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## Carbene Radicals in Cobalt(II)–Porphyrin-Catalysed Carbene Carbonylation Reactions; A Catalytic Approach to Ketenes

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### Keywords

carbenes; carbonylation; cobalt; ketenes; radicals; porphyrinoids

Ketenes have intrigued chemists with their unusual physical properties and their unique spectrum of chemical reactivity.<sup>[1]</sup> Ketenes are usually prepared by thermolysis, pyrolysis or in a stoichiometric manner from acyl chlorides using base-promoted elimination reactions.<sup>[2]</sup> Synthesis of ketenes from  $\alpha$ -diazoketones by means of the Wolff rearrangement<sup>[2d]</sup> is also noteworthy. However, all these synthetic methods have severe limitations and involve specialised equipment and/or highly unstable starting materials.

Carbonylation of metal–carbene species<sup>[3–6]</sup> is an interesting alternative method to produce such highly reactive ketenes, which find synthetic applications in various organic transformations.<sup>[1, 4, 5]</sup> The synthesis of medicinally important  $\beta$ -lactams by [2+2] ketene–imine cycloaddition reactions is especially important in this perspective.<sup>[5]</sup> Carbonylation reactions of Fischer carbene complexes have indeed been applied successfully to synthesise  $\beta$ -lactams.<sup>[5a, b]</sup> However, these are stoichiometric transformations, which hamper efficiency. Following the discovery of stoichiometric carbonylation reactions of Fischer-type carbene complexes, thus far only a few transition-metal-catalysed processes have been developed.<sup>[5, 6]</sup> While interesting results have recently been obtained with a noble (palladium) metal catalyst,<sup>[5c]</sup> carbene carbonylation by base-metal catalysts reported thus far were associated with low efficiencies and required quite harsh reaction conditions (elevated temperatures and high CO pressures).<sup>[6]</sup> Therefore, we focused on the development of new catalytic carbene carbonylation processes by catalysts based on abundant first-row transition metals that operate under comparably mild reaction conditions.

As stable metalloradicals with well-defined open-shell doublet  $d^7$ -electronic configuration, cobalt(II) complexes of porphyrins [ $\text{Co}^{\text{II}}(\text{Por})$ ] have emerged as a new class of catalysts capable of carbene-transfer reactions<sup>[7]</sup> proceeding through radical mechanisms involving discrete  $\text{Co}^{\text{III}}$ -carbene radical intermediates **C** (Scheme 1).<sup>[8]</sup>

In comparison with classic electrophilic Fischer-type carbenes, the increased nucleophilicity of the carbene radical intermediate **C** slows-down unwanted carbene dimerisation while allowing for catalytic cyclopropanation through radical addition to olefinic substrates, including electron-deficient olefins.<sup>[7, 8]</sup> In this respect, we envisioned that similar intermediates might well be effective in carbene carbonylation reactions, which can be considered as an attack of a nucleophilic cobalt-carbene radical (**C**) at the  $\pi$ -accepting CO substrate. At the same time, both the [ $\text{Co}(\text{Por})$ ] catalyst and the carbenoid intermediates are expected to interact only weakly with amines, alcohols, imines and the ketene reaction products. Hence, we expected smooth catalytic ketene formation under comparatively mild conditions and their subsequent in situ reactions with nucleophiles in one-pot tandem procedures (see Scheme 1).

Here in we report an efficient one-pot tandem protocol of the carbonylation of  $\alpha$ -diazocarbonyl compounds and a variety of *N*-tosylhydrazones catalysed by  $\text{Co}^{\text{II}}$ -porphyrin metalloradicals leading to the formation of ketenes, which subsequently react with a variety of nucleophiles and imines to form esters, amides and  $\beta$ -lactams. This system has a broad substrate scope and can be applied to various combinations of carbene precursors, nucleophiles and imines. The use of *N*-tosylhydrazones as precursors of diazo compounds in cobalt-porphyrin-based carbene-transfer reactions is unprecedented, and represents an efficient and convenient way to prepare the key carbenoid intermediates (**C** in Scheme 1) responsible for ketene formation. The key ketene formation steps were further investigated computationally (DFT).

Since ketenes are highly reactive<sup>[5, 6]</sup> and can generally only be trapped in the presence of a strong nucleophile, we first evaluated the activity of [ $\text{Co}^{\text{II}}(\text{P1})$ ] (**P1** = tetraphenylporphyrin; Figure 1) in the catalytic carbonylation of ethyl diazoacetate (EDA; **1**) in presence of aniline (**2a**) under 10 bar CO at 50 °C. Under these conditions, (ethoxycarbonyl) ketene was formed and trapped by aniline to produce ethyl 2-(phenylcarbamoyl)acetate (**3a**) in 57% isolated yield (Table 1, entry 1). Further initial experiments focused on the evaluation of ligand and solvent effects on the carbonylation of EDA in the presence of aniline. Four different  $\text{Co}^{\text{II}}$ -porphyrin catalysts, including two chiral ones, were employed in an attempt to improve the catalytic process and to investigate potential asymmetric induction of the reaction (Figure 1). The catalysts [ $\text{Co}^{\text{II}}(\text{P1})$ ], [ $\text{Co}^{\text{II}}(\text{P2})$ ], and [ $\text{Co}^{\text{II}}(\text{P3})$ ] (see Supporting Information for experimental details) showed more or less similar activity, while the catalyst [ $\text{Co}(\text{P4})$ ] was found to be ineffective for this reaction (Table 1). No enantioselectivity was obtained using the chiral catalysts [ $\text{Co}^{\text{II}}(\text{P3})$ ] and [ $\text{Co}^{\text{II}}(\text{P4})$ ] under the various reaction conditions applied. This suggests that the ketene intermediate is liberated from the catalyst to react subsequently with the amine, freely in solution.

