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The use of copper and vanadium mineral ores in catalyzed mechanochemical carbon–carbon bond formations

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Abstract: Under mechanochemical conditions in ball mills, copper- and vanadium-containing minerals initiate atom transfer radical cyclizations and oxidative couplings, respectively. Only catalytic quantities of the minerals are required, and the reactions proceed either under neat conditions or in the presence of a minimal amount of solvent.

In nature, minerals play a fundamental role as mediators and catalysts during the complex set of chemical reactions leading to the formation of hydrocarbons.^{1,2} This process generates structural complexity in light and heavier hydrocarbons, primarily through the formation and cleavage of carbon–carbon and carbon–hydrogen bonds. The ability of minerals to favor chemical reactions has been linked to their unique morphology and elemental composition, which consequently has inspired the design of materials resembling such structures. Recently, Fülöp and co-workers synthesized a Ag(I)Bi(III)-containing hybrid material mirroring naturally occurring layered double minerals.³ The silver-containing hybrid exhibited outstanding catalytic properties in DMSO towards the synthesis of organic nitriles from terminal alkynes and trimethylsilyl azide. Complementarily, the direct use of minerals for catalysis has been reported as well. For instance, the earth-abundant mineral pyrite (FeS₂) proved to be catalytically active for the selective hydrogenation of a broad class of functionalized nitroarenes to substituted anilines in a reaction medium composed of H₂O-THF,⁴ thus exemplifying the potential of minerals in catalysis research.⁵

As in the geochemical formation of hydrocarbons, organic chemists use metals to facilitate the formation of new C–C and C–H bonds. However, unlike in nature, the use of minerals as catalysts

in organic chemistry laboratories is far from being the mainstream choice. Practical hurdles such as the scarce solubility of minerals in commonly used reaction media may be responsible for the slow adoption of mineral-catalyzed organic transformations. Seeing the potential and the opportunities of recently implemented mechanochemical techniques to synthesize minerals^{6–9} and to facilitate the development of a myriad of reactions in organic chemistry,^{10–15} we started wondering about developing mechanochemical mineral-catalyzed transformations.

If achievable, such merging could clearly elevate the sustainability of mechanochemical reactions¹⁶ by harnessing the catalytic activity of bulk, readily available mineral ores, avoiding the need for the processing of the raw minerals into expensive metal catalysts.^{17–18} In a proof-of-concept study, we have here focused on two mechanochemical carbon–carbon bond formation processes, namely, a copper-catalyzed atom transfer radical cyclization reaction and a vanadium-catalyzed oxidative coupling (Figure 1). As natural sources for the metals, a copper sulphide mineral named covellite and a vanadium-containing ore known as vanadinite were chosen for the mechanochemical reactions.

Figure 1. Use of raw mineral ores in copper-catalyzed atom transfer radical cyclization (ATRC) reactions and vanadium-catalyzed oxidative couplings under mechanochemical conditions.

As initial system, a copper-catalyzed atom transfer radical cyclization (ATRC) was selected. Commonly, this reaction is catalyzed by transition metals, being, in most cases, copper(I) salts and, particularly, copper(I) complexes bearing organic ligands.¹⁹ Here, we chose the mineral covellite, which, despite its elemental formula of CuS suggesting the presence of copper(II) ions, predominantly consists of copper(I) species represented as $(\text{Cu}^+)_3(\text{S}^{2-})(\text{S}_2^-)$ or $(\text{Cu}^+)_4(\text{Cu}^{2+})_2(\text{S}_2)^{2-}_2(\text{S}^{2-})_2$.^{20–22}

Table 1. Optimization of the reaction conditions: use of covellite in mechanochemical ATRC of **1a**.^a

Entry	Ligand (mol%)	Reaction time (min)	2a:1a ^b
1	none	90	n.r.
2	I (20)	90	13:87
3	II (20)	90	80:20
4	III (20)	90	>99:1
5	III (15)	90	>99:1
6	III (10)	90	>99:1
7	III (5)	90	>99:1
8	III (2.5)	90	91:9
9	III (5)	60	>99:1
10	III (5)	30	>99:1
11	III (5)	5	55:45
12 ^c	III (5)	90	n.r.

^a Reaction conditions: **1a** (100.0 mg, 0.34 mmol), covellite (1.9 mg, 0.02 mmol, 5 mol%) and ligand **I-III** were milled in a mixer mill at 25 Hz under argon using a 10 mL ZrO₂-Y milling jar with one 10 mm Ø milling ball of the same material. For calculations covellite was considered as pure CuS. For an elemental analysis of the mineral samples, see ESI. ^b Determined by ¹H NMR spectroscopy using signal integrals of **2a** and **1a**. ^c Under air.

The first evaluation of the catalytic activity of covellite in a mechanochemical ATRC reaction involved neat grinding of amide **1a** with the mineral under argon in a mixer mill for 90 min (Table 1, entry 1). To our disappointment, these conditions proved unsuitable, and none of the expected 5-*exo-trig* cyclization product **2a** was observed. The outcome changed, when the experiment was performed in the presence of commonly used ligands **I-III** (20 mol%),¹⁹ which resulted in the formation of significant amounts of lactam **2a** identified by ¹H NMR spectroscopy of the crude mixture (Table 1, entries 2-4). In particular, tris[2-(dimethylamino)ethyl]amine (Me₆TREN, **III**) proved effective leading to full conversion of **1a** and exclusive formation of pyrrolidone **2a**. Reducing the amount of ligand **III** from 20 mol% to 5 mol% had no effect on the final ratio of **2a:1a**, which remained >99:1 (Table 1, entries 4-7). Applying only 2.5 mol% of **III** lowered the product amount and the **2a:1a** ratio changed to 91:9 (Table 1, entry 8). Shortening the milling time from 90 min to 30 min was possible without affecting the product/educt ratio (>99:1), but milling for only 5 min changed the **2a:1a** ratio to 55:45 (Table 1, entries 9-11). Noteworthy, no product

was observed when the argon atmosphere was changed to air (Table 1, entry 12). Performing the ATRC reaction under the optimized reaction conditions (Table 1, entry 10) allowed isolating product **2a** in 94% yield after column chromatography (Scheme 1). Carrying out the ATRC reaction under the optimized reaction conditions using 1.0 mmol of **1a** (ca. 3-fold scaled up) led to lactam **2a** in 91% yield. The generality of the concept with respect to the mineral was shown by applying a combination of Me₆TREN and bornite (Cu₅FeS₄)²³ instead of covellite, which provided lactam **2a** from amide **1a** in 97% yield.

Scheme 1. Scope of the ATRC reaction. Reaction conditions: **1a-f** (0.3 mmol or 100.0 mg), covellite (0.02 mmol, 5 mol%) and ligand **III** (Me₆TREN, 0.02 mmol, 5 mol%) were milled under argon in a 10 mL ZrO₂-Y milling jar with one 10 mm Ø milling ball of the same material for 30 min at 25 Hz. For calculations covellite was considered as pure CuS. For an elemental analysis of the mineral samples, see ESI. ^a Reaction conducted on 1.0 mmol scale of **1a**. ^b Bornite mineral was used instead of covellite. ^c 90 min of milling.

To further test the applicability of the mechanochemical ATRC reaction, the study was extended to amides **1b-f**, which were subjected to millings with covellite and Me₆TREN (Scheme 1). As *N*-benzyl derivative **1a**, also *N*-methyl- and *N*-tosyl-substituted amides **1b** and **1c**, respectively, underwent the cyclization reaction, although to a lesser extent compared to their *N*-benzyl analogue (Scheme 1). Probably, as shown in previous studies,^{24,25} the steric and electronic effects of the *N*-substituent affected the population of the required anti-amide conformer, thereby lowering the overall reaction efficiency. As studied for the conversion of **1c**, extending the reaction time had a positive effect on the yield of **2c**, which increased from 18% to 30% when the reaction was performed for 90 min instead of the standard 30 min (Scheme 1). Next, three other *N*-benzyl amides (**1d-f**) were tested. The results were mixed. While **1d** exhibited a similar reactivity as **1a** providing **2d** in 90% yield, **1e** reacted sluggish, leading to lactam **2e** in only 12% yield under standard conditions. As observed before, extending the reaction time proved beneficial, and after 90 min of milling **2e** was isolated in 27% yield. The results for the latter substrate were attributed to the pronounced stability of the presumed allyl radical being formed as intermediate after the initial cyclization step of **1e** and its reduced rate in bromide transfer closing the catalytic cycle (see ESI).²⁶ Finally, applying amide **1f** in the mechanochemical ATRC reaction afforded bromine-free isomeric lactams **2f** and **2f'** in 59% overall yield. Most likely, both compounds resulted from the same cyclization product having a 2-bromo-2-propyl substituent. Subsequent HBr elimination gave olefinic products **2f** and **2f'** (in a ratio of 61:39).

With the goal to validate the concept of using minerals in mechanosynthesis by a second example, the vanadium-promoted oxidative coupling of β -naphthol (**3a**) was set into the focus.^{27,28} The relatively high abundance of vanadium on earth compared to other transition metals has encouraged many studies on vanadium catalysis under homogeneous²⁷ and heterogeneous²⁹ reaction conditions. However, to the best of our knowledge, the direct use of a vanadium-containing mineral as catalyst for an organic reaction has remained unknown. For this part of the proof-of-concept study, we chose vanadinite [Pb₅(VO₄)₃Cl] being one of the most abundant vanadium-based minerals and therefore a primary source of this metal at the industrial level.³⁰ By using vanadinite in combination with dioxygen under mechanical milling we envisaged promoting the oxidative coupling of **3a** to 1,1'-bi-2-naphthol (BINOL, **4a**) (Table 2), while expanding the applicability of ball milling techniques to mechanochemical reactions involving gaseous reactants.^{31–35}

As in the case of the covellite-catalyzed ATRC reaction, the presence of an organic ligand proved critical here too. While in both the absence of vanadinite and the presence of the mineral alone the conversion of **3a** to **4a** was $\leq 1\%$ (Table 2, entries 1 and 2), the product formation was triggered by the addition of an organic acid (entries 3-7). Testing a series of acidic additives showed that (at 1 atm of dioxygen pressure) multicarboxylic acids such as tartaric acid and citric acid were superior over, for example, simple amino acids (see ESI for details). Finally, the presence of 2,6-dipicolinic acid (DPA)³⁶ led to be best result giving a 24:76 mixture of **4a** and **3a** after 2 h of milling at 600

Table 2. Optimization of the reaction conditions: use of vanadinite in mechanochemical oxidative coupling of **3a**.^a

Entry	O ₂ (atm)	Additive ^b	4a:3a ^c
1 ^d	1.0	None	0:100
2	1.0	None	1:99
3	1.0	Glutamic acid	3:97
4	1.0	Aspartic acid	8:92
5	1.0	Tartaric acid	7:93
6	1.0	Citric acid	4:96
7	1.0	DPA	24:76
8	4.0	DPA	33:67
9	4.0	DPA, LAG (MeOH, $\eta = 0.5$)	87:13
10^e	4.0	DPA, LAG (MeOH, $\eta = 0.5$)	89:11
11 ^f	4.0	DPA, LAG (MeOH, $\eta = 0.5$)	68:32

^a Reaction conditions: **3a** (100.0 mg, 0.69 mmol), vanadinite (1.0 g, equivalent to 1.70 mmol of vanadium) and additive (300.0 mg) were milled in a planetary ball mill under dioxygen in a 20 mL ZrO₂-Mg milling jar with five 10 mm Ø balls of the same material for 2 h at 600 rpm (1 h × 2; 20 min pause after each milling cycle). For an elemental analysis of the mineral sample, see ESI. ^b η is the volume of solvent (in μ L) divided by the total weight of the solid reactants (in mg). ^c Determined by ¹H NMR spectroscopy using signal integrals of **4a** and **3a**. ^d Without vanadinite. ^e Use of 500.0 mg of vanadinite (0.85 mmol of vanadium) and 150.0 mg of DPA (0.90 mmol). ^f Use of 250.0 mg of vanadinite (0.42 mmol of vanadium) and 75 mg of DPA (0.45 mmol).

rpm (Table 2, entry 7). Increasing the dioxygen pressure inside the milling vessel from 1 atm to 4 atm raised the product amount (**4a:3a** = 33:67; Table 2, entry 8). A further improvement was noted upon liquid-assisted grinding (LAG)³⁷ with methanol (Table 2, entry 9). The benefits of the LAG approach included reducing the vanadinite loading below stoichiometric amounts of vanadium, thereby achieving an oxidative coupling of β -naphthol (**3a**) in the ball mill under vanadinite catalysis (Table 2, entry 11). Intrigued by the remarkable effect of methanol on the mechanochemical reaction, LAG experiments with other liquid additives were carried out (Table 3). The screening revealed that the entire system was highly sensitive to even small changes. For example, adding MeOH-*d*₄ instead of MeOH changed the yield of **4a** (as determined by ¹H NMR spectroscopy with an internal standard) from 64% to 36% (Table 3, entries 2 and 3). Negative effects on the yield of **4a** were also noted when other common solvents were added (Table 3, entries 4-11). Finally, the amounts of methanol and DPA were fine-tuned to maximize the effects (Table 3, entries 12-15).

