Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

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

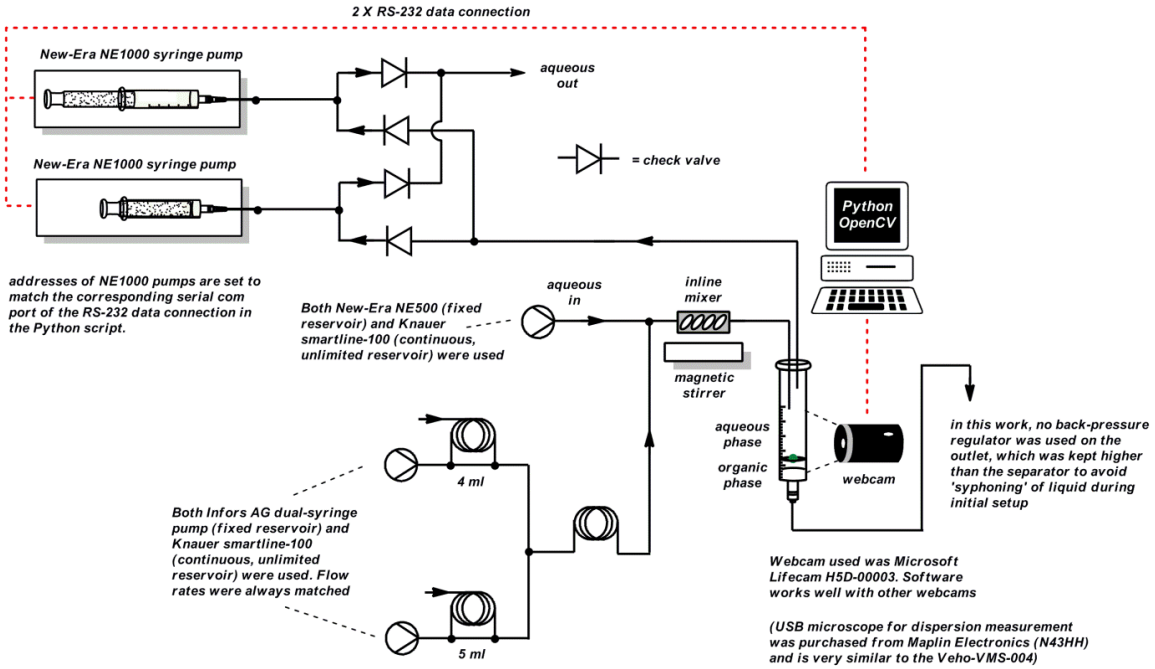
SUPPORTING INFORMATION

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

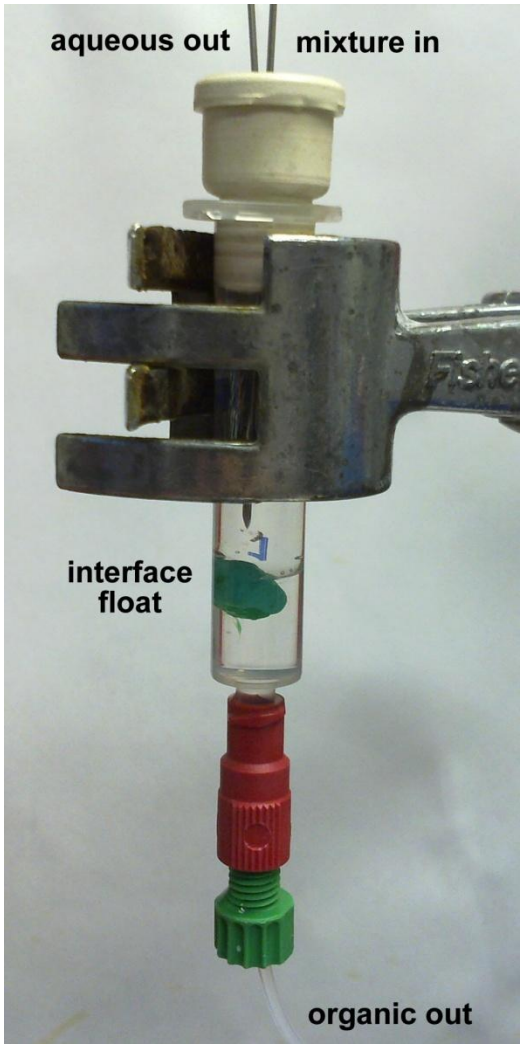
Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW

