Supplementary Material (ESI) for Chemical Communications

Supporting Information for:

Phase-Transfer Dynamic Combinatorial Chemistry

Ruth Pérez-Fernández, Michael Pittelkow, Ana M. Belenguer and Jeremy K. M. Sanders

University Chemical Laboratory, University of Cambridge,
Lensfield Road, Cambridge CB2 1EW, United Kingdom.
Fax: (+)44 (0)1223 336017
E-mail: jkms@cam.ac.uk

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Materials and Methods

All chemicals were purchased from commercial suppliers (Aldrich) and used without further purification. All solvents were reagent grade quality (MeOH, CH_2Cl_2) or HPLC grade (water, chloroform, acetonitrile 190 far UV gradient, Romil). Formic acid was acquired from Romil.

The thiol derivatives **2**, **4** were purchased from commercial suppliers.

The thiol derivatives **1**[1], **3**[2] and **5**[3] were prepared using slightly modified literature procedures.

[1] S. Otto, R. L. E. Furlan, J. K. M. Sanders, *Science* **2002**, *297*, 590-593.

[2] A. M. Tickner, G. K. Huang, K. Gombatz, R. J. Mills, V. Novack, K. S. Webb, *Synth. Commun.* **1995**, *25*, 2497-2505.

[3] B. M. R. Liénard, N. Selevsek, N. J. Oldham, C. J. Schofield, *ChemMedChem* **2007**, *2*, 175-179.

Dynamic Combinatorial Libraries

Aqueous phase: Building block **1** (5 mM overall) was dissolved in water and the pH was adjusted to pH 7-7.4 by addition of a base. When using borate buffer, the building block was dissolved in a borate buffer solution (10 mM, pH 7). In the case of tris-HCl (1M), 100 μL was added to the aqueous stock solution.

Organic phase: Thiols (building blocks **2** and **5**, 5 mM) were dissolved in chloroform and 10 equivalents of base were added.

Control experiments were performed in which the phase containing the building block was mixed with a pure solvent phase. The mixtures were allowed to oxidise and equilibrate during 4 weeks.

Library Analysis

Analyses were performed using an Agilent 1100 series HPLC with a diode array UV/VIS detector and interfaced to an Agilent XCT ion-trap mass spectrometer. Analyses were performed using reversed phase HPLC silica based columns: Kovasil MS-H (33mm × 4.6mm, 1.5 μm) for libraries set up with building blocks **1**-**4**, Agilent C8 Zorbax Eclipse XBD (4.6 × 150 mm, 5μm) for libraries with building blocks **1** and **5**. Using an injection volume of 0.3 μL, a flow rate of 1 mL/min and 0.2 mL/min respectively and gradient elution for Kovasil MS-H (30 to 40% over 1 min, 40 to 70% over 4 min and 70 to 90% over 1 min) of acetonitrile in water and for Agilent C8 Zorbax Eclipse XBD (60% isocratic over 1 min, 60 to 90% over 1 min, 90% over 1 min, 90 to 100% over 2 min, 100% isocratic over 9 min) of acetonitrile in water. Both acetonitrile and water contain 0.1% v/v formic acid. Analyses were monitored at 260 nm wavelength. The oven temperature was set up at 40 ºC. Alternate positive and negative ion mass spectra were acquired in the ultrascan mode (26000 $m/z \cdot sec^{-1}$) using electrospray ionization (drying gas temperature: 350 ºC, nebulizer pressure: 55 psi, drying gas flow: 12 L/min, HV capillary: 4000 V; ICC target: 200 000) and atmospheric pressure chemical ionization (drying gas temperature: 400 ºC, nebulizer pressure: 60 psi, drying gas flow: 7 L/min, HV capillary: 3500 V; corona current: 10000 nA, ICC target, 200 000).

Transport experiment

The transport experiment was performed using the U-tube cell represented in Figure S2. In the experiment the aqueous phase (**I**) consisted of 100 μL of a 5 mM solution of building block **1** at pH 7 by addition of tris HCl (1M, pH 7.4); the membrane phase (**M**) consisted of 400 μL of chloroform with tributylamine (10 μL); and the other aqueous phase (**II**) consisted of 100 μL of a 5 mM solution of building block **4** at pH 7 after addition of tris HCl. Stirring in this experiment was kept constant. Samples from the aqueous and organic phase were collected by a 25 μL Hamilton syringe and analysed by LC-MS under the previously described conditions with the Kovasil MS-H column.

