Supporting Information

Quantitative Reactivity Scales for Dynamic Covalent and Systems Chemistry

Yuntao Zhou[a,‡], Lijie Li [a,b,‡], Hebo Ye[a,‡], Ling Zhang[a], and Lei You[a,*]

a. State Key Laboratory of Structural Chemistry, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences, Fuzhou, Fujian, 350002, P. R. China

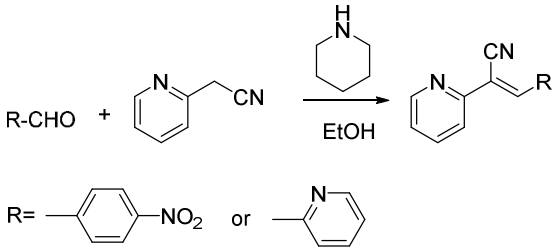
b. University of Chinese Academy of Sciences, Beijing, 100049, P. R. China

Experimental Section

General materials

All reagents were purchased from commercial sources unless otherwise specified. ^{1}HNMR and ^{13}CNMR spectra were recorded from Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences NMR facility (400 MHz).

Synthesis



Both α-[(4-nitrophenyl)methylene]-2-pyridineacetonitrile (**8**) and α-(2-pyridinylmethylene)-2-pyridineacetonitrile (**9**) are known compounds. Their synthesis followed the literature method.[1] Aldehyde (1.64 mmol, 1.0 equiv.) and 2-pyridylacetonitrile (1.80 mmol, 1.1 equiv.) were mixed in ethanol (12 mL), and piperidine (0.5 equiv.) was next added. The reaction mixture was stirred at room temperature overnight and quenched with water. The aqueous solution was extracted with dichloromethane. The combined organic layers were dried over $MgSO_4$, and the solvents were evaporated. Purification by column chromatography (silica gel, 4: 1 petroleum ether/EtOAc) afforded the desired compound.

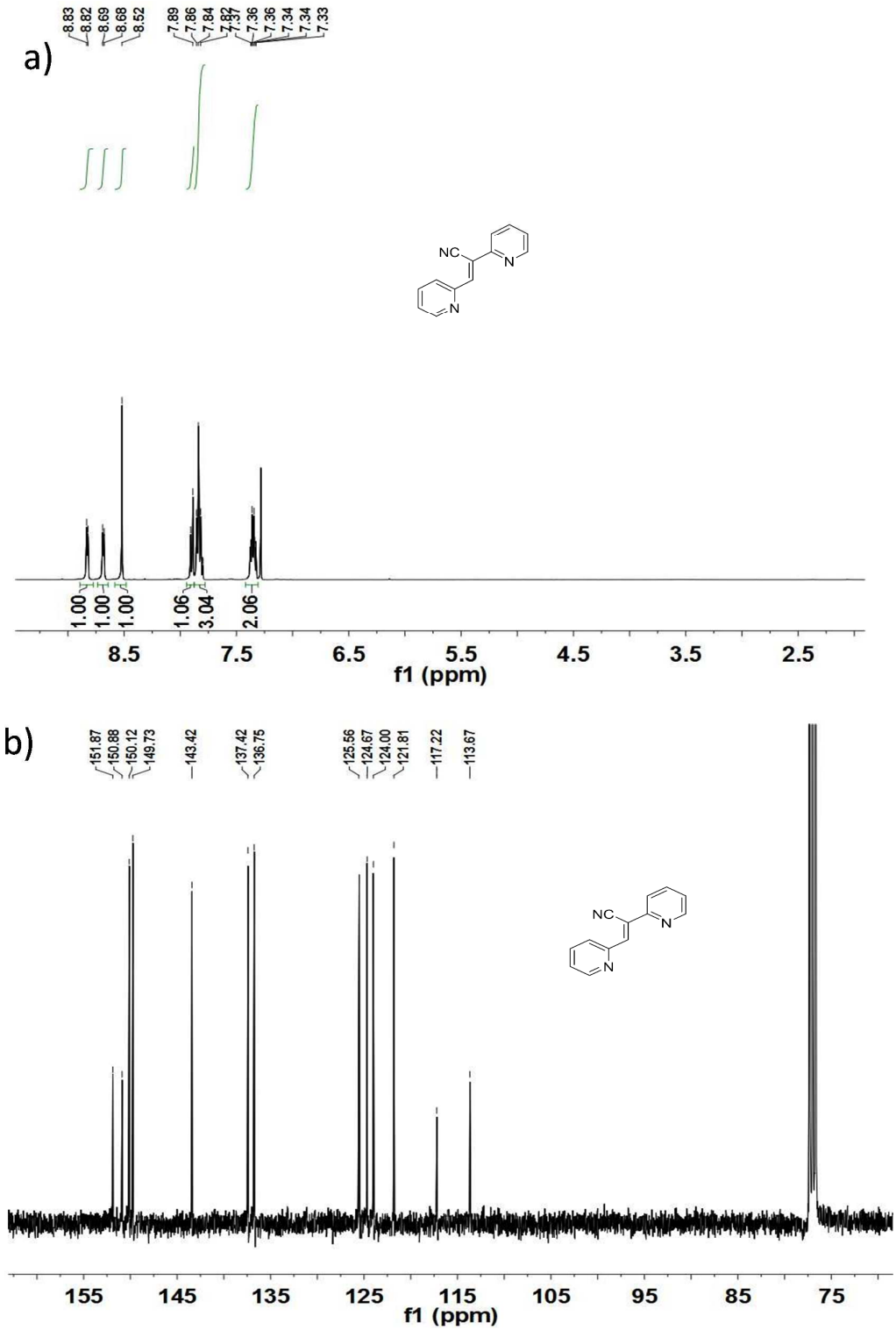


Figure S1. ^{1}HNMR (a) and ^{13}CNMR (b) of α-(2-pyridinylmethylene)-2-pyridineacetonitrile (**9**) in $CDCl_3$ (400 MHz).

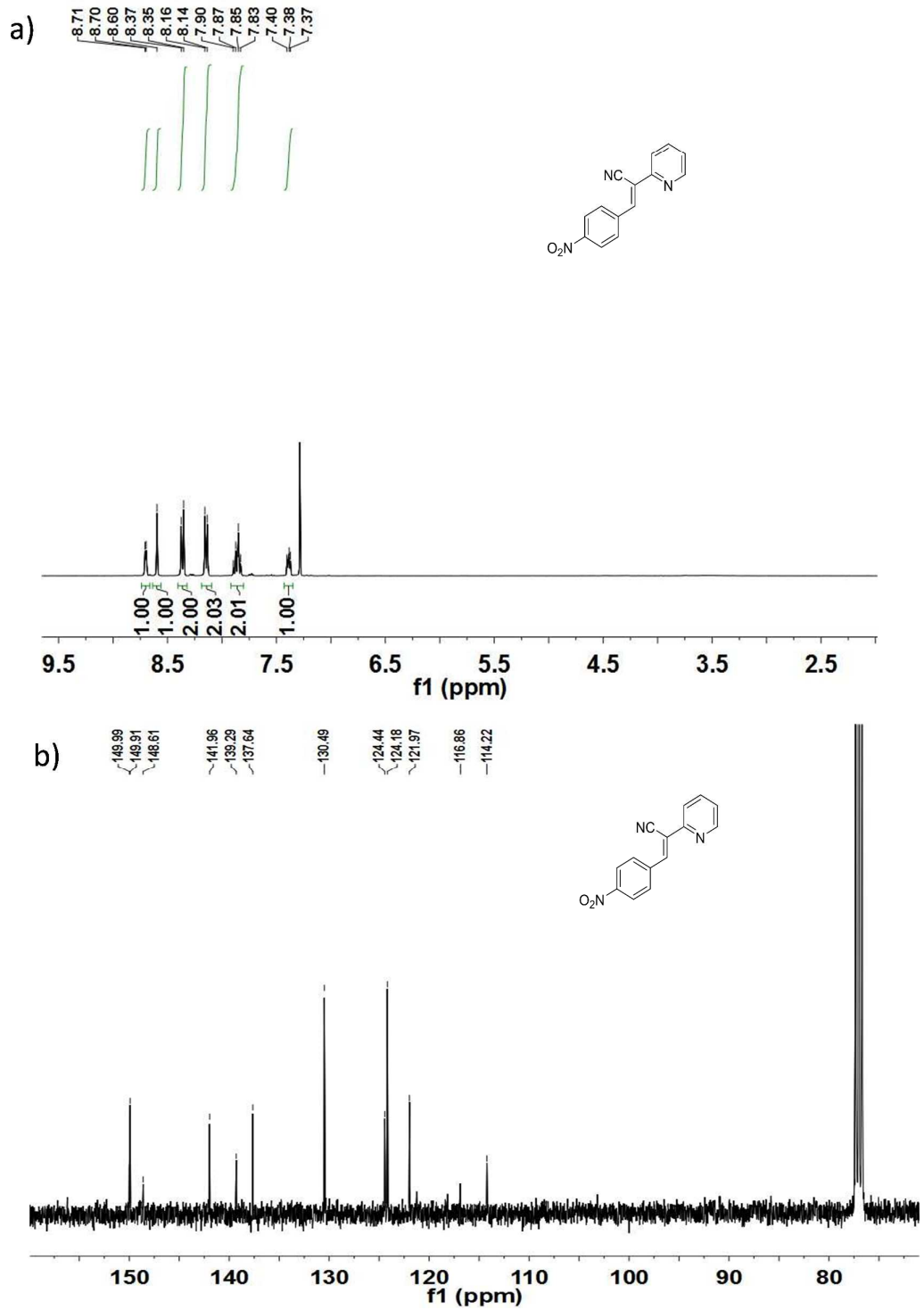
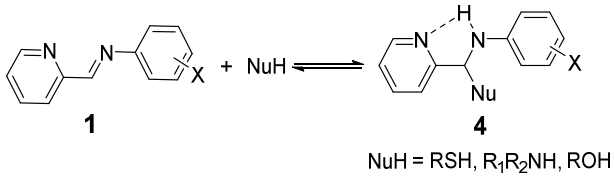


Figure S2. ^{1}HNMR (a) and ^{13}CNMR (b) of α-[(4-nitrophenyl)methylene]-2-pyridineacetonitrile (**8**) in $CDCl_3$ (400 MHz).

The dynamic multicomponent covalent assembly reaction.

Dynamic multicomponent reactions were performed *in situ* in CD_3CN without isolation and purification. To a stirred solution of pyridine-2-carboxaldehyde (**2-PA**, ~53.5 mM, 1.0 equiv.) in CD_3CN (0.6 mL), were added primary aromatic amines (1.0 equiv.), nucleophiles (ROH, RSH, R_1R_2NH, or RNH_2, 1.0-3.0 equiv. *See* the exact amount in the main text or SI), methanesulfonic acid (0.3 equiv. Note: only used for ROH and RSH), and activated 3 Å molecular sieves (4-8 mesh). The mixture was stirred at room temperature for 24 h and characterized by ^{1}HNMR.

Equilibrium constant



eq. 1

The equilibrium constant can be expressed as the following:

$$K = \frac{[\mathbf{4}]}{[\mathbf{1}]\,[\mathrm{NuH}]} \qquad \text{eq. 2}$$

According to the integrals in ^{1}HNMR spectra, define that

$$\frac{[\mathbf{1}]}{[\mathbf{4}]} = x,\ \frac{[\mathbf{2-PA}]}{[\mathbf{4}]} = y,\ \frac{[\mathrm{NuH}]}{[\mathbf{4}]} = z,\ \frac{[\mathbf{5}]+[\mathbf{6}]+[\mathbf{7}]}{[\mathbf{4}]} = n,$$

According to the mass balance of **2-PA**,

$$[\mathbf{1}] + [\mathbf{4}] + [\mathbf{2-PA}] + [\mathbf{5}] + [\mathbf{6}] + [\mathbf{7}] = [\mathbf{2-PA}]_{total}$$

$$[\mathbf{4}] + x[\mathbf{4}] + y[\mathbf{4}] + n[\mathbf{4}] = [\mathbf{2-PA}]_{total}$$

$$[\mathbf{4}] = \frac{[\mathbf{2\text{ - }PA}]_{total}}{1 + x + y + n} \qquad \text{eq. 3}$$

$$K = \frac{[\mathbf{4}]}{[\mathbf{1}]\,[\mathrm{NuH}]} = \frac{1}{x[\mathrm{NuH}]} = \frac{1}{x \cdot z[\mathbf{4}]}$$

$$K = \frac{1}{[\mathbf{2-PA}]_{total}} \cdot \frac{1 + x + y + n}{x \cdot z} \qquad \text{eq. 4}$$

Selected ^{1}HNMR spectra

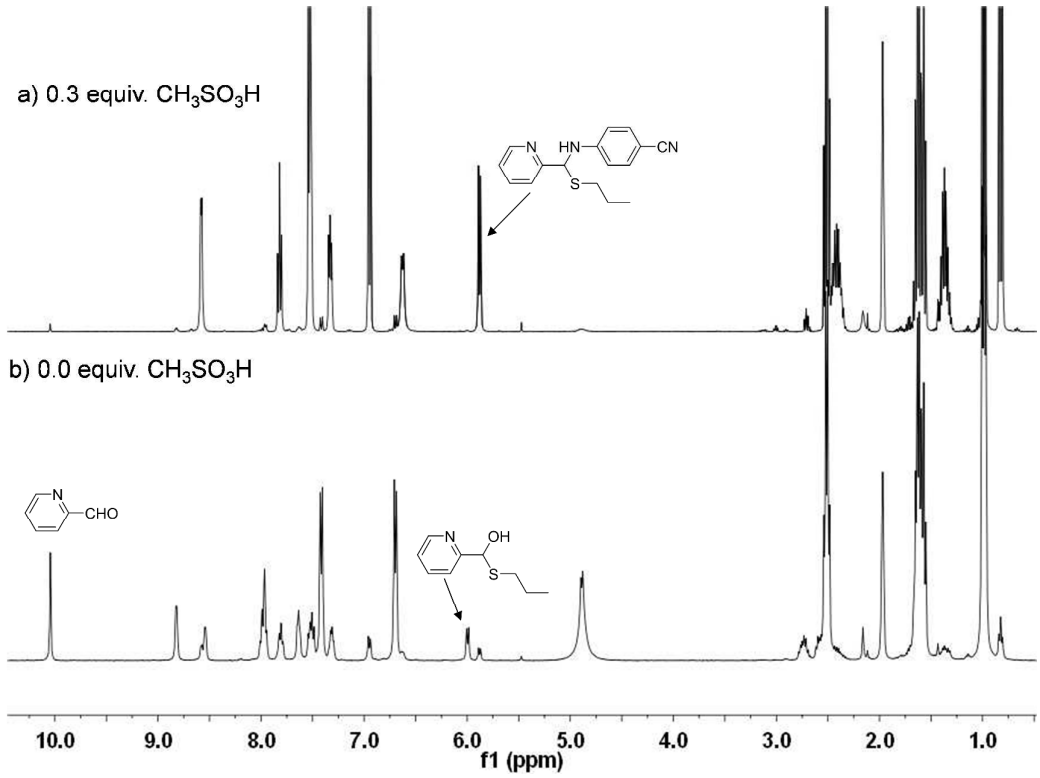


Figure S3. ^{1}HNMR of the reaction of **2-PA**, 4-cyanoaniline and 1-propanethiol with (a) and without (b) methanesulfonic acid.

