Supplementary Material (ESI) for Chemical Communications
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Target-driven selection in a dynamic nitrone library

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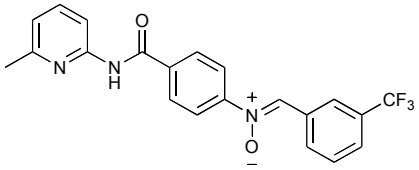
SUPPORTING INFORMATION

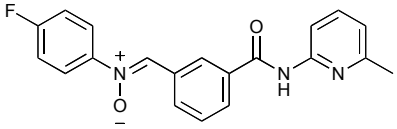
Spectroscopic Data:

Compound 1:



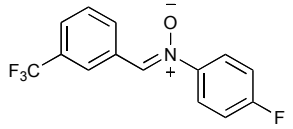
M.p. = 186.0-187.6 °C; ^{1}H NMR (300.1 MHz, CD_2Cl_2) δ_H = 8.86 (1H, s, Ar CH), 8.65 (1H, s, NH), 8.58 (1H, d, $J_{H,H}$ 8, Ar CH), 8.18 (1H, d, $J_{H,H}$ 8, Ar CH), 8.14 (1H, s, N=CH), 8.11 (2H, d, $J_{H,H}$ 9, Ar CH), 7.97 (2H, d, $J_{H,H}$ 9, Ar CH), 7.79 (1H, d, $J_{H,H}$ 8, Ar CH), 7.74-7.66 (2H, m, Ar CH), 7.02 (1H, d, $J_{H,H}$ 7, Ar CH), 2.50 (3H, s, CH_3); ^{13}C NMR (75.5 MHz CD_2Cl_2) δ_C = 164.4 (q), 157.7 (q), 151.5 (q), 151.0 (q), 139.0 (Ar CH), 136.5 (q), 133.5 (N=CH), 132.3 (Ar CH), 131.7 (q), 131.2 (C, q, $^{3}J_{C,F}$ 32, quart.), 129 (Ar CH), 128.8 (2C, Ar CH), 127.6 (C, q, $^{3}J_{C,F}$ 3, Ar CH), 125.6 (C, q, $^{3}J_{C,F}$ 4, Ar CH), 122.5 (2C, Ar CH), 120.0 (Ar CH), 111.1 (Ar CH), 24.2 (CH_3); ^{19}F NMR (282.3 MHz, CD_2Cl_2): δ_F = -63.58 (3F, s, CF_3); MS (ES-) m/z (%) = 398.0 (100) [M-H$^+$]: MS (ES+) m/z (%) = 422.1 (100) [M+Na$^+$]; HRMS (ES+): calcd for $C_{21}H_{16}N_3O_2F_3Na$ (422.1): 422.1092; found 422.095; FT-IR (thin film) ν_{max}/cm^{-1} = 3337, 1655, 1595, 1528, 1457, 1337, 1305, 1170, 1124, 1080, 690.

Compound 2:



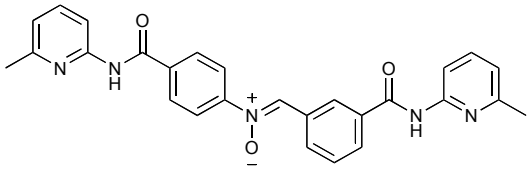
M.p. = 193-195 °C decomp.; ^{1}H NMR (300.1 MHz, $CDCl_3$) δ_H = 8.87 (1H, s, N=CH), 8.78 (1H, br. s, NH); 8.53 (1H, d, $J_{H,H}$ 9, Ar CH), 8.09 (1H, d, $J_{H,H}$ 9, Ar CH), 7.94 (1H, m, Ar CH), 7.92 (2H, s, Ar CH), 7.77-7.74 (2H, m, Ar CH), 7.61-7.51 (2H, m, Ar CH), 7.16-7.08 (2H, m, Ar CH), 6.88 (1H, d, $J_{H,H}$ 8, Ar CH), 2.36 (3H, s, CH_3); ^{13}C NMR (75.5 MHz $CDCl_3$) δ_C = 165.2 (q); 163.6 (C, d, $^{3}J_{C,F}$ 255, quart.), 157.6 (q), 151.3 (q), 145.6 (q), 138.9 (Ar CH), 135.3 (q), 133.3 (N=CH), 132.1 (Ar CH), 131.7 (q), 129.7 (Ar CH), 129.6 (Ar CH), 127.6 (Ar CH), 124.1 (2C, d, $^{3}J_{C,F}$ 9, Ar CH), 119.8 (Ar CH), 116.4 (2C, d, $^{3}J_{C,F}$ 23, Ar CH), 111.1 (Ar CH), 24.1 (CH_3); ^{19}F NMR (282.3 MHz, CD_2Cl_2): δ_F = -111.53 (F, s, Ar F); MS (MS CI+) m/z (%) = 334.1, 350.1 (100) [M+H$^+$]; HRMS (CI+): calcd for $C_{20}H_{17}N_3O_2F$ (350.1): 350.1305; found 350.1299.

