Highly efficient and time economical purification of olefin metathesis products from metal residues using an isocyanide scavenger

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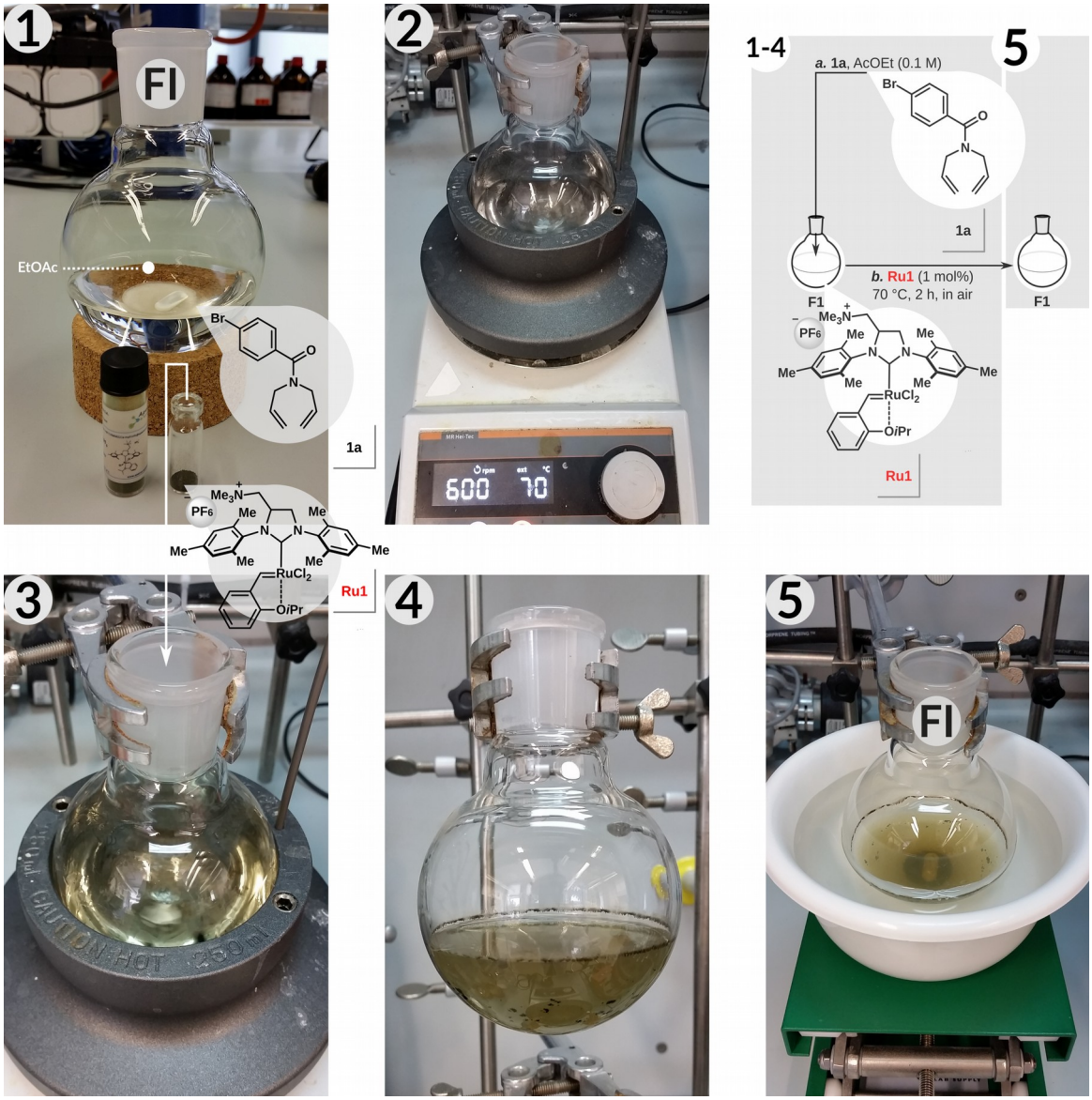
Supporting Information

General considerations

All reactions were carried out under air. The reactions from Tables 1 and 2 were performed using *Radleys Carousel*. Commercially available chemicals were used as received. Ruthenium catalysts were purchased from *Apeiron Synthesis S.A.* Bottles with ruthenium catalysts were stored under argon, but no special precautions were taken to avoid air or atmospheric moisture exposure after extracting catalysts from the bottles. NMR (^{1}H and ^{13}C) spectra were recorded on *Agilent Mercury* 400 MHz spectrometers with $CDCl_3$ used as the solvent. Chemical shifts (δ) are given in ppm, with the solvent peak of $CDCl_3$ used as a point of reference. Coupling constants (J) are reported in hertz (Hz). IR spectra were recorded on a *Thermo Scientific Nicolet iS 50 FT-IR* spectrometer; wave numbers ($\tilde{\upsilon}$) are given in cm^{-1}. Reactions were monitored by GC with measurements done on *Perkin-Elmer Clarus 580* with InertCap 5MS-Sil column. Filtration was performed using *Merck Millipore* silica gel (60, particle size 0.043–0.063 mm). Elemental analyses were performed by the Institute of Organic Chemistry, PAS, Warsaw. Ruthenium content was determined by inductively coupled plasma mass spectrometry (IPC-MS, *NexION 300D*, *Perkin Elmer*, USA).

Procedure for Scheme 1.

1. A 250-mL round-bottomed flask (**F1**) was equipped with a magnetic stir bar (egg shaped). *N,N*-diallyl-4-bromobenzamide (**1a**) (2.24 g, 8.0 mmol, 1.0 equiv.) was dissolved in ethyl acetate[1] (40 mL).
2. The reaction flask was placed in a *Heat-On*, and heated to 70 ℃.
3. The solid **Ru1** catalyst[2] (68 mg, 0.08 mmol, 1.0 mol%) was added, and the reaction mixture was stirred (600 rpm) for 2 h in an open flask..
4. The reaction flask (**FI**) was removed from the *Heat-On*.
5. The reaction flask (**FI**) was placed in an water bath for 5 min.



1 Ethyl acetate (*CHROMASOLV®*, for HPLC, ≥99.7%) was purchased from *SIGMA-ALDRICH* (product 34858-2.5L), and used as received.

2 **Ru1** (*StickyCat* PF_6) was purchased from *Apeiron Synthesis S.A.* (product AS2054) and used as received.

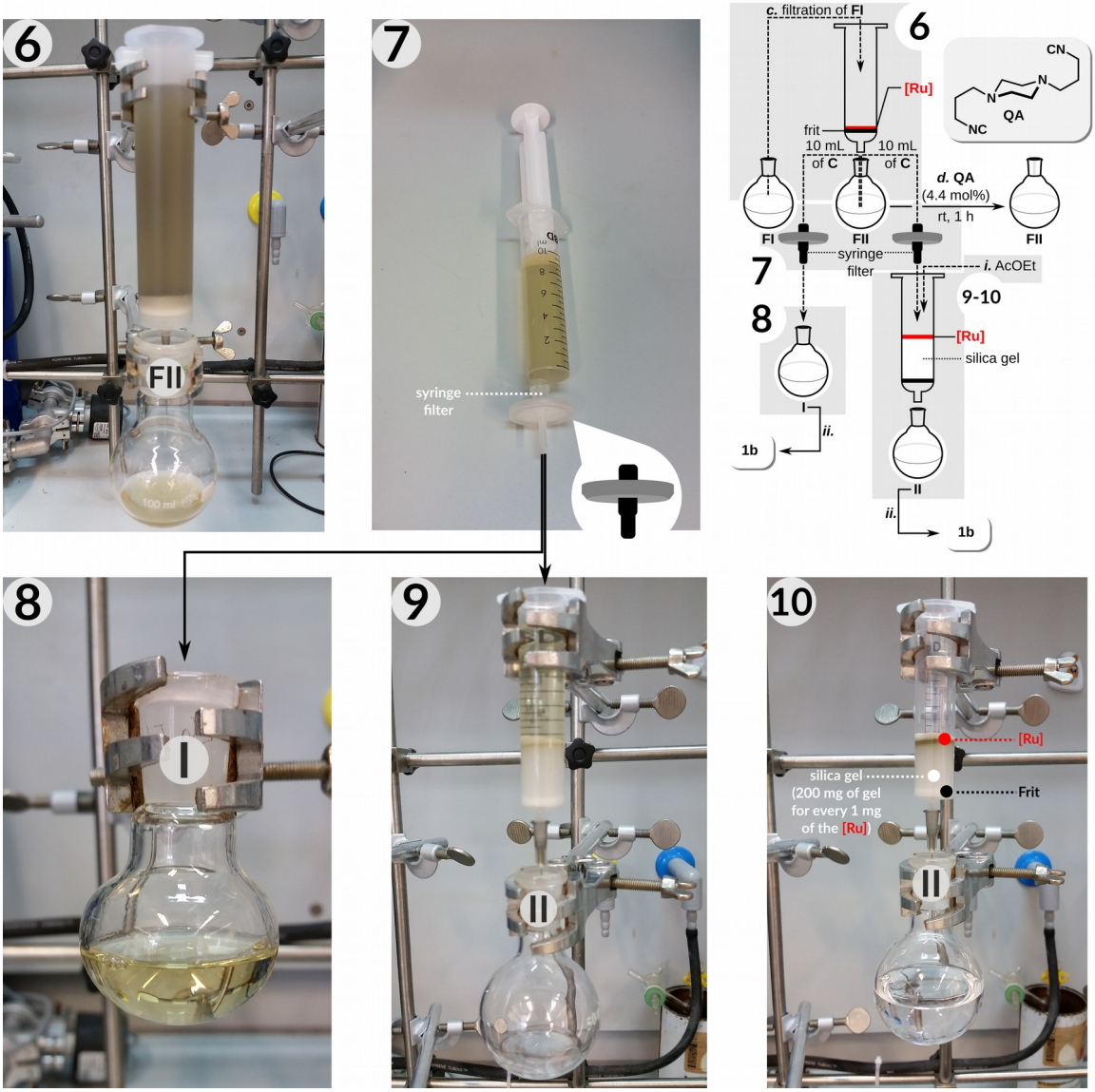
6. The mixture was transferred to a *RediSep*® cartridge (140 mm length and 27 mm diameter) and gravitationally filtered through a frit into a 100 mL round-bottomed flask (**FII**). Two aliquots (2×10 mL) were taken from the flask **FII** using a syringe.