Table 3. LAG effects upon addition of liquids to the vanadinite-catalyzed oxidative coupling of **3a**.^a

Entry	LAG additive (η)	Yield of 4a (%) ^b
1	---	39%
2	MeOH (0.5)	64%
3	MeOH- <i>d</i> ₄ (0.5)	36%
4	EtOH (0.5)	45%
5	CCl ₄ (0.5)	42%
6	<i>i</i> -PrOH (0.5)	12%
7	HFIP (0.5)	10%
8	H ₂ O (0.5)	12%
9	DMSO (0.5)	7%
10	DMF (0.5)	7%
11	MeCN (0.5)	11%
12 ^c	MeOH (0.5)	63%
13 ^c	MeOH (0.2)	50%
14 ^c	MeOH (0.1)	33%
15 ^c	MeOH (0.05)	63%

^a Reaction conditions: **3a** (100.0 mg; 0.69 mmol), vanadinite (250.0 mg; 0.42 mmol of vanadium), DPA (75.0 mg; 0.45 mmol) and the LAG solvent were milled under O₂ (4.0 atm) in a planetary ball mill using a 20 mL ZrO₂-Mg milling jar with five 10 mm Ø milling balls of the same material for 2 h at 600 rpm (1 h × 2; 20 min pause after each milling cycle). For an elemental analysis of the mineral sample, see ESI. ^b Determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. ^c Use of 0.42 mmol of DPA.

After having identified the best additive combination (DPA and MeOH), the vanadinite-catalyzed oxidative coupling of **3a** was carried out for 8 h of milling, which allowed to isolate of product **4a** in 86% yield (Scheme 2). Other naphthol derivatives showed a similar reactivity. For instance, the use of 7-methoxy 2-naphthol (**3b**) gave substituted BINOL **4b** in 96%. Bromo-substituted naphthols **3c** and **3d** proved less reactive affording the corresponding BINOLs **4c** and **4d** in yield of 53% and 36%, respectively (Scheme 2). Employing **3e** and **3f** with 6-aryl substituents led to yields of 72% for **4e** and 30% for **4f**. Overall, the results indicated that both electronic and steric

effects of the substrates have an impact of the coupling efficiency. In addition, solid-state properties (such as crystallinity) of both reactants and the products play a role.³⁸

Scheme 2. Scope of the mechanochemical vanadium-catalyzed oxidative coupling. Reaction conditions: **3a-f** (0.70 mmol), vanadinite (252.5 mg; 0.43 mmol), DPA (71.5 mg, 0.43 mmol) and methanol ($\eta = 0.05$) were milled under dioxygen in a planetary ball mill using a 20 mL ZrO₂-Mg milling jar with five 10 mm Ø milling balls of the same material for 8 h at 600 rpm (1 h $\times$ 8; 20 min pause after each milling cycle). For an elemental analysis of the mineral sample, see ESI.

In summary, we have demonstrated the potential of using raw mineral ores as catalysts in copper-catalyzed atom transfer radical cyclizations and vanadium-catalyzed oxidative couplings. Both carbon–carbon bond forming processes occurred in mixer and planetary ball mills, which enabled the reactions to proceed mechanochemically. Moreover, the implementation of ball milling techniques permitted the poorly soluble copper and vanadium minerals (i.e., covellite, bornite and vanadinite) to promote the reactions under neat and LAG conditions. Such approach significantly reduced mineral processing operations typically required to access commercial metal salts, by directly using mineral ores as catalysts in ball mills. Key to harness the catalytic activity of the metals within the minerals was the use of readily available organic ligands such as Me₆TREN and DPA. Thus, the approach avoided the need for highly engineered ligands or additive. Currently, this concept is further investigated in our laboratories applying it in other mechanochemical reactions, catalyzed by mineral ores.

Supporting Information. The following files are available free of charge. Experimental synthetic procedures and characterization (^1H and ^{13}C NMR, IR, MS (EI,CI)) of compounds **1a-f**, **2a-f**, **3e-f** and **4a-f**; HRMS data for compounds **1b-f** and **2b-f**; extended version of Table 2; considerations on the mechanism for the formation of **2e**.

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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Supporting Information

The use of copper and vanadium mineral ores in catalyzed mechanochemical carbon–carbon bond formations

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1. General information

Building blocks were commercially available and were used as received unless otherwise stated. Raw vanadinite samples were provided by the Mineral Processing Unit (AMR) RWTH Aachen University, and samples of covellite and bornite were purchased at a local mineral store. The elemental analysis of the minerals used was carried by the company ALS geochemistry (at the Loughrea, Co. Galway facility) and was performed by acid digestion followed by ICP-AES analysis; resulting data can be found in the Appendix 1 of the present document. Thin-layer chromatography (TLC) was performed using TLC plates (silica gel 60 on aluminum plates with fluorescence indicator F254) from MERCK. Qualitative analysis of the TLC plates was carried out using UV light ($\lambda = 254$ nm and/or $\lambda = 366$ nm) and/or by immersion in an aqueous solution of potassium permanganate (KMnO_4) and heating of the stained plates with a heat-gun at 300 °C until dryness. Dipping the TLC plates in a ninhydrin stain and heating them with a heat-gun until dryness or an iodine chamber could be used as well for visualisation of the samples. Flash column chromatography was conducted with silica gel 60 (40–63 μm) from MACHEREY-NAGEL and solvents for column chromatography were distilled prior to use. Nuclear magnetic resonance (NMR) spectra were recorded either on a Varian Mercury 300, Varian VNMRS 400, Varian VNMRS 600, Bruker Avance Neo 400 or Bruker Avance Neo 600 at 25 °C, if not otherwise stated and were processed and analysed with the program MestReNova.^[1] The chemical shifts δ are given in parts per million (ppm) relative to the residual solvent peak of the non-deuterated solvent (CHCl_3 : ^1H NMR: $\delta = 7.26$ ppm, $^{13}\text{C}\{^1\text{H}\}$ NMR: CDCl_3 : $\delta = 77.16$ ppm; Toluene- d_8 : ^1H NMR: $\delta = 2.08, 6.97, 7.01, 7.09$ ppm, $^{13}\text{C}\{^1\text{H}\}$ NMR: Toluene- d_8 : $\delta = 20.43, 125.13, 127.96, 128.87, 137.48$ ppm).^[2] Carbon spectra were measured broad band decoupled. The multiplicity was reported with the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal and combinations thereof. Coupling constants (J) were given in Hertz (Hz). Infrared spectra (IR) were recorded as transmission spectra on a PerkinElmer Spectrum 100 spectrometer using the attenuated total reflectance (ATR) technique. The wavenumbers ν of the absorption peaks are listed in cm^{-1} . Mass spectra were recorded on a Finnigan SSQ 7000 spectrometer [electron ionization (EI), 70 eV; chemical ionization (CI), methane, 100 eV] and the resulting signals are given according to their m/z values and their relative intensity is reported in parentheses. For high resolution mass spectra (HRMS) a Thermo Fisher Scientific LTQ Orbitrap XL spectrometer [electrospray ionization (ESI) in positive ion mode] was used. For powder X-ray diffraction (PXRD) analysis a Bruker D2 PHASER X-ray diffractometer with Copper- K_α radiation ($\lambda = 1.54056$ Å) was used and the PXRD pattern were recorded in a 2θ range of 15° to 70°. Data files for calculated PXRD patterns were downloaded from The Cambridge Crystallographic Data Centre (CCDC) database. CCDC codes for Covellite (1626445), Bornite (1591922), Vanadinite (1707631).^[3]

Mechanochemical reactions were carried out in a RETSCH MM400 mixer mill or in a FRITSCH planetary micro mill model “Pulverisette 7 premium line”. If not stated otherwise milling vessels and balls were always of the same material. Specifically, the zirconium oxide of the vessels and balls used for reactions conducted in the mixer mill RETSCH MM400 is yttrium oxide stabilized ($\text{ZrO}_2\text{-Y}$) while the one for the planetary mill FRITSCH “Pulverisette 7 premium line” is magnesium oxide stabilized ($\text{ZrO}_2\text{-Mg}$). In the cases mechanochemical reactions had to be conducted under an inert atmosphere, the jars were closed inside a MBraun Labmaster 130 glove box operating under an argon atmosphere.

2. Mineral processing

Covellite and bornite lumps were hammered into pieces of ca. 3 to 8 mm. Then, the samples were milled for 5 min at a milling amplitude of 1.5 mm in a Fritsch Pulverisette 0 Vibratory Micro Mill equipped with agate mortar and one 70 mm Ø ball of the same material. The mortar and the ball were washed with 1M HCl, deionized water and later oven dried for 1 h prior each use in order to avoid samples contamination from previous grindings. The obtained powder was transferred into a glass vial and used for elemental analysis and catalytic tests.

The vanadinite samples have been directly use for elemental analysis or catalytic tests as provided by the Mineral Processing Unit (AMR) RWTH Aachen University.

3. Synthesis of substrates 1a-f

N-Allyl-*N*-benzylamine (**S1a**)

A round bottom flask equipped with a magnetic stirring bar was charged with benzaldehyde (5.3076 g, 50.02 mmol, 1.00 equiv which was filtered over a short plug of Na₂CO₃ prior to use to remove benzoic acid. It was dissolved in 100 mL DCM and allylamine (3.76 mL, $\rho = 0.76 \text{ g}\cdot\text{mL}^{-1}$, 50.05 mmol, 1.00 equiv) and MgSO₄ (6.0210 g, 50.02 mmol, 1.00 equiv) were added. The reaction mixture was stirred at room temperature for 27 h. After that time, reaction mixture was filtered over Celite and the solvent was evaporated to yield the crude imine as a yellow oil, which was dissolved in 200 mL of MeOH and was cooled in an ice bath. Then, NaBH₄ (2.8388 g, 75.04 mmol, 1.50 equiv) was added in small portions to the ice-cooled reaction mixture. After the addition of NaBH₄ was completed the reaction mixture was allowed to warm up to room temperature overnight. The next day the solvent was evaporated, and the residue was dissolved and partitioned between 150 mL of H₂O and 75 mL EtOAc. After phase separation, the aqueous phase was extracted three times with EtOAc (75 mL), the organic phases were combined, dried over Na₂SO₄ and the solvent was evaporated. The product **S1a** was purified by column chromatography (SiO₂/acetone) to yield a slightly yellow oil (6.2966 g, 42.77 mmol, 86%).

$R_f = 0.63$ (acetone), UV-active (254 nm), stains with I₂.

¹H NMR (400 MHz, CDCl₃): δ = 7.37–7.21 (m, 5H, Ar–H), 5.94 (ddt, $^3J_{\text{H,H}} = 17.3, 10.3, 6.0 \text{ Hz}$, 1H, RCH=CH₂), 5.20 (dq, $^3J_{\text{H,H}} = 17.1, 1.6 \text{ Hz}$, 1H, RCH=CH_AH_B), 5.12 (dq, $^3J_{\text{H,H}} = 10.3, 1.4 \text{ Hz}$, 1H, RCH=CH_AH_B), 3.80 (s, 2H, PhCH₂NHR), 3.28 (dt, $^3J_{\text{H,H}} = 6.0, 1.5 \text{ Hz}$, 2H, RNHCH₂CH=CH₂), 1.45 (br s, 1H, NH) ppm.

¹³C{¹H} NMR (101 MHz, CDCl₃): δ = 140.4, 136.9, 128.5, 128.3, 127.1, 116.1, 53.4, 51.9 ppm.

IR (ATR): ν = 3855, 3653, 3315, 3071, 3027, 2913, 2811, 2331, 2088, 1993, 1870, 1738, 1641, 1601, 1492, 1451, 1357, 1243, 1201, 1106, 1028, 992, 916, 820, 734, 698 cm⁻¹.

MS (100 eV, CI): m/z (%): 148 (28) [$M+H$]⁺.

MS (70 eV, EI): m/z (%): 147 (25) [M]⁺, 146 (72) [$M-H$]⁺, 120 (11), 91 (100) [C_7H_7]⁺.

The NMR data closely match the ones previously reported in the literature.^[4]

***N*-Allyl-*N*-benzyl-2-bromo-2-methylpropanamide (1a)**

Secondary amine **S1a** (6.0000 g, 40.76 mmol, 1.00 equiv) was dissolved in 250 mL of distilled Et₂O and cooled in an ice bath before NEt₃ (11.3 mL, $\rho = 0.728 \text{ g}\cdot\text{mL}^{-1}$, 81.30 mmol, 2.00 equiv) was added. Then, to the cooled solution of **S1a**, α -bromoisobutyryl bromide (5.0 mL, $\rho = 1.86 \text{ g}\cdot\text{mL}^{-1}$, 40.45 mmol, 1.00 equiv) was added dropwise and a white precipitate formed immediately. The resulting reaction mixture was allowed to warm up to room temperature overnight. The next day the reaction was stopped by adding 50 mL of an aqueous saturated NH₄Cl solution and the biphasic reaction mixture was vigorously stirred for 5 min. It was concentrated under reduced pressure and the residue was partitioned between 100 mL distilled Et₂O and 100 mL of an aqueous saturated NaHCO₃ solution. After phase separation, the aqueous phase was extracted three times with distilled Et₂O (100 mL), the organic phases were combined and dried over Na₂SO₄. The solvent was evaporated to yield the title compound **1a** as a slightly yellow oil (11.2942 g, 38.13 mmol, 94%) after column chromatography (SiO₂/*n*-pentane:EtOAc 4:1 v/v).

$R_f = 0.84$ (*n*-pentane:EtOAc 1:1 v/v), UV-active, stains with KMnO₄.

¹H NMR (400 MHz, Toluene-*d*₈, 95 °C): δ = 7.19–6.93 (m, 5H, Ar-*H*), 5.51–5.70 (m, 1H, RCH=CH₂), 4.90–5.05 (m, 2H, RCH=CH₂), 4.65 (s, 2H, NCH₂Ph), 4.00 (s, 2H, NCH₂), 1.82 (s, 6H, 2×CH₃) ppm.

