Teflon AF-2400 mediated gas-liquid contact in continuous flow methoxycarbonylations and in-line FTIR measurement of CO concentration

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Supporting Information

Description of the synthesis of methyl carboxylate ***1b*** *in flow (this procedure - with modifications as indicated in the main manuscript - was used for all substrates)* (Figure S1)*:*

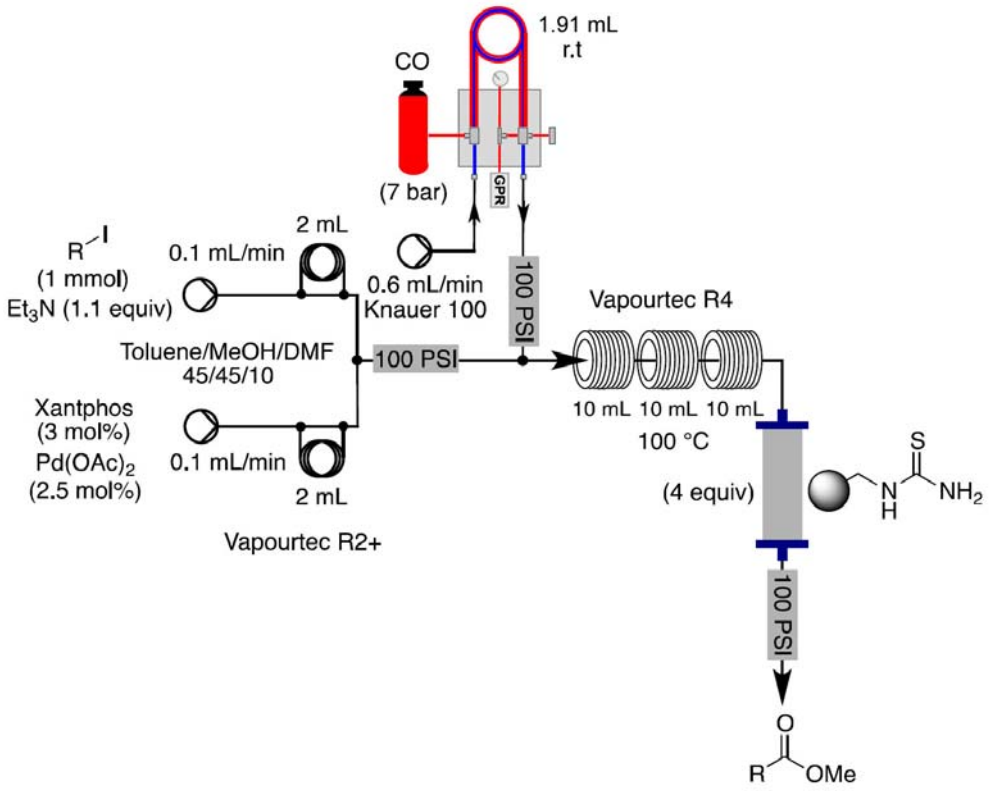
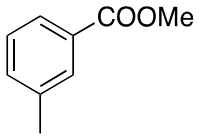


Figure S1. A schematic representation of the optimised gas-flow reactor configuration for the preparation of **1b**.

A solution of the aryl iodide **1a** (1.0 equiv., 1.0 mmol) and Et_3N (1.1 equiv.) dissolved in a mixture of toluene/MeOH/DMF (45/45/10) (2 mL) was loaded into a 2 mL PEEK sample loop and a solution of xantphos (3 mol%) and $Pd(OAc)_2$ (2.5 mol%) in toluene/MeOH/DMF (45/45/10) (2 mL) was loaded into a second 2 mL PEEK sample loop.

These mixtures were pumped (flow rate 0.1 mL/min) and mixed at a T-piece. The combined streams were united with a third solvent stream (toluene/MeOH/DMF = 45/45/10) (0.6 mL/min) enriched with CO (7 bar) from the gas-liquid reactor, via a second T-piece. The combined substrate, catalyst and enriched CO streams were directed to the heating coils (3 × 10 mL) of the Vapourtec R4 system. The total residence time in the heated flow coils was 38 min. The installation of backpressure regulators (2 × 100 psi) before the second T-piece (located before the heating coils) was used to ensure unidirectional flow through the heating coils. On exiting the heating coils, the product flow stream was directed through a glass Omnifit column (15 mm i.d. × 150 mm length) packed with QP-TU (5.0 g) to scavenge the palladium. A backpressure regulator (100 psi) was placed immediately after the glass Omnifit column to prevent out-gassing of the dissolved CO from the solvent mixture. The product stream was then collected into a round bottom flask and concentrated *in vacuo* to give the methyl carboxylate **1b**. Final product purification was achieved by column chromatography on silica gel (12:1 hexane:EtOAc) to afford **1b** as a colourless oil (105 mg, 70%).

Methyl 3-methylbenzoate 1b



^{1}H NMR ($CDCl_3$), δ, ppm: 7.82 (m, 2H), 7.31 (m, 2H), 3.88 (s, 3H), 2.37 (s, 3H). ^{13}C NMR, δ, ppm: 167.2, 138.1, 133.6, 133.4, 130.1, 128.2, 126.7, 52.0, 21.2.

Ref.: Marchal, J.; Bodiguel, J.; Fort, Y.; Caubere, P. *J. Org. Chem.* **1995**, *60*, 8336–8340. Li, A.-C.; Ren, J.; Liao, T.-G.; Jiang, J.-X.; Zhu, H.-J. *Eur. J. Org. Chem.* **2007**, *6*, 1026–1030. Molander, G. A.; Yun, C.-S.; Ribagorda, M.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 5534–5539.