

Raney Cobalt: An Effective and Recyclable Catalyst for the Pauson–Khand Reaction

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Abstract: Commercially available Raney cobalt is broadly applicable as a catalyst in intra- and intermolecular Pauson–Khand reactions (PKR). The activity of Raney cobalt compares favourably with that of previously described heterogeneous or heterogenised cobalt systems. The major reaction pathway appears to occur at the solid catalyst which can be efficiently separated and reused by filtration and/or exploiting its ferromagnetic properties.

Keywords: cyclopentenone; heterogeneous catalysis; Pauson–Khand reaction; Raney cobalt

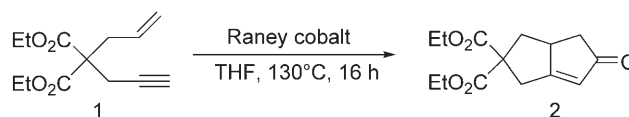
The [2+2+1] cycloaddition of alkynes with alkenes and carbon monoxide (CO) to form cyclopentenones is known as the Pauson–Khand reaction (PKR).^[1] The original protocol involved a stoichiometric reaction of cobalt complexes derived from [Co₂(CO)₈], but catalytic versions were developed more recently.^[2–4] The main drawback of the cobalt-catalysed PKR was initially its relatively low scope and, in many cases, low conversions. Many of these problems could be solved in the last decade leading to considerable improvements in the context of reaction conditions, selectivity and activity of the catalyst. Nevertheless, practical applications of this powerful synthesis are still hampered mainly due to catalyst separation problems and the volatile and toxic nature of cobalt carbonyls.^[1]

So far only few examples of heterogeneously cobalt-catalysed PKR are reported in the literature.^[5–8,16] Chung and co-workers deposited cobalt by thermal decomposition of [Co₂(CO)₈] onto various supports and demonstrated the catalytic activities of the resulting materials for the PKR.^[5,6] Cobalt on charcoal lead to ferromagnetic particles which could be separated from the reaction solution with a bar magnet.^[5] Colloidal cobalt nanoparticles in supported or unsupported form were also used as reusable catalysts for the PKR.^[7,8] These systems require very high

catalyst loadings approaching stoichiometric ratios in many cases.

Raney cobalt is widely used as catalyst for the chemoselective hydrogenation of α,β -unsaturated nitriles to amines, or aldehydes to alcohols.^[9–11] Raney cobalt is commercially available, cheap, easy to handle and not toxic. Besides these considerable advantages, it can easily be separated from reaction mixtures by filtration or by exploiting its ferromagnetic properties. Here we report that Raney cobalt serves as a broadly applicable and recyclable catalyst for the PKR operating at catalyst loadings in the range of 6.0 mol %.

In a first set of experiments we investigated the intramolecular benchmark PKR shown in Scheme 1.



Scheme 1. Intramolecular Pauson–Khand reaction with Raney cobalt.

Conversions of **1** were marginal at temperatures below 100°C, but excellent yields of **2** were obtained at 130°C within 16 h reaction time. Reducing the CO pressure from 23 to 10 bar resulted in a significant drop in reaction rate and also a somewhat reduced selectivity (Table 1).

In order to explore the scope of the new protocol, Raney cobalt was tested for a variety of different intra- and intermolecular PKR. Representative results obtained under standard conditions are given in Table 2. Almost quantitative conversions were achieved for the malonate-derived enynes **1** and **3** as well as for diol **5** under the standard reaction conditions. The catalyst loading corresponded to 5.8 mol % of cobalt in these experiments. Thus, the activity of Raney cobalt compares favourably with previously described heterogeneous systems which use almost 15–20 mol % of cobalt.^[5,6] The intermolecular PKR occurred also smoothly over Raney cobalt, although a

Table 1. Temperature and pressure dependence of the Raney cobalt-catalysed PKR of **1**.

