

COPPER-COIL REACTORS AS A PLATFORM FOR THE HYDROXYLATION OF ARYL BROMIDES

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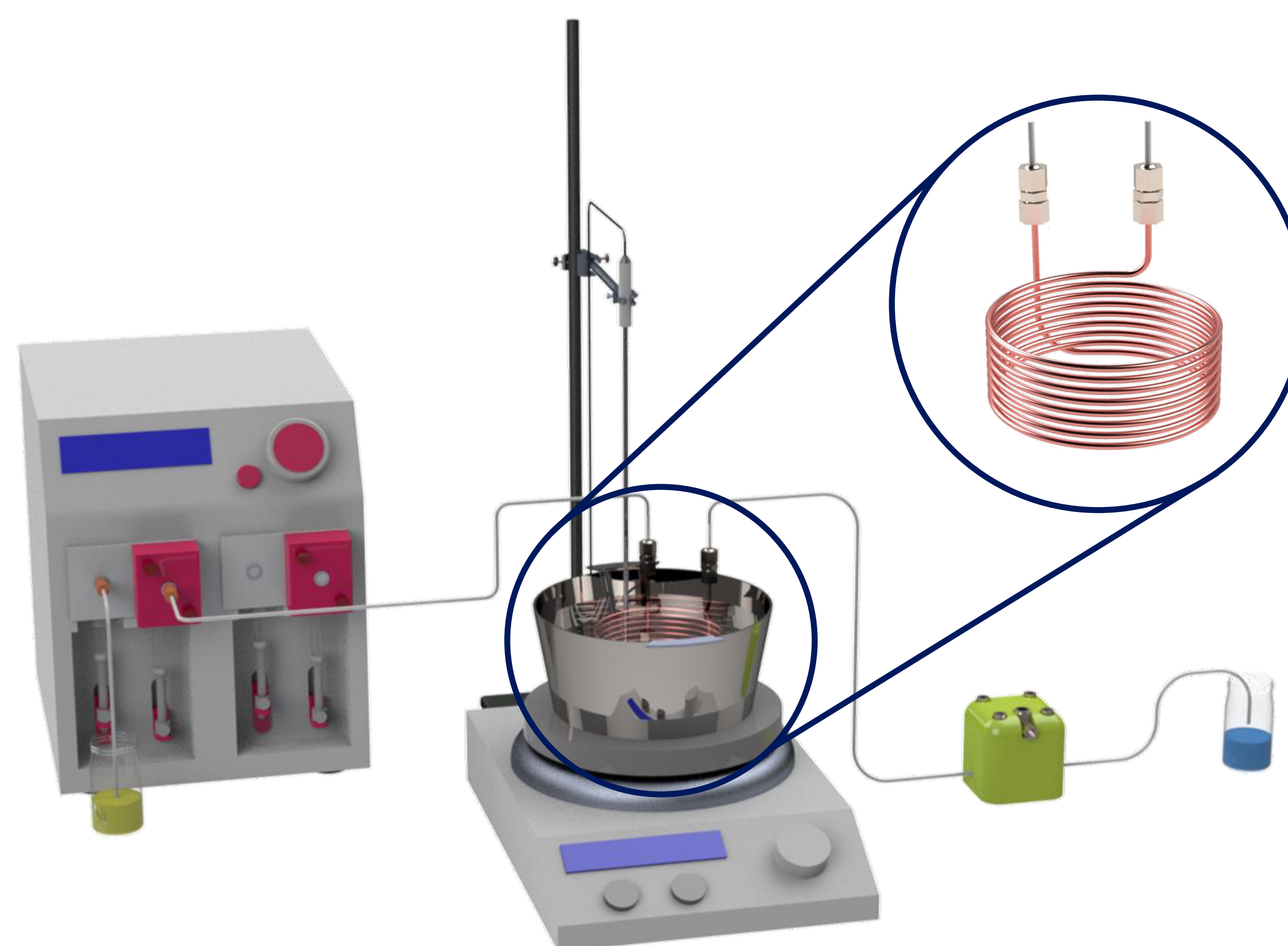
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Introduction

Processes based on **base metal catalysts**, such as iron, copper and nickel, are sought both from a **cost and a sustainability perspective**. Copper coils were unveiled as a simple alternative platform to carry out copper-catalyzed reactions under continuous flow around the year 2010. Its most attractive features were the use of simple setups, excellent heat transfer and ideal activation of the catalyst.

