A prototype continuous-flow liquid-liquid extraction system using open-source technology.

SUPPORTING INFORMATION

Matthew O’Brien,* Peter Koos, Duncan L. Browne and Steven V. Ley

Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW

Overall setup S2
Prototype separator S3
Inline mixer S4
Intensity/Concentration Calibration Curves S6
Comparison between linear and quartic calibration S7

Data for 3a S8
Data for 3b S8
Data for 3c S8
Data for 3d S8
Data for 3e S9
Data for 3f S9
Data for 3g S9
Data for 3h S9
Data for 3i S10

Data for 6a S10
Data for 6b S10
Data for 6c S10
Data for 6d S11

Data for 9a S11
Data for 9b S11
Data for 9c S11
General Experimental (Flow Apparatus)
Overall setup

2 x RS-232 data connection

Addresses of NE1000 pumps are set to match the corresponding serial com port of the RS-232 data connection in the Python script.

Both New Era NE500 (fixed reservoir) and Knaur smartline-100 (continuous, unlimited reservoir) were used.

Both Infors AG dual-syringe pump (fixed reservoir) and Knaur smartline-100 (continuous, unlimited reservoir) were used. Flow rates were always matched.

In this work, no back-pressure regulator was used on the outlet, which was kept higher than the separator to avoid ‘lymphing’ of liquid during initial setup.

Webcam used was Microsoft Lifecam HD-5000. Software works well with other webcams.
(USB microscope for dispersion measurement was purchased from Maplin Electronics (N43H01) and is very similar to the Veso-VMS-004)
Prototype Separator

The main body is a 2.5 mL plastic syringe barrel. Upper inlets are 120 mm stainless steel 21g needles going through the B10 suba-seal. The interface float was made by melting together roughly equal amounts (volume) of the polyethylene plunger from an HSW normject 1 mL syringe and a piece of green B-24 Keck clip.
Inline Mixer

Body of mixer is cut from the barrel of a 1 mL HSW normject syringe. The thread on the inlet side was made by heating to softness then screwing in the ¼-28-UNF connector, which cut a thread. PTFE tape was used to improve the seal. The outlet is a simple female luer to female ¼-28 UNF adapter.
Inline mixer, biphasic mixture (DCM/Water, DCM dyed red), stirrer on maximum speed:

Inline mixer, biphasic mixture, no stirring
Linear Regression between dye concentration and red intensity:

Quartic polynomial calibration:

\[
\text{Intensity} = 1.003 \text{ (conc)} - 0.0365 \\
R^2 = 0.9978
\]
Comparison between linear and quartic calibration (converting calculated concentration to 'observed' intensity) for 0.25 mL heavy phase dispersion measurements.
**Compound Data**

**1-benzylidene-2-phenylhydrazine (3a):**

![Chemical structure](image)

$^1H$ NMR (CDCl$_3$, 400 MHz) $\delta$ 7.65-7.69 (m, 3H), 7.38 (t, $J$ = 7.0 Hz, 2H), 7.34 - 7.24 (m, 3H), 7.11 – 7.15 (m, 2H), 6.89 (t, $J$ = 7.5 Hz, 1H) ppm. $^{13}C$ NMR (CDCl$_3$, 101 MHz) $\delta$ 144.7 (CH$_3$), 137.3, 135.4 (CH$_2$), 129.3, 128.6, 128.4, 126.2, 120.2, 112.8 ppm. IR (solid state): 3310 (w), 3058 (w), 1602 (m), 1594 (m), 1494 (m), 1262 (m) cm$^{-1}$. HRMS (ES): m/z [M+H]$^+$ calcd for C$_{13}$H$_{12}$N$_2$: 196.0995, found 196.1000.