General Experimental (Flow Apparatus)

Overall setup

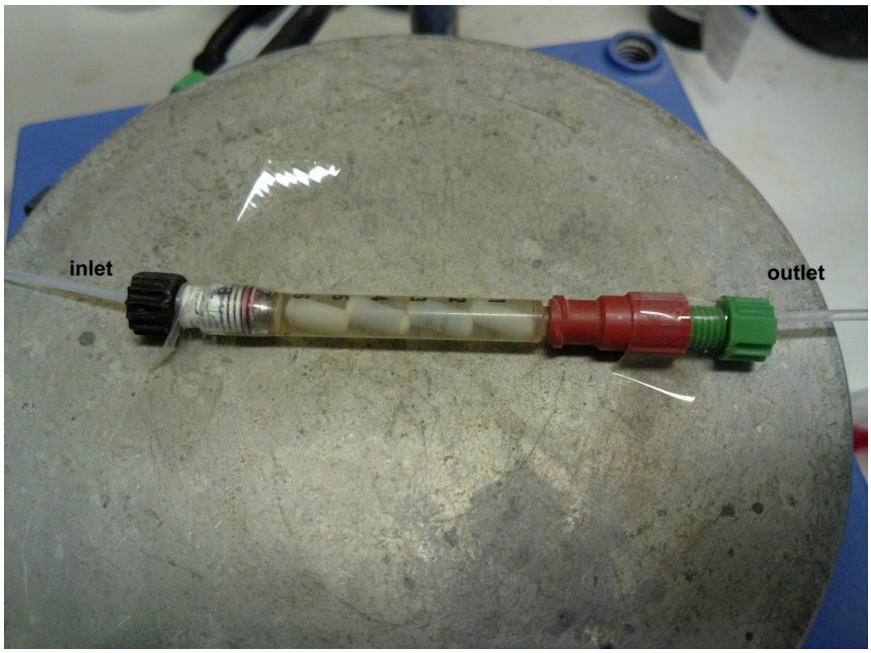


Prototype Separator



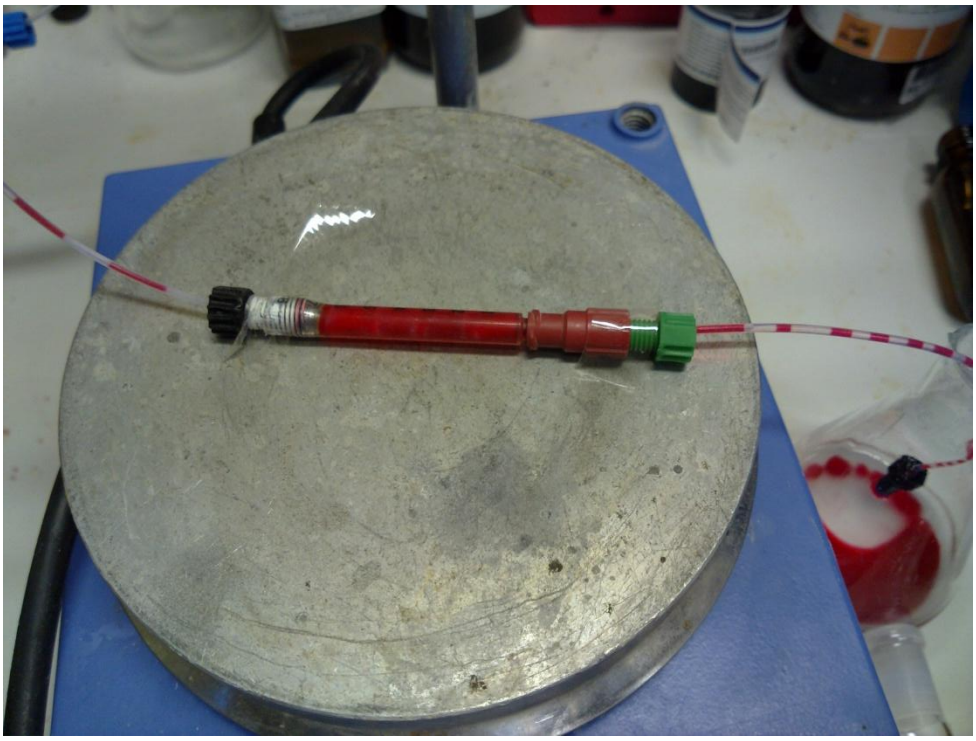
The main body is a 2.5 mL plastic syringe barrel. Upper inlets are 120 mm stainless steel 21g needles going through the B10 suba-seal. The interface float was made by melting together roughly equal amounts (volume) of the polyethylene plunger from an HSW normject 1 mL syringe and a peice of green B-24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