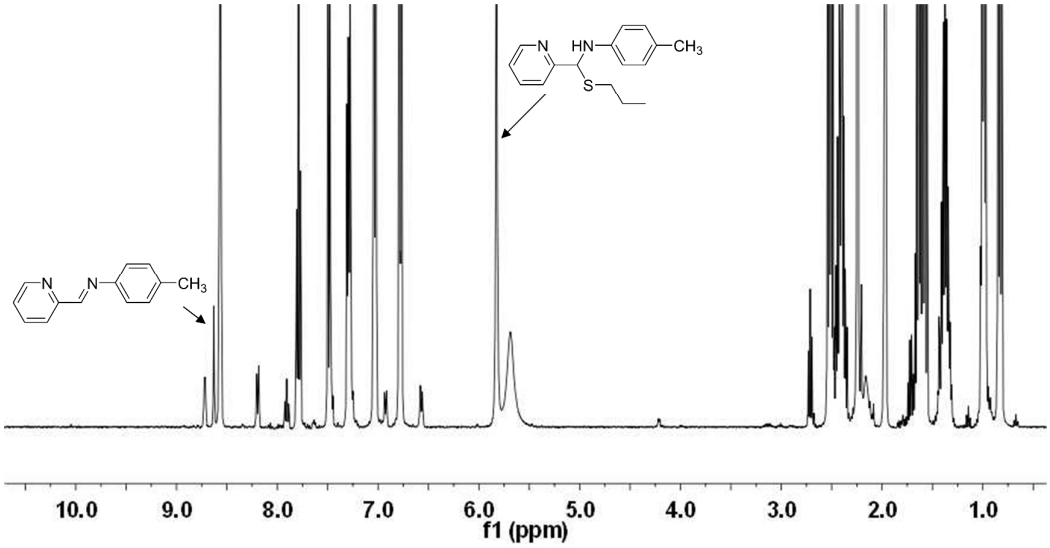


Figure S4. ^{1}HNMR of the reaction of **2-PA**, 4-methylaniline and 1-propanethiol in the presence of 0.3 equiv. methanesulfonic acid.

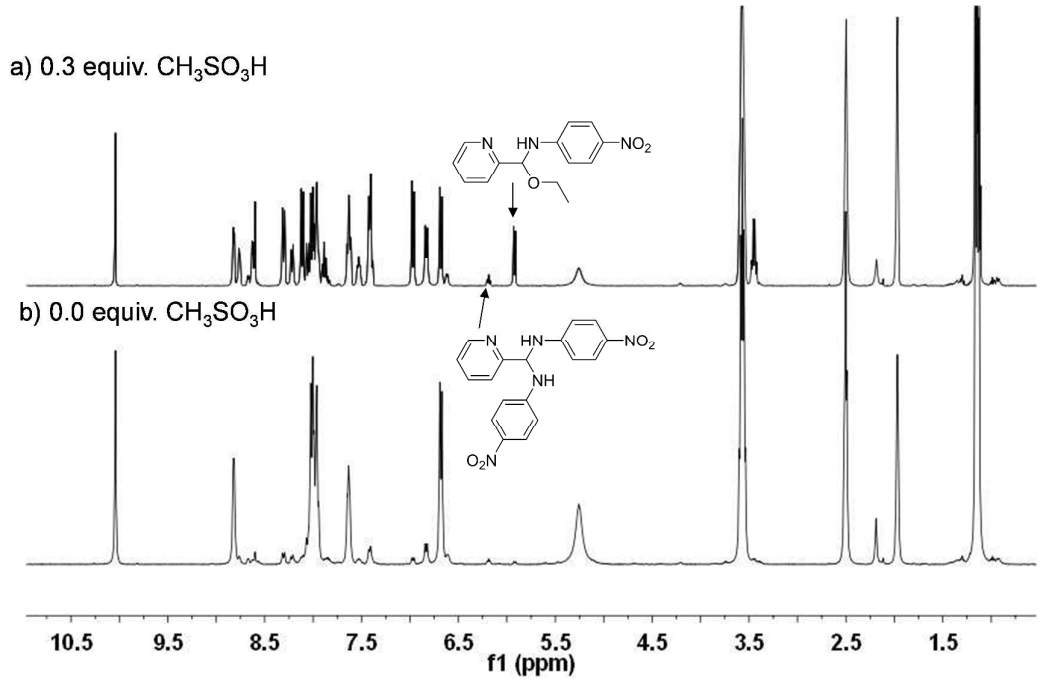


Figure S5. ^{1}HNMR of the reaction of **2-PA**, 4-nitroaniline and ethanol with (a) and without (b) 0.3 equiv. methanesulfonic acid.

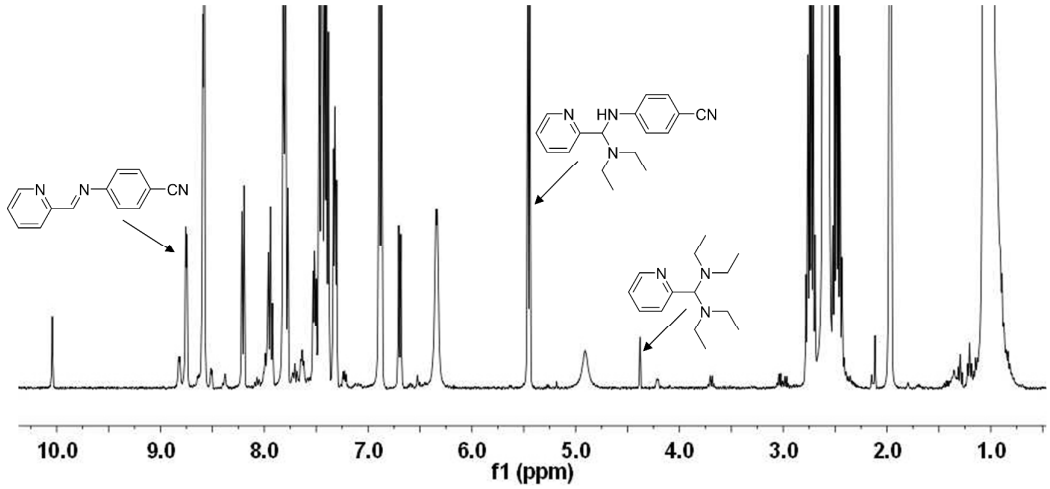


Figure S6. ^{1}HNMR of the reaction of **2-PA**, 4-cyanoaniline and diethylamine.

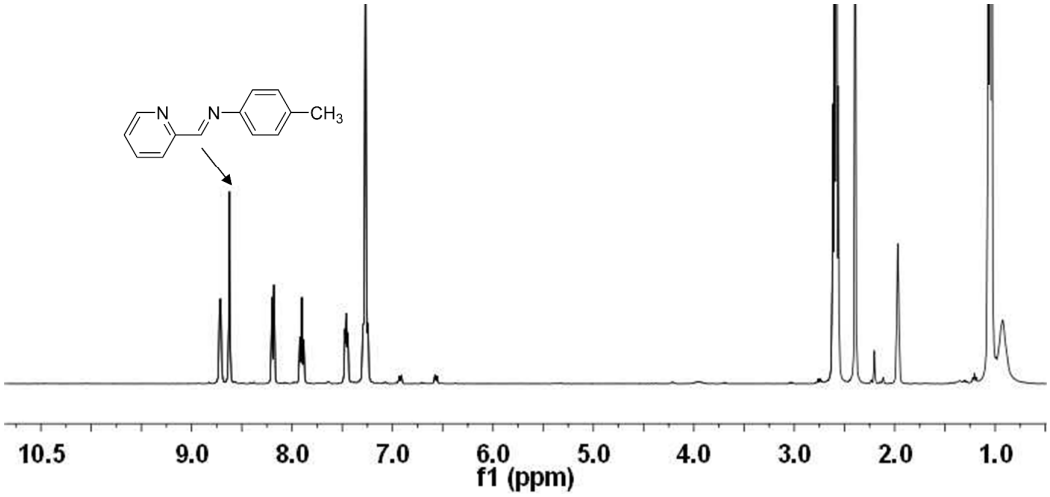


Figure S7. ^{1}HNMR of the reaction of **2-PA**, 4-methylaniline and diethylamine. Only imine was obtained.

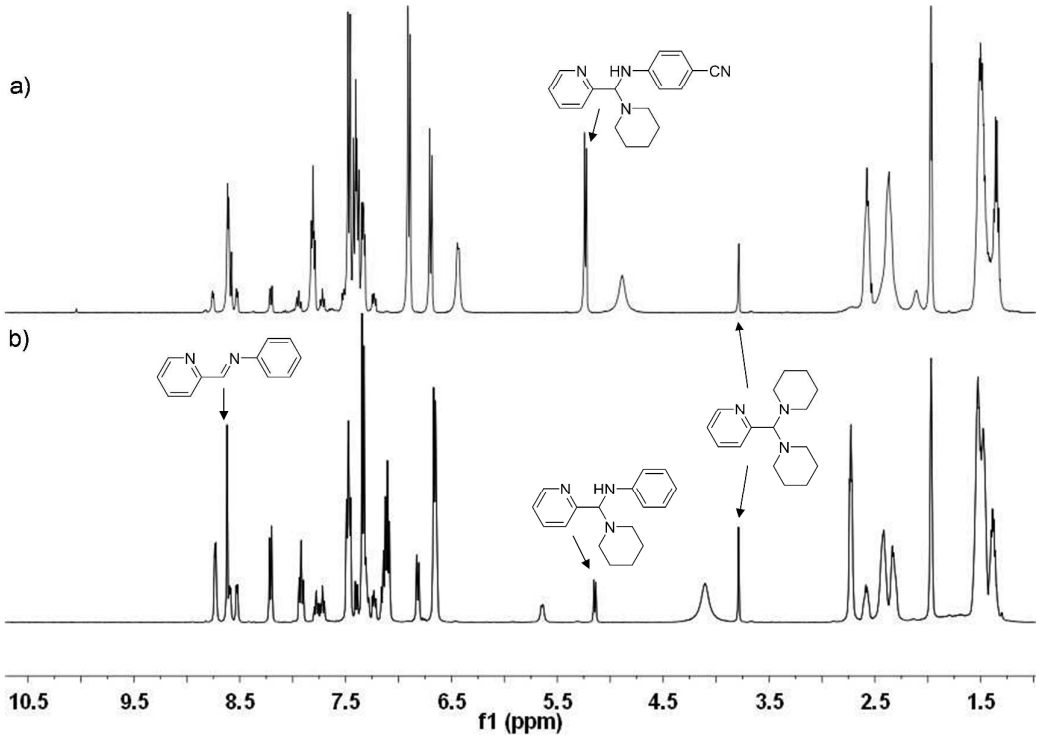


Figure S8. ^{1}HNMR of the reaction of **2-PA**, 4-cyanoaniline, and piperidine (a) as well as the reaction of **2-PA**, aniline, and piperidine (b).

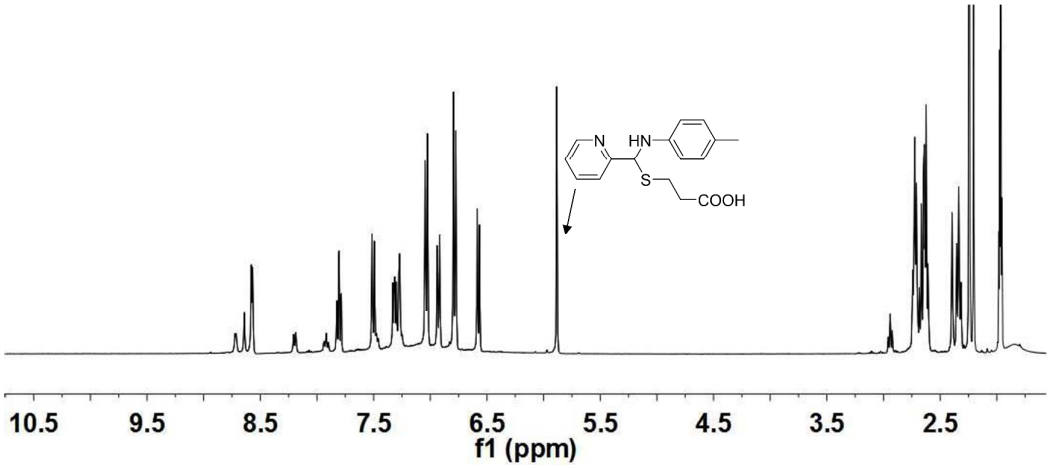


Figure S9. ^{1}HNMR of the reaction of **2-PA**, 4-methylaniline, and 3-mercaptopropionic acid in the presence of 0.3 equiv. methanesulfonic acid.

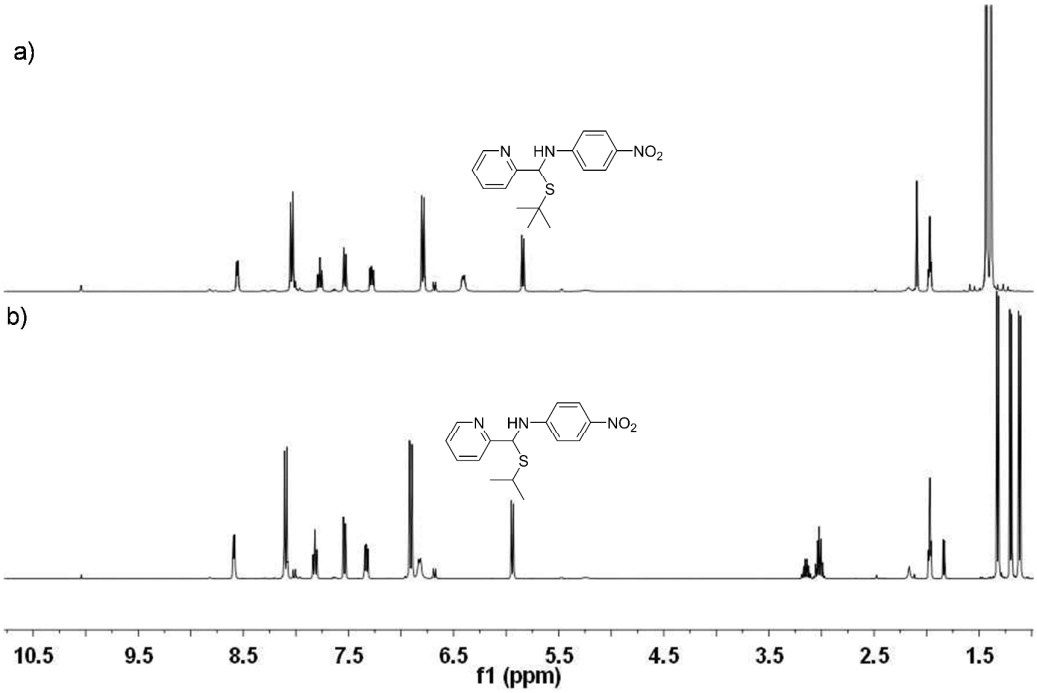


Figure S10. ^{1}HNMR of the reaction of **2-PA**, 4-nitroanline and *t*-butylthiol (a) or 2-propanethiol (b) in the presence of 0.3 equiv. methanesulfonic acid.

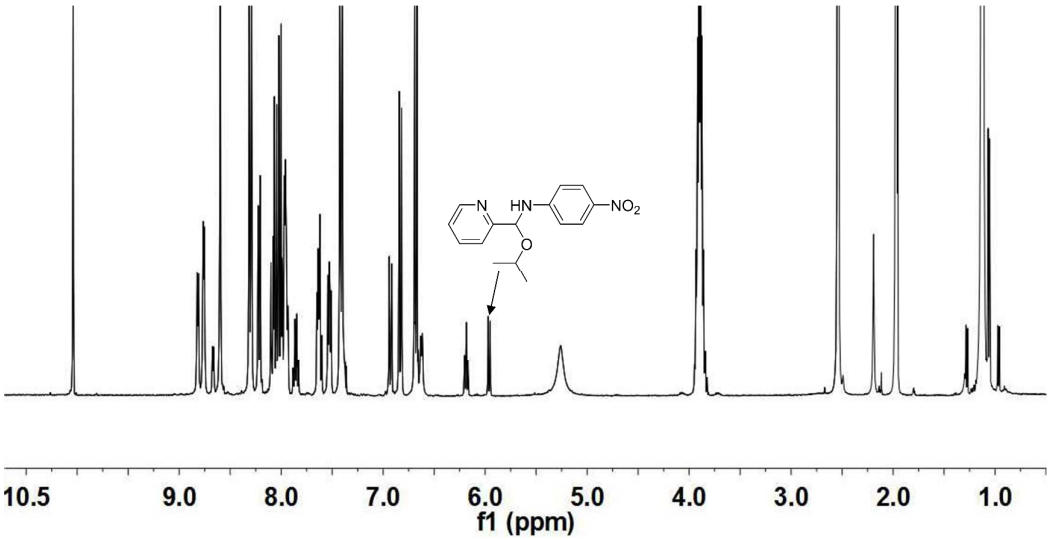


Figure S11. ^{1}HNMR of the reaction of **2-PA**, 4-nitroaniline, and 2-propanol in the presence of 0.3 equiv. methanesulfonic acid.