¹³C{¹H} NMR (101 MHz, Toluene-*d*₈, 95 °C): δ = 170.3, 137.6, 133.8, 128.9, 128.0, 127.5, 117.4, 57.9, 50.7, 50.4, 33.2 ppm.

IR (ATR): ν = 3261, 3066, 3012, 2980, 2930, 2662, 2334, 2195, 2098, 1950, 1635, 1494, 1460, 1411, 1364, 1285, 1247, 1169, 1108, 1026, 996, 927, 808, 730, 698 cm⁻¹.

MS (100 eV, CI): m/z (%): 296 (91) [$M+H$]⁺.

MS (70 eV, EI): m/z (%): 296 (12) [$M+H$]⁺, 216 (100), 91 (43) [C₇H₇]⁺.

The NMR data closely match the ones previously reported in the literature.^[5]

***N*-Allyl-2-bromo-*N*-2-dimethylpropanamide (1b)**

N-Allylmethylamine (0.9950 g, 13.99 mmol, 1.00 equiv) was dissolved in 50 mL distilled Et₂O, followed by addition of NEt₃ (3.9 mL, $\rho = 0.728 \text{ g}\cdot\text{mL}^{-1}$, 28.14 mmol, 2.01 equiv). The reaction mixture was cooled in an ice bath. Then, α -bromoisobutyryl bromide (1.74 mL, $\rho = 1.86 \text{ g}\cdot\text{mL}^{-1}$, 14.07 mmol, 1.01 equiv) was added. A white precipitate formed immediately upon addition. The reaction mixture was stirred overnight allowed to warm up to room temperature. The next day, the reaction was stopped by adding 40 mL of an aqueous saturated NH₄Cl solution. The biphasic reaction mixture was stirred for 5 min and was then partitioned between an aqueous saturated NaHCO₃ solution (50 mL) and distilled Et₂O (75 mL). After separating the phases, the aqueous phase was extracted three times with distilled Et₂O (75 mL), the organic phases were combined and dried over Na₂SO₄. The solvent was evaporated to yield the title compound **1b** as a colorless oil (2.5796 g, 11.71 mmol, 84%) after column chromatography (SiO₂/*n*-pentane:EtOAc 4:1 v/v).

$R_f = 0.37$ (*n*-pentane:EtOAc 4:1 v/v), UV-active, stains with KMnO_4 .

^1H NMR (400 MHz, Toluene- d_8 , 95 °C): $\delta = 5.52\text{--}5.61$ (m, 1H, $\text{RCH}=\text{CH}_2$), 4.94–4.96 (m, 1H, $\text{RCH}=\text{CH}_\text{A}\text{H}_\text{B}$), 4.91–4.93 (m, 1H, $\text{RCH}=\text{CH}_\text{A}\text{H}_\text{B}$), 3.88 (d, $^3J_{\text{H,H}} = 5.8$ Hz, 2H, CH_2), 2.82 (s, 3H, NCH_3), 1.78 (s, 6H, $2\times\text{CH}_3$) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, Toluene- d_8 , 95 °C): $\delta = 169.9, 133.9, 116.9, 57.7, 53.4, 36.4, 33.0$ ppm.

IR (ATR): $\nu = 3260, 3082, 2978, 2929, 2161, 2017, 1632, 1467, 1426, 1395, 1371, 1280, 1178, 1087, 988, 923, 756$ cm^{-1} .

MS (100 eV, CI): m/z (%): 220 (59) $[\text{M}+\text{H}]^+$.

MS (70 eV, EI): m/z (%): 220 (30) $[\text{M}+\text{H}]^+$, 219 (100) $[\text{M}]^+$, 140 (100), 112 (24), 98 (58), 70 (21).

HRMS (ESI): m/z calculated for $\text{C}_8\text{H}_{14}\text{BrNO}+\text{Na}^+$: 242.0151 $[\text{M}+\text{Na}]^+$; found: 242.0152.

***N*-Allyl-4-methylbenzenesulfonamide (S1c)**

A round bottom flask equipped with a magnetic stirring bar was charged with allylamine (1.97 mL, $\rho = 0.76$ $\text{g}\cdot\text{mL}^{-1}$, 26.27 mmol, 3.00 equiv) and dissolved in 44 mL of DCM. To this solution, 4-toluenesulfonyl chloride (1.67 g, 8.76 mmol, 1.00 equiv) dissolved in 6 mL of DCM was added dropwise. The reaction mixture was stirred at room temperature for 12 h. After that time, 50 mL of H_2O were added, and the aqueous phase extracted three times with DCM (20 mL). The combined organic fractions were dried over MgSO_4 and the solvent was removed under reduced pressure. The product **S1c** was obtained as a light yellow solid (1.70 g, 8.05 mmol, 92%). The product was considered pure enough for the next step and no further purification was needed.

m.p.: 60.5–60.9 °C.

^1H NMR (600 MHz, CDCl_3): $\delta = 7.70\text{--}7.80$ (m, 2H, Ar- H), 7.25–7.35 (m, 2H, Ar- H), 5.65–5.75 (m, 1H, $\text{RCH}=\text{CH}_2$), 5.16 (d, $^3J_{\text{H,H}} = 17.3$ Hz, 1H, $\text{RCH}=\text{CH}_\text{A}\text{H}_\text{B}$), 5.08 (d, $^3J_{\text{H,H}} = 9.9$ Hz, 1H, $\text{RCH}=\text{CH}_\text{A}\text{H}_\text{B}$), 4.65–4.85 (br s, 1H, NH), 3.55–3.60 (m, 2H, CH_2), 2.42 (s, 3H, Ar- CH_3) ppm;

$^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3): $\delta = 143.6, 137.1, 133.1, 129.8, 127.3, 117.8, 45.9, 21.6$ ppm.

IR (ATR): $\nu = 3247, 2928, 2855, 1649, 1594, 1493, 1422, 1317, 1155, 1092, 1062, 994, 933, 873, 809, 663$ cm^{-1} .

MS (EI, 70 eV): m/z (%): 212 (5) $[\text{M}+\text{H}]^+$, 211 (13) $[\text{M}]^+$, 155 (36), 157 (25), 92 (27), 91 (100) $[\text{C}_7\text{H}_7]^+$, 66 (27), 59 (38).

The NMR data closely match the ones previously reported in the literature.^[6]

***N*-Allyl-2-bromo-2-methyl-*N*-tosylpropanamide (**1c**)**

N-Allyl-4-methylbenzenesulfonamide **S1c** (1.0 g, 4.733 mmol, 1.00 equiv) was dissolved in 24 mL of distilled Et₂O, the solution cooled with an ice bath and NEt₃ (1.3 mL, $\rho = 0.728 \text{ g}\cdot\text{mL}^{-1}$, 9.47 mmol, 2.00 equiv) was added dropwise. The reaction mixture was stirred at the same temperature for 3 h. Then, α -bromoisobutyryl bromide (0.6 mL, $\rho = 1.86 \text{ g}\cdot\text{mL}^{-1}$, 4.73 mmol, 1.00 equiv) was added dropwise with the help of a syringe pump (40 drops/min). The solution was allowed to warm up to room temperature and stirred for additional 24 h. After this time, the reaction was stopped by adding 10 mL of an aqueous saturated NH₄Cl solution. The biphasic reaction mixture was stirred for additional 5 min, then 10 mL of an aqueous saturated NaHCO₃ solution were added and the aqueous phase was extracted three times with distilled Et₂O (10 mL). The organic phases were combined and dried over MgSO₄. The solvent was evaporated to yield the title compound **1c** as a yellowish powder (0.6243 mg, 1.73 mmol, 37% yield) after column chromatography (SiO₂/*n*-pentane:EtOAc 3:1 v/v).

$R_f = 0.54$ (*n*-pentane:EtOAc 2:1 v/v), UV-active, stains with KMnO₄.

m.p.: 79.6–80.4 °C.

¹H NMR (600 MHz, CDCl₃): δ = 7.80–7.90 (m, 2H, Ar-*H*), 7.25–7.35 (m, 2H, Ar-*H*), 5.95–6.05 (m, 1H, RCH=CH₂), 5.41 (d, ³*J*_{H,H} = 17.1 Hz, 1H, RCH=CH_AH_B), 5.34 (d, ³*J*_{H,H} = 10.6 Hz, 1H, RCH=CH_AH_B), 4.90–5.00 (m, 2H, CH₂), 2.43 (s, 3H, Ar-CH₃), 1.88 (s, 6H, 2×CH₃) ppm.

¹³C{¹H} NMR (151 MHz, CDCl₃): δ = 170.5, 144.8, 136.3, 133.7, 129.3, 129.0, 118.3, 57.2, 50.7, 32.2, 21.8 ppm.

IR (ATR): ν = 3336, 2988, 2927, 2166, 1674, 1593, 1460, 1348, 1315, 1460, 1438, 1315, 1236, 1160, 1090, 1051, 925, 805, 773, 716 cm⁻¹.

MS (EI, 70 eV): *m/z* (%): 362 (1) [*M*+H]⁺, 361 (1) [*M*]⁺, 359 (1) [*M*]⁺, 190 (100), 198 (98), 91 (78) [C₇H₇]⁺, 47 (40).

HRMS: calculated for C₁₄H₁₈BrNO₃S+Na⁺: 382.0091 [*M*+Na]⁺; found: 382.0083.

***N*-(2-Methallyl)benzylamine (**S1d**)**

A round bottom flask equipped with a magnetic stirring bar was charged with benzylamine (1.0737 g, 10.02 mmol, 1.00 equiv), which was dissolved in 100 mL MeCN. K₂CO₃ (2.7656 g, 20.01 mmol, 2.00 equiv), NaI (0.1500 g, 1.00 mmol, 0.10 equiv) and 3-chloro-2-methyl-1-propene (1.0 mL, $\rho = 0.92 \text{ g}\cdot\text{mL}^{-1}$, 9.96 mmol, 0.99 equiv) were added at room temperature in the given order. The reaction mixture was refluxed in an oil bath for 32 h and then cooled to room temperature. H₂O (100 mL) was added and the volatiles were removed under reduced pressure. The aqueous phase was extracted three times EtOAc (100 mL), the organic phases were combined, dried over MgSO₄, and the solvent was removed under reduced pressure. The crude secondary amine was purified by column chromatography (SiO₂/*n*-pentane:EtOAc 19:1 → 4:1 v/v) to yield the title compound **S1d** as a yellow oil (0.5289 g, 3.28 mmol, 33%).

$R_f = 0.16$ (*n*-Pentane:EtOAc 4:1 v/v), UV-active (254 nm), stains with I_2 .

^1H NMR (400 MHz, CDCl_3): $\delta = 7.40\text{--}7.19$ (m, 5H, Ar-H), 4.92 (s, 1H, $\text{R}=\text{CH}_\text{A}\text{H}_\text{B}$), 4.87 (s, 1H, $\text{R}=\text{CH}_\text{A}\text{H}_\text{B}$), 3.78 (s, 2H, RCH_2N), 3.21 (s, 2H, PhCH_2N), 1.78 (s, 3H, CH_3), 1.57 (br s, 1H, NH) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): $\delta = 144.0, 140.6, 128.5, 128.3, 127.0, 110.9, 55.1, 53.2, 20.9$ ppm.

IR (ATR): $\nu = 3868, 3651, 3329, 3071, 3029, 2971, 2910, 2817, 2332, 2097, 1944, 1873, 1801, 1651, 1449, 1364, 1235, 1200, 1114, 1027, 971, 893, 822, 734, 699$ cm^{-1} .

MS (100 eV, CI): m/z (%): 162 (100) $[\text{M}+\text{H}]^+$.

MS (70 eV, EI): m/z (%): 161 (21) $[\text{M}]^+$, 120 (17), 106 (9), 91 (43) $[\text{C}_7\text{H}_7]^+$.

The NMR data closely match the ones previously reported in the literature.^[4]

***N*-Benzyl-2-bromo-2-methyl-*N*-(2-methylallyl)propanamide (1d)**

A round bottom flask equipped with a magnetic stirring bar was charged with secondary amine **S1b** (0.4435 g, 2.75 mmol, 1.00 equiv), which was dissolved in 25 mL of distilled Et_2O . NEt_3 (0.76 mL, $\rho = 0.73$ $\text{g}\cdot\text{mL}^{-1}$, 5.48 mmol, 1.99 equiv) was added to the solution and the reaction mixture was cooled in an ice bath. α -Bromoisobutyryl bromide (0.34 mL, $\rho = 1.86$ $\text{g}\cdot\text{mL}^{-1}$, 2.75 mmol, 1.00 equiv) was added slowly and a white precipitate formed immediately upon addition. The reaction mixture was allowed to warm up to room temperature and

stirred overnight. The next day, 20 mL of an aqueous saturated NH_4Cl solution were added to stop the reaction. The biphasic reaction mixture was vigorously stirred for 15 min and then partitioned between 30 mL of an aqueous saturated NaHCO_3 solution and 25 mL of distilled Et_2O . After phase separation, the aqueous phase was extracted three times with distilled Et_2O (30 mL), the organic phases were combined, dried over Na_2SO_4 and the solvent removed under reduced pressure. The crude amide was purified by column chromatography (SiO_2 /*n*-pentane:EtOAc 19:1 v/v) to yield the title compound **1d** as a yellow oil (0.7163 g, 2.31 mmol, 84%).

$R_f = 0.63$ (*n*-pentane:EtOAc 9:1 v/v), UV-active (254 nm).

