CO_2 Utilization

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Ruthenium-Catalyzed Synthesis of Dialkoxymethane Ethers Utilizing Carbon Dioxide and Molecular Hydrogen

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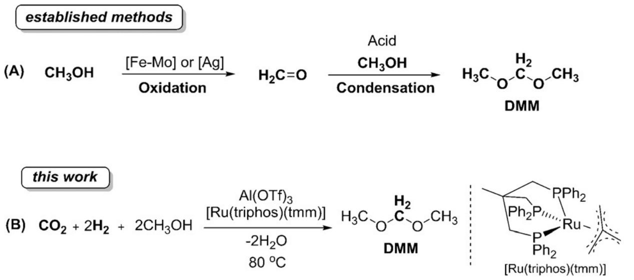
Abstract: *The synthesis of dimethoxymethane (DMM) by a multistep reaction of methanol with carbon dioxide and molecular hydrogen is reported. Using the molecular catalyst [Ru(triphos)(tmm)] in combination with the Lewis acid* $Al(OTf)_3$ *resulted in a versatile catalytic system for the synthesis of various dialkoxymethane ethers. This new catalytic reaction provides the first synthetic example for the selective conversion of carbon dioxide and hydrogen into a formaldehyde oxidation level, thus opening access to new molecular structures using this important* C_1 *source.*

Oxygenated compounds such as methanol, dimethyl ether (DME), and oxymethylene ethers (OMEs) are known to be attractive candidates for fuels or fuel additives because of their ability to reduce soot formation during the combustion in diesel engines.[1] Especially, oxymethylene dimethyl ethers such as dimethoxymethane (DMM or methylal) and poly(oxymethylene) dimethyl ethers (OMEx) have been gaining increasing interest in recent years because of their advantageous properties as fuel additives.[1,2] DMM is the first member in this homologous series and therefore sometimes referred to as OME_1. Moreover, this molecule represents an important building block and can thus be applied as a source for the synthesis of higher order OMEs.[1a,2,3] In addition, DMM has an attractive profile as a green solvent, and has been successfully used in pharmaceutical and perfume industries.

Industrially, DMM is produced by a two-step process comprising oxidation of methanol into formaldehyde over either silver or modified iron-molybdenum catalysts (ex. Formox Process),[4] and the condensation of formaldehyde with methanol in the presence of acid catalysts to afford the corresponding DMM product (Scheme 1 a).[5]

Many efforts have been dedicated to developing a one-step direct oxidation of methanol into DMM and a number of selective oxidation catalysts have been reported, thus yielding DMM in up to 100 % selectivity.[6] Most of these systems use bifunctional heterogeneous catalysts to control the sequential in situ formation of formaldehyde and its subsequent condensation in gas-phase continuous-flow processes.[6a–i] Recently, the group of Deng and Wang described a successful solution-phase batch reaction for the synthesis of DMM using $RuCl_3$ as a molecular catalyst for the oxidation/condensation of methanol into DMM.[6j]



Scheme 1. a) Industrial production of DMM starting from CH_3OH and/or formaldehyde. b) The new approach for synthesis of DMM starting from methanol using CO_2/H_2.

However, all current syntheses of DMM use methanol as a starting material and involve an oxidative step to attain the formaldehyde-level of the central CH_2-unit. To circumvent this redox-inefficient pathway, a reductive approach to generate DMM directly from MeOH and CO_2/H_2 would provide an attractive alternative route (Scheme 1 b). Herein, we describe the first catalytic process to achieve this goal, opening the possibility to harness renewable energy via the combination of CO_2 and H_2 directly into potential fuel candidates.[7]

Recently, our group described the first organometallic catalytic system for the hydrogenation of CO_2 into methanol by employing the highly versatile triphos-based ruthenium catalyst, [Ru(triphos)(tmm)] [triphos = 1,1,1-tris(diphenylphosphinomethyl)ethane, tmm = trimethylene methane], to catalyze this transformation through a series of hydride transfer and protonolysis steps promoted by an acid additive.[8] This system, which is very generally applicable to the hydrogenation of carboxylic and carbonic acid derivatives,[9] was also employed for the *N*-methylation of ammonia[10] and amines[11] using CO_2/H_2 as a C_1 synthon. Consequently, in the first set of experiments this complex was used in combination with selected acidic co-catalysts using methanol, CO_2, and H_2 as substrates. Reactions were carried out with a 1:3 ratio of the two gases under a total pressure of 80 bar (room temperature) and reaction temperatures between 80–120 °C. Using the [Ru(triphos)(tmm)] catalyst in the absence of acid