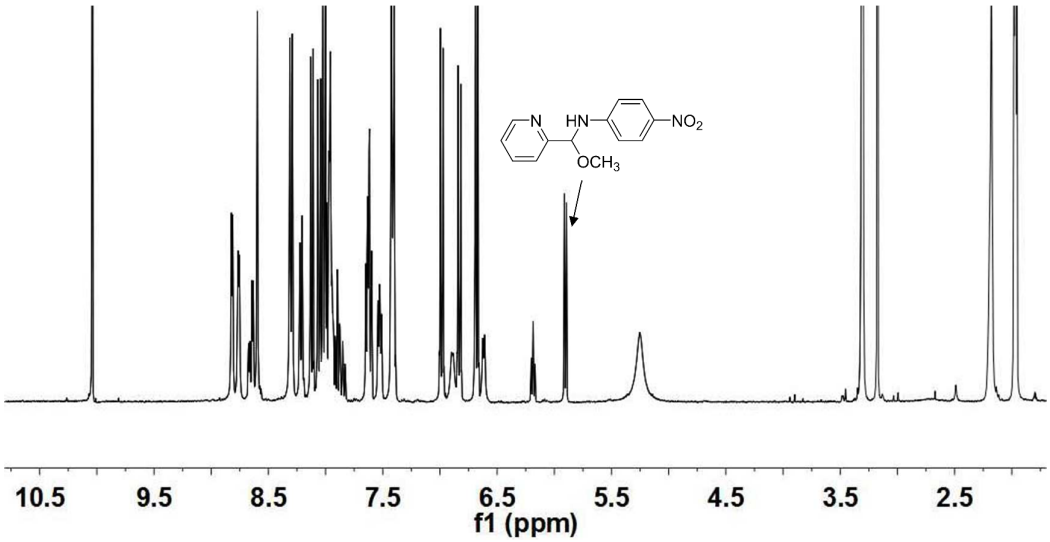


Figure S12. ^{1}HNMR of the reaction of **2-PA**, 4-nitroaniline, and methanol in the presence of 0.3 equiv. methanesulfonic acid.

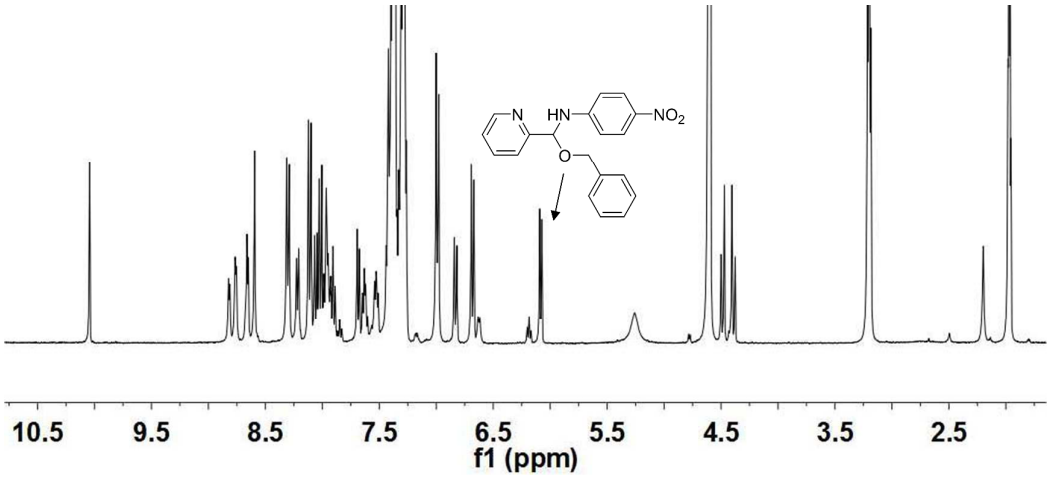


Figure S13. ^{1}HNMR of the reaction of **2-PA**, 4-nitroaniline, and benzyl alcohol in the presence of 0.3 equiv. methanesulfonic acid.

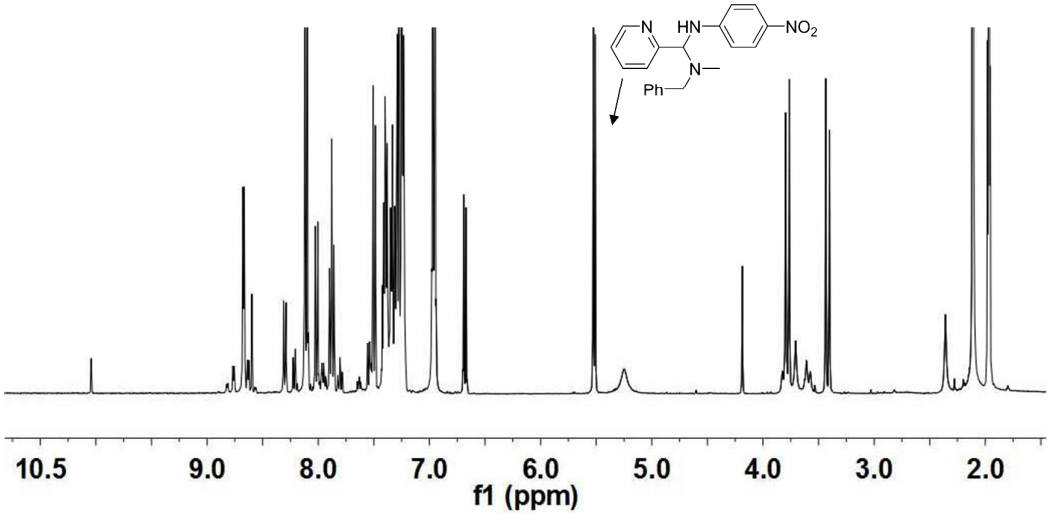


Figure S14. ^{1}HNMR of the reaction of **2-PA**, 4-nitroaniline, and N-methylbenzylamine.

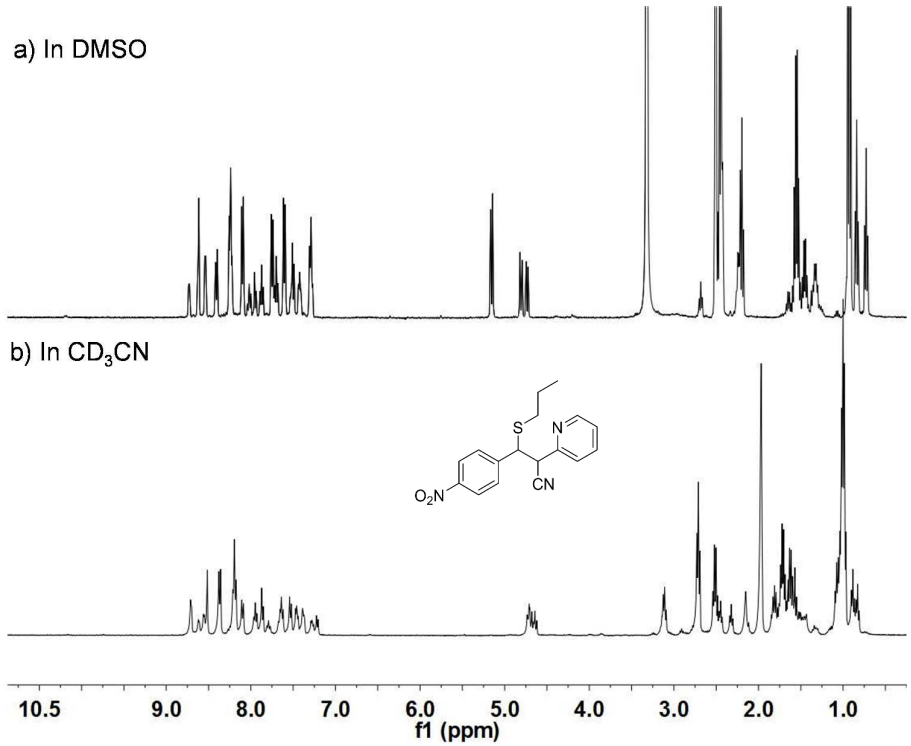


Figure S15. ^{1}HNMR of the reaction of α-[(4-nitrophenyl)methylene]-2-pyridineacetonitrile and 1-propanethiol in d^{6}-DMSO (a) and CD_3CN (b).

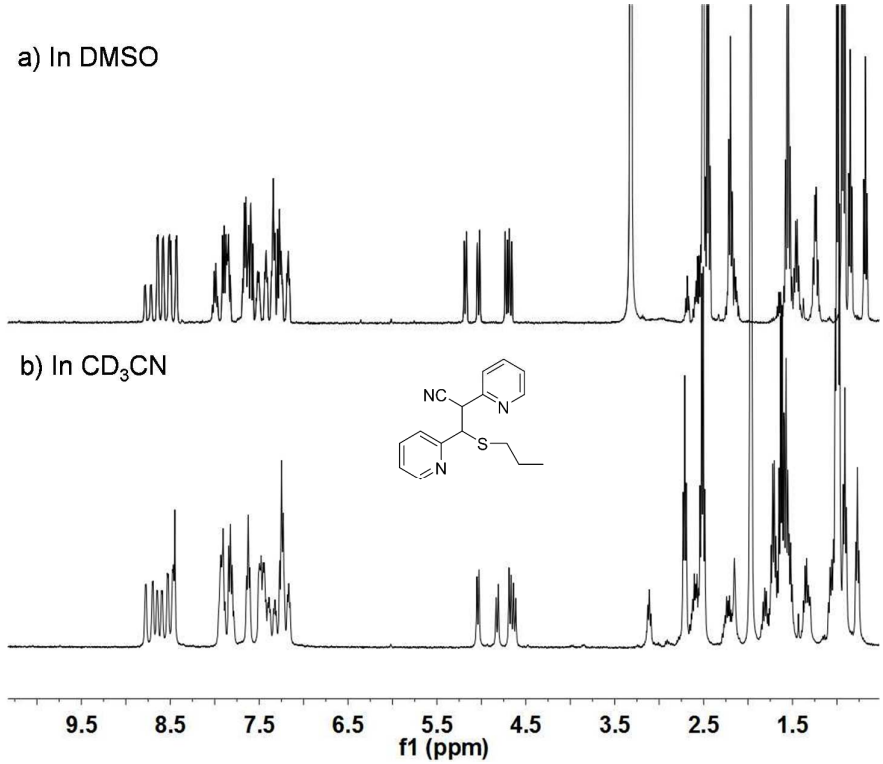


Figure S16. ^{1}HNMR of the reaction of (α-(2-pyridinylmethylene)-2-pyridineacetonitrile and 1-propanethiol in d^{6}-DMSO (a) and CD_3CN (b).

Hammett analysis

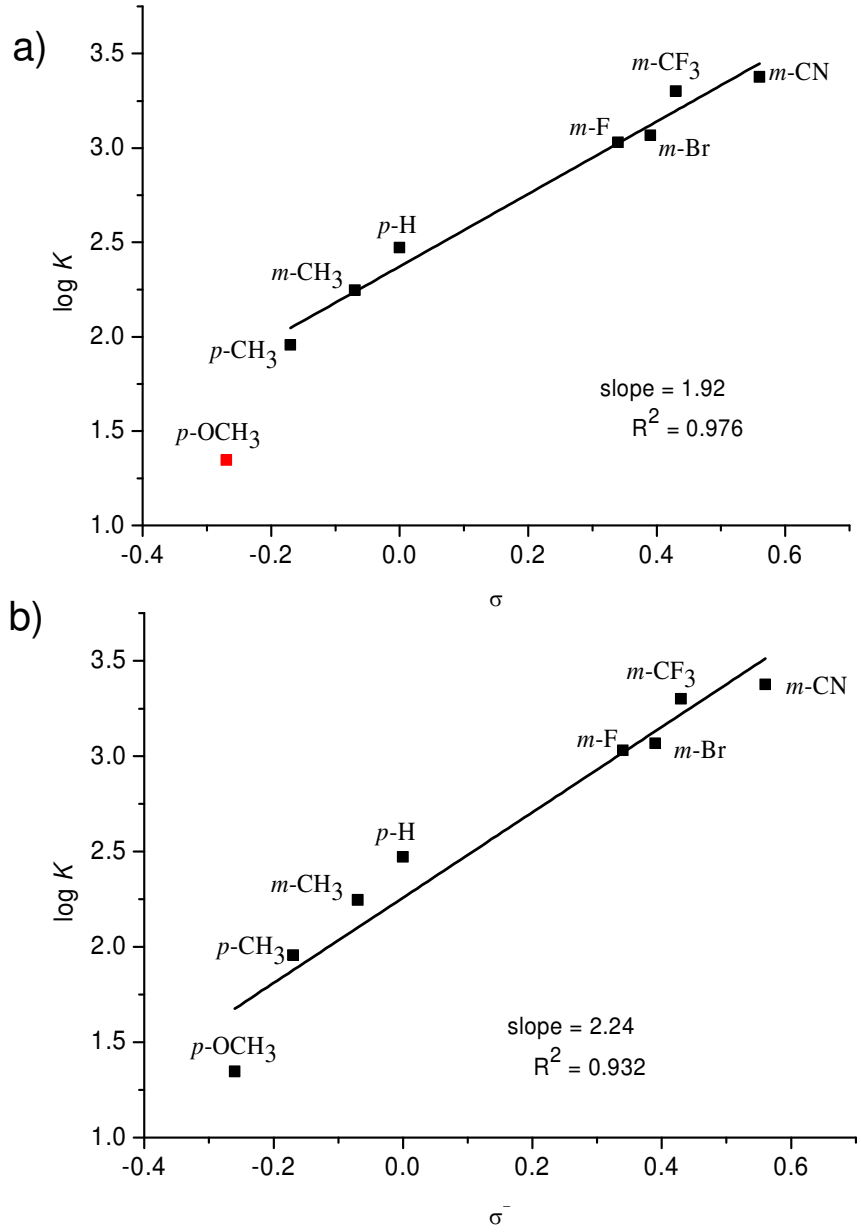


Figure S17. (a) Hammett plot of log *K* versus σ for the reaction of imine **1** with 1-propanethiol. Electron-donating *p*-OCH_3 significantly deviates from the line; (b) Hammett plot of log *K* versus σ^- for the reaction of imine **1** with 1-propanethiol.

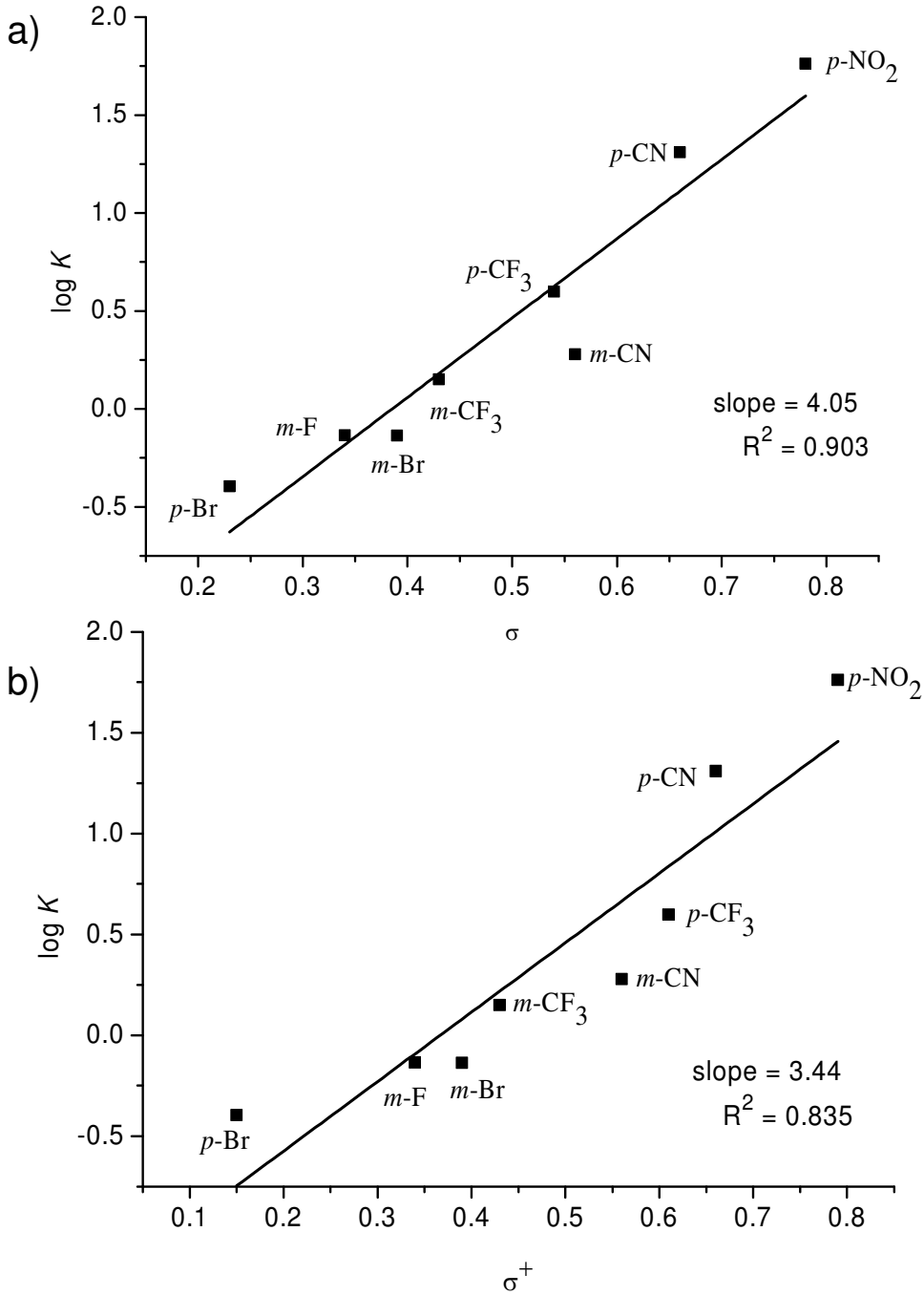


Figure S18. (a) Hammett plot of log *K* versus σ for the reaction of imine **1** with diethylamine; (b) Hammett plot of log *K* versus σ^+ for the reaction of imine **1** with diethylamine.

