

# A significant effect of anion binding ureas on the product ratio in the palladium(II)-catalyzed hydrocarbonylation of alkenes

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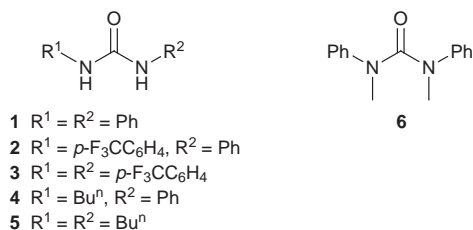
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**Hydrogen bonding of urea derivatives to the anionic ligands X of (dppp)PdX<sub>2</sub> catalysts significantly increases the hydroacylation of cyclopentene relative to the hydroformylation, most probably due to a decreased coordination strength of the anionic ligands.**

Transition metal complexes are important homogeneous catalysts for alkene polymerization<sup>1</sup> and alkene/CO copolymerization reactions.<sup>2</sup> In the L<sub>2</sub>PdX<sub>2</sub>-catalyzed hydrocarbonylation of alkenes with synthesis gas (CO/H<sub>2</sub>) either aldehydes (hydroformylation), ketones (hydroacylation), or polyketones (copolymerization) are formed. The type of reaction is determined mainly by the coordination strength of the anionic ligands X in L<sub>2</sub>PdX<sub>2</sub>.<sup>3</sup> Only Pd<sup>II</sup> catalysts with weakly coordinating anions (e.g. X = TFA) show sufficient activity in such hydrocarbonylation reactions. These catalysts are prepared by anion metathesis reactions of L<sub>2</sub>PdX<sub>2</sub> with the corresponding silver salt (X = Cl)<sup>4</sup> or Brønsted acid (X = OAc).<sup>5</sup> Alternatively, strong Lewis acids like methylalumoxane (MAO)<sup>6</sup> or SnCl<sub>2</sub><sup>7</sup> are added.

Our group has developed a variety of anion receptors based on multiple hydrogen bonding to (sulfon)amides<sup>8</sup> or (thio)ureas,<sup>9</sup> or coordination to a Lewis acidic uranyl center.<sup>10</sup> These anion receptors have been applied for anion-selective sensors (CHEMFETs)<sup>11</sup> and in membrane transport studies. Recently, we have described the catalytic activity of anion receptors in acyl transfer reactions.<sup>12</sup>

Here we show that *N,N'*-disubstituted urea derivatives **1–5**



significantly influence the performance of the (dppp)PdX<sub>2</sub> catalyst [dppp = 1,3-bis(diphenylphosphino)propane] in hydrocarbonylation reactions. The effect is attributed to the interaction<sup>13</sup> of the acidic urea protons with the counterions (X = OAc, TFA, OTs) leading to a decrease in their coordination strength. There are reports of hydrogen bonding to the anionic ligands of transition metal complexes in the solid state.<sup>14</sup> To the best of our knowledge this is the first report in which hydrogen bonding to the anionic ligands of a homogeneous catalyst alters the product ratio of the reaction.<sup>15</sup>

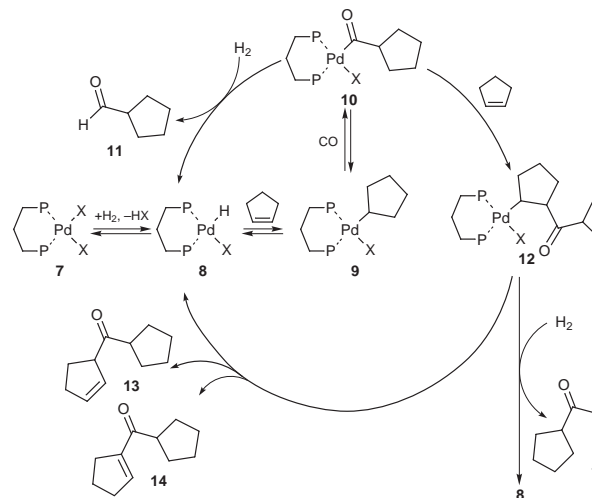
As a model reaction we used the Pd<sup>II</sup>-catalyzed hydrocarbonylation of cyclopentene with synthesis gas in anisole.<sup>†</sup> The mechanism for this reaction<sup>3</sup> is depicted in Scheme 1. Hydride **8** is formed by reaction of precatalyst (dppp)PdX<sub>2</sub> with H<sub>2</sub>. The rate of the subsequent exchange reaction of cyclopentene for X depends strongly on the coordination strength of the counterion to the Pd center.<sup>4,16</sup> Migratory insertion gives the  $\sigma$ -alkyl-Pd complex **9** and consecutive CO insertion yields the acyl-Pd intermediate **10**. The formation of **10** from **8** is

monitored by the turnover number of CO (TON<sub>CO</sub>), i.e. the number of CO insertions per Pd center. Intermediate **10** can react further in two different ways, either giving cyclopentane-carbaldehyde **11** or yielding one of the ketones **13–15** after insertion of a second molecule of cyclopentene. In all cases **8** is regenerated either by  $\beta$ -elimination or by oxidative addition of HX to the Pd<sup>0</sup> complex formed.