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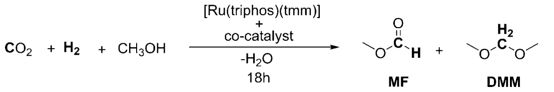
did not result in formation of any detectable CO_2 hydrogenation products. However, using the ruthenium precursor in combination with trifluoromethanesulfonylimide ($HNTf_2$) at 120 °C, resulted in the formation of DMM with a low turnover number (TON) of four, together with a similar amount of methylformate (MF; Table 1, entry 1). Interestingly, decreasing the reaction temperature to 100 °C caused a significant increase in DMM formation with a TON of 61 (entry 2). Applying the recently developed[10] catalyst system comprised of [Ru(triphos)(tmm)] and $Al(OTf)_3$ resulted in a significant increase in reactivity, thus giving a TON of 32 at 120 °C, and 94 at 100 °C (entries 3 and 4). An additional slight increase to a TON of 98 could be observed after 18 hours at a reaction temperature of 80 °C, but the formation of MF was also more pronounced (entry 5). Gratifyingly, when $Al(OTf)_3$ was used together with the Brønsted acid *p*-toluenesulfonic acid (*p*-TsOH), the TON of DMM increased to 125 at the expense of the reduction of formate (entry 6). A similar effect could be observed at higher loading of the Lewis-acidic co-catalyst, and with 25 μmol of $Al(OTf)_3$ a TON of 136 could be obtained (entry 7). Notably, the formation of either DMM or MF could not be detected in the reaction solution in the absence of CO_2.

Table 1: Ruthenium-catalyzed synthesis of MF and DMM using CO_2 and molecular hydrogen.[a]

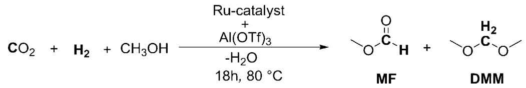


Entry	Acid	*x* [μmol]	*T* [°C]	TON[b] (MF)	TON[b] (DMM)
1	$HNTf_2$	12.5	120	7	4
2	$HNTf_2$	12.5	100	27	61
3	$Al(OTf)_3$	12.5	120	16	32
4	$Al(OTf)_3$	12.5	100	32	94
5	$Al(OTf)_3$	12.5	80	77	98
6	$Al(OTf)_3$/*p*-TsOH	12.5	80	53	125
7	$Al(OTf)_3$	25	80	54	136

[a] Reaction conditions: Catalyst = [Ru(triphos)(tmm)] (12.5 μmol), acid (*x* μmol), methanol (2 mL), CO_2/H_2 (20/60 bar), 18 h. [b] Turnover number (TON) was determined by NMR spectroscopy using mesitylene as an internal standard. Tf = trifluoromethanesulfonyl, Ts = 4-toluenesulfonyl.

In the subsequent experiments, the influence of the catalyst precursor and the catalyst concentration were investigated. Using an in situ system of $[Ru(cod)(methylallyl)_2]$ in combination with the triphos ligand resulted in the formation of DMM with a TON of 71 (Table 2, entry 1), thus corresponding to only around 50 % of the performance of the isolated catalyst. Using the complex [Ru(triphos)(CO)(H)(Cl)] did not yield any DMM (entry 2). Interestingly, a higher loading of [Ru(triphos)(tmm)] (25 μmol) resulted in a lower TON for DMM formation and decreased formation of MF with a low TON of 20 (entry 3). This result indicates that the performance of the catalytic system is dependent on the additive to catalyst ratio and additionally on the catalyst deactivation, by dimerization, at high loadings.[8b,12] This dependence became clearly evident when a lower loading of [Ru(triphos)(tmm)] was used (6 μmol), thus resulting in a significant increase of the TONs for MF and DMM formation to 104 and 214, respectively (Table 1, entry 7 and Table 2, entry 4). Introducing different CO_2 pressures to the reaction revealed that 20 bar of CO_2 was the optimal pressure for DMM formation with a favorable CO_2/H_2 pressure ratio of 1:3 (see the Supporting Information).

