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Dendritic effect in polymer-supported catalysis of the intramolecular Pauson–Khand reaction†

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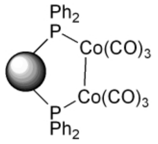
A remarkable increase in catalytic activity and selectivity in the intramolecular Pauson–Khand reaction is observed for Co complexes, immobilised on second- and third-generation dendron-functionalized polystyrene, as compared with their analogues on non-dendronized support.

Over the last decade, dendrimer-based soluble catalysts have been applied in numerous organic transformations.[1] Recently, increasing attention has been diverted to the synthesis of dendrons on solid support.[2,3] Surprisingly, thus far, only one research team have explored supported dendritic catalysts, for hydroformylation and the Heck reaction.[3]

Herein we report the first application of a dendritic catalyst for intramolecular Pauson–Khand reactions. The catalyst is built on polyether dendron-functionalized polystyrene, which was used for the first time in supported dendritic catalysis. The catalytic system demonstrates a remarkable positive dendritic effect on the catalyst activity and selectivity, never before observed in supported catalysis, and only rarely observed in solution.[4]

Pauson–Khand [2+2+1] cycloaddition of alkyne, alkene and carbon monoxide, promoted by $Co_2(CO)_8$, has been known since the 1970s,[5] but only during the last few years were catalytic versions, mainly for intramolecular reaction, developed.[6] Among other methods, the addition of phosphorus ligands (phosphines or phosphites) converts the stoichiometric reaction into a catalytic one.[6c,e] In 2000, Comely and coworkers reported catalysis of intramolecular Pauson–Khand annulation by a supported complex **1**, formed by the incubation of $Co_2(CO)_8$ with a commercial polystyrene-PPh_2 resin.[7]



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Nonselective coordination of two phosphines to the Co dimer must result in severe cross-linking of the polymer affecting its swelling properties. Moreover, the availability of two proximal phosphine moieties for every dimer coordinated can only be ‘ensured’ for high-loading resins. Bi- or polydentate supported ligands, on the other hand, seem highly suitable for the efficient bidentate coordination of cobalt dimers without inflicting a high degree of cross-linking. With this notion in mind, we decided to investigate catalytic systems that are based on ligands derived from dendronized resins **G1–G3** (Fig. 1).[8]

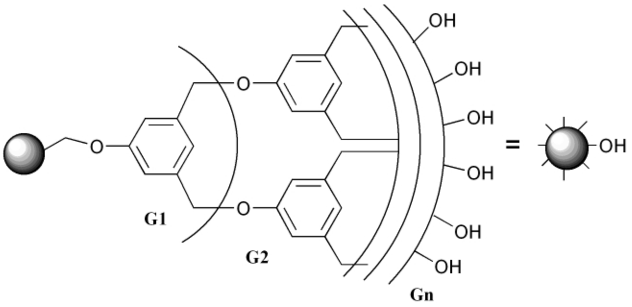


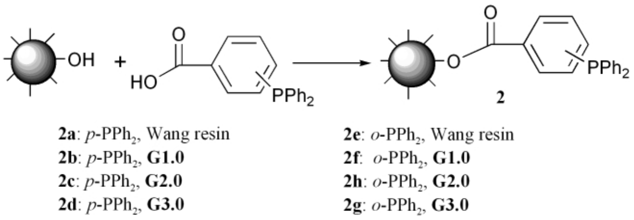
Fig. 1 Dendronized support (**Gn**).

For this study, Wang resin and the three dendronized supports were functionalized with 2- and 4-(diphenylphosphino)benzoic acid forming two series of ligands **2a–d** and **2e-h** (Scheme 1).‡ The resins were characterised using gel-phase ^{31}P and ^{13}C NMR as well as TFA-induced cleavage followed by ^1H NMR of the cleavage solution. Both ^{31}P and ^1H NMR were used for quantitative determination of the resin loading, usually with excellent agreement. Complete conversion of hydroxyl terminal groups into (diphenylphosphino)benzoyloxy moieties was achieved for all resins.

Incubation of the resins with $Co_2(CO)_8$ in dioxane at 75 °C yielded dark brown resins **3** (Scheme 2).[9] Gel-phase $^{31}P\{^1H\}$ NMR was used to determine the degree of complexation of the phosphines with cobalt and, accordingly, the loading of the active catalyst.

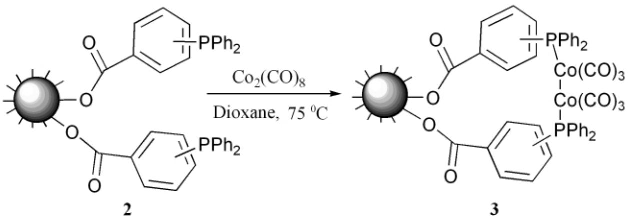
The reaction of the model compound **4** was chosen for comparison of the catalytic performance of the supported Co catalysts (Scheme 3). According to preliminary studies, the reaction product **5** is always accompanied by a cycloisomerisation byproduct **6**.[10,11] The catalytic experiments, performed in THF at 70 °C under 1 atm of CO,[9] revealed dramatic differences in the resin performance (Table 1).

The trends in the *p*-(diphenylphosphino)benzoate series are easier to follow. There is an increase in conversion and yield as we proceed from the non-dendronized support (**3a**) through the first-generation dendrimer (**3b**) to the second-generation resin (**3c**). This increase levels off when going from the second to the third generation (**3d**). The selectivity drops for the first-generation catalyst (**3b**) as compared with **3a** but then recovers (**3c**) and even improves for the third-generation resin (**3d**).



