Electronic Supplementary Information (ESI)

A pillar[5]arene with an amino-terminated arm stabilizes the formation of aliphatic hemiaminals and imines

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Contents

1. Materials and methods 3

2. Synthesis and characterization of related compounds 4

1) Ethyl 2-(4-ethoxyphenoxy)acetate 4

2) **DEP5A** and **ECP5A** 5

3) **R** 9

3. Determination of stoichiometry by Job's Plot method 13

1) **DEP5A** and caproaldehyde (**G3**) 13

2) **DEP5A** and benzaldehyde (**G1**) 14

3) **DEP5A** and 2-methylbutyraldehyde (**G2**) 15

4. Binding constants 16

5. Representative ^{1}H NMR signals of imines 18

6. Mixed aldehydes react with **PA** in the absence of **DEP5A** 19

7. Mixed aldehydes react with **PA** in the presence of **DEP5A** 21

8. Mixed aldehydes react with **PA** in the presence of 1,4-diethoxybenzene 25

9. Mixed aldehydes react with **R** 26

10. Mass spectra of unstable imines and hemiaminals 28

1) **G3** reacts with **R** 28

2) **G4** reacts with **R** 28

3) **G5** reacts with **R** 30

4) **G6** reacts with **R** 32

11. References and notes 37

1. Materials and methods

Materials:

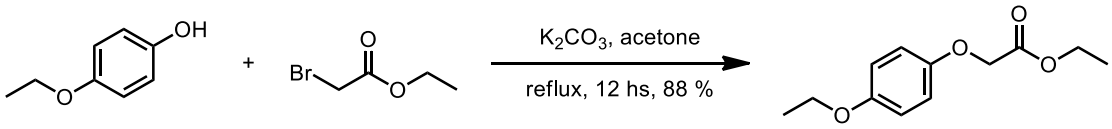
Ethyl bromoacetate, 1,4-diethoxylbenzene, *p*-ethoxyphenol, borontrifluoride diethyl etherate, paraformaldehyde, ethylenediamine, and *p*-anisidine (**PA**) were purchased from Aladin and used as received. Benzaldehyde (**G1**), 2-methylbutylaldehyde (**G2**), caproaldehyde (**G3**), benzenepropanal (**G4**), phenylacetaldehyde (**G5**), and 3,3-Dimethylbutyraldehyde (**G6**) were purchased from Aladin and distillated as described in the handbook.[S1] All solvents were used as purchased.

Methods:

Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker 400 MHz spectrometer (or a Bruker AVANCE III 300 MHz spectrometer) and 2D NMR were measured on a Bruker 600 MHz spectrometer. Chemical shifts for protons were reported in parts per million (ppm) and tetramethylsilane (TMS) was used as the reference, and those for carbon were reported in parts per million (ppm) and $CDCl_3$ (77.36 ppm) was used as the reference. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), integration. Low-resolution electrospray ionization mass spectra were obtained on a Bruker Esquire 3000 plus mass spectrometer (Bruker-Franzen Analytik GmbH Bremen, Germany) equipped with an ESI interface and an ion trap analyzer. Thin-layered chromatography (TLC) was performed using silica gel 60 F254 plates.

2. Synthesis and characterization of related compounds

1) Ethyl 2-(4-ethoxyphenoxy)acetate



To a solution of *p*-ethoxyphenol (6.9 g, 0.05 mol) and ethyl bromoacetate (8.4 g, 0.05 mol) in acetone (150 mL) was added K_2CO_3 (10.5 g, 0.075 mol), then the suspension was heated at reflux for 12 hours. The obtained yellow mixture was filtered and concentrated to a minimum volume and then subjected to column chromatography (SiO_2, PE: EA= 10 : 1) to get the pure product as colorless liquid (9.86 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$, 298K) δ 6.83 (m, 4H), 4.56 (s, 2H), 4.26 (q, J = 7.1 Hz, 2H), 3.97 (q, J = 7.0 Hz, 2H), 1.38 (t, J = 7.0 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$, 298K) δ 169.6, 154.2, 152.3, 116.2, 115.7, 66.7, 64.3, 61.6, 15.2, 14.5.

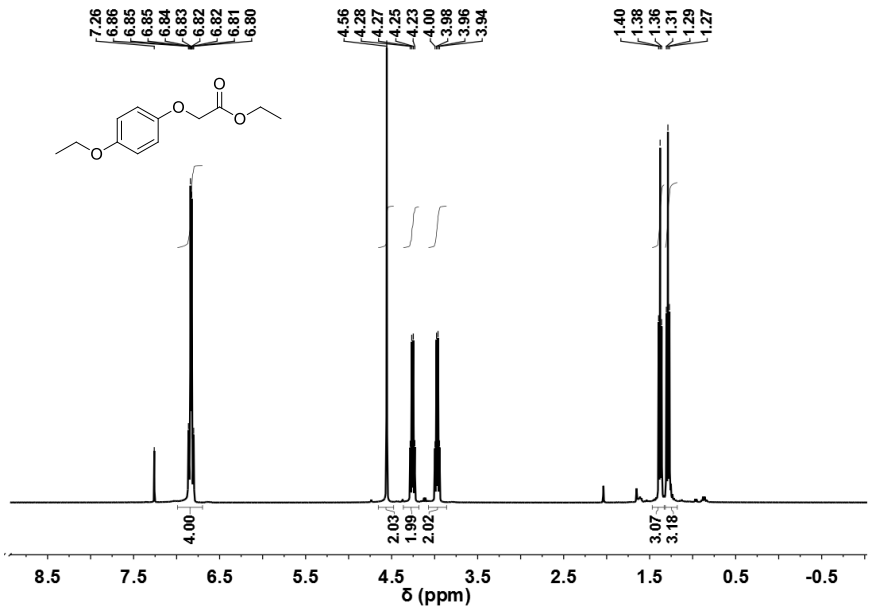


Figure S1. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 25 °C) of ethyl 2-(4-ethoxyphenoxy)acetate.

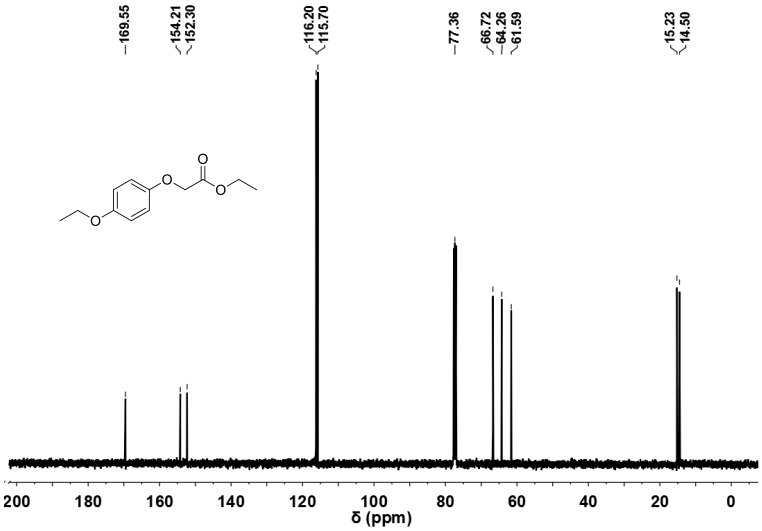
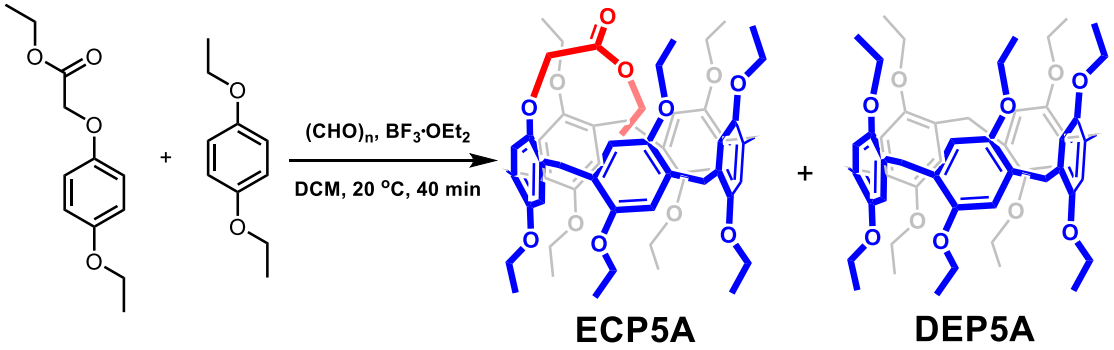


Figure S2. ^{13}C NMR spectrum (101 MHz, $CDCl_3$, 25 °C) of ethyl 2-(4-ethoxyphenoxy)acetate.

2) DEP5A and ECP5A



To a solution of 1,4-diethoxybenzene (2.76 g, 20.0 mmol) in dichloromethane (250.0 mL) was added paraformaldehyde (2.2 g, 73.0 mmol) and ethyl-4-ethoxy phenoxy acetate (0.84 g, 4.0 mmol), then the suspension was stirred at room temperature for 20 minutes. Then boron trifluoride diethyl etherate [$BF_3{\cdot}O(C_2H_5)_2$, 3.6 mL, 28.3 mmol] was added to the solution, and the mixture was stirred at room temperature for 40 minutes. Subsequently, the reaction was quenched with an aqueous solution of $NaHCO_3$ (200 mL). The obtained yellow mixture was filtered off and the organic phase was collected. The solvent was removed on rotor-vap and the crude product was purified by column chromatography (SiO_2, PE:DCM:EA = 22:1:1) to get the final product **DEP5A** (0.68 g) and **ECP5A** (0.62 g) as white powder. For **DEP5A**: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 6.78 (s, 10H), 3.88 (q, *J* = 6.9 Hz, 20H), 3.83 (s, 10H), 1.32 (t, *J* = 7.0 Hz, 30H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C) δ 150.1, 128.8, 115.4, 64.1, 30.2, 15.4. LC-ESI-MS: m/z calcd for $[M+H]^+$ $C_{55}H_{71}O_{10}^+$, calculated 891.5042; found 891.9648. For **ECP5A**: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 6.77 (ddd, *J* = 56.4, 27.5, 8.1 Hz, 10H), 4.49 (s, 2H), 4.15 – 3.55 (m, 28H), 2.49 (q, *J* = 7.0 Hz, 2H), 1.62 – 1.21 (m, 27H), -1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 169.41, 150.47, 150.34, 150.16, 149.86, 149.78, 149.70, 149.54, 149.42, 129.86, 129.51, 129.36, 129.08, 128.97, 128.86, 128.46, 128.02, 127.57, 127.50, 116.52, 116.15, 115.55, 115.16, 114.58, 114.52, 114.36, 113.75, 112.76, 77.36, 65.11, 64.64, 64.16, 64.10, 64.00, 63.93, 63.87, 63.53, 61.10, 31.85, 30.72, 30.12, 29.42, 29.22, 27.93, 15.71, 15.66, 15.62, 15.59, 15.53, 15.49, 15.47, 11.30. LC-ESI-MS: m/z calcd for $[M+H]^+$ $C_{57}H_{73}O_{12}^+$, 949.5097; found 949.9992.

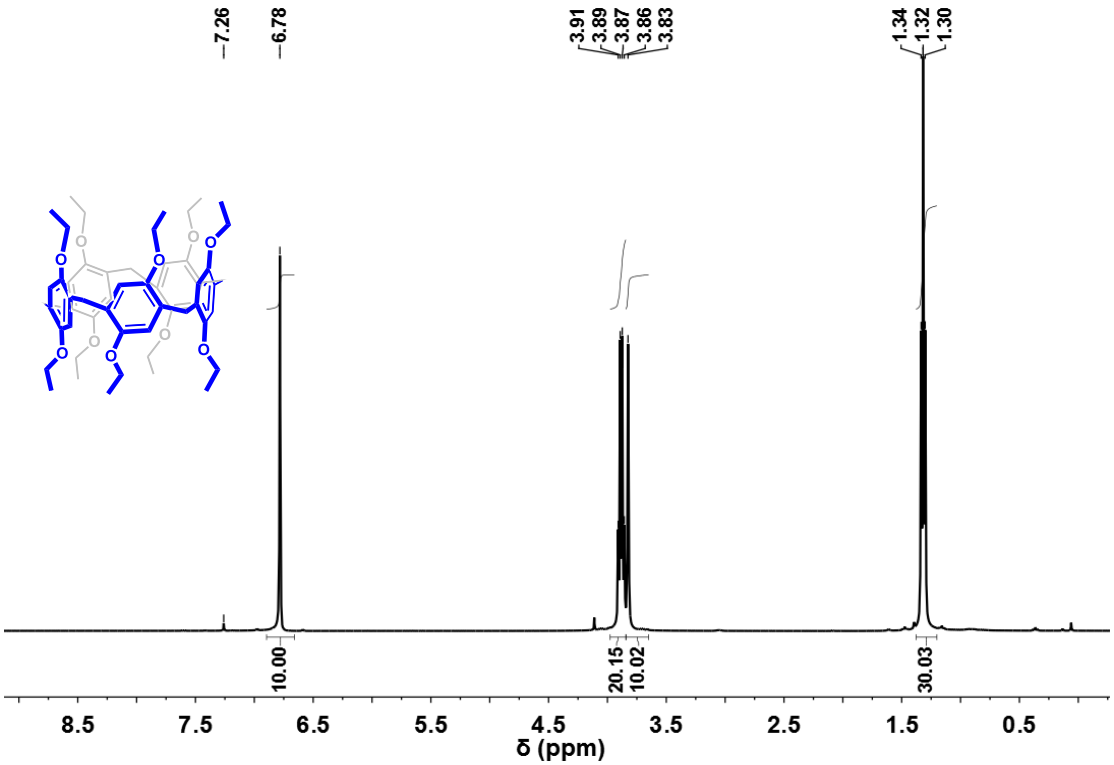


Figure S3. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 25 °C) of **DEP5A**.

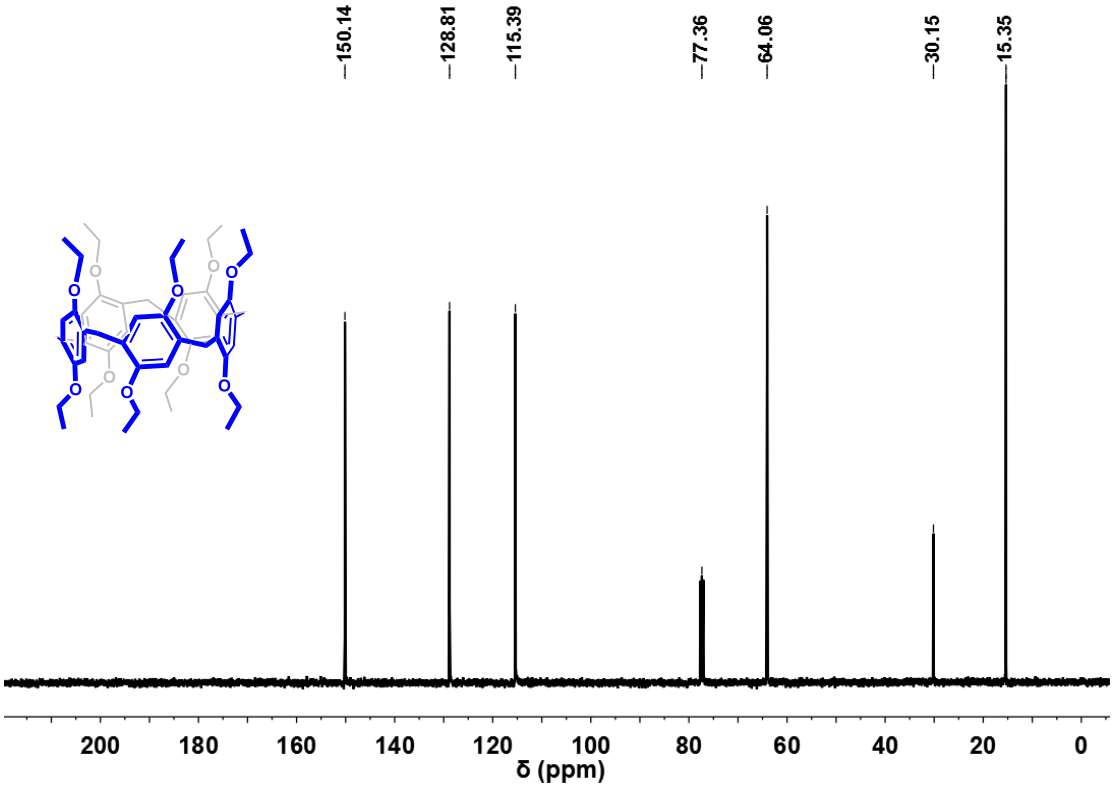


Figure S4. ^{13}C NMR spectrum (101 MHz, $CDCl_3$, 25 °C) of **DEP5A**.

