

Supporting Information for:

## **Production of Alkoxy-Functionalized Cyclohexylamines from Lignin-Derived Guaiacols**

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## Experimental Procedures

**Chemicals and materials.** Palladium hydroxide on carbon ( $\text{Pd}(\text{OH})_2/\text{C}$ , Pd 20% on carbon), morpholine (99%), 4-cyclohexylmorpholine (99%), 3-methylpiperidine (>98%), 4-methylpiperidine (>98%), 4-butoxyphenol (97%), 4-ethoxyphenol (99%), 3-ethoxyphenol (>97%), 3-isopropylphenol (>98%), *m*-cresol (98%), *p*-cresol (99%), cyclohexanol (>98.5%), 4-ethoxycyclohexanone (96%), ruthenium on carbon (Ru/C, 5 wt% Ru, reduced), and *m*-xylene (>99%) were purchased from Aladdin. Guaiacol (98%), phenol (99.5%), *n*-dodecane (99.5%), 2-methoxycyclohexanone (95%) and cyclohexanone (99%) were obtained from TCI. Methylmorpholine (97%), 2,2-dimethylmorpholine (97%), 4-propoxyphenol (97%), 2-propoxyphenol (97%), 3-methoxyphenol (95%) and 2-ethoxyphenol (98%) were purchased from ARK. *cis*-2,6-Dimethylmorpholine (97%), 4-methoxycyclohexanone (97%) and (1*S*, 2*S*)-(+)-2-methoxycyclohexanol (ChiPros 99%, ee 98%) were provided by Alfa. Palladium on carbon (Pd/C, 10 wt% Pd, reduced, anhydrous), 3-methoxy-cyclohexanone (96%), 2-ethoxycyclohexanone (98%), platinum on carbon (Pt/C, 10 wt% Pt, reduced, anhydrous) and 4-isopropylphenol (98%) were purchased from Innochem. Piperidine (>99%) was obtained from Sinopharm. 2-propoxy-cyclohexanone (97%), 3-butoxy-cyclohexanone (98%), 4-propoxy-cyclohexanone (96%), 3-ethoxycyclohexanone (96%), 4-butoxy-cyclohexanone (97%), 2-butoxy-cyclohexanone (96%) were obtained from Bide Pharmatech Ltd.

**Hydrogenation reaction.** In a typical experiment, 2-methoxycyclohexanone (1 mmol), morpholine (2.5 mmol), Pd/C (3 mol% Pd metal based on guaiacol), and *m*-xylene (3 mL) were added into a stainless-steel reactor of 15 mL with a Teflon coating. After the air in the autoclave was replaced by hydrogen (three times), the autoclave was pressurized to the desired pressure with  $\text{H}_2$  (2MPa). Then, the autoclave was placed into a constant-temperature air bath and heated to the desired temperature (120 °C), and the reactions were conducted with a stirring rate of 800 rpm for the desired reaction time (12 h). After the reaction, the products were analyzed quantitatively using *n*-

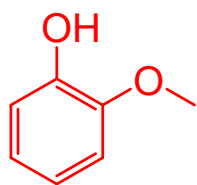
dodecane as the internal standard by gas chromatography (GC) and gas chromatography coupled with mass spectroscopy (GC-MS). In addition, to ensure the reliability of the obtained results, each experiment was repeated three times under the same reaction conditions.

**Examination of the recyclability.** To test the recyclability of Pd/C, the catalyst was separated from the reaction system by filtration, washed with ethanol for 4 times, and then dried under oven at 60 °C for 12 h. The sample was collected and transferred into a ceramic boat, then moved to a tubular furnace for reduction under H<sub>2</sub>/Ar atmosphere (containing 90% Ar) with a flow rate of 100 mL min<sup>-1</sup>. The sample was heated with a heating rate of 5 °C min<sup>-1</sup> from room temperature to 250 °C and held at this temperature for 5 h. Afterwards, the tubular furnace was cooled down to room temperature. Finally, the catalyst was used in the next catalytic cycle.

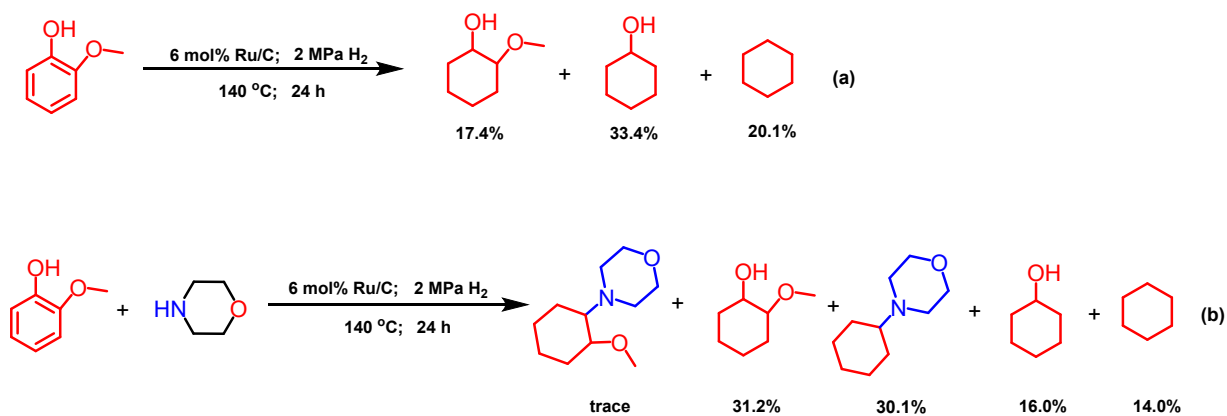
**Synthesis of the standard products.** Because there were no commercial resources, we pre-synthesized the products as the standards. Taking the synthesis of 4-(2-methoxycyclohexyl)morpholine as an example, guaiacol (1 mmol), morpholine (2.5 mmol), Pd/C (6 mol% Pd metal based on guaiacol), and m-xylene (3 mL) were added into a stainless-steel reactor of 15 mL with a Teflon coating. After the air in the reactor was replaced by hydrogen (three times), the reactor was pressurized to 2 MPa with H<sub>2</sub>. Then, the autoclave was placed into a constant-temperature air bath and heated to 140 °C, and the reactions were conducted with a stirring rate of 800 rpm for 24 h. After the reaction, pure 4-(2-methoxycyclohexyl)morpholine was obtained by column chromatography (silica gel) using petroleum ether/EtOAc (1:1, 500 mL), and subsequently pure EtOAc as the elution solvent. Additionally, similar routes were employed to prepare other standard products.

