for occasional small-scale synthesis. Instead, heterogeneous catalytic processes have the potential to offer sustainable continuous production on a large scale provided benign catalysts can be designed. So far, the only known heterogeneous route towards the production of 2,4-dmf is via triose that undergoes aldol condensation and dehydration to 4-hydroxymethylfurfural, which is hydrogenated to produce 2,4-dmf as in Scheme 1c).[13] However, this route depends on $CuCrO_4$ as a catalyst and the last step yields only 10% of product.[13] 2,5-dmf on the other hand can be neatly obtained from 5-hydroxymethylfurfural.[14]

Recently, we found 2,4-dmf to be a side product in the catalytic valorisation of biomass-derived 2,5-dimethylfuran (2,5-dmf) over zeolites.[15,16] We have elaborated further on this isomerisation reaction, and herein, we communicate an alternative green approach, namely the continuous selective syn-
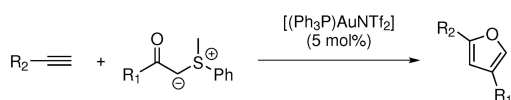
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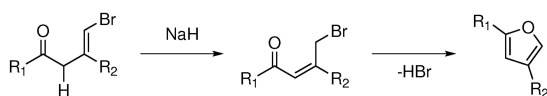
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Scheme 1. Synthesis of 2,4-dmf via a) Gold catalysed carbene transfer to alkynes[5] b) β-bromoenol phosphate route,[1] c) formose reaction and hydrogenation of 4-hydroxymethylfuran[13] and d) isomerisation of 2,5-dmf over zeolites/zeotypes (this work).

thesis of 2,4-dmf by heterogeneous catalytic isomerisation of readily available 2,5-dmf, shown in Scheme 1d).

We have observed the isomerisation of 2,5-dmf to 2,4-dmf, 2-methyl-2-cyclopentenone (2-mcpo) and 3-methyl-2-cyclopentenone (3-mcpo) as side reactions over the H-form of beta and MFI zeolites (with various aluminium or gallium contents) when targeting the formation of benzene, toluene and xylenes (BTX).[15,17] While screening catalyst formulations for enhanced BTX production, we discovered that Ga-silicate, i.e., Ga positioned in the MFI framework (Ga-MFI), exhibits much improved long-term activity and selectivity towards mentioned isomers, making it a suitable candidate for 2,4-dmf production.[16]

Here, we have studied Ga-MFI, using H-ZSM-5, Silicalite-1, and Ga$_2$O$_3$, as references. The physicochemical properties of the catalysts are summarised in Table S1. In brief, X-ray diffraction (XRD) confirms the MFI-type framework structure and the absence of other crystalline phases with long-range order (Figure S1) and scanning electron microscopy imaging shows highly crystalline crystals that are interconnected, resulting in a range of particle sizes.[15,16,18–20] From N$_2$-sorption measurements, the calculated BET-specific surface area falls within the rather narrow range of 365–412 $m^2 g^{-1}$ and likewise, the micropore volumes span the rather narrow range of 0.145–0.175 $cm^3 g^{-1}$, which are reasonable values for these materials.[21–23] Further analysis of the N$_2$-sorption isotherms shows a type H4 hysteresis (Figure S2) indicating that both meso- and micropores are present.[19] Concerning acidity, the acid site density follows the order of H-ZSM-5 > Ga-MFI≫Silicalite-1 as measured by temperature programmed desorption of ammonia (NH$_3$-TPD) that had been pre-adsorbed at 150 °C (Figure S3). By continuous flow-