^1H NMR (600 MHz, Toluene- d_8 , 95 $^\circ\text{C}$): $\delta = 7.14\text{--}6.93$ (m, 5H, Ar-H), 4.78 (s, 1H, $\text{R}=\text{CH}_\text{A}\text{H}_\text{B}$), 4.70 (s, 2H, PhCH_2N), 4.68 (s, 1H, $\text{R}=\text{CH}_\text{A}\text{H}_\text{B}$), 4.01 (s, 2H, NCH_2), 1.83 (s, 6H, $2\times\text{CH}_3$), 1.51 (s, 3H, $\text{CH}_2\text{CH}_3=\text{CH}_2$) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, Toluene- d_8 , 95 $^\circ\text{C}$): $\delta = 170.6, 141.1, 138.1, 128.9, 128.0, 127.6, 112.4, 58.2, 53.0, 51.2, 33.4, 20.0$ ppm.

IR (ATR): $\nu = 3264, 3068, 2976, 2931, 2327, 2094, 1994, 1882, 1637, 1494, 1457, 1414, 1369, 1290, 1247, 1168, 1108, 1079, 1053, 1029, 1001, 939, 896, 819, 731, 698$ cm^{-1} .

MS (100 eV, CI): m/z (%): 310 (4) $[\text{M}+\text{H}]^+$.

MS (70 eV, EI): m/z (%): 310 (14) $[\text{M}+\text{H}]^+$, 309 (20) $[\text{M}]^+$, 230 (100), 160 (15), 91 (46) $[\text{C}_7\text{H}_7]^+$.

HRMS (ESI): m/z calculated for $\text{C}_{15}\text{H}_{20}\text{BrNO}+\text{Na}^+$: 332.0621 $[\text{M}+\text{Na}]^+$; found: 332.0621.

***N*-Benzyl-2-bromo-*N*-(hexa-2,4-dien-1-yl)-2-methylpropanamide (**1e**)**

A round bottom flask equipped with a magnetic stirring bar was charged with benzylamine (3.1 mL, $\rho = 0.98 \text{ g}\cdot\text{mL}^{-1}$, 28.00 mmol, 1.00 equiv) and dissolved in 24 mL of MeOH. To this solution, 2,4-hexadienal (3.0 mL, $\rho = 0.90 \text{ g}\cdot\text{mL}^{-1}$, 28.00 mmol, 1.00 equiv) was added and the solution stirred for 2 h at room temperature. The mixture was then cooled with an ice bath for 30 minutes, NaBH_4 (2.12 g, 55.99 mmol, 2.00 equiv) added and the solution stirred for another hour. After this time, 20 mL of H_2O

were added, and the aqueous phase was extracted two times with DCM (15 mL). The combined organic fractions were washed with an aqueous 20% NaOH solution (10 mL), an aqueous saturated NaCl solution (10 mL), dried over MgSO_4 and the solvent was removed under reduced pressure. The crude mixture was purified by distillation using a glass oven apparatus (136.0 °C, 10 mbar) to obtain *N*-benzylhexa-2,4-dien-1-amine product **S1e** as a light-yellow oil (4831.6 g, 25.80 mmol, 95%). ^1H NMR (600 MHz, CDCl_3): $\delta = 7.29\text{--}7.36$ (m, 4H, Ar-*H*), 7.21–7.29 (m, 1H, Ar-*H*), 6.12–6.20 (m, 1H, $\text{RCH}=\text{CHR}'$), 6.04–6.11 (m, 1H, $\text{RCH}=\text{CHR}'$), 5.62–5.70 (m, 2H, $2\times\text{RCH}=\text{CHR}'$), 3.79 (s, 2H, NCH_2Ph), 3.29 (d, $^3J_{\text{H,H}} = 6.3 \text{ Hz}$, 2H, NCH_2R), 1.76 (d, $^3J_{\text{H,H}} = 6.3 \text{ Hz}$, 3H, RCH_3) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3): $\delta = 140.5, 132.1, 131.3, 129.3, 128.8, 128.5, 128.3, 127.0, 53.4, 51.0, 18.2$ ppm. The NMR data closely match the ones previously reported in the literature.^[7]

For the synthesis of product **1e**, compound **S1e** was directly used in the next reaction without any further purification.

A round bottom flask equipped with a magnetic stirring bar was charged with *N*-benzylhexa-2,4-dien-1-amine **S1e** (1.00 g, 5.34 mmol, 1.0 equiv), dissolved in 27 mL of dry DCM and cooled to with an ice bath, under argon atmosphere. To this solution were added first α -bromoisobutyryl bromide (0.7 mL, $\rho = 1.86 \text{ g}\cdot\text{mL}^{-1}$, 5.339 mmol, 1.0 equiv) all in once and afterward NEt_3 (747.3 μL , $\rho = 0.728 \text{ g}\cdot\text{mL}^{-1}$, 5.34 mmol, 1.0 equiv) dropwise. The reaction mixture was cooled in an ice bath and stirred for additional 3 h. After this time, the reaction was stopped by adding 10 mL of an aqueous saturated NH_4Cl solution. The biphasic reaction mixture was stirred for additional 5 min, then 10 mL of an aqueous saturated NaHCO_3 solution were added and the water phase extracted three times with DCM (15 mL). The organic phases were combined and dried over MgSO_4 . The solvent was evaporated to yield the title compound **1e** as a yellowish oil (1.496 g, 4.45 mmol, 83% yield) after column chromatography (SiO_2/n -pentane:EtOAc 4:1 v/v).

$R_f = 0.80$ (*n*-pentane:EtOAc 3:1 v/v), UV-active, stains with KMnO_4 .

^1H NMR (600 MHz, Toluene- d_8 , 95 °C): $\delta = 6.92\text{--}7.19$ (m, 5H, Ar-*H*), 5.80–5.99 (m, 2H, $\text{CH}_3\text{CH}=\text{CHR} + \text{NCH}_2\text{CH}=\text{CHR}$), 5.29–5.53 (m, 2H, $\text{CH}_3\text{CH}=\text{CHR} + \text{NCH}_2\text{CH}=\text{CHR}$), 4.68 (s, 2H, HCH_2Ph), 4.02–4.12 (m, 2H, $\text{NCH}_2\text{CH}=\text{CHR}$), 1.80–1.88 (m, 6H, $2\times\text{CH}_3$), 1.53–1.60 (m, 3H, $\text{CH}=\text{CHCH}_3$) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, Toluene- d_8 , 95 °C): $\delta = 170.3, 138.2, 134.1, 131.5, 129.4, 128.9, 128.1, 127.5, 125.8, 58.0, 50.7, 49.9, 33.3, 17.8$ ppm.

The bidimensional spectroscopic techniques carried out at a temperature of 95 °C in toluene- d_8 were not sufficient to identify the *E/Z* configuration of the two double bonds of the compound **1e**.

IR (ATR): $\nu = 3020, 2975, 2929, 2327, 2090, 1635, 1494, 1458, 1414, 1361, 1249, 1166, 1107, 990, 940, 728, 698 \text{ cm}^{-1}$.

MS (100 eV, CI): m/z (%): 339 (15) $[M+H]^+$, 338 (77) $[M+H]^+$.

MS (EI, 70 eV): m/z (%): 339 (3) $[M+H]^+$, 338 (16) $[M]^+$, 336 (17) $[M]^+$, 256 (100), 91 (71), 81 (32).

HRMS: calculated for $C_{17}H_{22}BrNONa$ $[M+Na]^+$: 358.0785; found: 358.0777.

***N*-Benzyl-*N*-prenylamine (**S1f**)**

A round bottom flask equipped with a magnetic stirring bar was charged with 3-methyl-2-butenal (1.0011 g, 11.90 mmol, 1.00 equiv), which was filtered over Na_2CO_3 before use to remove the corresponding carboxylic acid. Then, 3-methyl-2-butenal was dissolved in DCM (20 mL) and benzylamine (1.3 mL, $\rho = 0.981 \text{ g}\cdot\text{mL}^{-1}$, 11.90 mmol, 1.00 equiv) as well as $MgSO_4$ (1.4369 g, 11.94 mmol, 1.00 equiv) were added. The reaction mixture was stirred for 4 days at room temperature and then filtered over Celite. Next, the solvent was removed under reduced pressure and the crude imine was dissolved in MeOH (50 mL) and cooled in an ice bath. $NaBH_4$ (1.1286 g, 29.83 mmol, 2.51 equiv) was added in small portions and the reaction mixture was allowed to warm up to room temperature overnight. The next day, the solvent was evaporated and the residue was partitioned between H_2O (40 mL) and EtOAc (40 mL). After phase separation the aqueous phase was extracted three times with EtOAc (40 mL), the organic phases were combined and dried over Na_2SO_4 . The solvent was removed, and the crude secondary amine was purified by column chromatography (SiO_2 /EtOAc) to yield the title compound **S1f** as a yellow oil (1.2233 g, 6.98 mmol, 59%).

$R_f = 0.20$ (EtOAc), smears, UV-active (254 nm), stains with ninhydrin.

1H NMR (400 MHz, $CDCl_3$): $\delta = 7.36\text{--}7.29$ (m, 4H, Ar-H), 7.28–7.21 (m, 1H, Ar-H), 5.25–5.31 (m, 1H, $CH=(CH_3)_2$), 3.78 (s, 2H, $PhCH_2N$), 3.23 (dt, $^3J_{H,H} = 7.0, 1.1$ Hz, 2H, $NCH_2CH=R$), 1.73 (s, 3H, $RCH=CH_3(CH_3)$), 1.62 (s, 3H, $RCH=(CH_3)CH_3$), 1.45 (br s, 1H, NH) ppm.

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): $\delta = 140.6, 134.6, 128.5, 128.3, 127.0, 123.1, 53.6, 46.8, 25.9, 18.1$ ppm.

IR (ATR): $\nu = 3857, 3655, 3313, 3026, 2968, 2915, 2856, 2326, 2083, 1998, 1927, 1808, 1748, 1674, 1600, 1539, 1492, 1447, 1373, 1304, 1188, 1091, 1027, 976, 833, 733, 699 \text{ cm}^{-1}$.

MS (100 eV, CI): m/z (%): 176 (100) $[M+H]^+$.

MS (70 eV, EI): m/z (%): 176 (23) $[M+H]^+$, 175 (17) $[M]^+$, 160 (18), 135 (23), 134 (12), 120 (17), 106 (36), 91 (100) $[C_7H_7]^+$, 77 (14), 65 (14).

The NMR data closely match the ones previously reported in the literature.^[8]

***N*-Benzyl-2-bromo-2-methyl-*N*-(3-methylbut-2-en-1-yl)propanamide (1f)**

A round bottom flask equipped with a magnetic stirring bar was charged with secondary amine **S1c** (1.2208 g, 6.96 mmol, 1.00 equiv), which was dissolved in 50 mL distilled Et₂O. The solution was cooled in an ice bath and NEt₃ (1.6 mL, $\rho = 0.73 \text{ g}\cdot\text{mL}^{-1}$, 11.83 mmol, 1.70 equiv) were added. α -Bromoisobutyryl bromide (0.9 mL, $\rho = 1.86 \text{ g}\cdot\text{mL}^{-1}$, 6.96 mmol, 1.00 equiv) was added slowly and a white precipitate formed immediately upon addition. The reaction mixture was allowed to warm up to room temperature and stirred overnight. The

next day the reaction was stopped by adding 20 mL of an aqueous saturated NH₄Cl solution. The biphasic reaction mixture was stirred vigorously for 15 min and was then partitioned between 50 mL of an aqueous saturated NaHCO₃ solution and 50 mL of distilled Et₂O. The phases were separated, and the aqueous phase was extracted three times distilled Et₂O (50 mL). The organic phases were combined, dried over MgSO₄ and the solvent was removed under reduced pressure. The crude amide was purified by column chromatography (SiO₂/*n*-pentane:EtOAc 39:1 v/v) to yield the title compound **1f** as a colorless oil (1.6207 g, 5.00 mmol, 72%).

R_f = 0.56 (*n*-pentane:EtOAc 9:1 v/v), UV-active (254 nm).

¹H NMR (600 MHz, Toluene-*d*₈, 95 °C): δ = 7.15–6.93 (m, 5H, Ar-*H*), 5.12–5.17 (m, 1H, RCH=(CH₃)₂), 4.67 (s, 2H, PhCH₂N), 4.11 (d, ³*J*_{H,H} = 6.5 Hz, 2H, NCH₂CH), 1.86 (s, 6H, 2×CH₃), 1.55 (s, 3H, RCH=CH₃(CH₃)), 1.32 (s, 3H, RCH=(CH₃)CH₃) ppm.

¹³C{¹H} NMR (151 MHz, Toluene-*d*₈, 95 °C): δ = 170.3, 138.4, 135.9, 128.8, 128.1, 127.5, 121.1, 58.1, 50.9, 46.3, 33.3, 25.6, 17.8 ppm.

IR (ATR): ν = 3510, 3257, 2975, 2925, 2661, 2323, 2089, 1996, 1913, 1733, 1632, 1422, 1370, 1249, 1163, 1106, 1030, 1001, 942, 890, 841, 730 cm⁻¹.

MS (100 eV, CI): *m/z* (%): 324 (20) [*M*+H]⁺.

MS (70 eV, EI): *m/z* (%): 324 (16) [*M*+H]⁺, 325 (15) [*M*]⁺, 244 (100), 91 (42) [C₇H₇]⁺, 69 (18).

HRMS (ESI): *m/z* calculated for C₁₆H₂₂BrNO+H⁺: 324.0958 [*M*+H]⁺; found: 324.0957.