**Preparation of Ni/C.** Ni/C (10 wt%) was prepared *via* incipient wetness impregnation based on a reported procedure with some modifications.<sup>S1</sup> Initially, active carbon (C, 2

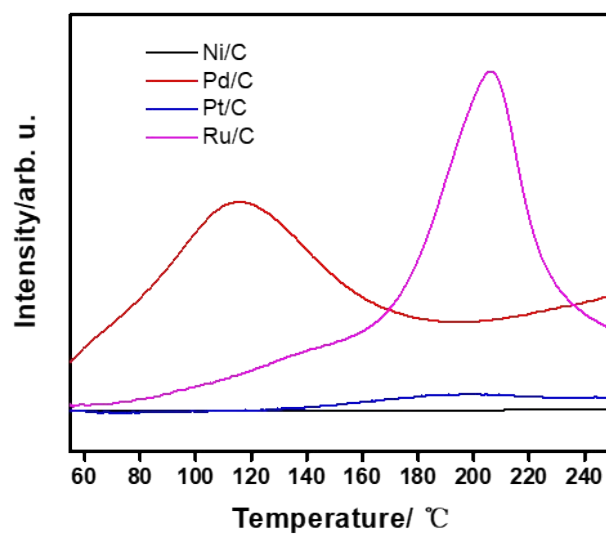
g) was impregnated with an aqueous solution (30 mL) of  $\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$  (1.1 g) for 10 h. Subsequently, the water was removed by rotary evaporation at 80 °C, and the fine solid mixture of C and  $\text{Ni}(\text{NO}_3)_2$  was obtained. Finally, the obtained solid was reduced (3 h, 2 °C min<sup>-1</sup>, 100 mL min<sup>-1</sup> 10% H<sub>2</sub> in Ar), and then passivated (1 h, 100 mL min<sup>-1</sup> 1% O<sub>2</sub> in Ar) at room temperature. The obtained Ni/C was stored in a vacuum dryer.



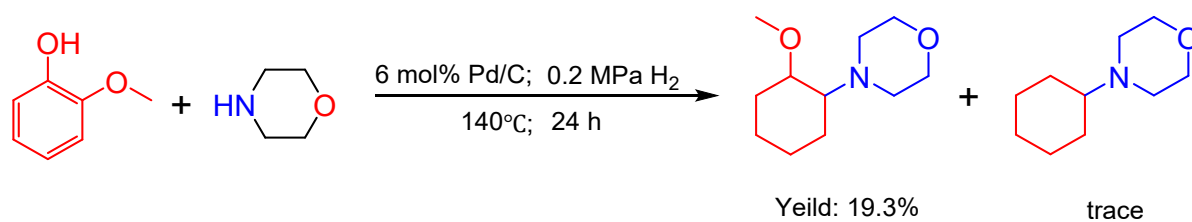
**Fig. S1.** The chemical structure of guaiacol.



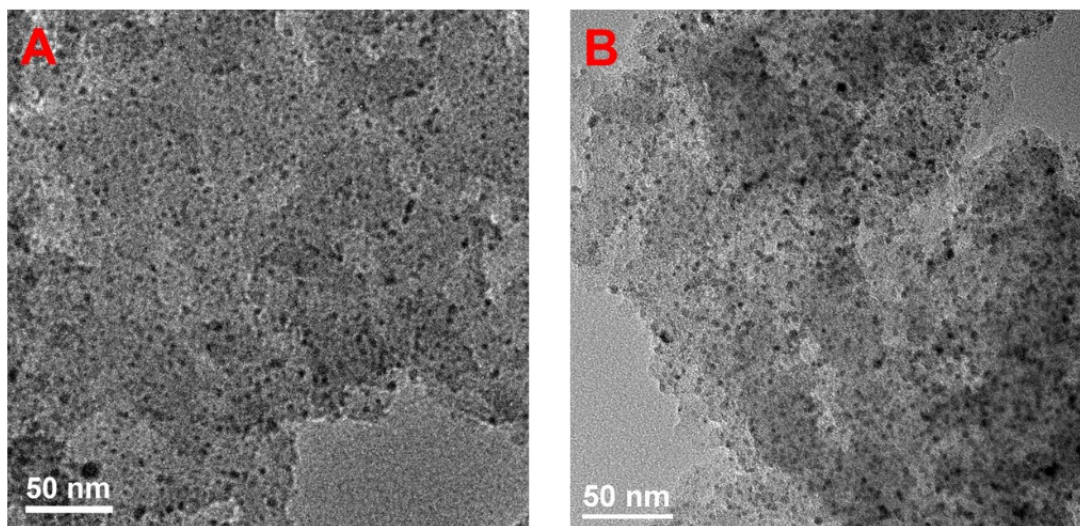
**Fig. S2.** Activity of Ru/C in several control experiments.



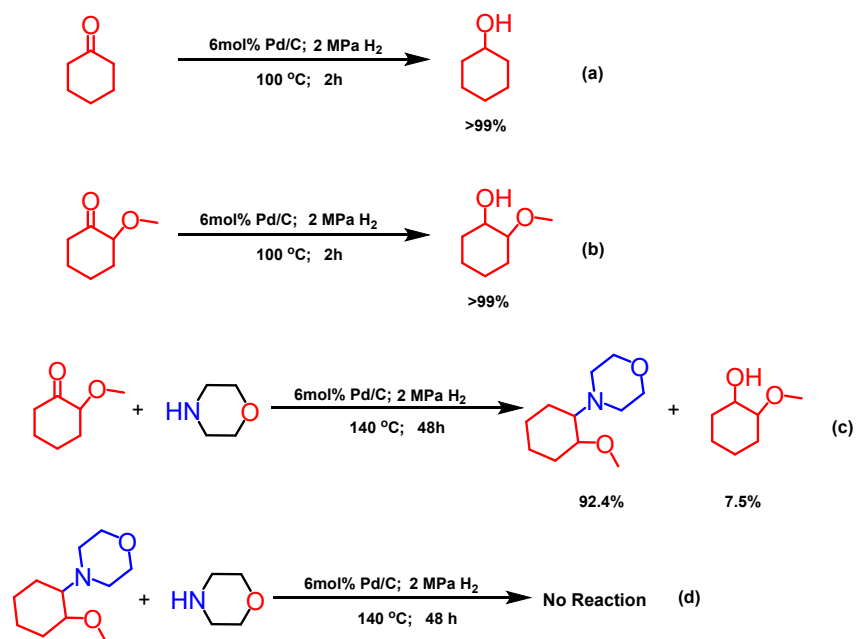
**Fig. S3.** The profiles of H<sub>2</sub>-TPR.