Optimisation of the reaction conditions revealed that the reaction proceeded most efficiently in nonpolar solvents, such as toluene and chlorobenzene, whereas reactions in solvents of

high polarities, such as THF, dioxane, MeCN and DMF, afforded poor yields (Table 1, entries 2–6). The use of inorganic bases  $K_2CO_3$  or  $K_3PO_4$  further improved the yields (Table 1, entries 8–11).

Reactions with other nucleophiles were evaluated to investigate the versatility of the reaction. The experiments indeed showed that the ketenes generated by the  $Co^{II}$ -porphyrin-catalysed carbene carbonylation could be trapped by a wide range of nucleophiles (Table 2). The reaction occurred smoothly with substituted aromatic amines (Table 2, entries 1–5), primary and secondary aliphatic amines (Table 2, entries 6–8) and alcohols (Table 2, entries 9 and 10).

To further investigate the scope of the reaction, imines were introduced into the reaction medium in an attempt to produce  $\beta$ -lactams in a one-pot tandem procedure involving [2+2] cycloaddition of the intermediate ketene with the imine. Indeed, a 1:2 mixture of ethyl diazoacetate (EDA; **1**) and *N*-methylbenzaldimine (**4a**) in dichloroethane (DCE) under a carbon monoxide atmosphere (20 bar) at 50°C in the presence of a catalytic amount of  $[Co^{II}(\mathbf{P1})]$  (2 mol%) led to formation of *trans-N*-methyl- $\alpha$ -ethoxycarbonyl- $\beta$ -phenyl- $\beta$ -lactam (**5a**) in 60% isolated yield (Table 3). Similar reactions using other imines  $PhCH=NR$  ( $R=CH_2Ph$  (**4b**) and *t*Bu (**4c**)) also produced the desired  $\beta$ -lactams (Table 3). Notably, the (ethoxycarbonyl)ketene generated by  $[Co^{II}(\mathbf{P1})]$ -catalysed carbene carbonylation participates selectively in [2+2] cycloaddition reactions with imines to produce the desired  $\beta$ -lactams (Table 3).

Reactions of other diazoacetates with imines also produced the desired  $\beta$ -lactams (Table 3). This behaviour is markedly different from the [4+2] cycloaddition reactions producing 1,3-dioxin-4-ones reported by Wang and co-workers in related palladium-catalysed reactions (see Scheme 2).<sup>[5c]</sup>

Again, the use of chiral catalyst  $[Co^{II}(\mathbf{P3})]$  and  $[Co^{II}(\mathbf{P4})]$  did not lead to any enantioselectivity, pointing to liberation of free ketene in solution reacting subsequently with the imine. Introduction of Cinchona alkaloid, quinidine and its derivatives into the reaction mixture in an attempt to trap the liberated ketene with a chiral organocatalysts<sup>[9]</sup> for chirality transfer in a one-pot cascade manner produced the  $\beta$ -lactams with a low *ee* of only 5% at 30 °C. This temperature is probably much too high for efficient chirality transfer with these organocatalysts (typically operating at  $-78^\circ C$ ), but this is the lowest possible temperature at which still some conversion can be achieved with these cobalt(II)-based catalysts. Nonetheless, this result reveals the potential of combining metallo and organo catalysts in cascade processes, which may become a useful concept to achieve enantioselective ketene reactivity when combined with more active cobalt catalysts working at lower temperatures in the future.

To expand the scope of the catalytic ketene synthesis methodology, carbonylation reactions were carried out with *N*-tosylhydrazones,<sup>[10]</sup> which are widely used as precursors for in-situ generation of non-stabilised diazo compounds. The use of *N*-tosylhydrazones as precursors of diazo compounds in cobalt-porphyrin-based carbene-transfer reactions was thus far unprecedented. The easy synthesis of these *N*-tosylhydrazones from ketones and aldehydes

combined with the above described [Co(Por)]-catalysed carbene carbonylation methodology offers a convenient method to convert an organic carbonyl moiety into a ketene functionality, applicable in one-pot three-component tandem transformations.