7. The first aliquot was filtered through a syringe filter[3] into a 25 mL round-bottomed flask (**I**). The solvent was removed under reduced pressure to give **1b** (1265 ppm Ru).

8. The second aliquot (10 mL) was filtered through a syringe filter onto the top of a silica gel plug.

9. The mixture was gravitationally filtered through silica gel[4] into a 50 mL round-bottomed flask (**II**). The silica gel plug was washed with an additional portion of ethyl acetate (20 mL). The solvent was removed under reduced pressure to give **1b** (40 ppm Ru).

10. The flask **FII** was equipped with a magnetic stir bar (egg shaped). 1,4-Bis(3-isocyanopropyl)piperazine (**QA**) (58 mg, 0.26 mmol, 4.4 mol%) was added. The resulting mixture was stirred (600 rpm) at rt for 1 h.



3 Syringe filter (*CHROMAFIL*®, pore size: 0.45 µm, filter diameter: 15 mm) was purchased from *ROTH* (product XH64.1).

4 200 mg of silica gel per 1 mg of Ru catalyst; column diameter: 1.6 cm (10 mL syringe). Silica gel (60, particle size 0.043–0.063 mm) was purchased from *Merck Millipore* and used as received.

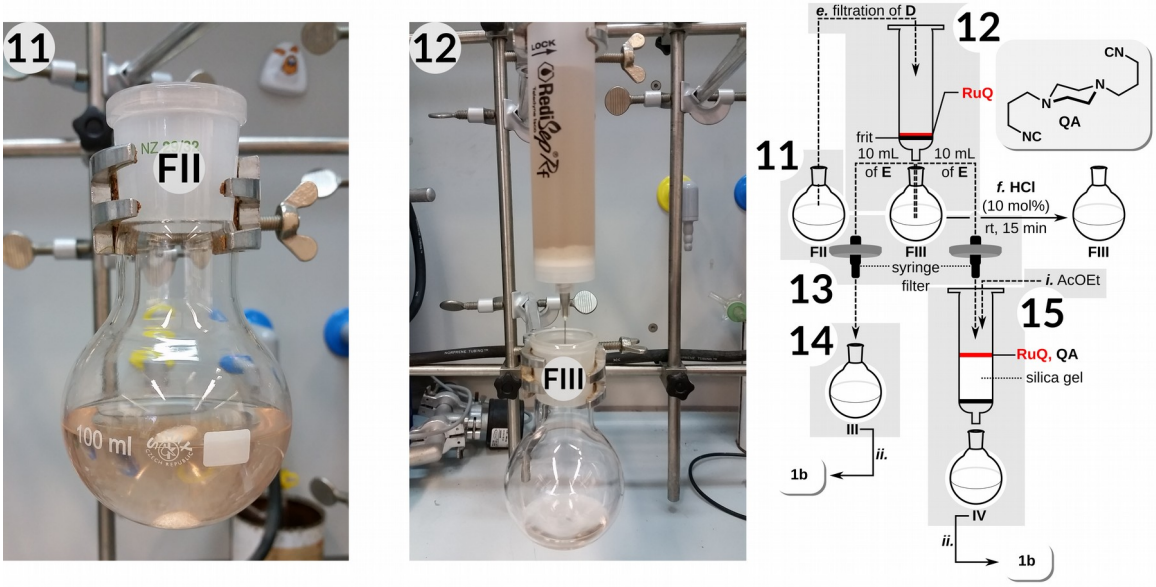
11. Picture 11 shows the reaction mixture after scavenging.

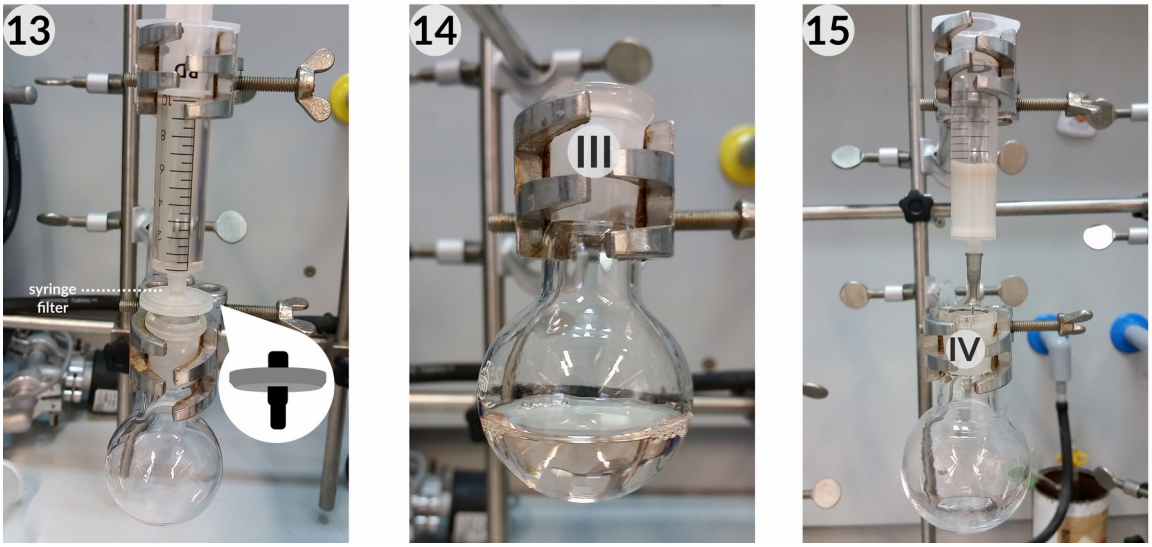
12. The mixture from flask **FI** was transferred to a *RediSep*® cartridge (140 mm length and 27 mm diameter), and gravitationally filtered through sand into a 100 mL round-bottomed flask (**FII**).

13. Two aliquots (2×10 mL) were extracted from the flask **FII** uisng a syringe. One of them was filtered through a syringe filter into a 25 mL round-bottomed flask (**III**). The solvent was removed under reduced pressure to give **1b** (269 ppm Ru).

14. Picture 14 shows the reaction mixture after filtration.

15. The second aliquot (10 mL) was filtered through a syringe filter onto the top of a silica gel plug and then gravitationally filtered into a 50 mL round-bottomed flask (**IV**). The silica gel plug was washed with an additional portion of ethyl acetate (20 mL). The solvent was removed under reduced pressure to give **1b** (0.9 ppm Ru).





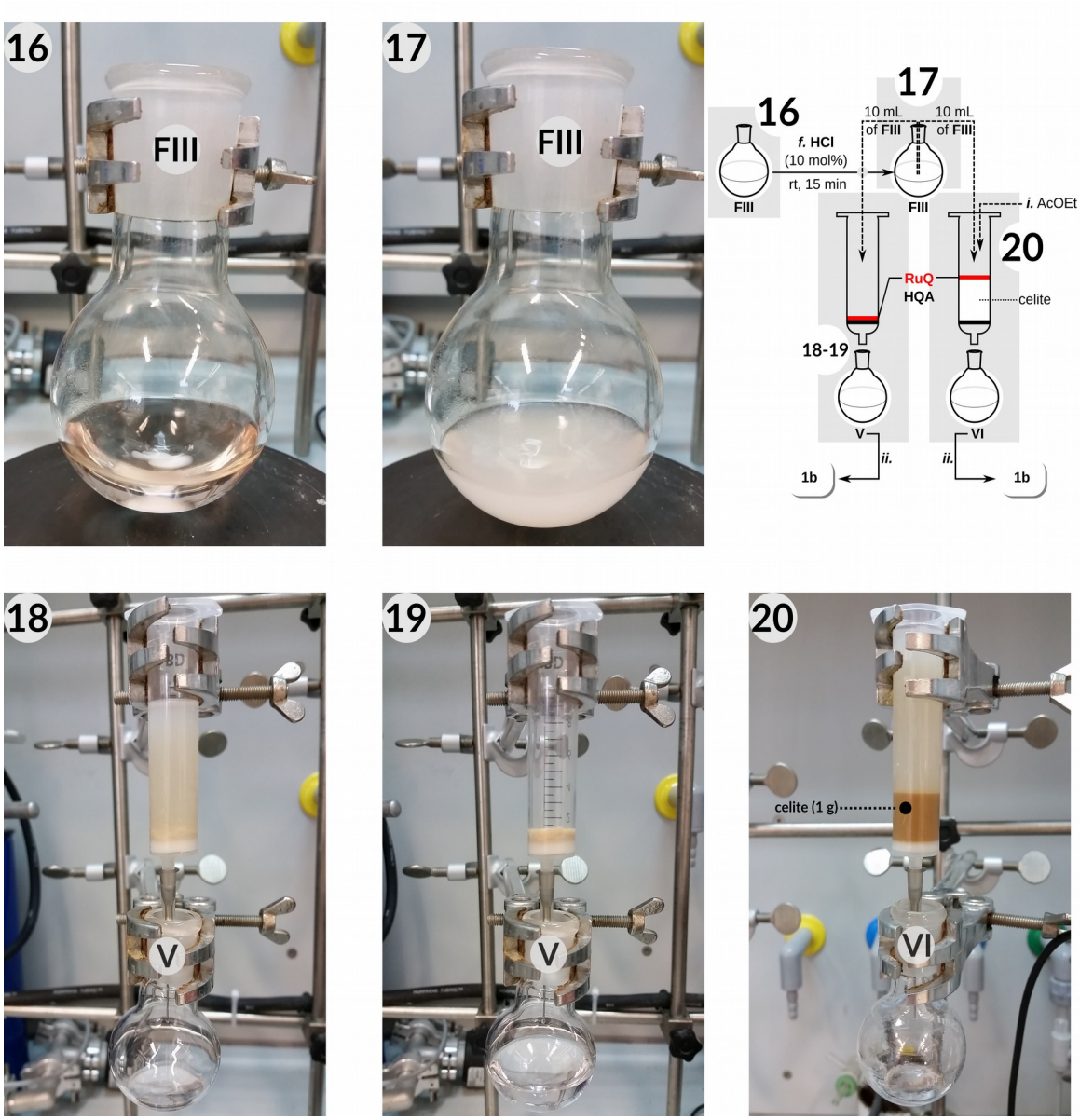
16. The flask FIII was equipped with a magnetic stir bar (egg shaped).