4. Mechanochemical synthesis of 2a-f

General procedure for optimization of reaction conditions

A 10 mL ZrO₂-Y milling vessel equipped with one milling ball (10 mm in diameter) was charged with amide **1a** (100.0 mg, 0.34 mmol), covellite (5-20 mol%; covellite considered to be pure CuS for calculation). The milling vessel was transferred inside a glove box and ligand **I-III** 5-20 mol% was added. The milling vessel was closed, sealed at the seam with parafilm and took out of the glove box. The mechanochemical reaction was conducted for the time indicated in Table 1 at a frequency of 25 Hz. At the end of this time, 1 mL of CDCl₃ was added to the reaction vessel and the crude mixture filtered through a short silica plug directly into a NMR tube. The reported ratio of **2a:1a** was calculated based on the integrals of the signals at 2.36–2.48 ppm (**2a**, CH) and 5.63–5.95 ppm (**1a**, RCH=CH₂).

General procedure for the mechanochemical ATRC of tertiary amides with copper ores

A 10 mL ZrO₂-Y milling vessel equipped with one milling ball (10 mm in diameter) was charged with amide **1a-f** (0.30 mmol) and covellite (1.4 mg, 0.015 mmol, 5 mol%; covellite considered to be pure CuS for calculation). The jar was transferred inside a glove box and tris[2-(dimethylamino)ethyl]amine (**III**, 3.5 mg, 4.1 μL ($\rho = 0.851 \text{ g}\cdot\text{mL}^{-1}$), 0.015 mmol, 5 mol%) was added. The vessel was closed, sealed at the seam with parafilm and took out of the glove box. The mechanochemical reaction was conducted for 30 min at a frequency of 25 Hz. The reaction mixture was transferred in a round bottom flask by adding CHCl₃ (5 mL) to the jar, which was closed and shaken (5 times). The products were purified by performing a dry loaded column chromatography.

1-Benzyl-4-(bromomethyl)-3,3-dimethylpyrrolidin-2-one (**2a**)

The title compound was synthesized using the general procedure stated above, to yield **2a** after column chromatography (SiO₂/*n*-pentane:EtOAc 4:1 v/v) as a colorless oil (93.5 mg, 0.32 mmol, 94%).

Upscaling: **1a** 297.5 mg, Covellite 4.8 mg, Me₆TREN 11.6 mg (13.6 μL). Obtained 269.3 mg product after column chromatography (*n*-pentane:EtOAc 3:1 v/v, *R_f* = 0.11).

Bornite (Cu₅FeS₄): 100.4 mg **1a**, 1.7 mg Bornite, 4.6 μL Me₆TREN, 97.0 mg product after column chromatography (*n*-pentane:EtOAc 3:1 v/v, *R_f* = 0.11).

R_f = 0.11 (*n*-Pentane:EtOAc 3:1 v/v), slightly UV-active, stains with KMnO₄.

¹H NMR (600 MHz, CDCl₃): δ = 7.33 (m, 2H, Ar-H), 7.29 (m, 1H, Ar-H), 7.21 (m, 2H, Ar-H), 4.53 (d, ³*J*_{H,H} = 14.6 Hz, 1H, PhCH_AH_BN), 4.38 (d, ³*J*_{H,H} = 14.6 Hz, 1H, PhCH_AH_B), 3.49 (dd, ³*J*_{H,H} = 10.1, 4.8 Hz, 1H, CH_AH_BBr), 3.38 (dd, ³*J*_{H,H} = 10.1, 7.6 Hz, 1H, CH_AH_BBr), 3.25 (t, ³*J*_{H,H} = 10.4 Hz, 1H, NCH_AH_B), 2.90 (dd, ³*J*_{H,H} = 10.1, 8.6 Hz, 1H, NCH_AH_B), 2.43 (dddd, ³*J*_{H,H} = 10.8, 8.6, 7.6, 4.8 Hz, 1H, CH), 1.26 (s, 3H, CH₃), 1.01 (s, 3H, CH₃) ppm.

¹³C{¹H} NMR (151 MHz, CDCl₃): δ = 178.6, 136.5, 128.9, 128.2, 127.8, 49.0, 46.8, 46.2, 44.2, 31.5, 24.4, 18.5 ppm.

IR (ATR): ν = 3474, 3029, 2965, 2927, 2868, 2325, 2082, 1894, 1685, 1491, 1434, 1360, 1321, 1269, 1165, 1079, 1035, 998, 947, 809, 748, 700, 673 cm⁻¹.

MS (100 eV, CI): *m/z* (%): 296 (27) [*M*+H]⁺.

MS (70 eV, EI): m/z (%): 296 (50) $[M+H]^+$, 295 $[M]^+$ (46), 216 (9), 202 (10), 92 (20), 91 (100) $[C_7H_7]^+$, 65 (20), 55 (11).

The NMR data closely match the ones previously reported in the literature.^[5]

4-(Bromomethyl)-1,3,3-trimethylpyrrolidin-2-one (2b)

The title compound was synthesized using the general procedure stated above. **1b** (102.3 mg, 0.46 mmol), covellite (2.2 mg, 0.02 mmol, 5 mol%) and ligand **III** (= Me₆TREN, 5.3 mg, 6.2 μ L (ρ = 0.851 g·mL⁻¹), 0.02 mmol, 5 mol%) were used, to yield **2b** after column chromatography (SiO₂/*n*-pentane:EtOAc 1:1 v/v) as a colorless oil (80.7 mg, 0.36 mmol, 79 %).

R_f = 0.40 (*n*-pentane:EtOAc 1:1 v/v), not UV-active, stains with KMnO₄ after heating.

¹H NMR (600 MHz, CDCl₃): δ = 3.43–3.53 (m, 2H, BrCH_AH_BCH + CHCH_AH_BN), 3.30 (dd, ³*J*_{H,H} = 11.0, 11.0 Hz, 1H CHCH_AH_BN), 3.05 (dd, ³*J*_{H,H} = 9.7, 8.4 Hz, 1H, BrCH_AH_BCH), 2.84 (s, 3H, NCH₃), 2.40–2.49 (m, 1H, BrCH₂RCHCH₂), 1.19 (s, 3H, CH₃(A)), 0.97 (s, 3H, CH₃(B)) ppm.

¹³C{¹H} NMR (151 MHz, CDCl₃): δ = 178.6, 51.8, 46.2, 44.0, 31.7, 29.9, 24.5, 18.5 ppm.

IR (ATR): ν = 3482, 2964, 2928, 2870, 2161, 162, 1496, 1438, 1401, 1363, 1274, 1174, 1083, 1025, 971, 731, 673 cm⁻¹.

MS (70 eV, EI): m/z (%): 223 (11) $[M+H]^+$, 222 (100) $[M]^+$, 221 (23) $[M+H]^+$, 220 (95) $[M]^+$, 219 (14), 140 (64), 126 (19), 83 (14), 69 (24), 55 (22).

HRMS: calculated for C₈H₁₄BrNONa $[M+Na]^+$: 242.0157; found: 242.0151.

4-(Bromomethyl)-3,3-dimethyl-1-tosylpyrrolidin-2-one (2c)

The title compound was synthesized using the general procedure stated above to yield **2c** after column chromatography (SiO₂/*n*-pentane:EtOAc 3:1 v/v) as a white solid (20.0 mg, 0.05 mmol, 18%; for an extended milling time of 90 min: 32.4 mg, 0.09 mmol, 30%).

R_f = 0.20 (*n*-pentane:EtOAc 3:1 v/v), UV-active.

m.p.: 127.4–128.1 °C.

¹H NMR (600 MHz, CDCl₃): δ = 7.80–7.85 (m, 2H, Ar-*H*), 7.30–7.35 (m, 2H, Ar-*H*), 4.14 (dd, ³*J*_{H,H} = 10.1, 7.5 Hz, 1H, BrCH_AH_BCH), 3.40–3.50 (m, 2H, BrCH_AH_BCH + CHCH_AH_BN), 3.24 (dd, ³*J*_{H,H} = 11.0, 11.0 Hz, 1H, CHCH_AH_BN), 2.41–2.48 (m, 4H, BrCH₂RCHCH₂ + CH₃(A)), 1.18 (s, 3H, Ar-CH₃), 0.89 (s, 3H, CH₃(B)) ppm.

¹³C{¹H} NMR (151 MHz, CDCl₃): δ = 177.0, 145.5, 135.0, 129.9, 128.1, 48.9, 45.5, 45.2, 29.9, 23.6, 21.8, 18.0 ppm.

IR (ATR): ν = 3286, 2972, 2922, 2854, 2162, 1724, 1597, 1455, 1352, 1237, 1163, 1115, 939, 881, 811, 749, 659 cm⁻¹.

MS (EI, 70 eV): m/z (%): 362 (31) $[M+H]^+$, 360 (35) $[M+H]^+$, 297 (78), 295 (100), 92 (22), 91 (61), 69 (37), 65 (28), 56 (25).

HRMS: calculated for $C_{14}H_{18}BrNO_3S+Na^+$: $[M+Na]^+$: 382.0091; found: 382.0083.

1-Benzyl-4-(bromomethyl)-3,3,4-trimethylpyrrolidin-2-one (2d)

The title compound was synthesized using the general procedure stated above. **1d** (93.1 mg, 0.30 mmol), covellite (1.4 mg, 0.015 mmol, 5 mol%) and ligand **III** (= Me_6TREN , 3.5 mg, 4.1 μ L ($\rho = 0.851$ g·mL $^{-1}$), 0.015 mmol, 5 mol%) were used, to yield **2d** after column chromatography (SiO_2/n -pentane:EtOAc 4:1 $\rightarrow$ 1:1 v/v) as a transparent oil (83.7 mg, 0.27 mmol, 90%).

$R_f = 0.48$ (n -pentane:EtOAc 1:1 v/v), UV-active (254 nm), stains with I_2 .

1H NMR (600 MHz, $CDCl_3$): δ = 7.33 (m, 2H, Ar- H), 7.28 (m, 1H, Ar- H), 7.22 (m, 2H, Ar- H), 4.32–4.50 (m, 2H, $PhCH_2N$), 3.42 (d, $^3J_{H,H} = 10.2$ Hz, 1H, CH_AH_BBr), 3.34 (d, $^3J_{H,H} = 10.2$ Hz, 1H, CH_AH_BBr), 3.19 (d, $^3J_{H,H} = 10.2$ Hz, 1H, NH_AH_B), 2.84 (d, $^3J_{H,H} = 10.2$ Hz, 1H, NH_AH_B), 1.13 (s, 3H, $(C=O)C(CH_3)CH_3$), 1.10 (s, 3H, CH_3), 1.07 (s, 3H, $(C=O)CCH_3(CH_3)$) ppm.

$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ = 178.4, 136.5, 128.9, 128.3, 127.8, 54.4, 47.2, 46.8, 43.0, 40.5, 20.3, 20.0, 19.4 ppm.

IR (ATR): ν = 3870, 3479, 3030, 2972, 2928, 2871, 2662, 2327, 2085, 1989, 1908, 1805, 1686, 1492, 1432, 1376, 1310, 1263, 1165, 1110, 1079, 1028, 949, 853, 814, 748, 700, 668 cm^{-1} .

MS (100 eV, CI): m/z (%): 310 (95) $[M+H]^+$.

MS (70 eV, EI): m/z (%): 310 (37) $[M+H]^+$, 309 (58) $[M]^+$, 294 (24), 230 (20), 218 (9), 106 (10), 91 (100) $[C_7H_7]^+$, 65 (15), 55 (15).

HRMS (ESI): m/z calculated for $C_{15}H_{20}BrNO+Na^+$: 332.0621 $[M+Na]^+$; found: 332.0619.

(*E*)-1-Benzyl-4-(3-bromobut-1-en-1-yl)-3,3-dimethylpyrrolidin-2-one (2e)

The title compound was synthesized using the general procedure stated above. **1e** (101.0 mg, 0.30 mmol), covellite (1.4 mg, 0.02 mmol, 5 mol%) and ligand **III** (= Me_6TREN , 3.5 mg, 4.1 μ L ($\rho = 0.851$ g·mL $^{-1}$), 0.02 mmol, 5 mol%) were used, to yield **2e** after column chromatography (SiO_2/n -pentane:EtOAc 3:1 v/v) as a transparent oil mixture of two diastereomers in 1:1 *d.r.* (12.3 mg, 0.04 mmol, 12%).

After 90 min of milling: 28.9 mg, 0.09 mmol, 27%.