Reaction of the benzaldehyde tosylhydrazone sodium salt (**6a**) and aniline (**2a**) was catalysed by [Co<sup>II</sup>(**P1**)] under similar reaction conditions as mentioned above (50 °C, 10 bar CO). The benzyl ketene, thus generated in-situ, reacted with aniline to produce *N*-2-diphenylacetamide (**7a**) in 70% isolated yield (Table 4, entry 1). Further optimisation of the reaction conditions revealed that the yield could be improved by adding a phase transfer agent (Aliquat 336, trioctyl-methylammonium chloride; Table S1 in the Supporting Information). Both polar and nonpolar solvents were suitable for this reaction (Table S1 in the Supporting Information), and again toluene was the best solvent. The use of inorganic bases K<sub>2</sub>CO<sub>3</sub> or K<sub>3</sub>PO<sub>4</sub> further improved the yields (Table S1 in the Supporting Information).

Reactions with nucleophiles other than aniline were also investigated. The experiments showed that the ketenes generated from the tosylhydrazone sodium salts by means of [Co<sup>II</sup>(**P1**)]-catalysed carbene carbonylation method could also be trapped by different nucleophiles. Expected products were obtained with several amines and alcohols (Table 4, entries 1–8).

These results prompted us to explore the scope of the catalytic carbene carbonylation reactions using a series of *N*-tosylhydrazone sodium salts under the above optimised reaction conditions. The reactions produced the expected acetamide derivatives in good to high yields (Table 4, entries 9– 13). The reaction also worked well with disubstituted *N*-tosylhydrazones, although requiring longer reaction times (Table 4, entry 14). Also  $\alpha,\beta$ -unsaturated *N*-tosylhydrazones could be converted to amides, albeit in modest yields (Table 4, entry 15).

Upon introduction of imines to the reaction medium, the ketenes generated from these *N*-tosylhydrazone salts also reacted smoothly to produce the desired  $\beta$ -lactams. The use of a phase-transfer agent in this case did not have any influence. A series of *N*-tosylhydrazone salts were subjected to the reaction conditions with different benzaldimines (Table 5). In all cases, the corresponding  $\beta$ -lactams were obtained in good yields. Interestingly, for most of the substrates, the reactions afforded *trans* products with excellent diastereoselectivity. However, again no enantioselectivity was obtained using either chiral catalysts or by adding quinidine-based chiral organocatalysts into the reaction mixture.

To obtain more insight into the mechanistic aspects of [Co(Por)]-catalysed ketene formation, several controlled infrared studies of the reaction mixtures were carried out. Since, diphenylketene is known to be more stable than the corresponding monosubstituted ketenes, diphenyl tosylhydrazone sodium salt was intentionally chosen as the carbene source for IR analysis of the carbene carbonylation reaction mixtures (see Supporting Information Figure S1–S4). Indeed, carbonylation of the diphenyl tosylhydrazone sodium salt with 20 bar CO produces free diphenyl ketene, as indicated by observation of a characteristic IR stretch frequency at 2102 cm<sup>-1</sup> directly after the reaction.<sup>[11]</sup> Formation of the diphenyl diazo

compound<sup>[12]</sup> from the diphenyl tosylhydrazone sodium salt was also detected by IR spectroscopy, as revealed by observation of a characteristic stretch frequency at 2042 cm<sup>-1</sup>. These data are in excellent agreement with the proposed reaction mechanism shown in Scheme 1.

Repeated attempts to detect the more reactive benzyl ketene directly after reaction of the corresponding tosylhydrazone sodium salt with 20 bar CO were unsuccessful. This is likely due to too rapid dimerisation/oligomerisation and/or other side-reactions of the ketene in absence of a nucleophile or imine. The reaction mixture obtained directly after reacting the benzaldehyde tosylhydrazone salt with 20 bar CO in the presence of *N*-methylbenzaldimine does show characteristic C=O stretch frequency of the  $\beta$ -lactam at 1752 cm<sup>-1</sup>.<sup>[5c]</sup>

The mechanism of the above carbene carbonylation reactions was further investigated computationally by using DFT methods (see Supporting Information for details). In these studies, in contrast to previous investigations reported by our groups, we decided to include dispersion (VdW) corrections in the geometry optimisations. Remarkably, this modification had a profound influence on the affinity of the cobalt center for the diazo compound (bound through carbon), shifting the association equilibrium from **A** to **B** and resulting in a somewhat lower transition state barrier **TS1** (from **B**) for formation of the key Co<sup>III</sup>-carbene radical intermediate **C** (Scheme 1) than reported previously. It is also worth noting that with dispersion forces, the carbonbound methyl diazoacetate (MDA) adduct **B** was calculated to be more stable than the nitrogen-bound MDA adduct **B'**, while this was reversed in previous calculations without dispersion corrections.<sup>[8]</sup> Apart from this interesting effect of inclusion of dispersion forces in the calculations, this part of the catalytic mechanism is in fact identical to carbenoid formation in the calculated mechanism for olefin cyclopropanation.<sup>[8]</sup> Carbene radicals **C** are in equilibrium with "bridging carbenes" **C'** according to these calculations (nearly thermoneutral), and both **C**- and **C'**-type species were previously detected by EPR spectroscopy after reacting [Co<sup>II</sup>(**P3**)] with ethyl diazoacetate.<sup>[8a]</sup>