17. HCl (0.2 mL, 1 M in Et_2O, 0.2 mmol, 10 mol%) was added. The resulting mixture was stirred (600 rpm) at rt for 15 min.

18. Two aliquots (10 mL) were extracted from flask **FIII** using a syringe. One of them was filtered through a frit into a 25 mL round-bottomed flask (**V**). The solvent was removed under reduced pressure to give **1b** (32 ppm **Ru**).

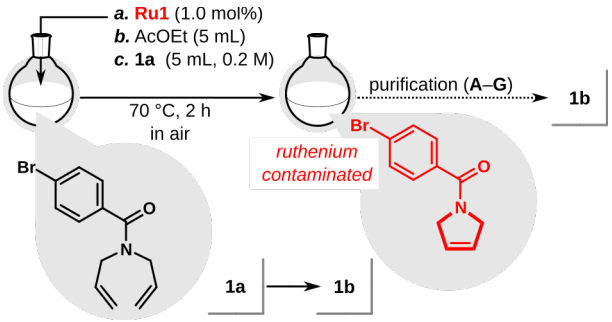
19. Picture 19 shows the reaction mixture after filtration.

20. The second aliquot (10 mL) was transferred onto a plug of celite[5] and gravitationally filtered into a 25 mL round-bottomed flask (**VI**). The celite plug was washed with an additional portion of ethyl acetate (5 mL). The solvent was removed under reduced pressure to give **1b** (9 ppm **Ru**).

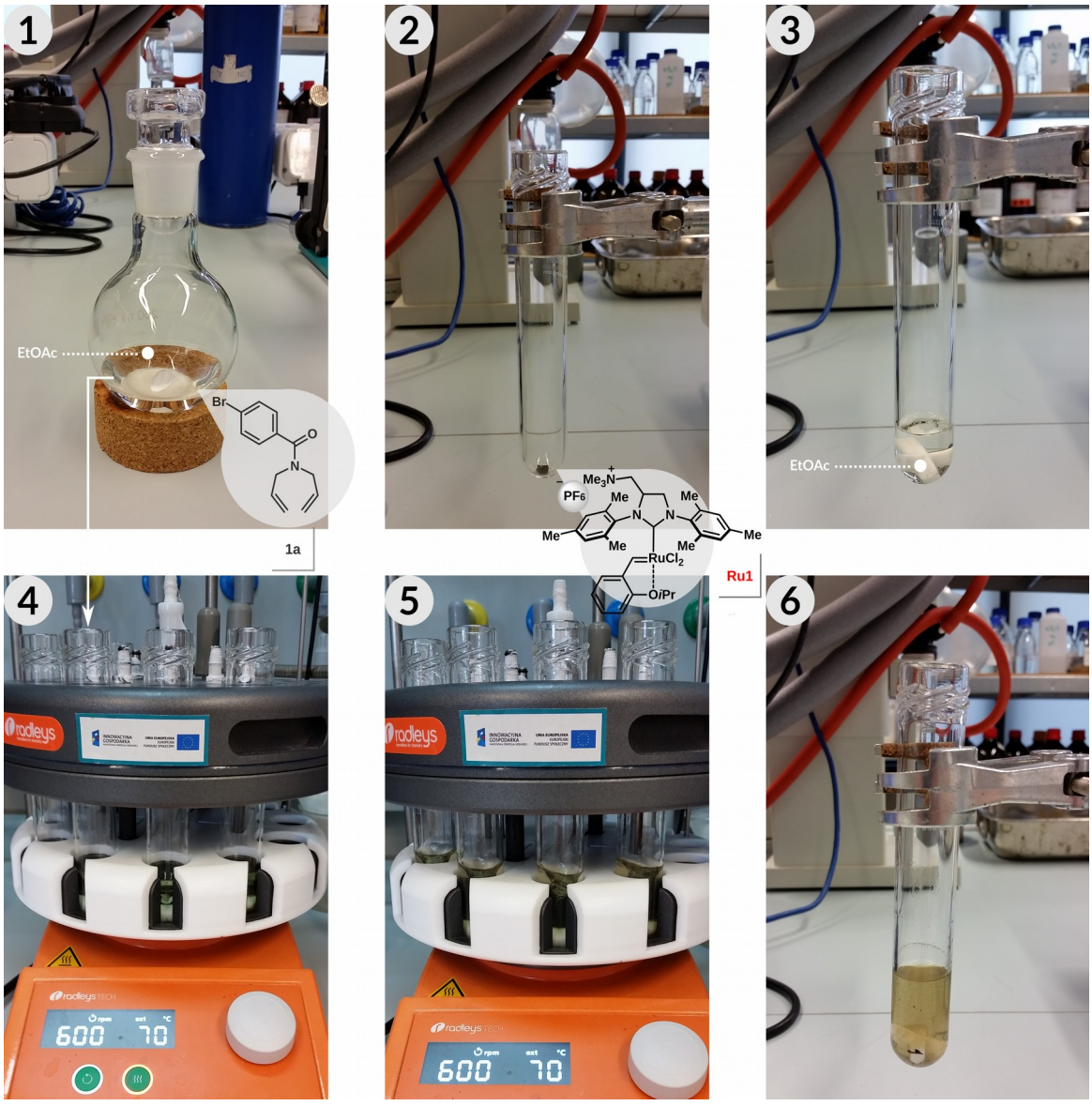


5 Celite® Standard Super Cel® was purchased from *ROTH*, and used as received.

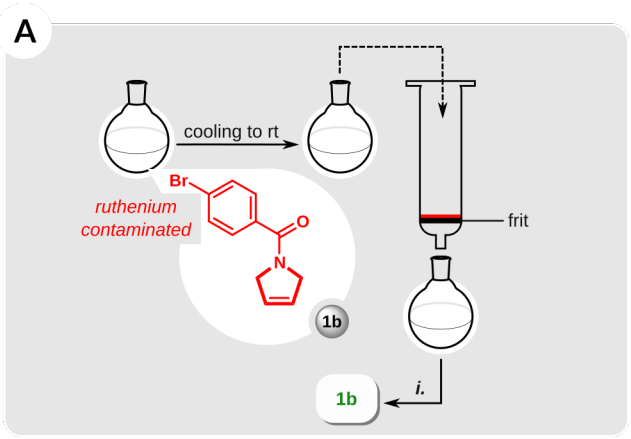
General procedure for RCM (Table 1)



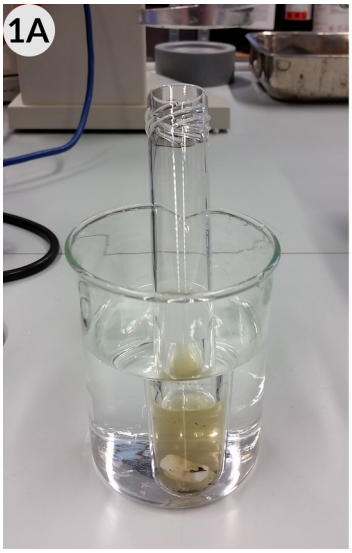
1. A 250 mL round-bottomed flask was equipped with a magnetic stir bar (egg shaped). *N,N*-diallyl-4-bromobenzamide (**1a**) (1.96g, 7.0 mmol) was dissolved in ethyl acetate (35 mL)[1].
2. The solid **Ru** catalyst (0.01 mmol, 1.0 mol%) was placed in a *Radleys* glass tube.
3. Ethyl acetate (5.0 mL) was added.
4. The *Radleys* glass tube was placed in a *Radleys Carousel* and heated to 70 °C, after which **1a** (5.0 mL, 0.2 M in AcOEt) was added.
5. The reaction mixture was stirred (600 rpm) for 2 h under an ambient atmosphere.
6. The heating was turned off and the reaction mixture was further purified by method **A**–**G**.



