

Supporting Information

Efficient Claisen Rearrangement of Allyl *para* substituted Phenyl Ethers Using Microreactors

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Experimental

¹H NMR spectra was recorded on JEOL ECA NMR spectrometer at 400 MHz. ¹H NMR chemical shifts were determined relative to internal tetramethylsilane at δ 0.0 ppm. Yields were determined by HPLC analysis using Agilent 1200 (DAD: 215 nm, column: agilent zorbax eclipse XDB-C18 (4.6*150 mm, I.D. 5 μ m)) using an internal standard.

Fabrication of microreactors systems

MR-1

The microchannel we used is one kind of stainless steel pipe that is commonly used in high-performance liquid chromatography (HPLC). It is acid/base resistant and high-temperature durable. We fabricated a microreactor system, MR-1, with a pump connected micro syringe (0.005 - 36 ml h⁻¹) and a 120 cm long pipe (170 μ m in I.D.) with a maximal heating length of 106 cm. The necessary cooling and collection devices linked in sequence following the reaction section. The substrate is injected through the pipe, heated in the oil bath, subsequently cooled in the second bath, and finally collected from the other end of the pipe.

MR-2

The fabrication of MR-2 is the same to MR-1 except that the heating length is twice

as MR-1.

General procedure for the Claisen rearrangement reactions using microreactor

Substrates **1-6** were synthesized according to the procedures reported by White, et al.¹ Substrates **1-4** were injected into the steel micro reactor, MR-1. The reaction residence time can be adjusted by changing the flow rate, which is controlled by the micro-pump. The crude product was collected at the end of the micro channel, and then characterized by HPLC. After purified through column chromatography, the target product was characterized by ¹HNMR (Substrates **3&4** are not needed purification.) The solid substrates **5** and **6** were dissolved in diphenyl ether, with the mole proportion of 1:4 and 2:3, respectively. The remaining experiment procedures are the same as the substrates **1-4**.

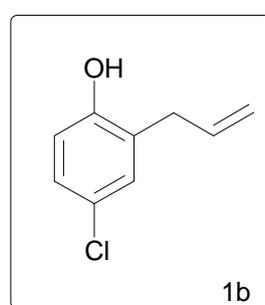
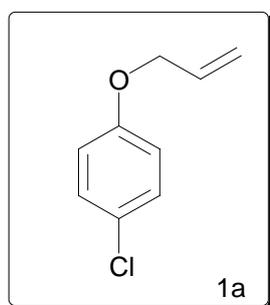
In the study of the influence of the flow rate on the Claisen rearrangement reaction in the micro-channel, the microreactors MR-1 and MR-2 were both used. For each compared experiment, in order to provide the same residence time, the injection rate of the micro-pump in MR-2 is twice than that in MR-1. The substrate **4** was heated to 220 °C by using an oil bath. The remained experiment procedure is same as before.

General procedure for the conventional Claisen rearrangement reactions

The allyl *p*-x-phenyl ether (substrates **1-4**, 0.05 mole) was stirred at the same temperature for the same reaction time (corresponding residence time of the microreaction) as in the microreactor. The crude product was then characterized by HPLC. After purified through column chromatography, the target product was

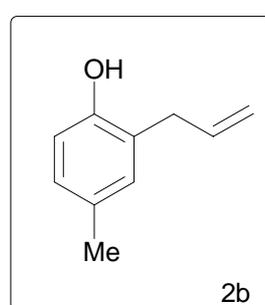
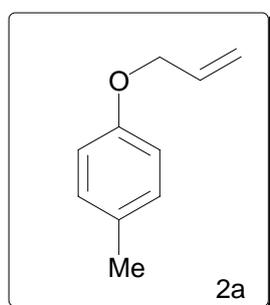
characterized by ^1H NMR. Solid substrates **5** and **6** were dissolved in diphenyl ether, with the mole proportion of 1:4 and 2:3, respectively. The remaining experiment procedures are the same as the substrates **1-4**.