Subsequent carbonylation of terminal carbenoid **C** proceeds by means of a concerted one-step CO addition to the carbene moiety with simultaneous homolysis of the Co-C bond to produce the free ketene, according to DFT. The ketene has little to no affinity for cobalt, and spontaneously dissociates from the cobalt center directly after its formation. These calculations are in good agreement with the detection of free ketene in the above-mentioned IR experiments. The computed carbene carbonylation step has a somewhat lower energy barrier ( $G^*(\mathbf{TS2})=8.6$  kcalmol<sup>-1</sup> from **C**;  $G^*(\mathbf{TS2})=9.2$  kcalmol<sup>-1</sup> from **C'**) than the barrier for formation of **C** through dinitrogen loss from diazo adduct **B** (**TS1**=13.6 kcalmol<sup>-1</sup>).<sup>[8a]</sup> The rate-limiting step in the catalytic cycle according to these calculations under standard conditions in the gas phase is therefore the formation of carbene radical **C**. However, the energy differences between **TS1** and **TS2** are not large and at relative low CO concentrations and relative high EDA concentrations (i.e., non-standard conditions as in the catalytic experiments) the entropy contributions lower the relative barrier of **TS1** compared to **TS2**, allowing side reactions of **C** (e.g., carbene dimerisation, reaction with the solvent). This, in combination with the relatively low solubility of CO in common organic solvents,<sup>[13]</sup> most likely explains why CO pressures >10 bar are required in the experimental catalytic runs.

The ketene, thus generated in-situ, has no affinity for the [Co(Por)] catalyst according to these DFT calculations, and hence most likely reacts subsequently in a noncatalysed manner with nucleophiles or imines present in solution, leading to the final ester, amide or  $\beta$ -lactam products.<sup>[5c, 6]</sup> Given that carbon monoxide has a weak affinity for the cobalt(II) center,<sup>[14]</sup> it is unlikely for carbon monoxide to bind to the catalyst and thus influence the carbonylation of diazo compounds under the applied catalytic reaction conditions. The more nucleophilic character of **C** compared to Fischertype carbenes further reduces its reactivity towards nucleophiles, which is likely an important feature in preventing unwanted side-reactions.

In summary, we have demonstrated [Co<sup>II</sup>(Por)] are effective metalloradical catalysts for carbene carbonylation, producing ketenes from CO and diazo compounds or tosylhydrazones under mild conditions. The [Co<sup>II</sup>(Por)]-catalysed reaction, which involves a low-barrier carbene carbonylation step, provides a valuable synthetic alternative for the production of ketenes, which can be trapped in situ with amines, alcohols or imines to produce esters, amides or  $\beta$ -lactams in a one-pot cascade manner. This straightforward methodology has a broad substrate scope and can be applied for various combinations of diazo compounds and nucleophiles or imines. In addition to diazo compounds, [Co<sup>II</sup>(Por)]-catalysed carbonylation process can also employ tosylhydrazones derived from aldehydes and ketones as carbene sources. Consequently, this procedure offers an efficient way for the homologation of ketones and aldehydes, and also provides a diastereoselective method for the transformation of aldehydes to  $\beta$ -lactam derivatives. Future research in this area will focus on achieving enantioselective one-pot cascade reactions involving ketene intermediates.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