The selectivity for ketones increases from 14 to 98% reflecting the decrease in coordination strength of the anionic ligands X in the series of (dppp)PdX<sub>2</sub> (X = TFA, OMs, OTs, OTf, entries 1–4 in Table 1) with  $6.0 \times 10^2 < \text{TON}_{\text{CO}} < 9.2 \times 10^2 \text{ mol (mol Pd)}^{-1} \text{ h}^{-1}$ . With (dppp)Pd(OAc)<sub>2</sub> (entry 5) the TON<sub>CO</sub> is reduced to  $0.2 \times 10^2 \text{ mol (mol Pd)}^{-1} \text{ h}^{-1}$  because of the stronger coordinating acetate, and the selectivity for ketones is 24%. Weaker coordinating anions may enhance the (intrinsic) electrophilicity of the Pd<sup>II</sup> center and, of course, these anions are more easily displaced from the (fourth) coordination site which facilitates the formation of intermediates **10** (increased TON<sub>CO</sub>) and **12** (increased selectivity for ketones).

We found that in the presence of 0.6 mol% [7.5 equiv. with respect to the (dppp)Pd(TFA)<sub>2</sub> catalyst] of *N,N'*-diphenylurea **1** the selectivity for ketones increases from 14 to 25% (entry 6 in Table 1), whereas the TON<sub>CO</sub> increases from  $6.0 \times 10^2$  to  $7.8 \times 10^2 \text{ mol (mol Pd)}^{-1} \text{ h}^{-1}$ .<sup>‡</sup> With 0.6 mol% of the urea derivatives **2** and **3**, containing either one or two electron-withdrawing substituents at the phenyl rings that will increase the anion affinity of the urea moiety,<sup>17</sup> the selectivity for ketones shows a sharp increase from 14 to 49 and 61%, respectively (entries 7 and 8). In both cases the TON<sub>CO</sub> is similar to that in the presence of urea **1**. Both *N*-butyl-*N'*-phenylurea **4** and *N,N'*-dibutylurea **5** do not significantly change the selectivity for ketones (entries 9 and 10), which is in accordance with the much lower acidity and anion binding strength of (di)alkyl ureas compared to diaryl ureas.<sup>18</sup>

The altered selectivities of the catalyst upon addition of diarylureas **1** or **3** were also observed for the catalysts



**Scheme 1** Catalytic cycle for the Pd<sup>II</sup>-catalyzed hydrocarbonylation of cyclopentene.

**Table 1** Selectivity for ketones and turnover number for the hydrocarbonylation of cyclopentene with CO and H<sub>2</sub> in the presence of urea derivatives **1–6**<sup>a</sup>

| Entry | Anion            | Receptor <sup>b</sup> | Selectivity (%) <sup>c</sup> | TON <sub>CO</sub> /10 <sup>2</sup> mol (mol Pd) <sup>-1</sup> h <sup>-1</sup> <sup>d</sup> |
|-------|------------------|-----------------------|------------------------------|--|
| 1     | OTf              | —                     | 98                           | 8.7  |
| 2     | OTs              | —                     | 54                           | 8.2  |
| 3     | OMs              | —                     | 41                           | 9.2  |
| 4     | TFA              | —                     | 14                           | 6.0  |
| 5     | OAc              | —                     | 24                           | 0.2  |
| 6     | TFA              | <b>1</b>              | 25                           | 7.8  |
| 7     | TFA              | <b>2</b>              | 49                           | 7.8  |
| 8     | TFA              | <b>3</b>              | 61                           | 8.3  |
| 9     | TFA              | <b>4</b>              | 16                           | 5.9  |
| 10    | TFA              | <b>5</b>              | 10                           | 5.1  |
| 11    | OAc              | <b>1</b>              | 45                           | 0.4  |
| 12    | OAc              | <b>3</b>              | 80                           | 0.4  |
| 13    | OTs <sup>e</sup> | <b>1</b>              | 82                           | 7.0  |
| 14    | OTs              | <b>3</b>              | 95                           | 10   |
| 15    | TFA              | <b>6</b>              | 14                           | 6.4  |
| 16    | TFA <sup>f</sup> | <b>6</b>              | 12                           | 5.8  |
| 17    | OAc              | <b>6</b>              | 25                           | 0.3  |
| 18    | OTs              | <b>6</b>              | 51                           | 9.6  |

<sup>a</sup> Cyclopentene (5 ml), anisole (10 ml), (dppp)PdX<sub>2</sub> (0.08 mol%), 110 °C, 80 bar (CO:H<sub>2</sub> = 1:1), analysis by GC FID, integrals were not corrected for sensitivities. <sup>b</sup> 7.5 equiv. cocatalyst compared to Pd catalyst. <sup>c</sup> Percentage of hydroacylation products (**13–15**) of the total amount of products formed, accuracy ±2%. <sup>d</sup> Turnover number of CO determined as the sum of TONs of all products **11**, **13**, **14** and **15**; accuracy ±5% (see note ¶). <sup>e</sup> 10 equiv. cocatalyst **5**. <sup>f</sup> 13 equiv. cocatalyst **6**.