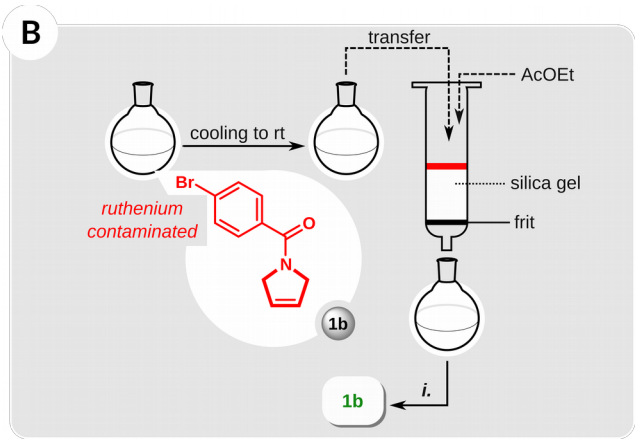
Purification method A (Table 1)



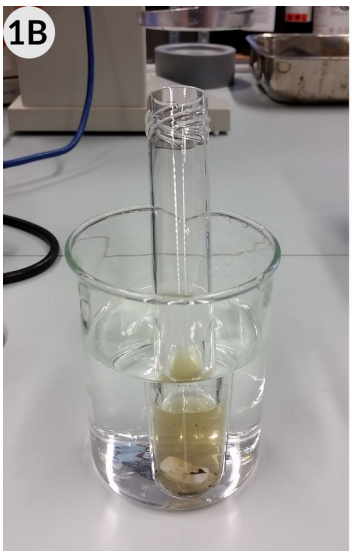
1. The *Radleys* glass tube containing the reaction mixture was placed in a water bath (room temperature) for 5 min.
2. The reaction mixture was gravitationally filtered through a frit.
3. Pictures **2A** and **3A** show the reaction mixture after filtration (experiment with **Ru1** catalyst). The solvent was removed under reduced pressure to give **1b**. The ruthenium content in the product was determined by inductively coupled plasma mass spectrometry (ICP-MS).

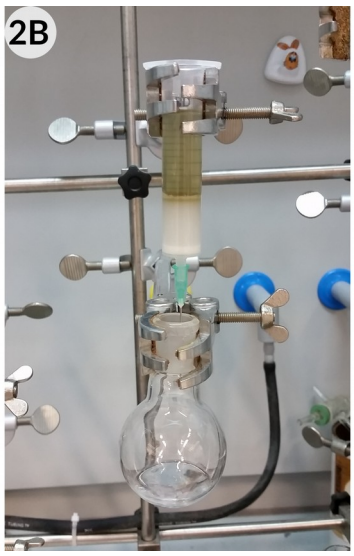


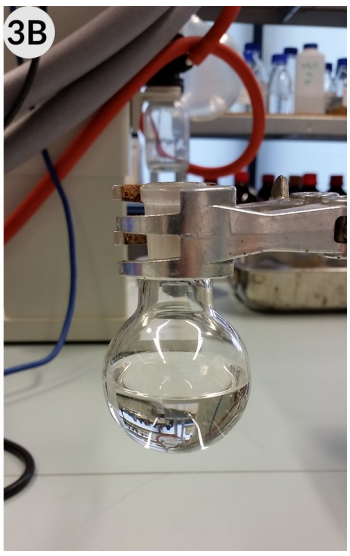
Purification method B (Table 1)



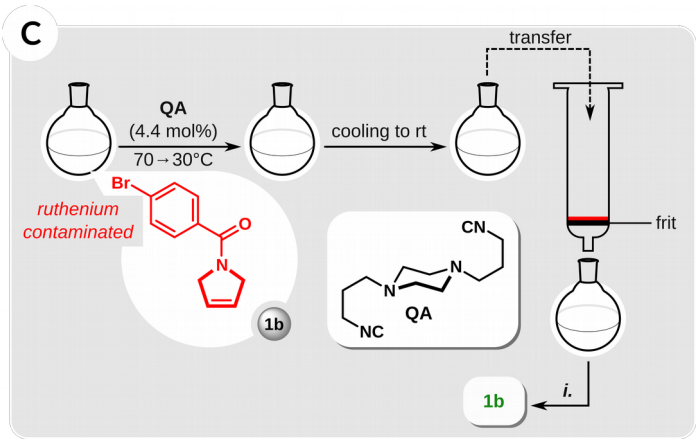
1. The *Radleys* glass tube containing the reaction mixture was placed in a water bath (room temperature) for 5 min.
2. The reaction mixture was gravitationally filtered through silica gel (200 mg of silica gel per 1 mg of catalyst; column diameter: 1.6 cm). The silica gel plug was washed with an additional portion of EtOAc (20 mL).
3. Picture **3B** shows the reaction mixture after filtration (experiment with **Ru1** catalyst). The solvent was removed under reduced pressure to give **1b**. The ruthenium content in the product was determined by inductively coupled plasma mass spectrometry (ICP-MS).



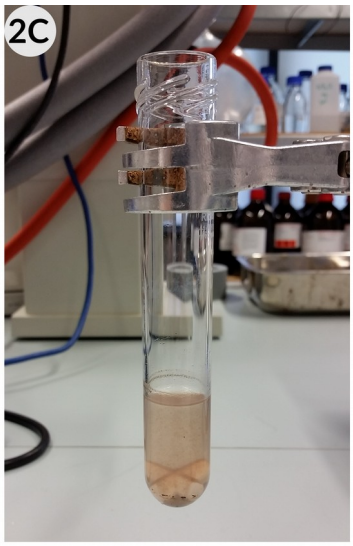


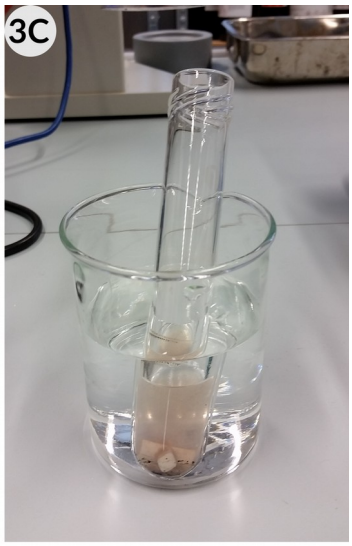


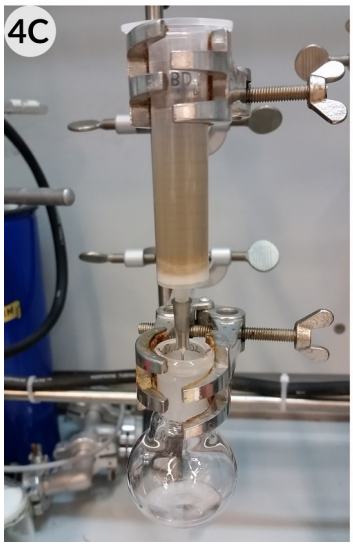
Purification method C (Table 1)

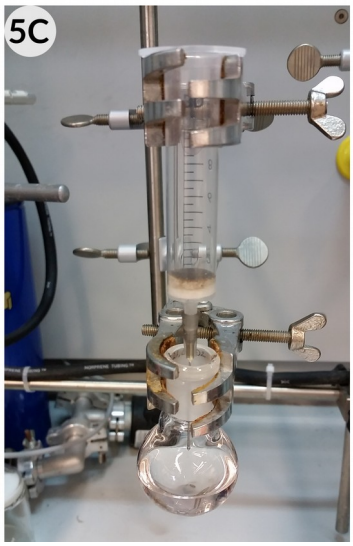


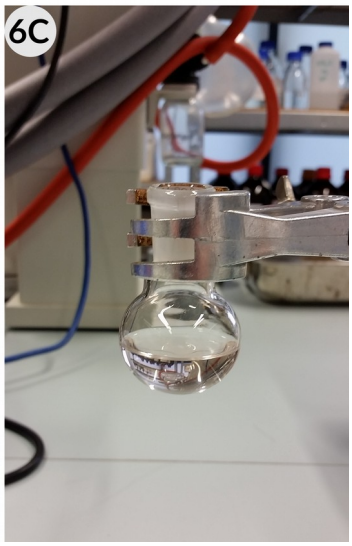
1. The scavenger **QA** (1.0 mL, 0.044 M in EtOAc, 0.044 mmol, 4.4 equiv.[6]) was added directly into the *Radleys* glass tube containing the reaction mixture. The contents of the tube were stirred (600 rpm) for 1 h.
2. Picture **2C** shows the reaction mixture after treatment with **QA** (experiment with **Ru1** catalyst).
3. The tube was placed in a water bath (room temperature) for 5 min.
4. The reaction mixture was gravitationally filtered through a frit.
5. Pictures **5C** and **6C** shows the reaction mixture after filtration (experiment with **Ru1** catalyst). The solvent was removed under reduced pressure to give **1b**. The ruthenium content in the product was determined by inductively coupled plasma mass spectrometry (ICP-MS).





