

# Computer-Assisted Drug Design

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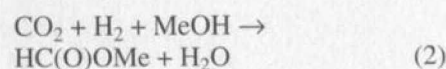
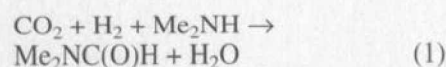
## Novel Homogeneous and Heterogeneous Catalysts for the Synthesis of Formic-Acid Derivatives from CO<sub>2</sub>

Oliver Kröcher, René A. Köppel, and Alfons Baiker\*

**Abstract.** Recently developed homogeneous and heterogeneous catalysts for the synthesis of *N,N*-dimethylformamide (DMF) and methyl formate (MF) from carbon dioxide are compared with respect to their catalytic performance. Among all catalysts known today, ruthenium catalysts with bidentate phosphine ligands show best performance in the synthesis of DMF and MF, affording turnover frequencies of 360 000 h<sup>-1</sup> at 100% selectivity (DMF) and 830 h<sup>-1</sup> (MF), respectively. Among the heterogeneous catalysts, a hybrid gel made up of [RuCl<sub>2</sub>{P(CH<sub>3</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>Si(OC<sub>2</sub>H<sub>5</sub>)<sub>3</sub>}<sub>3</sub>] incorporated into a silica matrix exhibits best performance, reaching turnover frequencies of 1860 h<sup>-1</sup> for DMF and 85 h<sup>-1</sup> for MF synthesis, respectively.

### Previous Developments

In the past two decades, the synthesis of *N,N*-dimethylformamide (DMF, Eqn. 1) and methyl formate (MF, Eqn. 2) from carbon dioxide has gained considerable attention as an interesting alternative route for producing these basic chemicals [1–3].



Both reactions are exothermic but, depending on the reaction conditions, neutral or slightly exergonic due to the unfavorable entropy change. To reach high product yields, high pressures and relatively low temperatures have to be applied. In order to stabilize the formic acid,

which is regarded as a crucial intermediate, the addition of a basic additive is beneficial. In MF synthesis the stabilizing additive is a tertiary amine such as tri-

ethylamine. In DMF synthesis, dimethylamine acts as a basic additive and as reactant, forming the product on reacting with the formic-acid intermediate. To reach high reaction rates, the use of a catalyst is crucial for this type of reactions. Here we compare the performance of the most active known homogeneous and heterogeneous catalysts with highly active Ru-based catalysts recently developed in our laboratory.

Over the past two decades, various group(VIII)-based transition-metal complexes have been tested as catalysts in the synthesis of DMF and MF from CO<sub>2</sub> in liquid solvents [1–3]. In 1970, Haynes *et al.* [4] reported the homogeneously catalyzed formation of DMF from H<sub>2</sub>, CO<sub>2</sub>, and dimethylamine using various transition-metal complexes with Ph<sub>3</sub>P or dppe (= Ph<sub>2</sub>P(CH<sub>2</sub>)<sub>2</sub>PPh<sub>2</sub>) ligands. With benzene as a solvent, up to 1200 catalytic cycles per metal center (turnover number, TON) corresponding to turnover frequencies (TOF/h<sup>-1</sup> = TON per hour) up to 71 h<sup>-1</sup> were achieved at 125° with [(Ph<sub>3</sub>P)<sub>2</sub>(CO)IrCl]. Among the group(VIII) metals tested in the following years by various groups, Rh- and Ru-based systems with phosphine ligands proved to be most effective for DMF synthesis. However, overall catalytic activity remained low, as can be seen from the comparison of activity data shown in Fig. 1. Till 1993, the most