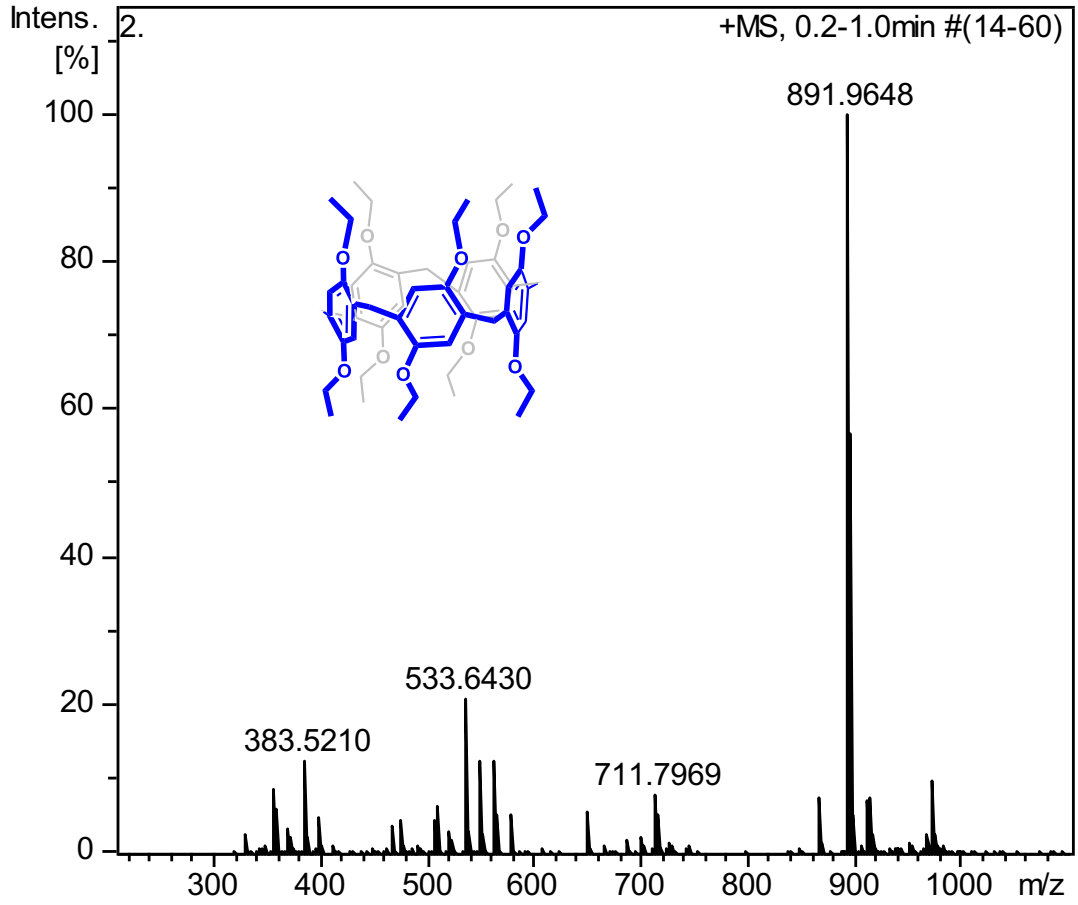


Figure S5. LC-ESI-MS of **DEP5A**: m/z calculated for $[M+H]^+$ (100.00 %) $C_{55}H_{71}O_{10}^+$, 891.5042; found 891.9648.

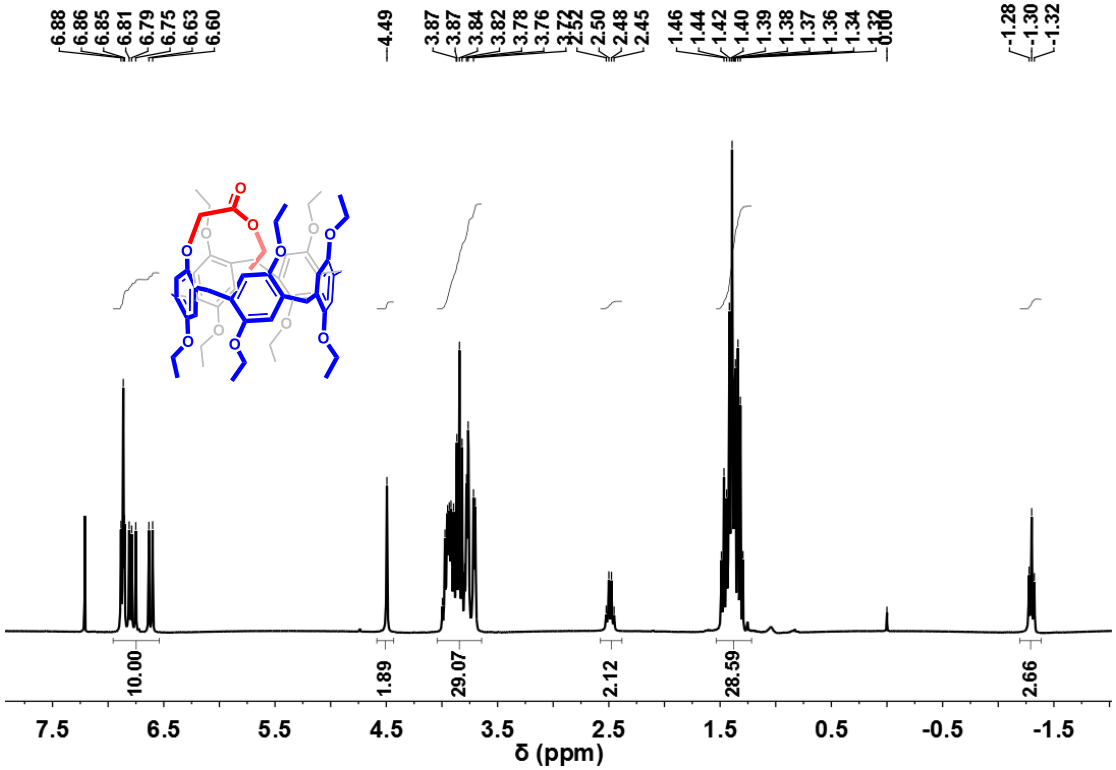


Figure S6. ^{1}H NMR spectrum (300 MHz, $CDCl_3$, 25 °C) of **ECP5A**.

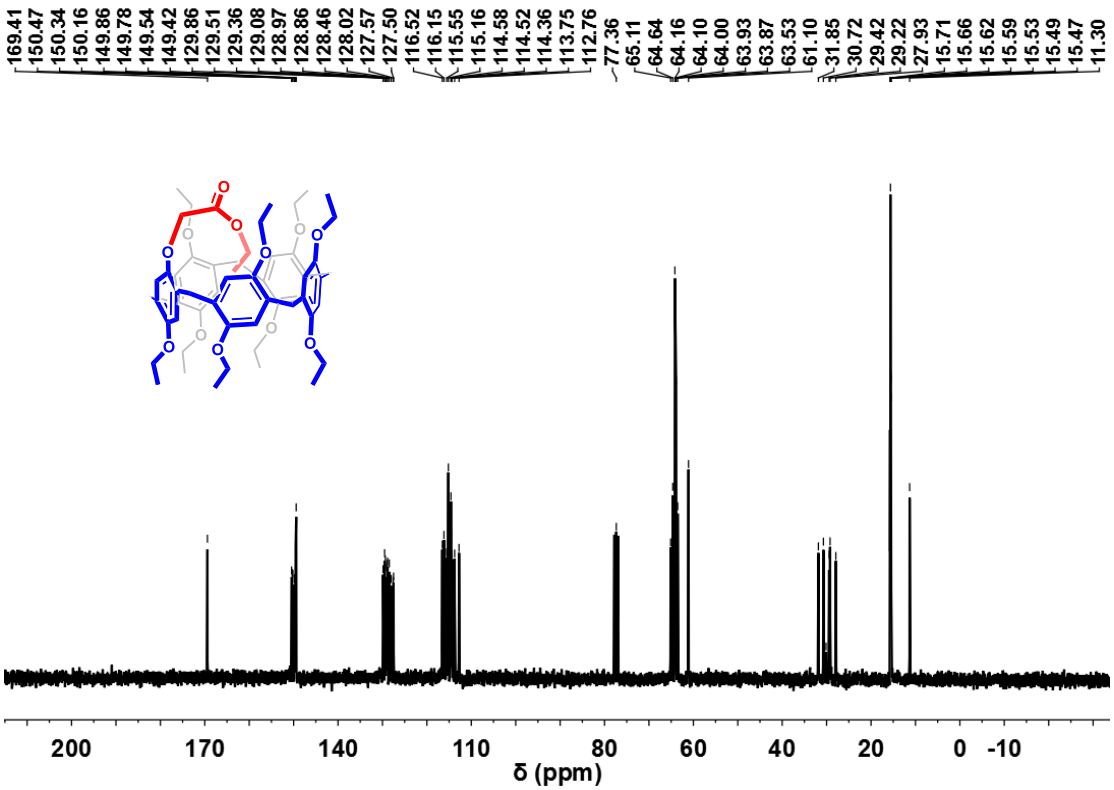


Figure S7. ^{13}C NMR spectrum (75 MHz, $CDCl_3$, 25 °C) of **ECP5A**.

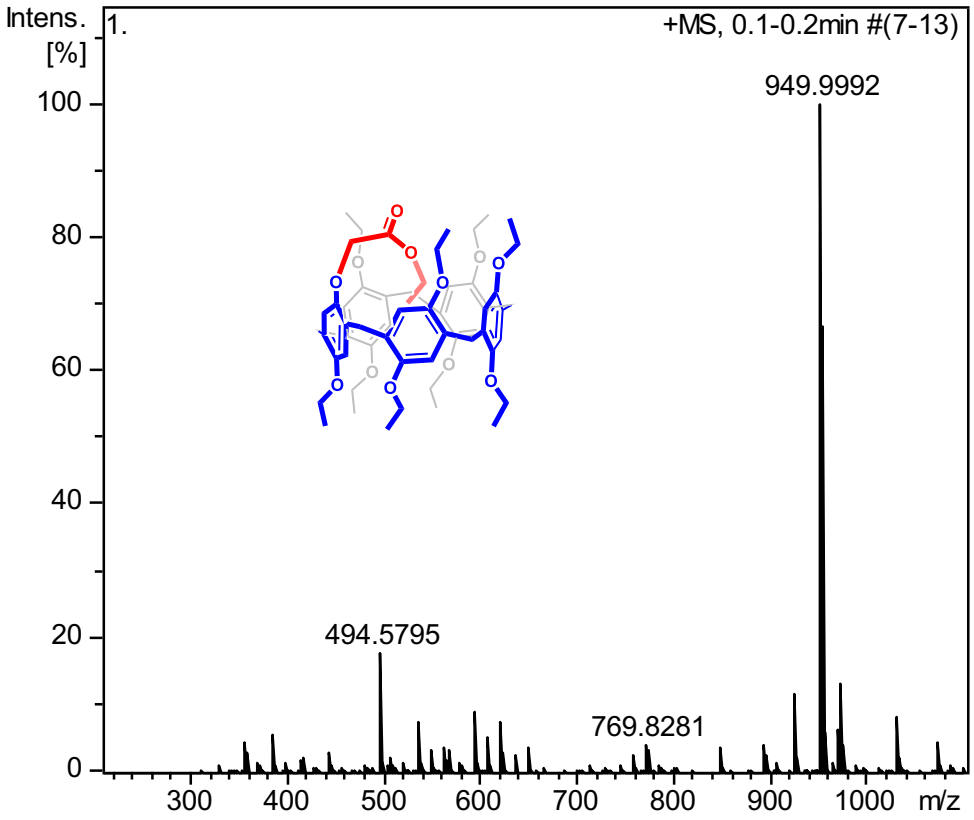
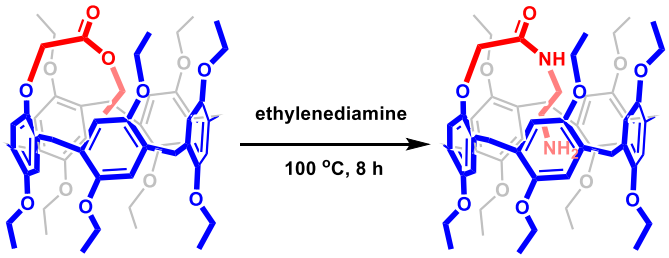


Figure S8. LC-ESI-MS of **ECP5A**: m/z calcd for $[M+H]^+$ $C_{57}H_{73}O_{12}^+$, 949.5097; found 949.9992.

3) R



ECP5A R

To a 50 mL round-bottom flask was dispersed **ECP5A** (214 mg, 0.22 mmol) in ethylenediamine (10 mL). The mixture was heated at 100 ºC for 8 hours. After being cooled down, the suspension was filtered off and washed there times with distillated water (3×10 mL) and then separated by column chromatography (SiO_2, DCM:MeOH = 10:1), the white powder was collected for analysis (208 mg, 96 %). ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C) δ 7.00 – 6.96 (m, Ar*H*, 3H), 6.96 – 6.92 (m, Ar*H*, 3H), 6.89 (s, Ar*H*, 1H), 6.80 (d, *J* = 2.5 Hz, Ar*H*, 2H), 6.58 (s, Ar*H*, 1H), 4.47 (s, -C*H*$_2$CO-, 2H), 4.30 (t, *J* = 5.3 Hz, -CON*H*-, 1H), 4.16 – 3.63 (m, ArC*H*$_2$-, 10H, -C*H*$_2$CH$_3$, 18H), 1.48 (dddd, *J* = 16.6, 13.8, 13.0, 7.0 Hz, -CH$_2$C*H*$_3$, 27H, -NHC*H*$_2$-, 2H), -0.87 (t, *J* = 4.7 Hz, -C*H*$_2$NH$_2$, 2H), -2.22 (s, -CH$_2$N*H*$_2$, 2H). ^{13}C NMR (151 MHz, $CDCl_3$, 25 °C) δ 169.00, 151.17, 151.00, 150.64, 150.37, 150.09, 150.02, 149.81, 149.53, 148.39, 147.97, 131.15, 129.31, 128.94, 128.74, 127.91, 117.08, 115.39, 115.15, 114.74, 114.47, 113.95, 113.08, 73.47, 68.44, 66.55, 66.03, 65.87, 65.01, 64.42, 64.25, 63.96, 63.39, 51.72, 36.47, 32.24, 31.56, 30.40, 30.22, 30.07, 29.78, 29.19, 28.81, 27.05, 15.76, 15.62, 15.56, 15.35, 15.22, 15.07. LC-ESI-MS: m/z calcd for $[M+H]^+$ (100.00 %) $C_{57}H_{75}N_2O_{11}^+$, 963.5365; found 963.5408; m/z calcd for $[M+2H]^{2+}$ (4.47 %) $C_{57}H_{76}N_2O_{11}^{2+}$, 964.5438; found 964.5538.