Compound 3:



M.p. = 105.9-107.2 °C decomp.; ^{1}H NMR (300.1 MHz, CD_2Cl_2) δ_H = 8.82 (1H, s, Ar CH), 8.52 (1H, d, $J_{H,H}$ 8, Ar CH), 8.02 (1H, s, N=CH), 7.82 (2H, d, $J_{H,H}$ 9, Ar CH), 7.75 (1H, d, $J_{H,H}$ 8, Ar CH), 7.65 (1H, dd, $J_{H,H}$ 8, $J_{H,H}$ 8, Ar CH), 7.22 (2H, d, $J_{H,H}$ 9, Ar CH); ^{13}C NMR (75.5 MHz CD_2Cl_2) δ_C = 163.7 (C, d, $^{3}J_{C,F}$ 250, quart.), 145.6 (q), 133.0 (N=CH), 132.2 (Ar CH), 131.9 (q), 131.2 (C, q, $^{3}J_{C,F}$ 37, quart.), 129.6 (Ar CH), 127.4 (C, q, $^{3}J_{C,F}$ 4, quart.), 125.5 (C, q, $^{3}J_{C,F}$ 4, quart.), 124.1 (2C, d, $^{3}J_{C,F}$ 9, Ar CH), 123.3 (q), 116.4 (2C, d, $^{3}J_{C,F}$ 23, Ar CH); ^{19}F NMR (282.3 MHz, CD_2Cl_2): δ_F = -63.53 (3F, s, CF_3), -111.27 (F, s, Ar F) MS (Cl+) m/z (%) = 248.1 (20), 264.1 (60), 284.1 (100) [M+H$^+$]: HRMS (Cl+): calcd for $C_{14}H_{10}NOF_4$ (284.1): 284.0699; found 284.0692; FT-IR (thin film) ν_{max}/cm^{-1} = 3117, 3039, 1599, 1553, 1499, 1435, 1332, 1124, 1074, 841, 809.

Compound 4:



M.p. = 138.8-140.1 °C., ^{1}H NMR (300.1 MHz, CD_2Cl_2) δ_H = 8.96 (1H, s, Ar CH), 8.79 (1H, s, NH), 8.70 (1H, s, NH), 8.54 (1H, d, $J_{H,H}$ 8, Ar CH), 8.09 (1H, d, $J_{H,H}$ 8, Ar CH), 8.08 (1H, d, $J_{H,H}$ 8, Ar CH), 8.05 (1H, s, N=CH), 8.00 (2H, d, $J_{H,H}$ 9, Ar CH), 8.00-7.96 (1H, m, Ar CH), 7.87 (2H, d, $J_{H,H}$ 9, Ar CH), 7.61 (1H, dd, $J_{H,H}$ 8, $J_{H,H}$ 8, Ar CH), 7.60 (1H, dd, $J_{H,H}$ 8, $J_{H,H}$ 8, Ar CH), 7.57 (1H, dd, $J_{H,H}$ 8, $J_{H,H}$ 8, Ar CH), 6.90 (1H, d, $J_{H,H}$ 7, Ar CH), 6.89 (1H, d, $J_{H,H}$ 7, Ar CH), 2.39 (6H, s, Ar CH); ^{13}C NMR (75.5 MHz CD_2Cl_2) δ_C = 165.2 (q), 164.5 (q), 157.5 (q), 151.6 (q), 151.2 (q), 151.0 (q), 139.2 (Ar CH), 139.1(Ar CH), 136.4 (q), 135.3 (q), 134.0 (N=CH), 132.5 (Ar CH), 131.6 (2q), 130.1 (Ar CH), 129.6 (Ar CH), 128.8 (Ar CH), 127.8 (Ar CH), 122.5 (Ar CH), 120.0 (Ar CH), 119.8 (Ar CH), 111.2 (Ar CH), 111.1 (Ar CH), 24.1 (CH_3); MS (ES+) m/z (%) = 488.18 (100) [M+Na$^+$]; HRMS (ES+): calcd for $C_{27}H_{24}N_5O_3$ (466.2): 466.1879; found 466.1888.

