SUPPLEMENTARY INFORMATION

Effect of Ligand Sequence-Specific Modification on DNA Hybrid Catalysis

H. Zhou,[a] D. Chen,[a] J. K. Bai,[a] X. L. Sun,[a] C. Li*[a] and R. Z. Qiao*[ab]

[a] *State Key Laboratory of Chemical Resource Engineering, Beijing University of Chemical Technology, Beijing 100029, P. R. China*

[b] *State Key Laboratory of Natural and Biomimetic Drugs School of Pharmaceutical Sciences, Peking University Health Science Center, Beijing, 100083, P. R. China*

Correspondence: Prof. Renzhong Qiao, State Key Laboratory of Chemical Resource Engineering, Beijing University of Chemical Technology, Beijing 100029, P. R. China

E-mail: qiao_group@163.com

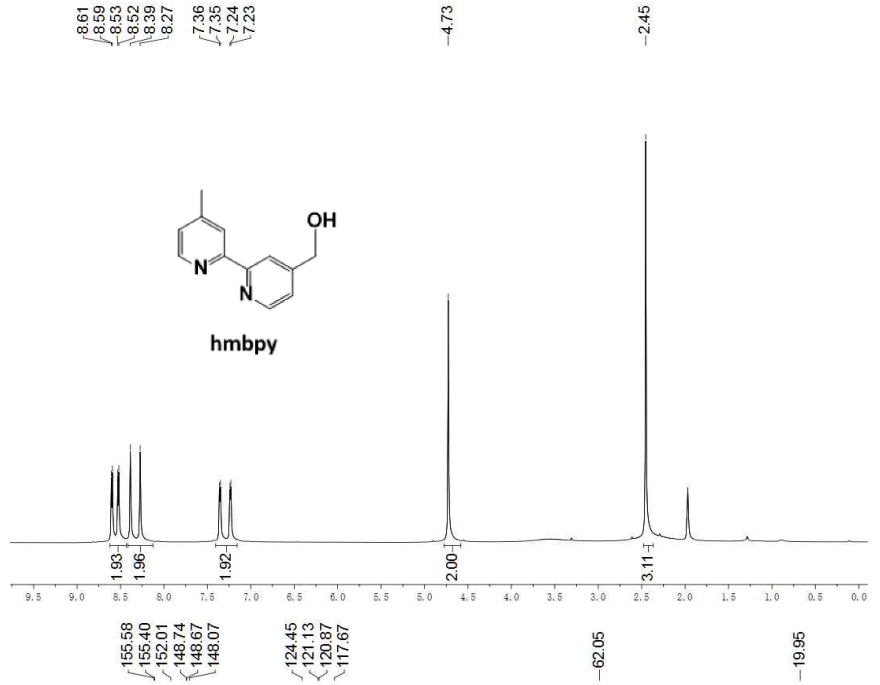
Prof. Chao Li, State Key Laboratory of Chemical Resource Engineering, Beijing University of Chemical Technology, Beijing 100029, P. R. China

