Selective hydrogenation of *N*-heterocyclic compounds using Ru nanocatalysts in ionic liquids

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Experimental

General methods

All manipulations involving the [Ru(2-methylallyl)$_2$COD] complex were carried out in a *MBraun Labmaster 200* glovebox under an argon atmosphere.

The chemicals isoquinoline, pyridine, 2,6-dimethylpyridine, 2-picolylamine, *N*-methylpyrrole, 1-methylimidazol, 1,2-dimethylimidazol, 2-phenylpyridine, 1-phenylpyrazole, [Ru(2-methylallyl)$_2$COD] and Ruthenium (5%) on activated charcoal were purchased from *SigmaAldrich.* Pyrimidine and carbazole were purchased from *ABCR*. Quinoline and indole were purchased from the chemical stock of the institute. Imiadzole was purchased from *Alfa Aesar* and 4-dimethylaminopyridine was purchased from *Carbolution Chemicals*. The ionic liquid 1-(2-hydroxyethyl)-methylimidazolium bis(trifluoromethanesulfonimide) [C_2OHMIM]NTf$_2$ was purchased from *Merck*.

The ionic liquids 1,2-dimethyl-3-butylimidazolium bis(trifluoromethanesulfonimide) [BMMIM]NTf$_2$[1], 1-butyl-3-methylimidazolium bis(trifluoromethanesulfonimide) [BMIM]NTf$_2$[1], 1-*n*-decyl-2,3-dimethylimidazolium bis(trifluoromethanesulfonimide) and [C_{10}MMIM]NTf$_2$[1, 2], 1-(2,3-dihydroxypropyl)-2,3-dimethylimidazolium bis(trifluoromethanesulfonimide) [C_1C_1(EG)IM]NTf$_2$[3] were prepared according to known literature procedures and were dried in vacuo before they were placed in the glove box. All other commercially available chemicals were used without further purification.

Analytical methods

Transmission electron spectroscopy was recorded on Zeiss LEO912 with 120 kV. For the sample preparation one drop of the NP-dispersion embedded in ionic liquid was diluted in 2 ml acetone. Of this solution one drop was placed onto a holey carbon-coated copper grid.

^{1}H-, ^{13}C-APT- and ^{19}F-NMR spectroscopy were recorded on a *Bruker* AVANCE II spectrometer at 298 K (300 MHz, 75 MHz, 182 MHz).

Fourier Transform spectra were recorded on Bruker alpha Platinum ATR with a diamond ATR module.

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Gas Chromatography with Mass Spectrometry (GC-MS) and Gas Chromatography with Flame Ionization Detector (GC-FID) were performed using Agilent 5973 Network Mass Selective Detector with injection, auto sample, mass detector and flame ionization detector. As column MN Optima 5 MS Accent was used. As standard temperature program 50-300.MF was used (50 °C (2.0 min, 25 °C/min → 300 °C (5 min) with 0.7 bar and a flow rate of 1.7 ml/min).

Synthesis of Ru-NPs

In a typical experiment, adapted from previous protocols,[4, 5] a screw-capped vial with butyl/PTFE septum was loaded with [Ru(2-methylallyl)$_2$COD]] (12.1 mg, 0.038 mmol) and the appropriate ionic liquid (0.3 g) under argon. The suspension was heated to 90 °C and stirred under argon for 18 h resulting in a black suspension. The NP-suspension was evaporated under reduced pressure to remove volatile by-products from the decomposition of the organometallic precursor. The monometallic Ru-NPs in [C_1C_1(EG)IM]NTf_2 were prepared adapted from a literature method using a concentration of 0.1 M precursor in the IL.[6] The monometallic Ru-NPs in [C_2OHMIM]NTf_2 were synthesised using 0.1 M precursor in IL suspension at 90 °C for 18 h.

Hydrogenation reactions

In a typical experiment to the freshly prepared Ru-NPs in IL was added 1.9 mmol of the *N*-heteroaromatic compound. Then the vial was placed in a stainless steel autoclave, the reactor was sealed, charged with hydrogen and was placed into a preheated aluminium heating block (600 rpm) at the appropriate temperature. For certain compounds mesitylene was added as co-solvent for better solubility of the substrate. After the appropriate reaction time the reactor was cooled down to room temperature. For the work-up procedure the reaction mixture was extracted with 5 x 2 ml *n*-pentane or diethyl ether, the solvent was evaporated under reduced pressure and 20 µl (0.01 mmol) hexamethyldisilane as internal standard was added. Alternatively for more volatile compounds, the IL was used as internal standard. The residue was analysed using ^{1}H- and ^{13}C-APT-NMR spectroscopy and was compared to literature data.