1H NMR (600 MHz, $CDCl_3$): δ = 7.30–7.35 (m, 2H, Ar- H), 7.30–7.35 (m, 2H, Ar- H), 7.26–7.30 (m, 1H, Ar- H), 7.26–7.30 (m, 1H, Ar- H), 7.19–7.23 (m, 2H, Ar- H), 7.19–7.23 (m, 2H, Ar- H), 5.75–5.81 (m, 1H, $BrCHCH=CHR$), 5.75–5.81 (m, 1H, $BrCHCH=CHR$), 5.52–5.60 (m, 1H, $BrCHCH=CHR$), 5.52–5.60 (m, 1H, $BrCHCH=CHR$), 4.61–4.69 (m, 1H, $BrCH$), 4.61–4.69 (m, 1H, $BrCH$), 4.51 (d, $^2J_{H,H} = 14.8$ Hz, 1H, NCH_AH_BPh), 4.51 (d,

$^2J_{\text{H,H}} = 14.8$ Hz, 1H, $\text{NCH}_\text{A}\text{H}_\text{B}\text{Ph}$), 4.40 (d, $^2J_{\text{H,H}} = 14.8$ Hz, 1H, $\text{NCH}_\text{A}\text{H}_\text{B}\text{Ph}$), 4.40 (d, $^2J_{\text{H,H}} = 14.8$ Hz, 1H, $\text{NCH}_\text{A}\text{H}_\text{B}\text{Ph}$), 3.16–3.23 (m, 1H, $\text{CHCH}_\text{A}\text{H}_\text{B}\text{N}$), 3.16–3.23 (m, 1H, $\text{CHCH}_\text{A}\text{H}_\text{B}\text{N}$), 2.94–3.01 (m, 1H, $\text{CHCH}_\text{A}\text{H}_\text{B}\text{N}$), 2.94–3.01 (m, 1H, $\text{CHCH}_\text{A}\text{H}_\text{B}\text{N}$), 2.53–2.60 (m, 1H, $\text{BrCH}_2\text{RCHCH}_2$), 2.53–2.60 (m, 1H, $\text{BrCH}_2\text{RCHCH}_2$), 1.75 (d, $^3J_{\text{H,H}} = 6.8$ Hz, 3H, BrCHCH_3), 1.74 (d, $^3J_{\text{H,H}} = 6.8$ Hz, 3H, BrCHCH_3), 1.18 (s, 3H, $\text{CH}_3(\text{A})$), 1.19 (s, 3H, $\text{CH}_3(\text{A})$), 0.96 (s, 3H, $\text{CH}_3(\text{B})$), 0.95 (s, 3H, $\text{CH}_3(\text{B})$) ppm;

$^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3): $\delta = 179.0, 178.9, 136.6, 136.6, 136.5, 136.4, 128.9, 128.2, 128.0, 127.9, 127.8, 127.8, 48.7, 48.5, 48.1, 48.0, 46.9, 46.8, 46.7, 44.5, 44.4, 26.2, 26.0, 23.6, 23.6, 19.3, 19.2$ ppm.

The configuration of the double bond was determined after 1D Selective Gradient H,H-COSY analysis on the multiplet at 5.75–5.81 ppm: $^3J_{\text{H,H}} = 16.4$ Hz, which indicated an *E*-configuration.

IR (ATR): $\nu = 3029, 2964, 2924, 2866, 2327, 2099, 1685, 1491, 1431, 1361, 1266, 1170, 1003, 969, 750, 700$ cm^{-1} .

MS (EI, 70 eV): m/z (%) = 338 (15) $[\text{M}+\text{H}]^+$, 337 (38) $[\text{M}]^+$, 336 (19) $[\text{M}+\text{H}]^+$, 335 (51) $[\text{M}]^+$, 256 (68), 202 (46), 123 (29), 91 (100), 81 (24) .

MS (100 eV, CI): m/z (%): 338 (56) $[\text{M}+\text{H}]^+$, 336 (59) $[\text{M}+\text{H}]^+$, 257 (20), 256 (100).

HRMS: calculated for $\text{C}_{18}\text{H}_{23}\text{BrNO}$ $[\text{M}+\text{H}]^+$: 336.0964; found: 336.0958.

1-Benzyl-3,3-dimethyl-4-(prop-1-en-2-yl)pyrrolidin-2-one (2f) and 1-benzyl-3,3-dimethyl-4-(propan-2-ylidene)pyrrolidin-2-one (2f')

The title isomeric mixture was synthesized using the general procedure described above. **1f** (97.3 mg, 0.30 mmol), covellite (1.4 mg, 0.015 mmol, 5 mol%) and ligand **III** (= Me_6TREN , 3.5 mg, 4.1 μl ($\rho = 0.851$ $\text{g}\cdot\text{mL}^{-1}$), 0.015 mmol, 5 mol%) were used, to yield a mixture of isomers **2f** and **2f'** (61:39) after column chromatography (SiO_2/n -pentane:EtOAc 4:1 v/v) as a transparent oil (43.5 mg, 0.18 mmol, 59%). For a milling time of 90 min (71.6 mg, 0.29 mmol, 98%, **2f:2f'** 46:54).

The expected bromine derivative was not obtained as it underwent elimination to yield the olefins **2f** and **2f'**.

$R_f = 0.46$ – 0.58 (n -pentane:EtOAc 1:1 v/v), stains with KMnO_4 .

^1H NMR (600 MHz, CDCl_3): δ (**2f**) = 7.35 (m, 2H, Ar-H), 7.30 (m, 1H, Ar-H), 7.25 (m, 2H, Ar-H), 4.90 (m, 1H, R= $\text{CH}_\text{A}\text{H}_\text{B}$), 4.70 (m, 1H, R= $\text{CH}_\text{A}\text{H}_\text{B}$), 4.50 (m, 2H, PhCH_2N), 3.19 (m, 2H, NCH_2CHR_2), 2.61 (t, $^3J_{\text{H,H}}$ = Hz, 1H, CH), 1.73 (s, 3H, $\text{H}_2\text{C}=\text{CRCH}_3$), 1.31 (s, 3H, $(\text{C}=\text{O})\text{C}(\text{CH}_3)\text{CH}_3$), 0.98 (s, 3H, $(\text{C}=\text{O})\text{CCH}_3(\text{CH}_3)$) ppm; δ (**2f'**) = 7.35 (m, 2H, Ar-H), 7.30 (m, 1H, Ar-H), 7.25 (m, 2H, Ar-H), 4.54 (s, 2H, PhCH_2N), 3.75 (s, 2H, NCH_2R), 1.80 (s, 3H, R= $(\text{CH}_3)\text{CH}_3$), 1.53 (s, 3H, R= $\text{CH}_3(\text{CH}_3)$), 1.40 (s, 6H, $(\text{C}=\text{O})\text{C}(\text{CH}_3)_2$) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3): δ (**2f**) = 179.0, 142.4, 136.7, 128.8, 128.3, 127.7, 113.2, 50.7, 46.9, 46.8, 43.8, 25.4, 23.1, 19.2 ppm; δ (**2f'**) = 179.6, 136.6, 130.5, 128.8, 128.1, 127.6, 126.1, 49.4, 46.4, 44.2, 24.4, 21.4, 20.2 ppm.

IR (ATR): ν = 3866, 3372, 2966, 2925, 2661, 2328, 2095, 1996, 1910, 1685, 1491, 1437, 1363, 1264, 1157, 1079, 1029, 896, 815, 745, 701 cm^{-1} .

MS (100 eV, CI): m/z (%): 244 (100) $[\text{M}+\text{H}]^+$.

MS (70 eV, EI): m/z (%): 244 (50) $[\text{M}+\text{H}]^+$, 243 (96) $[\text{M}]^+$, 228 (36), 152 (17), 91 (100) $[\text{C}_7\text{H}_7]^+$, 65 (20), 55 (13).

5. Considerations on the mechanism for the formation of **2e**

It is assumed that the stability of intermediate **11e** reduced the rate in the formation of product **2e**, thus lowering its yield after the same reaction time compared to other substrates used.

Scheme S1 - Proposed reaction mechanism for the formation of **2e**.

6. Synthesis of substrates 3e and 3f

6-Phenylnaphthalen-2-ol (3e)

A round bottom Schlenk flask equipped with a magnetic stirring bar was flushed with argon and charged with 22 mL of toluene and 23 mL of an aqueous 2% Na₂CO₃ solution. To this mixture, 6-bromo-2-naphthol (1000.0 mg, 4.48 mmol, 1.00 equiv), phenylboronic acid (546.6 mg, 4.48 mmol, 1.00 equiv) and [Pd(PPh₃)₄] (517.7 mg, 0.448 mmol, 0.10 equiv) were added under argon flow and the mixture stirred at 80 °C for 22 h in an oil bath. At the end of this time, 15 mL of water were added, the crude mixture was vacuum filtrated and extracted three times with DCM (20 mL). The combined organic phases were washed once with 10 mL of an aqueous saturated NaCl solution, dried over MgSO₄ and the solvent removed under reduced pressure. The 6-phenylnaphthalen-2-ol product (**3e**) was obtained as a yellow solid (423.7 mg, 1.93 mmol, 43%) after column chromatography (SiO₂/*n*-pentane:EtOAc 4:1 v/v).

R_f = 0.60 (*n*-pentane:EtOAc 2:1 v/v), UV-active.

m.p.: 174.1–175.6 °C.

¹H NMR (400 MHz, DMSO-*d*₆): δ = 9.98–9.63 (br s, 1H, Ar–OH), 8.00–8.12 (m, 1H, Ar–H), 7.86–7.82 (m, 1H, Ar–H), 7.79–7.74 (m, 3H, Ar–H), 7.74–7.70 (m, 1H, Ar–H), 7.51–7.45 (m, 1H, Ar–H), 7.38–7.33 (m, 2H, Ar–H), 7.16–7.13 (m, 1H, Ar–H), 7.12–7.08 (m, 1H, Ar–H).

¹³C{¹H} NMR (101 MHz, DMSO-*d*₆): δ = 155.6, 140.3, 134.3, 133.9, 129.8, 128.9, 128.0, 127.0, 126.7, 126.6, 125.2, 125.1, 119.1, 108.4 ppm.

IR (ATR): ν = 3327, 3056, 3030, 2922, 2853, 2696, 2321, 2109, 1897, 1814, 1772, 1630, 1601, 1491, 1451, 1354, 1273, 1227, 1192, 1150, 960, 861, 807, 755, 696, 667 cm^{−1}.

MS (EI, 70 eV): *m/z* (%): 221 (17) [M+H]⁺, 220 (100) [M]⁺, 191 (20), 189 (22), 165 (16).

The NMR data closely match the ones previously reported in the literature.^[9]

[1,2'-Binaphthalen]-6'-ol (3f)

A round bottom Schlenk flask equipped with a magnetic stirring bar was flushed with argon and charged with 6-bromo-2-naphthol (500.0 mg, 2.24 mmol, 1.00 equiv), [Pd(PPh₃)₄] (207.1 mg, 0.179 mmol, 0.08 equiv), Na₂CO₃ (1.0 g, 9.86 mmol, 4.40 equiv), 7 mL of H₂O and 7 mL of toluene. To this mixture, a solution of 1-naphthylboronic acid (500.5 mg, 2.91 mmol, 1.30 equiv) in 9 mL of EtOH was added. The reaction mixture was heated to reflux for 6 h under stirring, allowed to cool to room temperature and was then concentrated in vacuo. To the residue were added 10 mL of EtOAc and 10 mL of water. The suspension was filtrated and the filtrate acidified with 1 M HCl until pH = 2. The aqueous layer was extracted three times with EtOAc (20 mL) and the combined organic phases washed first with water (10 mL) and

then with an aqueous saturated NaCl solution (10 mL). The organic phase was dried over MgSO₄ and the solvent removed under reduced pressure. The [1,2'-binaphthalen]-6'-ol product **3f** was obtained as yellow solid (477.7 mg, 1.77 mmol, 79%) after column chromatography (SiO₂/*n*-pentane:EtOAc 5:1 v/v).

R_f = 0.42 (*n*-pentane:EtOAc 2:1 v/v), UV-active.

m.p.: 146.5–146.9°C.

¹H NMR (400 MHz, DMSO-*d*₆): δ = 9.79–9.91 (br, 1H, Ar–OH), 7.99–8.04 (m, 1H, Ar–H), 7.94–7.99 (m, 1H, Ar–H), 7.80–7.91 (m, 4H, Ar–H), 7.58–7.64 (m, 1H, Ar–H), 7.53–7.58 (m, 1H, Ar–H), 7.45–7.53 (m, 3H, Ar–H), 7.19–7.25 (m, 1H, Ar–H), 7.10–7.18 (m, 1H, Ar–H) ppm.

¹³C{¹H} NMR (101 MHz, DMSO-*d*₆): δ = 155.7, 139.7, 134.3, 133.8, 133.5, 131.1, 129.7, 128.4, 128.3, 128.2, 127.7, 127.5, 127.1, 126.3, 126.0, 125.9, 125.6, 125.4, 119.1, 108.6 ppm.

IR (ATR): ν = 3304, 3048, 2922, 2853, 2663, 2322, 2094, 1933, 1738, 1631, 1605, 1483, 1446, 1360, 1279, 1236, 1201, 1152, 1020, 958, 913, 867, 799, 773, 674 cm^{–1}.

MS (EI, 70 eV): *m/z* (%) = 271 (20) [*M*+H]⁺, 270 (100) [*M*]⁺, 240 (16), 239 (47).

The NMR data closely match the ones previously reported in the literature.^[10]

7. Mechanochemical synthesis of **4a–f**

General procedure for solid additive screening (Table S1)

A 10 mL ZrO₂-Mg milling vessel equipped with five milling balls (10 mm in diameter) of the same material was charged with 2-naphthol (**3a**, 100.0 mg, 0.69 mmol, 1.0 equiv), vanadinite (1.0 g, 2.44 equiv of the corresponding vanadium content) and a solid additive (300.0 mg). The jar was closed, flushed with oxygen and loaded with 1.0 atm of the gas. The mechanochemical reaction was conducted for 1 h at 600 rpm, for a total of two repetitions with 20 min break in between each one. At the end of this time the remaining pressure was released through one of the lid valves, ca. 3 mL of 1.0 M HCl were added and the crude mixture partitioned between water and EtOAc (ca. 3 mL). After phase separation, the aqueous phase was extracted three times with EtOAc (3 mL) and the organic phases combined. Next, the solvent removed under reduced pressure. To the remaining crude solid 1 mL of CDCl₃ was added and the mixture filtered on a shot silica plug directly into an NMR tube. The reported ratio of **4a:3a** was calculated based on the signals at 7.95–8.01 ppm (**4a**) and 7.73–7.81 ppm (**3a**).