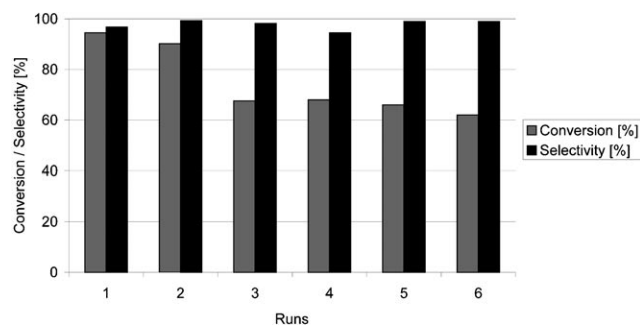
Entry	Temperature [°C]	Pressure [bar] ^[a]	Conversion [%]	Selectivity for 2 [%]
1	65	23	<1	-
2	95	23	11.1	83.3
3	130	23	94.5	96.5
4	130	10	51.1	87.0

^[a] Pressure in the autoclave at the reaction temperature. *Reaction conditions:* All reactions were performed in 4 mL THF, in a 10-mL, window-equipped stainless steel autoclave. Substrate/catalyst ratio: 17.0; reaction time: 16 h.

higher catalyst loading and increased CO pressure was required. Fair to excellent yields were obtained upon cyclisation of norbornene **7** with various substituted acetylenes. Again, the activities compare well with other heterogeneous systems.^[5,6]

The recyclability of the catalyst was tested for the intramolecular PKR depicted in Scheme 1. After cooling and venting, the autoclave was opened under

a flow of argon. The supernatant solution could be readily separated by syringe from the ferromagnetic catalyst particles which were mainly attached on the magnetic stir bar. The conversion decreased in the first three runs, but remained then fairly stable for at least six cycles (Figure 1). Cobalt leaching can be excluded as a major deactivation pathway because the

**Figure 1.** Recycling experiments with Raney cobalt. *Reaction conditions:* All reactions were performed in 4 mL THF in a 10-mL, window-equipped stainless steel autoclave. Substrate/Co ratio: 17.0. CO pressure: 23 bar at 130°C. Reaction time: 16 h.**Table 2.** Raney cobalt-catalysed intra- and intermolecular PKR.^[a]

Entry	Substrate	Product	Conversion [%]	Selectivity [%]
1			94.5	96.8
2			99.5	94.7
3			99.4	98.0
4	+		94.2	91.5
5	+		54.2	96.8
6	+		58.3	96.0
7	+		58.4	94.6

^[a] *Reaction conditions:* All reactions were performed in 4 mL THF, in a 10-mL, window-equipped stainless steel autoclave. Reaction time: 16 h. Entries 1–3: substrate/Co ratio 17.0, CO pressure 23 bar at 130°C; entries 4–7: substrate/Co ratio 6.0, CO pressure 35 bar at 130°C.

cobalt content in the entire product samples of the recycling experiments was less than 8 ppm as determined by ICP measurements. The selectivity for the formation of the product **2** remained uniformly high throughout the experiments. The total turnover number (TON) achieved in this series of experiments amounts to 76.1 mol of **2** per mol cobalt, corresponding to a productivity of 344.1 g of **2** per gram of catalyst.

A series of control experiments was carried out in order to elucidate if the reaction is truly heterogeneous or if the activity is due to catalytically active cobalt carbonyl species in solution. No significant further conversion occurred when the product samples of the recycling experiments (entry 2 and entry 4 in Figure 1) were re-submitted to the reaction after removal of the Raney cobalt, indicating that an efficient separation of products and active metal is achieved. However, a small increase in conversion was observed when the reaction solution was filtered under turnover conditions.^[12] After 2 h reaction time with a stoichiometric loading of catalyst, the solution was transferred to a second high pressure vessel through a closed filter system. Conversion in the original reactor was 43 % at this stage and increased to 57 % in the filtrate over the next 10 h, indicating that small amounts of active species were present in the reaction solution.