For recycling experiments the solvent residues were removed under reduced pressure after the work up procedure. Afterwards new substrate was added and the reaction mixture was hydrogenated using the standard reaction conditions.

Transmission Electron Microscopy (TEM)

TEM measurements of NPs in [BMIM]NTf_2 and [C_1C_1(EG)IM]NTf_2 were conducted after the synthesis of the NPs, whereas the formed NPs in [BMMIM]NTf_2, [C_{10}MMIM]NTf_2 and [C_2OHMIM]NTf_2 were measured after use in a hydrogenation reaction of quinoline (80 °C, 10 bar H_2, 5 h and 19 h, respectively).

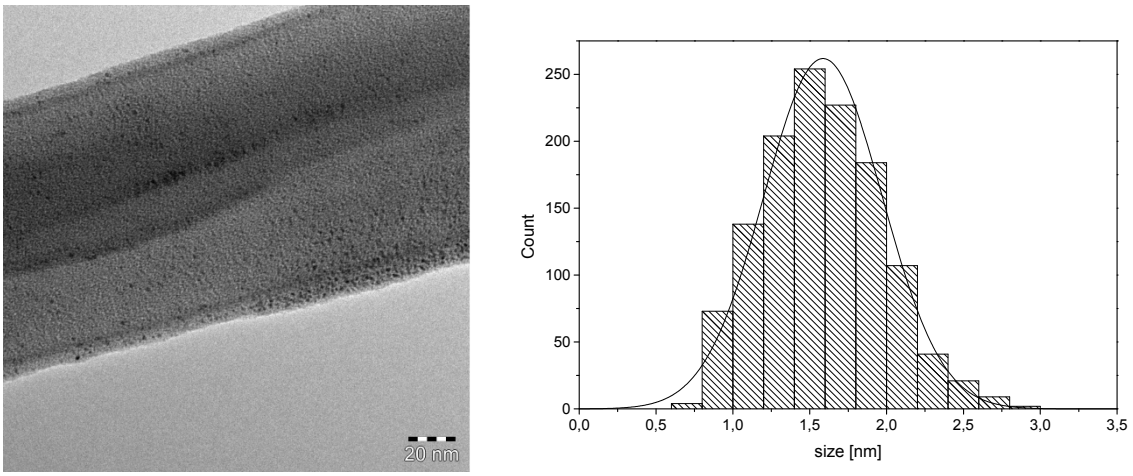


Figure S 1: TEM picture of Ru-NPs dispersed in [BMMIM]NTf_2 (38 µmol metal in 0.3 g IL, 90 °C, 18 h, after catalysis, hydrogenation of quinoline, 80 °C, 10 bar H_2, 5h) and histogram of size distribution. The mean particle diameter is 1.6 ± 0.4 nm.