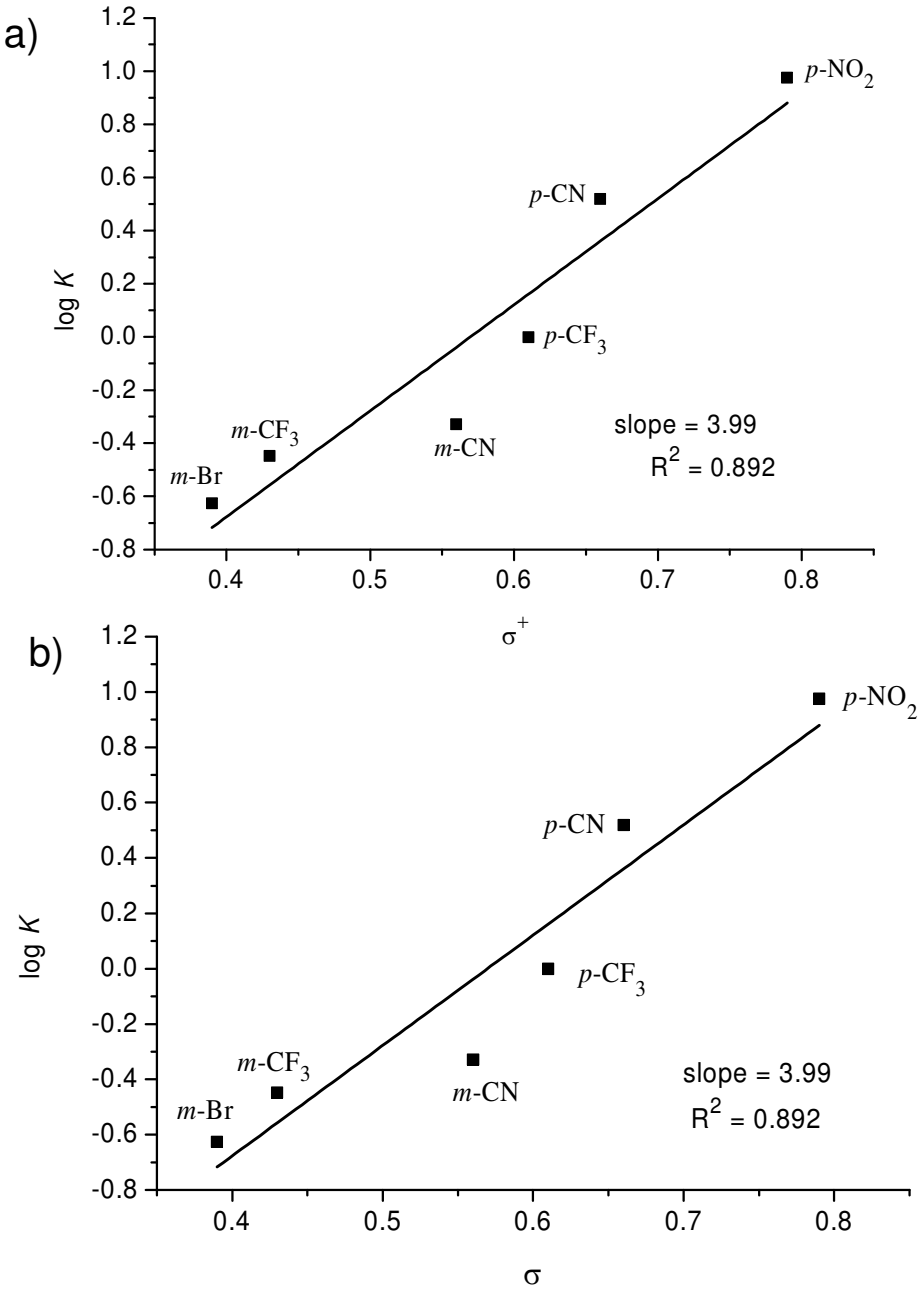


Figure S19. (a) Hammett plot of log *K* versus σ^+ for the reaction of imine **1** with ethanol; (b) Hammett plot of log *K* versus σ for the reaction of imine **1** with ethanol.

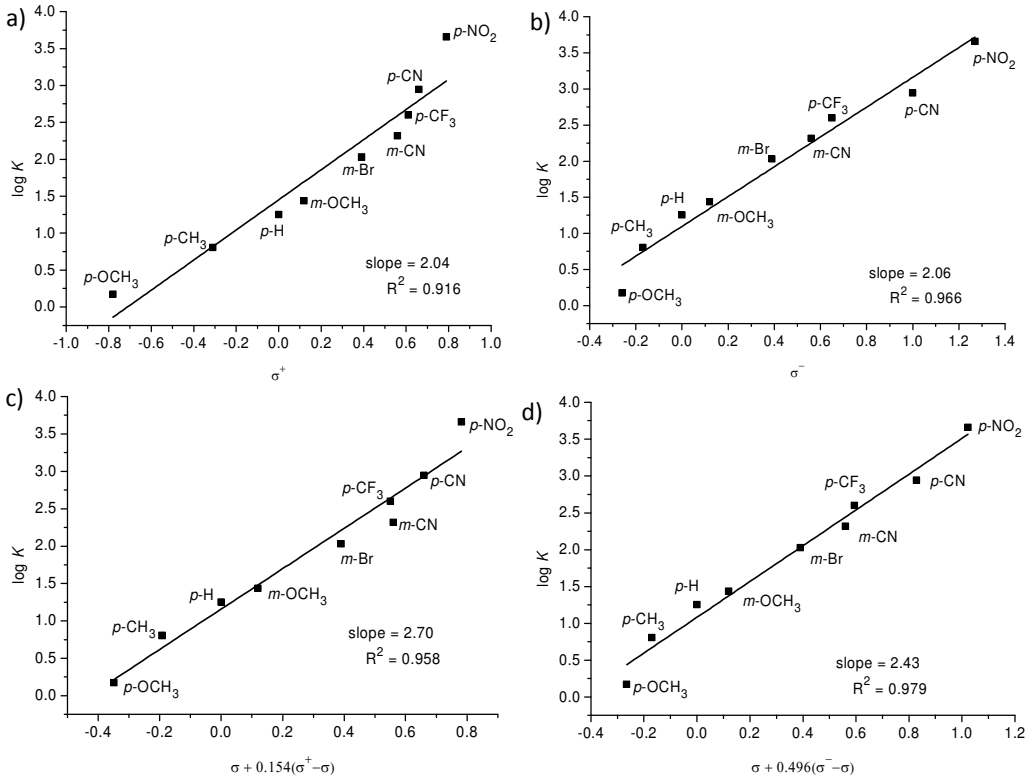


Figure S20. Hammett plot of log *K* versus σ^+ (a) and σ^- (b) for the reaction of imine **1** with piperidine. The corresponding plot using Yukawa-Tsuno equation (c and d) for the reaction of imine **1** with piperidine.

Reaction Screen

Table S1. The component distribution of the reaction of **2-PA**, 4-cyanoaniline, and 1-propanethiol with or without methanesulfonic acid.

Equiv. of acid	**2-PA**(%)	Thiohemiacetal **5**(%)	Product **4**(%)
0.0	53	33	14
0.1	6	4	90
0.3	2	0	98
0.5	1	0	99

Table S2. The component distribution of the reaction of **2-PA**, 4-nitroaniline, and ethanol with or without methanesulfonic acid.

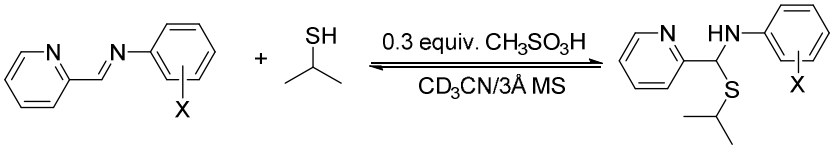
Equiv. of acid	**2-PA**(%)	Imine **1**(%)	Aminal **6**(%)	Product **4**(%)
0.0	85	9	4	2
0.1	49	20	7	24
0.2	39	27	7	27
0.3	37	29	6	28
0.4	35	31	6	28
0.5	37	31	6	27

Table S3. The component distribution of the reaction of **2-PA**, 4-cyanoaniline, and diethylamine with or without methanesulfonic acid.

Equiv. of acid	**2-PA**(%)	Imine **1**(%)	Aminal **7**(%)	Product **4**(%)
0.0	5	30	3	62
0.1	7	33	2	58
0.3	11	35	3	51
0.5	13	38	2	47
1.0	15	48	0	37

Component distribution, equilibrium constant, and Hammett plot for imine based DCRs

Table S4. The component distribution, equilibrium constant, and Hammett plot with σ^+ for imine **1** based DCRs with 2-propanethiol (3.0 equiv.).



X	σ^+	**4**(%)	**1**(%)	$K(M^{-1})$
p-OCH_3	-0.78	27	73	5.04
p-CH_3	-0.31	50	50	20.1
p-H	0.00	68	32	50.1
m-Br	0.39	58	42	202
m-CF_3	0.43	65	35	282
m-CN	0.56	70	30	369

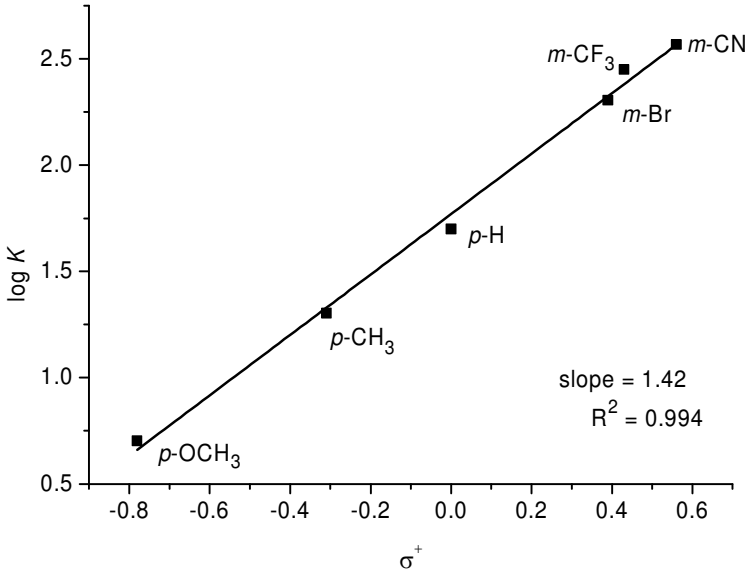
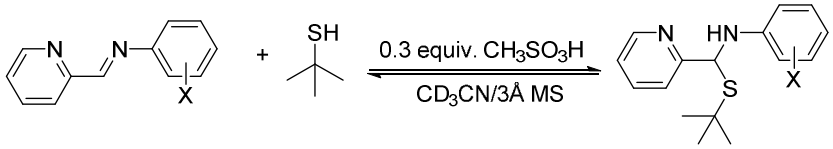


Table S5. The component distribution, equilibrium constant, and Hammett plot with σ^+ for imine **1** based DCRs with *t*-butylthiol (3.0 equiv.).



X	σ^+	**4**(%)	**1**(%)	**2-PA**(%)	$K(M^{-1})$
p-OCH_3	-0.78	5	95	0	0.47
p-CH_3	-0.31	17	83	~1	2.00
p-H	0.00	30	69	~1	4.86
m-Br	0.39	32	66	~1	19.3
m-CN	0.56	41	58	~1	34.4

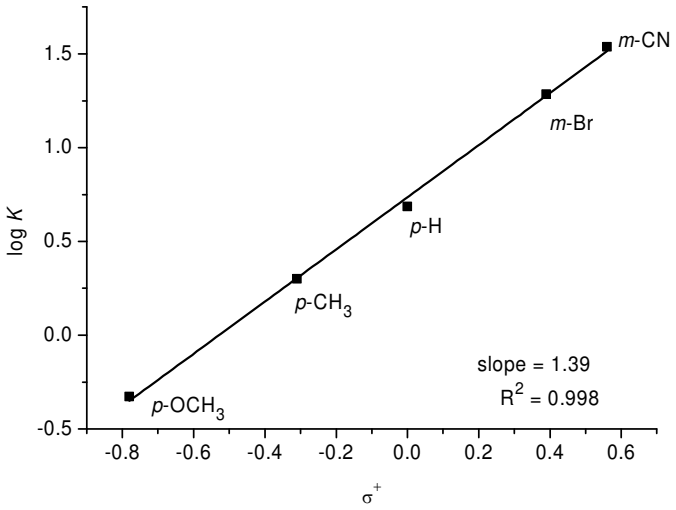
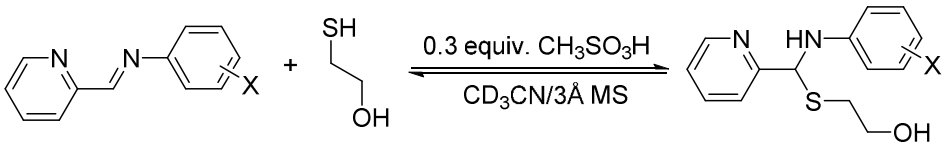


Table S6. The component distribution, equilibrium constant, and Hammett plot with σ^+ for imine **1** based DCRs with 2-mercaptoethanol.



X	σ^+	**4**(%)	**1**(%)	$K(M^{-1})$
p-CH_3[a]	-0.31	84	16	67.2
p-H[a]	0.00	93	7	190
m-Br[b]	0.39	88	12	538
m-CN[b]	0.56	93	7	1000

Note: a.2.0 equiv. 2-mercaptoethanol; b. 1.1 equiv. 2-mercaptoethanol.