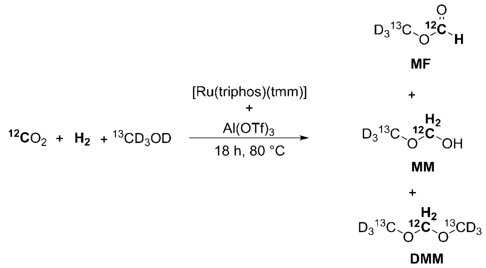
Table 2: Optimization of the ruthenium catalysts for the synthesis of DMM with CO_2 and molecular hydrogen.[a]



Entry	Catalyst/ligand	*x* [μmol]	TON[b] (MF)	TON[b] (DMM)
1	$[Ru(cod)(methylallyl)_2]$/triphos	12.5	33	71
2	[Ru(triphos)(CO)(H)(Cl)]	12.5	–	–
3	[Ru(triphos)(tmm)]	25	20	90
4	[Ru(triphos)(tmm)]	6.0	104	214

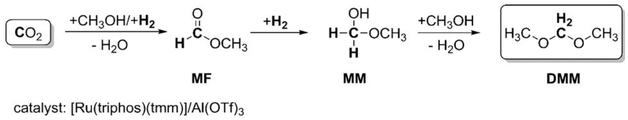
[a] Reaction conditions: Ruthenium catalyst (*x* μmol), $Al(OTf)_3$ (25 μmol), methanol (2 mL), CO_2/H_2 (20/60 bar), 18 h, 80 °C. [b] TON was determined by NMR spectroscopy using mesitylene as an internal standard. cod = 1,5-cyclooctadiene.

Further insight into the formation of DMM was obtained from a labeling experiment using the catalyst system [Ru(triphos)(tmm)]/$Al(OTf)_3$ in the presence of $^{13}CD_3OD$ in combination with nonlabelled CO_2 and H_2. The NMR analysis revealed the expected formation of MF with the ^{12}C at the formyl group and ^{13}C in the ester functionality (Scheme 2). Moreover, the formation of methoxymethanol (MM) could be observed with the anticipated labeling resulting from the sequential reduction of labeled MF (Scheme 2). The final product DMM was found to have the ^{13}C label incorporated only at the methyl groups, thus confirming their origin from methanol and the generation of the CH_2O unit from CO_2 and H_2. These results clearly indicate the construction of the corresponding carboxyl group of MF and the methylene groups of MM and DMM from CO_2 as the C_1 source.



Scheme 2. Isotopic labeling observed by NMR spectroscopy for the [Ru(triphos)(tmm)]/$Al(OTf)_3$-catalyzed synthesis of DMM from $^{13}CD^{3}OD$.

Thus, these experimental observations lead us to propose a sequential pathway of DMM formation starting from methanol, CO_2, and H_2. First, MF is formed by the well-known hydrogenation to the formic acid oxidation level

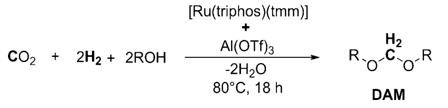


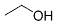
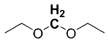
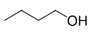
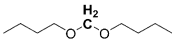
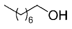
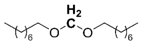
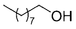
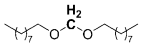
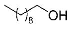
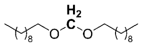
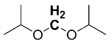
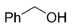
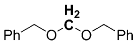
Scheme 3. Possible reaction pathway for the [Ru(triphos)(tmm)]/Al(OTf)$_3$-catalyzed synthesis of DMM using methanol and CO_2/H_2 as a C_1 synthon.