To further estimate the contribution of homogeneously dispersed active centres to the overall turnover number, a direct comparison was made for the PKR of solid phase-bound substrate **10** with a soluble cobalt carbonyl catalyst and Raney cobalt (Scheme 2).^[13] The substrate was attached to carboxypolystyrene beads using standard techniques.^[14] The PKR with norbonene occurred smoothly in the presence of $[\text{Co}_2(\text{CO})_8]$ as homogeneous catalyst. After cleavage with trifluoroacetic acid (TFA) the product **11** was obtained in almost quantitative yield.

In contrast, a conversion of only 10 % of the polymer-bound substrate was achieved with Raney cobalt even at a stoichiometric substrate to cobalt ratio (**10**/Co = 1/1) under otherwise identical conditions. Together with the filtration tests described above, these results suggest that small amounts of soluble cobalt species may contribute to the conversion, but the major catalytic pathway seems to occur at the solid catalyst particles.

In conclusion, we have shown that commercially available Raney cobalt is broadly applicable as catalyst in intra- and intermolecular Pauson–Khand reac-

tions (PKR). The activity of Raney cobalt compares favourably with that of previously described heterogeneous or heterogenised cobalt systems. The major reaction pathway appears to occur at the solid catalyst which can be efficiently separated and reused by filtration and/or exploiting its ferromagnetic properties. Therefore, we believe that the use of Raney cobalt offers an interesting practical approach to catalytic PKR on laboratory and production scale.

Experimental Section

General Remarks

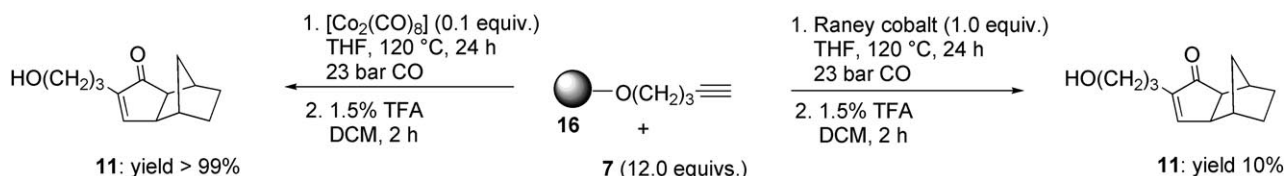
All reactions were conducted using 10-mL, window-equipped stainless steel autoclaves. THF was dried and distilled according to standard methods.^[15] Reagents were purchased from Aldrich Chemical Co. and were used as received. Raney cobalt 2724 was purchased as an aqueous suspension from Davison catalysts and used in dry form after filtration and washing with diethyl ether (Et_2O). ^1H and ^{13}C NMR spectra were measured on a DPX Bruker 300 spectrometer. GC-MS analyses were carried out with a Varian CP 3800 instrument. ICP measurements were carried out in the group of Prof. Dr. A. Behr at the University of Dortmund.

General Procedure for the Intramolecular PKR using Raney Cobalt (Entries 1–3, Table 2)

Raney cobalt (2.0 mg, 3.4×10^{-2} mmol) was added to a dry and degassed window-equipped, 10-mL stainless steel autoclave under a counter current flow of argon. A solution of enyne (5.8×10^{-1} mmol) in 4 mL THF was added. The reactor was charged with 15 bar of CO at room temperature and heated under stirring at 130 °C for 16 h. Under these reaction conditions the pressure in the autoclave increased to 23 bar. After the reaction the reactor was cooled to room temperature and vented carefully to the exhaust line. The remaining solution was filtered, concentrated and analysed by GC-MS and NMR.

General Procedure for the Intermolecular PKR using Raney Cobalt (Entries 4–7, Table 2)

Raney cobalt (4.0 mg, 6.8×10^{-2} mmol) was added to a dry and degassed window-equipped, 10-mL stainless steel autoclave under a counter current flow of argon. A solution of alkyne (40.8×10^{-2} mmol) and norbonene **7** (61.2×10^{-2} mmol, 1.5 equivs.) in 4 mL THF was added. The reactor was charged with 25 bar of CO at room temperature and heated under stirring to 130 °C for 16 h. Under these reaction conditions the pressure in the autoclave increased to



Scheme 2. Intermolecular PKR with the solid phase-bound alkyne **16**.