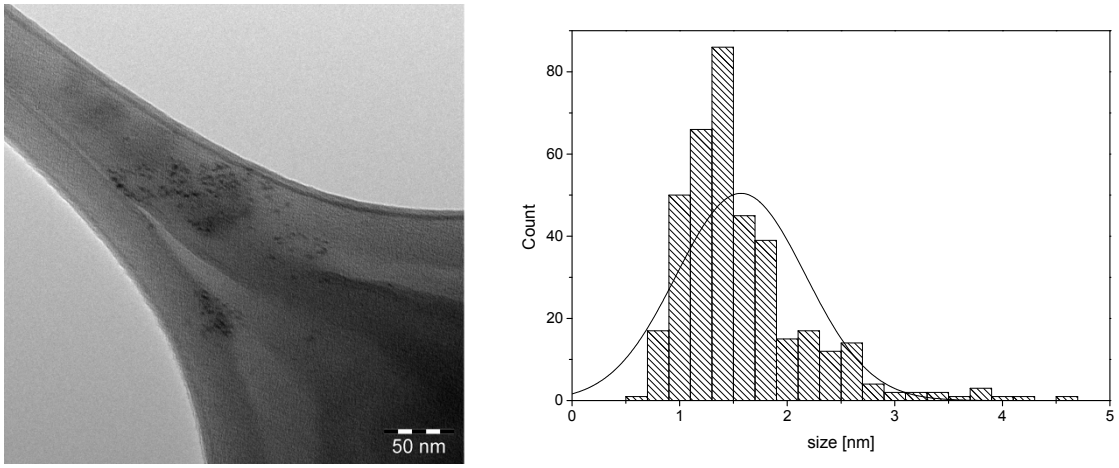


Figure S 2: TEM picture of Ru-NPs dispersed in [BMIM]NTf_2 (38 µmol metal in 0.3 g IL, 90 °C, 18 h) and histogram of size distribution. The mean particle diameter is 1.6 ± 0.6 nm.

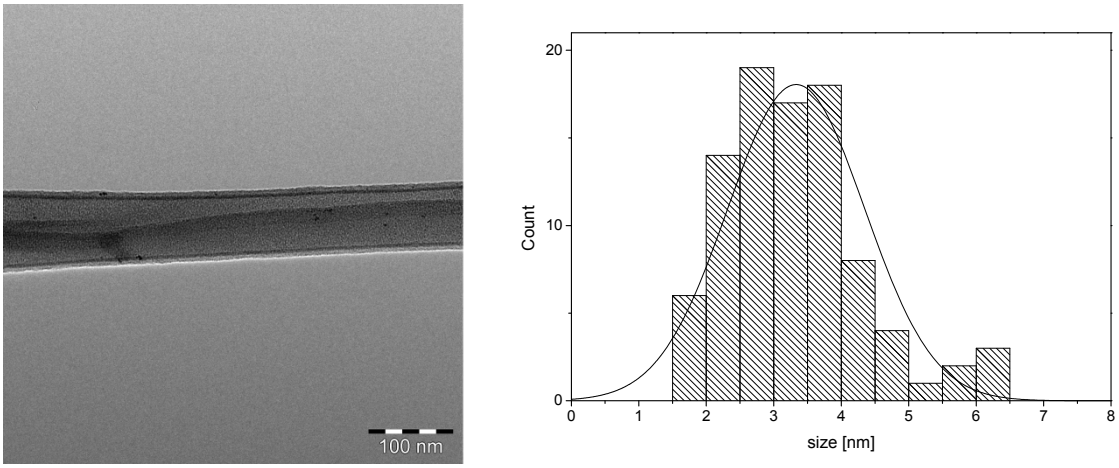


Figure S 3: TEM picture of Ru-NPs dispersed in [C_1C_1(EG)MIM]NTf_2 (30 µmol metal in 0.3 ml IL, 90 °C, 1 h) and histogram of size distribution. The mean particle diameter is 3.3 ± 1.0 nm.

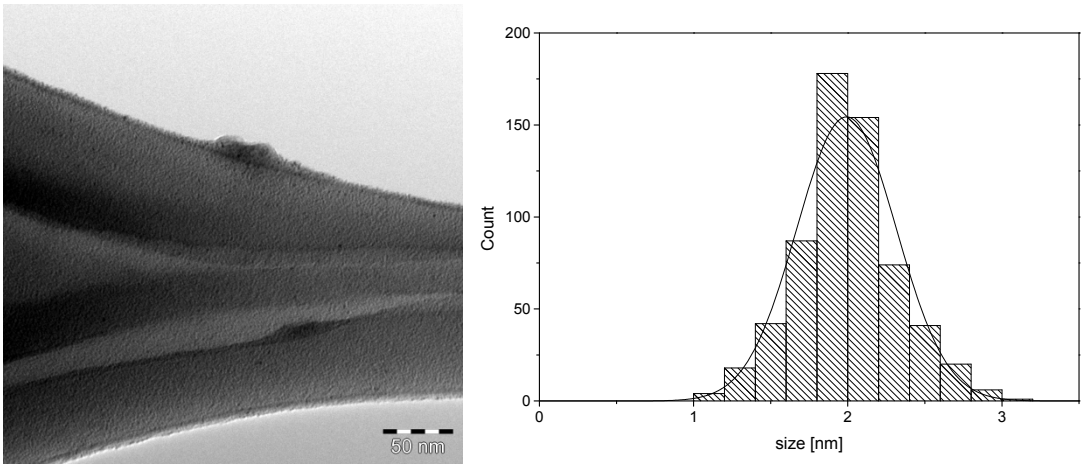


Figure S 4: TEM picture of Ru-NPs dispersed in $[C_{10}MMIM]NTf_2$ (38 µmol metal in 0.3 g IL, 90 °C, 18 h, after catalysis, hydrogenation of quinoline, 80 °C, 10 bar H_2, 5 h) and histogram of size distribution. The mean particle diameter is 2.0 ± 0.3 nm.