**Fig. S4.** The control experiments for studying the roles of H<sub>2</sub>.

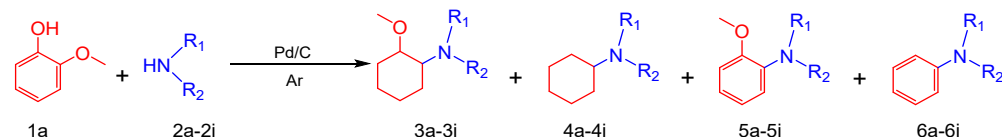


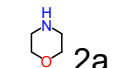
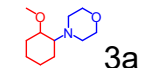
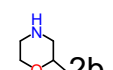
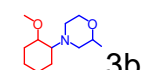
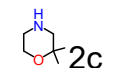
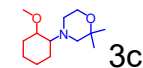
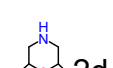
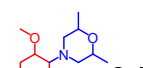
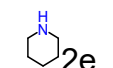
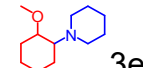
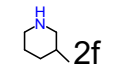


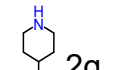


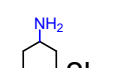




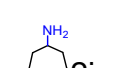


**Fig. S5.** (A) The original Pd/C, and (B) the recycled Pd/C.



**Fig. S6.** The control experiments for studying the pathway of reactions

**Table S1.** Pd-catalyzed reductive coupling of guaiacol with various amines at Ar. <sup>a</sup>



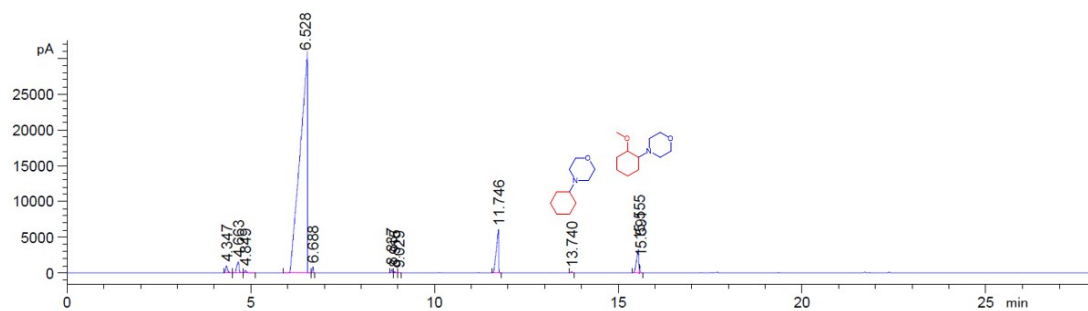
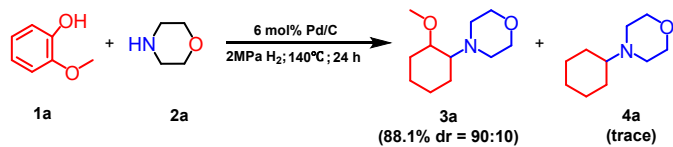
Entry	Substrates	Main Products	Yields (%) <sup>b,c</sup>
1	 2a	 3a	trace
2	 2b	 3b	trace
3	 2c	 3c	trace
4	 2d	 3d	trace
5	 2e	 3e	trace
6	 2f	 3f  4f	20.1/18.1
7	 2g	 3g  4g	25.2/20.2
8	 2h	 3h  4h  5h  6h	10.1/23.2/20.1/52.3
9	 2i	 3i  5i	43.2/20.1

<sup>a</sup> Reaction conditions: 1, 1.0 mmol; 2, 2.5 mmol; catalyst, 6 mol% metal based on 1; *m*-xylene, 3.0 mL; reaction temperature, 140 °C; Ar pressure, 2 MPa; reaction time, 24 h. <sup>b</sup> The yields were determined by GC using dodecane as a standard. <sup>c</sup> The values in the parentheses were the standard deviations.

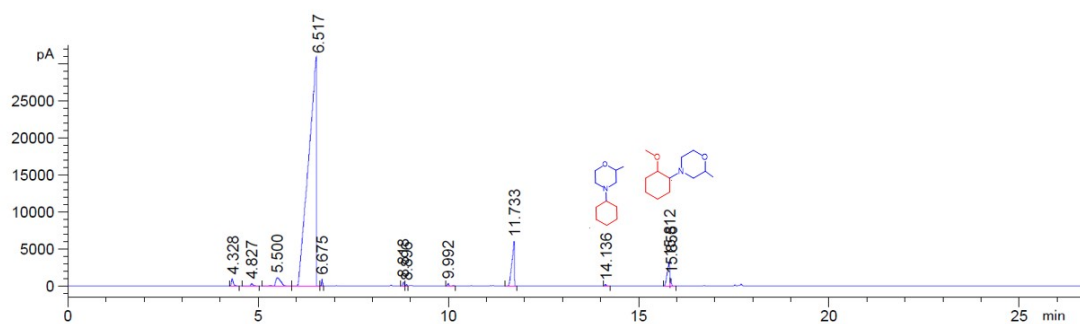
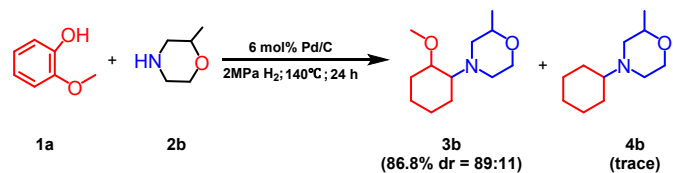


## Chromatograms for GC-measurements

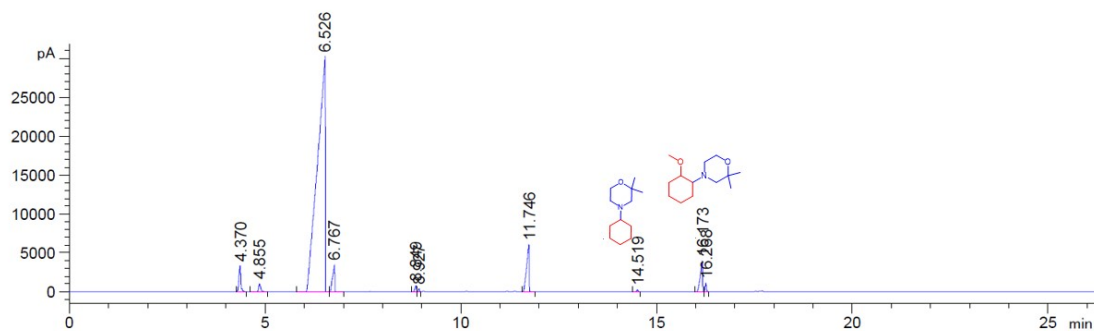
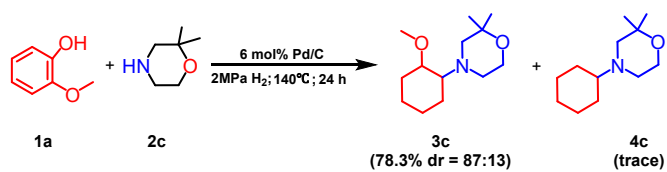
### Reaction 1