35 bar. After the reaction, the reactor was cooled to room temperature and worked-up as described above.

Recycling Experiments

After the reaction, the reactor was cooled to room temperature and depressurised. The reaction solution was carefully removed from the autoclave by syringe under argon. The Raney cobalt remained in the reactor, mainly attached to the stir bar and was washed twice with 2.5 mL THF. The combined solutions were concentrated and analysed by GC-MS. A new substrate/THF solution was added and the reaction was repeated in the same manner.

PKR of Solid Phase-Bound Substrate 16

Raney cobalt (15.0 mg, 0.25 mmol) was added to a dry and degassed window-equipped, 10-mL stainless steel autoclave under a counter current flow of argon. The substrate-containing carboxy-polystyrene beads (249.1 mg, loading: 0.25 mmol pentynol **10**) were added to the reaction vessel. A solution of norbornene **7** (282.2 mg, 2.90 mmol, 12 equivs.) in 4.0 mL THF was added. The reactor was charged with 15 bar of CO at room temperature and heated under rigorous shaking to 120 °C for 16 h. Under these reaction conditions the pressure in the autoclave increased to 21 bar. After cooling and venting, the solution was filtered and 170.1 mg of the remaining polymer were swollen in 2 mL dichloromethane (DCM) for 10 min. Afterwards 2 mL of a solution of TFA in DCM were added and mixed for 1 h to cleave of the product **11**. The remaining solution was filtered and stirred over 0.5 g K₂CO₃ for 10 min. The cleavage procedure was repeated twice with each sample to ensure quantitative recovery of the bound substrate/product. The combined solutions were concentrated and analysed by GC with 1-decanol as standard.

Characterisation of the Products

Diethyl 3,3a,4,5-tetrahydro-5-oxopentalene-2,2(IH)-dicarboxylate (2): ¹H NMR (300 MHz, CDCl₃): δ = 1.22 (q, 6H), 1.67 (t, 1H), 2.10 (m, 2H), 2.53–2.77 (m, 2H), 3.24 (q, 2H), 4.17 (m, 4H), 5.87 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ = 13.0, 34.1, 37.9, 41.1, 44.0, 59.8, 61.1, 124.6, 170.5, 184.7, 208.7; MS (CI, methane): *m/z* (%) = 266 (4.7%, M⁺), 244 (27.0%), 221 (4.7%, M⁺–C₂H₅O), 215 (B), 192 (8.8%, M⁺–C₂H₆), 119 (20.0%, M⁺–147), 93 (61.2%), 65 (25.3%), 55 (24.7%).

Diethyl 3,3a,4,5-tetrahydro-6-methyl-5-oxopentalene-2,2(IH)-dicarboxylate (4): ¹H NMR (300 MHz, CDCl₃): δ = 1.22 (q, 6H), 1.58 (m, 1H), 1.65 (s, 3H), 2.05 (d, 2H), 2.53–2.75 (m, 2H), 3.13 (m, 2H), 4.16 (m, 4H); ¹³C NMR (75 MHz, CDCl₃): δ = 8.5, 14.0, 34.0, 39.7, 41.39, 42.7, 61.0, 61.9, 126.1, 171.0, 177.8, 209.4; MS (CI, methane): *m/z* (%) = 280 (22.0%, M⁺), 235 (10.8%, M⁺–C₂H₅O), 206 (70.8%, M⁺–C₄H₁₀O), 178 (21.7%, M⁺–C₃H₁₁O₂), 133 (B, M⁺–C₆H₁₀O₄), 105 (40.4%), 91 (25.0%).

4,5,6,6a-Tetrahydro-5,5-bis(hydroxymethyl)pentalene-2(IH)-one (6): ¹H NMR (300 MHz, DMSO): δ = 1.02 (t, 2H), 1.93 (m, 2H), 2.47 (d, 2H), 3.28 (m, 1H), 3.42 (m, 4H), 4.63 (t, 1H), 4.74 (t, 1H), 5.79 (s, 1H); ¹³C NMR (75 MHz, DMSO): δ = 32.8, 35.8, 42.3, 44.0, 51.4, 65.3, 123.63, 191.0, 209.7.