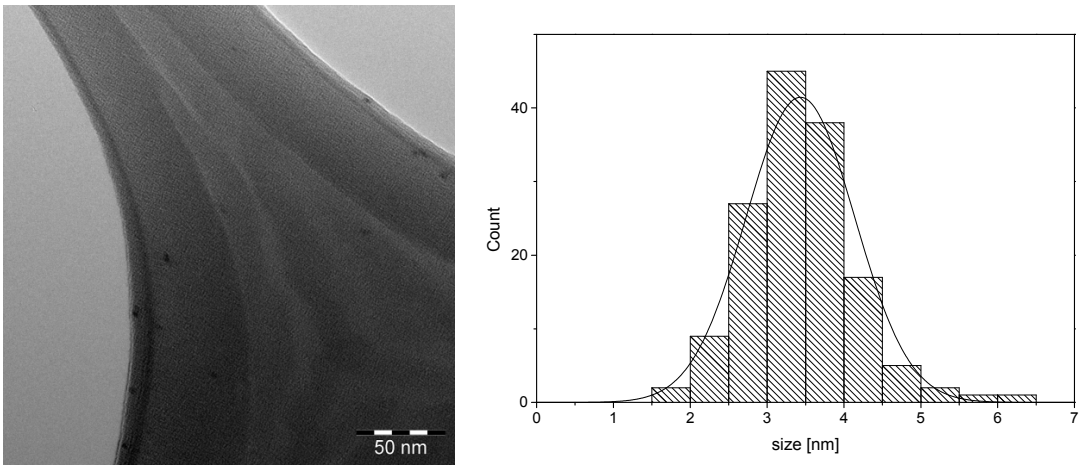


Figure S 5: TEM picture of Ru-NPs dispersed in $[C_2OHMIM]NTf_2$ (30 µmol metal in 0.3 ml IL, 90 °C, 18 h, after catalysis, hydrogenation of quinoline, 80 °C, 10 bar H_2, 19 h) and histogram of size distribution. The mean particle diameter is 3.4 ± 0.7 nm.

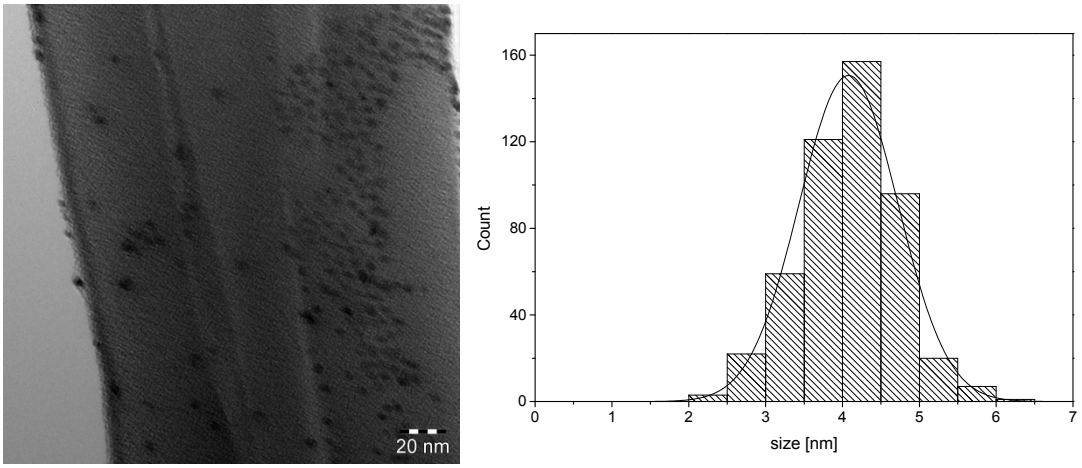


Figure S 6: TEM picture of Ru-NPs dispersed in $[C_1C_1(EG)MIM]NTf_2$ (30 µmol metal in 0.3 ml IL, 90 °C, 1 h, after six runs of recycling of the hydrogenation of quinoline, 80 °C, 10 bar H_2, 19 h) and histogram of size distribution. The mean particle diameter is 4.1 ± 0.6 nm.