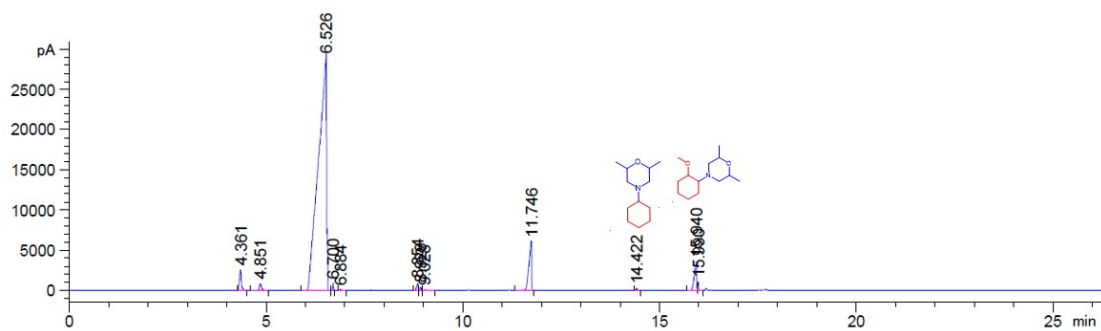
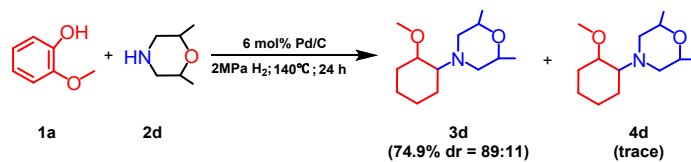
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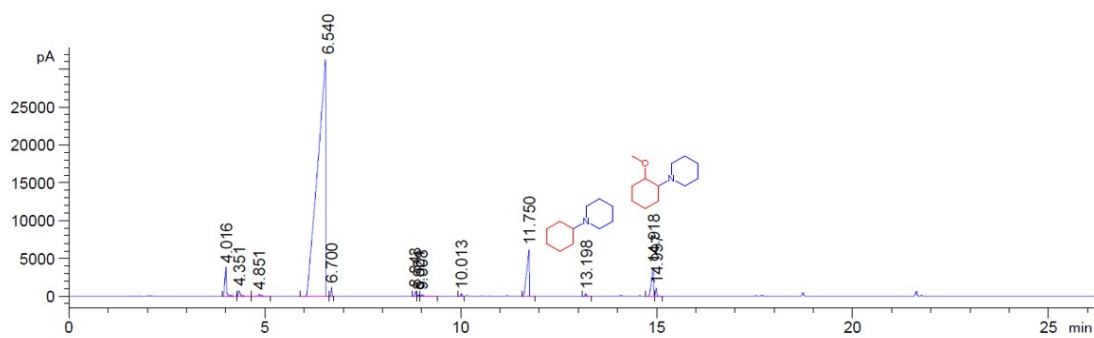
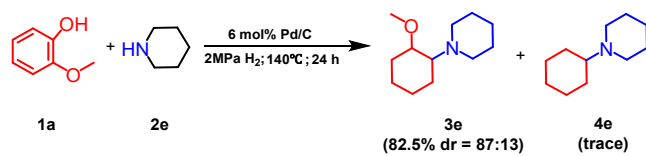
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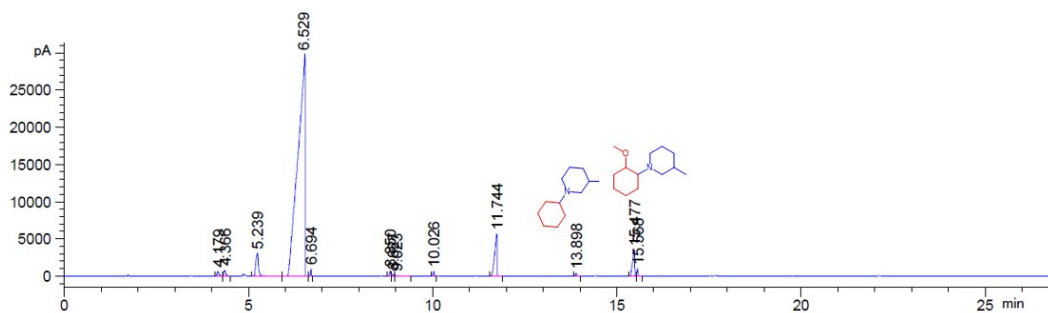
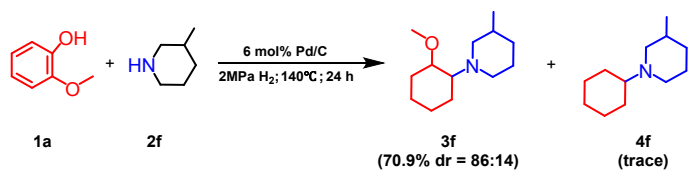
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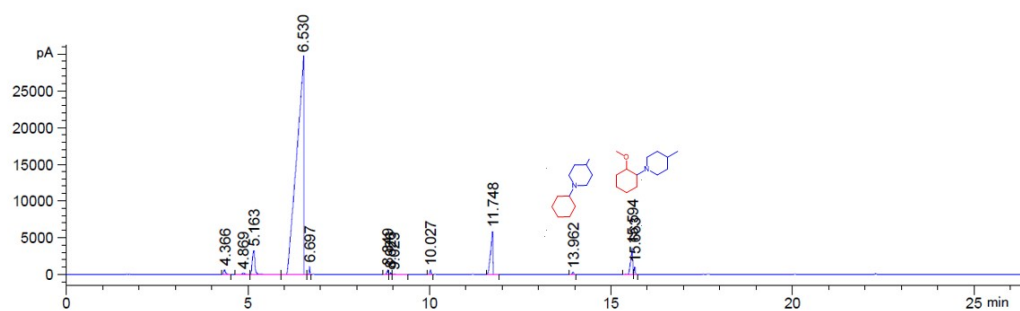
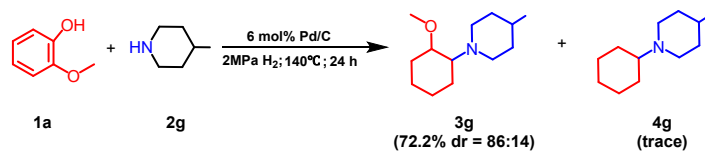
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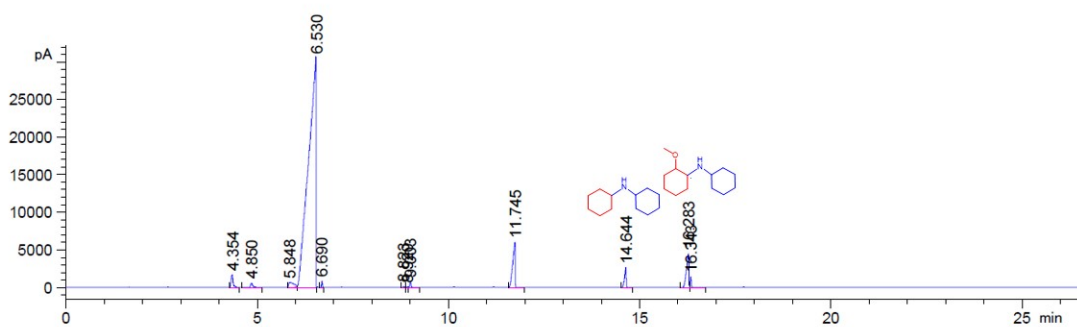