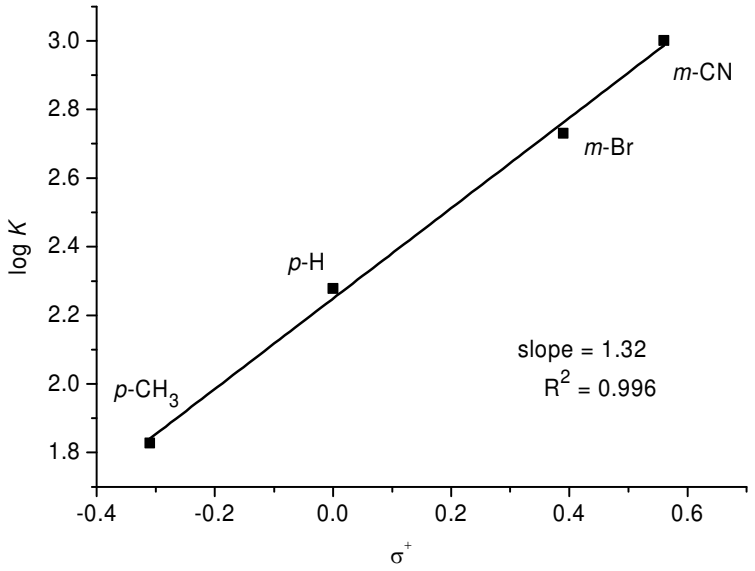
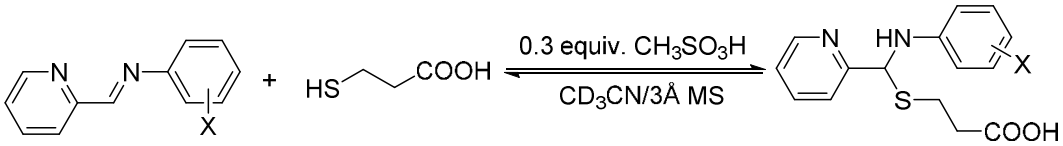


Table S7. The component distribution, equilibrium constant, and Hammett plot with σ^+ for imine **1** based DCRs with 3-mercaptopropionic acid.



X	σ^+	**4**(%)	**1**(%)	**2-PA**(%)	$K(M^{-1})$
p-CH_3[a]	-0.31	77	23	0	67.1
p-H[a]	0.00	85	15	0	152
m-Br[b]	0.39	91	9	0	786
m-CN[b]	0.56	80	8	12	1010

Note: a.2.0 equiv. 2-mercaptoethanol; b. 1.1 equiv. 2-mercaptoethanol.

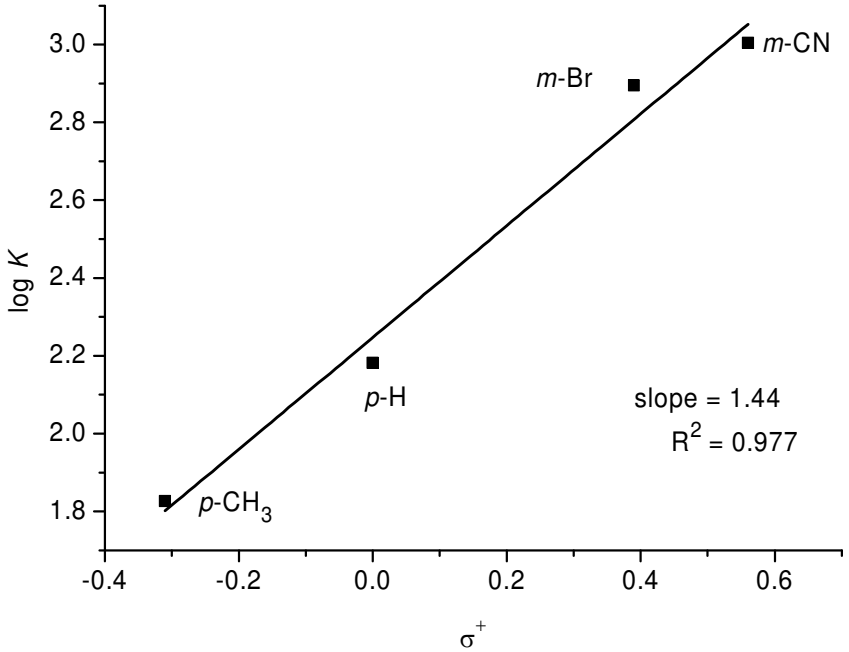
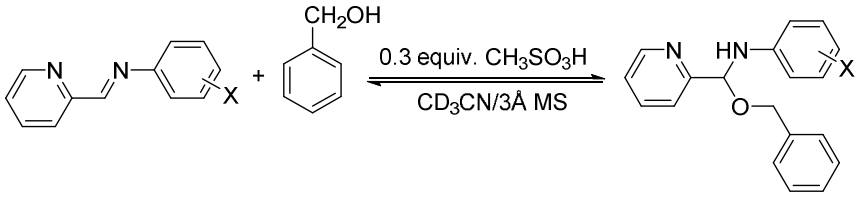


Table S8. The component distribution, equilibrium constant, and Hammett plot with σ^- for imine **1** based DCRs with benzyl alcohol (3.0 equiv.).



X	σ^-	**4**(%)	**1**(%)	**2-PA**(%)	**6**(%)	$K(M^{-1})$
p-NO_2	1.27	33	37	23	7	6.86
p-CN	1.00	21	65	9	5	2.37
p-CF_3	0.65	13	79	4	3	1.16

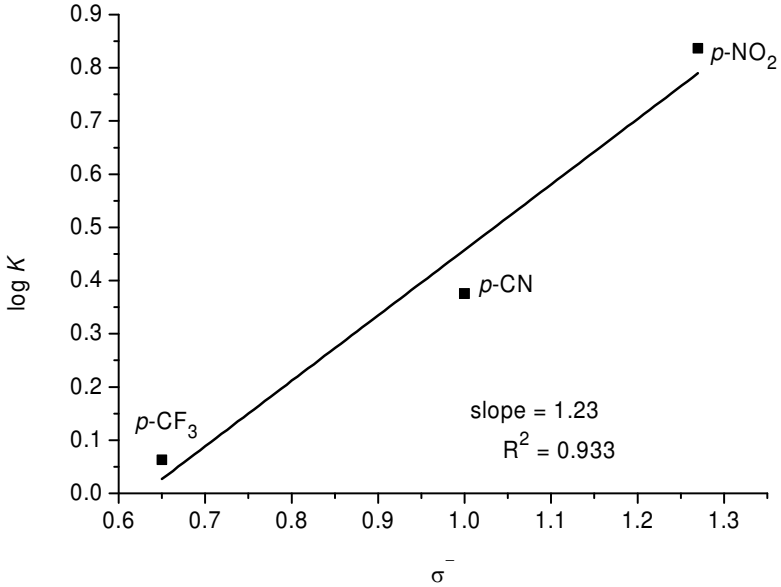
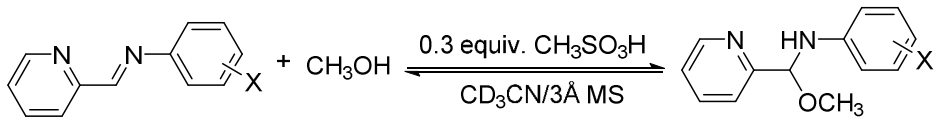


Table S9. The component distribution, equilibrium constant, and Hammett plot with σ^- for imine **1** based DCRs with methanol (3.0 equiv.).



X	σ^-	**4**(%)	**1**(%)	**2-PA**(%)	**6**(%)	$K(M^{-1})$
p-NO_2	1.27	22	34	35	10	30.0
p-CN	1.00	12	64	19	5	10.1
p-CF_3	0.65	4	87	7	2	2.95

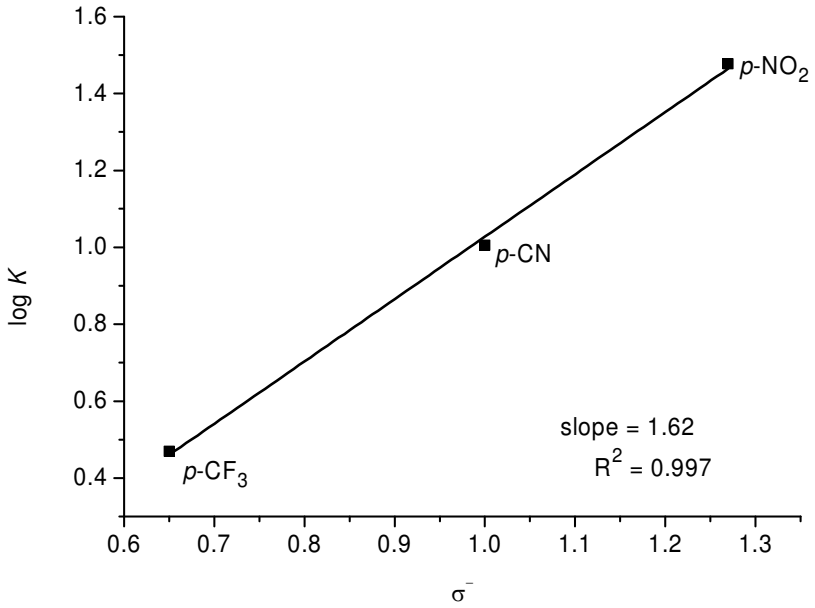
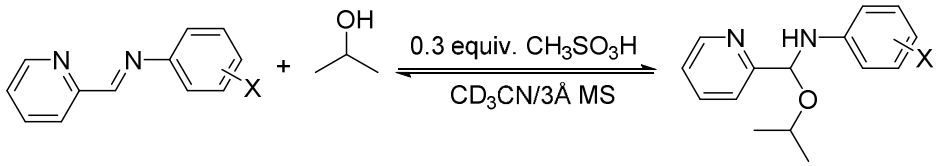


Table S10. The component distribution, equilibrium constant, and Hammett plot with σ^- for imine **1** based DCRs with 2-propanol (3.0 equiv.).



X	σ^-	**4**(%)	**1**(%)	**2-PA**(%)	**6**(%)	K(M^{-1})
p-NO_2	1.27	10	49	30	11	1.82
p-CN	1.00	8	73	13	5	0.91
p-CF_3	0.65	2	93	3	2	0.13

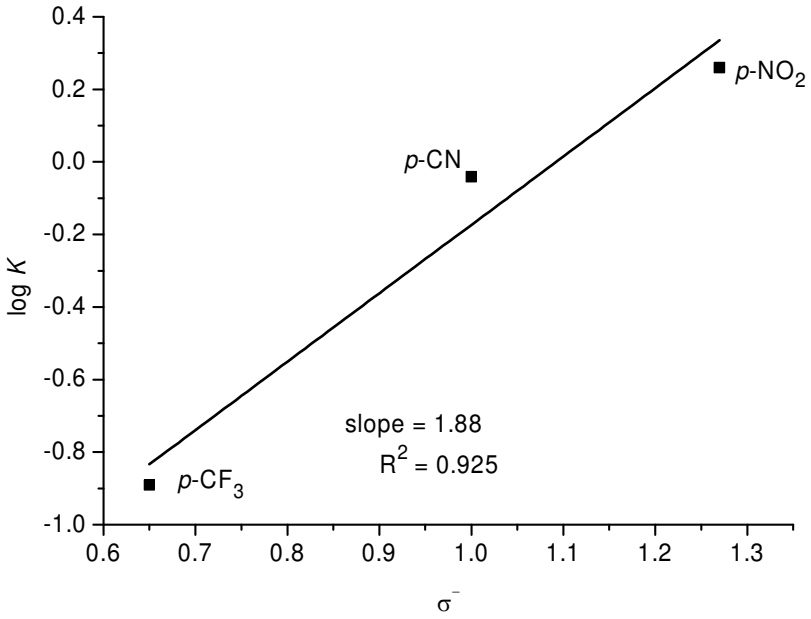
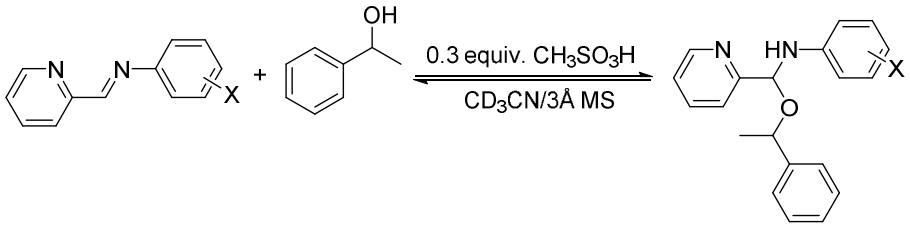


Table S11. The component distribution, equilibrium constant, and Hammett plot with σ^- for imine **1** based DCRs with 1-phenylethanol (3.0 equiv.).



X	σ^-	**4**(%)	**1**(%)	**2-PA**(%)	**6**(%)	$K(M^{-1})$
p-NO_2	1.27	6	52	30	12	0.86
p-CN	1.00	3	80	13	4	0.25
p-CF_3	0.65	1	93	4	2	0.09

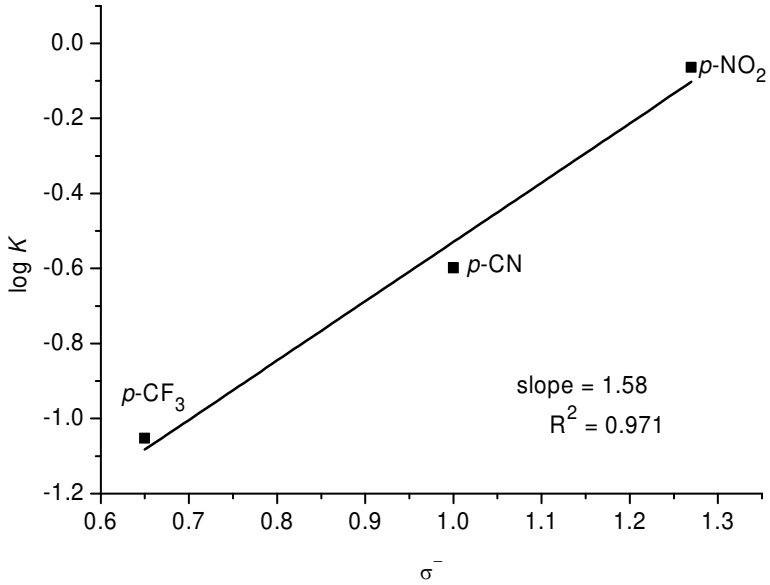
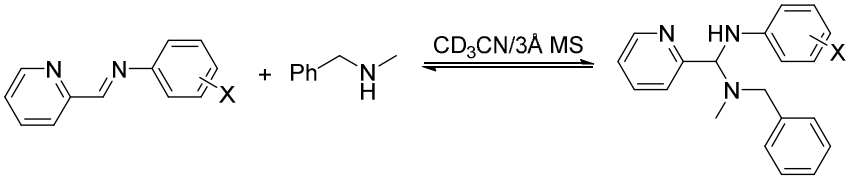


Table S12. The component distribution, equilibrium constant, and Hammett plot with σ^- for imine **1** based DCRs with N-methylbenzylamine (1.1 equiv.).



X	σ^-	**4**(%)	**1**(%)	**7**(%)	$K(M^{-1})$
m-Br	0.39	38	50	12	27.7
m-CN	0.56	52	41	7	50.3
p-CN	1.00	60	23	17	290
p-NO_2	1.27	76	10	14	1170

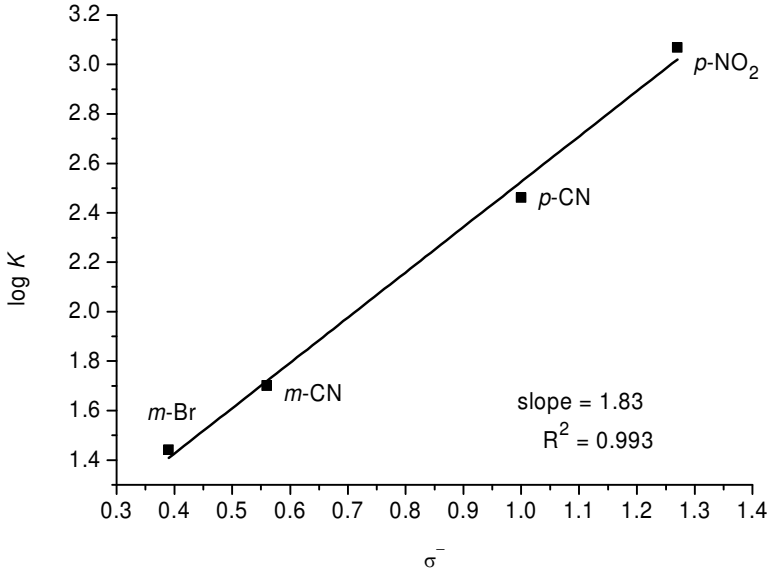
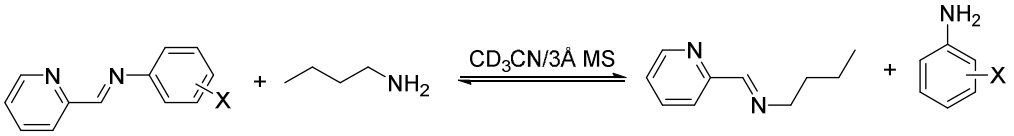


Table S13. The equilibrium constant and Hammett plot with σ^+ for dynamic imine exchange with 1-butylamine (1.3 equiv.).