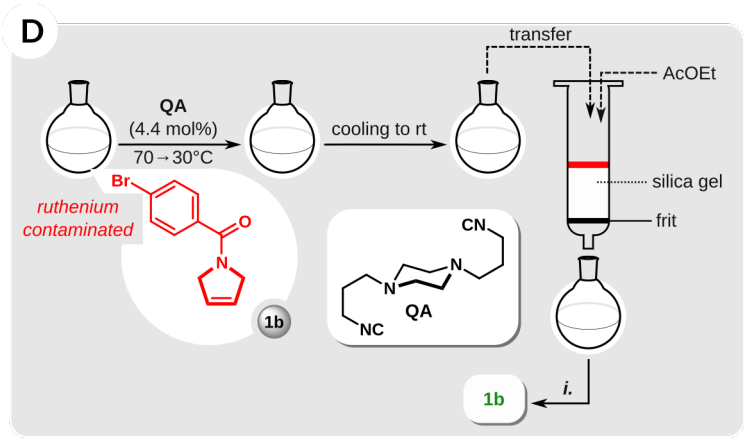




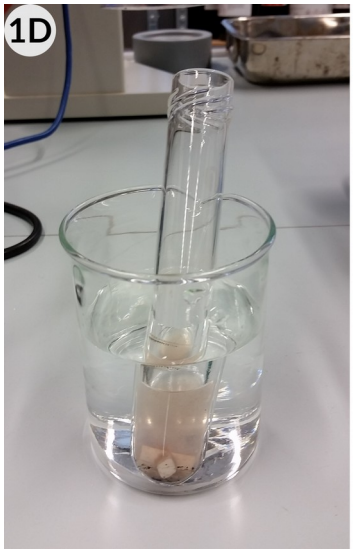


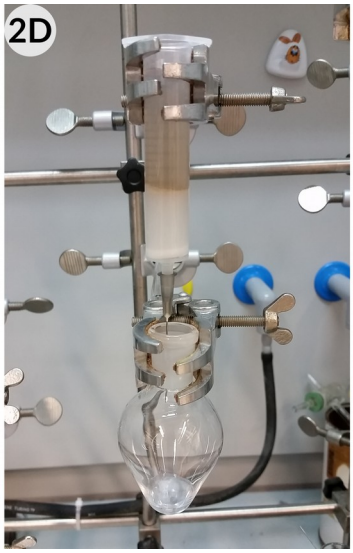
6 Equivalents with respect to the catalyst.

Purification method D (Table 1)

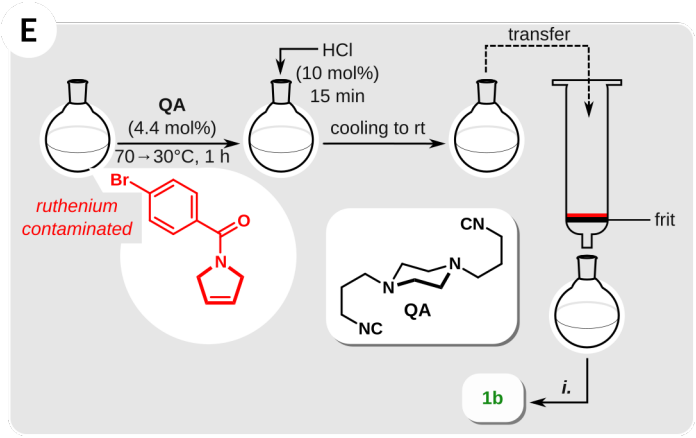


1. The scavenger **QA** (1.0 mL, 0.044M in EtOAc, 0.044 mmol, 4.4 equiv.[6]) was added directly into the *Radleys* glass tube containing the reaction mixture. The contents of the tube were stirred (600 rpm) for 1 h.
2. The tube was placed in a water bath (room temperature) for 5 min.
3. The reaction mixture was gravitationally filtered through silica gel (200 mg of silica gel per 1 mg of catalyst; column diameter: 1.6 cm). The silica gel plug was washed with an additional portion of EtOAc (20 mL).
4. Picture **3D** shows the reaction mixture after filtration (experiment with **Ru1** catalyst). The solvent was removed under reduced pressure to give **1b**. The ruthenium content in the product was determined by inductively coupled plasma mass spectrometry (ICP-MS).

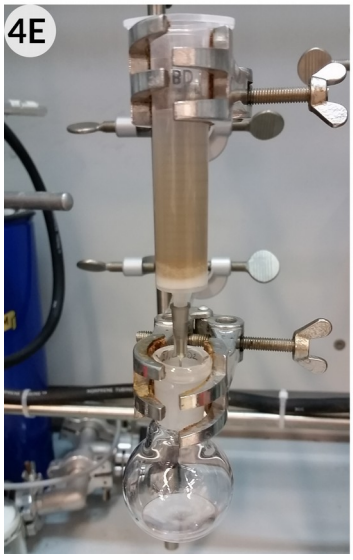


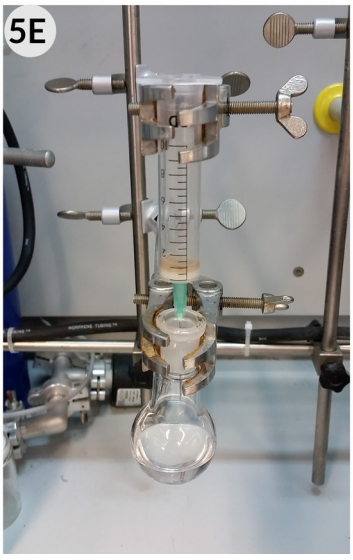


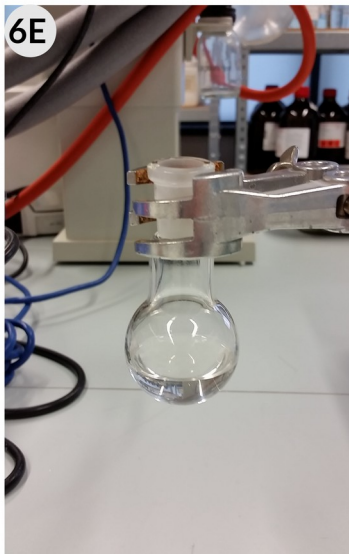
Purification method E (Table 1)



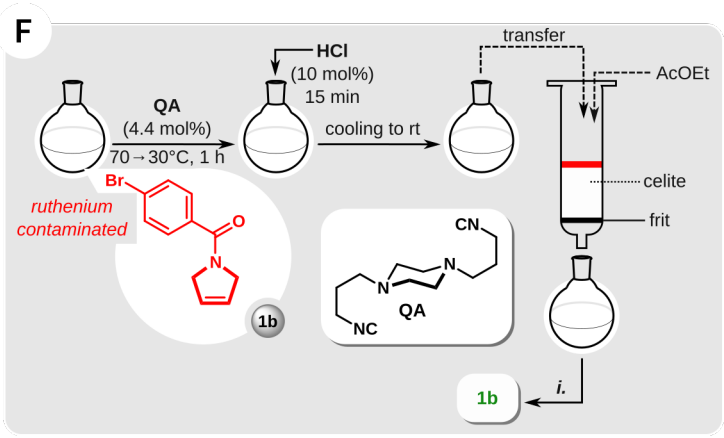
1. The scavenger **QA** (1.0 mL, 0.044 M in EtOAc, 0.044 mmol, 4.4 equiv.[6]) was added directly into the *Radleys* glass tube containing the reaction mixture. The contents of the tube were stirred (600 rpm) for 1 h.
2. HCl (0.1 mL, 1M in Et_2O, 0.1 mmol, 10 equiv.) was added and the resulting mixture was stirred (600 rpm) for 15 min.
3. The tube was placed in a water bath (room temperature) for 5 min.
4. The reaction mixture was gravitationally filtered through a frit.
5. Pictures **5E** and **6E** show the reaction mixture after filtration (experiment with **Ru1** catalyst). The solvent was removed under reduced pressure to give **1b**. The ruthenium content in the product was determined by inductively coupled plasma mass spectrometry (ICP-MS).



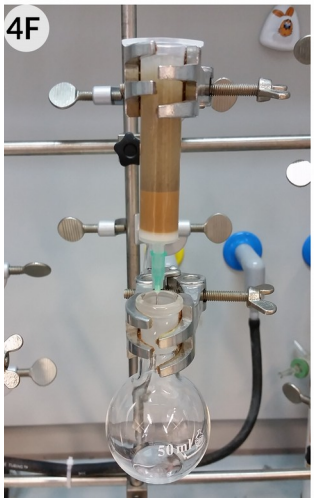




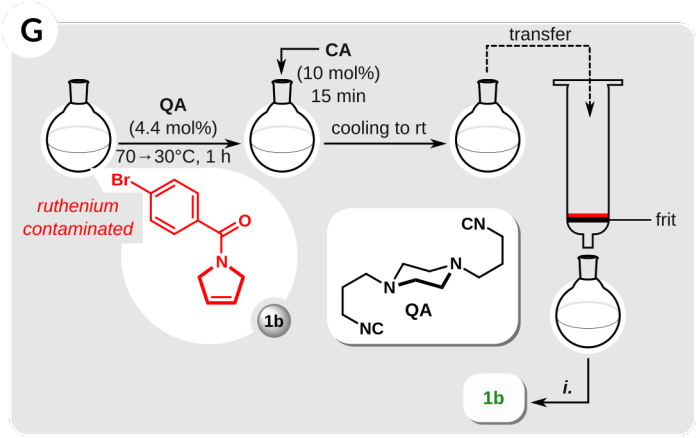
Purification method F (Table 1)



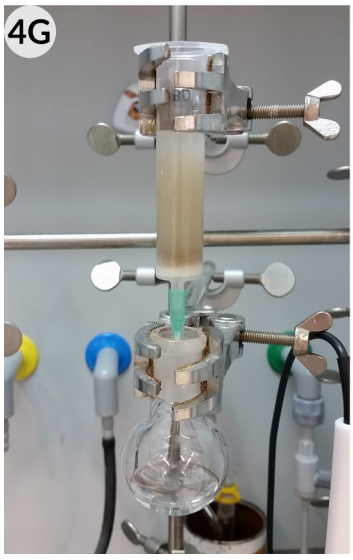
1. The scavenger **QA** (1.0 mL, 0.044 M in EtOAc, 0.044 mmol, 4.4 equiv.[6]) was added directly into the *Radleys* glass tube containing the reaction mixture. The contents of the tube were stirred (600 rpm) for 1 h.
2. HCl (0.1 mL, 1M in Et_2O, 0.1 mmol, 10 equiv.) was added and the resulting mixture was stirred (600 rpm) for 15 min.
3. The tube was placed in a water bath (room temperature) for 5 min.
4. The reaction mixture was gravitationally filtered through celite (1.0 g of celite; column diameter: 1.6 cm). The celite plug was washed with an additional portion of EtOAc (5 mL).
5. Pictures **5F** and **6F** show the reaction mixture after filtration (experiment with **Ru1** catalyst). The solvent was removed under reduced pressure to give **1b**. The ruthenium content in the product was determined by inductively coupled plasma mass spectrometry (ICP-MS).