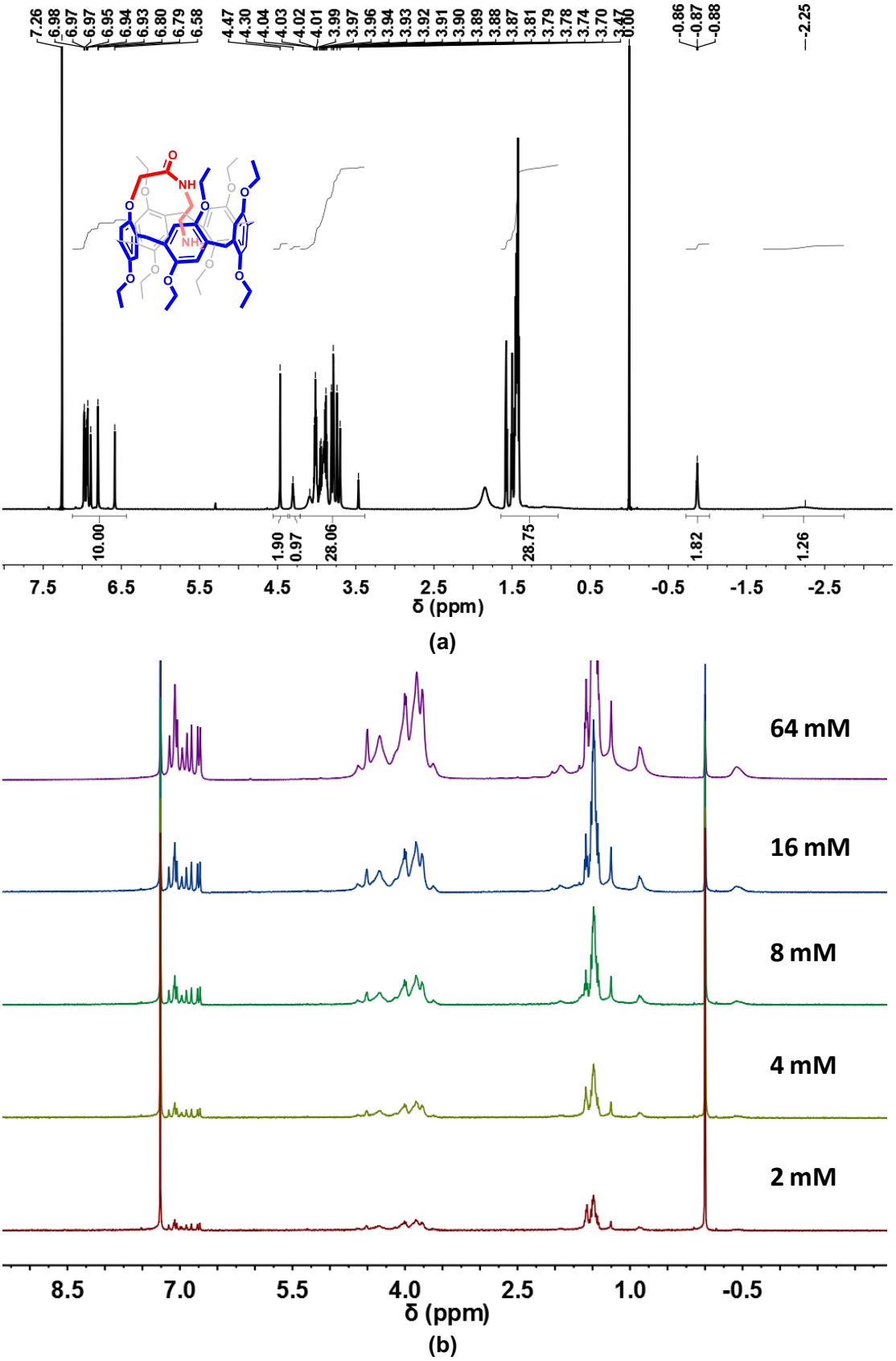


Figure S9. (a) ^{1}H NMR spectrum (600 MHz, $CDCl_3$, 25 °C) of **R**; (b) ^{1}H NMR spectra (300 MHz, $CDCl_3$, 25 °C) of **R** with varying concentration.

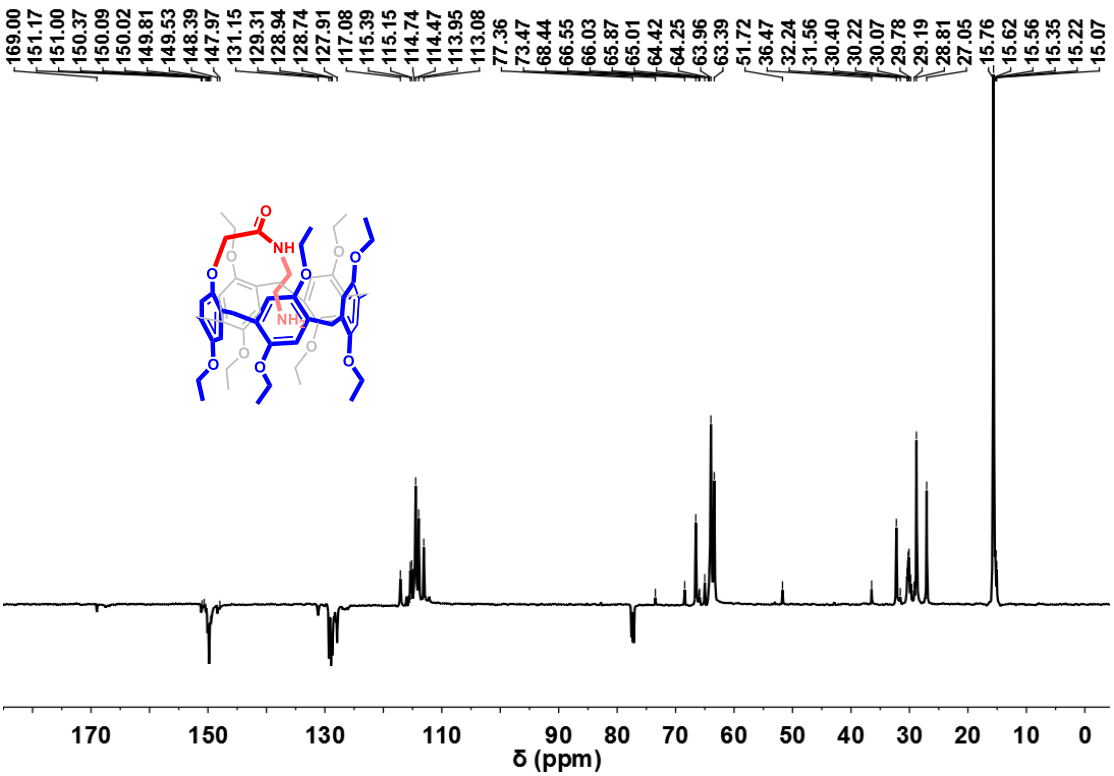


Figure S10. ^{13}C NMR spectrum (151 MHz, $CDCl_3$, 25 °C) of **R**.

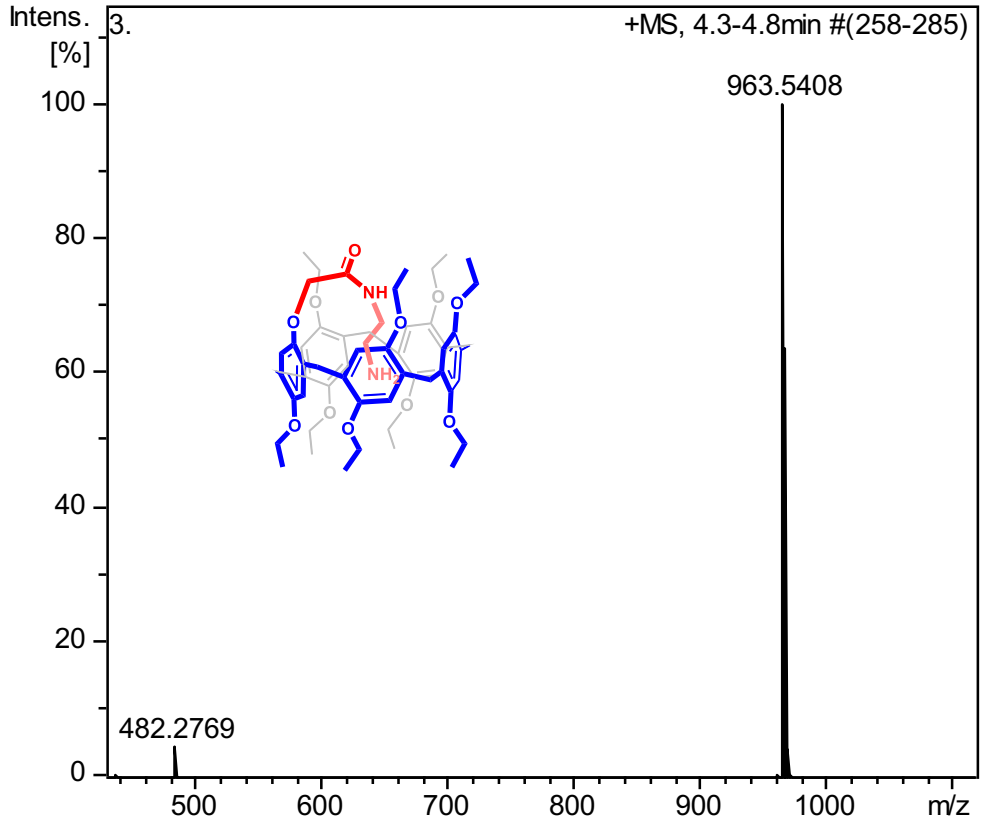


Figure S11. LC-ESI-MS of **R**: m/z calcd for $[M+H]^+$ (100.00 %) $C_{57}H_{75}N_2O_{11}^+$, 963.5365; found 963.5408; m/z calcd for $[M+2H]^{2+}$ (4.47 %) $C_{57}H_{76}N_2O_{11}^{2+}$, 964.5438; found 964.5538.

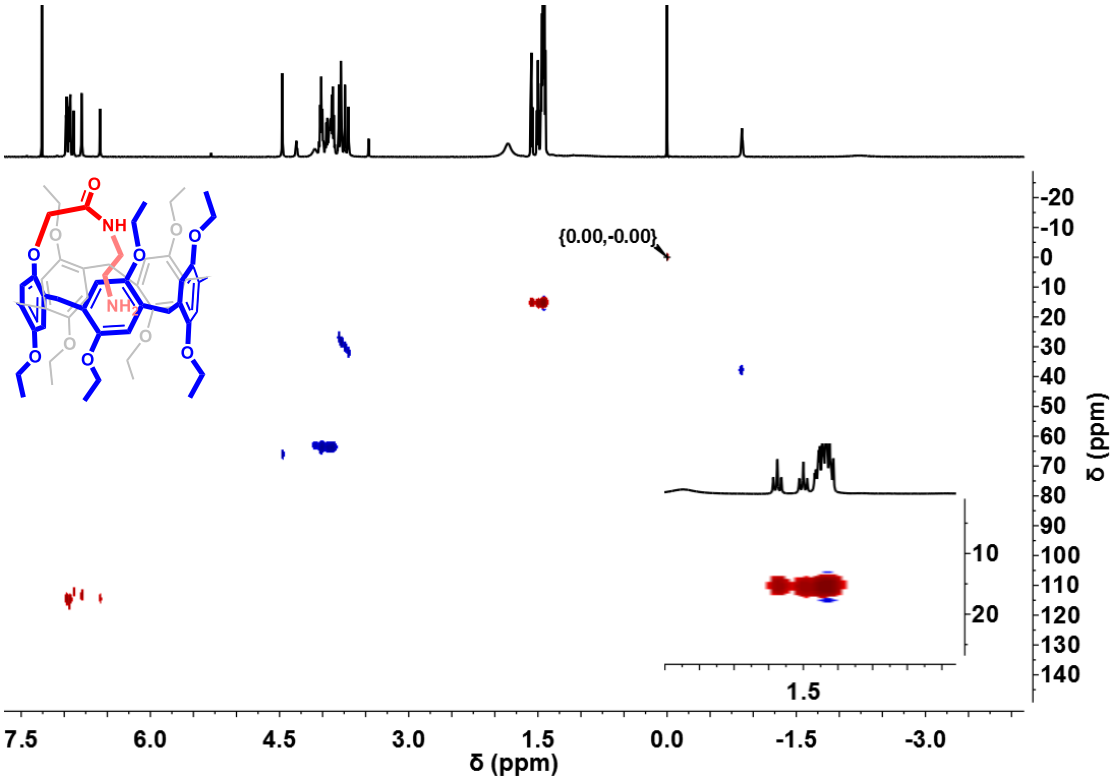


Figure S12. ^{1}H-^{13}C HSQC spectrum (600 MHz, $CDCl_3$, 25 °C) of **R**, in which color in blue represents the signal of –C*H*$_2$- and in red stands for –OCH$_2$C*H*$_3$ and Ar*H*.

3. Determination of stoichiometry by Job's Plot method

1) DEP5A and caproaldehyde (G3)

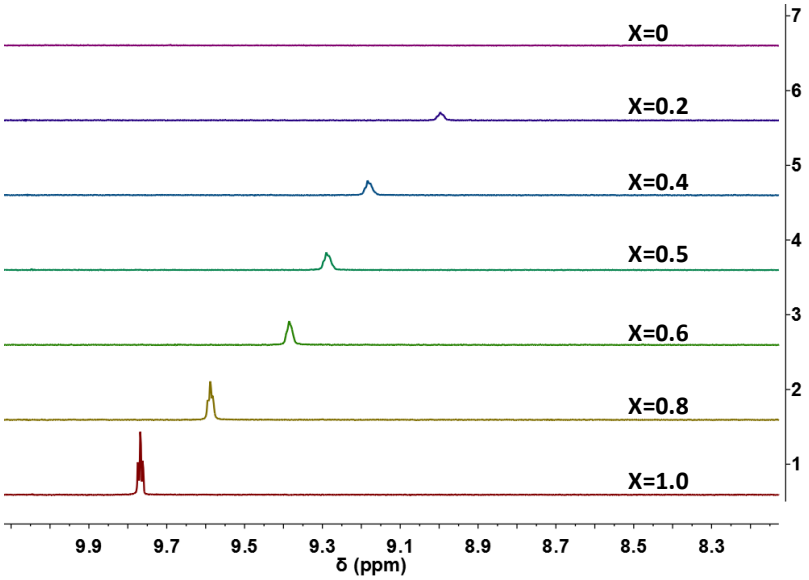


Figure S13. Partial ^{1}H NMR (300 MHz, $CDCl_3$, 25 ^{o}C) chemical shifts of the **G3**.

Table S1 Original data for Job's plot of **DEP5A** and **G3**

groups	[H]/mM	[G]/mM	X_{guest}	δ_{guest}	Δδ	Δδ ·X_{guest}
7	10	0	0			0
6	8	2	0.2	9.002	0.762	0.1524
5	6	4	0.4	9.186	0.578	0.2312
4	5	5	0.5	9.290	0.474	0.2370
3	4	6	0.6	9.384	0.380	0.2280
2	2	8	0.8	9.587	0.177	0.1416
1	0	10	1.0	9.764	0	0

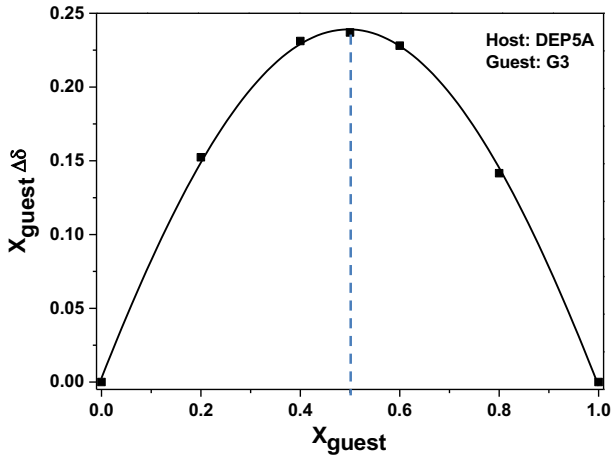


Figure S14. Job's plot of **DEP5A** and **G3**.

2) DEP5A and benzaldehyde (G1)

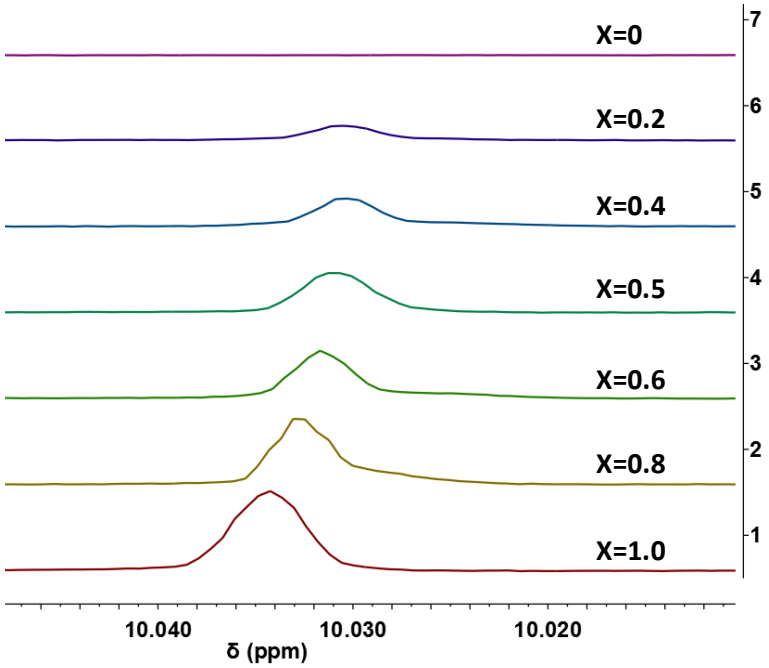


Figure S15. Partial ^{1}H NMR (300 MHz, $CDCl_3$, 25 ^{o}C) chemical shifts of the **G1**.