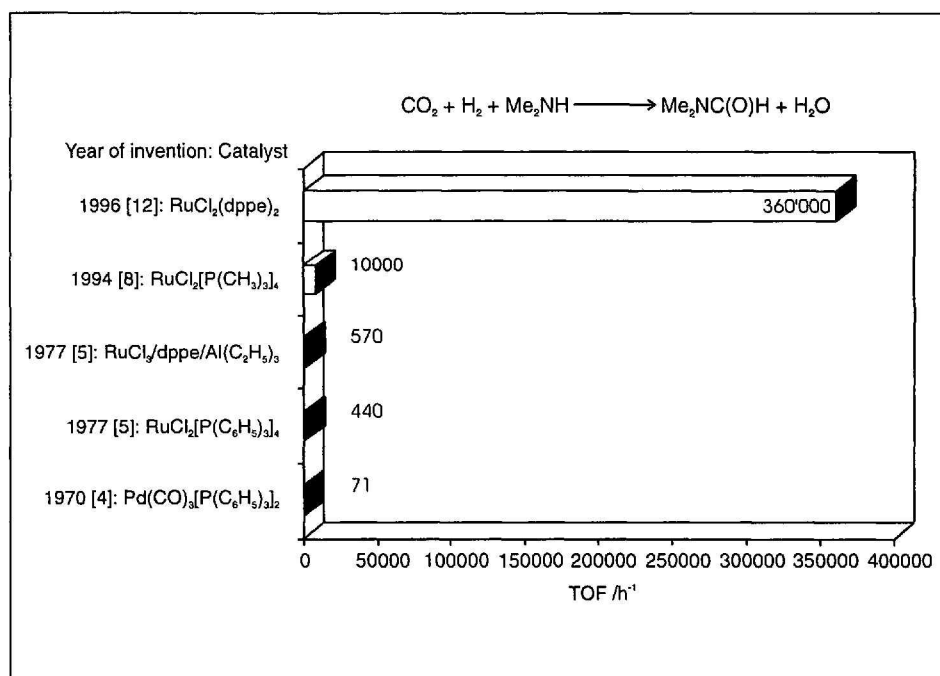


Fig. 1. Comparison of turnover frequencies (TOF) of catalysts in DMF synthesis from CO<sub>2</sub>

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active catalysts for DMF formation were still ruthenium(II)-phosphine complexes reported by *Kiso and Saeki* [5] in 1977. In hexane as a solvent, a TON of 3400 (TOF =  $570 \text{ h}^{-1}$ ) was observed with dppe as a ligand.

Similar as with DMF synthesis, phosphine complexes of group(VIII) transition metals were found to be active homogeneous catalysts for the formation of MF from  $\text{CO}_2$ ,  $\text{H}_2$ , and MeOH in the presence of organic solvents (Fig. 2). The phosphine complexes with basic cocatalysts give mixtures of formate salts and MF. *Lodge and Smith* [6] used insoluble metal oxides as bases. With  $[\text{RuCl}_2(\text{PPh}_3)_3]$  as a catalyst, a TOF of  $7.3 \text{ h}^{-1}$  was observed in MF formation from  $\text{CO}_2$ ,  $\text{H}_2$ , and MeOH in THF in the presence of  $\text{Al}_2\text{O}_3$ . Among the catalysts tested till 1985, highest yields were reported by *Phala et al.* [7] using