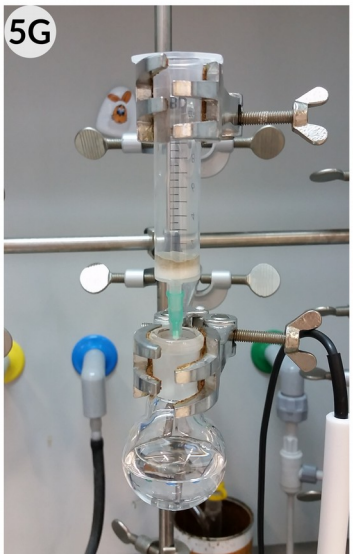


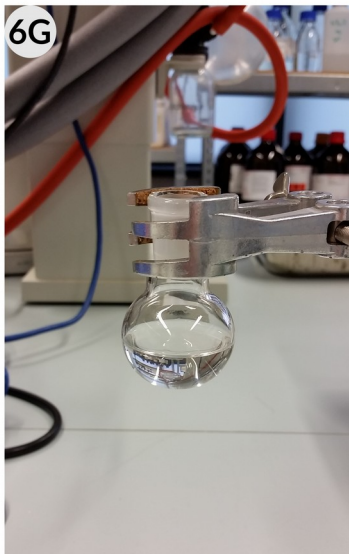
Purification method G (Table 1)



1. The scavenger QA (1.0 mL, 0.044 M in EtOAc, 0.044 mmol, 4.4 equiv.[6]) was added directly into the *Radleys* glass tube containing the reaction mixture. The contents of the tube were stirred (600 rpm) for 1 h.
2. Citric acid **CA** (19.2 mg, 0.1 mmol, 10 equiv.) was added and the resulting mixture was stirred (600 rpm) for 1 h.
3. The tube was placed in a water bath (room temperature) for 5 min.
4. The reaction mixture was gravitationally filtered through a frit.
5. Pictures **5G** and **6G** show the reaction mixture after filtration (experiment with **Ru1** catalyst). The solvent was removed under reduced pressure to give **1b**. The ruthenium content in the product was determined by inductively coupled plasma mass spectrometry (ICP-MS).







General procedure for RCM (Table 2)

A *Radleys* glass tube was charged with **Ru** catalyst (0.01 mmol). Ethyl acetate (5.0 mL) was added. The stirrer was set to 600 rpm. The solution was heated to 70 °C, after which the substrate (**2a**–**19a**) (5.0 mL, 0.2 M in EtOAc, 1.0 mmol) was added. The reaction mixture was stirred at 70 °C for 2 h under ambient atmosphere. The heating was turned off, the scavenger **QA** (9.7 mg, 0.044 mmol, 4.4 equiv.[6]) was added and the resulting mixture was stirred for 1 h. Subsequently, HCl (0.1 mL, 1M in Et_2O, 0.1 mmol, 10 mol%) was added and stirring continued for 15 min. Finally, the reaction mixture was gravitationally filtered through a frit and the solvent was removed under reduced pressure to give crude **2b**–**19b**.[7]

7 Reaction conversions were determined by GC analysis and are based on the ratio of product/(product + starting material).

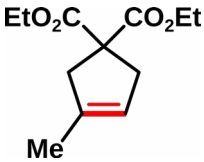
Diethyl cyclopent-3-ene-1,1-dicarboxylate (2b)

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.65 – 5.55 (m, 2H), 4.19 (q, J = 7.1 Hz, 4H), 3.06 – 2.96 (m, 4H), 1.25 (t, J = 7.1 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 127.8, 61.51, 58.8, 40.8, 14.0.

Spectral data are in agreement with those reported in the literature.[8]

Diethyl 3-methyl-3-cyclopentene-1,1-dicarboxylate (3b)

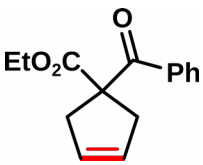


^{1}H NMR (400 MHz, $CDCl_3$): δ 5.21 – 5.16 (m, 1H), 4.18 (q, J = 7.1 Hz, 4H), 2.98 – 2.94 (m, 2H), 2.92 – 2.87 (m, 2H), 1.74 – 1.68 (m, 3H), 1.24 (t, J = 7.1 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 137.4, 121.2, 61.4, 59.3, 44.6, 40.5, 16.0, 14.0.

Spectral data are in agreement with those reported in the literature.[9]

Ethyl 1-benzoylcyclopent-3-enecarboxylate (4b)



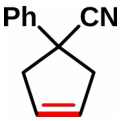
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 – 7.83 (m, 2H), 7.56 – 7.49 (m, 1H), 7.47 – 7.37 (m, 2H), 5.64 – 5.58 (m, 2H), 4.08 (q, J = 7.1 Hz, 2H), 3.29 – 3.20 (m, 2H), 3.16 – 3.07 (m, 2H), 0.98 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9, 174.3, 135.0, 132.9, 128.9, 128.6, 127.7, 62.3, 61.7, 41.4, 13.8.

Spectral data are in agreement with those reported in the literature.[10]

8 D. F. Taber and K. J. Frankowski, *J. Org. Chem.*, 2003, **68**, 6047–6048.
9 Z. Xi, H. S. Bazzi and J. A. Gladysz, *Org. Lett.*, 2011, **13**, 6188–6191.
10 G. K. Zieliński, C. Samojłowicz, T. Wdowik and K. Grela, *Org. Biomol. Chem.*, 2015, **13**, 2684–2688.

1-phenylcyclopent-3-enecarbonitrile (5b)

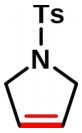


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 – 7.44 (m, 2H), 7.42 – 7.34 (m, 2H), 7.34 – 7.28 (m, 1H), 5.86 – 5.80 (m, 2H), 3.37 – 3.26 (m, 2H), 3.01 – 2.91 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 129.1, 128.5, 127.9, 125.4, 125.0, 48.5, 45.0.

Spectral data are in agreement with those reported in the literature.[11]

1-tosyl-2,5-dihydro-1*H*-pyrrole (6b)

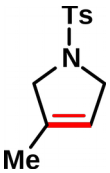


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 – 7.70 (m, 2H), 7.35 – 7.28 (m, 2H), 5.67 – 5.63 (m, 2H), 4.13 – 4.09 (m, 4H), 2.42 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 134.4, 129.9, 127.5, 125.6, 55.0, 21.6.

Spectral data are in agreement with those reported in the literature.[12]

3-methyl-1-tosyl-2,5-dihydro-1*H*-pyrrole (7b)

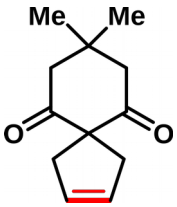


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 8.1 Hz, 1H), 7.32 (d, J = 8.5 Hz, 1H), 5.43 – 5.07 (m, 0H), 4.11 – 4.03 (m, 1H), 4.00 – 3.93 (m, 1H), 2.43 (s, 2H), 1.69 – 1.63 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 135.2, 134.5, 129.9, 127.6, 119.2, 57.8, 55.3, 21.7, 14.2.

Spectral data are in agreement with those reported in the literature.[13]

5-(cyclopent-3-enyl)-2,2-dimethyl-clohexane-4,6-dione (8b)



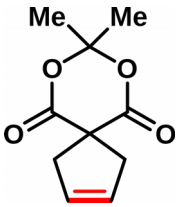
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.55 – 5.50 (m, 2H), 2.87 – 2.83 (m, 4H), 2.64 – 2.62 (m, 4H), 0.99 (s, 6H).

11 O. Ablialimov, M. Kędziorek, M. Malińska, K. Woźniak and K. Grela, *Organometallics*, 2014, **33**, 2160–2171.
12 C. Hongfa, J. Tian, H. S. Bazzi and D. E. Bergbreiter, *Org. Lett.*, 2007, **9**, 3259–3261.
13 K. Skowerski, J. Białecki, A. Tracz and T. K. Olszewski, *Green Chem.*, 2014, **16**, 1125–1130.

^{13}C NMR (100 MHz, $CDCl_3$): δ 207.1, 127.2, 69.8, 51.6, 39.2, 30.5, 28.4.

Spectral data are in agreement with those reported in the literature.[14]

5-(cyclopent-3-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (9b)

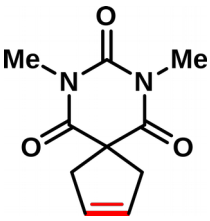


^{1}H NMR (400 MHz, $CDCl_3$): δ 5.74 – 5.69 (m, 1H), 3.17 – 3.13 (m, 2H), 1.77 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 127.3, 105.0, 50.8, 46.9, 28.8.