X	σ^+	$K(M^{-1})$
p-OCH_3	-0.78	39.8
p-CH_3	-0.31	138
p-H	0.00	482

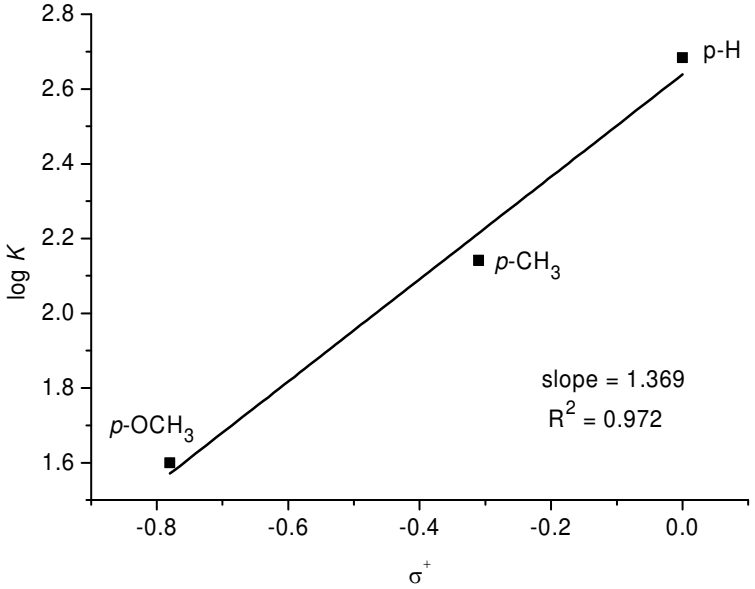
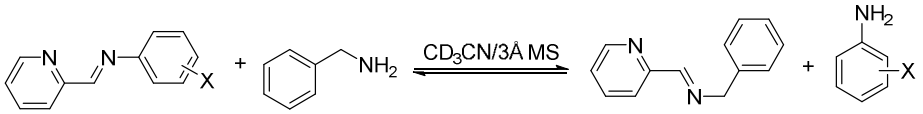


Table S14. The equilibrium constant and Hammett plot with σ^+ for dynamic imine exchange with benzylamine (1.3 equiv.).



X	σ^+	$K(M^{-1})$
p-OCH_3	-0.78	30.9
p-CH_3	-0.31	95.3
p-H	0.00	179

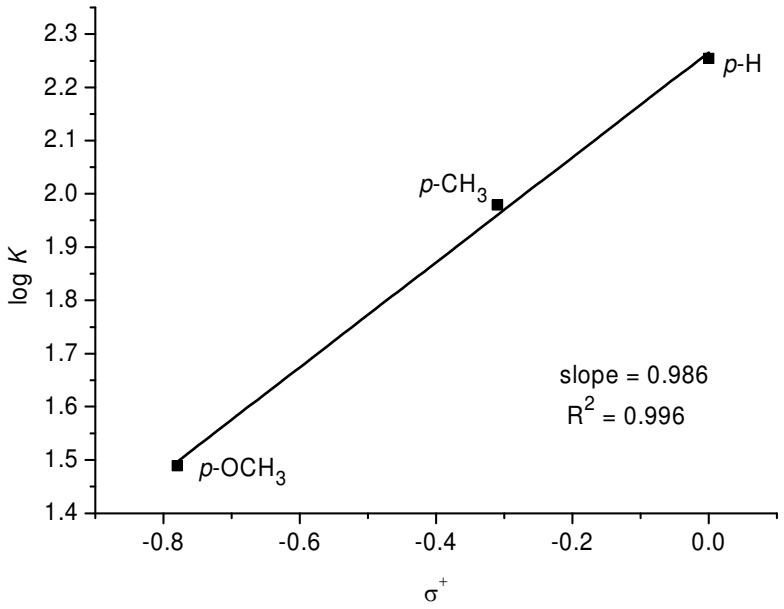
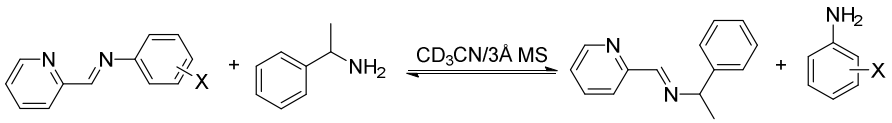
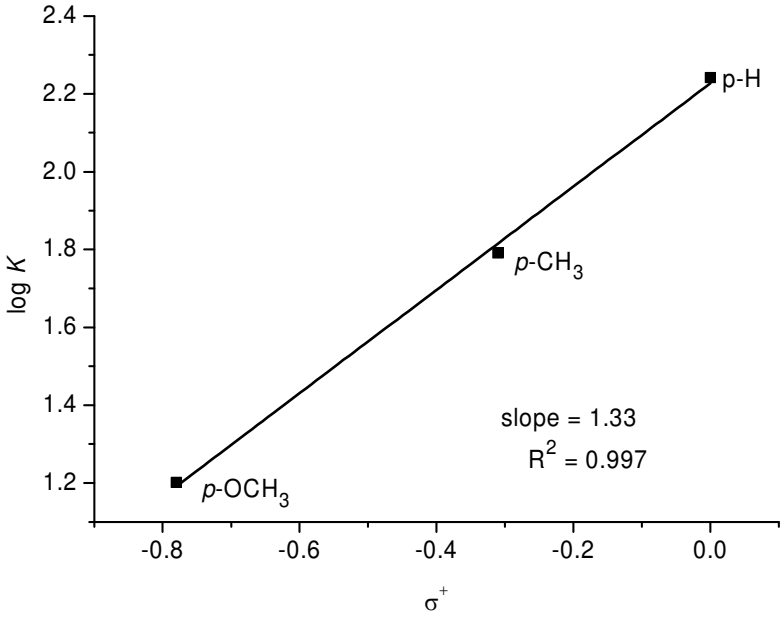


Table S15. The equilibrium constant and Hammett plot with σ^+ for dynamic imine exchange with α-methylbenzylamine (1.3 equiv.).

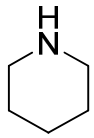


X	σ^+	$K(M^{-1})$
p-OCH_3	-0.78	15.9
p-CH_3	-0.31	61.8
p-H	0.00	175



Data for correlation analysis

Table S16. Imine **1** based DCRs with piperidine.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-OCH_3)	-1.86	0.17	**1.00**	**2.03**
	1(*p*-CH_3)	-1.22	0.81		
	1(*p*-H)	-0.78	1.25		
	1(*m*-Br)	0.00	2.03		
	1(*m*-CN)	0.29	2.32		
	1(*p*-NO_2)	1.63	3.66		
	1(*p*-CN)	0.92	2.95		
	1(*p*-CF_3)	0.57	2.60		
	1(*m*-OCH_3)	-0.59	1.44		

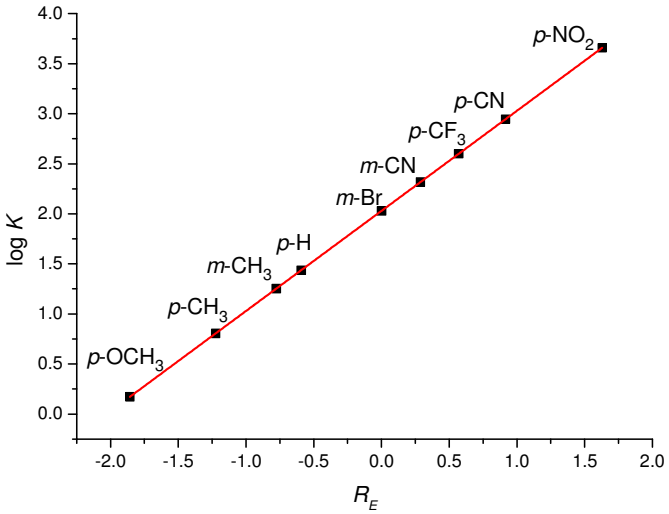


Table S17. Imine **1** based DCRs with 2-propanethiol.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	1(*p*-OCH_3)	-1.86	0.70	**0.86**	**2.71**
	1(*p*-CH_3)	-1.22	1.30		
	1(*p*-H)	-0.78	1.70		
	1(*m*-Br)	0.00	2.30		
	1(*m*-CF_3)	0.16	2.45		
	1(*m*-CN)	0.29	2.57		

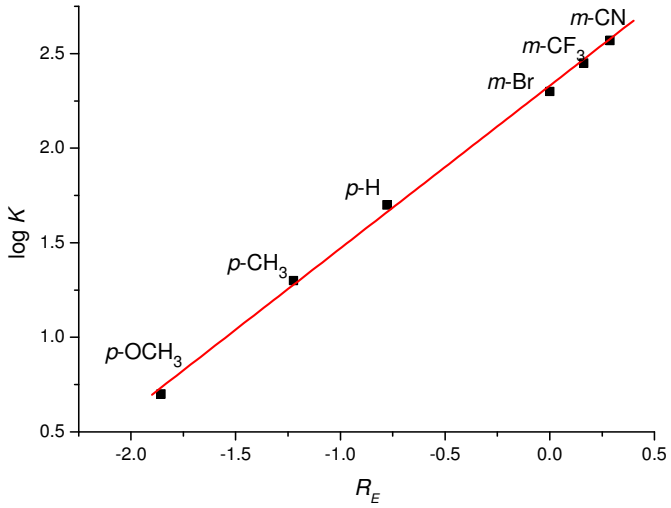
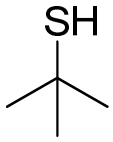


Table S18. Imine **1** based DCRs with *t*-butylthiol.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-OCH_3)	-1.86	-0.33	**0.86**	**1.52**
	1(*p*-CH_3)	-1.22	0.30		
	1(*p*-H)	-0.78	0.69		
	1(*m*-Br)	0.00	1.29		
	1(*m*-CN)	0.29	1.54		

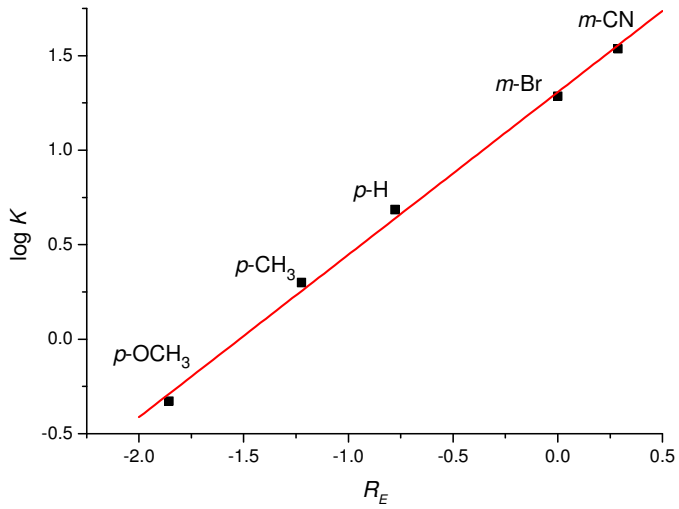
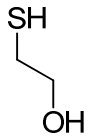


Table S19. Imine **1** based DCRs with 2-mercaptoethanol.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-CH_3)	-1.22	1.83	**0.74**	**3.76**
	1(*p*-H)	-0.78	2.28		
	1(*m*-Br)	0.00	2.73		
	1(*m*-CN)	0.29	3.00		

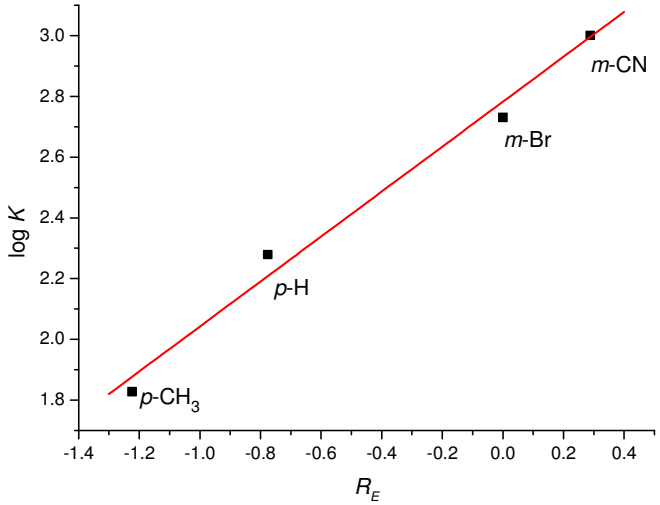
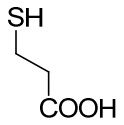


Table S20. Imine **1** based DCRs with 3-mercaptopropionic acid.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-CH_3)	-1.22	1.83	**0.81**	**3.48**
	1(*p*-H)	-0.78	2.18		
	1(*m*-Br)	0.00	2.90		
	1(*m*-CN)	0.29	3.00		

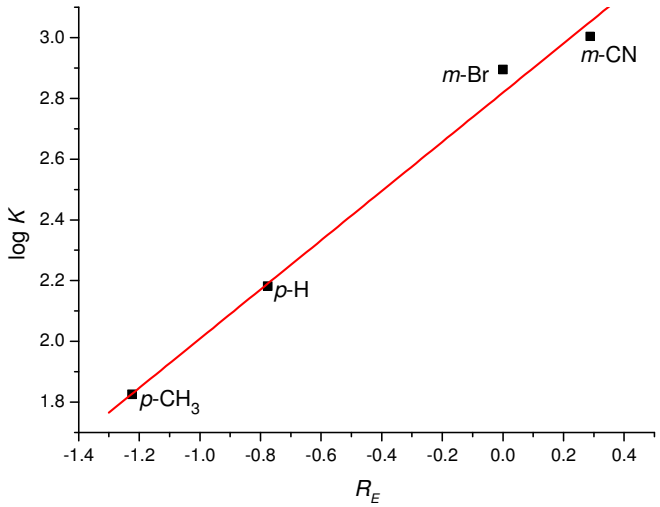
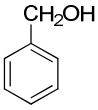


Table S21. Imine **1** based DCRs with benzyl alcohol.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-NO_2)	1.63	0.84	**0.72**	**-0.45**
	1(*p*-CN)	0.92	0.38		
	1(*p*-CF_3)	0.57	0.06		

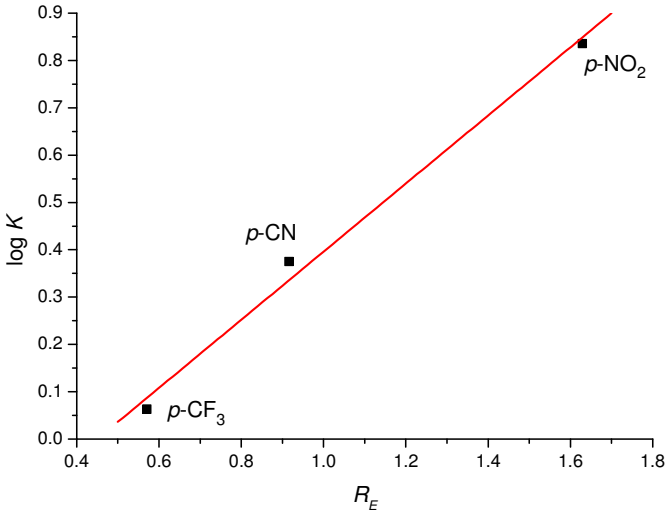


Table S22. Imine **1** based DCRs with methanol.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
CH_3OH	**1**(*p*-NO_2)	1.63	1.48	**0.91**	**0.04**
	1(*p*-CN)	0.92	1.00		
	1(*p*-CF_3)	0.57	0.47		