reactor measurements, the 2,5-dmf conversion and the product selectivities (excluding coke selectivity) were studied as a function of time-on-stream (TOS) upon a sudden introduction of the 2,5-dmf reactant at different reaction temperatures (Figures 1 and 2). Figure 1 shows the conversion and selectivities at 450 °C using Ga-silicate. Initially, during the first ten minutes, olefins and aromatics are the preferred reaction products and selectivity to 2,4-dmf is relatively low. During this period, the conversion of 2,5-dmf drops rather quickly. After the initial transient behaviour, an induction period of approximately four hours continues, during which the formation of olefins and aromatics diminishes to negligible levels (selectivities nearing zero) while the selectivity towards 2,4-dmf increases and reaches a remarkable 60%. The 2,4-dmf selectivity then remains stable for up to ten hours of TOS. Besides 2,4-dmf, the structural isomers 2-mcpo and 3-mcpo are also produced, though in smaller amounts. At this stage, the conversion decreases slowly due to coke formation on the surface of the catalyst. Upon stepwise increase of reactant concentrations after 10 hours TOS
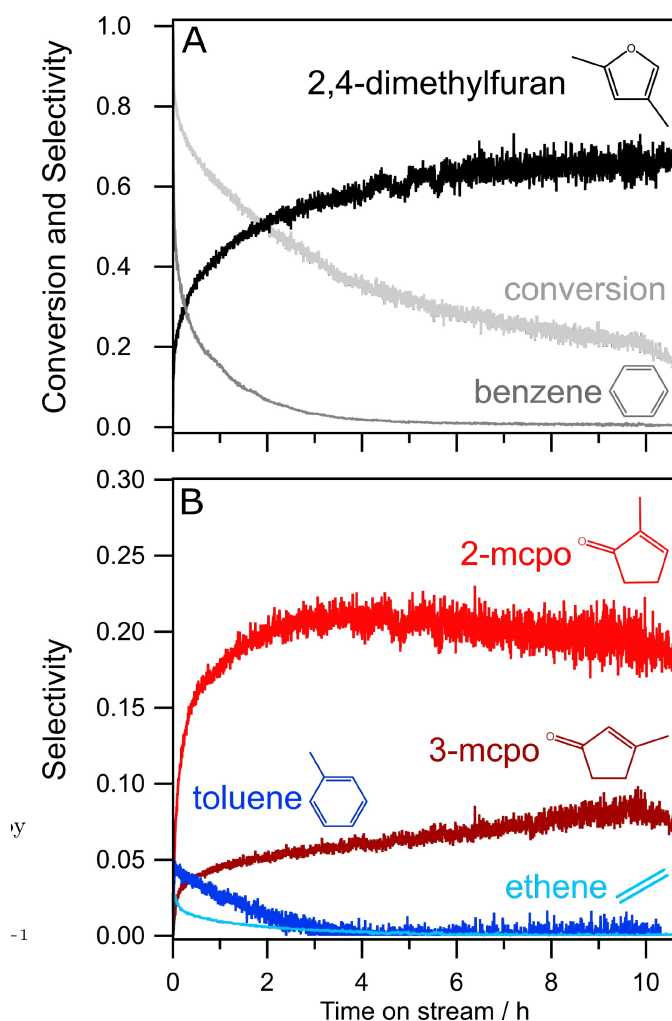

Figure 1. Conversion of 2,5-dmf and selectivities of 2,4-dimethylfuran and benzene (panel A) and selectivities of 3-mcpo, 2-mcpo, toluene and ethene (panel B) as a function of time on stream during a 10 h long experiment at 450 °C over Ga-silicate (68.8 mg).
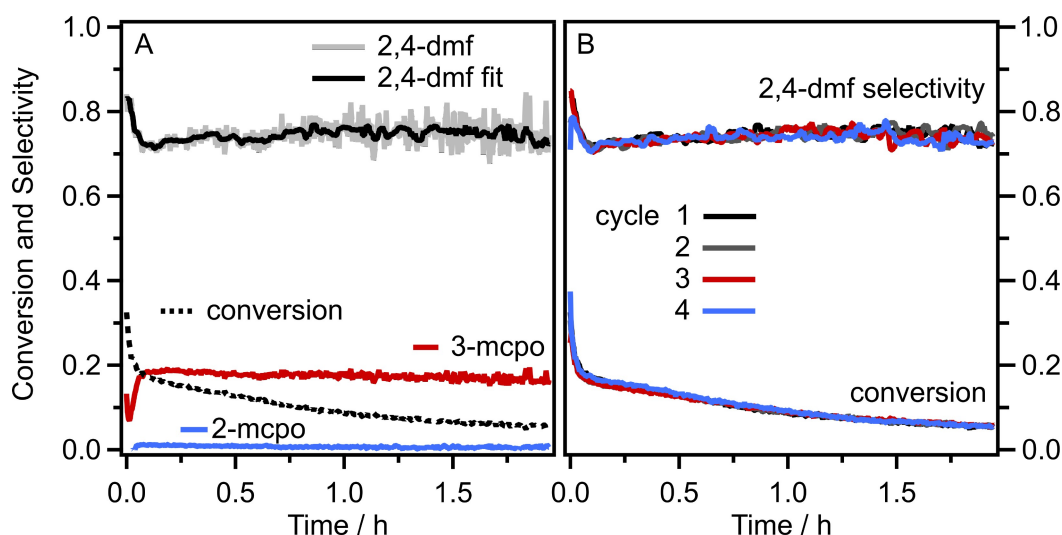
Figure 2. Conversion and selectivities of selected products during two hours of 2,5-dmf conversion over Ga-silicate at 350 °C (panel A) and smoothed 2,4-dmf selectivities and conversion during 4 cycles of two hours 2,5-dmf conversion at 350 °C (panel B). Ga-silicate was oxidised in 20 % O$_2$ at 625 °C between each cycle.