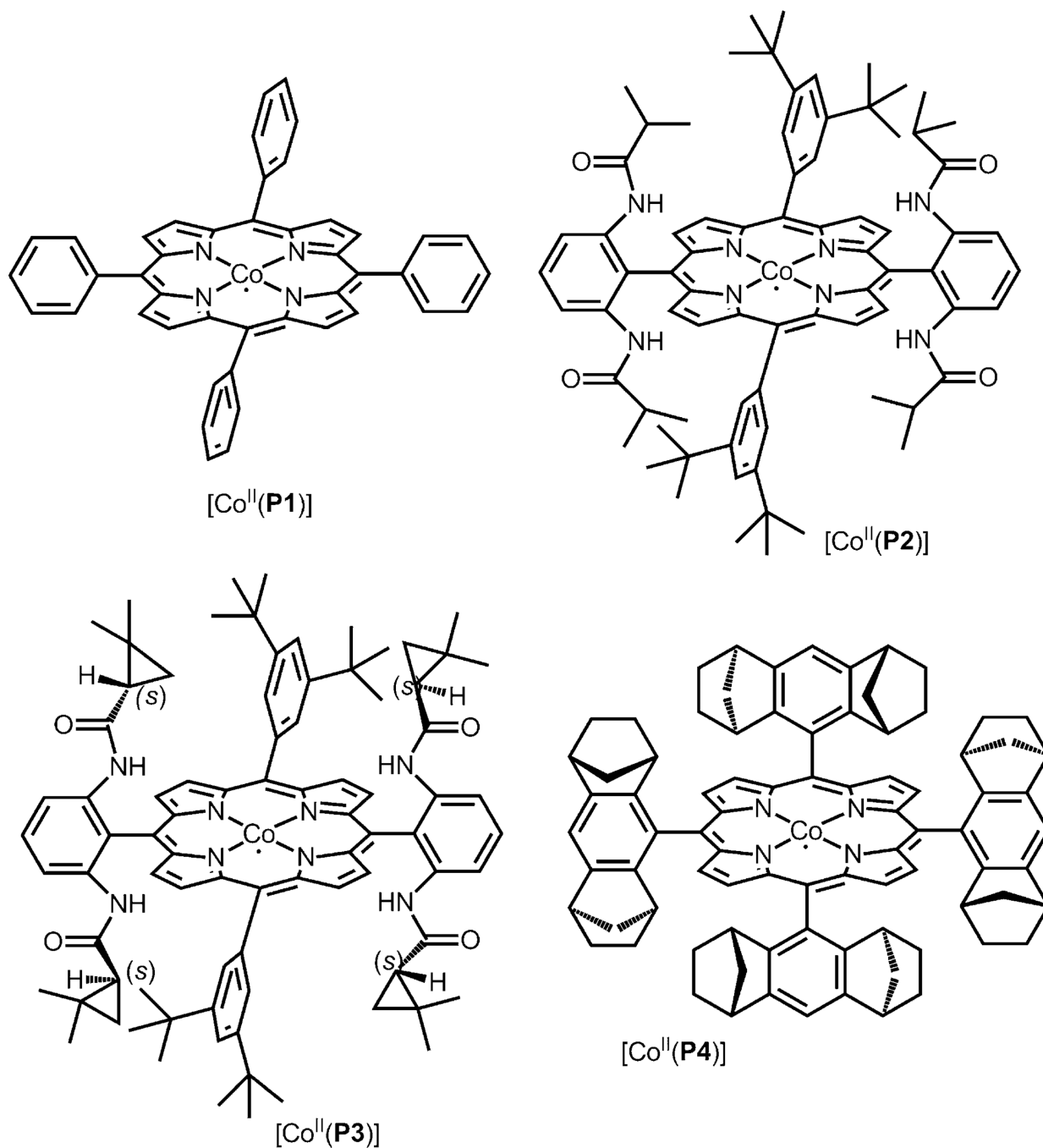
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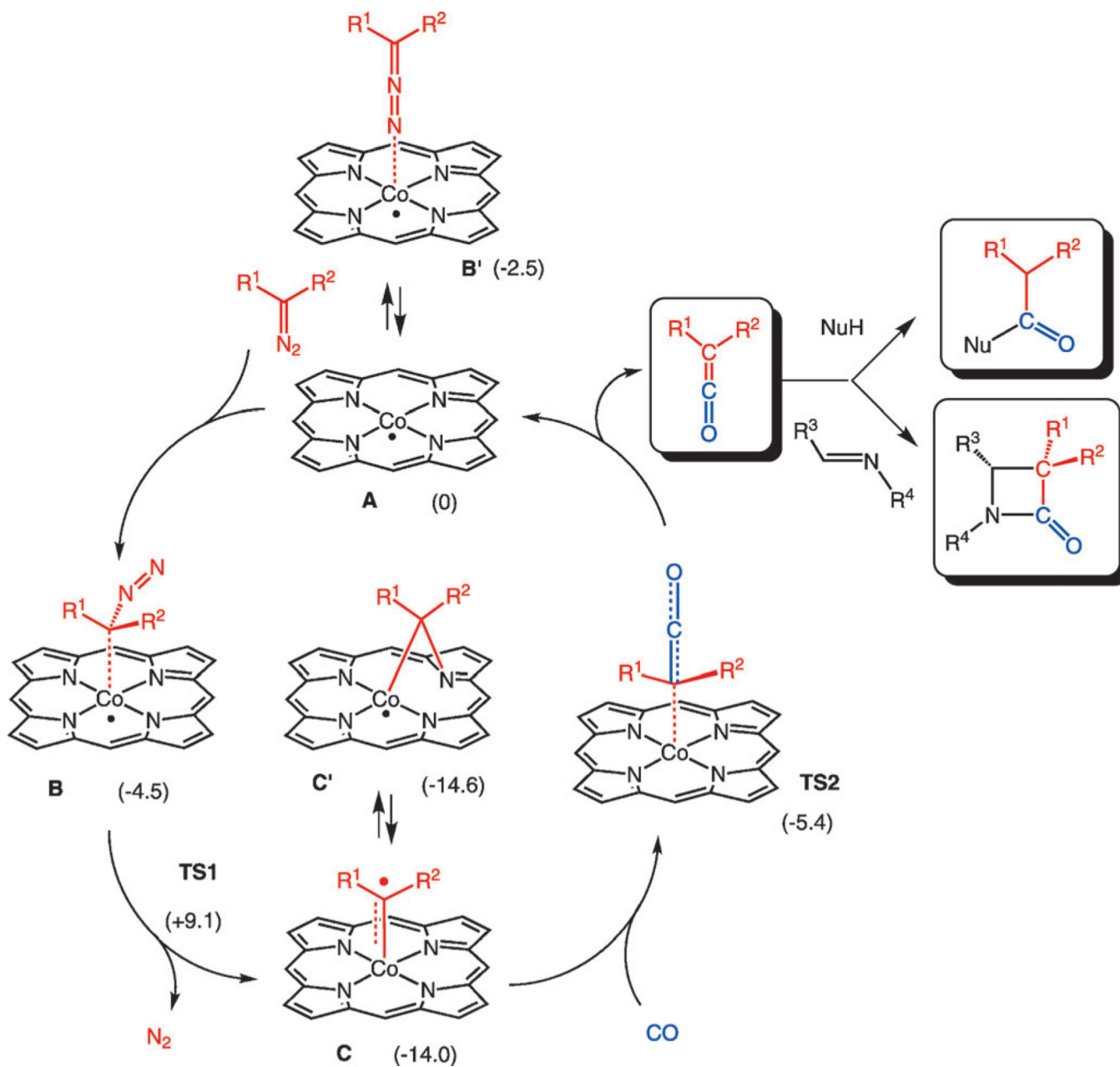