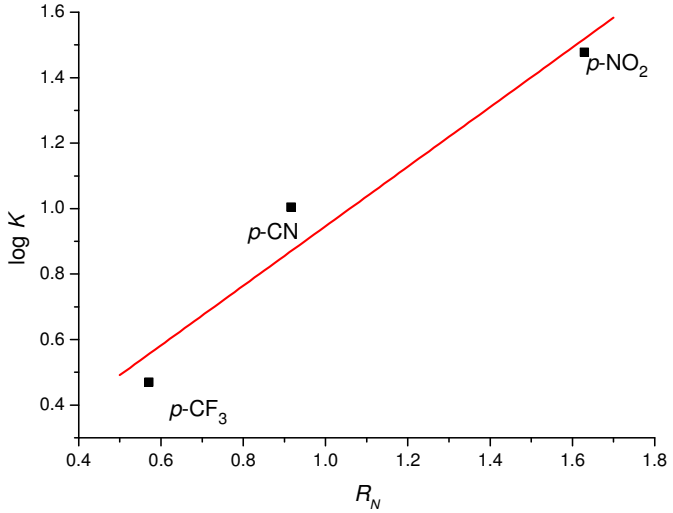


Table S23. Imine **1** based DCRs with 2-propanol.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	1(*p*-NO_2)	1.63	0.26	**0.99**	**-1.27**
	1(*p*-CN)	0.92	-0.04		
	1(*p*-CF_3)	0.57	-0.89		

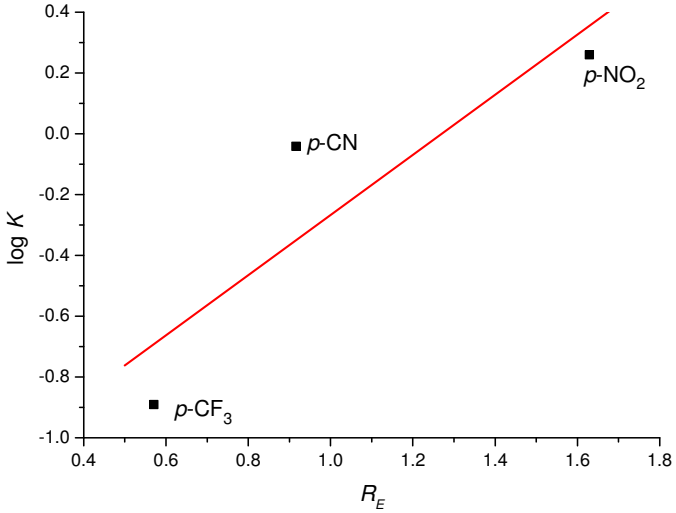
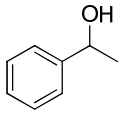


Table S24. Imine **1** based DCRs with 1-phenylethanol.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-NO_2)	1.63	-0.06	**0.91**	**-1.67**
	1(*p*-CN)	0.92	-0.60		
	1(*p*-CF_3)	0.57	-1.05		

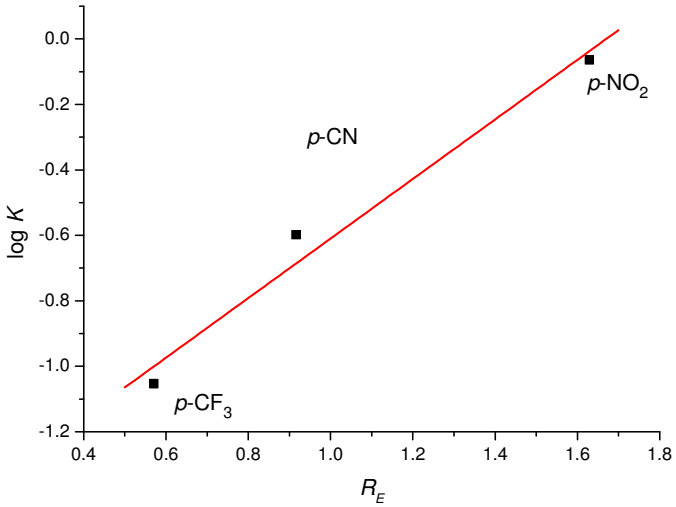
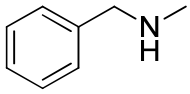


Table S25. Imine **1** based DCRs with N-methylbenzylamine.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*m*-Br)	0.00	1.44	**1.02**	**1.42**
	1(*m*-CN)	0.29	1.70		
	1(*p*-NO_2)	1.63	3.07		
	1(*p*-CN)	0.92	2.46		

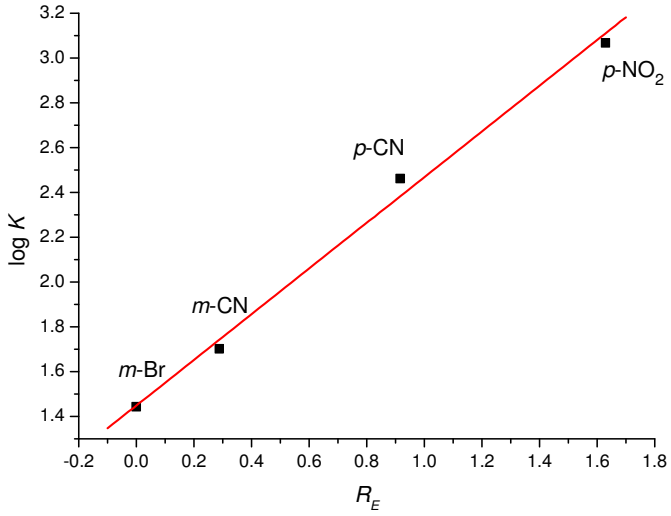
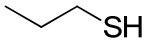


Table S26. Imine **1** based DCRs with 1-propanethiol.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-OCH_3)	-1.86	1.35	**0.93**	**3.33**
	1(*p*-CH_3)	-1.22	1.96		
	1(*m*-CH_3)	-0.92	2.25		
	1(*p*-H)	-0.78	2.47		
	1(*m*-F)	-0.08	3.03		
	1(*m*-Br)	0.00	3.07		
	1(*m*-CF_3)	0.16	3.30		
	1(*m*-CN)	0.29	3.38		

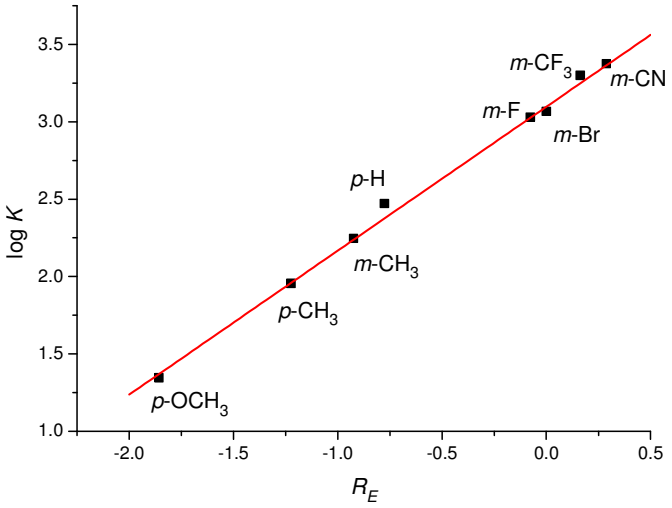


Table S27. Imine **1** based DCRs with ethanol.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
C_2H_5OH	**1**(*m*-Br)	0.00	-0.63	**1.01**	**-0.58**
	1(*m*-CF_3)	0.16	-0.45		
	1(*m*-CN)	0.29	-0.33		
	1(*p*-NO_2)	1.63	0.98		
	1(*p*-CN)	0.92	0.52		
	1(*p*-CF_3)	0.57	0.00		

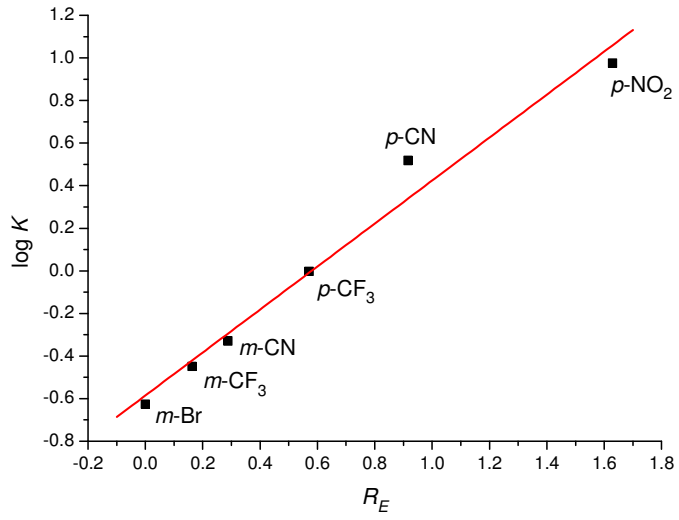
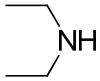


Table S28. Imine **1** based DCRs with diethylamine.

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	1(*m*-F)	-0.08	-0.14	**1.20**	**-0.04**
	1(*m*-Br)	0.00	-0.14		
	1(*m*-CF_3)	0.16	0.15		
	**1**(*m*-CN)	0.29	0.28		
	1(*p*-NO_2)	1.63	1.76		
	1(*p*-CN)	0.92	1.31		
	1(*p*-CF_3)	0.57	0.60		
	1(*p*-Br)	-0.29	-0.40		

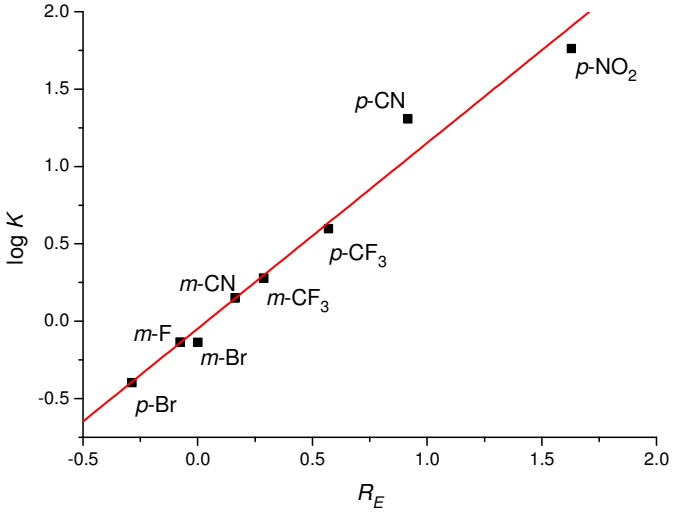
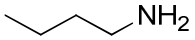


Table S29. Imine **1** based DCRs with 1-butylamine (Scheme 2a).

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-OCH_3)	-1.86	1.60	**0.99**	**3.44**
	1(*p*-CH_3)	-1.22	2.14		
	1(*p*-H)	-0.78	2.68		

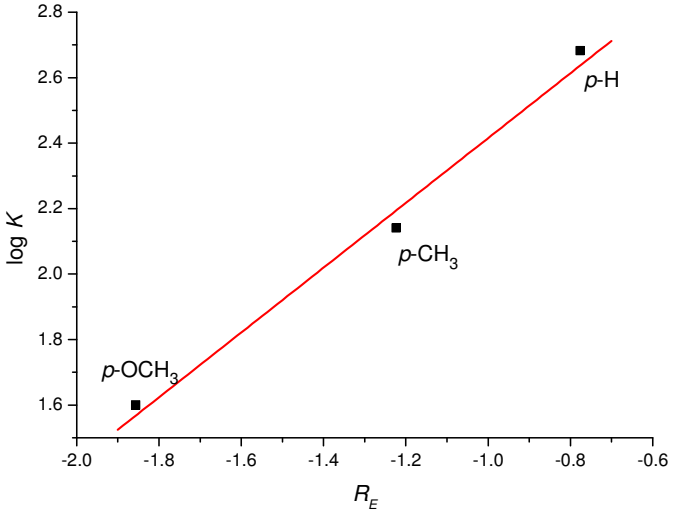
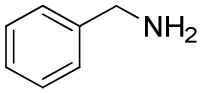


Table S30. Imine **1** based DCRs with benzylamine (Scheme 2a).

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-OCH_3)	-1.86	1.49	**0.71**	**3.96**
	1(*p*-CH_3)	-1.22	1.98		
	1(*p*-H)	-0.78	2.25		

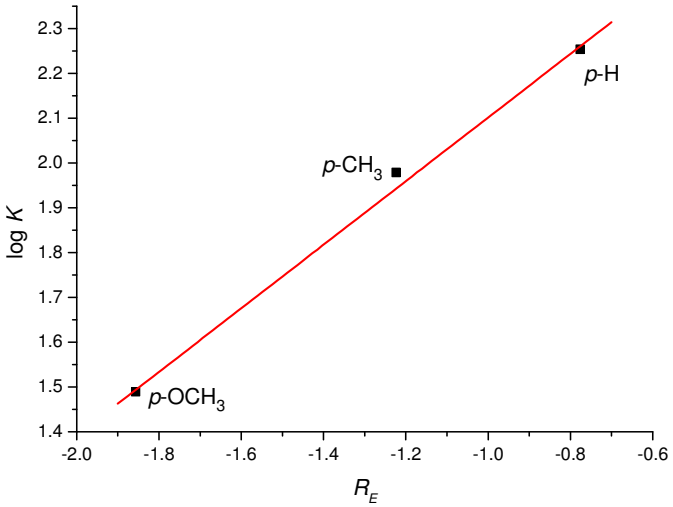
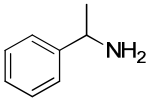


Table S31. Imine **1** based DCRs with α-methylbenzylamine (Scheme 2a).

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-OCH_3)	-1.86	1.20	**0.96**	**3.10**
	1(*p*-CH_3)	-1.22	1.79		
	1(*p*-H)	-0.78	2.24		

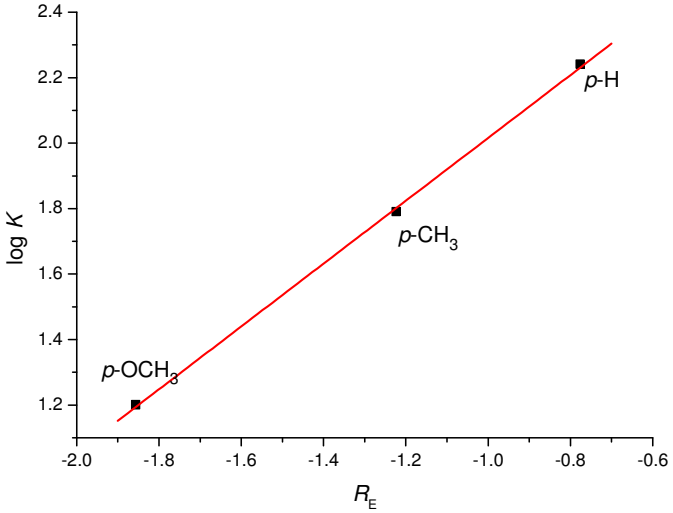
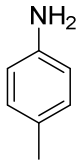


Table S32. Imine **1** based DCRs with 4-methylaniline (Scheme 2b).

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-OCH_3)	-1.86	-0.54	**0.92**	**1.25**
	1(*p*-CH_3)	-1.22	0.00		
	1(*p*-CF_3)	0.57	1.68		
	1(*p*-Br)	-0.29	0.88		

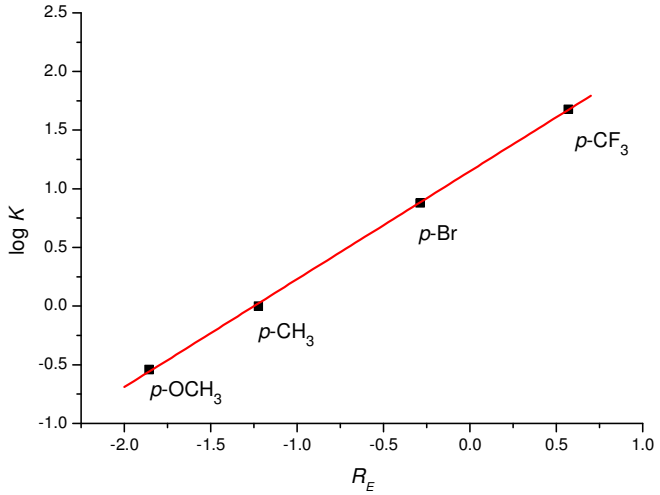
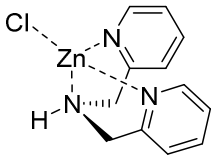


Table S33. Imine **1** based DCRs with Zn^{2+}-DPA complex (Scheme 2c).