2-Phenyl-3a,4,5,6,7,7a-hexahydro-4,7-methanoinden-1-one (9): ¹H NMR (300 MHz, CDCl₃): δ = 1.03 (m, 2H), 1.23 (m, 2H), 1.53 (m, 2H), 2.15 (m, 1H), 2.25 (m, 1H), 2.39 (m, 1H), 2.57 (m, 1H), 7.27 (m, 3H), 7.52 (d, 1H), 7.61 (m, 2H); ¹³C NMR (75 MHz, CDCl₃): δ = 28.4, 29.2, 31.3, 38.4, 39.5, 47.7, 55.0, 127.1, 128.4, 131.6, 146.1, 160.3, 209.0.

2-(3-Hydroxypropyl)-3a,4,5,6,7,7a-hexahydro-4,7-methanoinden-1-one (11): ¹H NMR (300 MHz, DMSO): δ = 0.91 (m, 2H), 1.26 (m, 2H), 1.58 (m, 4H), 2.11 (m, 5H), 2.57 (s, 1H), 3.36 (m, 2H), 4.44 (t, 1H), 7.27 (s, 1H); ¹³C NMR (75 MHz, DMSO): δ = 20.8, 27.8, 28.5, 30.6, 30.6, 37.4, 38.4, 47.4, 52.9, 60.2, 148.1, 159.1, 209.8; MS (CI, methane): *m/z* (%) = 206 (36.5%, M⁺), 188 (93.6%, M⁺–H₂O), 173 (33.33%, M⁺–H₂O₂), 150 (39.7%), 145 (30.15%), 131 (21.0%, M⁺–C₃H₇O₂), 122 (77.8%, M⁺–C₅H₈O), 105 (30.16%), 91 (B), 77 (58.7%), 67 (71.4%), 53 (23.8%), 41 (42.8%), 31 (22.7%).

2-Propyl-3a,4,5,6,7,7a-hexahydro-4,7-methanoinden-1-one (13): ¹H NMR (300 MHz, CDCl₃): δ = 0.99 (m, 5H), 1.27 (m, 2H), 1.42 (m, 2H), 1.59 (m, 2H), 2.11 (m, 4H), 2.36 (m, 1H), 2.55 (m, 1H), 7.09 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ = 13.9, 21.1, 26.7, 28.4, 29.1, 31.0, 38.0, 40.0, 48.1, 53.9, 149.2, 158.9, 211.3; MS (CI, methane): *m/z* (%) = 190 (B, M⁺), 175 (32.5%, M⁺–CH₃), 162 (55%, M⁺–CO), 161 (62.5%, M⁺–C₂H₅), 147 (31%, M⁺–C₃H₇), 124 (56%), 95 (50%, M⁺–C₆H₈O), 91 (67.5%), 79 (60%), 67 (31%).

2-Hexyl-3a,4,5,6,7,7a-hexahydro-4,7-methanoinden-1-one (15): ¹H NMR (300 MHz, CDCl₃): δ = 0.92 (m, 5H), 1.19 (m, 8H), 1.36 (m, 2H), 1.52 (m, 2H), 2.05 (m, 4H), 2.30 (m, 1H), 2.49 (m, 1H), 7.03 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ = 14.1, 22.5, 24.7, 27.8, 28.4, 29.1, 31.0, 31.6, 38.0, 39.0, 48.1, 53.9, 149.5, 158.7, 211.3; MS (CI, methane): *m/z* (%) = 232 (M⁺, 34.8%), 203 (19.6%, M⁺–C₂H₅), 189 (12.7%, M⁺–C₃H₇), 175 (15.2%, M⁺–C₄H₉), 163 (B), 91 (34.2%), 67 (34.3%), 41 (21.0%).

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