(see Figure S4) the concentrations as well as the selectivities (not shown) of the products remain steady.

At lower temperatures (350 °C), the conversion is somewhat lower, as shown in Figure 2A. However, the selectivity to 2,4-dmf quickly reaches approximately 70 % and remains stable for 2 h, as shown here. In contrast to 2,5-dmf conversion at 450 °C, no significant amounts of olefins and aromatics are formed ($\leq$ 3 %).

To test the repeatability, the same sample was used for three more cycles under identical conditions as shown in Figure 2B. Between each cycle, the catalyst was regenerated with an oxidative treatment to remove carbon deposits (coke). Both selectivity and conversion remain stable over the course of the four cycles, suggesting an intact catalyst framework hosting active sites that can be regenerated without significant permanent deactivation.

For comparison, ZSM-5, Ga$_2$O$_3$ and pure Silicalite-1 were considered as catalysts beside the Ga-MFI. Tests without a catalyst as well as tests with pure Silicalite-1 did not result in any isomerisation of 2,5-dmf, nor did tests with Ga$_2$O$_3$. H-ZSM-5 produces the target 2,4-dmf product for shorter times but becomes completely inactive after approximately three hours (Figure S5).

The Ga-MFI sample was further evaluated in a continuous long-term catalytic test lasting for 48 hours (Figure S6). This measurement shows that Ga-MFI isomerises 2,5-dmf to 2,4-dmf for the entire duration of the measurement. Besides 2,4-dmf, smaller amounts of 2-mcpo and 3-mcpo are also produced during TOS.

The superior performance, i.e., high selectivity towards isomerisation and significantly improved long-term activity, of the Ga-containing sample is in essence thanks to slower deactivation by coke. This performance, as well as the inactivity of Silicalite-1 and Ga$_2$O$_3$, indicates that for catalytic isomerisation, both the microporous framework structure and catalytically active acid sites are necessary. Thus we envisage that the

isomerisation of 2,5-dmf is promoted by the MFI framework structure, with a maximum pore size of 5.5 and 5.6 Å for the two types of channels; slightly smaller than the kinetic diameter of 2,5-dmf (5.7 Å). However, at elevated reaction temperatures, the zeolite pores are dilated and their effective size is better described by applying Norman radii corrections, resulting in a maximum pore size of 6.2 and 6.3 Å.[24] This allows for 2,5-dmf to enter and be converted inside the pores of the Ga-MFI zeolite, similar to what was observed for benzene (5.85 Å) and p-xylene (5.85 Å) over ZSM-5 and silicalite-1, respectively.[25,26] A previous work on MFI and beta zeolites shows that MFI is more efficient in producing 2,4-dmf than beta zeolite,[17] which has a bigger pore size and thus fewer steric interactions promoting 2,4-dmf production. It is, however, not yet clear if the Ga-MFI is superior to other Ga-modified frameworks, for example, a Ga-BEA catalyst. Concerning the presence of acid sites, we combined continuous flow experiments, with intermittent NH$_3$-TPD measurements (Figure S3) in the same reactor as to monitor the change of available acid sites as a function of TOS. Even though the Ga-MFI sample has very few acid sites available after ten hours of catalytic conversion, it is still active for the isomerisation of 2,5-dmf. On the contrary, the ZSM-5 sample is completely inactive while it still has a major part of acid sites available for NH$_3$ adsorption. This suggests that mainly weak acid sites are responsible for isomerisation reactions, whereas strong acid sites are responsible for cracking, decarbonylation and aromatisation reactions. Ga-silicate has, in a recent study, been shown to contain even weaker acid sites as well, on which ammonia readily adsorbs and desorbs at temperatures below 150 °C.[16] Complementary targeted studies are necessary to determine the most beneficial Ga content of the catalyst.