Experimental data



(**1a**) Allyloxy-4-chlorobenzene: IR ν /cm⁻¹ 3078, 1648, 1606, 1583, 1513, 827. ^1H NMR (400 MHz, CDCl₃) δ 4.50–4.51 (m, CH₂, 2H), 5.30–5.43 (m, C=CH₂, 2H), 6.00–6.04 (m, C=CH, 1H), 6.83–6.85 (m, ArH, 2H), 7.22–7.24 (m, ArH, 2H);

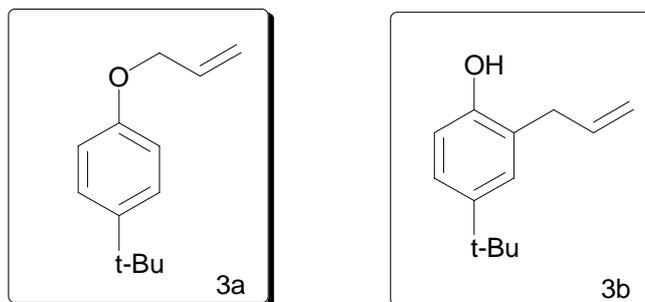
(**1b**) 2-Allyl-4-chlorophenol: IR ν /cm⁻¹ 3437, 3078, 1639, 1606, 1583, 1490, 866, 815. ^1H NMR (400 MHz, CDCl₃) δ 3.38 (d, J=6.3 Hz, CH₂, 2H), 4.95 (s, OH, 1H), 5.14–5.19 (m, C=CH₂, 2H), 5.95–6.02 (m, C=CH, 1H), 6.73–6.85 (m, ArH, 1H), 7.07–7.09 (m, ArH, 2H);



(**2a**) Allyloxy-4-methylbenzene: IR ν /cm⁻¹ 3078, 3027, 1649, 1615, 1586, 1511, 1459, 817. ^1H NMR (400 MHz, CDCl₃) δ 2.28 (s, CH₃, 3H), 4.50–4.52 (m, CH₂,

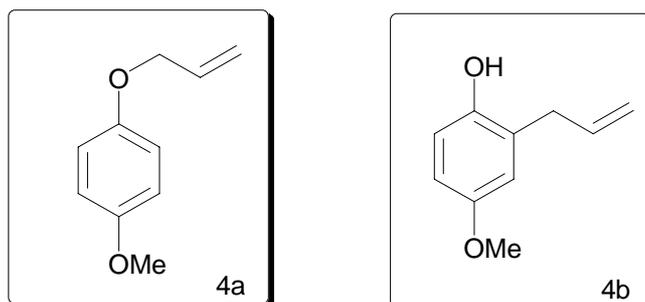
2H), 5.29–5.43 (m, C=CH₂, 2H), 6.03–6.06 (m, C=CH, 1H), 6.81–6.83 (m, ArH, 2H), 7.07–7.09 (m, ArH, 2H);

(2b) 2-Allyl-4-methylphenol: IRv/cm⁻¹ 3426, 3078, 1639, 1511, 901, 825. ¹H NMR (400 MHz, CDCl₃) δ2.28 (s, CH₃, 3H), 3.38 (d, J=6.4 Hz, CH₂, 2H), 4.51 (s, OH, 1H), 5.26–5.42 (m, C=CH₂, 2H), 6.02–6.05 (m, C=CH, 1H), 6.72 (d, J=8.0 Hz, ArH, 1H), 6.90–6.92 (m, ArH, 2H);



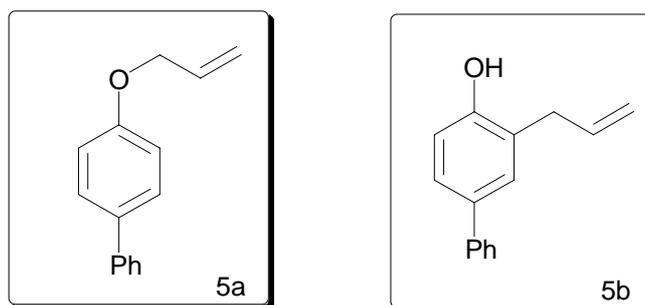
(3a) Allyloxy-4-tert-butylbenzene: IRv/cm⁻¹ 3083, 1646, 1596, 1581, 1491, 1460, 1363, 822. ¹H NMR (400 MHz, CDCl₃) δ1.30 (s, C(CH₃)₃, 9H), 4.49–4.52 (m, CH₂, 2H), 5.26–5.43 (m, C=CH₂, 2H), 6.02–6.05 (m, C=CH, 1H), 6.84–6.87 (m, ArH, 2H), 7.25–7.28 (m, ArH, 2H);

(3b) 2-Allyl-4-tert-butylphenol: IRv/cm⁻¹ 3456, 3082, 1639, 1608, 1508, 1465, 1362, 881, 820. ¹H NMR (400 MHz, CDCl₃) δ1.29 (s, C(CH₃)₃, 9H), 3.42 (d, J=6.4, CH₂, 2H), 4.80 (s, OH, 1H), 5.15–5.20 (m, C=CH₂, 2H), 6.00–6.04 (m, C=CH, 1H), 6.74 (d, J=8.3, ArH, 1H), 7.12–7.14 (m, ArH, 2H);