$CDCl_3$ treatment

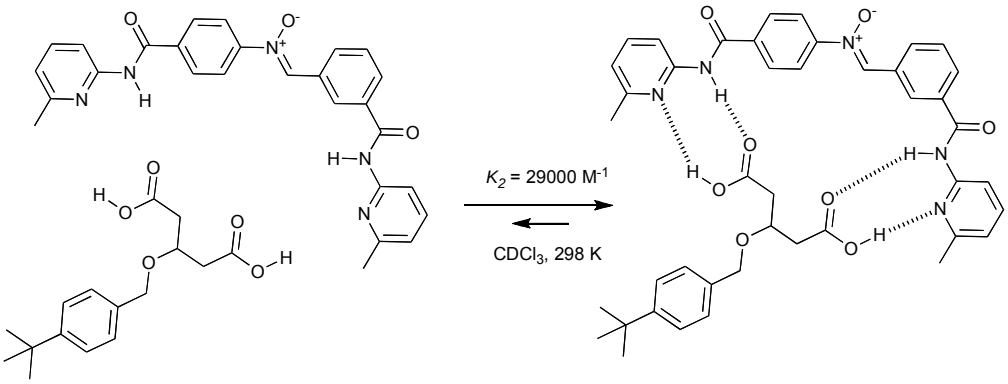
$CDCl_3$ (20 ml) was dried over $CaCl_2$ in the absence of light for 18 h. The $CDCl_3$ was then filtered through a 3 cm^3 plug of activated neutral type I Brockman alumina. The dried $CDCl_3$ was stored over 4 Å molecular sieves and used within 24 h of filtration.

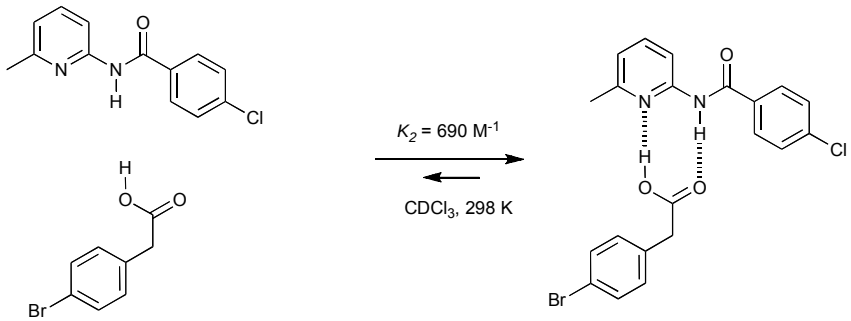
Nitrone exchange experiments

In a typical experiment, an NMR sample was prepared in a 5 mm NMR tube (Wilmad 527PP) by mixing appropriate volumes of stock solutions of the required nitrones (**1** and **2**), acid (either 4-bromophenylacetic acid or the diacid target **5**) and hydroxylamine **6** such that the total volume of the sample was 0.7 ml. The NMR tubes were placed in a thermostatically-controlled water bath at 298 K. Every 24 hours, the tube was transferred to an NMR spectrometer (Bruker Avance), regulated at 298 K, and 300 MHz ^{1}H NMR and 282.3 MHz ^{19}F (with ^{1}H decoupling) spectra were acquired. The ratios of **3**:**2** and **3**:**1** can be calculated readily by deconvolution of the appropriate resonances for compounds **1** and **3** which appear in the CF_3 region (around –63 ppm) and the appropriate resonances for compounds **2** and **3** which appear in the aryl fluoride region (between –100 and –130 ppm) of the 282.3 MHz ^{19}F NMR spectra of the exchanging mixtures of nitrones. Deconvolution was carried out using iNMR (Version 2.5, Nucleomatica, 2008) running on Mac OS X (Version 10.5.2). The ratios of **3**:**2** and **3**:**1** are not identical because of the differential rates of hydrolysis of nitrones **1** and **2**. The associated equilibrium positions for the hydrolyses of **1** and **2** are coupled to the exchange processes and so, given different hydrolytic stabilities of **1** and **2**, slight differences in the corresponding concentrations with respect to **3** would be expected. Analysis of the ^{1}H NMR spectra of the exchanging mixtures confirm the presence of differing amounts of the aldehydes derived from **1** and **2** in the exchanging mixture – with the aldehyde derived from **2** being present in a larger amount. The amount of hydrolysis is <10% of the reaction mixture.