Table S1 Optimization of reaction conditions for the mechanochemical oxidative coupling of **3a** in the presence of vanadinite. An extract of this table is reported in the manuscript under the name of Table 2.

Entry	O ₂ (atm)	Additive	4a:3a ^a
1 ^b	1.0	None	0:100
2	1.0	None	1:99
3	1.0	Glycine	1:99
4	1.0	Arginine	1:99
5	1.0	Methionine	1:99
6	1.0	Histidine	1:99
7	1.0	Glutamine	1:99
8	1.0	L-Proline	1:99
9	1.0	Glutamic acid	3:97
10	1.0	Aspartic acid	8:92
11	1.0	Tartaric acid	7:93
12	1.0	Citric acid	4:96
13	1.0	DPA	24:76
14	4.0	DPA	33:67
15	4.0	DPA, LAG (MeOH η = 0.5) ^c	87:13
16 ^d	4.0	DPA, LAG (MeOH η = 0.5)	89:11
17 ^e	4.0	DPA, LAG (MeOH η = 0.5)	68:32

Reaction conditions: **3a** (100.0 mg; 0.69 mmol), vanadinite ore (1.0 g; equivalent to 1.70 mmol of vanadium) and additive (300.0 mg) were milled in a planetary ball mill under an O₂ atmosphere in a 20 mL ZrO₂-Mg milling jar with five 10 mm Ø balls of the same material for 2 h at 600 rpm (1 h $\times$ 2; 20 min pause after each milling cycle).

^a Determined by ¹H NMR spectroscopy. ^b No vanadinite was added. ^c η is the volume of solvent (in μ L) divided by the total weight of the solid reactants (in mg). ^d Vanadinite 500.0 mg (0.85 mmol of vanadium) and DPA (150.0 mg, 0.90 mmol) were used. ^e Vanadinite 250.0 mg (0.42 mmol of vanadium) and DPA (75.0 mg, 0.45 mmol) were used.

General procedure for LAG screening (Table 3)

A 10 mL ZrO₂-Mg milling vessel equipped with five milling balls (10 mm in diameter) of the same material was charged with 2-naphthol (**3a**, 100.0 mg, 0.69 mmol, 1.0 equiv), vanadinite (250.0 mg, 0.6 equiv of the corresponding vanadium content), pyridine-2,6-dicarboxylic acid (75.0 mg, 0.45 mmol, 0.7 equiv) and a liquid additive (η = 0.05–0.5 μ L/mg). The jar was closed, flushed with oxygen, loaded with 4.0 atm of the gas. The mechanochemical reaction was conducted for 1 h at 600 rpm, for a total of two repetitions with 20 min break in between each one. At the end of this time the remaining pressure was released through one of the lid valves, ca. 3 mL of 1.0 M HCl were added and the crude mixture partitioned between water and EtOAc (ca. 50 mL). The biphasic mixture was filtrated on a short silica plug and the organic phase separated. The water phase was extracted three times with EtOAc (10 mL), the organic phases combined, and the solvent evaporated under reduced pressure. To the remaining crude solid was added 1,3,5-trimethoxybenzene as internal standard and ca.

3 mL of CDCl_3 . The mixture filtered through a short silica plug directly into an NMR tube. The reported yield was calculated based on the signals at 7.95–8.01 ppm (**4s**) and 6.11–6.19 ppm (internal standard).

General procedure for the mechanochemical synthesis of 1,1'-bi-2-naphthols (**4a-f**) with vanadinite

A 10 mL ZrO_2 -Mg milling vessel equipped with five milling balls (10 mm in diameter) of the same material was charged with 2-naphthol (**3a**) (100.0 mg, 0.69 mmol, 1.0 equiv), vanadinite (250.0 mg, 0.6 equiv of the corresponding vanadium content), pyridine-2,6-dicarboxylic acid (70.9 mg, 0.42 mmol, 0.6 equiv) and MeOH (21.0 μL , $\eta = 0.05 \mu\text{L/mg}$). The jar was closed, flushed with oxygen, loaded with 4.0 atm of the gas. The mechanochemical reaction was conducted for 1 h at 600 rpm, for a total of eight repetitions with 20 min break in between each cycle. At the end of this time the remaining pressure was released through one of the lid valves, ca. 3 mL of 1.0 M HCl were added and the crude mixture partitioned between water and EtOAc (ca. 50 mL). The biphasic mixture was filtrated through a short silica plug and the organic phase separated. The water phase was extracted three times with EtOAc (10 mL), the organic phases combined, and the solvent evaporated under reduced pressure. The [1,1'-binaphthalene]-2,2'-diol (**4a**) was obtained as pale yellow solid (85.6 mg, 0.30 mmol, 86% yield) after column chromatography (SiO_2/n -pentane:EtOAc 6:1 v/v).

[1,1'-Binaphthalene]-2,2'-diol (**4a**)

$R_f = 0.60$ (n -Pentane:EtOAc 2.5:1 v/v), UV-active.

m.p.: 217.9–218.5 °C.

^1H NMR (400 MHz, CDCl_3): δ = 7.93–8.02 (m, 2H, Ar-H), 7.85–7.93 (m, 2H, Ar-H), 7.34–7.42 (m, 4H, , Ar-H), 7.28–7.34 (m, 2H, Ar-H), 7.12–7.20 (m, 2H, Ar-H), 5.01–5.14 (br, 2H, 2xAr-OH) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ = 152.9, 135.5, 131.5, 129.6, 128.5, 127.6, 124.3, 124.2, 117.9, 111.0 ppm.

IR (ATR): ν = 3484, 3399, 3048, 3232, 2084, 1917, 1617, 1592, 1511, 1466, 1379, 1320, 1272, 1252, 1212, 1170, 1142, 958, 819, 749, 666 cm^{-1} .

MS (EI, 70 eV): m/z (%) = 287 (14) $[\text{M}+\text{H}]^+$, 286 (100) $[\text{M}]^+$, 257 (23), 239 (23), 120 (27).

The NMR data closely match the ones previously reported in the literature.^[11]

7,7'-Dimethoxy-[1,1'-binaphthalene]-2,2'-diol (4b)

The title compound was synthesized using the general procedure stated above.

7-Methoxy-2-naphthol (121.9 mg, 0.70 mmol, 1.0 eq), vanadinite (252.2 mg, 0.6 equiv of the corresponding vanadium content), pyridine-2,6-dicarboxylic acid (71.5 mg, 0.42 mmol, 0.6 equiv) and MeOH (22.3 μ L, η = 0.05 μ L/mg) were used.

Product **4b** was obtained as a pale yellow solid (116.3 mg, 0.34 mmol, 96%) after column chromatography (SiO_2/n -pentane:EtOAc 3:1 v/v) and washing with warm distilled *n*-pentane.

R_f = 0.18 (*n*-pentane:EtOAc 2:1 v/v), UV-active.

m.p.: 150.8–151.2 $^{\circ}\text{C}$.

^1H NMR (400 MHz, CDCl_3): δ = 7.83–7.92 (m, 2H, Ar-*H*), 7.74–7.82 (m, 2H, Ar-*H*), 7.25–7.19 (m, 2H, Ar-*H*), 7.00–7.07 (m, 2H, Ar-*H*), 6.45–6.53 (m, 2H, Ar-*H*), 4.97–5.11 (br, 2H, 2 $\times$ Ar-OH) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ = 159.2, 153.5, 134.8, 131.3, 130.1, 124.9, 116.2, 115.2, 110.2, 103.3, 55.3 ppm.

IR (ATR): ν = 3376, 3004, 2933, 2834, 2318, 2112, 2077, 1906, 1742, 1620, 1510, 1456, 1431, 1377, 1333, 1267, 1215, 1145, 1068, 1028, 1000, 955, 871, 825, 695 cm^{-1} .

MS (EI, 70 eV): m/z (%) = 347 (13) [$M+H$] $^+$, 346 (100) [M] $^+$.

The NMR data closely match the ones previously reported in the literature.^[11]

6,6'-Dibromo-[1,1'-binaphthalene]-2,2'-diol (4c)

The title compound was synthesized using the general procedure stated above.

6-Bromo-2-naphthol (156.1 mg, 0.7 mmol, 1.0 equiv), vanadinite (252.5 mg, 0.6 equiv of the corresponding vanadium content), pyridine-2,6-dicarboxylic acid (71.5 mg, 0.42 mmol, 0.6 equiv) and MeOH (24.0 μ L, η = 0.05 μ L/mg) were used. Product **4c** was obtained as a pale yellow solid (82.0 mg, 0.18 mmol, 53%) after column chromatography (SiO_2/n -Pentane:EtOAc 3:1 v/v) and washing with warm distilled *n*-pentane.

R_f = 0.13 (*n*-Pentane:EtOAc 2:1 v/v), UV-active.

m.p.: 189.3–191.0 $^{\circ}\text{C}$.

^1H NMR (400 MHz, CDCl_3): δ = 8.02–8.08 (m, 2H, Ar-*H*), 7.94–7.85 (m, 2H, Ar-*H*), 7.33–7.44 (m, 4H, Ar-*H*), 6.91–7.01 (m, 2H, Ar-*H*), 4.96–5.05 (br, 2H, 2 $\times$ Ar-OH) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ = 153.1, 132.0, 131.0, 130.9, 130.7, 130.6, 126.0, 119.1, 118.2, 110.7 ppm.

IR (ATR): ν = 3465, 3409, 3255, 2921, 2852, 2658, 2324, 2108, 1909, 1762, 1583, 1493, 1409, 1379, 1316, 1262, 1212, 1168, 1146, 1066, 961, 924, 875, 812, 770, 670 cm^{-1} .

MS (EI, 70 eV): m/z (%) = 446 (45) $[M+2H]^+$, 444 (100) $[M]^+$, 442 (76) $[M-2H]^+$, 256 (31), 255 (31), 226 (36), 142 (31), 118 (23), 113 (23).

The NMR data closely match the ones previously reported in the literature.^[11]

3,3'-Dibromo-[1,1'-binaphthalene]-2,2'-diol (**4d**)

The title compound was synthesized using the general procedure stated above.

3-Bromo-2-naphthol (156.1 mg, 0.7 mmol, 1.0 equiv), vanadinite (252.5 mg, 0.6 equiv of the corresponding vanadium content), pyridine-2,6-dicarboxylic acid (71.5 mg, 0.42 mmol, 0.6 equiv) and MeOH (24.0 μL , η = 0.05 $\mu\text{L}/\text{mg}$) were used. Product **4d** was obtained as a pale yellow solid (56.7 mg, 0.13 mmol, 36%) after column chromatography (SiO_2/n -pentane:EtOAc 6:1 v/v) and washing with warm distilled n -pentane.

R_f = 0.65 (n -pentane:EtOAc 3:1 v/v), UV-active.

m.p.: 286.7–287.3 $^{\circ}\text{C}$.

^1H NMR (400 MHz, CDCl_3): δ = 8.21–8.30 (m, 2H, Ar- H), 7.78–7.87 (m, 2H, Ar- H), 7.35–7.42 (m, 2H, Ar- H), 7.28–7.34 (m, 2H, Ar- H), 7.05–7.13 (m, 2H, Ar- H), 5.49–5.58 (br, 2H, 2 $\times$ Ar-OH) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ = 148.2, 132.9, 129.9, 127.8, 127.6, 125.0, 124.8, 114.8, 112.4 ppm.

IR (ATR): ν = 3486, 3151, 3095, 2924, 2668, 2324, 2084, 1910, 1837, 1733, 1574, 1495, 1419, 1376, 1314, 1216, 1143, 1002, 929, 876, 855, 791, 748, 685 cm^{-1} .

MS (EI, 70 eV): m/z (%) = 446 (45) $[M+2H]^+$, 444 (100) $[M]^+$, 442 (76) $[M-2H]^+$, 256 (20), 255 (33), 226 (44), 142 (31), 133 (22), 113 (30).

The NMR data closely match the ones previously reported in the literature.^[12]

6,6'-Diphenyl-[1,1'-binaphthalene]-2,2'-diol (4e)

The title compound was synthesized using the general procedure stated above.

6-Phenylnaphthalen-2-ol **3e** (154.2 mg, 0.7 mmol, 1.0 equiv), vanadinite (252.5 mg, 0.6 equiv of the corresponding vanadium content), pyridine-2,6-dicarboxylic acid (71.5 mg, 0.42 mmol, 0.6 equiv) and MeOH (23.9 μ L, η = 0.05 μ L/mg) were used. Product **4e** was obtained as a pale yellow solid (111.1 mg, 0.25 mmol, 72%) after column chromatography (SiO₂/*n*-pentane:EtOAc 7:1 v/v).

R_f = 0.45 (*n*-Pentane:EtOAc 2:1 v/v), UV-active.

m.p.: 171.7–172.6 °C.

¹H NMR (400 MHz, CDCl₃): δ = 8.09–8.15 (m, 2H, Ar-*H*), 8.01–8.09 (m, 2H, Ar-*H*), 7.65–7.63 (m, 4H, Ar-*H*), 7.56–7.64 (m, 2H, Ar-*H*), 7.53–7.41 (m, 6H, Ar-*H*), 7.33–7.41 (m, 2H, Ar-*H*), 7.25–7.32 (m, 2H, Ar-*H*), 5.07–5.18 (m, 2H, 2×Ar-OH) ppm.

¹³C{¹H} NMR (101 MHz, CDCl₃): δ = 153.0, 140.9, 137.1, 132.7, 131.9, 129.9, 129.0, 127.4, 127.4, 127.3, 126.5, 124.9, 118.4, 110.9 ppm.