Table S2 Original data for Job's plot of **DEP5A** and **G1**

groups	[H]/mM	[G]/mM	X_{guest}	δ_{guest}	$\Delta\delta$	$\Delta\delta \cdot X_{guest}$
7	10	0	0	0	0	0
6	8	2	0.2	10.0306	0.00037	0.00074
5	6	4	0.4	10.0304	0.0039	0.00156
4	5	5	0.5	10.0310	0.0033	0.00165
3	4	6	0.6	10.0316	0.0027	0.00162
2	2	8	0.8	10.0328	0.0015	0.00012
1	0	10	1.0	10.0343	0	0

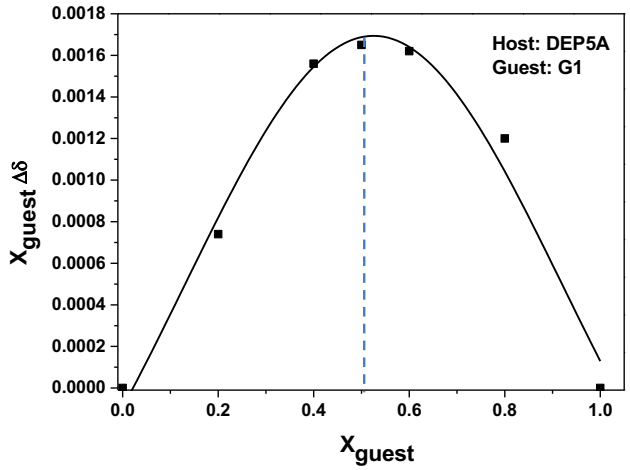


Figure S16. Job's plot of **DEP5A** and **G1**.

3) DEP5A and 2-methylbutyraldehyde (G2)

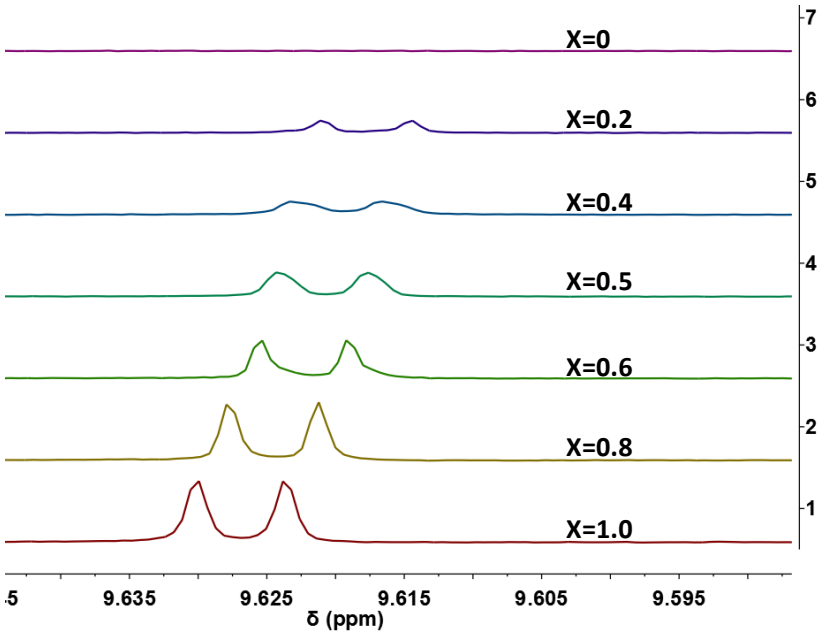


Figure S17. Partial ^{1}H NMR (300 MHz, $CDCl_3$, 25 ^{o}C) chemical shifts of **G2**.

Table S3 Original data for Job's plot of **DEP5A** and **G2**

groups	[H]/mM	[G]/mM	X_{guest}	δ_{guest}	Δδ	Δδ ·X_{guest}
7	10	0	0	0	0	0
6	8	2	0.2	9.6145	0.0092	0.00184
5	6	4	0.4	9.6166	0.0071	0.00284
4	5	5	0.5	9.6176	0.0061	0.00305
3	4	6	0.6	9.6191	0.0046	0.00276
2	2	8	0.8	9.6213	0.0024	0.00192
1	0	10	1.0	9.6237	0	0

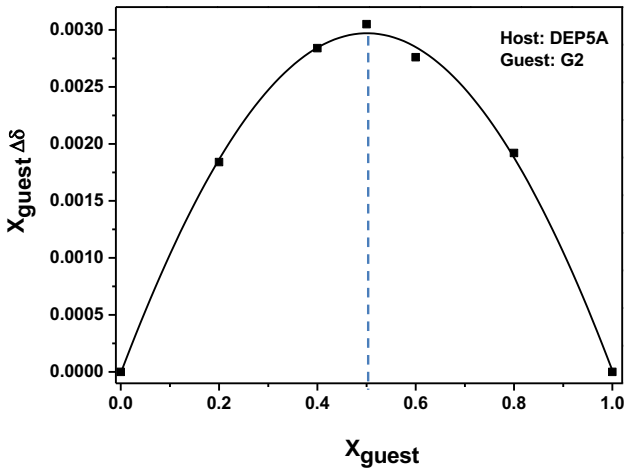


Figure S18. Job's plot of **DEP5A** and **G2**.

4. Binding constants

Table S4 Original data for binding constant of **DEP5A** and **G3**

group	$[G_i]$ (mM)	$CDCl_3$ (uL)	DEP5A (100mM) [H](uL)	[H] (mM)	[H] (equiv.)	Δ_{guest} (ppm)	Δδ (ppm)
1		440	0	0	0	9.769	0
2	4	430	10	2	0.5	9.649	0.12
3		425	15	3	0.75	9.583	0.186
4		415	25	5	1.25	9.466	0.303
5		410	30	6	1.5	9.417	0.352
6		400	40	8	2	9.334	0.435
7		390	50	10	2.5	9.250	0.519
8		380	60	12	3	9.181	0.588
9		360	80	16	4	9.059	0.710
10		340	100	20	5	8.955	0.814
11		320	120	24	6	8.878	0.891
12		300	140	28	7	8.812	0.957
13		280	160	32	8	8.740	1.029
14		260	180	36	9	8.696	1.073
15		240	200	40	10	8.650	1.119
16		220	220	44	11	8.611	1.158
17		200	240	48	12	8.576	1.193
18		180	260	52	13	8.548	1.221
19		160	280	56	14	8.523	1.246
20		140	300	60	15	8.499	1.270
21		120	320	64	16	8.473	1.296
22		100	340	68	17	8.452	1.317
23		80	360	72	18	8.435	1.334
24		60	380	76	19	8.424	1.345
25		40	400	80	20	8.404	1.365
26		20	420	84	21	8.391	1.378
27		0	440	88	22	8.380	1.389
			DEP5A (200mM)				
28		210	230	92	23	8.378	1.391
29		200	240	96	24	8.361	1.408
30		190	250	100	25	8.351	1.418

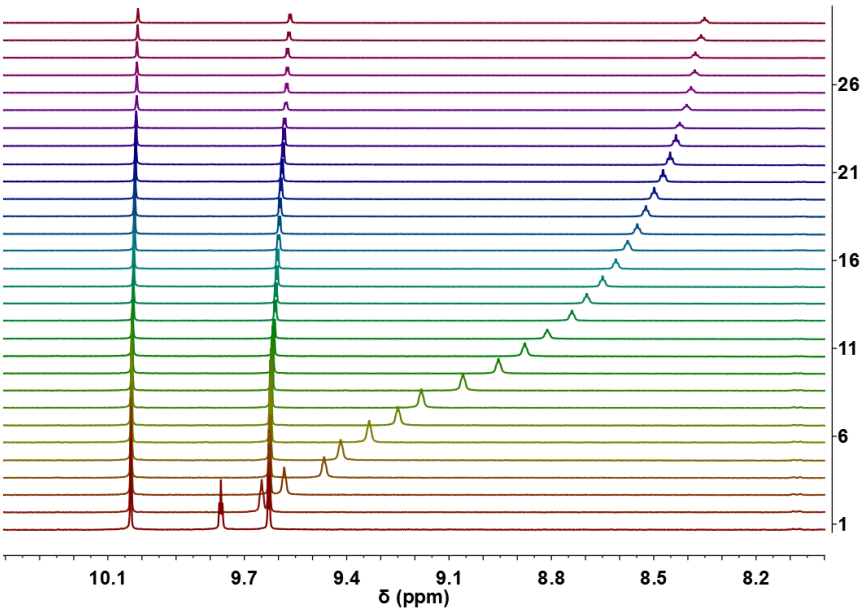


Figure S19. Partial ^{1}H NMR titration spectra (400 MHz, $CDCl_3$, 25 °C) of 3 aldehydes at the concentration of 4 mM respectively upon addition of **DEP5A**: (1) 0 mM; (2) 2 mM; (3) 3 mM; (4) 5 mM; (5) 6 mM; (6) 8 mM; (7) 10 mM; (8) 12mM; (9) 16 mM; (10) 20 mM;(11) 24 mM; (12) 28 mM; (13) 32 mM; (14) 36 mM; (15) 40 mM; (16) 44 mM; (17) 48 mM; (18) 52 mM; (19) 56 mM; (20) 60 mM; (21) 64 mM; (22) 68 mM; (23) 72 mM; (24) 76 mM; (25) 80 mM; (26) 84 mM; (27) 88 mM; (28) 92 mM; (29) 96 mM; (30) 100 mM.

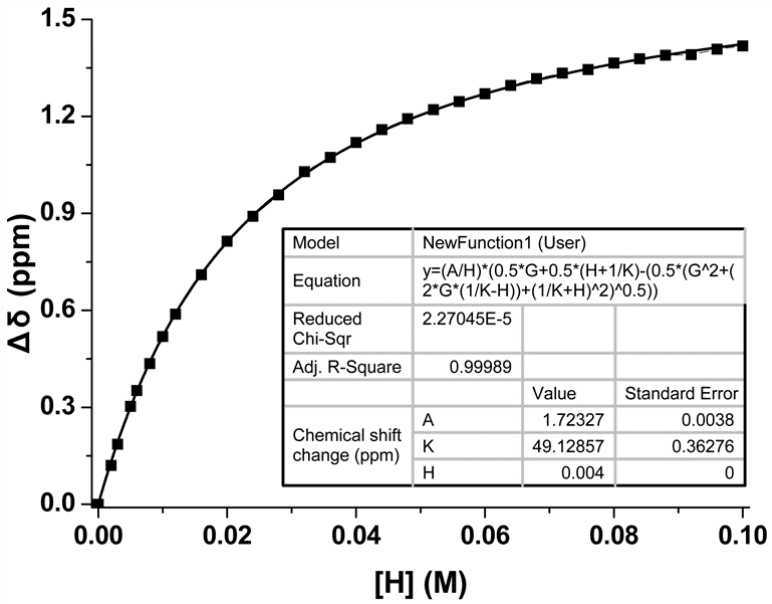


Figure S20. The non-linear curve-fitting [S2] for the complexation of **G3** (4 mM) in the mixed solution and **DEP5A** in $CDCl_3$ at 25 °C. The concentration of **DEP5A** was in accordance with ^1H NMR titration. The association constant (K_a) is calculated to be 49.1 M^{-1}.

5. Representative ^{1}H NMR signals of imines

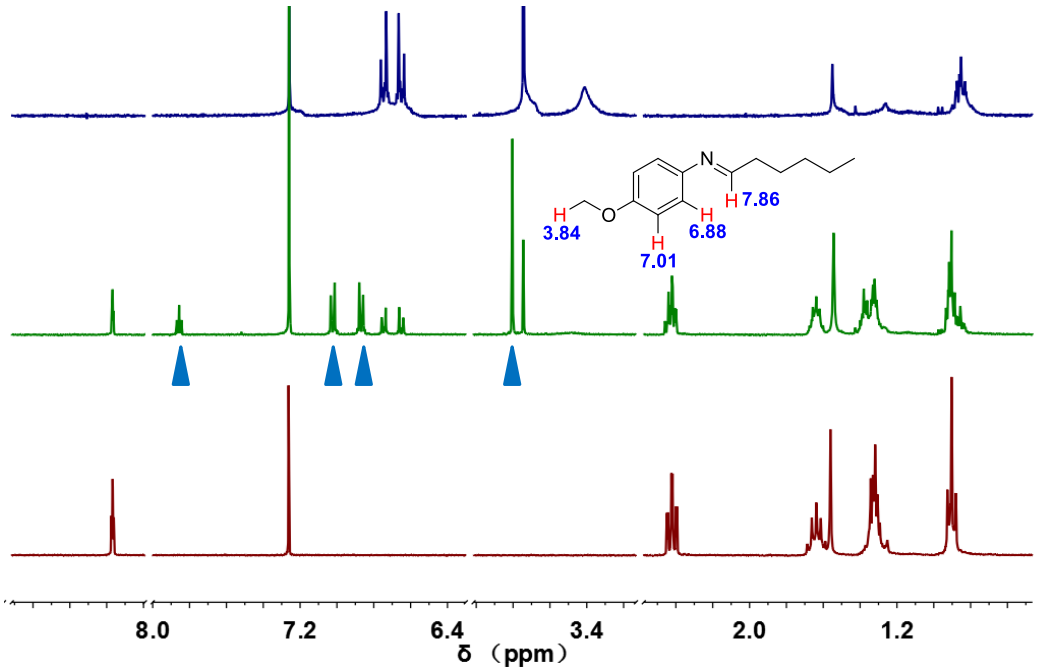


Figure S21. ^{1}H NMR spectra (400 MHz, $CDCl_3$, 25 °C) of the imine formation reaction between caproaldehyde (**G3**, 6 mM) on the bottom and *p*-anisidine (**PA**, 4 mM) on the top in a NMR tube with a total volume of 0.5 mL.

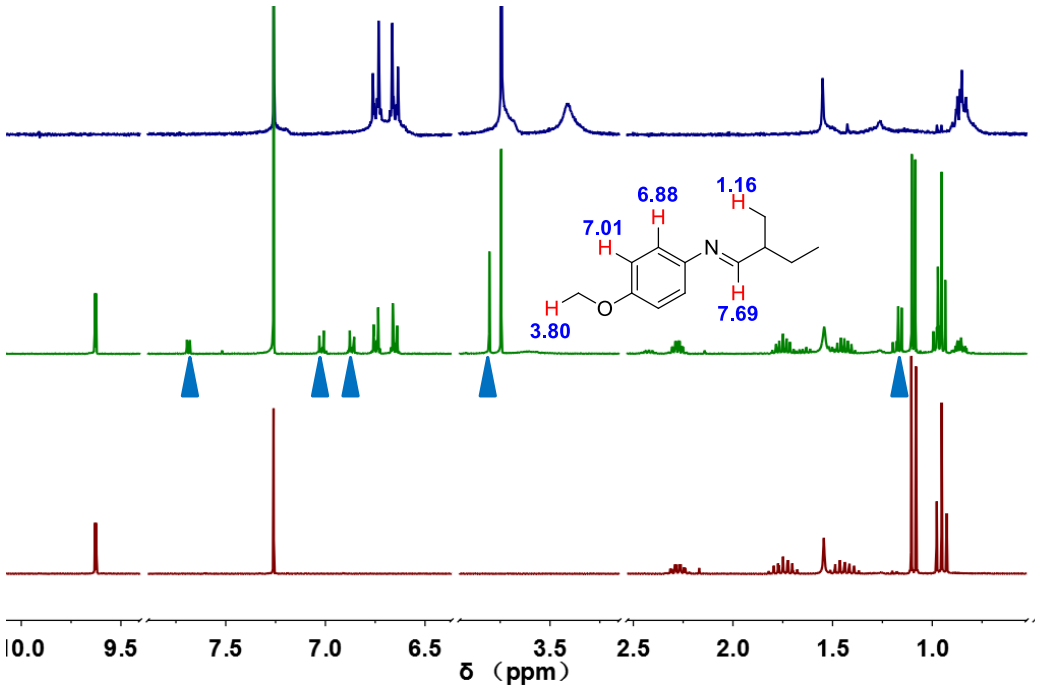


Figure S22. ^{1}H NMR spectra (400 MHz, $CDCl_3$, 25 °C) of the imine formation reaction between 2-methylbutanal (**G2**, 6 mM) on the bottom and *p*-anisidine (**PA**, 4 mM) on the top in a NMR tube with a total volume of 0.5 mL.