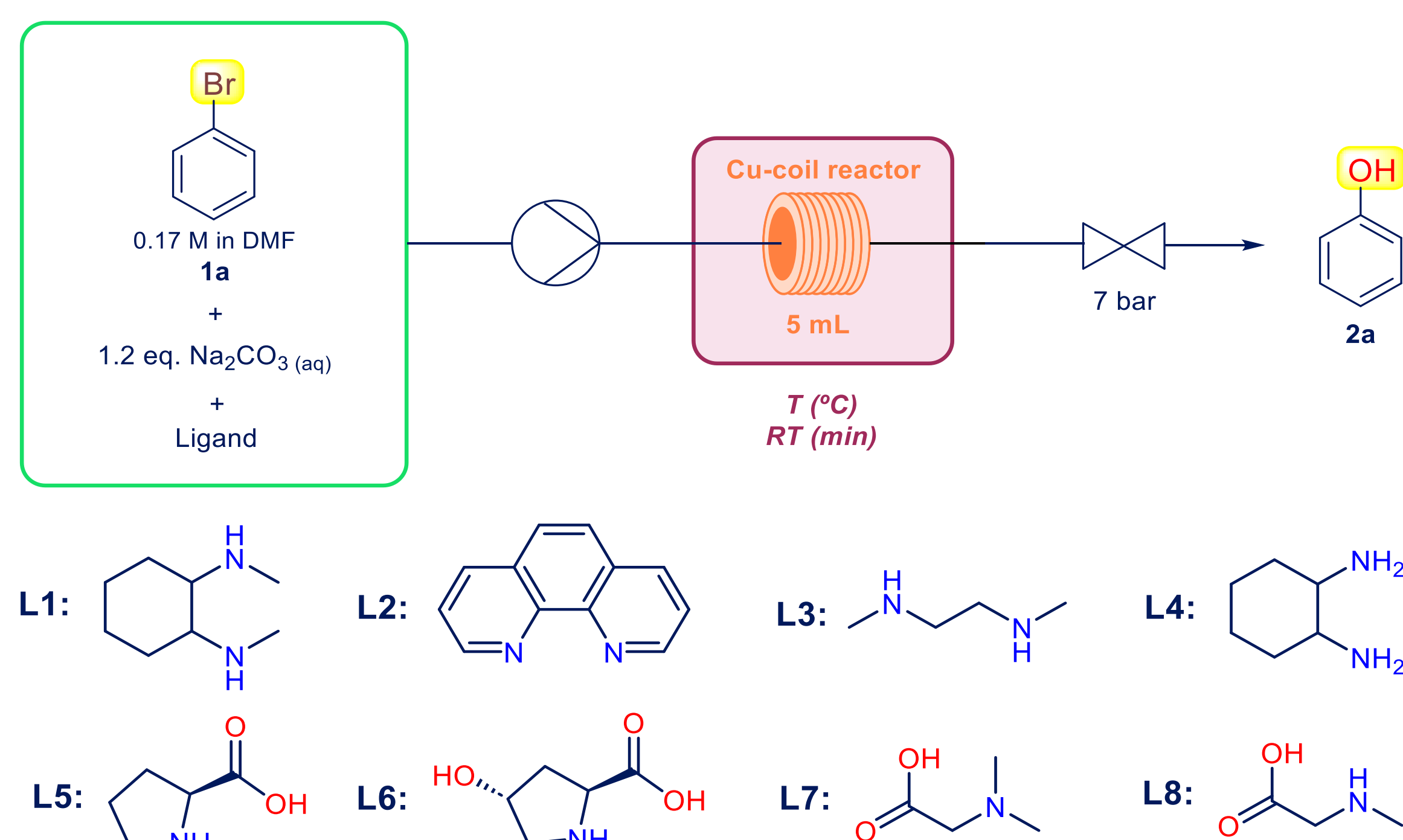
77 Ir Iridium 137.90 €/g*	45 Rh Rhodium 158.50 €/g*	48 Pd Palladium 31.60 €/g*	78 Pt Platinum 31.55 €/g*
27 Co Cobalt 0.0332 €/g*	28 Ni Nickel 0.0149 €/g*	29 Cu Copper 0.0101 €/g*	26 Fe Iron 0.0004 €/g*