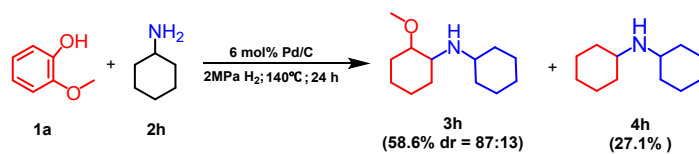
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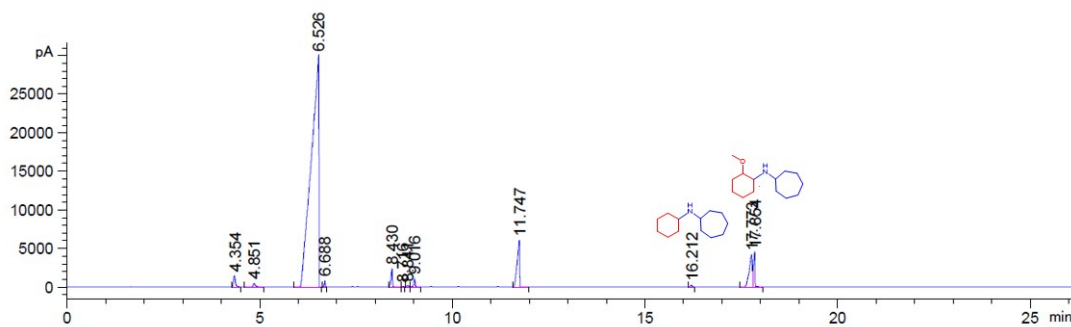
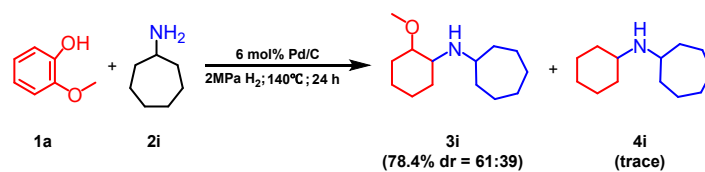
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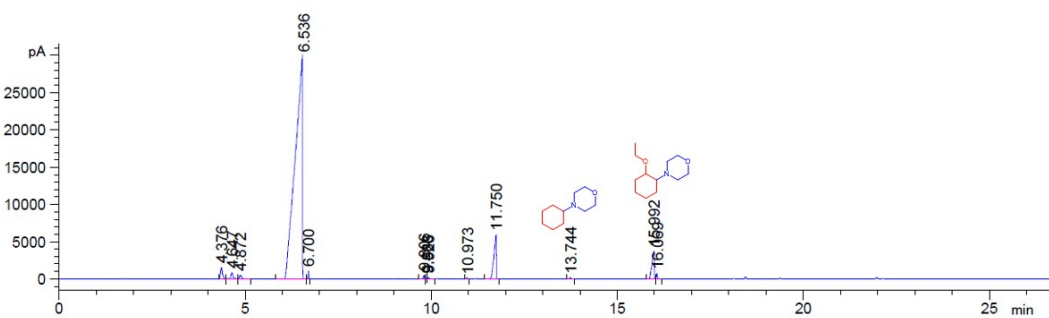
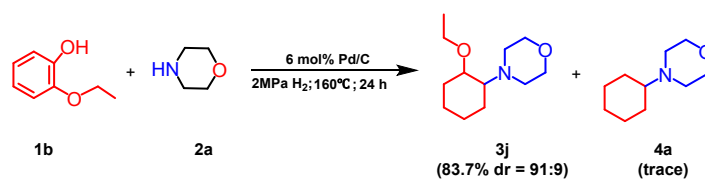
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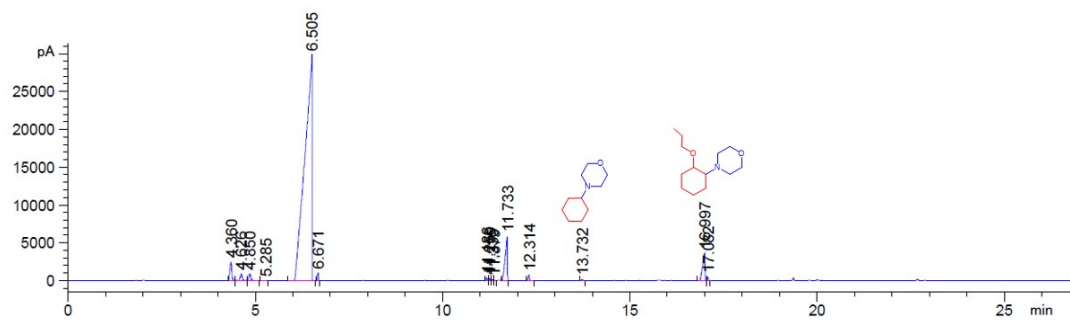
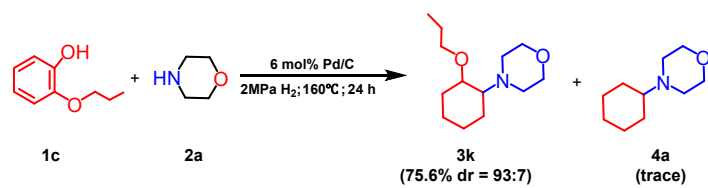
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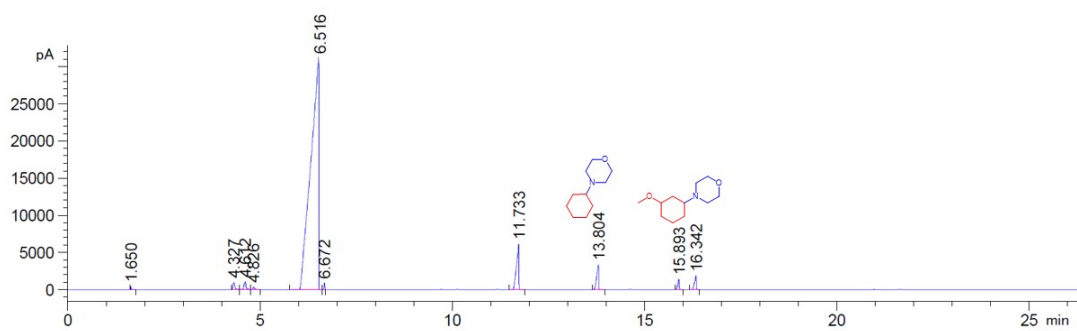
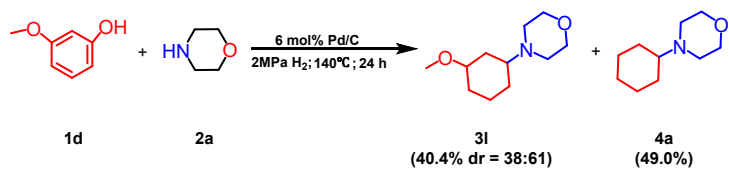