Inline Mixer



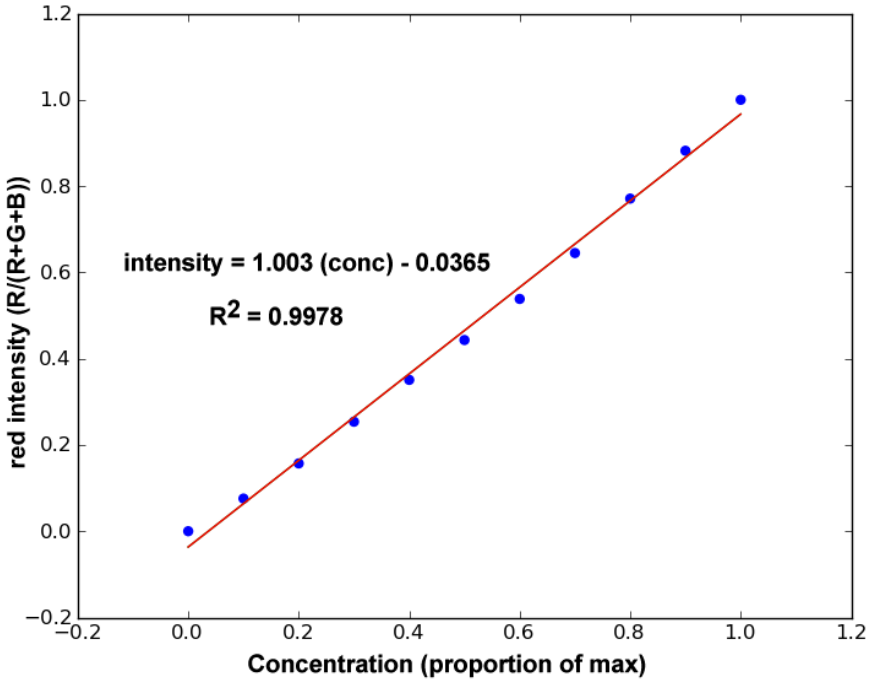
Body of mixer is cut from the barrel of a 1 mL HSW normject syringe. The thread on the inlet side was made by heating to softness then screwing in the ¼-28-UNF connector, which cut a thread. PTFE tape was used to improve the seal. The outlet is a simple female luer to female ¼-28 UNF adapter.

Inline mixer, biphasic mixture (DCM/Water, DCM dyed red), stirrer on maximum speed:

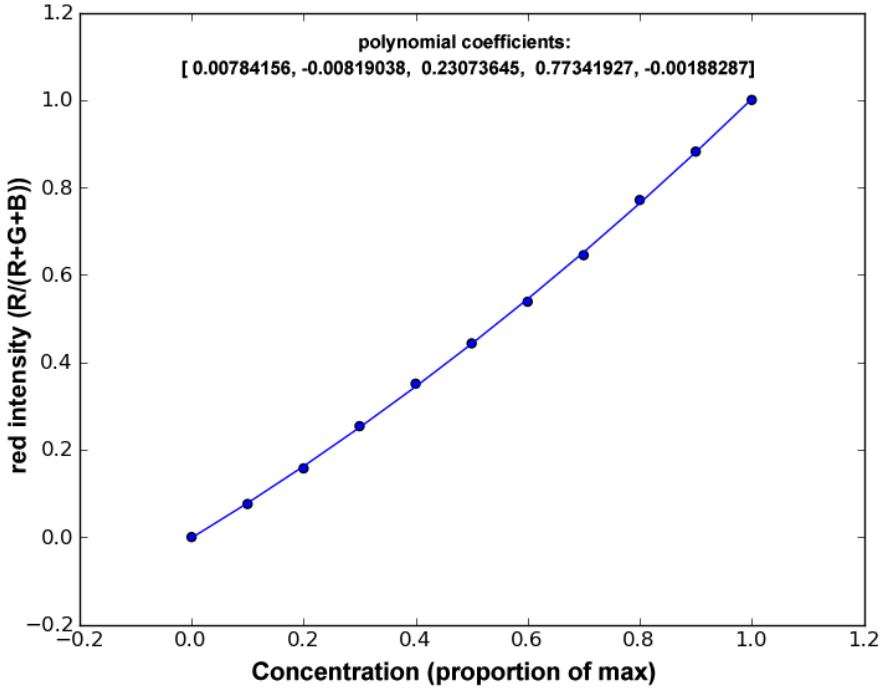


Inline mixer, biphasic mixture, no stirring

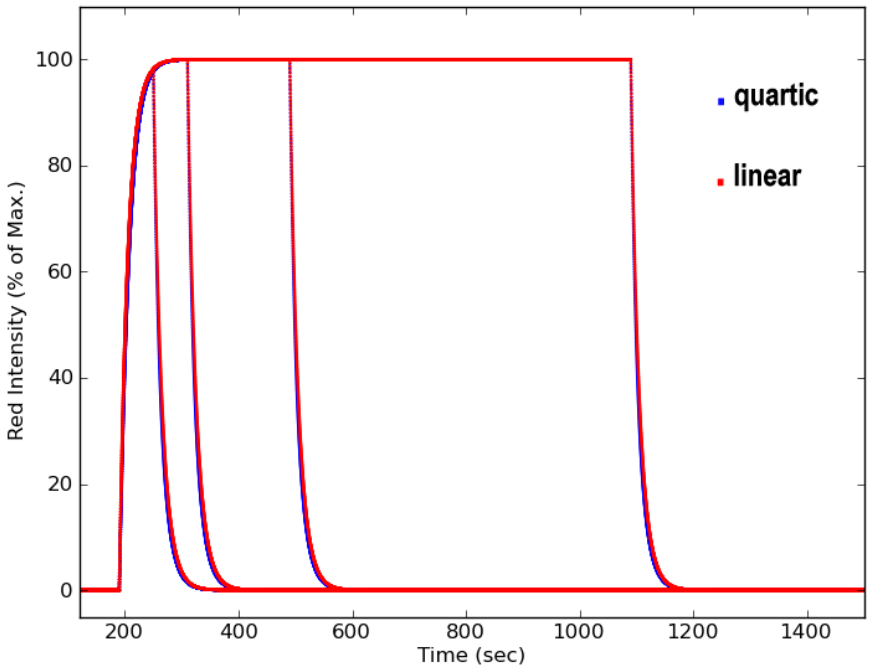
Linear Regression between dye concentration and red intensity:



Quartic polynomial calibration:



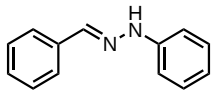
Comparison between linear and quartic calibration (converting calculated concentration to 'observed' intensity) for 0.25 mL heavy phase dispersion measurements.



Compound Data

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

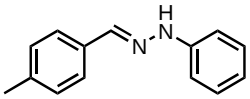
M. S. Gordon, S. A. Sojka and J. G. Krause, *J. Org. Chem.*, 1984, **49**, 97-100.



^{1}H NMR ($CDCl_3$, 400 MHz) δ 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) δ 144.7 (CH_0), 137.3, 135.4 (CH_0), 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* $[MH]^+$ calcd for $C_{13}H_{12}N_2$: 196.0995, found 196.1000.

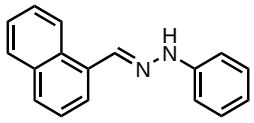
1-(4-methylbenzylidene)-2-phenylhydrazine (**3b**):

M. S. Gordon, S. A. Sojka and J. G. Krause, *J. Org. Chem.*, 1984, **49**, 97-100.



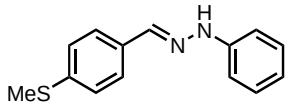
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68 (s, 1H), 7.54-7.58 (m, 2H), 7.24-7.30 (m, 2H), 7.17-7.21 (m, 2H), 7.09-7.14 (m, 2H), 6.83-6.90 (m, 1H), 2.37 (s, 3H) ppm. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 144.9 (CH_0), 138.5 (CH_0), 137.6, 132.6 (CH_0), 129.4, 129.3, 126.2, 120.0, 112.8, 21.4 (CH_3) ppm. **IR** (solid state): 3312 (w), 3029 (w), 1597 (m), 1507 (m), 1493 (m), 1259 (m) cm^{-1}. **HRMS** (ES): *m/z* $[MH]^+$ calcd for $C_{14}H_{14}N_2$: 210.1151, found 210.1152.