Infrared Spectroscopy (IR)

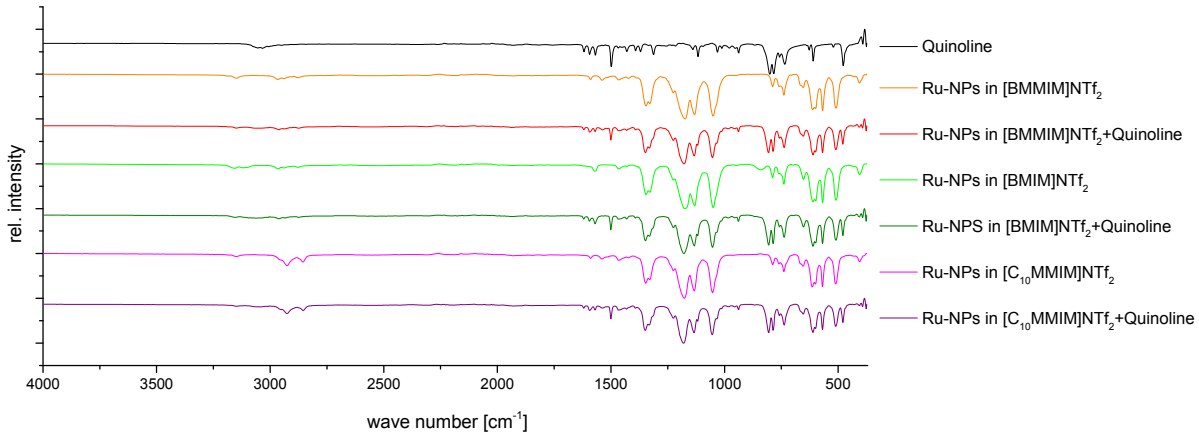


Figure S 7: IR spectra of quinoline, Ru-NPs embedded in different imidazolium based ILs and mixtures of both.

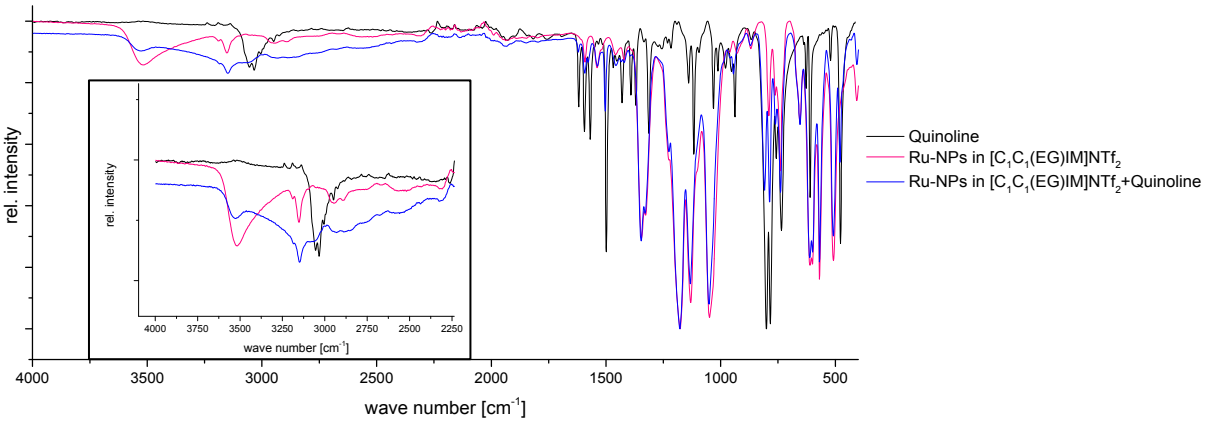


Figure S 8: IR spectra of quinoline, Ru-NPs embedded in $[C_1C_1(EG)IM]NTf_2$ and a mixture of both.