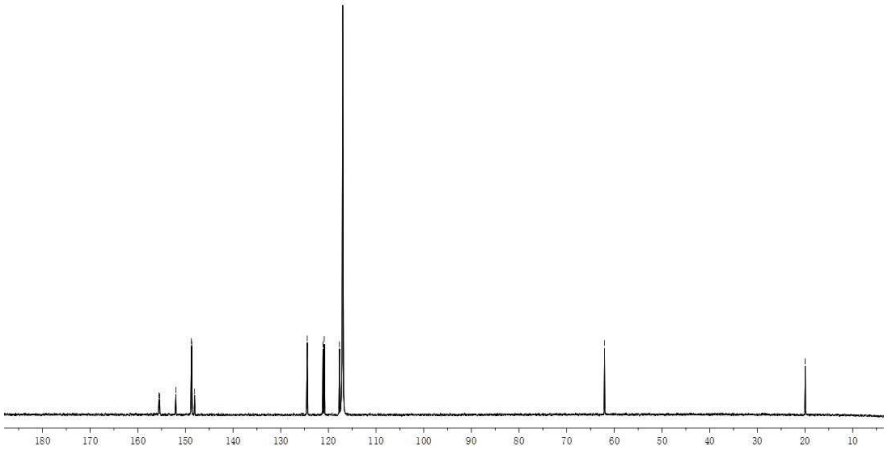
E-mail: lichao@mail.buct.edu.cn

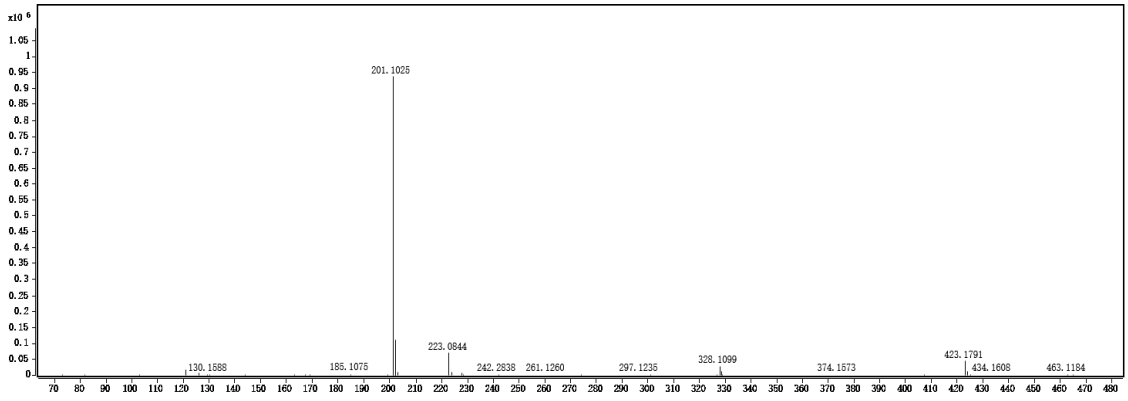
Fax: 86-010-64416428

Contents

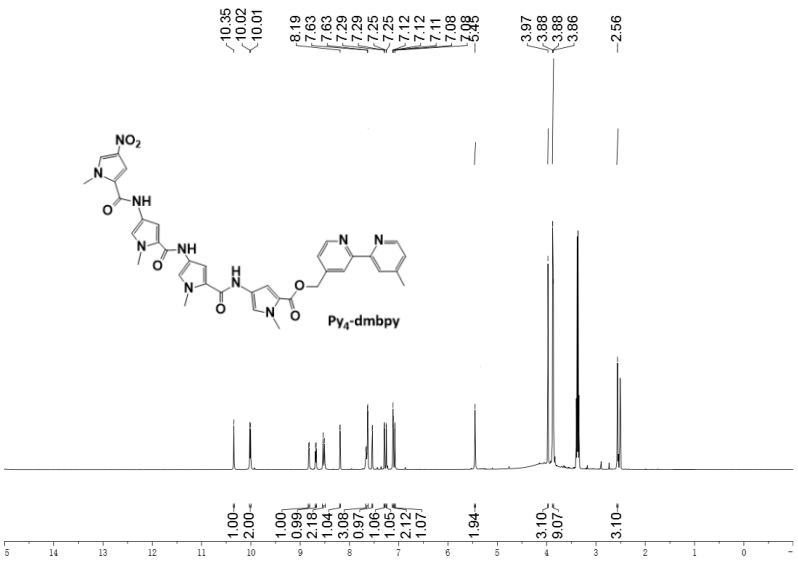
NMR and HRMS spectra of hmbpy