The setup



Results

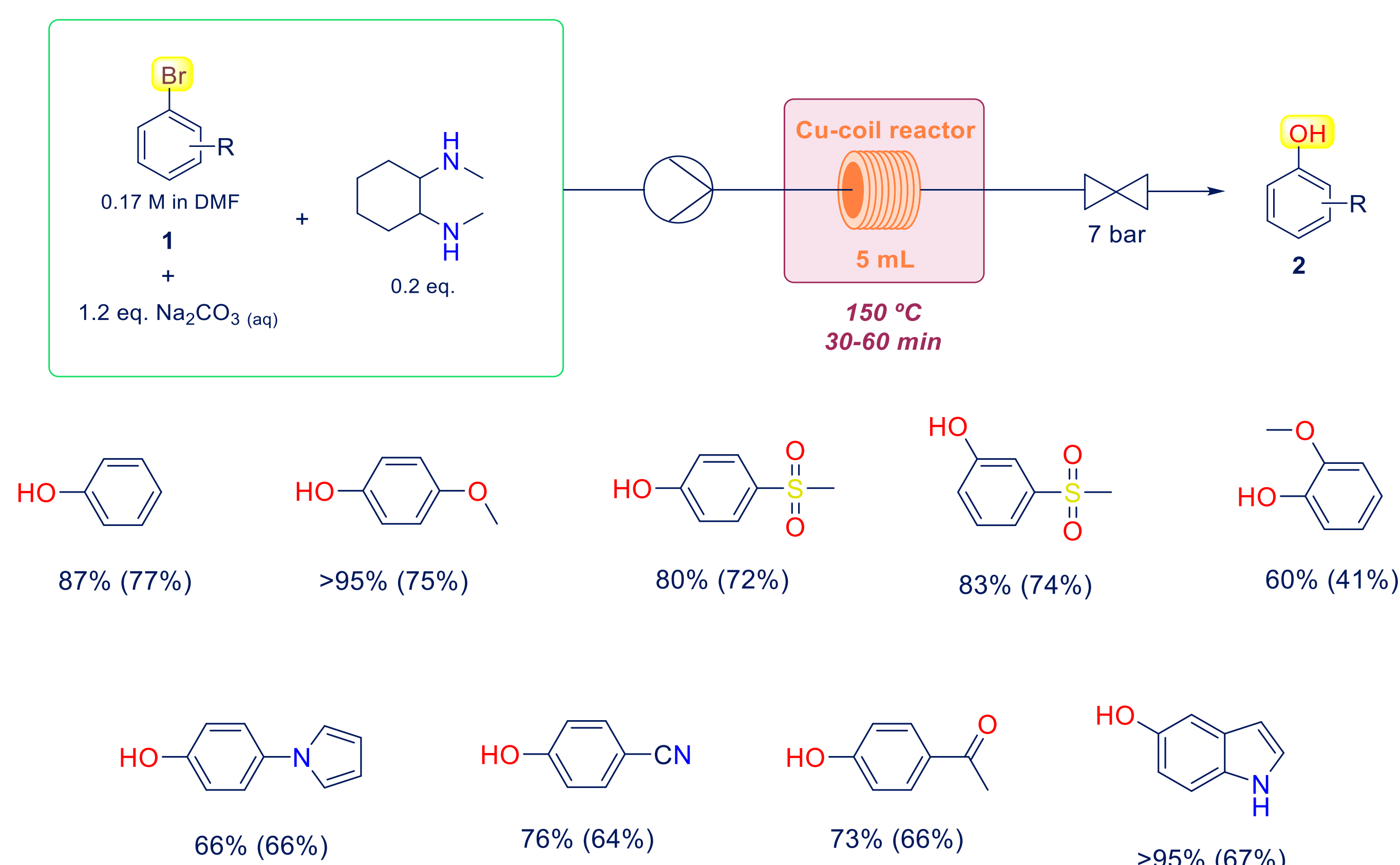
Optimization table



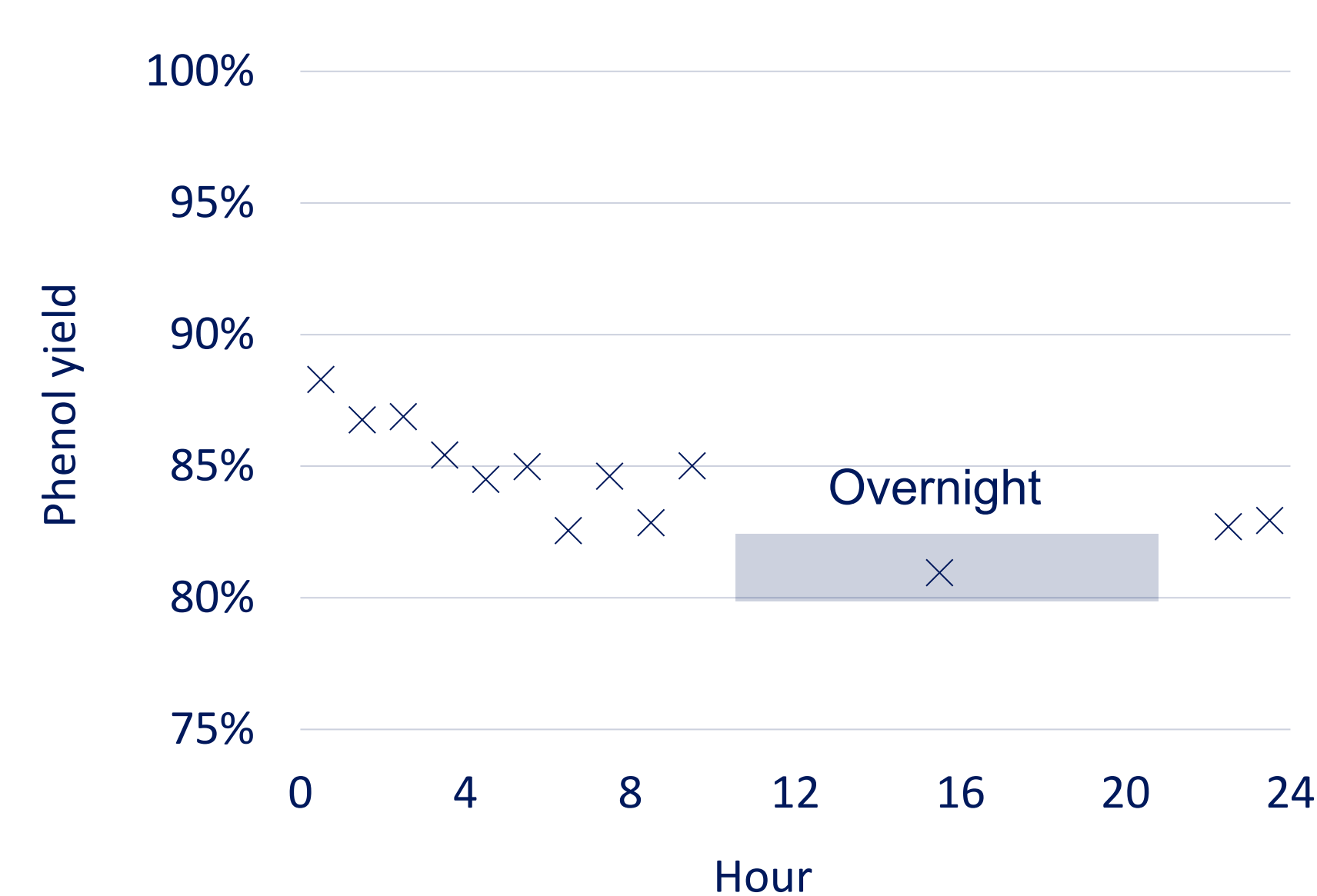
Entry	Ligand	Eq. Ligand	Temp (°C)	RT (min)	Conversion (%) ^[a]	Yield (%) ^[a]	Cu (ppm)
1	L1	0.2	150	30	92	88	94 (2%)
2	L4	0.2	150	30	85	82	150
3	L3	0.2	150	30	43	38	24
4	L5	0.2	150	30	28	14	35
5	L6	0.2	150	30	50	15	-
6	L7	0.2	150	30	30	4	-
7	L8	0.2	150	30	38	9	-
8	L2	0.2	150	30	0	0	511
9	-	-	150	30	0	0	26
10	L1	0.1	150	30	64	60	31
11	L1	0.5	150	30	94	87	224
12	L1	0.2	170	30	81	75	67
13	L1	0.2	150	60	98	91	92

Reaction conditions: aryl bromide (2 mmol), DMF (12 mL), Na₂CO₃ (aq) 0.17 M (14 mL). ^[a] Calculated with internal standard.

Scope



Gram-scale reaction



Conclusions

- Copper-coil reactors are feasible platforms for the hydroxylation of aryl bromides.
- Copper-coil reactors outperform other copper sources such as Cu(I) and Cu(II) salts in terms of minimum catalyst loading for the reaction and in terms of the reaction rate.
- The reaction has been tested with electron-donor, electron-acceptor aromatic rings and sterically hindered substrates.
- The model has been scaled to the gram scale to prove the robustness of the catalyst over 24 hours.

[1] *Org. Process Res. Dev.* 2024, 28, 4477–4484. DOI: 10.1021/acs.oprd.4c00402

[2] *Synlett* 2014, 25(10), 1409–1412. DOI: 10.1055/s-0033-1338634

[3] *Synthesis* 2019, 51, 251–257. DOI: 10.1055/s-0037-1610398

[4] *Adv. Synth. Catal.* 2009, 351, 849–854. DOI: 10.1002/adsc.200800758

* <https://pmm.umicore.com> (18/03/2025) and <https://www.dailymetalprice.com> (18/03/2025)

Research funded by:

- Ministerio de Universidades: FPU 21/05233