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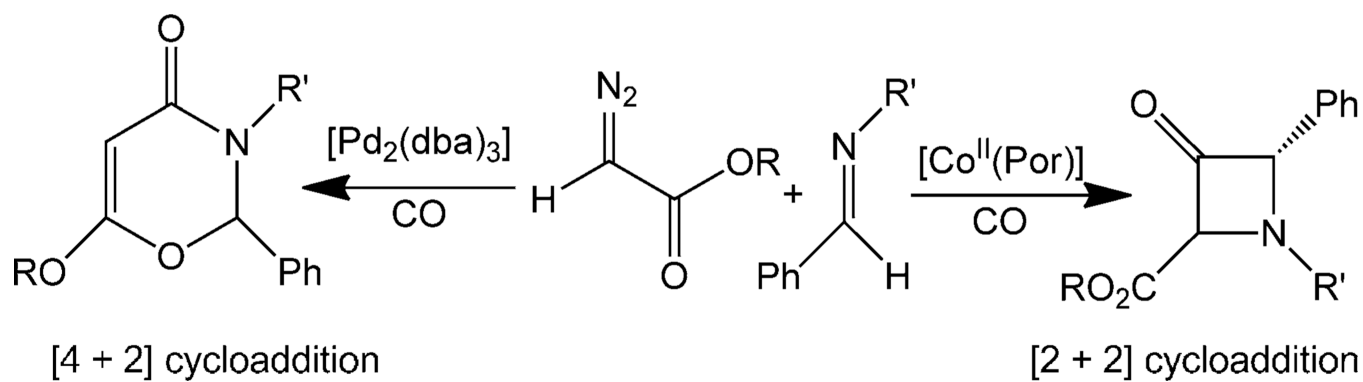


**Figure 1.** Structures of cobalt(II) complexes of porphyrins. **P1** = Tetraphenylporphyrin; **P2** = 3,5-Di*t*Bu-IbuPhyrin; **P3** = 3,5-Di*t*Bu-ChenPhyrin; **P4** = 21*H*,23*H*-porphine-5,10,15,20-tetrakis[(1*R*,4*S*,5*S*,8*R*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracen-9-yl].



**Scheme 1.**

$[\text{Co}^{\text{II}}(\text{Por})]$ -catalysed carbene carbonylation leading to ketene formation in one-pot tandem transformations producing amides, esters and  $\beta$ -lactams. DFT calculated relative free energies ( $G^\circ$ ) in kcalmol<sup>-1</sup> between brackets (Turbomole, BP86, def2-TZVP, employing Grimme's disp3 dispersion corrections).

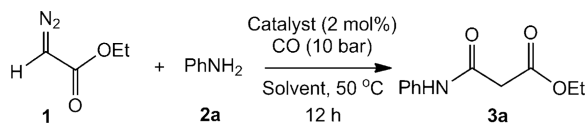


[4 + 2] cycloaddition

[2 + 2] cycloaddition

**Scheme 2.**

Markedly different behaviour of  $[\text{Co}^{\text{II}}(\text{Por})]$  compared to  $[\text{Pd}_2(\text{dba})_3]$  in reactions with  $\alpha$ -diazo carbonyl compounds and imines.