IR (ATR): ν = 3463, 3396, 3027, 2923, 2320, 2108, 1989, 1908, 1717, 1593, 1491, 1446, 1383, 1352, 1281, 1213, 1148, 1074, 1022, 964, 934, 885, 813, 752, 692 cm⁻¹.

MS (EI, 70 eV): *m/z* (%) = 439 (31) [*M*+H]⁺, 438 (100) [*M*]⁺, 77 (15).

The NMR data closely match the ones previously reported in the literature.^[13]

[1,2':5',1'':6'',1'''-Quaternaphthalene]-2'',6'-diol (4f)

The title compound was synthesized using the general procedure stated above.

1,2'-Binaphthalen-6'-ol **3f** (189.2 mg, 0.7 mmol, 1.0 equiv), vanadinite (252.5 mg, 0.6 equiv of the corresponding vanadium content), pyridine-2,6-dicarboxylic acid (71.5 mg, 0.42 mmol, 0.6 equiv) and MeOH (25.6 μ L, η = 0.05 μ L/mg) were used. Product **4f** was obtained as a brown solid (56.9 mg, 0.11 mmol, 30%) after column chromatography (SiO₂/*n*-pentane:EtOAc 7:1 v/v).

R_f = 0.18 (*n*-pentane:EtOAc 2:1 v/v), UV-active.

m.p.: 166.2–167.8 °C.

^1H NMR (400 MHz, CDCl_3): δ = 8.04–8.08 (m, 4H, Ar–H), 7.88–7.99 (m, 6H, Ar–H), 7.47–7.59 (m, 9H, Ar–H), 7.38–7.45 (m, 4H, Ar–H), 5.11–5.28 (br, 2H, 2×Ar–OH) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ = 153.2, 140.0, 136.8, 134.0, 132.7, 131.8, 130.3, 129.7, 129.5, 128.5, 127.9, 127.4, 126.3, 126.2, 126.0, 125.6, 124.2, 118.4, 111.0 ppm.

IR (ATR): ν = 3857, 3510, 3048, 2924, 2324, 2113, 2068, 1925, 1710, 1591, 1476, 1382, 1349, 1280, 1145, 932, 895, 777, 689 cm^{-1} .

MS (EI, 70 eV): m/z (%) = 540 (1) $[M+2\text{H}]^+$, 539 $[M+\text{H}]^+$, 538 $[M]^+$.

The NMR data closely match the ones previously reported in the literature.^[14]

8. References

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9. NMR spectra

N-Allyl-*N*-benzylamine (S1a)

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

***N*-Allyl-*N*-benzyl-2-bromo-2-methylpropanamide (1a)**¹H NMR (400 MHz, Toluene-*d*₈, 95 °C)

***N*-Allyl-2-bromo-*N*-2-dimethylpropanamide (1b)**¹H NMR (400 MHz, Toluene-*d*₈, 95 °C) ¹³C{¹H} NMR (101 MHz, Toluene-*d*₈, 95 °C)

***N*-Allyl-4-methylbenzenesulfonamide (S1c)**¹H NMR (600 MHz, CDCl₃) ¹³C{¹H} NMR (151 MHz, CDCl₃)

***N*-Allyl-2-bromo-2-methyl-*N*-tosylpropanamide (1c)**¹H NMR (600 MHz, CDCl₃) ¹³C{¹H} NMR (151 MHz, CDCl₃)

***N*-(2-Methylallyl)benzylamine (S1d)**¹H NMR (400 MHz, CDCl₃) ¹³C{¹H} NMR (101 MHz, CDCl₃)

***N*-Benzyl-2-bromo-2-methyl-*N*-(2-methylallyl)propanamide (1d)**¹H NMR (600 MHz, Toluene-*d*₈, 95 °C) ¹³C{¹H} NMR (151 MHz, Toluene-*d*₈, 95 °C)

***N*-benzylhexa-2,4-dien-1-amine product (S1e)**¹H NMR (600 MHz, CDCl₃) ¹³C{¹H} NMR (151 MHz, CDCl₃)

***N*-Benzyl-2-bromo-*N*-(hexa-2,4-dien-1-yl)-2-methylpropanamide (1e)**¹H NMR (600 MHz, Toluene-*d*₈, 95 °C) ¹³C{¹H} NMR (151 MHz, Toluene-*d*₈, 95 °C)

***N*-Benzyl-*N*-prenylamine (S1f)** ^1H NMR (400 MHz, CDCl_3)

***N*-Benzyl-2-bromo-2-methyl-*N*-(3-methylbut-2-en-1-yl)propanamide (1f)**¹H NMR (600 MHz, Toluene-*d*₈, 95 °C) ¹³C{¹H} NMR (151 MHz, Toluene-*d*₈, 95 °C)

1-Benzyl-4-(bromomethyl)-3,3-dimethylpyrrolidin-2-one (2a)
 ^1H NMR (600 MHz, CDCl_3)

 $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3)

4-(Bromomethyl)-1,3,3-trimethylpyrrolidin-2-one (2b) ^1H NMR (600 MHz, CDCl_3) $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3)

4-(Bromomethyl)-3,3-dimethyl-1-tosylpyrrolidin-2-one (2c) ^1H NMR (600 MHz, CDCl_3) $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3)

1-Benzyl-4-(bromomethyl)-3,3,4-trimethylpyrrolidin-2-one (2d) ^1H NMR (600 MHz, CDCl_3)

(E)-1-benzyl-4-(3-bromobut-1-en-1-yl)-3,3-dimethylpyrrolidin-2-one (2e)¹H NMR (600 MHz, CDCl₃) ¹³C{¹H} NMR (151 MHz, CDCl₃)

1D Selective Gradient COSY, freq: 5.698 ppm

1-Benzyl-3,3-dimethyl-4-(prop-1-en-2-yl)pyrrolidin-2-one (2f) and 1-Benzyl-3,3-dimethyl-4-(propan-2-ylidene)pyrrolidin-2-one (2f')

^1H NMR (600 MHz, CDCl_3)

$^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3)

6-Phenylnaphthalen-2-ol (3e) ^1H NMR (400 MHz, $\text{DMSO}-d_6$) $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, $\text{DMSO}-d_6$)

[1,2'-Binaphthalen]-6'-ol (3f) ^1H NMR (400 MHz, $\text{DMSO}-d_6$) $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, $\text{DMSO}-d_6$)

[1,1'-binaphthalene]-2,2'-diol (4a) ^1H NMR (400 MHz, CDCl_3) $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

7,7'-dimethoxy-[1,1'-binaphthalene]-2,2'-diol (4b) ^1H NMR (400 MHz, CDCl_3) $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

6,6'-dibromo-[1,1'-binaphthalene]-2,2'-diol (4c)¹H NMR (400 MHz, CDCl₃) ¹³C{¹H} NMR (101 MHz, CDCl₃)

3,3'-dibromo-[1,1'-binaphthalene]-2,2'-diol (4d) ^1H NMR (400 MHz, CDCl_3) $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

6,6'-diphenyl-[1,1'-binaphthalene]-2,2'-diol (4e) ^1H NMR (400 MHz, CDCl_3) $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

[1,2':5',1'':6'',1''':quaternaphthalene]-2'',6'-diol (4f) ^1H NMR (400 MHz, CDCl_3) $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

10. Minerals PXRD and elemental analysis

Code references:

Covellite – RWTHFPCUC

Bornite – RWTHFPCUB

Vanadinite – RWTHFPV1

PXRD analysis of the minerals used in this work

Elemental analysis of the minerals used in this work

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CERTIFICATE LR19093865

P.O. No.: 4910033301
This report is for 5 Pulp samples submitted to our lab in Loughrea, Ireland on 19-Apr-2019.
The following have access to data associated with this certificate:
FRANCESCO PUCETTI

SAMPLE PREPARATION	
ALS CODE	DESCRIPTION
WEI-21	Received Sample Weight
LOG-24	Pulp Login - Rcd w/o Barcode
ANALYTICAL PROCEDURES	
ALS CODE	DESCRIPTION
As-OG62	Ore Grade As - Four Acid
ME-OG62	Ore Grade Elements - Four Acid
S-OG62	Ore Grade S - Four Acid
V-OG62	Ore Grade V - Four Acid
ME-ICP61	33 element four acid ICP-AES
Ag-OG62	Ore Grade Ag - Four Acid
Cu-OG62	Ore Grade Cu - Four Acid
Pb-OG62	Ore Grade Pb - Four Acid
	ICP-AES
	ICP-AES

This is the Final Report and supersedes any preliminary report with this certificate number. Results apply to samples as submitted. All pages of this report have been checked and approved for release.
***** See Appendix Page for comments regarding this certificate *****
Comments: AMENDMENT TO CERTIFICATE ISSUED MAY 28TH 2019 IN ORDER TO REPORT ME-ICP61 RESULTS FOR SAMPLE RWHFPCUB.

Signature:
Andrey Tarrow, Technical Manager, Ireland

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CERTIFICATE OF ANALYSIS

LR19093865

Sample Description	Method Analyte Units LOD	WEI-21 Recd Wt. kg	ME-ICP61 Ag ppm	ME-ICP61 Al %	ME-ICP61 As ppm	ME-ICP61 Ba ppm	ME-ICP61 Be ppm	ME-ICP61 Bi ppm	ME-ICP61 Ca %	ME-ICP61 Cd ppm	ME-ICP61 Co ppm	ME-ICP61 Cr ppm	ME-ICP61 Cu ppm	ME-ICP61 Fe %	ME-ICP61 Ga ppm	ME-ICP61 K %
RWTHPEVY		<0.02	3.8	0.02	>10000	30	<0.5	28	0.20	<0.5	<1	13	<1	0.03	<10	<0.01
RWTHPEVR		<0.02	4.1	0.08	2690	1400	<0.5	29	0.26	20.9	<1	186	<1	0.05	<10	0.03
RWTHPEV1		<0.02	3.3	0.03	>10000	110	<0.5	25	0.81	1.7	<1	12	<1	0.04	<10	0.01
RWTHPEUC		<0.02	>100	0.02	3970	10	<0.5	21	0.04	20.5	67	2	>10000	9.75	310	0.02
RWTHPEUCB		<0.02	18.1	0.09	40	<10	<0.5	<2	0.01	0.5	8	4	>10000	13.30	20	0.02

Comments: AMENDMENT TO CERTIFICATE ISSUED MAY 28TH 2019 IN ORDER TO REPORT ME-ICP61 RESULTS FOR SAMPLE RWTHPEUCB.

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Sample Description	Method Analyte Units LOD	ME-ICP61 La ppm	ME-ICP61 Mg %	ME-ICP61 Mn ppm	ME-ICP61 Mo ppm	ME-ICP61 Na %	ME-ICP61 Ni ppm	ME-ICP61 P ppm	ME-ICP61 Pb ppm	ME-ICP61 S %	ME-ICP61 Sb ppm	ME-ICP61 Sc ppm	ME-ICP61 Sr ppm	ME-ICP61 Th ppm	ME-ICP61 Ti %	ME-ICP61 Tl ppm
RWTHPEVY		10	0.04	119	3	0.01	<1	5890	>10000	0.03	19	<1	338	<20	<0.01	<10
RWTHPEVR		10	0.06	14	<1	<0.01	<1	9870	>10000	0.07	49	<1	354	<20	<0.01	<10
RWTHPEV1		10	0.23	427	5	0.01	<1	5820	>10000	0.03	21	<1	309	<20	<0.01	<10
RWTHPEUC		<10	<0.01	18	411	0.01	14	50	958	>10.0	119	<1	<1	<20	<0.01	<10
RWTHPEUCB		<10	<0.01	<5	19	0.01	<1	<10	746	>10.0	13	<1	1	<20	<0.01	<10

Comments: AMENDMENT TO CERTIFICATE ISSUED MAY 28TH 2019 IN ORDER TO REPORT ME-ICP61 RESULTS FOR SAMPLE RWTHPEUCB.

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CERTIFICATE OF ANALYSIS

LR19093865

Sample Description	Method Analyte Units LOD	ME-ICP61 U ppm 10	ME-ICP61 V ppm 1	ME-ICP61 W ppm 10	ME-ICP61 Zn ppm 2	Ag-OC62 Ag ppm 1	Cu-OC62 Cu ppm 0.001	Pb-OC62 Pb ppm 0.001	As-OC62 As ppm 0.001	S-OC62 S ppm 0.01	V-OC62 V ppm 0.01
RWTHPEVY		<10	>10000	<10	117			>20.0	1.535		8.67
RWTHPEVR		<10	>10000	450	1510			>20.0			9.54
RWTHPEV1		<10	>10000	<10	485			>20.0	1.535		8.64
RWTHPEUC		<10	24	30	1680	1220	61.1			18.30	
RWTHPEUCB		<10	35	10	379		50.6			19.75	

Comments: AMENDMENT TO CERTIFICATE ISSUED MAY 28TH 2019 IN ORDER TO REPORT ME-ICP61 RESULTS FOR SAMPLE RWTHPEUCB.

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CERTIFICATE COMMENTS	
Applies to Method:	<p>The methods immediately below this line are ISO 17025:2005 Accredited. INAB Registration No: 173T</p> <p>Ag-OG62 As-OG62 Cu-OG62 ME-OG62 Pb-OG62 S-OG62</p> <p> </p> <p>Processed at ALS Loughrea located at Dublin Road, Loughrea, Co. Galway, Ireland.</p> <p>Ag-OG62 As-OG62 Cu-OG62 ME-ICP61 ME-OG62 Pb-OG62 V-OG62 WEI-21</p> <p>ME-ICP61 V-OG62</p> <p>LOG-24 S-OG62</p>

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