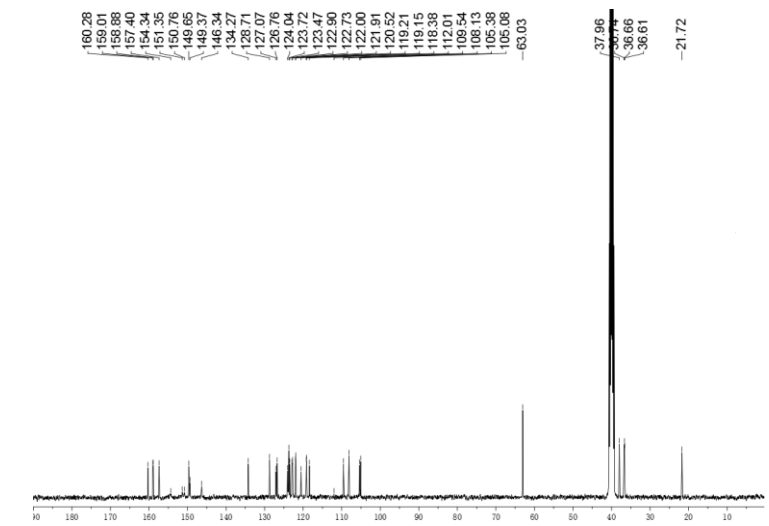


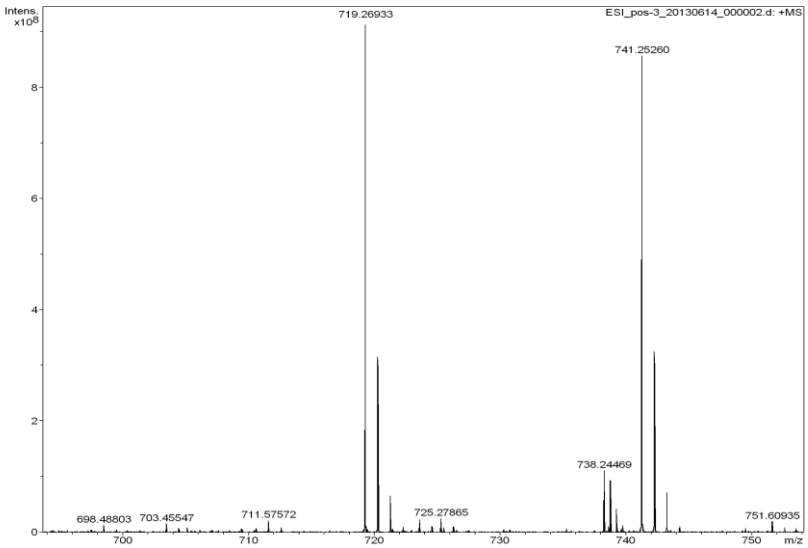




NMR and HRMS spectra of Py_4-dmbpy

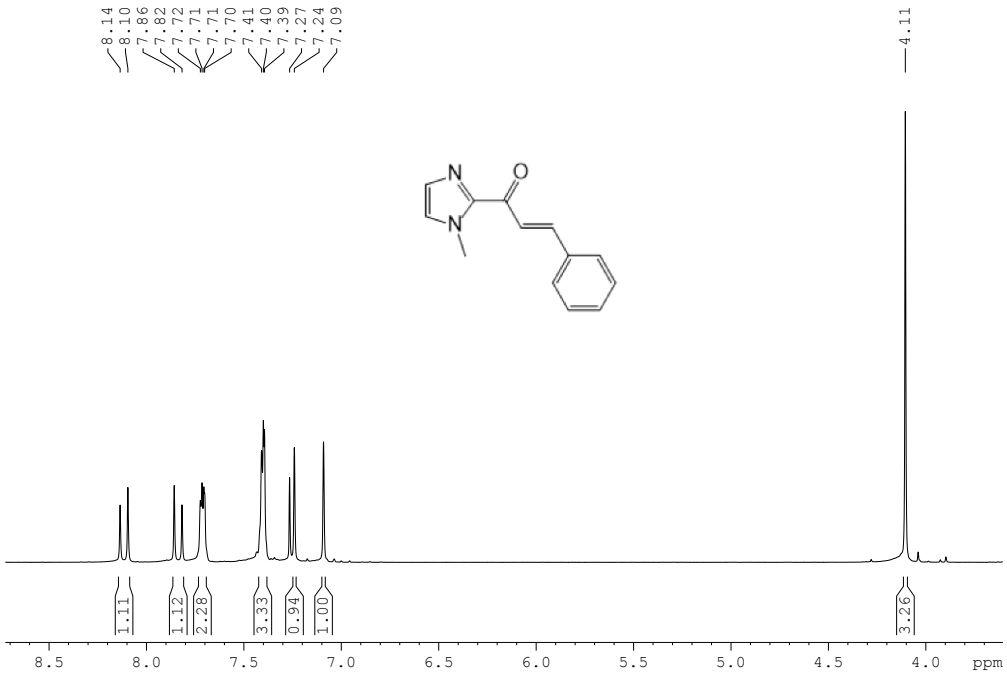






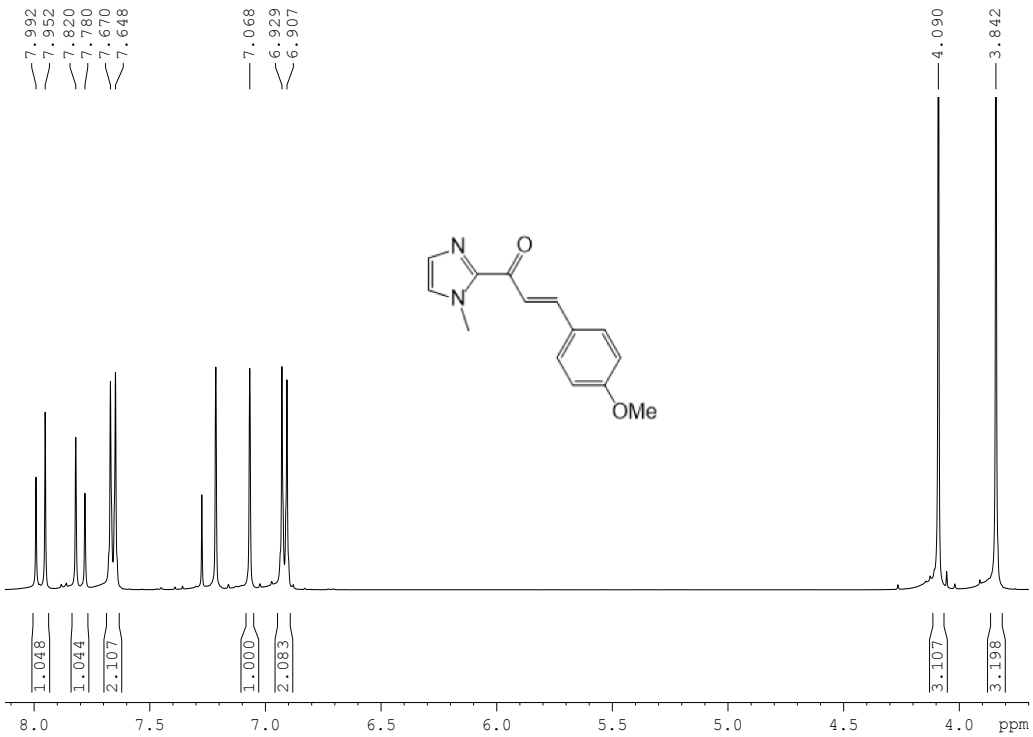