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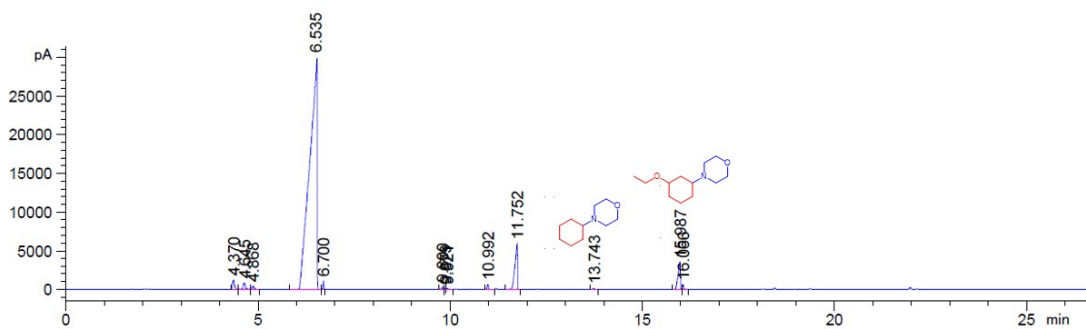
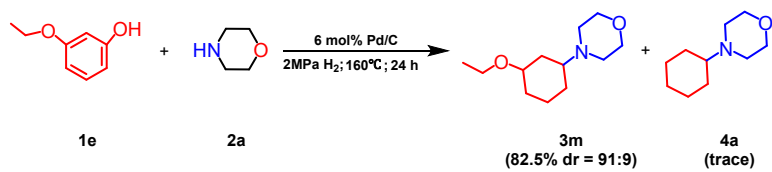
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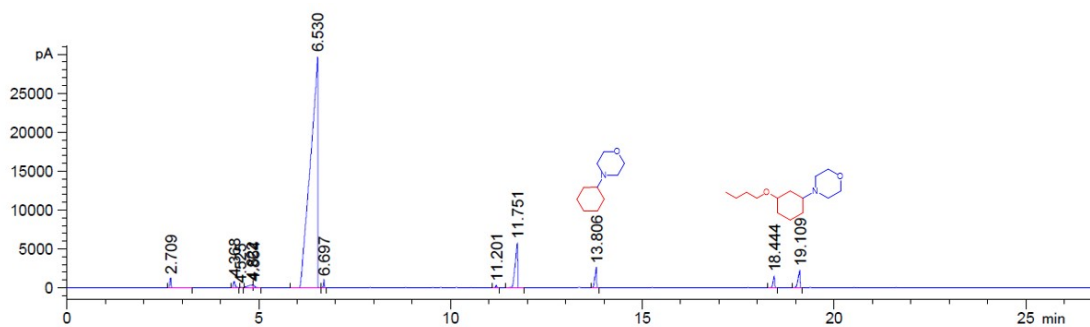
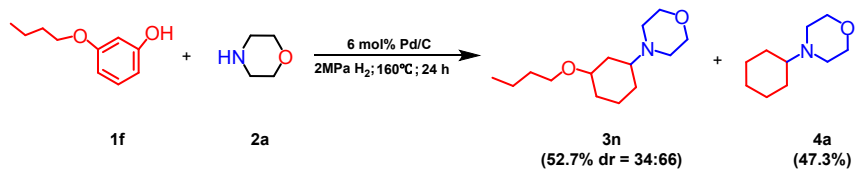
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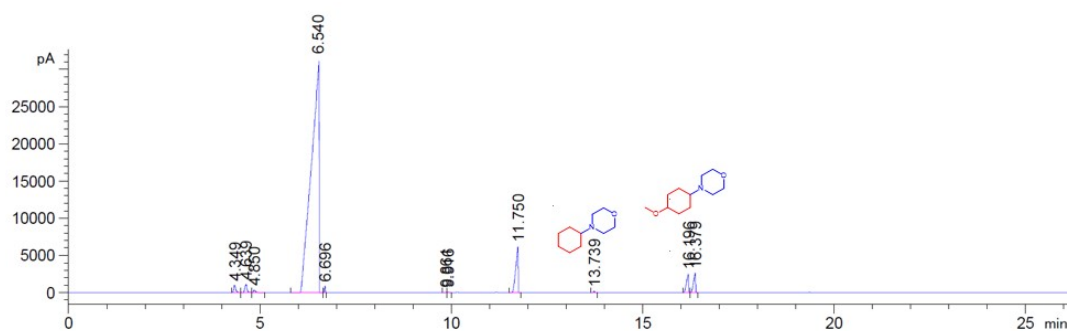
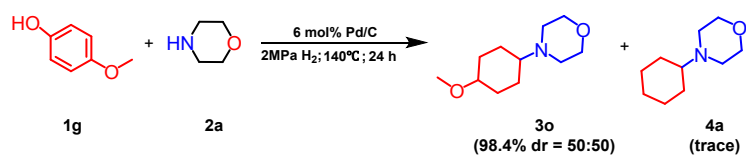
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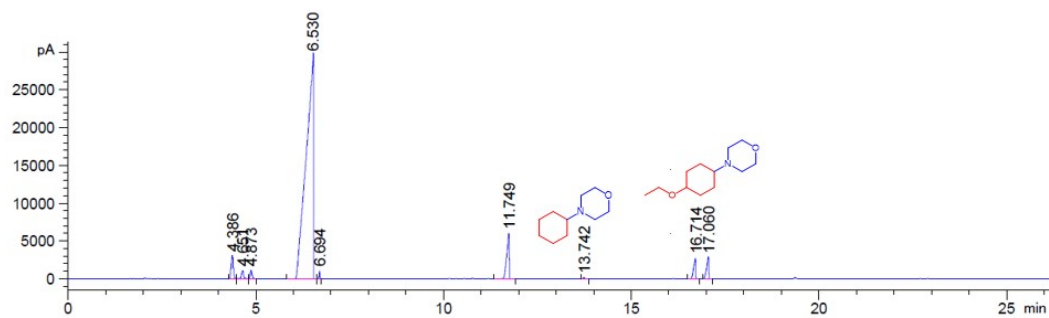
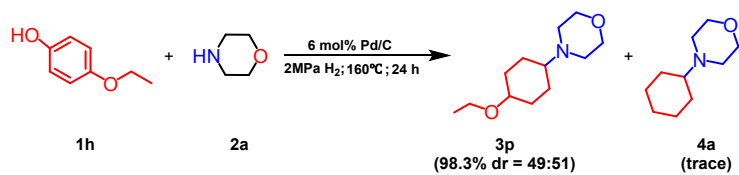
### Reaction 14