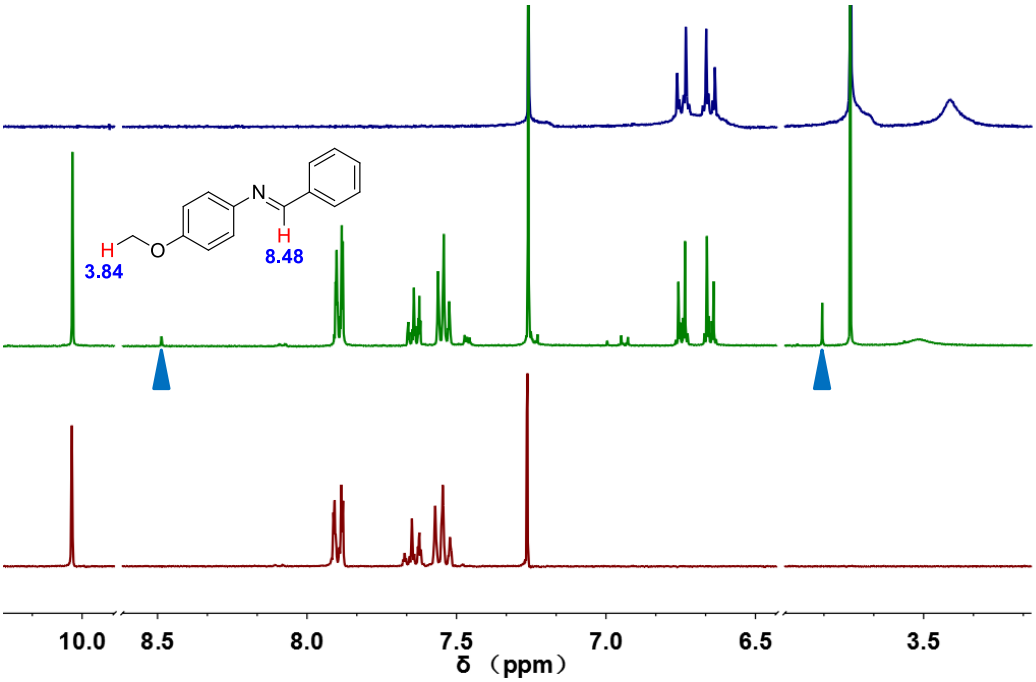


Figure S23. ^{1}H NMR spectra (400 MHz, $CDCl_3$, 25 °C) of the imine formation reaction between benzaldehyde (**G1**, 6 mM) on the bottom and *p*-anisidine (**PA**, 4 mM) on the top in a NMR tube with a total volume of 0.5 mL.

6. Mixed aldehydes react with PA in the absence of DEP5A

Table S5 Original data for the reactions of 3 studied aldehydes with **PA** and without **DEP5A**

groups	t/min	G1 %	$G1_i^{PA}$%	G2	G2 %	$G2_i^{PA}$%	G3	G3 %	$G3_i^{PA}$ -OCH_3	$G3_i^{PA}$%
0	0	100.0	0	85.38	100.0	0. 1	88.16	100.0	0	0
1	6	100.0	0	84.55	99.0	0. 1	87.21	98.9	2.78	1.05
2	9	100.0	0	84.04	98.4	0.1	87.25	98.9	4.29	1.62
3	12	100.0	0	84.27	98.7	0.1	86.85	98.5	4.94	1.87
4	15	100.0	0	85.80	100.0	0.1	86.10	97.6	3.24	1.23
5	18	100.0	0	85.29	99.9	0.1	87.08	98.8	6.50	2.46
6	21	100.0	0	85.83	100.0	0.1	86.08	97.6	4.98	1.88
7	25	100.0	0	84.41	98.8	0.1	85.01	96.4	6.36	2.40
8	28	100.0	0	84.82	99.3	0.1	85.21	96.6	7.36	2.78
9	31	100.0	0	84.64	99.1	0.1	84.43	95.7	8.36	3.16
10	34	100.0	0	84.32	98.7	0.1	83.75	94.9	10.2	3.86
11	37	100.0	0	84.86	99.4	0.1	84.04	95.3	11.98	4.53
12	40	100.0	0	83.89	98.3	0.1	83.22	94.4	15.38	5.81
13	44	100.0	0	84.81	99.3	0.1	82.76	93.8	14,95	5.65
14	47	100.0	0	84.93	99.5	0.1	82.16	93.2	15.41	5.83
15	50	100.0	0	84.56	99.0	0.1	81.55	92.5	19.76	7.47
16	53	100.0	0	84.61	99.1	0.1	81.24	92.1	23.38	8.84
17	57	100.0	0	84.38	98.8	0.1	80.31	91.1	21.14	7.99
18	61	100.0	0	85.40	100.0	0.1	80.32	91.1	23.37	8.84
19	72	100.0	0	85.07	99.6	0.1	79.59	90.2	30.72	11.6

[NOTE]

1) Benzaldehyde (**G1**) did not react in this experiment and was regarded as the reference where the integration of RC***H***O was normalized to 100 to get the above data.

2) Definition:

$$\textit{Decay of aldehyde \% } = (Y_i/Y_0)*100\%$$

wherein, Y_i and Y_0 stand for the integral value of RC***H***O belonging to aldehyde after and before the addition of *p*-anisidine respectively.

$$\textit{formation of imine \% } = (Y_{ii}/Y_0)*100\%$$

wherein, Y_{ii} is the integral value of -C***H***=N- after adding the *p*-anisidine to the mixture of aldehydes and Y_0 is the integral value of RC***H***O belonging to aldehyde before the addition of *p*-anisidine.

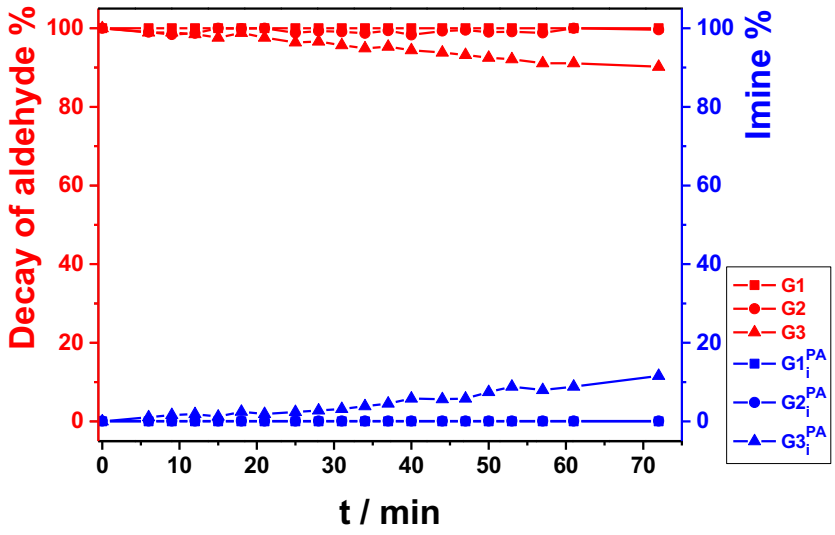


Figure S24. Dynamic studies of the constituent distribution of the reaction between 3 mixed aldehydes (with equal concentration 4 mM) and **PA** (with the concentration 4 mM) in the absence of **DEP5A** in $CDCl_3$, monitored by 400 MHz at 25 °C.

7. Mixed aldehydes react with PA in the presence of DEP5A

Table S6 Original data for the reactions of 3 studied aldehydes with **PA** and with **DEP5A**

group	t/min	G1	G1 %	$G1_i^{PA}$	$G1_i^{PA}$ %	G2	G2%	$G2_i^{PA}$	$G2_i^{PA}$%	G3	G3 %	$G3_i^{PA}$	$G3_i^{PA}$ %	G1-G2 (aldol)	G1-G2 %
0	0	15.49	100.0	0	0	12.44	100.0	0	0	11.96	100.0	0	0	0	0
1	6	15.21	98.2	0.314	2.0	9.01	72.4	3.467	27.8	12.14	100.0	0	0	0.131	1.1
2	10	15.24	98.4	0.390	2.5	8.16	65.6	2.636	21.2	11.90	99.5	0	0	0.260	2.1
3	15	13.41	86.6	0.779	5.0	7.07	56.8	2.514	20.2	11.62	97.2	0	0	0.587	4.7
4	19	12.07	77.9	1.089	7.0	6.23	50.1	2.389	19.2	11.84	99.0	0	0	0.709	5.7
5	23	11.60	74.9	1.152	7.4	5.76	46.3	1.943	15.6	12.19	100.0	0	0	0.792	6.4
6	26	11.59	74.9	1.231	7.9	5.49	44.1	1.414	11.4	12.65	100.0	0	0	0.913	7.3
7	30	10.51	74.3	1.551	10.0	4.98	40.0	1.856	14.9	12.36	100.0	0	0	0.900	7.2
8	33	10.71	69.1	1.671	10.8	4.94	39.7	1.794	14.4	12.56	100.0	0	0	0.939	7.5
9	36	10.13	65.4	1.685	10.9	4.76	38.3	1.616	13.0	12.31	100.0	0	0	0.929	7.5
10	40	10.06	64.9	1.638	10.6	4.93	39.6	1.225	9.8	12.97	100.0	0	0		
11	46	10.11	65.3	1.919	12.4	4.63	37.2	1.557	12.5	12.52	100.0	0	0	0.835	6.7
12	49	10.13	65.4	1.992	12.8	4.66	37.4	1.264	10.2	12.52	100.0	0	0	0.951	7.6
13	52	11.43	67.3	2.070	13.4	4.58	36.8	1.110	8.9	12.39	100.0	0	0	0.937	7.5
14	62	10.12	65.4	2.202	14.2	4.27	34.3	1.27	10.2	11.78	98.5	0	0	0.890	7.2
15	71	10.16	65.6	1.903	12.3	4.26	34.2	0.404	3.2	11.61	97.1	0	0	0.883	7.1

[NOTE]

1) TMS used as the reference whose integral values was normalized to 100 to get the above data.

2) Definition:

$$decay\ of\ aldehyde\ \% = (Y_i/Y_0)*100\%$$

wherein, Y_i and Y_0 stand for the integral value of RC***H***O belonging to aldehyde after and before the addition of *p*-anisidine respectively.

$$formation\ of\ imine\ \% = (Y_{ii}/Y_0)*100\%$$

wherein, Y_{ii} is the integral value of -C***H***=N- after adding the *p*-anisidine to the mixture of aldehydes and Y_0 is the integral value of RC***H***O belonging to aldehyde before the addition of *p*-anisidine.

$$formation\ of\ aldol\ product\ \% = (Y_{iii}/Y_0)*100\%$$

Where Y_{iii} is the integral value of –C***H***O belonging to aldol product and Y_0 is the integral value of RC***H***O belonging to aldehyde before the addition of *p*-anisidine.

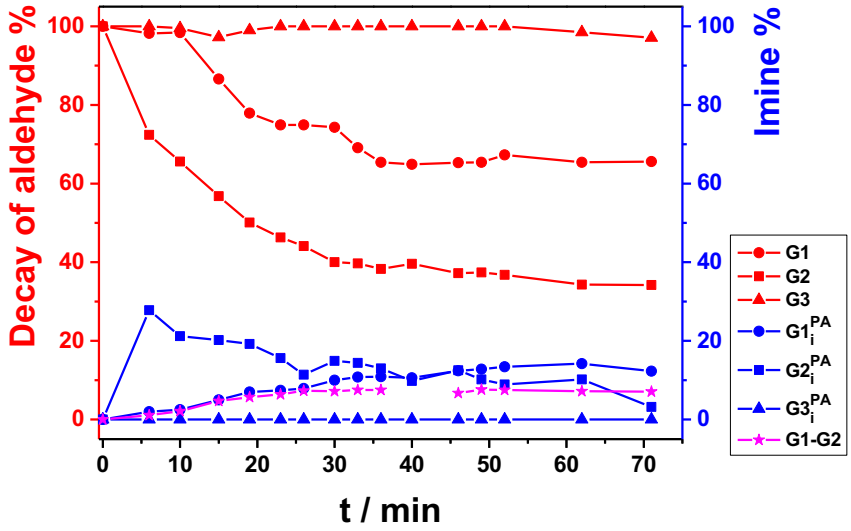


Figure S25. Dynamic studies of the constituent distribution of the reaction between 3 mixed aldehydes (with equal concentration 4 mM) and **PA** (with the concentration 4 mM) in the presence of **DEP5A** in $CDCl_3$, monitored by 400 MHz at 25 °C, ★ aldol product formed from the aldehydes, **G1** and **G2**.

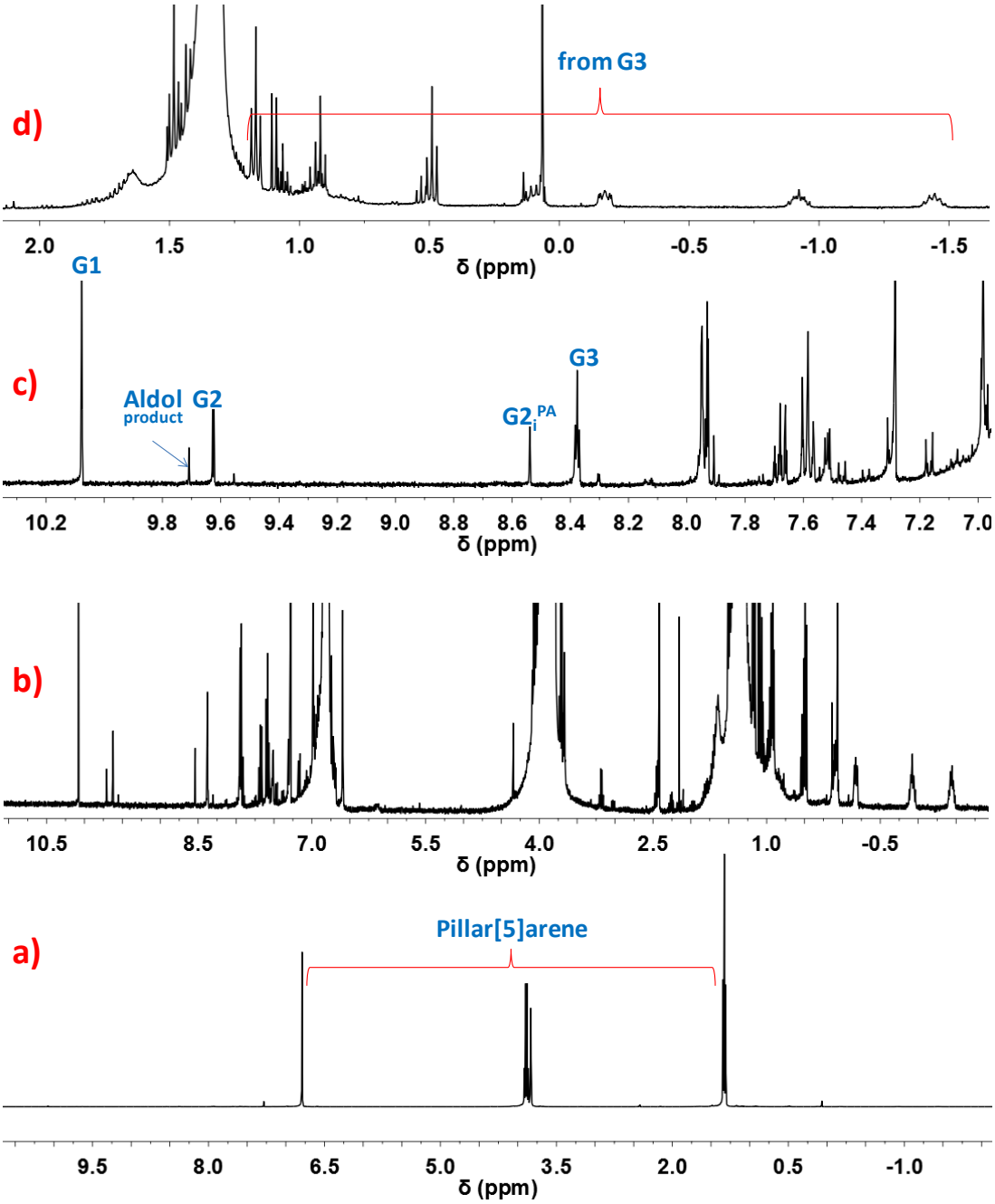


Figure S26. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) studies on the reaction mixture of 3 aldehydes and **PA** and in the presence of **DEP5A**, a) shows the **DEP5A** exists in the reaction; b) is an enlarged figure of a); c) and d) are partial expanded figure of b).