LC-MS analysis

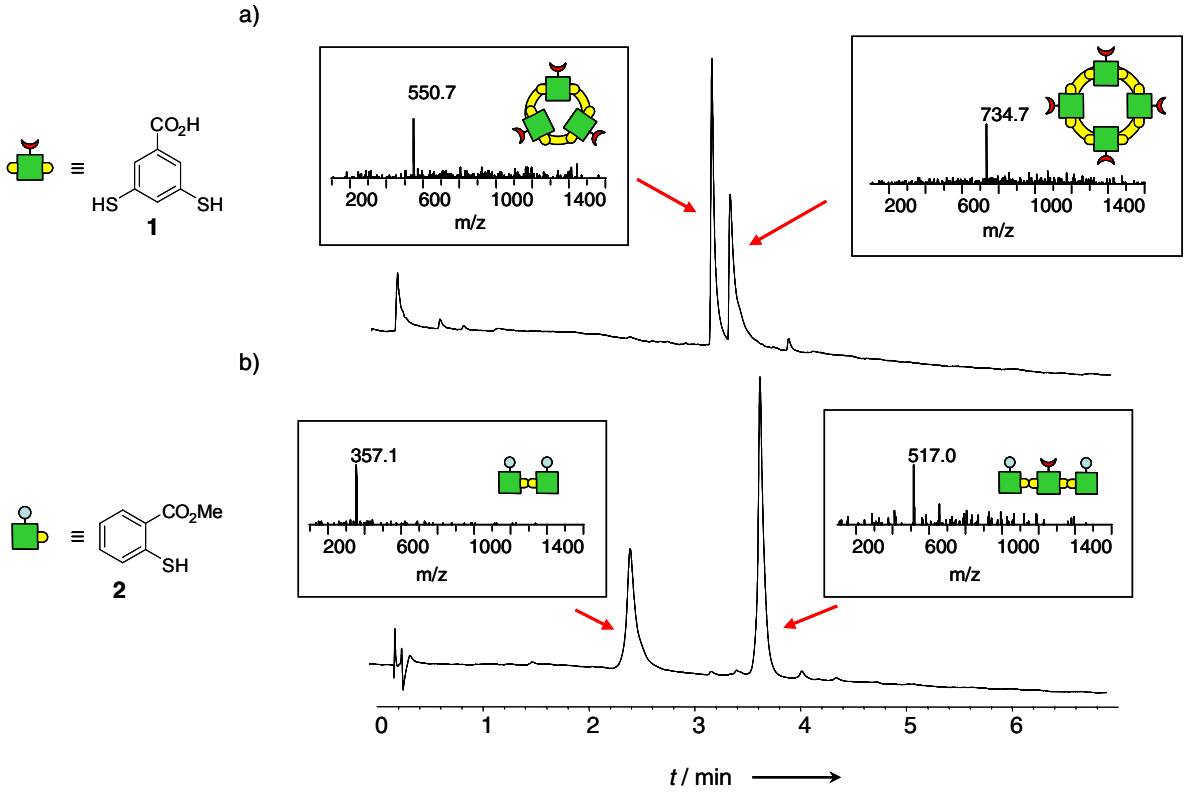

Figure S1. HPLC (monitored at 260 nm wavelength) and MS analysis of library set up with building blocks **1** and **2** after equilibration, (a) aqueous phase injection; (b) organic phase injection.

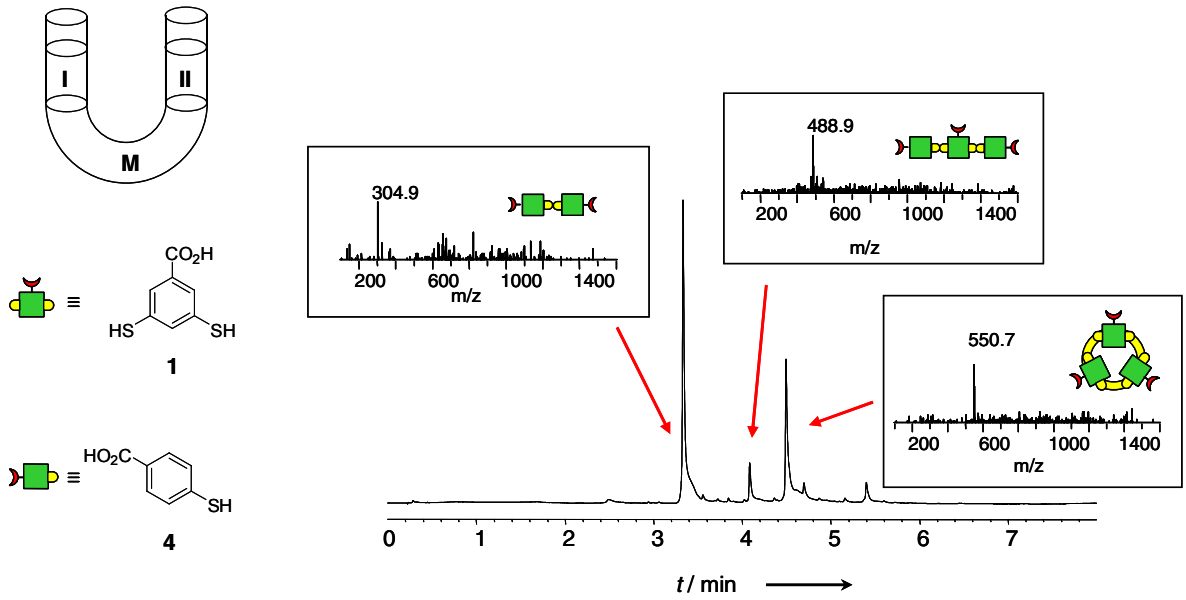

Figure S2. HPLC (monitored at 260 nm wavelength) and MS analysis of the transport experiment set up with building blocks **1** and **4**, organic phase (**M**) injection after equilibration.