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-OCH_3)	-1.86	0.93	**0.63**	**3.39**
	1(*p*-CH_3)	-1.22	1.39		
	1(*p*-CF_3)	0.57	2.45		
	1(*p*-Br)	-0.29	2.03		

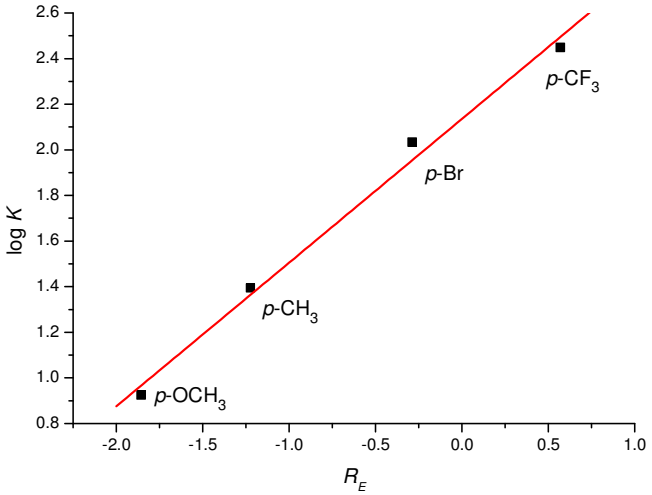
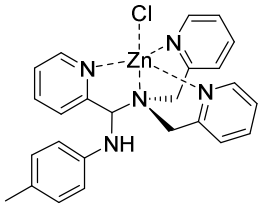


Table S34. Imine **1** based DCRs with aminal based metal complex (Scheme 2d).

Nucleophile	Electrophile	R_E	log K	S_N	R_N
	**1**(*p*-OCH_3)	-1.86	-0.54	**0.58**	**1.05**
	1(*p*-CH_3)	-1.22	0.00		
	1(*p*-CF_3)	0.57	0.93		
	1(*p*-Br)	-0.29	0.42		

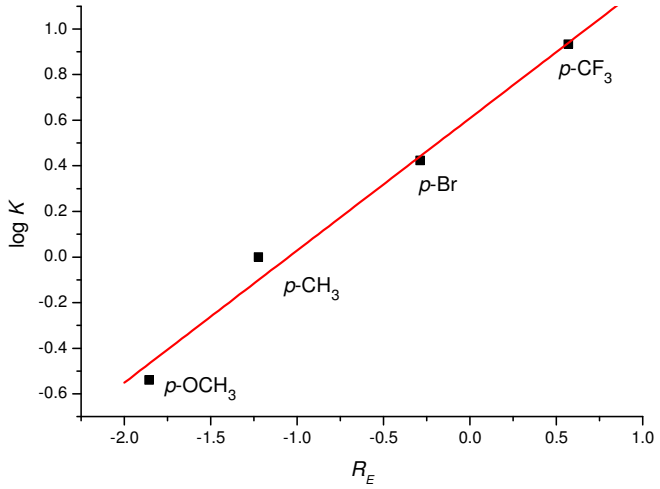
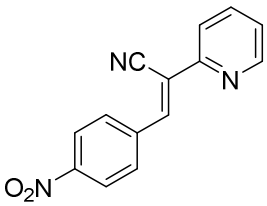
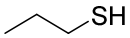
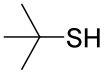
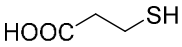


Table S35. α-[(4-nitrophenyl)methylene]-2-pyridineacetonitrile (**8**) based DCRs with thiols in CD_3CN (Scheme 2e).

Electrophile	Nucleophile	S_N	R_N	(log K)/S_N	R_E
		0.93	3.33	1.70	**-1.43**
		0.86	2.71	1.50	
		0.86	1.52	-0.03	
		0.81	3.48	2.16	

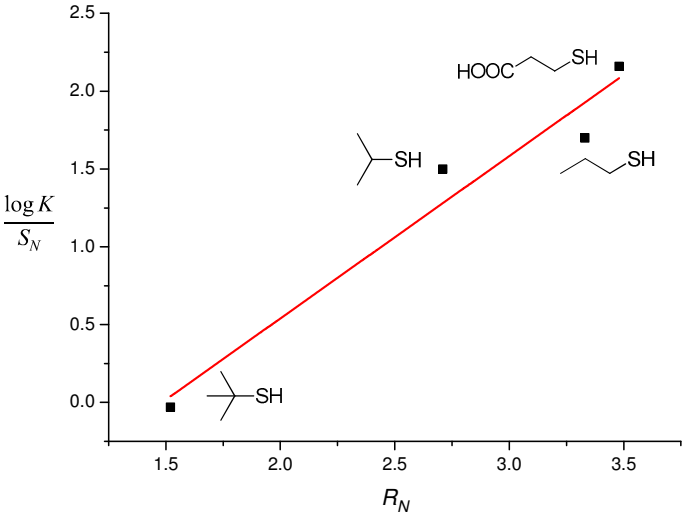
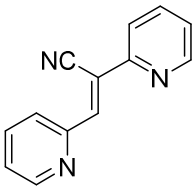
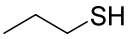
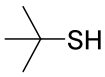
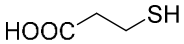


Table S36. α-(2-pyridinylmethylene)-2-pyridineacetonitrile (**9**) based DCRs with thiols in CD_3CN (Scheme 2f).

Electrophile	Nucleophile	S_N	R_N	(log K)/S_N	R_E
		0.93	3.33	1.90	**-1.55**
		0.86	2.71	1.09	
		0.86	1.52	-0.54	
		0.81	3.48	2.40	

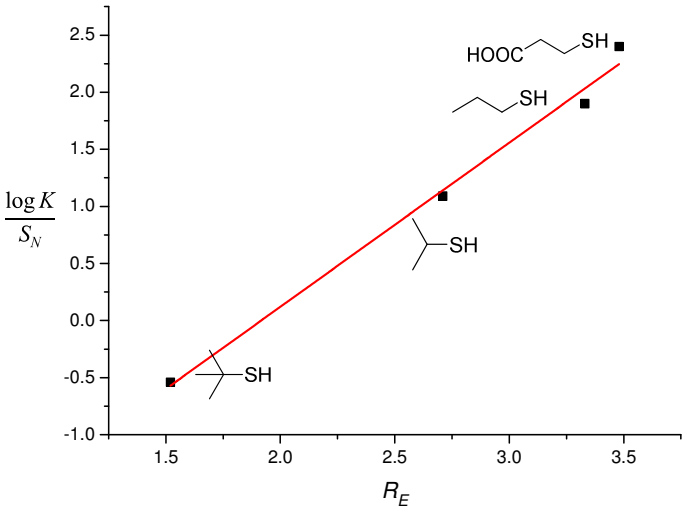
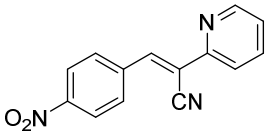
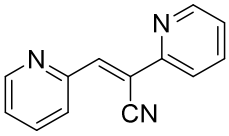
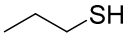
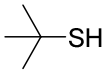
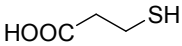


Table S37. Equilibrium constants (M^{-1}) for DCRs of α-[(4-nitrophenyl)methylene]-2-pyridineacetonitrile (**8**) or α-(2-pyridinylmethylene)-2-pyridineacetonitrile (**9**) with thiols in d^6-DMSO.

RSH		
	98.0	137
	71.6	118
	17.3	21.8
	109	220

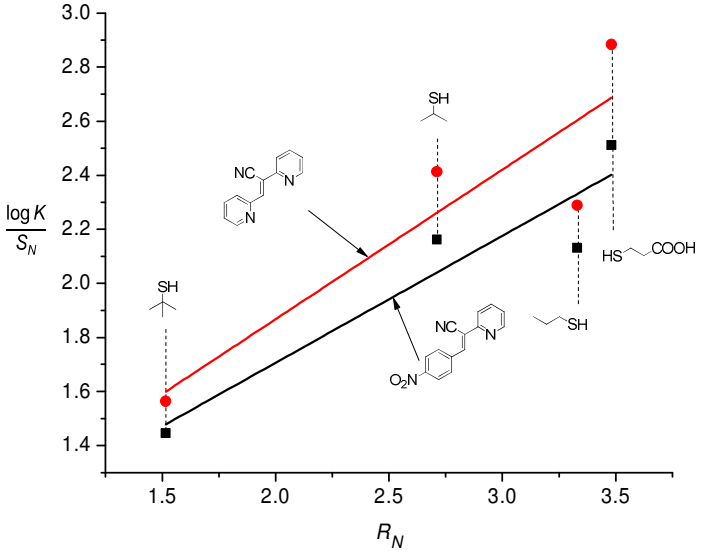
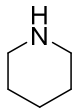
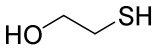
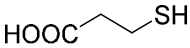
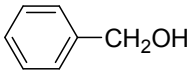


Table S38. The measured log *K* and predicted log *K* values in Figure 4.

Nucleophile	Electrophile	R_E	Measured log *K*	Predicted log *K*
 $R_N = 2.03$ $S_N = 1.00$	**1**(*p*-OCH_3)	-1.86	0.17	0.17
	1(*p*-CH_3)	-1.22	0.81	0.81
	1(*p*-H)	-0.78	1.25	1.25
	1(*m*-Br)	0.00	2.03	2.03
	1(*m*-CN)	0.29	2.32	2.32
	1(*p*-NO_2)	1.63	3.66	3.66
	1(*p*-CN)	0.92	2.95	2.95
	1(*p*-CF_3)	0.57	2.60	2.60
	1(*m*-OCH_3)	-0.59	1.44	1.44
$R_N = 2.71$ $S_N = 0.86$	**1**(*p*-OCH_3)	-1.86	0.70	0.73
	1(*p*-CH_3)	-1.22	1.30	1.28
	1(*p*-H)	-0.78	1.70	1.66
	1(*m*-Br)	0.00	2.30	2.33
	1(*m*-CF_3)	0.16	2.45	2.47
	1(*m*-CN)	0.29	2.57	2.58
$R_N = 1.52$ $S_N = 0.86$	**1**(*p*-OCH_3)	-1.86	-0.33	-0.29
	1(*p*-CH_3)	-1.22	0.30	0.26
	1(*p*-H)	-0.78	0.69	0.64
	1(*m*-Br)	0.00	1.29	1.31
	1(*m*-CN)	0.29	1.54	1.56
 $R_N = 3.76$ $S_N = 0.74$	**1**(*p*-CH_3)	-1.22	1.83	1.88
	1(*p*-H)	-0.78	2.28	2.21
	1(*m*-Br)	0.00	2.73	2.78
	1(*m*-CN)	0.29	3.00	3.00
 $R_N = 3.48$ $S_N = 0.81$	**1**(*p*-CH_3)	-1.22	1.83	1.83
	1(*p*-H)	-0.78	2.18	2.19
	1(*m*-Br)	0.00	2.90	2.82
	1(*m*-CN)	0.29	3.00	3.05
 $R_N = 1.52$ $S_N = 0.74$	**1**(*p*-NO_2)	1.63	0.84	0.85
	1(*p*-CN)	0.92	0.38	0.34
	1(*p*-CF_3)	0.57	0.06	0.09
CH_3OH $R_N = 0.04$ $S_N = 0.91$	**1**(*p*-NO_2)	1.63	1.48	1.52
	1(*p*-CN)	0.92	1.00	0.87
	1(*p*-CF_3)	0.57	0.47	0.56

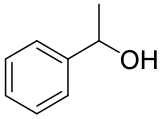
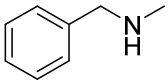
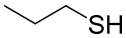
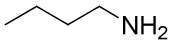
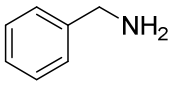
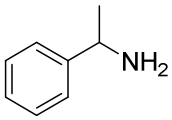
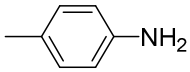
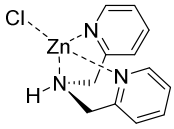
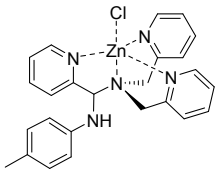
 R_N = -1.27 S_N = 0.99	**1**(*p*-NO_2)	1.63	0.26	0.36
	1(*p*-CN)	0.92	-0.04	-0.35
	1(*p*-CF_3)	0.57	-0.89	-0.69
 R_N = -1.67 S_N = 0.91	**1**(*p*-NO_2)	1.63	-0.06	-0.04
	1(*p*-CN)	0.92	-0.60	-0.68
	1(*p*-CF_3)	0.57	-1.05	-1.00
 R_N = 1.42 S_N = 1.02	**1**(*m*-Br)	0.00	1.44	1.45
	1(*m*-CN)	0.29	1.70	1.74
	1(*p*-NO_2)	1.63	3.07	3.11
	1(*p*-CN)	0.92	2.46	2.39
 R_N = 3.33 S_N = 0.93	**1**(*p*-OCH_3)	-1.86	1.35	1.37
	1(*p*-CH_3)	-1.22	1.96	1.96
	1(*m*-CH_3)	-0.92	2.25	2.24
	1(*p*-H)	-0.78	2.47	2.37
	1(*m*-F)	-0.08	3.03	3.02
	1(*m*-Br)	0.00	3.07	3.10
	1(*m*-CF_3)	0.16	3.30	3.25
	1(*m*-CN)	0.29	3.38	3.37
C_2H_5OH R_N = -0.58 S_N = 1.01	**1**(*m*-Br)	0.00	-0.63	-0.59
	1(*m*-CF_3)	0.16	-0.45	-0.42
	1(*m*-CN)	0.29	-0.33	-0.29
	1(*p*-NO_2)	1.63	0.98	1.06
	1(*p*-CN)	0.92	0.52	0.34
	1(*p*-CF_3)	0.57	0.00	-0.01
 R_N = -0.04 S_N = 1.20	**1**(*m*-F)	-0.08	-0.14	-0.14
	1(*m*-Br)	0.00	-0.14	-0.05
	1(*m*-CF_3)	0.16	0.15	0.14
	1(*m*-CN)	0.29	0.28	0.30
	1(*p*-NO_2)	1.63	1.76	1.91
	1(*p*-CN)	0.92	1.31	1.06
	1(*p*-CF_3)	0.57	0.60	0.64
	1(*p*-Br)	-0.29	-0.40	-0.40

Table S39. The measured log *K* and predicted log *K* values in Figure 5d.

Nucleophile	R_N (S_N)	Electrophile	R_E	Measured log *K*	Predicted log *K*
	3.44 (0.99)	**1**(*p*-OCH_3)	-1.86	1.60	1.56
		1(*p*-CH_3)	-1.22	2.14	2.20
		1(*p*-H)	-0.78	2.68	2.63
	3.96 (0.71)	**1**(*p*-OCH_3)	-1.86	1.49	1.49
		1(*p*-CH_3)	-1.22	1.98	1.95
		1(*p*-H)	-0.78	2.25	2.26
	3.10 (0.96)	**1**(*p*-OCH_3)	-1.86	1.20	1.19
		1(*p*-CH_3)	-1.22	1.79	1.80
		1(*p*-H)	-0.78	2.24	2.23
	1.25 (0.92)	**1**(*p*-OCH_3)	-1.86	-0.54	-0.56
		1(*p*-CH_3)	-1.22	0.00	0.03
		1(*p*-CF_3)	0.57	1.68	1.67
		1(*p*-Br)	-0.29	0.88	0.88
	3.39 (0.63)	**1**(*p*-OCH_3)	-1.86	0.93	0.96
		1(*p*-CH_3)	-1.22	1.39	1.37
		1(*p*-CF_3)	0.57	2.45	2.49
		1(*p*-Br)	-0.29	2.03	1.95
	1.05 (0.58)	**1**(*p*-OCH_3)	-1.86	-0.54	-0.47
		1(*p*-CH_3)	-1.22	0.00	-0.10
		1(*p*-CF_3)	0.57	0.93	0.94
		1(*p*-Br)	-0.29	0.42	0.44

SH	3.33 (0.93)		1.59	1.77
SH	2.71 (0.86)	-1.43	1.29	1.10
SH	1.52 (0.86)		-0.03	0.08
HOOC SH	3.48 (0.81)		1.76	1.66
SH	3.33 (0.93)		1.78	1.66
SH	2.71 (0.86)	-1.55	0.94	1.00
SH	1.52 (0.86)		-0.47	-0.03
HOOC SH	3.48 (0.81)		1.95	1.56

References

(1) Kumpf, J.; Schwaebel, S. T.; Bunz, U. H. F. *J. Org. Chem.* **2015**, *80*, 5159-5166.