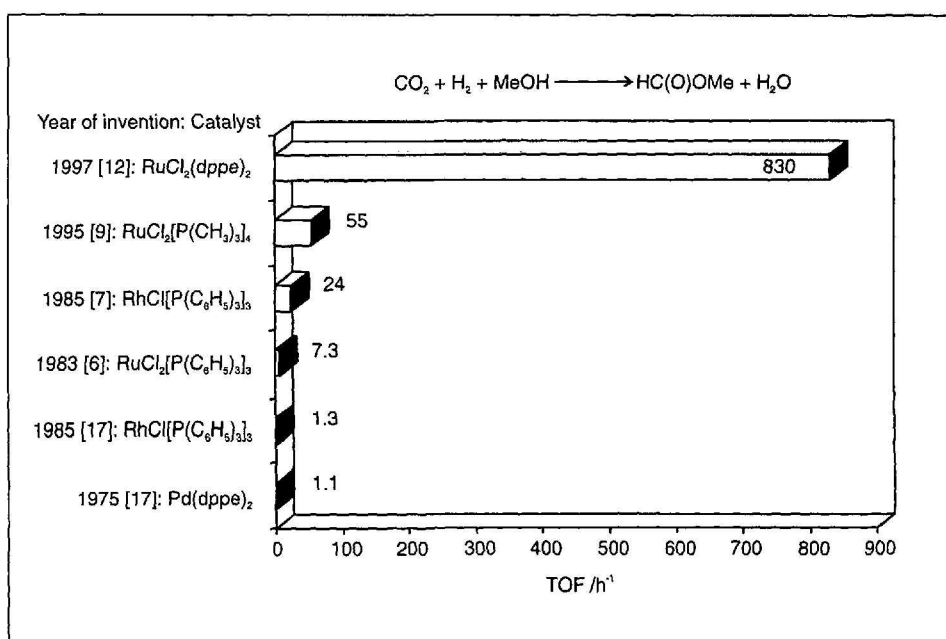


Fig. 2. Comparison of turnover frequencies (TOF) of catalysts in MF synthesis from  $\text{CO}_2$

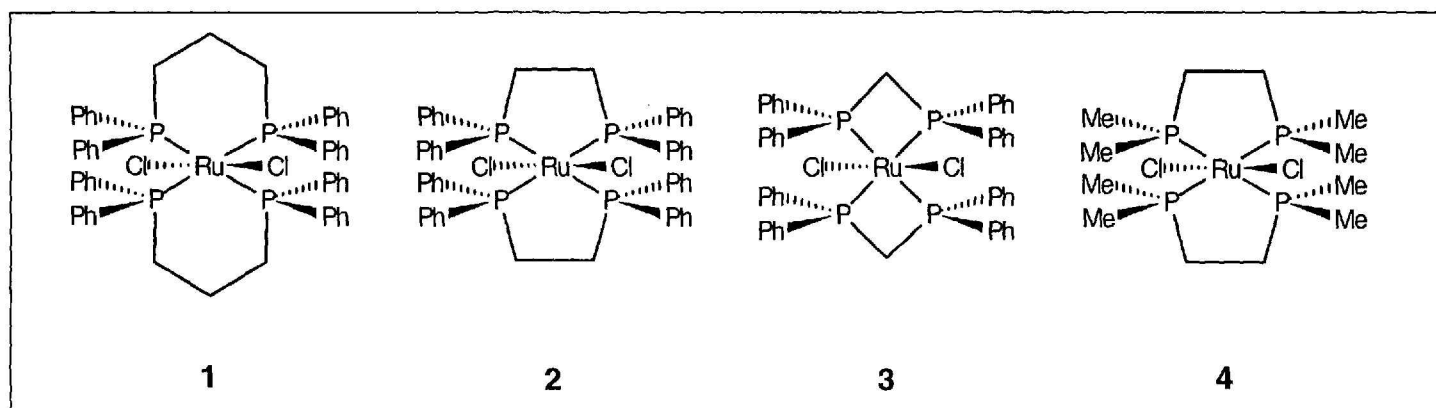


Fig. 3. Novel bidentate Ru complexes used for the homogeneous catalytic synthesis of DMF and MF from  $\text{CO}_2$

$[\text{RhCl}(\text{PPh}_3)_3]$  as a catalyst and triethylenediamine as a base, affording TOFs up to  $24^{-1}$  (Fig. 2).

A substantially more efficient reaction system for DMF and MF synthesis, not requiring any additional solvent, was recently reported by *Jessop et al.* [3][8][9], making use of a supercritical phase of  $\text{CO}_2$  and  $\text{H}_2$  in which the catalyst is dissolved. In this case  $\text{CO}_2(\text{sc})$  serves as both a reactant and a solvent. In the presence of  $[\text{RuCl}_2(\text{PMe}_3)_4]$  and  $\text{NEt}_3$ , TON values in MF synthesis up to 3500 were obtained in 64 h at  $80^\circ$ , with corresponding TOF values of  $55 \text{ h}^{-1}$  [9]. In DMF synthesis, a maximum TON of 370000 with a corresponding TOF of  $10000 \text{ h}^{-1}$  was reported [3][8], which exceeded the previously reported values by a factor of 17. The high reaction rate was attributed to favorable mass transfer effects, high solubility of  $\text{H}_2$ , and weak solvation of the catalyst compared to liquid solvents [9]. The application of complexes soluble in  $\text{CO}_2(\text{sc})$  was reported to be crucial for achieving high activities in this reaction system, and