2a: *p*-PPh_2, Wang resin
2b: *p*-PPh_2, **G1.0**
2c: *p*-PPh_2, **G2.0**
2d: *p*-PPh_2, **G3.0**
2e: *o*-PPh_2, Wang resin
2f: *o*-PPh_2, **G1.0**
2h: *o*-PPh_2, **G2.0**
2g: *o*-PPh_2, **G3.0**

Scheme 1 *Reagents and conditions*: DIC, DMAP, DMF or DCM.



Scheme 2 Complexation of $Co_2(CO)_8$ with **2**.

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† Electronic supplementary information (ESI) available: characterization data for resins **2** and **3** and a general procedure for catalysis. See http://www.rsc.org/suppdata/cc/b2/b207625j/

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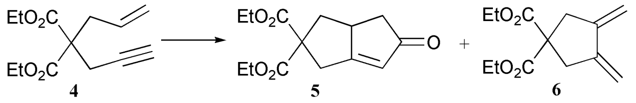

Scheme 3 *Reagents and conditions*: **3** (5% of Co dimer), CO (1 atm), THF, 70 °C, 24 h.

Table 1 Results of the catalytic reaction

Catalyst	Conversion (%)[a]	Selectivity (**5**:**6**)[a]	Yield of **5** (%)[a]
3a	32	4.3	26
3b	40	3.0	35(31[b])
3c	61	3.7	48
3d	59	12.2	55
3e	26	4.8	22
3f	0	—	0
3g	75	9.7	68
3h	74	5.4	63

[a] Determined using ^{1}H NMR. [b] Isolated yield.

The (*o*-diphenylphosphino)benzoate series demonstrated improved performance for the second and third generation-derived catalysts (**3g**, **3h**) as compared with the non-dendronized analogue (**3e**). The improvement is expressed in both higher conversion and selectivity. Surprisingly, catalyst **3f**, derived from the first generation dendrimeric resin, is absolutely inactive. Such outstanding behaviour of **3f** does not have a clear explanation at the moment and is currently under investigation. With the exception of **3f**, however, both series demonstrated superiority of dendritic architecture of the linking units and are excellent examples of the positive dendritic effect.

Based on the literature and our own observation, we suggest the following two factors as a rationale for this remarkable behaviour. The most active compound on solid support is, according to the literature, a complex of type L(CO)$_3$Co-CoL(CO)$_3$ (L = phosphine), while the mono-phosphine species are less active.[7] The bidentate coordination to the dimer must be much more available with dendritic ligands than simple polymer-bound monodentate phosphines. Indeed, IR and ^{31}P NMR analyses of resins **3** reveal differences in population of Co species on dendronized and non-dendronized ligands. IR spectra of all complexes exhibit two strong carbonyl absorptions at 1940–1954 and 2032–2037 cm^{-1}. However, only for non-dendronized resins **3a**, **3e** and **1**, is an additional peak around 2077 cm^{-1} observed. In the literature, this peak is attributed to the L(CO)$_3$Co-Co(CO)$_4$ complex.[12] Moreover, for resins **3a** and **3e**, ^{31}P NMR demonstrates a distinctive shoulder (not observed for other resins **3**), attributed to L(CO)$_3$Co-Co(CO)$_4$, in addition to the main peak of the L(CO)$_3$Co-CoL(CO)$_3$ complex. We must therefore assume that dendronized resins are predominantly populated by L(CO)$_3$Co-Co(CO)$_3$L complexes, while a notable portion of the population on non-dendronized supports are mono-phosphine species.

The second factor responsible for the dendritic effect is, very likely, the degree of the resin cross-linking. For non-dendronized catalysts, each Co-dimer, coordinated to two phosphines, provides an additional cross-linking connection while, for the dendronized catalysts, such a coordination mode can easily be obtained without extra cross-linking. The higher the dendrimer generation, the lesser the chances for cross-linking in the bidentate coordination mode. The substantially increased cross-linking strongly affects the resin properties. Thus, we observed that the swelling of resin **1** in the reaction media decreases dramatically. Accordingly, the resin is barely suitable for gel-phase NMR and the phosphorous signal observed for the resin is extremely broad.[13] The swelling of resins **3a** and **3e** is also badly affected (although to a lesser extent than that of **1**, as a result of more flexible cross-linking). Decreased swelling inhibits transport inside the resin, thus taking its ‘toll’ on catalysis.

The increased distance of the active site from the polymer matrix in the second and third generation catalysts can contribute, somewhat, to the improved performance but, as experiments with linear spacers demonstrated, is in no way a dominant factor.[14]

In conclusion, we prepared novel dendritic catalysts on solid support and used them for intramolecular Pauson–Khand annulation. This is the first case in which dendritic catalysis has been applied (on support or in solution) to this reaction. A significant dendritic effect was observed and a rationale for it was suggested and supported by experimental evidence.

Notes and references

‡ General procedure: diisopropylcarbodiimide (2.5 eq.) was added to a solution of diphenylphosphinobenzoic acid (5 eq.) in DCM (20 ml g^{-1}), cooled to 0 °C and the mixture was stirred for 20 min. For the 2-isomer, the solution was added directly to the resin swollen in DCM (10 ml g^{-1}), while for the 4-isomer the solvent was evaporated, the residue redissolved in DMF (20 ml g^{-1}) and added to the resin swollen in DMF (10 ml g^{-1}). 4-(Dimethylamino)pyridine (0.5 eq.) was added and the suspension stirred overnight at ambient temperature. The resin was filtered, washed extensively with DCM (2-isomer) or DMF, THF, and DCM (4-isomer) and dried in vacuum. For the **G2** and **G3** resins with 2-isomer, the procedure has to be performed twice to achieve complete conversion.

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14 We prepared resins, where a non-branched spacer was used in order to imitate the distance between the phosphine moieties and the polystyrene core in resins **2c** and **g**, but the catalytic performance of their corresponding Co complexes was clearly inferior to that of **3**.