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

Peter Koos, Ulrike Gross, Anastasios Polyzos, Matthew O’Brien, Ian Baxendale and Steven V. Ley

Whiffen Laboratory

University Chemical Laboratory, University of Cambridge, Lensfield Road, Cambridge, UK, CB2 1EW; E-mail: svl1000@cam.ac.uk

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](https://example.com/figure1.png)

**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$_3$N (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**

![Methyl 3-methylbenzoate 1b](image)

$^1$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.