(dppp)Pd(OAc)<sub>2</sub> (entries 11 and 12) and (dppp)Pd(OTs)<sub>2</sub> (entries 13 and 14). In both cases the stronger anion binding urea **3** causes the largest change in the selectivity for ketones, *i.e.* from 24 to 80% for (dppp)Pd(OAc)<sub>2</sub> and from 54 to 95% for (dppp)Pd(OTs)<sub>2</sub>. The TON<sub>CO</sub> is enhanced from 0.2 × 10<sup>2</sup> to 0.4 × 10<sup>2</sup> and from 8.2 × 10<sup>2</sup> to 10 × 10<sup>2</sup> mol (mol Pd)<sup>-1</sup> h<sup>-1</sup>, respectively. These results suggest that the observed increase in ketone formation is the result of complexation of the anionic ligands by the urea derivatives **1–3** via hydrogen bonding which decreases the coordination strength of the counterions to the Pd center.

Experiments carried out in the presence of a large excess of tetrasubstituted urea **6**, which is unable to bind anions via hydrogen bonding, show that neither the selectivity for ketones nor the TON<sub>CO</sub> is affected to a significant extent (entries 15–18 in Table 1). This excludes the possibility that the observed effect is due to coordination of the urea carbonyl to the Pd center or to a change in the polarity of the reaction medium. §

Our results show that hydrogen bond formation to the anionic ligands X of (dppp)Pd catalysts can significantly change the selectivity of the catalyst in the hydrocarbonylation of cyclopentene with synthesis gas. Addition of *N,N'*-diarylureas **1–3** strongly favours hydroacylation with respect to hydroformylation. The maximum effect is observed with the stronger anion binding urea **3**.

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## Notes and references

† *Experimental procedure:* Hydrocarbonylation experiments were performed in a 100 ml autoclave at 110 °C. 10 ml anisole, 5 ml cyclopentene, 0.08 mol% of (dppp)PdX<sub>2</sub> catalyst, and urea cocatalyst were brought under a H<sub>2</sub> atmosphere whereafter the autoclave was pressurized with 40 bar CO and 40 bar H<sub>2</sub>. After a reaction time of 20 h the autoclave was cooled down and the gas (pressure drop < 15 bar) was vented off. The products were analysed by GC FID (CPSIL-5, 50 m).

‡ The amount of added *N,N'*-diphenylurea **1** correlates well with the selectivity for ketones formed in the reaction and the TON<sub>CO</sub>. With varying amounts (2–18 equiv.) of **1** as cocatalyst in the (dppp)Pd(TFA)<sub>2</sub> catalyzed reaction both the selectivity for ketones and the TON<sub>CO</sub> are increased. A maximum of 37% and 8.9 × 10<sup>2</sup> mol (mol Pd)<sup>-1</sup> h<sup>-1</sup> was reached with 1.5 mol% (18 equiv.) of **1** (limited by the solubility of **1** in the reaction medium).

§ Additional evidence for hydrogen bond formation of **1–5** to the anionic ligands X of (dppe)PdX<sub>2</sub> (X = Cl, TFA, OTs) was obtained by IR, <sup>1</sup>H and <sup>31</sup>P NMR spectroscopic studies in CDCl<sub>3</sub> at room temperature (ref. 19). Addition of 2 equiv. (dppe)PdCl<sub>2</sub> to an 1 mM solution of *N,N'*-diphenylurea **1** (free N–H vibration at 3422 cm<sup>-1</sup>) gave rise to an additional N–H stretch frequency at 3330 cm<sup>-1</sup> in the FT–IR spectrum. The <sup>1</sup>H NMR spectra of ureas **1–5** show in all cases downfield shifts (0.40 > Δδ > 0.15 ppm) for the urea proton signals upon addition of 1 equiv. of (dppp)PdX<sub>2</sub>, which is indicative for hydrogen bond formation. Furthermore the <sup>31</sup>P NMR resonances of the (dppe)PdX<sub>2</sub> complexes shift over 1 ppm downfield upon addition of 2 equiv. of **1**. Similar downfield shifting of the <sup>31</sup>P NMR resonances is also observed upon weakening of the coordination strength of the anions of (dppe)PdX<sub>2</sub> (X = TFA: δ 63.1; X = OTs: δ 69.9). In contrast to this the addition of 1,3-dimethyl-1,3-diphenylurea **6** to the Pd complexes did not induce any significant shift of the <sup>31</sup>P NMR resonances.

¶ The TONs based on conversion of cyclopentene (TON<sub>c</sub>) can easily be calculated from Table 1 according to TON<sub>c</sub> = TON<sub>CO</sub> × (1 + selectivity).

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