Mechanistically, we hypothesise that the isomerisation of 2,5-dmf to 2,4-dmf happens through an acid catalysed methyl-migration that is facilitated by steric confinement in the MFI

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structure. To test this hypothesis for the isomerisation, we calculated the reaction landscape using density functional calculations (calculation details are accounted for in the SI). In short, the mechanism includes the adsorption of 2,5-dmf, followed by a proton transfer from the Brønsted acid site to one of the carbons close to oxygen, i.e., site 2 or 5 in the 2,5-dmf notation. Both sites are equivalent; however, we will focus on site 5 in the calculations. As a result, the sp^2 hybridisation of that carbon will change to an sp^3 hybridisation. The protonated 2,5-dmf can rotate without a barrier thanks to confinement effects in the zeolite pore. This is followed by the transfer of the $-CH_3$, and consequently, the sp^3 hybridisation, from site 5 to site 4. Once the $-CH_3$ is at site 4, the proton will be transferred back to the Brønsted acid site, thereby forming the 2,4-dmf. Finally, the 2,4-dmf will desorb and leave the zeolite. Hence, the acid site is important for the initiation of the reaction; although, the highest barrier is connected to the shift of the methyl group.

The Gibbs free energy calculated at 450 °C is shown in Figure 3 (for the total energy of the reaction landscape, see S7). From the figure, it is clear that the proton transfers, although essential, are associated with relatively low barriers. Instead, the $-CH_3$ transfer from site 5 to site 4 has the highest barrier throughout the reaction landscape. We construct a microkinetic model from the suggested reaction mechanism via PyCatKin,[27] and the analysis is performed according to the energetic span model.[28] The analysis shows that the $-CH_3$ transfer is the rate controlling step, and that the estimated turnover frequency is 0.002 s^{-1} at 450 °C. This is in good agreement with the experimentally estimated turn-over frequencies ranging from 0.002 s^{-1} to 0.02 s^{-1} (see SI for conditions). Further, according to first-principles calculations, the equilibrium ratio between the partial pressure of 2,5-dmf and 2,4-dmf is 6.5/1 and 5/1 at 350 °C and 450 °C, respectively. These ratios are lower

than the experimentally observed ones of 23/1 at 350 °C and 11/1 at 450 °C for close to steady formation of 2,4-dmf, indicating that the experiments are in the regime of kinetic control at this point.

This methyl-migration is possibly analogous to industrially applied xylene isomerisation. However, we want to stress that in contrast to xylenes, furans are subject to cracking, decarbonylation, dehydration and oligomerisation reactions when in contact with zeolites, especially at elevated temperatures, which often prohibits selective product formation that keeps the furan structure intact.[29]

Before concluding this communication, we comment on the utilisation of bio-derived 3-mcpo to methylcyclopentadiene (mcpd), which is of special interest.[30] It is described as an important precursor for high-energy-density rocket fuel,[31] and various valuable products, such as medicines, dye additives, antiknock agents and many others.[30,32] Currently, mcpd is mainly obtained from the by-products of petroleum cracking, and a path building on the utilisation of cellulose was described only recently.[30] The route we describe in this work adds another path using bio-based raw materials and, at the same time, utilises the 3-mcpo side product. If furans become potential supplements to BTX aromatics as platform molecules, the isomerisation described here is of significant importance for the coming biorefinery era, where the increased use of PEF is just one example.