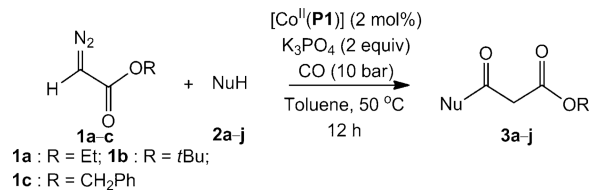
**Table 1**Conditions of [Co<sup>II</sup>(Por)]-catalysed  $\beta$ -ketoester synthesis using CO, EDA and aniline.<sup>[a]</sup>

Entry	Catalyst	Solvent	Yield [%] <sup>[b]</sup>
1	[Co <sup>II</sup> ( <b>P1</b> )]	PhMe	57
2	[Co <sup>II</sup> ( <b>P1</b> )]	THF	25
3	[Co <sup>II</sup> ( <b>P1</b> )]	dioxane	50
4	[Co <sup>II</sup> ( <b>P1</b> )]	DCE	10–15
5	[Co <sup>II</sup> ( <b>P1</b> )]	MeCN	<5
6	[Co <sup>II</sup> ( <b>P1</b> )]	DMF	–
7	[Co <sup>II</sup> ( <b>P1</b> )]	PhCl	55
8	[Co <sup>II</sup> ( <b>P1</b> )]	PhMe/K <sub>3</sub> PO <sub>4</sub>	69
9	[Co <sup>II</sup> ( <b>P1</b> )]	PhMe/K <sub>2</sub> CO <sub>3</sub>	65
10	[Co <sup>II</sup> ( <b>P1</b> )]	PhMe/KHCO <sub>3</sub>	58
11	[Co <sup>II</sup> ( <b>P1</b> )]	PhMe/NEt <sub>3</sub>	63
12	[Co <sup>II</sup> ( <b>P2</b> )]	PhMe/K <sub>3</sub> PO <sub>4</sub>	70
13	[Co <sup>II</sup> ( <b>P3</b> )]	PhMe/K <sub>3</sub> PO <sub>4</sub>	72
14	[Co <sup>II</sup> ( <b>P4</b> )]	PhMe/K <sub>3</sub> PO <sub>4</sub>	35

<sup>[a]</sup>Stoichiometry EDA:aniline = 1:2.<sup>[b]</sup>Isolated yields after column chromatography.

**Table 2**

[Co<sup>II</sup>(Por)]-catalysed  $\beta$ -ketoester synthesis using CO,  $\alpha$ -diazocarbonyl compounds and different nucleophiles.  
[a]



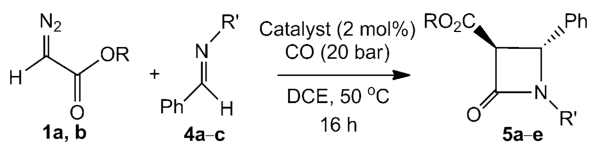
Entry	R	NuH	Yield[%] <sup>[b]</sup>
1	Et	PhNH <sub>2</sub>	69 ( <b>3a</b> )
2	Et	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	64 ( <b>3b</b> )
3	Et	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	61 ( <b>3c</b> )
4	Et	3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> NH <sub>2</sub>	64 ( <b>3d</b> )
5	Et	Ph <sub>2</sub> NH	63 ( <b>3e</b> )
6	Et	PhCH <sub>2</sub> NH <sub>2</sub>	67 ( <b>3f</b> )
7	Et	<i>n</i> BuNH <sub>2</sub>	57 ( <b>3g</b> )
8	Et	Morpholine	53 ( <b>3h</b> )
9	Et	Ph(CH <sub>2</sub> ) <sub>3</sub> OH	63 ( <b>3i</b> )
10	Et	EtOH	62 ( <b>3j</b> )
11	<i>t</i> Bu	PhNH <sub>2</sub>	75 ( <b>3k</b> )
12	CH <sub>2</sub> Ph	PhNH <sub>2</sub>	72 ( <b>3l</b> )

[a] Stoichiometry EDA:NuH = 1:2.

[b] Isolated yields after column chromatography

**Table 3**

[Co<sup>II</sup>(Por)]-catalysed *trans*-selective  $\beta$ -lactam synthesis from diazocarbonyl compounds.<sup>[a]</sup>



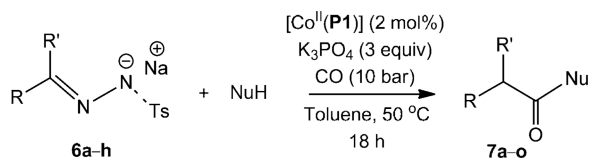
Entry	Catalyst	Diazo	Imine	Yield [%] <sup>[b]</sup> ( <i>trans:cis</i> )
1	[Co <sup>II</sup> ( <b>P1</b> )]	R = Et	R' = Me	65 ( <b>5a</b> ) (>95:5)
2	[Co <sup>II</sup> ( <b>P2</b> )]	R = Et	R' = Me	65 ( <b>5a</b> ) (>95:5)
3	[Co <sup>II</sup> ( <b>P3</b> )]	R = Et	R' = Me	67 ( <b>5a</b> ) (>95:5)
4	[Co <sup>II</sup> ( <b>P1</b> )]	R = Et	R' = CH <sub>2</sub> Ph	50 ( <b>5b</b> ) (>90:5)
5	[Co <sup>II</sup> ( <b>P1</b> )]	R = Et	R' = <i>t</i> Bu	55 ( <b>5c</b> ) (>95:5)
6	[Co <sup>II</sup> ( <b>P1</b> )]	R = <i>t</i> Bu	R' = Me	66 ( <b>5d</b> ) (>95:5)

<sup>[a]</sup>Stoichiometry EDA:imine = 1:2.