## Reaction 15

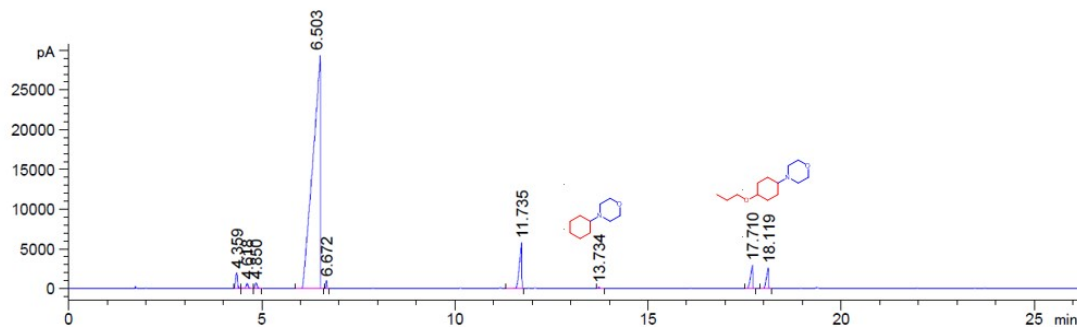
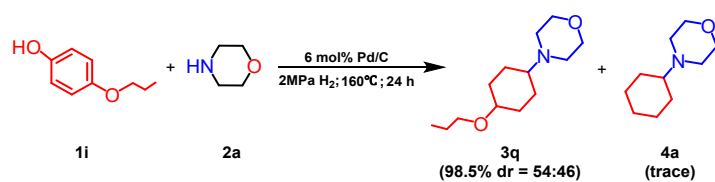


## Reaction 16

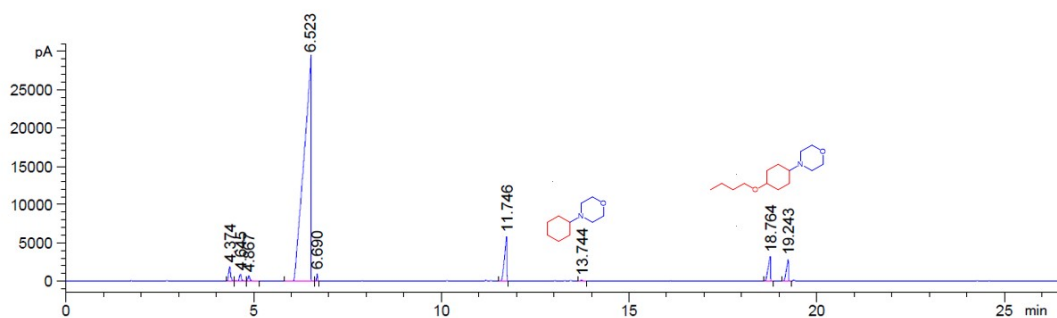
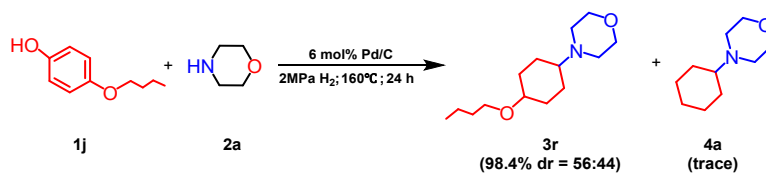




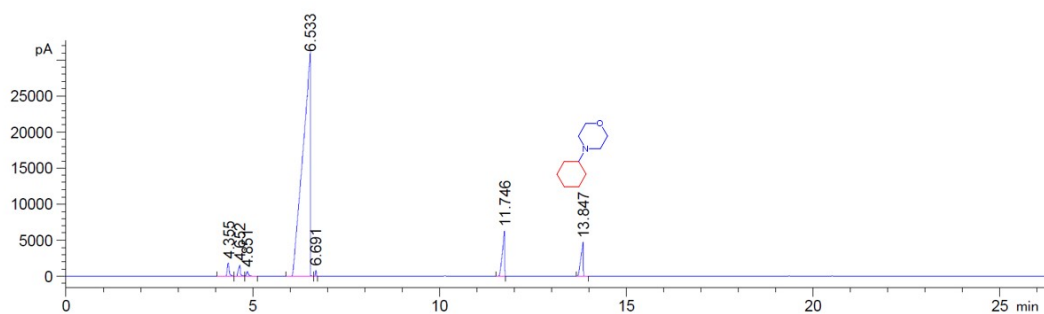
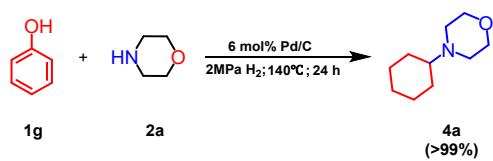
## Reaction 17



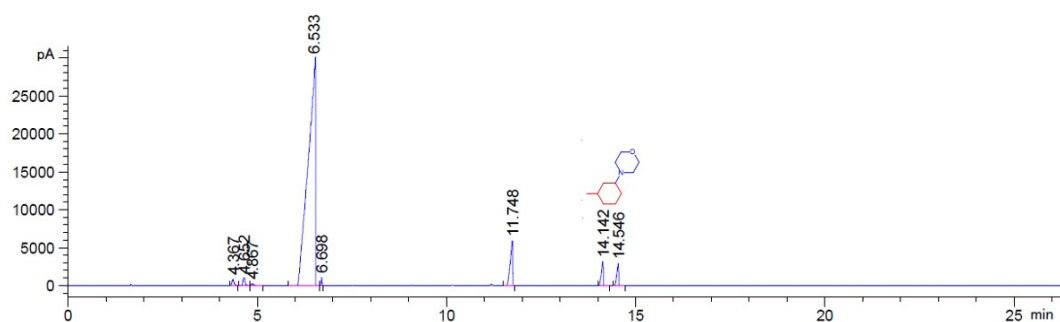
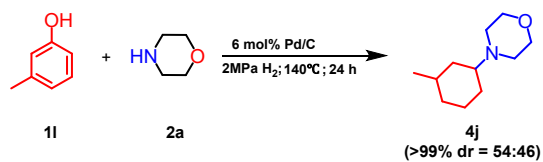
## Reaction 18



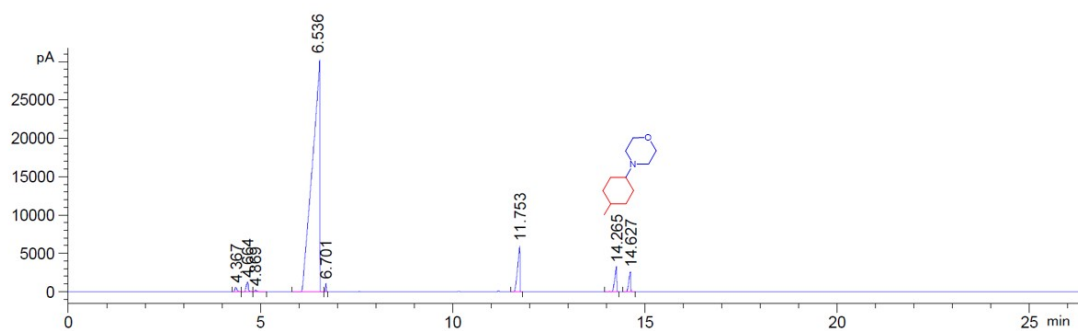
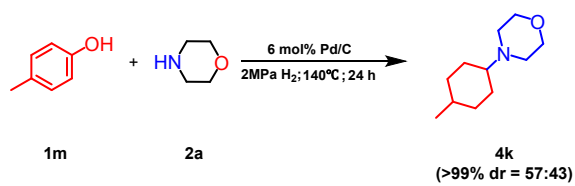
## Reaction 19