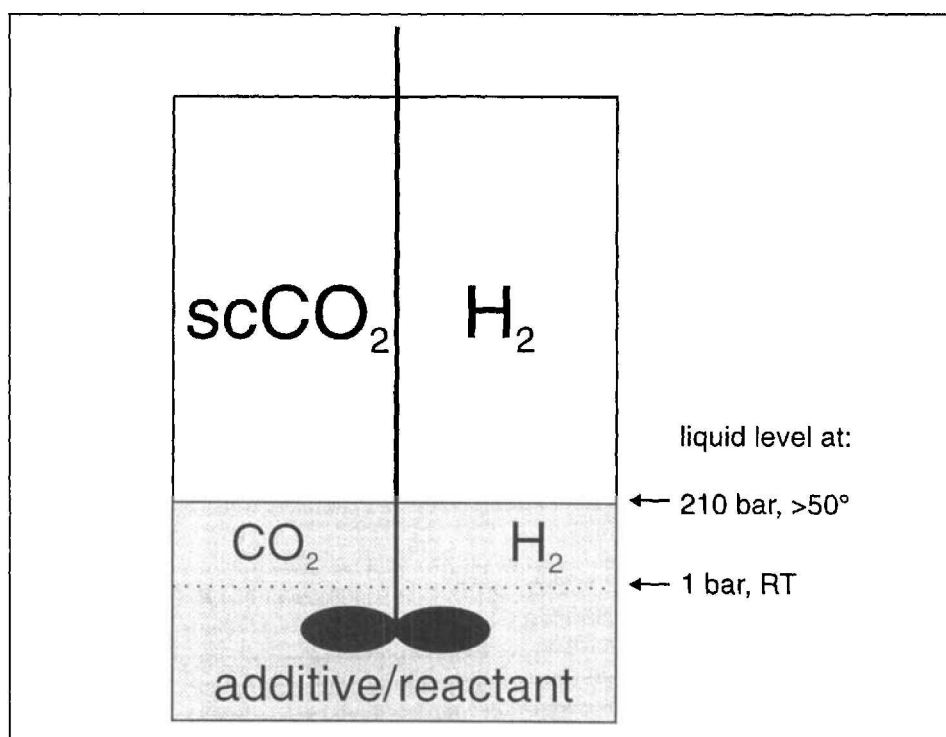


Fig. 4. Distribution of the reactants in the supercritical and the liquid phase in the autoclave under standard reaction conditions

it seemed unlikely that a similar increase in hydrogenation activity could be achieved with subcritical CO<sub>2</sub>.

### New Developments

Although the processes reported by Jessop *et al.* [3][8][9] are far more efficient than the corresponding liquid-phase synthesis of DMF and MF, overall reaction rates are still relatively low and the catalysts are sensitive to air, rendering this route rather troublesome for economic technical utilization. In order to find more active and stable catalysts for the synthesis of DMF and MF, we have recently investigated the potential of Ru complexes with bidentate ligands of the type dppm (= Ph<sub>2</sub>PCH<sub>2</sub>PPh<sub>2</sub>), dppe (= Ph<sub>2</sub>P(CH<sub>2</sub>)<sub>2</sub>PPh<sub>2</sub>), dppp (= Ph<sub>2</sub>P(CH<sub>2</sub>)<sub>3</sub>PPh<sub>2</sub>), and dmpe (= Me<sub>2</sub>P(CH<sub>2</sub>)<sub>2</sub>PMe<sub>2</sub>) (Fig. 3). These