**1-(4-methylbenzylidene)-2-phenylhydrazine (3b):**

![Chemical structure](image)

$^1H$ NMR (CDCl$_3$, 400 MHz) $\delta$ 7.68 (s, 1H), 7.54-7.58 (m, 2H), 7.24-7.30 (m, 2H), 7.17-7.21 (m, 2H), 7.09-7.14 (m, 2H), 6.83-6.90 (m, 1H), 2.37 (s, 3H) ppm. $^{13}C$ NMR (CDCl$_3$, 101 MHz) $\delta$ 144.9 (CH$_3$), 138.5 (CH$_2$), 137.6, 132.6 (CH$_3$), 129.4, 129.3, 126.2, 120.0, 112.8, 21.4 (CH$_3$) ppm. IR (solid state): 3312 (w), 3029 (w), 1597 (m), 1507 (m), 1493 (m), 1259 (m) cm$^{-1}$. HRMS (ES): m/z [M+H]$^+$ calcd for C$_{14}$H$_{14}$N$_2$: 210.1151, found 210.1152.

**1-(naphthalen-1-ylmethylene)-2-phenylhydrazine (3c):**

![Chemical structure](image)

$^1H$ NMR (CDCl$_3$, 400 MHz) $\delta$ 8.81 (d, $J$ = 8.5 Hz, 1H), 8.26 (s, 1H), 7.81-7.92 (m, 3H), 7.74 (s, 1H), 7.60-7.64 (m, 1H), 7.48-7.56 (m, 2H), 7.32-7.37 (m, 2H), 7.18-7.22 (m, 2H), 6.94 (t, $J$ = 7.0 Hz, 1H) ppm. $^{13}C$ NMR (CDCl$_3$, 101 MHz) $\delta$ 144.7 (CH$_3$), 137.0, 134.0 (CH$_2$), 130.8 (CH$_3$), 130.4 (CH$_2$), 129.5, 129.1, 128.8, 126.8, 126.4, 126.0, 125.5, 124.5, 120.2, 112.9 ppm. IR (solid state): 3308 (w), 3053 (w), 1600 (s), 1506 (m), 1493 (m), 1253 (m) cm$^{-1}$. HRMS (ES): m/z [M+H]$^+$ calcd for C$_{15}$H$_{14}$N$_2$: 246.1151, found 246.1147.

**1-(4-(methylthio)benzylidene)-2-phenylhydrazine (3d):**

![Chemical structure](image)

$^1H$ NMR (CDCl$_3$, 400 MHz) $\delta$ 7.63-7.67 (s, 1H), 7.58-7.61 (m, 2H), 7.25-7.32 (m, 5H), 7.11-7.15 (m, 2H), 6.90 (t $J$ = 7.0 Hz, 1H), 2.53 (s, 3H) ppm. $^{13}C$ NMR (CDCl$_3$, 101 MHz) $\delta$ 145.0 (CH$_3$), 139.3 (CH$_2$), 137.3, 133.7 (CH$_2$), 129.2, 127.0, 126.9, 120.5, 16.1 (CH$_3$) ppm. IR (solid state): 3315 (w), 1594 (m), 1493 (m), 1264 (m) cm$^{-1}$. Elemental Analysis calcd for C$_{14}$H$_{14}$N$_2$S : C = 69.39%, H= 5.82%, N = 11.56%, found C = 69.37%, H = 5.74%, N= 11.57%.
1-(4-ethoxybenzylidene)-2-phenylhydrazine (3e):

\[
\text{HN}
\]

**1H NMR** (CDCl₃, 400 MHz) \(\delta\) 7.59-7.65 (m, 3H), 7.47 (s, 1H), 7.28-7.35 (m, 2H), 7.11-7.15 (m, 2H), 6.87-6.95 (m, 3H), 4.09 (q, \(J = 7.0\) Hz, 2H), 1.46 (t, \(J = 7.0\) Hz, 3H) ppm. **13C NMR** (CDCl₃, 101 MHz) \(\delta\) 159.8 (CH=), 145.1 (CH₂), 137.6, 129.3, 128.0 (CH₃), 127.6, 119.8, 114.8, 112.7, 63.6 (CH₃), 14.9 (CH₃) ppm. **IR** (solid state): 3315 (w), 2978 (w), 1597 (m), 1504 (m), 1494 (m), 1262 (m), 1239 (m) cm⁻¹. **Elemental Analysis** calcld for C₁₅H₁₄N₂O: C = 74.97%, H = 6.71%, N = 11.66%, found C = 74.77%, H = 6.70%, N = 11.28%.