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



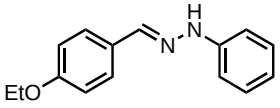
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.81 (d, *J* = 8.5 Hz, 1H), 8.26 (s, 1H), 7.81-7.92 (m, 3H), 7.74 (s, 1H), 7.60-7.64 (m, 1H), 7.48-7.56 (m, 2H), 7.32-7.37 (m, 2H), 7.18-7.22 (m, 2H), 6.94 (t, *J* = 7.0 Hz, 1H) ppm. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 144.7 (CH_0), 137.0, 134.0 (CH_0), 130.8 (CH_0), 130.4 (CH_0), 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* $[MH]^+$ calcd for $C_{17}H_{14}N_2$: 246.1151, found 246.1147.

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



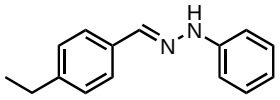
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.63-7.67 (s, 1H), 7.58-7.61 (m, 2H), 7.25-7.32 (m, 5H), 7.11-7.15 (m, 2H), 6.90 (t *J* = 7.0 Hz, 1H), 2.53 (s, 3H) ppm. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 145.0 (CH_0), 139.3 (CH_0), 137.3, 133.7 (CH_0), 129.2, 127.0, 126.9, 120.5, 16.1 (CH_3) ppm. **IR** (solid state): 3315 (w), 1594 (m), 1493 (m), 1264 (m) cm^{-1}. **Elemental Analysis** calcd for $C_{14}H_{14}N_2S$: 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**):



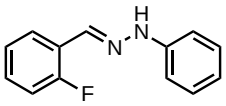
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59-7.65 (m, 3H), 7.47 (s, 1H), 7.28-7.35 (m, 2H), 7.11-7.15 (m, 2H), 6.87-6.95 (m, 3H), 4.09 (q, *J* = 7.0 Hz, 2H), 1.46 (t, *J* = 7.0 Hz, 3H) ppm. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 159.5 (CH_0), 145.1 (CH_0), 137.6, 129.3, 128.0 (CH_0), 127.6, 119.8, 114.8, 112.7, 63.6 (CH_2), 14.9 (CH_3) ppm. **IR** (solid state): 3315 (w), 2978 (w), 1597 (m), 1504 (m), 1494 (m), 1262 (m), 1239 (m) cm^{-1}. **Elemental Analysis** calcd for $C_{15}H_{16}N_2O$: 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**):



^{1}H NMR ($CDCl_3$, 400 MHz) δ 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. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 144.9 (2C, CH_0), 137.6, 132.9 (CH_0), 129.3, 128.2, 126.3, 120.0, 112.8, 28.8 (CH_2), 15.5 (CH_3) 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 $C_{15}H_{16}N_2$: 224.1308, found 224.1307.

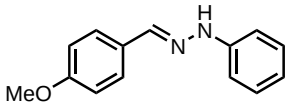
1-(2-fluorobenzylidene)-2-phenylhydrazine (**3g**):



^{1}H NMR ($CDCl_3$, 400 MHz) δ 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. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 160.5 (d, J_{C-F} = 252 Hz), 144.5 (CH_0), 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, CH_0) 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** calcd for $C_{13}H_{11}FN_2$: 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**):

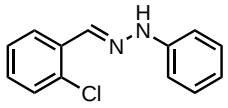
M. S. Gordon, S. A. Sojka and J. G. Krause, *J. Org. Chem.*, 1984, **49**, 97-100.



^{1}H NMR ($CDCl_3$, 400 MHz) δ 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. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 160.1 (CH_0), 145.0 (CH_0), 137.5, 129.3, 128.2 (CH_0), 127.7, 119.8, 114.2, 112.7, 55.3 (CH_3) ppm. **IR** (solid state): 3309 (w), 3054 (w), 1598 (m), 1587 (m), 1482 (m), 1446 (m), 1256 (m), 1236 (m) cm^{-1}. **Elemental Analysis** calcd for $C_{14}H_{14}N_2O$: 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**):

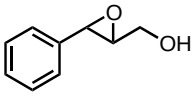
R. Liu, Y. Zhu, L. Qin and S. Ji, *Synthetic Communications*, 2008, **38**, 249-254.