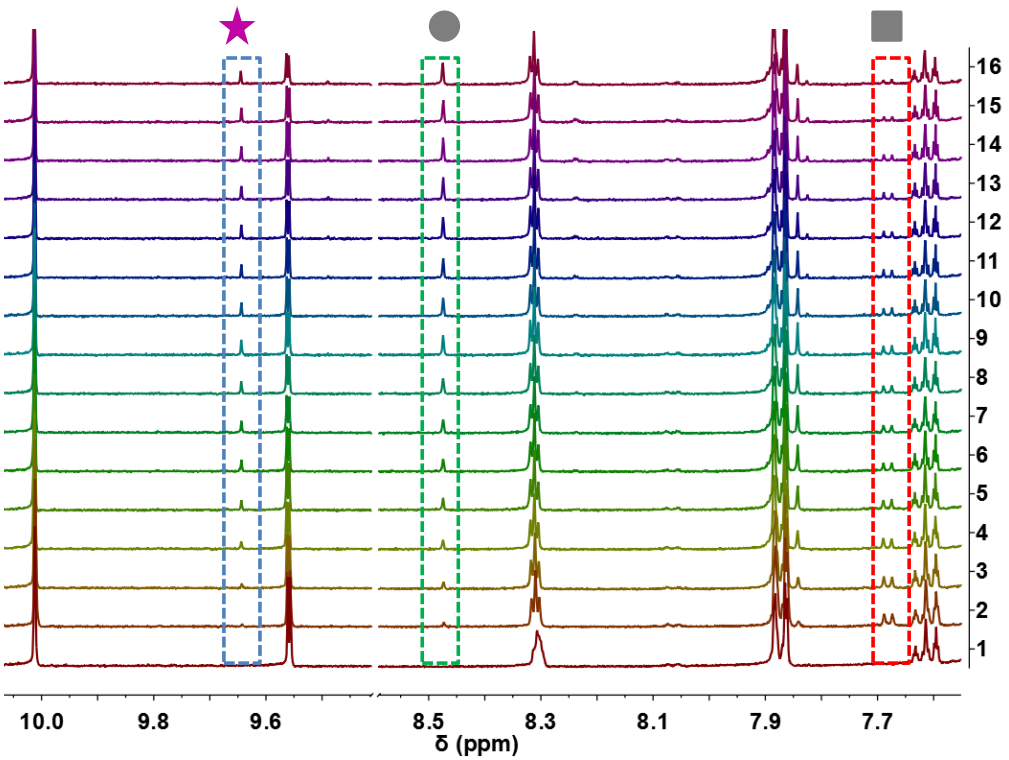
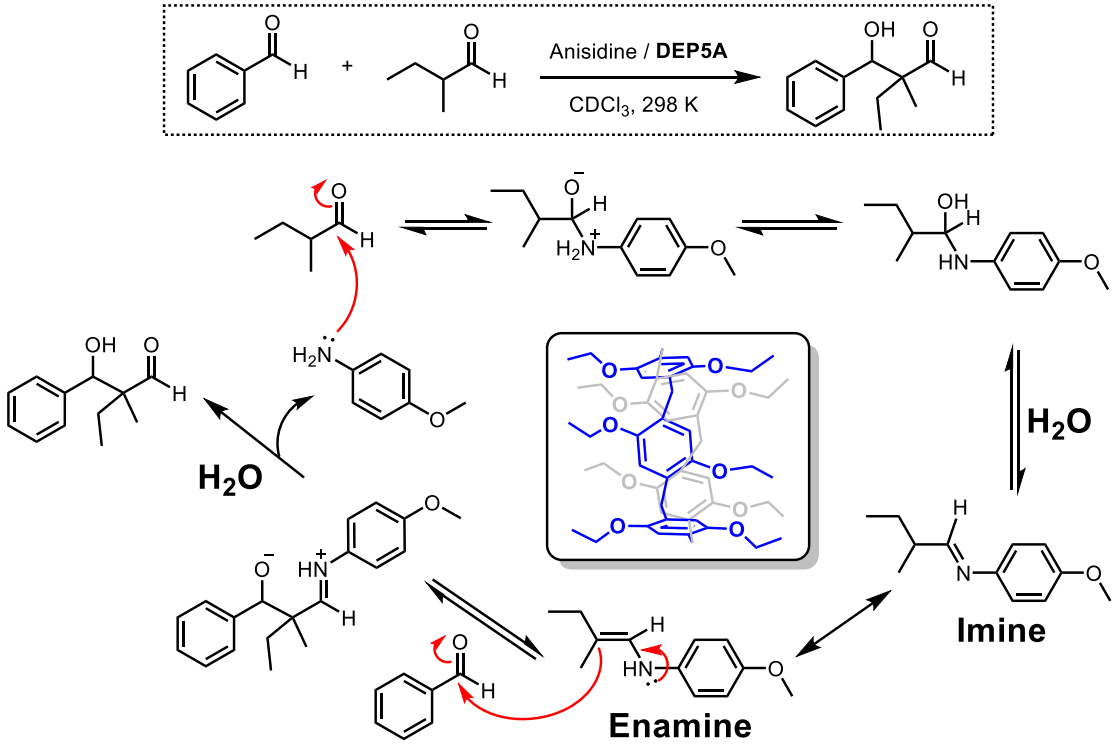


Figure S27. Partial ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) spectra of the dynamic imines formation between 3 mixed aldehydes (with equal concentration 4 mM) and **PA** (with the concentration 4 mM) in the presence of **DEP5A** at a concentration of 100 mM, ● **G1$_i^{PA}$**, ■ **G2$_i^{PA}$**, ★ aldol product.



Scheme S1 A proposed mechanism of the aldol reaction catalysed by the *p*-anisidine in the DCLs with the aid of high concentration of **DEP5A**.

8. Mixed aldehydes react with PA in the presence of 1,4-diethoxybenzene

Table S7 Original data for the reactions of 3 studied aldehydes with **PA** and with 1,4-diethoxybenzene

group	t/min	G1 %	G3	G3 %	$G3_i^{PA}$	$G3_i^{PA}$ %	G2	G2 %	$\Delta G2_i^{PA}$	$G2_i^{PA}$%
0	0	100.00	89.63	100.00	0	0	87.01	100.00	0	0
1	7	100.00	85.38	95.26	6.62	7.4	85.58	98.36	0.49	0.5
2	11	100.00	82.44	91.98	10.46	11.7	85.85	98.67	0.27	0.3
3	15	100.00	81.03	90.40	11.62	12.9	86.01	98.85	0.54	0.6
4	19	100.00	77.61	86.59	9.49	10.6	84.68	97.32	0.56	0.6
5	23	100.00	76.46	85.31	11.02	12.3	84.55	97.17	1.03	1.2
6	30	100.00	72.53	80.92	16.14	18.0	84.25	96.83	1.03	1.2
7	35	100.00	71.76	80.06	23.61	26.3	84.62	97.25	1.92	2.2
8	39	100.00	70.05	78.15	15.99	17.8	84.37	96.96	1.92	2.2
9	43	100.00	69.55	77.60	22.93	25.6	84.01	96.55	1.60	1.8
10	48	100.00	67.18	74.95	21.24	23.7	82.84	95.21	1.60	1.8
11	52	100.00	66.16	73.81	28.27	31.5	83.06	95.46	2.39	2.7
12	56	100.00	65.03	72.55	28.31	31.6	83.13	95.54	2.39	2.7
13	60	100.00	65.68	73.27	27.35	30.5	84.40	97.00	2.47	2.8
14	70	100.00	62.07	69.25	29.52	32.9	82.37	94.67	2.38	2.7

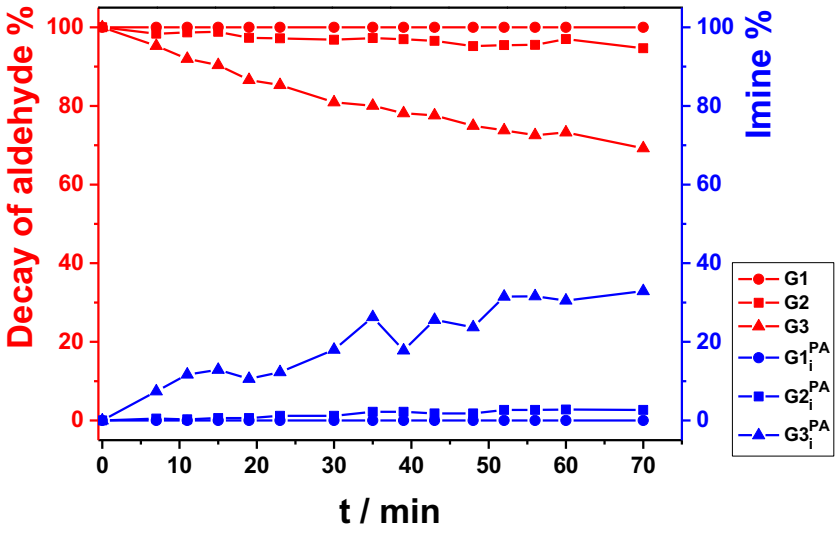


Figure S28. Dynamic studies of the constituent distribution of the reaction between 3 mixed aldehydes (with equal concentration 4 mM) and **PA** (with the concentration 4 mM) in the absence of 1,4-diethoxybenzene in $CDCl_3$, monitored by 400 MHz at 25 °C.

9. Mixed aldehydes react with R

Table S8 Original data for reactions of 3 aldehydes with **R**

group	t/min	G1	G1 %	G3	G3 %	G2	G2 %	$G3_i^R$	$G3_i^R$%
0	0	100.00	100.0	95.198	100.0	71.309	100.0	0	0
1	6	100.00	100.0	80.948	85.0	70.390	100.0	12.956	13.6
2	10	100.00	100.0	75.553	79.4	70.926	100.0	16.755	17.6
3	14	100.00	100.0	73.637	77.4	71.443	100.0	18.488	19.4
4	22	100.00	100.0	72.339	75.9	70.881	100.0	20.393	21.4
5	29	100.00	100.0	72.089	75.7	71.057	100.0	20.836	21.9
6	38	100.00	100.0	71.695	75.3	70.366	100.0	20.440	21.5
7	56	100.00	100.0	72.625	76.3	70.650	100.0	21.743	22.8
8	79	100.00	100.0	72.290	75.9	69.592	100.0	20.887	21.9
9	88	100.00	100.0	72.860	76.5	70.276	100.0	21.031	22.1

[NOTE]

1) Benzaldehyde did not react in this experiment and was regarded as the reference where the integration of RC***H***O was normalized to 100 to get the above data.

2) Definition:

$$Decay\ of\ aldehyde\ \% = (Y_i/Y_0)*100\%$$

wherein, Y_i and Y_0 stand for the integral value of RC***H***O belonging to aldehyde after and before the addition of **R** respectively.

$$formation\ of\ imine\ \% = (Y_{ii}/Y_0)*100\%$$

wherein, Y_{ii} is the integral value of -C***H***=N- after adding the *p*-anisidine to the mixture of aldehydes and Y_0 is the integral value of RC***H***O belonging to aldehyde before the addition of **R**.

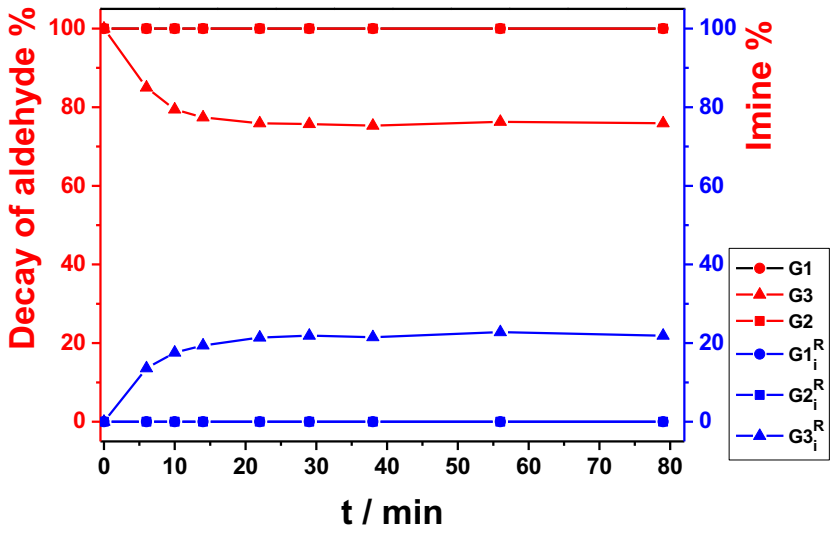


Figure S29. Dynamic studies of the constituent distribution of the reaction between 3 mixed aldehydes (each aldehyde with equal concentration of 4 mM) and **R** (with the concentration of 4 mM) in $CDCl_3$, monitored by 400 MHz at 25 °C.

Table S9 Original data for reactions of 3 aldehydes with **R**

group	t/min	G1	G1 %	G3	G3 %	G2	G2 %	$G3_i^R$	$G3_i^R$%
0	0	100.00	100.0	108.523	100.0	78.123	100.0	0	0
1	6	100.00	100.0	79.742	73.5	77.333	100.0	21.076	19.4
2	13	100.00	100.0	58.373	53.8	76.563	100.0	44.578	41.1
3	21	100.00	100.0	52.777	48.6	77.314	100.0	50.073	46.1
4	29	100.00	100.0	51.860	47.8	76.894	100.0	52.692	48.6
5	39	100.00	100.0	51.842	47.8	77.074	100.0	54.697	50.4
6	48	100.00	100.0	51.657	47.6	77.068	100.0	53.345	49.2
7	61	100.00	100.0	52.516	48.4	75.424	100.0	50.888	46.9
8	71	100.00	100.0	51.965	47.9	77.347	100.0	53.457	49.3
9	82	100.00	100.0	52.620	48.5	76.424	100.0	51.280	47.3

[NOTE]

1) Benzaldehyde did not react in this experiment and was regarded as the reference where the integration of RC***H***O was normalized to 100 to get the above data.

2) Definition:

$$Decay\ of\ aldehyde\ \% = (Y_i/Y_0)*100\%$$

wherein, Y_i and Y_0 stand for the integral value of RC***H***O belonging to aldehyde after and before the addition of **R** respectively.

$$formation\ of\ imine\ \% = (Y_{ii}/Y_0)*100\%$$

wherein, Y_{ii} is the integral value of -C***H***=N- after adding the anisidine to the mixture of aldehydes and Y_0 is the integral value of RC***H***O belonging to aldehyde before the addition of **R**.

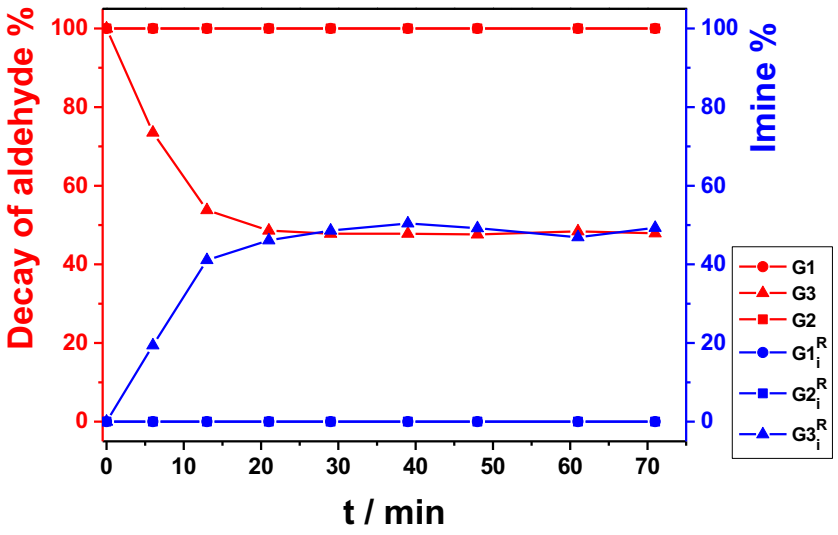


Figure S30. Dynamic studies of the constituent distribution of the reaction between 3 mixed aldehydes (each aldehyde with equal concentration of 4 mM) and **R** (with the concentration of 12 mM) in $CDCl_3$, monitored by 400 MHz at 25 °C.

10. Mass spectra of unstable imines and hemiaminals

Unstable imines and hemiaminals traced by LC-ESI-MS

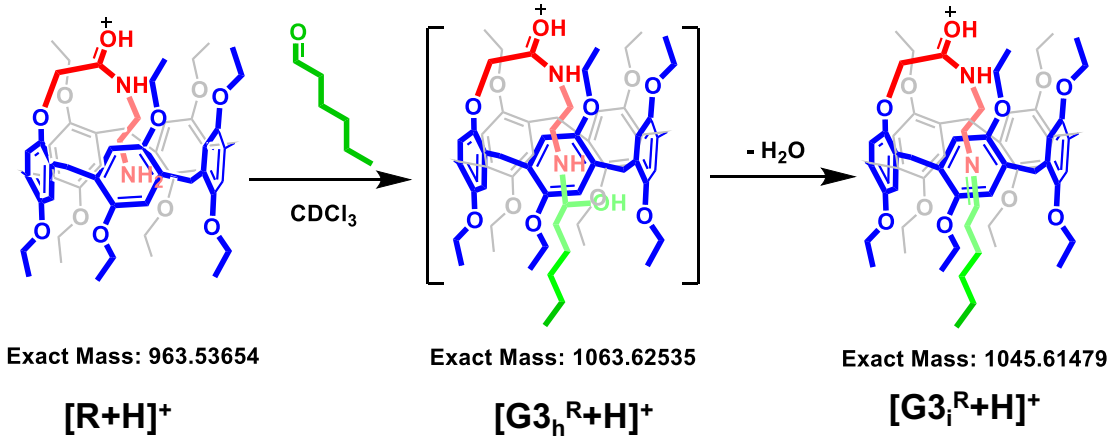
1) In a 5.0 mL vial was added **R** (5.1 mg) and CH_2Cl_2 (2.0 mL) to get a solution, which was divided equally into 4 parts for use;

2) **G3**, **G4**, **G5** and **G6** (5.0 μL) was added to four vials with CH_2Cl_2 (500 μL), respectively, to get four solutions;

3) **G3**, **G4**, **G5** and **G6** (200 μL) was added respectively to the solution of **R**, and the reaction mixture was kept at 20 °C for 2 hours;

4) The reaction mixtures (200 μL) were transferred to 4 vials, then diluted by CH_3OH (500 μL), and then subjected to LC-ESI-MS at 27 °C.