1-(4-ethylbenzylidene)-2-phenylhydrazine (3f):

\[
\text{HN}
\]

**1H NMR** (CDCl₃, 400 MHz) \(\delta\) 7.68 (s, 1H), 7.60-7.64 (m, 2H), 7.55 (s, 1H), 7.28-7.33 (m, 2H), 7.23-7.26 (m, 2H), 7.13-7.17 (m, 2H), 6.88-6.93 (m, 1H), 2.70 (q, \(J = 7.5\) Hz, 2H), 1.29 (t, \(J = 7.5\) Hz, 3H) ppm. **13C NMR** (CDCl₃, 101 MHz) \(\delta\) 144.9 (2C, CH₃), 137.6, 132.9 (CH₃), 129.3, 128.2, 126.3, 120.0, 112.8, 28.8 (CH₂), 15.5 (CH₃) ppm. **IR** (solid state): 3312 (w), 2966 (w), 1598 (m), 1507 (m), 1262 (m), 1258 (m) cm⁻¹. **HRMS** (ES): m/z [MH⁺] calcd for C₁₅H₁₆N₂: 224.1308, found 224.1307.

1-(2-fluorobenzylidene)-2-phenylhydrazine (3g):

**1H NMR** (CDCl₃, 400 MHz) \(\delta\) 8.04-8.10 (m, 1H), 7.91 (s, 1H), 7.71 (s, 1H), 7.28-7.38 (m, 3H), 7.16-7.24 (m, 3H), 7.08-7.15 (m, 1H), 6.94-7.00 (m, 1H) ppm. **13C NMR** (CDCl₃, 101 MHz) \(\delta\) 160.5 (d, \(J_{C,F} = 252\) Hz), 144.5 (CH₃), 130.6, 129.6 (d, \(J_{C,F} = 8\) Hz), 129.4, 126.2 (d, \(J_{C,F} = 4\) Hz) 124.4 (d, \(J_{C,F} = 4\) Hz) 123.2 (d, \(J_{C,F} = 10\) Hz, CH₃), 120.5, 115.6, (d, \(J_{C,F} = 30\) Hz) 112.9 ppm. **IR** (solid state): 3309 (w), 3054 (w), 1598 (m), 1587 (m), 1482 (m), 1446 (m), 1256 (m), 1236 (m) cm⁻¹. **Elemental Analysis** calcld for C₁₃H₁₁FN₂: C = 72.88%, H = 5.18%, N = 13.08%, found C = 72.80%, H = 5.09%, N = 13.00%.

1-(4-methoxybenzylidene)-2-phenylhydrazine (3h):

**1H NMR** (CDCl₃, 400 MHz) \(\delta\) 7.60-7.65 (m, 3H), 7.47 (s, 1H), 7.28-7.34 (m, 2H), 7.11-7.15 (m, 2H), 6.88-6.97 (m, 3H), 3.86 (s, 3H) ppm. **13C NMR** (CDCl₃, 101 MHz) \(\delta\) 160.1 (CH₃), 145.0 (CH₃), 137.5, 129.3, 128.2 (CH₃), 127.7, 119.8, 114.2, 112.7, 55.3 (CH₃) ppm. **IR** (solid state): 3309 (w), 3054 (w), 1598 (m), 1587 (m), 1482 (m), 1446 (m), 1256 (m), 1236 (m) cm⁻¹. **Elemental Analysis** calcld for C₁₄H₁₄N₂O: C = 74.31%, H = 6.24%, N = 12.38%, found C = 74.39%, H = 6.23%, N = 12.44%.