^{1}H NMR ($CDCl_3$, 400 MHz) δ 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. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 144.4 (CH_0), 133.6, 132.8 (CH_0), 132.6 (CH_0), 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}. **Elemental Analysis** calcd for $C_{13}H_{11}ClN_2$: C = 67.68%, H= 4.81%, N = 12.14%, found C = 67.67%, H = 4.78%, N= 12.14%.

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

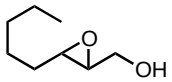
K. Oh and W. E. Knabe, *Tetrahedron*, 2009, **65**, 2966-2974.



^{1}H NMR ($CDCl_3$, 400 MHz) δ 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. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 136.7 (CH_0), 128.6, 128.4, 125.8, 62.5, 61.3 (CH_2), 55.63 ppm. **IR** (solid state): 3408 (br), 2924 (w), 1496 (m), 1461 (m), 1069 (m) cm^{-1}. **HRMS** (ES): *m/z* $[MNa]^+$ calcd for $C_9H_{10}NaO$: 173.0573, found 173.0575.

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

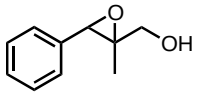
A. Mordini, S. Bindi, S. Pecchi, A. Degl'Innocenti, G. Reginato and A. Serci, *J. Org. Chem.*, 1996, **61**, 4374-4378.



^{1}H NMR ($CDCl_3$, 400 MHz) δ 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. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 61.8, 58.5 (CH_1), 56.1 (CH_1), 31.6, 31.5, 25.6, 22.6, 14.0 (CH_3) ppm. **IR** (solid state): 3415 (br), 2926 (w), 2860 (w), 1467 (m), 1081 (m) cm^{-1}. **Elemental Analysis** calcd for $C_8H_{16}O_2$: C = 66.63%, H= 11.18%, found C = 66.60%, H = 10.94%.

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

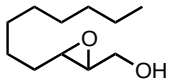
R. Balamurugan, R. B. Kothapalli and G. K. Thota, *European Journal of Organic Chemistry*, 2011, 1557-1569.



^{1}H NMR ($CDCl_3$, 400 MHz) δ 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. **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 135.6 (CH_0), 128.15, 127.6, 126.5, 65.1 (CH_0), 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}. **Elemental Analysis** calcd for $C_{10}H_{12}O_2$: C = 73.15%, H= 7.37%, found C = 72.39%, H = 7.30%.

E-(3-octyloxiran-2-yl)methanol (**6d**):

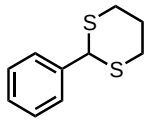
J. S. Yadav, P. K. Deshpande and G. V. M. Sharma, *Tetrahedron*, 1990, **46**, 7033-7046.
J. K. Karjalainen, O. E. O. Hormi and D. C. Sherrington, *Tetrahedron-Asymmetry*, 1998, **9**, 1563-1575.



^{1}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}C NMR** ($CDCl_3$, 101 MHz) δ 61.8, 58.5 (CH_1), 56.0 (CH_1), 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**):

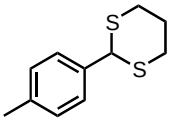
C.-T. Chen, Y.-D. Lin and C.-Y. Liu, *Tetrahedron*, 2009, **65**, 10470-10476.



^{1}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}C NMR** ($CDCl_3$, 101 MHz) δ 139.2 (CH_0), 128.8, 128.5, 127.8, 51.5, 32.2 (CH_2), 25.2 (CH_2)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*-tolyl)-1,3-dithiane (**9b**):

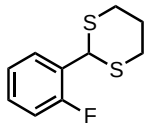
D. Dong, Y. Ouyang, H. Yu, Q. Liu, J. Liu, M. Wang and J. Zhu, *J. Org. Chem.*, 2005, **70**, 4535-4537



^{1}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}C NMR** ($CDCl_3$, 101 MHz) δ 138.3 (CH_0), 136.3 (CH_0), 129.5, 127.7, 51.3 (CH_1), 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**):

S. Goswami and A. C. Malty, *Tetrahedron Lett.*, 2008, **49**, 3092-3096.
P. C. B. Page, A. E. Graham and B. K. Park, *Tetrahedron*, 1992, **48**, 7265-7274.



^{1}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}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%.