<sup>[b]</sup>Isolated yields after column chromatography.

Table 4

[Co<sup>II</sup>(Por)]-catalysed amide/ester synthesis using *N*-tosylhydrazone sodium salt and different nucleophiles.<sup>[a]</sup>



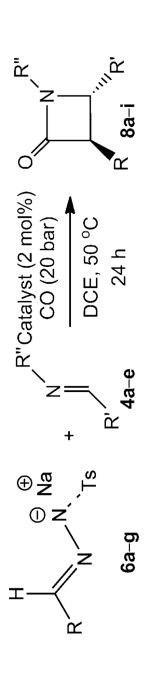
Entry	R	R'	NuH	Yield [%] <sup>[b]</sup>
1	Ph	H	PhNH <sub>2</sub>	75 ( <b>7a</b> )
2	Ph	H	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	79 ( <b>7b</b> )
3	Ph	H	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	72 ( <b>7c</b> )
4	Ph	H	PhCH <sub>2</sub> NH <sub>2</sub>	75 ( <b>7d</b> )
5	Ph	H	Ph <sub>2</sub> NH	79 ( <b>7e</b> )
6	Ph	H	<i>n</i> BuNH <sub>2</sub>	75 ( <b>7f</b> )
7	Ph	H	Morpholine	77 ( <b>7g</b> )
8	Ph	H	Ph(CH <sub>2</sub> ) <sub>3</sub> OH	65 ( <b>7h</b> )
9	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	H	PhNH <sub>2</sub>	82 ( <b>7i</b> )
10	<i>o</i> -MeC <sub>6</sub> H <sub>4</sub>	H	PhNH <sub>2</sub>	75 ( <b>7j</b> )
11	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	H	PhNH <sub>2</sub>	72 ( <b>7k</b> )
12	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	H	PhNH <sub>2</sub>	80 ( <b>7l</b> )
13	2-naph	H	PhNH <sub>2</sub>	77 ( <b>7m</b> )
14	Ph	CH <sub>3</sub>	PhNH <sub>2</sub>	56 ( <b>7n</b> )
15	PhCH=CH	H	PhNH <sub>2</sub>	65 ( <b>7o</b> )

<sup>[a]</sup>Stoichiometry *N*-Tosylhydrazone:NuH = 1:3, PTA used.

<sup>[b]</sup>Isolated yields after column chromatography.

Table 5

[Co<sup>II</sup>(Por)]-catalysed *trans*-selective  $\beta$ -lactam synthesis using different *N*-tosylhydrazone sodium salts and imines.<sup>[a]</sup>



Entry	Catalyst	R	R'	R''	Yield (%) <sup>[b]</sup> ( <i>trans</i> : <i>cis</i> )
1	[Co <sup>II</sup> ( <b>P1</b> )]	Ph	Ph	Me	64 ( <b>8a</b> ) (>95:5)
2	[Co <sup>II</sup> ( <b>P2</b> )]	Ph	Ph	Me	65 ( <b>8a</b> ) (>95:5)
3	[Co <sup>II</sup> ( <b>P3</b> )]	Ph	Ph	Me	65 ( <b>8a</b> ) (>95:5)
4	[Co <sup>II</sup> ( <b>P1</b> )]	Ph	Ph	PhCH <sub>2</sub>	62 ( <b>8b</b> ) (>90:10)
5	[Co <sup>II</sup> ( <b>P1</b> )]	Ph	<i>p</i> ClC <sub>6</sub> H <sub>4</sub>	Me	63 ( <b>8c</b> ) (>95:5)
6	[Co <sup>II</sup> ( <b>P1</b> )]	Ph	<i>p</i> OMeC <sub>6</sub> H <sub>4</sub>	Me	73 ( <b>8d</b> ) (>90:10)
7	[Co <sup>II</sup> ( <b>P1</b> )]	<i>p</i> MeC <sub>6</sub> H <sub>4</sub>	Ph	Me	77 ( <b>8e</b> ) (>95:5)
8	[Co <sup>II</sup> ( <b>P1</b> )]	<i>p</i> ClC <sub>6</sub> H <sub>4</sub>	Ph	Me	62 ( <b>8f</b> ) (>95:5)
9	[Co <sup>II</sup> ( <b>P1</b> )]	<i>p</i> MeOC <sub>6</sub> H <sub>4</sub>	Ph	Me	73 ( <b>8g</b> ) (>85:15)
10	[Co <sup>II</sup> ( <b>P1</b> )]	2-naphthyl	Ph	Me	67 ( <b>8h</b> ) (>95:5)
11	[Co <sup>II</sup> ( <b>P1</b> )]	PhCH = CH	Ph	Me	52 ( <b>8i</b> ) (>95:5)

<sup>[a]</sup>Stoichiometry: *N*-tosylhydrazone:imine=1:2.

<sup>[b]</sup>Isolated yields after column chromatography.