complexes, which are stable against water and air, can be easily prepared from RuCl<sub>3</sub> and the corresponding phosphine ligands [10][11]. The resulting catalysts proved to be extremely active in DMF synthesis from CO<sub>2</sub>, H<sub>2</sub>, and Me<sub>2</sub>NH, affording turnover frequencies of 360 000 h<sup>-1</sup> with **1** (Fig. 3) ( $n[\text{catalyst}] = 0.58 \mu\text{mol}$ ,  $n[\text{Me}_2\text{NH}] = 2.44 \text{ mol}$ ,  $p[\text{H}_2] = 85 \text{ bar}$ ,  $p[\text{CO}_2] = 130 \text{ bar}$ ,  $t = 2.05 \text{ h}$ ,  $T = 100^\circ$ ), 2650 h<sup>-1</sup> with **2**, 190 000 h<sup>-1</sup> with **3**, and 2000 h<sup>-1</sup> with **4** [12]. In addition, MF could be produced very efficiently with TOFs up to 830 h<sup>-1</sup> ( $n[\text{catalyst}] = 3.8 \mu\text{mol}$ ,  $n[\text{MeOH}] = 0.74 \text{ mol}$ ,  $n[\text{N}(\text{Et}_3)] = 0.37 \text{ mol}$ ,  $p[\text{H}_2] = 85 \text{ bar}$ ,  $p[\text{CO}_2] = 130 \text{ bar}$ ,  $t = 15.5 \text{ h}$ ,  $T = 100^\circ$ ). The extremely good results can be explained by high amounts of dissolved gases in the liquid phase at the bottom of the reactor under reaction conditions. A simplified scheme illustrating the distribution of the reactants in the

supercritical and the liquid phase is shown in Fig. 4. Jessop *et al.* have observed high swelling of the liquid phase at the bottom of the reactor by dissolved gases under comparable conditions [13]. Thus, high concentrations of CO<sub>2</sub> and possibly H<sub>2</sub> could be assumed in the liquid phase. High reaction rates (TOF = 36 500 h<sup>-1</sup>) were also obtained under subcritical conditions ( $n[\text{catalyst}] = 0.86 \mu\text{mol}$ ,  $n[\text{Me}_2\text{NH}] = 0.71 \text{ mol}$ ,  $p[\text{H}_2] = 30 \text{ bar}$ ,  $p[\text{CO}_2] = 12 \text{ bar}$ ,  $t = 2.0 \text{ h}$ ,  $T = 100^\circ$ ), indicating that this phase behavior is not limited to the supercritical region of CO<sub>2</sub>.

To overcome difficulties in separating the homogeneous catalysts from the products, the 'solvent-free' reaction design was extended to a heterogeneously catalyzed variant of these CO<sub>2</sub> hydrogenation reactions. Anchoring of catalytically active metal complexes *via* organic groups within oxide networks offers the possibility to combine the advantages of both homogeneous and heterogeneous catalysts. Silylether-complex analogues (**9–12**) of different group(VIII)-metal complexes, *e.g.* Ru catalysts (**5**, **6**) and Wilkinson-type catalysts (**7**, **8**) (Fig. 5), have been incorporated successfully into a silica matrix applying the sol-gel method (Scheme) [14][15]. These heterogeneous hybrid-gel catalysts can easily be separated from the reaction mixture by simple filtration and are stable under reaction conditions, except the Rh-containing catalyst.