1-(2-chlorobenzylidene)-2-phenylhydrazine (3i):


\[
\text{H NMR (CDCl}_3\text{, 400 MHz) \delta 8.08-8.14 (m, 2H), 7.82 (s, 1H), 7.23-7.42 (m, 5H), 7.15-7.19 (m, 2H), 6.93-6.98 (m, 1H) ppm. C NMR (CDCl}_3\text{, 101 MHz) \delta 144.4 (CH}_3\text{), 133.6, 132.8 (CH}_2\text{), 132.6 (CH}_3\text{), 129.7, 129.4, 129.2, 127.0, 126.7, 120.5, 112.9 ppm. IR (solid state): 3313 (w), 3057 (w), 1603 (m), 1580 (m), 1493 (m), 1442 (m), 1257 (m) cm}^{-1}. \text{Elemental Analysis calcd for C}_{13}\text{H}_{11}\text{ClN}_2\text{: C} = 76.68\%, \text{H} = 4.81\%, \text{N} = 12.14\%, \text{found C} = 67.67\%, \text{H} = 4.78\%, \text{N} = 12.14\%.
\]

E-(3-phenyloxiran-2-yl)methanol (6a):


\[
\text{H NMR (CDCl}_3\text{, 400 MHz) \delta 7.30-7.40 (m, 5H), 7.47 (s, 1H), 4.07 (dd, J = 12.5, 2.5 Hz, 1H), 3.95 (d, J = 2.0 Hz, 1H), 3.70 (dd, J = 12.5, 4.0 Hz, 1H), 3.25 (dt, J = 4.0, 2.5 Hz, 1H) ppm. C NMR (CDCl}_3\text{, 101 MHz) \delta 136.7 (CH}_3\text{), 128.6, 128.4, 125.8, 62.5, 61.3 (CH}_2\text{), 55.63 ppm. IR (solid state): 3408 (br), 2924 (w), 1496 (m), 1461 (m), 1069 (m) cm}^{-1}. \text{HRMS (ES): m/z [M+Na}^+\text{] calcd for C}_{9}\text{H}_{10}\text{NaO: 173.0573, found 173.0575.}
\]

E-(3-pentyloxiran-2-yl)methanol (6b):


\[
\text{H NMR (CDCl}_3\text{, 400 MHz) \delta 3.91 (dd, J = 12.5, 2.5 Hz, 1H), 3.63 (dd, J = 12.5, 4.5 Hz, 1H), 2.89-3.00 (m, 2H), 2.06 (br, 1H), 1.54-1.63 (m, 2H), 1.39-1.52 (m, 2H), 1.33 (m, 4H), 0.86-0.95 (m, 3H) ppm. C NMR (CDCl}_3\text{, 101 MHz) \delta 61.8, 58.5 (CH}_2\text{), 56.1 (CH}_3\text{), 31.6, 31.5, 25.6, 22.6, 14.0 (CH}_2\text{) ppm. IR (solid state): 3415 (br), 2926 (w), 2860 (w), 1467 (m), 1081 (m) cm}^{-1}. \text{Elemental Analysis calcd for C}_{8}\text{H}_{10}\text{O}_2\text{: C} = 66.63\%, \text{H} = 11.18\%, \text{found C} = 66.60\%, \text{H} = 10.94\%.
\]

E-(2-methyl-3-phenyloxiran-2-yl)methanol (6c):


\[
\text{H NMR (CDCl}_3\text{, 400 MHz) \delta 7.18-7.47 (m, 5H), 4.24 (s, 1H), 3.88 (d, J = 12.5 Hz, 1H), 3.78 (d, J = 12.5 Hz, 1H), 1.12 (s, 3H) ppm. C NMR (CDCl}_3\text{, 101 MHz) \delta 135.6 (CH}_3\text{), 128.15, 127.6, 126.5, 65.1 (CH}_2\text{), 63.8, 60.3, 13.5 ppm. IR (solid state): 3428 (br), 2927 (w), 1497 (w), 1450 (m), 1384 (w), 1070 (m), 1030 (m) cm}^{-1}. \text{Elemental Analysis calcd for C}_{10}\text{H}_{12}\text{O}_2\text{: C} = 73.15\%, \text{H} = 7.37\%, \text{found C} = 72.39\%, \text{H} = 7.30\%.
\]
**E-(3-octyloxiran-2-yl)methanol (6d):**