Determinination of K_a by the ^{1}H NMR dilution method

A series of ^{1}H NMR samples were prepared in 5 mm NMR tubes (Wilmad 527PP) at concentrations of 0.8 to 100 mM in $CDCl_3$ of equimolar amounts of the host and guest. The NMR tubes were equilibrated at 298 K using a thermostatically controlled water bath. In turn, each tube was transferred promptly to a 500 MHz NMR spectrometer (Varian UNITYplus) regulated at 298 K and a ^{1}H NMR spectrum was acquired on each sample. Chemical shift changes of appropriate resonances in these spectra were analyzed by non-linear least squares fitting to a 1:1 binding isotherm to afford K_a values for each complex studied. For a detailed discussion of this method for Ka determination, see C. A. Wilcox in *Frontiers in Supramolecular Organic Chemistry and Photochemistry*, H. -J. Schneider and H. Dürr (Eds.), VCH, Weinheim, 1991, p.123–143.





Coordinates for unbound receptor 4

38

C	1	0.175	0.387	0.449
C	2	-0.705	-1.720	0.784
C	3	-2.001	-1.248	0.553
C	4	-2.179	0.104	0.259
C	5	-1.082	0.956	0.200
C	6	1.574	2.456	0.215
C	7	5.526	4.093	0.610
C	8	4.499	4.823	0.010
C	9	3.242	4.249	-0.117
C	10	2.987	2.956	0.364
C	11	4.025	2.250	0.989
C	12	5.295	2.813	1.114
C	13	7.934	4.055	0.626
C	14	11.961	5.435	0.846
C	15	11.674	4.092	0.554
C	16	10.343	3.674	0.497
C	17	9.281	4.574	0.736
C	18	9.594	5.915	1.050
C	19	10.924	6.328	1.102
C	20	12.846	3.194	0.267
C	21	14.954	-1.496	-0.200
C	22	13.648	-1.533	0.297
C	23	13.479	0.765	0.175
C	24	14.783	0.909	-0.325
C	25	15.516	-0.257	-0.510
C	26	12.975	-2.832	0.668
C	27	-0.432	-3.164	1.125
H	28	2.176	0.518	0.621
H	29	7.803	3.006	0.395
H	30	11.728	1.540	0.799
N	31	0.364	-0.909	0.730
N	32	1.379	1.114	0.442
N	33	6.817	4.757	0.741
N	34	12.609	1.843	0.407
N	35	12.925	-0.416	0.477
O	36	0.669	3.226	-0.094
O	37	6.757	6.022	0.928
O	38	13.932	3.658	-0.062

Coordinates for [4•5] complex

49

C	1	0.260	0.335	0.536
C	2	-0.415	-1.876	0.833
C	3	-1.742	-1.541	0.570
C	4	-2.055	-0.208	0.294
C	5	-1.056	0.755	0.272
C	6	1.347	2.572	0.592
C	7	5.230	4.363	0.827
C	8	4.145	4.945	1.485
C	9	2.888	4.364	1.365
C	10	2.709	3.202	0.600
C	11	3.794	2.678	-0.115
C	12	5.053	3.262	-0.013
C	13	7.611	4.171	1.027
C	14	11.692	5.172	1.682
C	15	11.315	3.869	1.313
C	16	9.966	3.586	1.104
C	17	8.978	4.585	1.252
C	18	9.378	5.887	1.620
C	19	10.727	6.161	1.836
C	20	12.432	2.886	1.117
C	21	14.491	-1.736	0.222
C	22	13.181	-1.836	0.684
C	23	12.960	0.487	0.744
C	24	14.278	0.667	0.284
C	25	15.035	-0.465	0.026
C	26	12.531	-3.175	0.932
C	27	0.004	-3.288	1.156
C	28	3.975	-1.124	1.528
C	29	5.263	-1.544	2.210
C	30	6.512	-0.871	1.634
C	31	7.772	-1.283	2.402
C	32	9.059	-0.683	1.864
H	33	2.269	0.713	0.549
H	34	7.420	3.121	0.856
H	35	11.115	1.265	1.165
H	36	2.084	-1.456	1.478
H	37	10.943	-1.083	1.636
N	38	0.562	-0.947	0.821
N	39	1.363	1.189	0.501
N	40	6.543	4.953	1.053
N	41	12.084	1.545	1.004
N	42	12.438	-0.738	0.940
O	43	0.325	3.239	0.707
O	44	6.552	6.208	1.317
O	45	13.596	3.271	1.061
O	46	2.916	-1.803	1.944
O	47	3.920	-0.226	0.694
O	48	10.097	-1.487	2.035
O	49	9.136	0.431	1.352