The Ru catalysts proved to be most active, affording TONs up to 110 800 with corresponding TOFs up to 1860 h<sup>-1</sup> in DMF synthesis ( $n[\text{catalyst}] = 50 \mu\text{mol}$ ,  $n[\text{Me}_2\text{NH}] = 6.4 \text{ mol}$ ,  $p[\text{H}_2] = 85 \text{ bar}$ ,  $p[\text{CO}_2] = 130 \text{ bar}$ ,  $t = 60 \text{ h}$ ,  $T = 133^\circ$ ) with **9**. This turnover frequency exceeds those previously achieved with heterogeneous catalysts [16] by a factor of 600, and this in conjunction with much higher selectivities. Under standard conditions ( $n[\text{catalyst}] = 50 \mu\text{mol}$ ,  $n[\text{Me}_2\text{NH}] = 0.7 \text{ mol}$ ,  $p[\text{H}_2] = 85 \text{ bar}$ ,  $p[\text{CO}_2] = 130 \text{ bar}$ ,  $t = 15 \text{ h}$ ,  $T = 100^\circ$ ), a maximum TOF of 900 h<sup>-1</sup> could be achieved with **9** and a TOF of 290 h<sup>-1</sup> was obtained with **10**. Lower TOFs were reached with **11** (190 h<sup>-1</sup>) and **12** (35 h<sup>-1</sup>), containing Ir and Rh, respectively, as a group(VIII) metal. The catalysts could be used at least three times without any deactivation. In MF synthesis ( $n[\text{catalyst}] = 14.1 \mu\text{mol}$ ,  $n[\text{MeOH}] = 0.74 \text{ mol}$ ,  $n[\text{N}(\text{Et}_3)] = 0.074 \text{ mol}$ ,  $p[\text{H}_2] = 85 \text{ bar}$ ,  $p[\text{CO}_2] = 130 \text{ bar}$ ,  $t = 15.0 \text{ h}$ ,  $T = 120^\circ$ ), turnover frequencies up to 116 h<sup>-1</sup> were achieved with **9**, which exceeds the TOF for the best hitherto known homogeneous catalyst [9] by a factor of two, and this at lower amine concentration.