Spectral data are in agreement with those reported in the literature.[15]

7,9-dimethyl-9-diazaspiro[4.5]dec-2-ene-6,8,10-trione (10b)

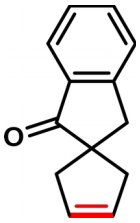


^{1}H NMR (400 MHz, $CDCl_3$): δ 5.68 – 5.65 (m, 2H), 3.31 (s, 7H), 3.02 – 3.00 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 151.4, 127.3, 54.6, 45.5, 29.0.

Spectral data are in agreement with those reported in the literature.[16]

Spiro[cyclopent[3]ene-1,2'-inden]-1'(3'*H*)-one (11b)



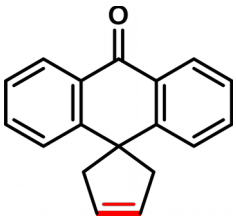
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (ddd, J = 7.6, 1.2, 0.7 Hz, 1H), 7.59 (td, J = 7.4, 1.2 Hz, 1H), 7.44 (dp, J = 7.7, 0.9 Hz, 1H), 7.39 – 7.38 (m, 1H), 5.76 – 5.69 (m, 2H), 3.17 (s, 2H), 2.98 – 2.82 (m, 2H), 2.41 – 2.28 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.6, 152.9, 136.4, 134.9, 128.9, 127.6, 126.6, 124.4, 55.6, 45.6.

Spectral data are in agreement with those reported in the literature.[17]

10*H*-spiro[anthracene-9,1'-cyclopent[3]en]-10-one (12b)

14 S. Kotha, E. Manivannan, T. Ganesh, N. Sreenivasachary and A. Deb, *Synlett*, 1999, **10**, 1618–1620.
15 C. Kammerer, G. Prestat, T. Gaillard, D. Madec and G. Poli, *Org. Lett.*, 2008, **10**, 405–408.
16 S. Kotha, A. C. Deb and R. V. Kumar, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 1039–1043.
17 S. Kotha, K. Mandal, A. Tiwari and S. M. Mobin, *Chem. Eur. J.*, 2006, **12**, 8024–8038.

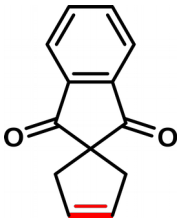


^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (ddd, J = 7.9, 1.6, 0.6 Hz, 2H), 7.62 (ddd, J = 8.1, 7.1, 1.6 Hz, 2H), 7.51 (ddd, J = 8.1, 1.2, 0.6 Hz, 2H), 7.41 (ddd, J = 7.9, 7.1, 1.2 Hz, 2H), 6.06 – 6.00 (m, 2H), 3.18 (s, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 184.0, 153.2, 134.4, 130.2, 129.3, 126.7, 126.5, 110.1, 56.2, 45.7.

Spectral data are in agreement with those reported in the literature.[18]

Spiro[cyclopent[3]ene-1,2'-indene]-1',3'-dione (13b)

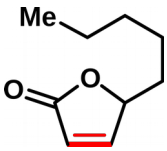


1H NMR (400 MHz, CDCl3): δ 8.03 – 7.96 (m, 2H), 7.88 – 7.81 (m, 2H), 5.77 – 5.69 (m, 2H), 2.78 – 2.74 (m, 4H).

13C NMR (100 MHz, CDCl3): δ 203.5, 141.7, 135.7, 128.3, 123.5, 77.0, 57.7, 41.7.

Spectral data are in agreement with those reported in the literature.[14]

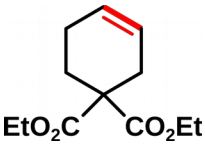
2-nonen-4-olide (14b)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (dd, J = 5.7, 1.5 Hz, 1H), 6.09 (dd, J = 5.7, 2.0 Hz, 1H), 5.02 (ddt, J = 7.3, 5.3, 1.8 Hz, 1H), 1.81 – 1.59 (m, 3H), 1.52 – 1.37 (m, 1H), 1.36 – 1.21 (m, 4H), 0.94 – 0.81 (m, 3H).

Spectral data are in agreement with those reported in the literature.[19]

Diethyl cyclohex-3-ene-1,1-dicarboxylate (15b)



^{1}H NMR (400 MHz, $CDCl_3$): δ 5.68 – 5.65 (m, 2H), 4.18 (q, J = 7.1, 4H), 2.57 – 2.53 (m, 2H), 2.17 – 2.05 (m, 4H), 1.24 (t, J = 7.1 Hz, 6H).

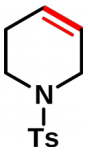
18 V. César, Y. Zhang, W. Kośnik, A. Zieliński, A. A. Rajkiewicz, M. Ruamps, S. Bastin, N. Lugan, G. Lavigne and K. Grela, *Chem. Eur. J.*, 2017, **23**, 1950–1955.

19 P. Bonete and C. Najera, *J. Org. Chem.*, 1994, **59**, 3202–3209.

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 126.2, 124.1, 61.4, 53.1, 30.6, 27.5, 22.7, 14.2.

Spectral data are in agreement with those reported in the literature.[10]

1-tosyl-1,2,5,6-tetrahydropyridine (16b)

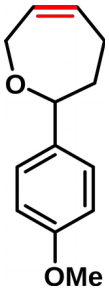


H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 5.79 – 5.71 (m, 1H), 5.64 – 5.57 (m, 1H), 3.57 (p, J = 2.8 Hz, 2H), 3.16 (t, J = 5.7 Hz, 2H), 2.42 (s, 3H), 2.21 (tq, J = 5.8, 2.8 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 133.5, 129.7, 127.8, 125.2, 122.7, 44.9, 42.8, 25.4, 21.6.

Spectral data are in agreement with those reported in the literature.[20]

2-(4-methoxyphenyl)-2,3,4,7-tetrahydrooxepine (17b)

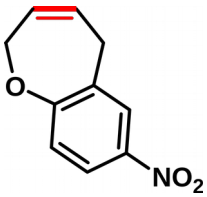


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.27 (m, 2H), 6.92 – 6.84 (m, 2H), 5.95 – 5.83 (m, 1H), 5.82 – 5.72 (m, 1H), 4.66 (dd, J = 8.3, 3.8 Hz, 1H), 4.40 – 4.29 (m, 1H), 4.18 (ddq, J = 15.9, 3.9, 2.0 Hz, 1H), 3.80 (s, 3H), 2.51 – 2.37 (m, 1H), 2.34 – 2.22 (m, 1H), 2.21 – 2.11 (m, 1H), 2.01 – 1.85 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 136.2, 132.4, 130.3, 127.2, 113.8, 82.8, 67.0, 55.4, 35.7, 26.2.

Spectral data are in agreement with those reported in the literature.[18]

7-nitro-2,5-dihydrobenzo[b]oxepine (18b)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (dd, J = 8.7, 2.8 Hz, 1H), 8.00 (d, J = 2.8 Hz, 1H), 7.11 (d, J = 8.7 Hz, 1H), 5.98 – 5.89 (m, 1H), 5.63 – 5.53 (m, 1H), 4.70 – 4.65 (m, 2H), 3.60 – 3.56 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): 164.0, 143.4, 135.8, 127.0, 126.0, 124.6, 123.8, 122.2, 70.6, 31.5.

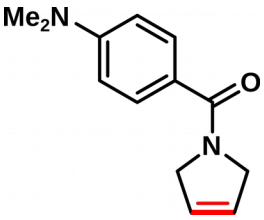
IR (film $CHCl_3$**):** ῡ = 3093, 3072, 3033, 2948, 2903, 2855, 1612, 1581, 1518, 1486, 1431, 1398, 1341, 1276, 1243, 1202, 1171, 1120, 1085, 1055, 1020, 977, 942, 901, 869, 787, 763, 733.

20 C. Hongfa, H.-L. Su, H. S. Bazzi and D. E. Bergbreiter, *Org. Lett.*, 2009, **11**, 665–667.

MS (EI): m/z: 191.6 [M^+], 191.0 (100%).

Elemental analysis calcd (%) for $C_{10}H_9NO_3$ C 62.82; H 4.74; N 7.33; O 25.11 found: 62.60; 4.84; N 7.15.

(2,5-dihydro-1*H*-pyrrol-1-yl)(4-(dimethylamino)phenyl)methanone (19b)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 – 7.46 (m, 2H), 6.72 – 6.63 (m, 2H), 5.89 (brs, 1H), 5.75 (brs, 1H), 4.45 (brs, 2H), 4.34 (brs, 2H), 3.00 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 151.6, 129.2, 126.2, 125.4, 123.7, 111.1, 56.1, 53.8, 40.3.

IR (neat): $\tilde{\upsilon}$ = 3071, 2888, 2856, 1633, 1585, 1542, 1476, 1463, 1398, 1364, 1323, 1236, 1206, 1187, 1155, 1082, 1069, 1000, 961, 947, 910, 820, 803, 792.

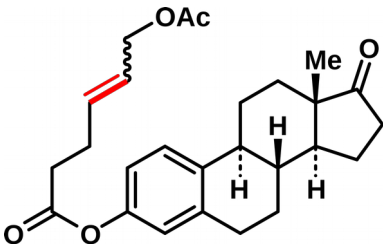
MS (ESI): m/z: 239.12 [M+Na]$^+$, 455.24 [2M+Na]$^+$.