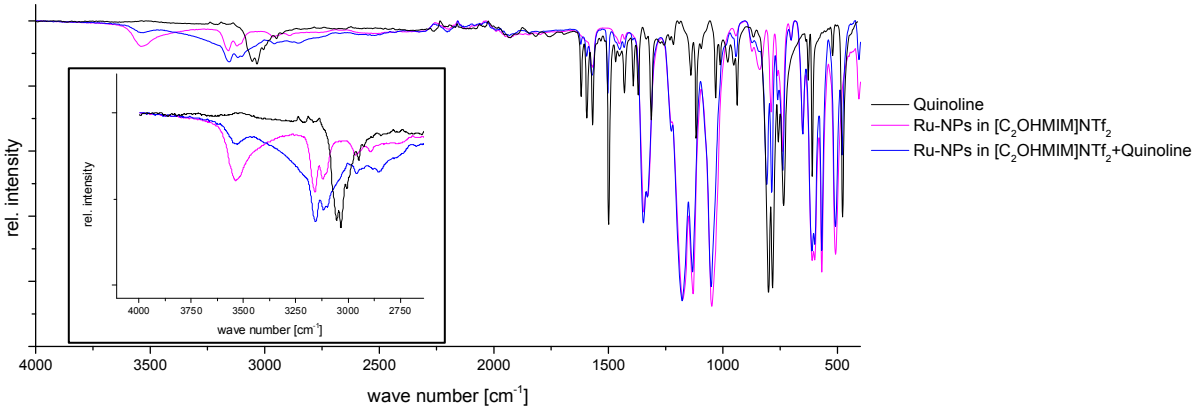


Figure S 9: IR spectra of quinoline, Ru-NPs embedded in $[C_2OHmIM]NTf_2$ and a mixture of both**.**

Hydrogenation of quinoline using different catalysts

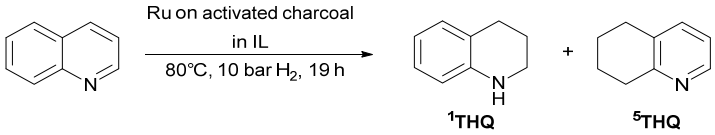
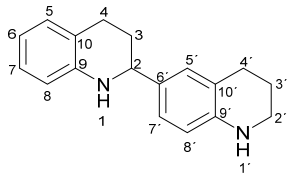


Table S 1: Hydrogenation of quinoline using Ru on activated charcoal in $[C_1C_1(EG)IM]NTf_2$.

Entry	Catalyst	Ionic Liquid	Conversion [%]	Yield ^{1}THQ [%]	Yield ^{5}THQ [%]
1[a]	Ruthenium on activated carbon	$[C_1C_1(EG)IM]NTf_2$	100	85	2

Reaction conditions: catalyst loading: 2 mol% Ru, 80 °C, 10 bar H_2, 19 h.
[a] In the NMR spectra as well as GC-MS measurement unidentified side products were detected, 11% yield of 1´,2,2´,3,3´,4,4´-octahydro-2,6´-biquinoline was identified.

For identification of the unknown side products of this reaction column chromatography was used to isolate the main side product. Isolation of different side products, identified by TLC and GC-MS, were not successful due to too low concentration in the reaction mixture.
Using 2D NMR techniques a dimer of ^{1}THQ was identified: 1,1´,2,2´,3,3´,4,4´-octahydro-2,6´-biquinoline:



R_f = 0.17 (cyclohexane/ethyl acetate 8:1). GC-MS: m/z = 264 [M^+]. ^{1}H-NMR (300 MHz, Acetone-d_6): δ(ppm)=6.92-6.82 (m, 4H, H-5, H-7, H-5´, H-7´), 6.62-6.55 (m, 1H, H-8), 6.51-6.41 (m, 2H, H-6, H-8´), 4.85 (NH, 2H), 4.21 (dd, *J* = 9.1, 2.5 Hz, 1H, H-2), 3.32-3.20 (m, 2H, H-2´), 2.88-2.61 (m, 4H, H-4, H-4´), 1.99-1.82 (m, 4H, H-3, H-3´). ^{13}C-APT (75 MHz, Acetone-d_6): δ(ppm)= 146.7 & 145.5 (C_q, C-9 & C-9´), 133.2 (C_q, C-6´), 129.7 (*C*H), 128.2 (*C*H), 127.3 (*C*H), 125.6 (*C*H), 121.1& 121.0 (C_q, C-10 & C-10´), 116.7 (C-6), 114.6 & 114.5 (C-8 & C-8´), 56.5 (C-2), 42.4 (C-2´), 32.0 (C-3), 28.0 (CH_2), 27.4 (CH_2), 23.0 (C-3´).