$$\text{OH}$$

$^1\text{H NMR}$ (CDCl$_3$, 400 MHz) δ 3.93 (dd, $J = 12.5, 2.5$ Hz, 1H), 3.64 (dd, $J = 12.5, 4.5$ Hz, 1H), 2.89-3.02 (m, 2H), 1.54-1.65 (m, 2H), 1.40-1.51 (m, 2H), 1.17-1.38 (m, 10H), 0.84-0.94 (m, 3H), 1.71-1.99 (m, 1H) ppm. $^{13}\text{C NMR}$ (CDCl$_3$, 101 MHz) δ 61.8, 58.5 (CH$_3$), 56.0 (CH$_2$), 31.9, 31.6, 29.5, 29.4, 29.2, 26.0, 22.7, 14.1 (CH$_3$) ppm. IR (solid state): 3264 (br), 3138 (br), 2918 (s), 2848 (s), 1459 (m), 1333 (w), 1058 (m), 1017 (m) cm$^{-1}$. **Elemental Analysis** calcd for C$_{11}$H$_{22}$O$_2$: C = 70.92%, H = 11.90% found C = 70.89%, H = 11.82.

**2-phenyl-1,3-dithiane (9a):**


$^1\text{H NMR}$ (CDCl$_3$, 400 MHz) δ 7.45-7.55 (m, 2H), 7.27-7.41 (m, 3H), 5.20 (s, 1H), 3.03-3.16 (m, 2H), 2.93 (m, 2H), 2.14-2.24 (m, 1H), 1.90-2.03 (m, 1H) ppm. $^{13}\text{C NMR}$ (CDCl$_3$, 101 MHz) δ 139.2 (CH$_3$), 128.8, 128.5, 127.8, 51.5, 32.2 (CH$_2$), 25.2 (CH$_3$)ppm. IR (solid state): 2949 (w), 2892 (m), 1451 (m), 1275 (m) 1171 (w) cm$^{-1}$. **Elemental Analysis** calcd for C$_{10}$H$_{12}$S$_2$: C = 61.18%, H = 6.16% found C = 60.45%, H = 6.09%.

**2-(p-toly)-1,3-dithiane (9b):**


$^1\text{H NMR}$ (CDCl$_3$, 400 MHz) δ 7.33-7.50 (m, 2H), 7.11-7.24 (m, 2H), 5.15 (s, 1H), 3.00-3.19 (m, 2H), 2.82-2.99 (m, 2H), 2.28-2.47 (s, 3H), 2.13-2.27 (m, 1H), 1.85-2.07 (m, 1H) ppm. $^{13}\text{C NMR}$ (CDCl$_3$, 101 MHz) δ 138.3 (CH$_3$), 136.3 (CH$_2$), 129.5, 127.7, 51.3 (CH$_2$), 32.2, 25.2, 21.2 (CH$_3$) ppm. IR (solid state): 2932 (w), 2894 (m), 1513 (m), 1421 (m), 1277 (m) 1169 (w) cm$^{-1}$. **Elemental Analysis** calcd for C$_{11}$H$_{14}$S$_2$: C = 62.81%, H = 6.71% found C = 62.92%, H = 6.70%.

**2-(2-fluorophenyl)-1,3-dithiane (9c):**


$^1\text{H NMR}$ (CDCl$_3$, 400 MHz) δ 7.53-7.73 (m, 1H), 7.22-7.36 (m, 1H), 7.13-7.20 (m, 1H), 6.99-7.12 (m, 1H), 5.57 (s, 1H), 3.09-3.26 (m, 2H), 2.88-2.99 (m, 2H), 2.14-2.25 (m, 1H), 1.89-2.03 (m, 1H) ppm. $^{13}\text{C NMR}$ (CDCl$_3$, 101 MHz) δ 159.0 (d, $J_{C-F} = 249$ Hz), 130.0 (d, $J_{C-F} = 8$ Hz), 129.6 (d, $J_{C-F} = 3$ Hz), 126.3 (d, $J_{C-F} = 14$ Hz) 124.7 (d, $J_{C-F} = 4$ Hz), 115.5 (d, $J_{C-F} = 22$ Hz) 43.1, 32.3, 25.1 ppm. IR (solid state): 2897(w), 1586 (m), 1456 (m), 1421 (m), 1275 (m), 1231 (m), 1088 (m) cm$^{-1}$. **Elemental Analysis** calcd for C$_{10}$H$_{11}$FS$_2$: C = 56.04%, H = 5.17% found C = 56.16%, H = 5.17%.