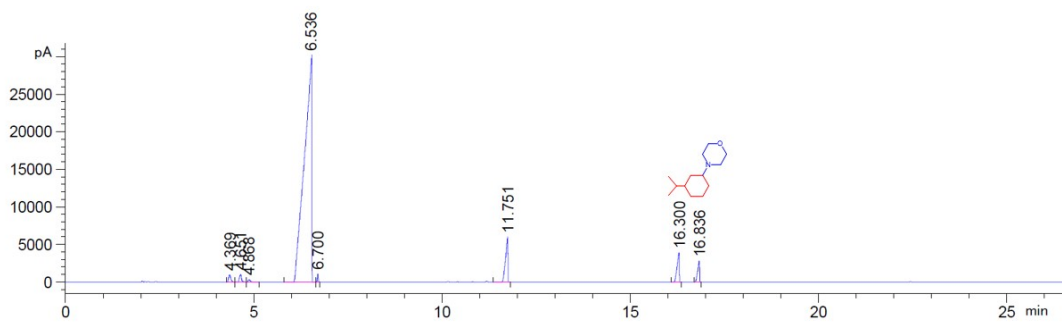
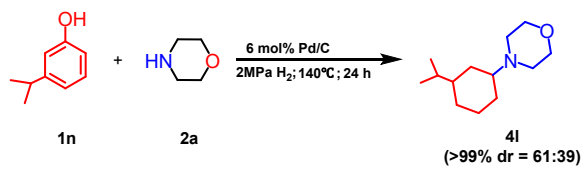
## Reaction 20



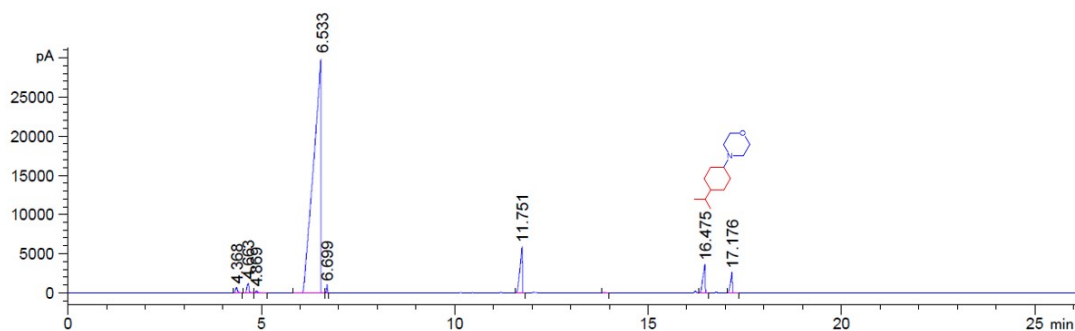
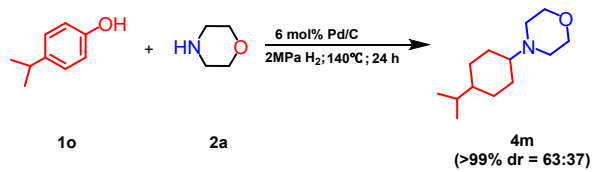
## Reaction 21



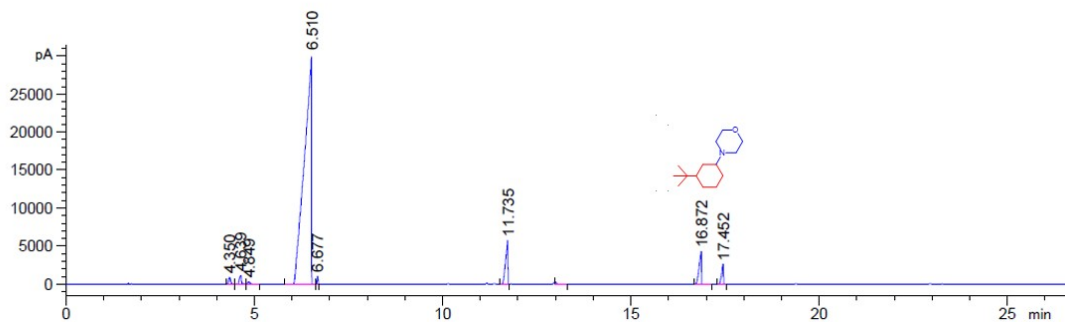
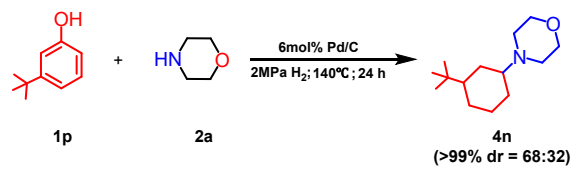
## Reaction 22



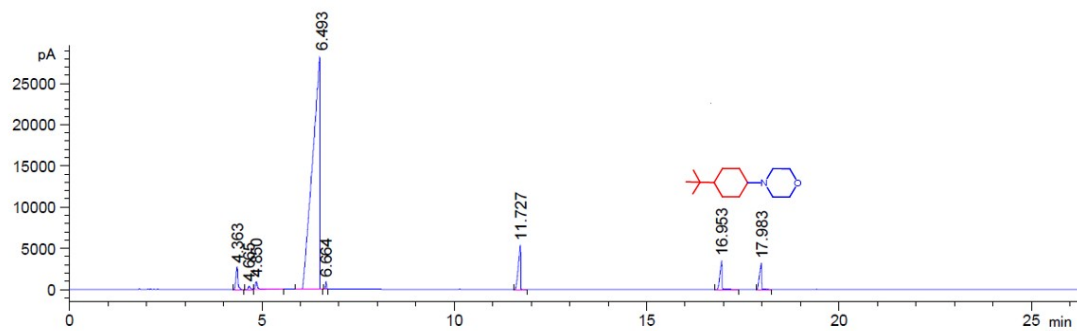
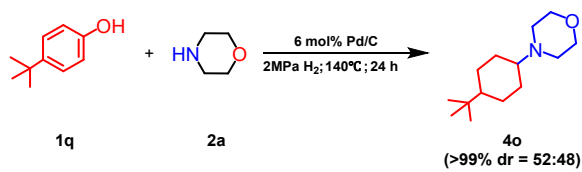
## Reaction 23



## Reaction 24



## Reaction 25



## Reference

S1. T. Cuypers, T. Morias, S. Windels, C. Marquez, C. V. Goethem, I. Vankelecom and D. E. D. Vos, *Green Chem.*, 2020, **22**, 1884-1893.