Elemental analysis calcd (%) for $C_{13}H_{16}N_2O$: C 72.19, H 7.46, N 12.95, O 7.40 found: C 72.06, H 7.67, N 12.85

CM of 22a with 21 (fig. 5B)

A *Radleys* glass tube was charged with the steroid substrate **22a** (352 mg, 1 mmol) and *cis*-1,4-diacetoxy-2-butene (689 mg, 4.0 mmol, 4.0 equiv.). Ethyl acetate (5.0 mL) was added. The stirrer was set to 600 rpm, the solution was heated to 70 ℃ and the **Ru1** catalyst (7.34 mg, 0.01 mmol, 1.0 mol%) was added. The reaction mixture was stirred at 70 ℃ for 2 h under ambient atmosphere. The heating was turned off, the scavenger **QA** (0.1 mL, 0.044 M in AcOEt, 0.044 mmol, 4.4 equiv.[6]) was added and the resulting mixture was stirred for 1 h. Subsequently, HCl (0.1 mL, 1M in Et_2O, 0.1 mmol, 10 mol%) was added and stirring continued for 15 min. Finally, the reaction mixture was gravitationally filtered through a frit and the solvent was removed under reduced pressure to give crude **22b** (99%,[21] 1.6 ppm Ru).

Mixture of isomers *E/Z* = 3:1.



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, J = 8.2 Hz, 1H), 7.04 – 6.39 (m, 2H), 5.93 – 5.77 (m, 1H), 5.76 – 5.56 (m, 1H), 4.52 (d, J = 6.0 Hz, 2H), 3.08 – 2.76 (m, 2H), 2.71 – 2.43 (m, 5H), 2.43 – 2.21 (m, 2H), 2.19 – 1.86 (m, 7H), 1.72 – 1.30 (m, 6H), 0.89 (s, 3H).

^{13}CNMR (100 MHz, $CDCl_3$): δ 220.7, 171.6, 171.5, 170.9, 170.8, 148.6, 138.0, 137.4, 133.4, 132.4, 126.4, 125.6, 125.3, 121.6, 118.8, 64.8, 63.6, 62.2, 60.2, 53.4, 53.2, 50.4, 48.0, 44.2, 38.0, 35.9, 34.0, 33.6, 31.6, 29.4, 27.6, 26.4, 25.8, 23.1, 21.6, 21.0, 21.0, 20.8, 13.8.

IR (film CH_2Cl_2)**:** ῡ = 3427, 2932, 2865, 1739, 1608, 1494, 1474, 1368, 1227, 1153, 1025, 1008, 966, 905, 821, 758, 607, 581, 560.

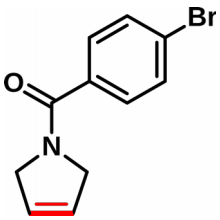
MS (ESI): m/z: 239.12 $[M+Na]^+$, 871.44 $[2M+Na]^+$.

Elemental analysis calcd (%) for $C_{26}H_{31}O_5$ (424.54) C 73.56; H 7.60; O 18.84 found: 73.27; H 7.52

21 Reaction conversion was determined by TLC analysis.

Large scale RCM of 1a (fig. 5A)

A 50 mL round-bottomed flask was charged with **Ru1** catalyst (10.5 mg, 0.0125 mmol, 0.25 mol%). Ethyl acetate (25.0 mL) was added. The stirrer was set to 600 rpm, the solution was heated to 70 ℃ and *N*,*N*-diallyl-4-bromobenzamide (**1a**) (1.4 g, 5.0 mmol, 1.0 equiv.) was added. The reaction mixture was stirred at 70 ℃ for 2 h under ambient atmosphere. The heating was turned off, the scavenger **QA** (1.0 mL 0.055 M in AcOEt, 0.055 mmol, 4.4 equiv.[6]) was added and the resulting mixture was stirred for 1 h. Subsequently, HCl (0.125 mL, 1M in Et_2O, 0.125 mmol, 10 equiv.) was added and stirring continued for 15 min. Finally, the reaction mixture was gravitationally filtered through a frit and the solvent was removed under reduced pressure to give crude **1b** (98%,[7] 6.4 ppm Ru).



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 – 7.51 (m, 2H), 7.44 – 7.37 (m, 2H), 5.94 – 5.88 (m, 1H), 5.78 – 5.71 (m, 1H), 4.48 – 4.37 (m, 2H), 4.23 – 4.14 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 135.7, 131.8, 128.7, 126.2, 125.2, 124.3, 55.9, 53.6.

Spectral data are in agreement with those reported in the literature.[22]

22 G. Szczepaniak, K. Urbaniak, C. Wierzbicka, K. Kosiński, K. Skowerski and K. Grela, *ChemSusChem*, 2015, **8**, 4139–4148.

Telescope synthesis of 1d (fig. 6)

A 10 mL vial was charged with **1a** (280 mg, 1.0 mmol) and dissolved in ethyl acetate (2.0 mL). **NHII** (3.36 mg, 0.5 mo %) was added and the mixture was stirred (600 rpm) at rt for 10 min. Afterwards, the contents of the vial were transferred to a *Radleys* glass tube containing a solution of phenylboronic acid (189 mg, 1.5 mmol) and Cs_2CO_3 (652 mg, 2.0 mmol) in ethanol (4.0 mL) prepared ahead of time and heated to 80 ℃. $(PPh_3)_2PdCl_2$ (35.1 mg, 5.0 mol%) was added to the combined contents of the *Radleys* tube and the mixture was stirred (600 rpm) at 80 ℃ for 10 min. The heating was turned off and the reaction mixture was purified using procedures **A** or **B**, described below.

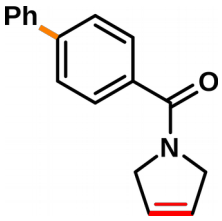
Procedure A; Purification of 1d using QA, CA and aluminium oxide

The scavenger **QA** (53.3 mg, 0.24 mmol, 24.2 mol%) was added directly into the *Radleys* tube and the resulting mixture was stirred (600 rpm) for 1 h. Ethanol (5.0 mL) was added, followed by citric acid (480 mg, 2.5 mmol) and the contents were stirred (800 rpm) for 10 min. The solvent was removed under reduced pressure and the solid residue was loaded onto the top of an aluminium oxide[23] plug (2.0 g, column diameter: 1.6 cm). The plug was washed with three portions of EtOAc (2×10 mL and 5 mL). Finally, the solvent was removed under reduced pressure to give crude **1d** (1.17 ppm of **Ru** and 0.79 ppm of **Pd**).

Procedure B; purification of 1d using aluminium oxide (Control experiment)

The solvent was removed under reduced pressure and the solid residue was loaded onto the top of an aluminium oxide plug (2.0 g, column diameter: 1.6 cm). The plug was washed with three portions of EtOAc (2×10 mL and 5 mL). Finally, the solvent was removed under reduced pressure to give crude **1d** (49 ppm of **Ru** and 467 ppm of **Pd**).

[1,1'-biphenyl]-4-yl(2,5-dihydro-1H-pyrrol-1-yl)methanone (1d)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 – 7.57 (m, 6H), 7.48 – 7.42 (m, 2H), 7.41 – 7.32 (m, 1H), 5.92 (dt, J = 6.5, 2.1 Hz, 1H), 5.75 (dt, J = 6.5, 2.1 Hz, 1H), 4.47 (td, J = 4.0, 1.9 Hz, 2H), 4.27 (td, J = 4.0, 1.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 142.8, 140.3, 135.6, 129.0, 127.8, 127.5, 127.2, 127.1, 126.1, 125.3, 55.9, 53.6.

IR (neat): ῡ = 3080, 3033, 2940, 2860, 1630, 1602, 1488, 1398, 1351, 1332, 1195, 1165, 1117, 1090, 1076, 1037, 1005, 963, 913, 855, 837, 804.

MS (ESI): m/z: 272.10 $[M+Na]^+$, 521.22 $[2M+Na]^+$.

Elemental analysis calcd (%) for $C_{17}H_{15}NO$ (249.12): C 81.90; H 6.06, N 5.62, O 6.42; found: C 81.87; H 5.99, N 5.64.

23 Aluminum oxide activated, basic Brockmann I was purchased from *SIGMA-ALDRICH (product 199443-1KG),* and used as received.

Analytical determination of ruthenium concentration

Ruthenium content was determined by inductively coupled plasma mass spectrometry (IPC-MS, NexION 300D, *Perkin Elmer*, USA) equipped with a traditional sample introduction system, which requires samples to be in solution in order to be analyzed.

Mineralization

Samples ranging in mass from 30 to 300 mg were digested in capped glass vessels placed in a microwave assisted sample preparation system (single reaction cell - *UltraWAVE* system, *Milestone*, Italy) with 4 mL of 65% HNO_3 (*Suprapur*, *Merck*, Germany) and 0.125 mL of 70% $HClO_4$ (ultra pure, *Chem-Lab NV*, Belgium). Different digestion methods, including different combination of acids and different digestion conditions, were tested on the chosen samples. Finally the microwave program was set to a 270 ℃ for 20 min after 25 min heat up period at 120 bar and 1500 W. Most samples were pre-digested before microwaving by aging the sample mixed with acids for 12 h at room temperature. Final digests were diluted with deionized water and measured within 24 h.

ICP-MS

The ICP-MS apparatus was calibrated by measuring a series of reference solutions with concentrations ranging from 0.001 mg L^{-1} to 0.200 mg L^{-1} (obtained by diluting a standard solution of ruthenium, 1000 mg L^{-1} in 20% HCl, *VHG Labs*, USA). The measurement was obtained as a count of ions with mass-to-charge ratio of 102 and 104. The apparatus was purged with a neutral solution for 60 s after each sample and was allowed to equilibrate for 40 s before the first measurement. Three measurements were obtained for each sample and averaged. The limit of quantification calculated from results obtained for blank solutions was 0.02 ppm.