coupled with esterification (Scheme 3). The Ru-Triphos system is able to induce further hydrogenation to MM corresponding to the formaldehyde oxidation level. Transacetalization with the solvent methanol leads to the DMM product. Whereas the reduction sequence is resulting from the hydrogenation activity, the esterification and acetalization steps are expected to be largely facilitated by the Brønsted and/or Lewis acidity of the multifunctional catalytic system. It is noteworthy that this is the first example for a catalytic hydrogenation of CO_2 which terminates selectively at the formaldehyde level.[7c]

To study the versatility of this new approach towards the synthesis of dialkoxymethanes, the synthetic scope of this transformation with selected alcohols was investigated (Table 3). Under the presented reaction conditions and in presence of ethanol, the reaction afforded the target product diethoxymethane (DEM) with a TON of 118 (entry 1). The use of 1-butanol in the reaction yielded dibutoxymethane diether (DBM) with a TON of 110 (entry 2). However, the linear alcohols with a longer carbon chain resulted in a slight decrease of the TONs, and 1-octanol (entry 3), 1-nonanol (entry 4), and 1-decanol (entry 5) afforded the products (DOM, DNM, and DDM) with TONs of 78, 60, and 51, respectively. Similarly, the use of the secondary alcohol, isopropanol, resulted in the formation of diisopropoxymethane diether (D*i*PrM) with a low TON of 29 (entry 6). Benzyl alcohol was also tested for this reaction, and gave dibenzyloxymethane diether (DBnM) with a TON of 99 (entry 7).

Table 3: Ruthenium-catalyzed synthesis of dialkoxymethanes (DAM) using variable alcohols with CO_2 and molecular hydrogen.[a]



Entry	ROH	TON[b] (DAM)
1		 **DEM** (118)
2		 **DBM** (110)
3		 **DOM** (78)
4		 **DNM** (60)
5		 **DDM** (51)
6		 **D^{i}PrM** (29)
7		 **DBnM** (99)

[a] Reaction conditions: [Ru(triphos)(tmm)] (6 μmol), Al(OTf)$_3$ (25 μmol), ROH (2 mL), CO_2/H_2 (20/60 bar), 18 h, 80 °C. [b] TON was determined by NMR spectroscopy using mesitylene as an internal standard.

In conclusion, we have described a novel catalytic synthesis towards dimethoxymethane (DMM or methylal) starting from methanol, CO_2, and H_2. This reaction pathway provides the first direct reductive access to DMM, and constitutes the starting member of the oxymethylene-ether series (OME_1), currently discussed as potential fuel candidates based on renewable hydrogen. The catalytic system was based on the Ru-Triphos unit in combination with Lewis and/or Brønsted cocatalysts. The multifunctionality of the catalyst system was crucial for the complex reaction sequence, comprising various hydrogenation and esterification/acetalization steps. Moreover, the reaction was found to be general for the synthesis of dialkoxymethane ethers from CO_2, H_2, and the respective alcohols. Furthermore, the formation of methoxymethanol (MM) and methylformate (MF) could be identified as possible intermediates on the pathway to the construction of the methylene group from the CO_2/H_2. Consequently, this new catalytic reaction provides the first synthetic example for the selective conversion of CO_2 and H_2 into a compound having the formaldehyde oxidation level, thus opening access to new fields on the catalytic chess board of CO_2 hydrogenation.[7e] Future work in our laboratories will be directed towards the synthesis of cyclic and poly(oxymethylene) ethers using this newly established catalytic pathway.

Experimental Section

General procedure for the synthesis of dimethoxymethane DMM from methanol, CO_2, and H_2: A 2.0 mL solution of [Ru(triphos)(tmm)] (0.009 g, 12.5 μmol) and Al(OTf)$_3$ (0.012 g, 25 μmol) in methanol was prepared under an argon atmosphere in a Schlenk tube containing a stirring bar. After stirring for 5 minutes, the solution was transferred to a carefully degassed and dried 20 mL stainless-steel autoclave. The autoclave was pressurized at room temperature with 20 bar CO_2 and then H_2 was added up to a total pressure of 80 bar. The reaction mixture was stirred with a magnetic stir bar and heated to 80 °C using a preheated aluminum cone. After 18 h the autoclave was cooled in an ice bath and then carefully vented. The turnover number (TON) of DMM in solution was analyzed by ^1H NMR spectroscopy using mesitylene as an internal standard.

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