1) G3 reacts with R



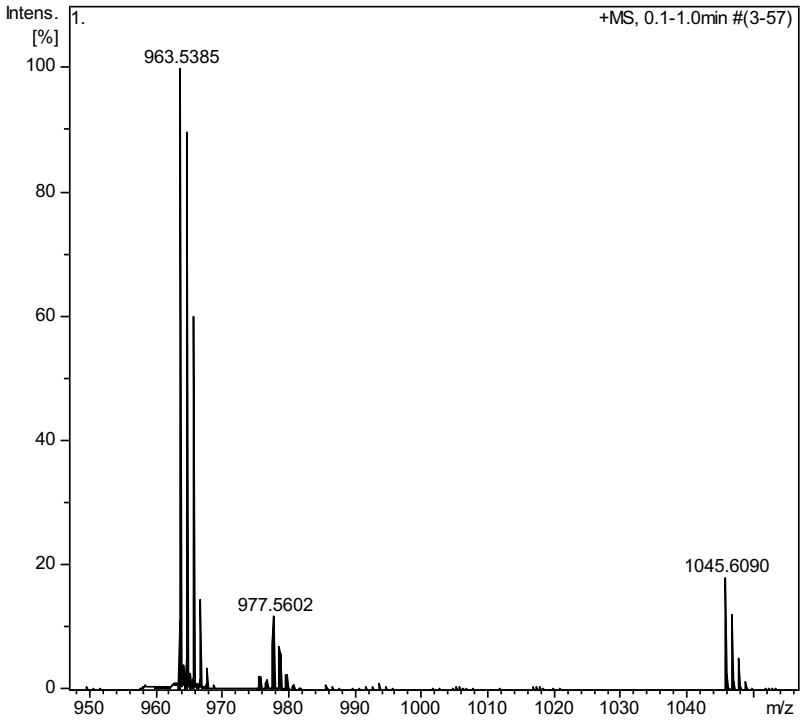


Figure S31. LC-ESI-MS of the reaction mixture of **R** and **G3**. The exact mass of $[\mathbf{R}+H]^+$ is 963.5365, which was used as an internal reference, and the experimental value is 963.5385. The imine $[\mathbf{G3_i}^{\mathbf{R}}+H]^+$ is corrected as 1045.6090, in line with the exact mass, 1045.6148.

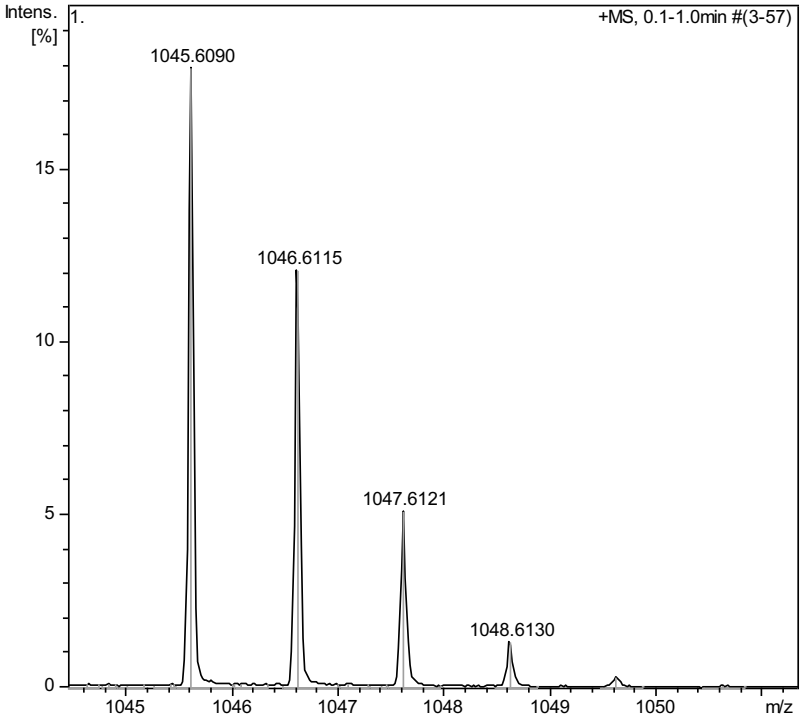


Figure S32. Partial LC-ESI-MS of the expanded Figure S31.

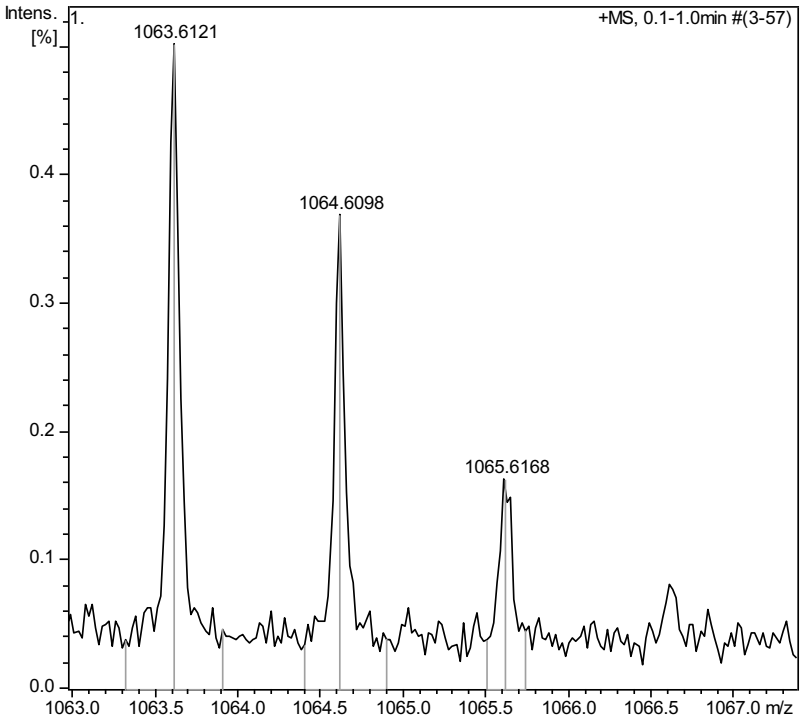
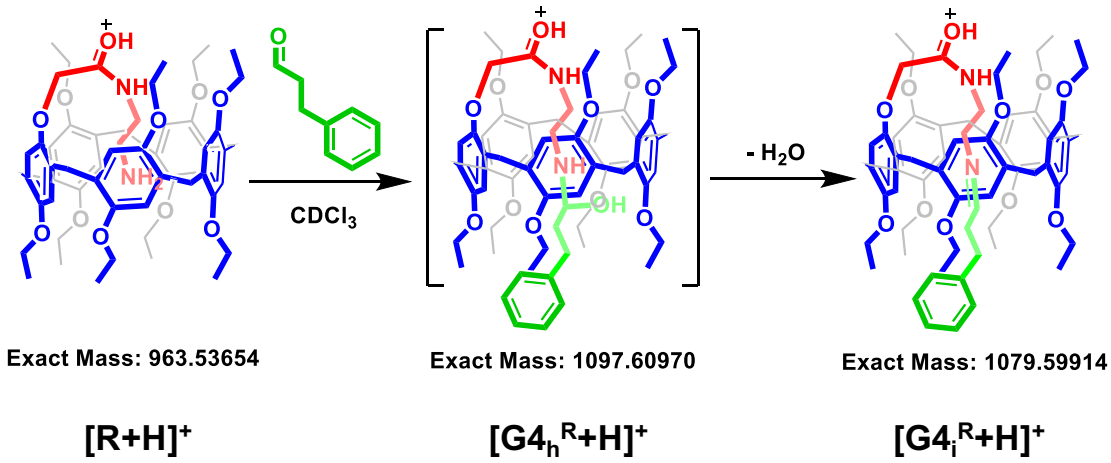


Figure S33. Partial LC-ESI-MS of the expanded Figure S23. The mass of hemiaminal $[\mathbf{G3_h}^{\mathbf{R}} + H]^+$ is 1063.6121, in line with the exact mass, 1063.6254.

2) G4 reacts with R



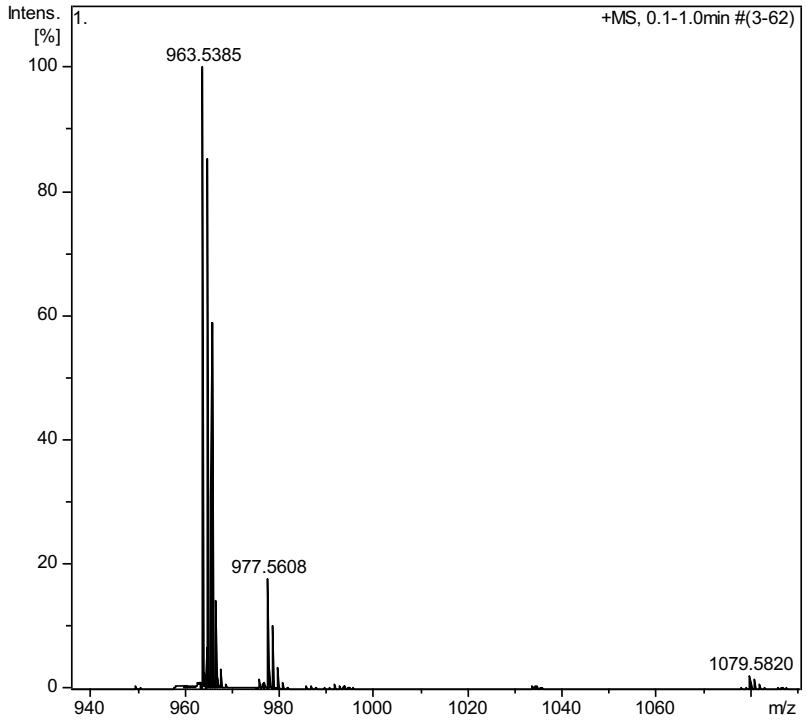


Figure S34. LC-ESI-MS of the reaction mixture of **R** and **G4**. The exact mass of [**R**+H]$^+$ is 963.5365, which was used as an internal reference, and the experimental value is 963.5385.

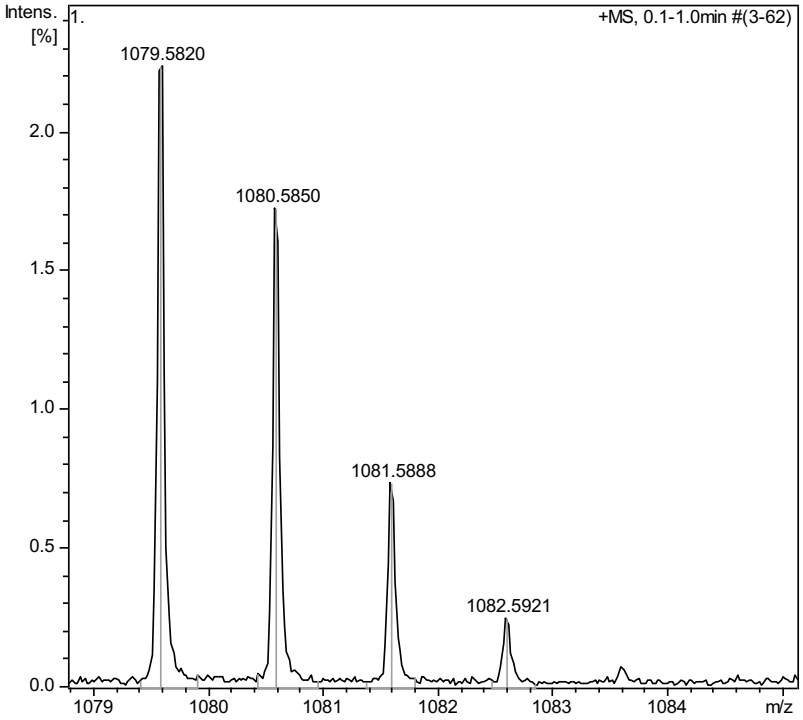


Figure S35. Partial LC-ESI-MS of the expanded Figure S34. The mass of imine $[\mathbf{G4_i^R}+H]^+$ is 1079.5820, in line with the exact mass, 1079.5991.

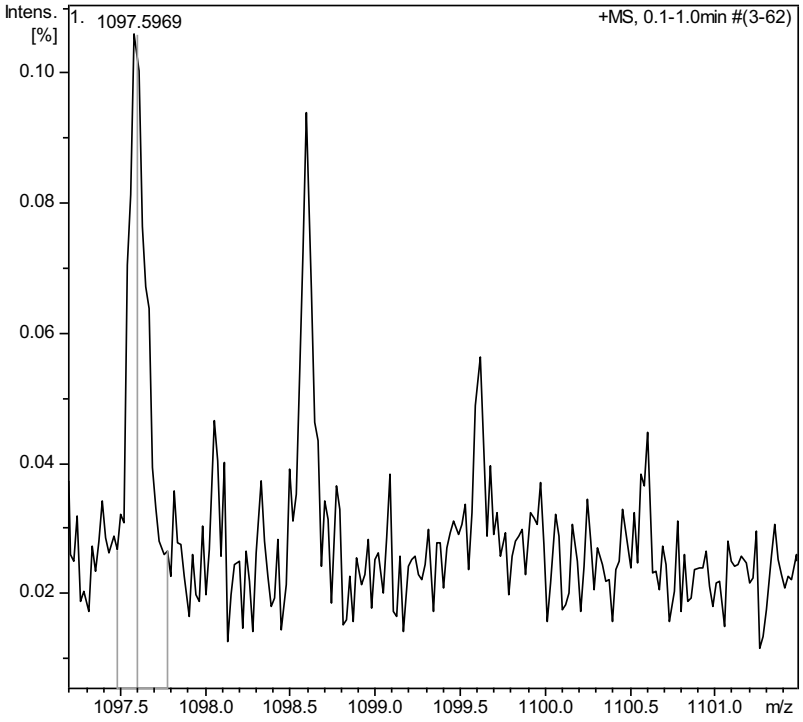
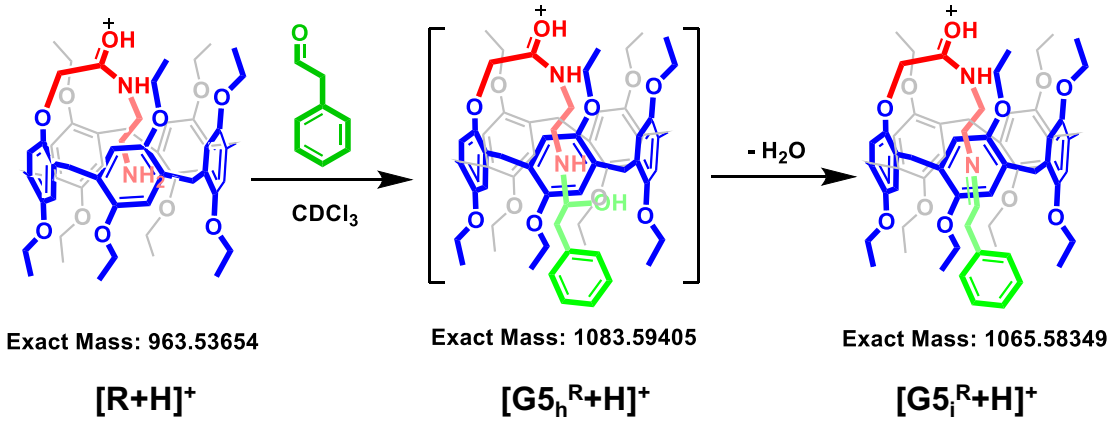


Figure S36. Partial LC-ESI-MS of the expanded Figure S34. The mass of hemiaminal $[\mathbf{G4_h^R}+H]^+$ is 1097.5969, in line with the exact mass, 1097.6097.