In summary, we present the discovery of Ga-silicate as a promising, potential catalyst for the isomerisation of 2,5-dimethylfuran to 2,4-dimethylfuran, a five-membered heterocycle with a substitution pattern that is otherwise difficult to access. The continuous production of the desired 2,4-disubstituted furan occurs in a chemical flow reactor under heterogeneous catalytic conditions. The catalyst shows stability over several regeneration cycles and is active for many hours of
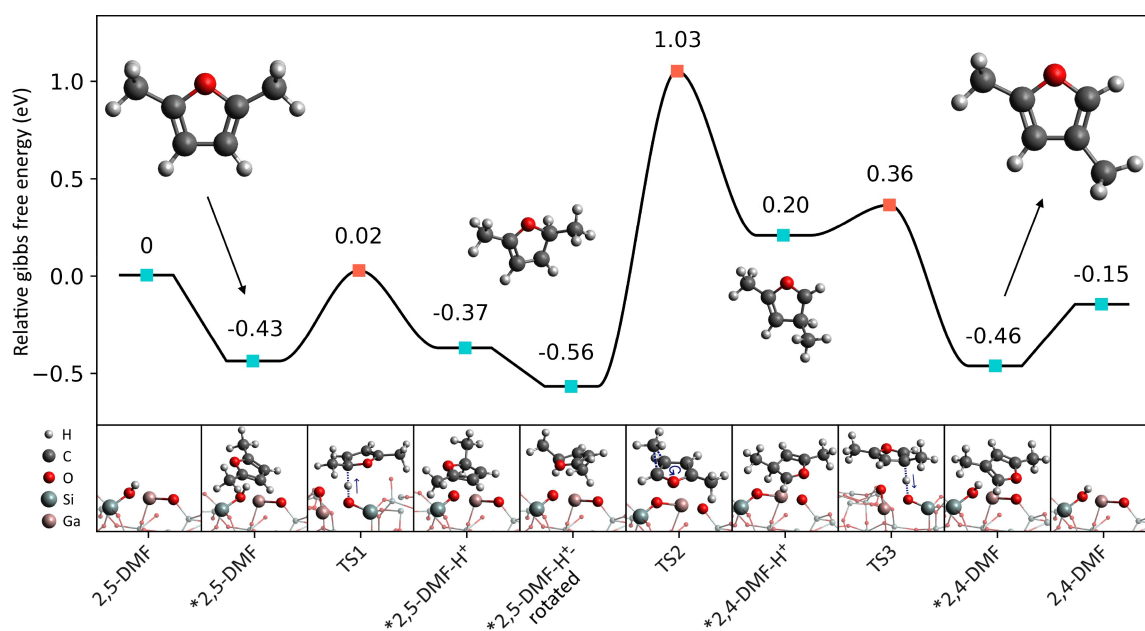

Figure 3. Suggested reaction mechanism and the calculated reaction landscape for the isomerisation of 2,5-dmf to 2,4-dmf at 450 °C.

time-on-stream, but experiences some deactivation. The role of Ga in the framework seems crucial for the long-term activity and selectivity, as pure silicalite-1 does not yield any isomerisation and the aluminium zeolite tested here deactivates more rapidly. Future work is necessary to fully understand the role of the gallium content and its influence on the acid site for this reaction. In line with this, it would be interesting to also study whether or not a further reduced acid site strength could suppress initial aromatisation and thus increase the 2,4-dmf selectivity.

Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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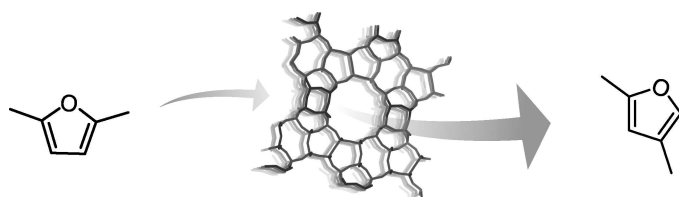[32] D. Lan, L. Ma, Y. Chun, C. Wu, L. Sun, J. Zhu, *J. Catal.* **2010**, *275*, 257.

RESEARCH ARTICLE

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Continuous isomerisation of 2,5-dimethylfuran to 2,4-dimethylfuran over Ga-silicate

MFI framework zeolites and zeotypes enable the isomerisation of 2,5-dimethylfuran to 2,4-dimethylfuran through a heterogeneously catalysed route. Incorporating gallium instead of aluminium increases the selectivity and durability of the catalyst. This reaction is promoted by suitable acidity of the catalyst and steric confinement in the micropores.