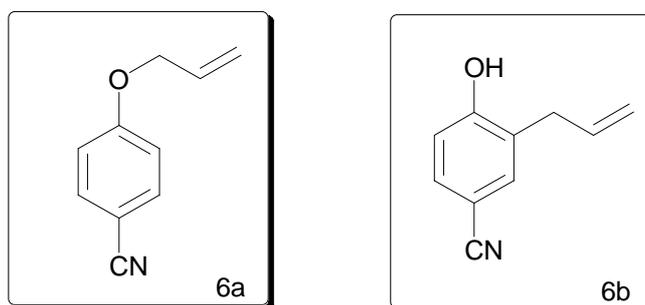
(4a) Allyloxy-4-methoxybenzene: IRv/cm⁻¹ 3078, 1644, 1593, 1508, 1463, 1178, 825. ¹H NMR (400 MHz, CDCl₃) δ3.75 (s, CH₃, 3H), 4.47–4.48 (m, CH₂, 2H), 5.27–5.42 (m, C=CH₂, 2H), 6.01–6.05 (m, C=CH, 1H), 6.83–6.85 (m, ArH, 4H);

(4b) 2-Allyl-4-methoxyphenol: IRv/cm⁻¹ 3410, 3078, 1639, 1613, 1507, 1194, 871, 805. ¹H NMR (400 MHz, CDCl₃) δ3.37 (d, J=6.4 Hz, CH₂, 2H), 3.76 (s, CH₃, 3H), 4.64 (s, OH, 1H), 5.14–5.17 (m, C=CH₂, 2H), 5.97–6.04 (m, C=CH, 1H), 6.68–6.74 (m, ArH, 3H);



(**5a**) 4-Allyloxy-biphenyl: IRv/cm⁻¹ 3094, 3057, 3027, 3011, 2991, 2919, 2883, 2847, 1644, 1606, 1523, 1489, 830, 758, 692. ¹H NMR (400 MHz, CDCl₃) δ4.58–4.59 (m, CH₂, 2H), 5.30–5.47 (m, C=CH₂, 2H), 6.05–6.10 (m, C=CH, 1H), 6.98–7.00 (d, ArH, 2H), 7.28–7.32 (m, ArH, 1H), 7.39–7.44 (m, ArH, 1H), 7.51–7.54 (m, ArH, 4H);

(**5b**) 2-Allyl-biphenyl-4-ol: IRv/cm⁻¹ 3411, 3058, 1639, 1585, 1516, 1488, 871, 825, 687, 748. ¹H NMR (400 MHz, CDCl₃) δ3.48 (d, CH₂, 2H), 4.98 (s, OH, 1H), 5.20–5.23 (m, C=CH₂, 2H), 6.02–6.07 (m, C=CH, 1H), 6.90 (d, ArH, 1H), 7.37–7.43 (m, ArH, 4H), 7.50–7.55 (m, ArH, 3H);



(**6a**) 4-Allyloxybenzonitrile: IRv/cm⁻¹ 3073, 3037, 2223, 1644, 1608, 1582, 1506, 1488, 1460, 830. ¹H NMR (400 MHz, CDCl₃) δ4.58–4.60 (m, CH₂, 2H), 5.35–5.44 (m, C=CH₂, 2H), 6.00–6.04 (m, C=CH, 1H), 6.95–6.97 (m, ArH, 2H), 7.57–7.59 (m, ArH, 2H);

(**6b**) 2-Allyl-4-cyanophenol: IRv/cm⁻¹ 3326, 3078, 2227, 1639, 1604, 1573, 1508, 881, 832. ¹H NMR (400 MHz, CDCl₃) δ3.44 (d, J=6.4Hz, CH₂, 2H), 5.18–5.24 (m, C=CH₂, 2H), 5.99 (s, OH, 1H), 6.05 (m, C=CH, 1H), 6.89 (d, ArH, 1H), 7.46 (m, ArH, 2H).

References

1. White, W. N.; Gwynn, D.; Schlitt, R.; Girard, C.; Fife, W., The Ortho-Claisen Rearrangement .1. the Effect of Substituents on the Rearrangement of Allyl Para-X-Phenyl Ethers. *Journal of the American Chemical Society* **1958**, 80, (13), 3271-3277.