In literature a dehydrogenative polycondensation of ^{1}THQ or a mixture of quinoline/^{1}THQ has been reported for the synthesis of oligomeric structures of 2,3´- and 2,6´-biquinoline-units using Re- or Ru-sulphide catalyst systems. In the reaction mixture also partial hydrogenated dimer, trimers have been found.[7, 8] Similar surface reactions of the Ru on activated charcoal catalyst are assumed, although under hydrogenative conditions further hydrogenation of the *N*-heterocyclic moiety might form the partially hydrogenated derivative. In future work further studies have to be evaluated to clarify the reaction mechanism.

Hydrogenation of quinoline with protic additives

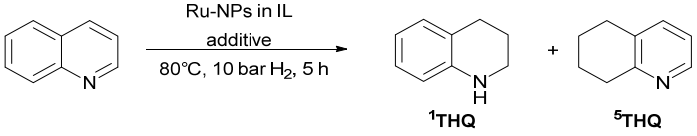
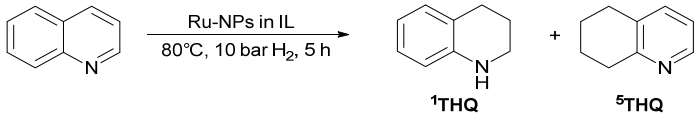


Table S 2: Hydrogenation of quinoline with Ru-NPs in $[BMMIM]NTf_2$ with different additives.

Entry	Ionic Liquid	Additive	Amount of additive[a] [eq]	Conversion [%]	Yield ^{1}THQ [%]	Yield ^{5}THQ [%]
1	$[BMMIM]NTf_2$	Ethanol	0.5	100	93	7
2	$[BMMIM]NTf_2$	*n*-Butanol	0.5	100	88	10
3	$[BMMIM]NTf_2$	Ethylene glycol	0.5	100	91	7
4	$[BMMIM]NTf_2$	Ethylene glycol	1	100	97	3

Reaction conditions: catalyst loading: 2 mol% Ru-NPs based on Ru-precursor, 80 °C, 10 bar H_2, 5 h.
[a]The amount of the additive is based on the used amount of OH-groups per Ru surface atoms with regard to the diol IL $[C_1C_1(EG)IM]NTf_2$.

Hydrogenation of quinoline and isoquinoline in non-polar solvents

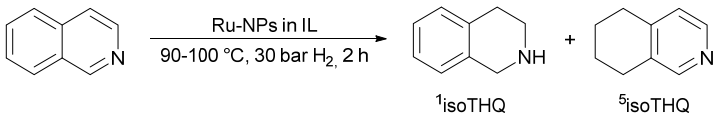


^{1}THQ ^{5}THQ

Table S 3: Hydrogenation of quinoline with Ru-NPs in different imidazolium based ILs and different solvents.

Entry	Ionic Liquid	Co-solvent	Conversion [%]	Yield ^{1}THQ [%]	Yield ^{5}THQ [%]	Selectivity ^{1}THQ [%]
1	$[BMMIM]NTf_2$	-	100	90	9	90
2	$[BMMIM]NTf_2$	*n*-Heptane	100	77	21	77
3	$[C_{10}MMIM]NTf_2$	-	100	93	5	93
4	$[C_{10}MMIM]NTf_2$	*n*-Heptane	100	92	5	92

Reaction conditions: catalyst loading: 2 mol% Ru-NPs based on Ru-precursor, 80 °C, 10 bar H_2, 5 h, all reactions were conducted with 1 ml co-solvent.



^{1}isoTHQ ^{5}isoTHQ

Table S 4: Hydrogenation reactions of isoquinoline with Ru-NPs in $[BMMIM]NTf_2$ and different solvents.

Entry	T [°C]	Co-solvent	Conversion [%]	Yield ^{1}isoTHQ [%]	Yield ^{5}isoTHQ [%]	Selectivity ^{1}isoTHQ [%]
1	100	-	25	15	10	59
2	90	*n*-Heptane	22	10	10	47
3	100	Mesitylene	41	23	17	55
4	100	Cyclooctane	21	13	81	60

Reaction conditions: catalyst loading: 2 mol% Ru-NPs based on Ru-precursor, 30 bar H_2, 2 h, all reactions were conducted with 1 ml co-solvent.

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