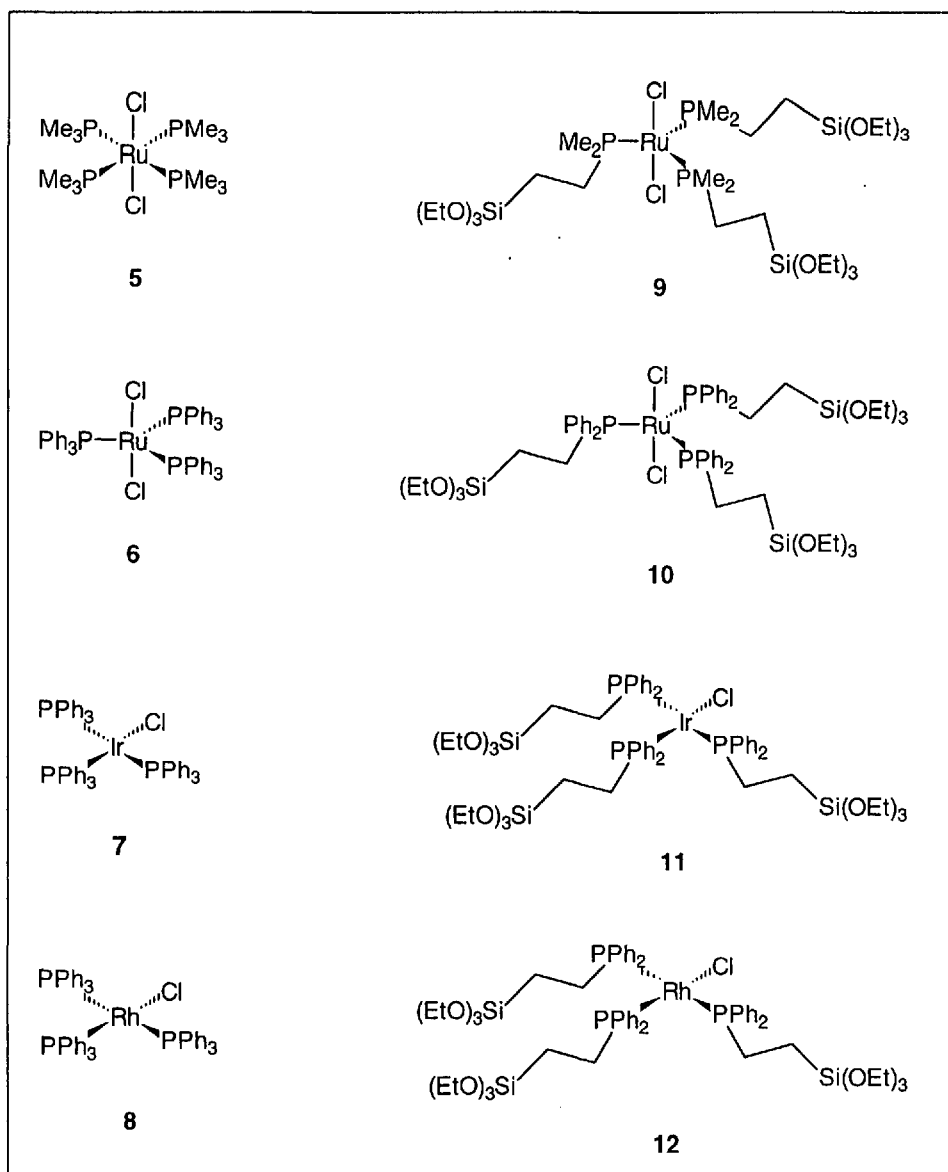
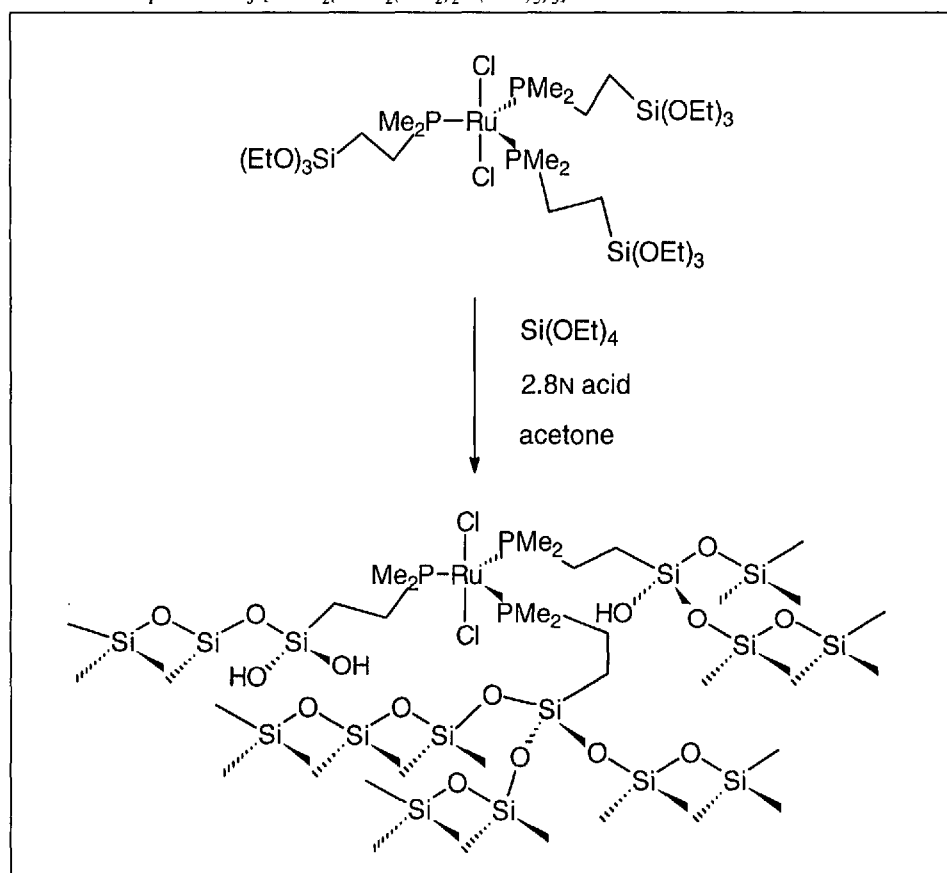


Fig. 5. Comparison of homogeneous group(VIII)-metal complexes (left) and corresponding silylether analogues (right) used as precursors for hybrid-gel catalysts

Scheme. Incorporation of  $[RuCl_2(PMe_2(CH_2)_2Si(OEt)_3)_3]$  into a Silica Matrix

Present research in our laboratory aims at combining the excellent catalytic properties of ruthenium bidentate-phosphine complexes with the technical advantages of heterogeneous hybrid-gel catalysts.

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