3) G5 reacts with R



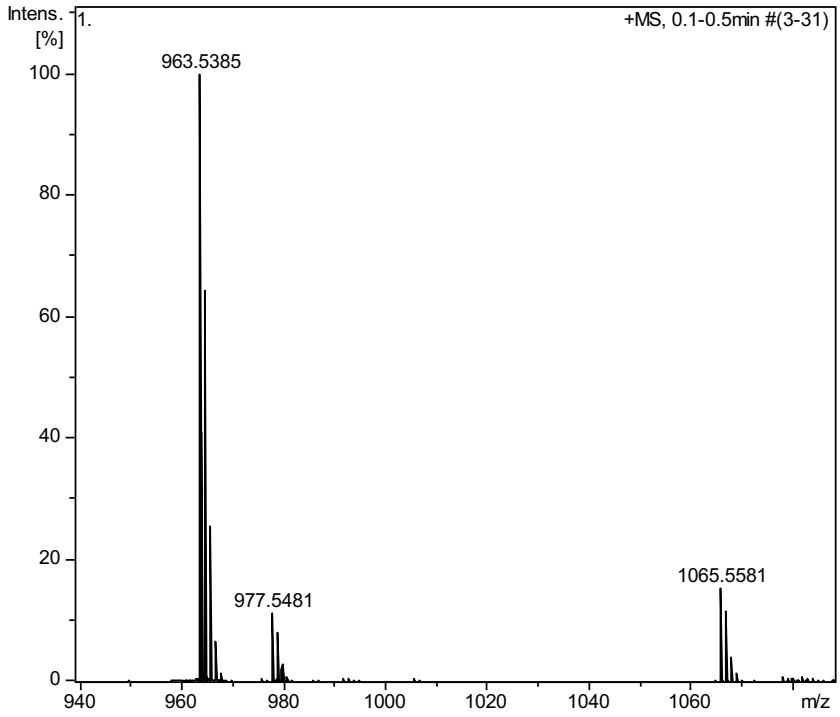


Figure S37. LC-ESI-MS of the reaction mixture of **R** and **G5**. The exact mass of [**R**+H]$^+$ is 963.5365, which was used as an internal reference, and the experimental value is 963.5385. The mass of imine [**G5$_i^R$** +H]$^+$ is 1065.5581, in line with the exact mass, 1065.5835.

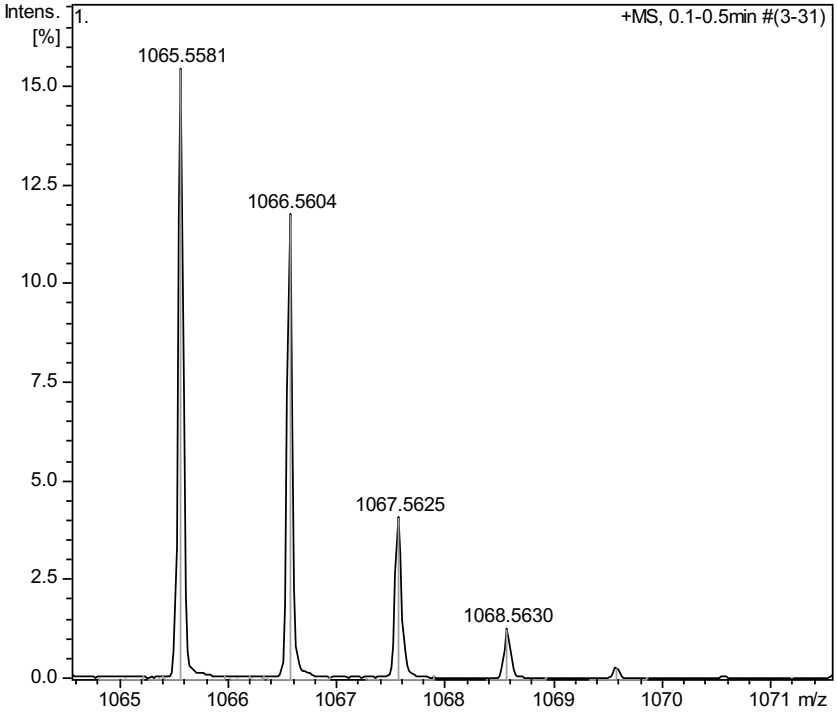


Figure S38. Partial LC-ESI-MS of the expanded Figure S37.

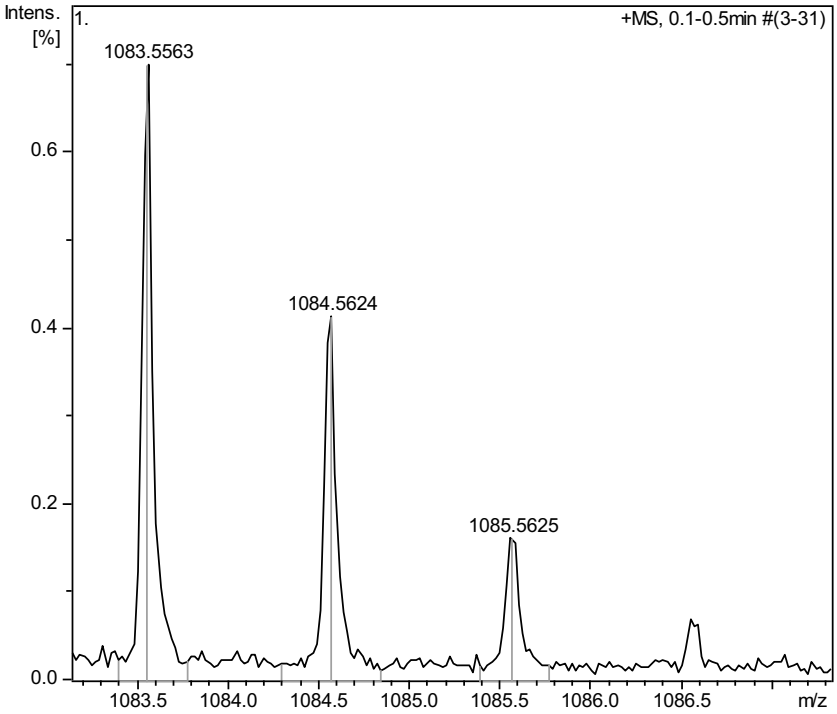
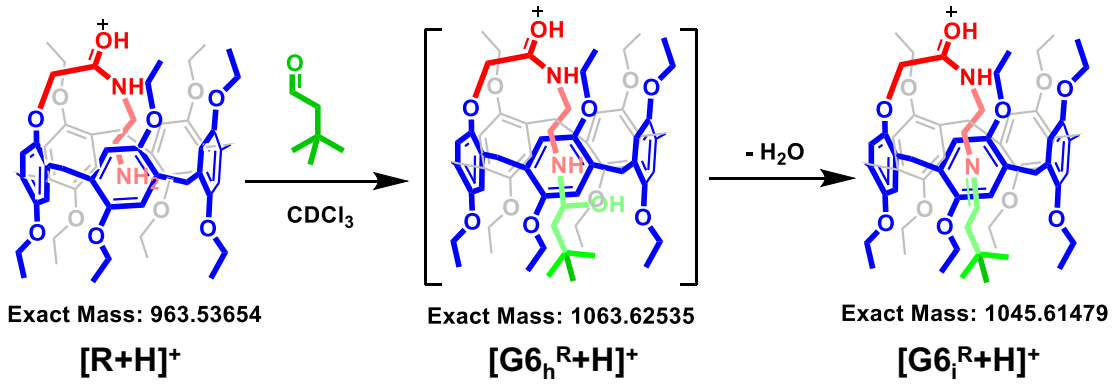


Figure S39. Partial LC-ESI-MS of the expanded Figure S37. The mass of hemiaminal $[\mathbf{G5_h}^{\mathbf{R}} + H]^+$ is 1083.5563, in line with the exact mass, 1083.5940.

4) G6 reacts with R



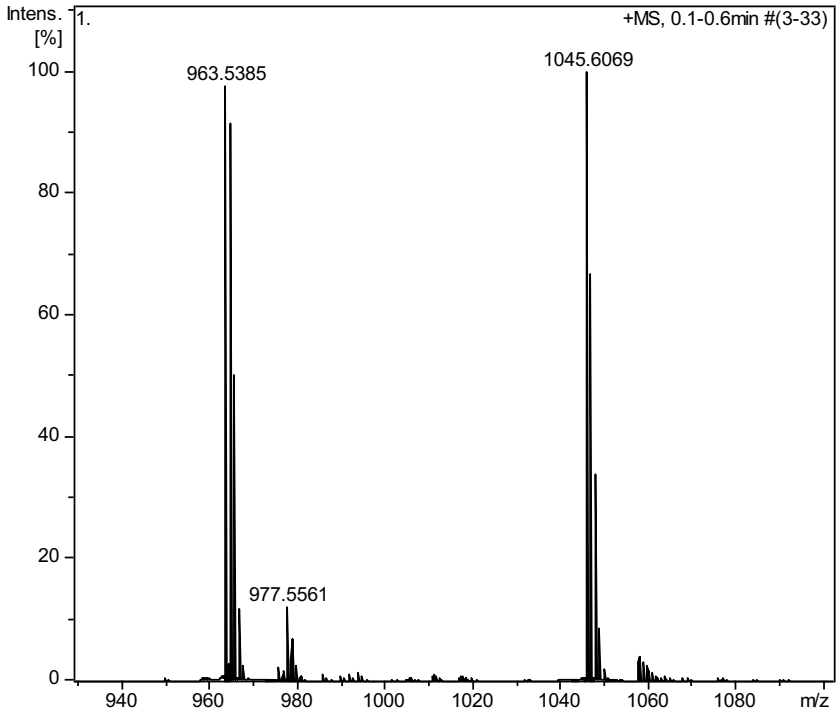


Figure S40. LC-ESI-MS of the reaction mixture of **R** and **G6**. The exact mass of [**R**+H]$^+$ is 963.5365, which was used as an internal reference, and the experimental value is 963.5385. The mass of imine [$\mathbf{G6_h}^{\mathbf{R}}$ +H]$^+$ is 1045.6069, in line with the exact mass, 1045.6148.

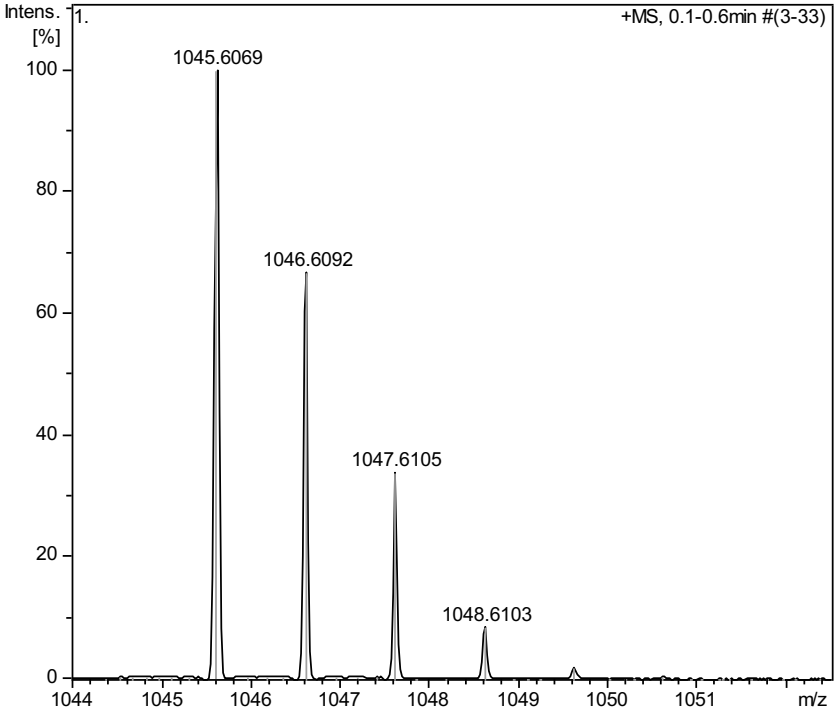


Figure S41. Partial LC-ESI-MS of the expanded Figure S40.

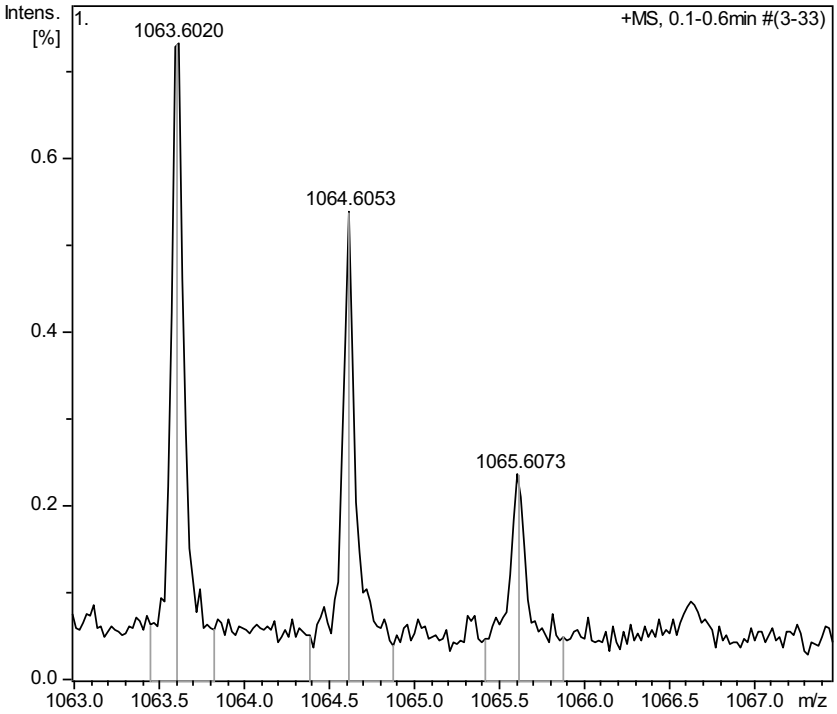
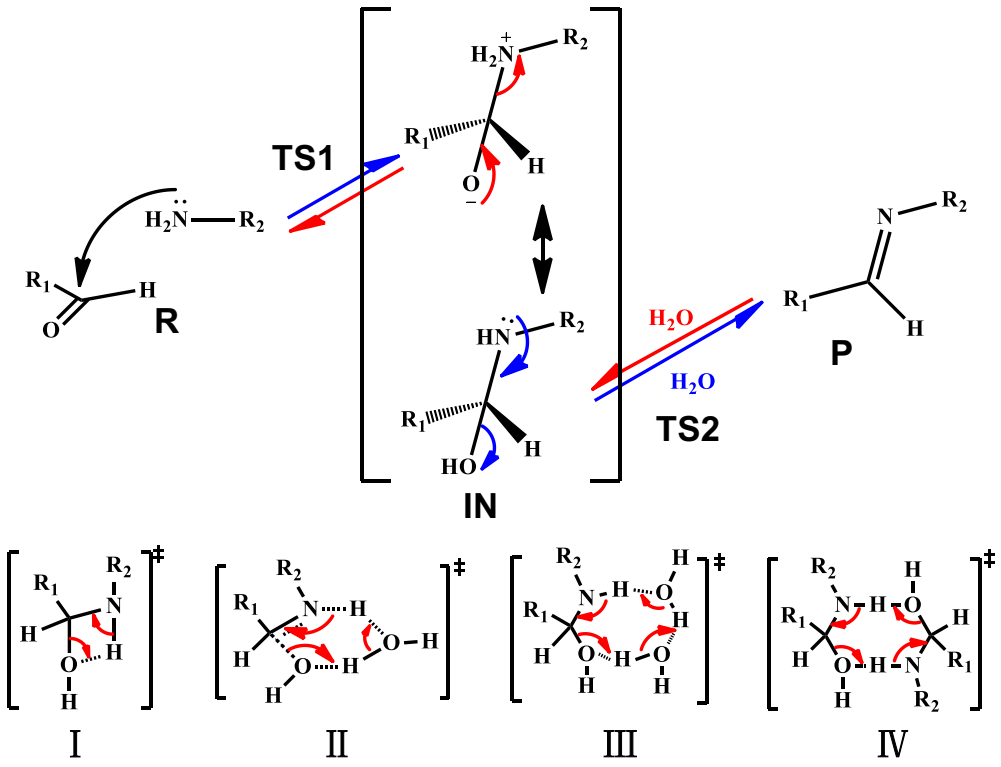


Figure S42. Partial LC-ESI-MS of the expanded Figure S40. The mass of hemiaminal $[\mathbf{G6_h}^{\mathbf{R}} + H]^+$ is 1063.6020, in line with the exact mass, 1063.6254.



Scheme S2 Proposed mechanism and possible transition state without acid catalysis.

11. References and notes

[S1] *Purification of Laboratory Chemicals (Seventh Edition)*, eds. W. L. F. Armarego and C. Chai, Butterworth-Heinemann, Boston, 2013.

[S2] P. R. Ashton, R. Ballardini, V. Balzani, M. Bělohradský, M. T. Gandolfi, D. Philp, L. Prodi, F. M. Raymo, M. V. Reddington, N. Spencer, J. F. Stoddart, M. Venturi, D. J. Williams, *J. Am. Chem. Soc.,*1996, ***118***, 4931-4951.

$$\Delta\delta = (\Delta\delta_\infty/[G]_0)\,(0.5[H]_0 + 0.5([G]_0+1/K_a) - (0.5\,([H]_0^2+(2[H]_0(1/K_a - [G]_0)) + (1/K_a + [G]_0)^2)^{0.5}))$$

Where $\Delta\delta$ is the chemical shift change of H_a on G1 at $[H]_0$, $\Delta\delta_\infty$ is the chemical shift change of H_a when the guest is completely complexed, $[G]_0$ is the fixed initial concentration of the guest, and $[H]_0$ is the varying concentrations.