^{1}H NMR spectra of 1a-d

(*E*)-1-(1-methyl-1*H*-imidazol-2-yl)-3-phenylprop-2-en-1-one (**1a**)



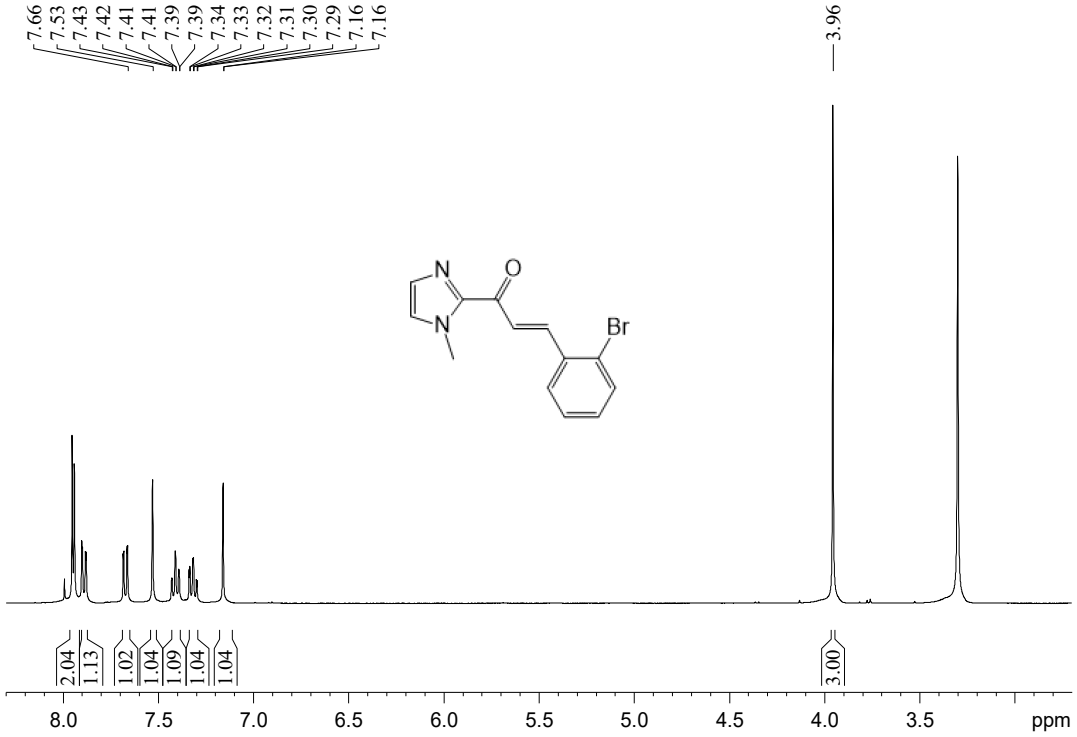
^{1}H-NMR(400 MHz, $CDCl_3$) δ/ppm= 4.11 (s, 3H), 7.09 (s, 1H), 7.24 (s, 1H), 7.39-7.41 (m, 3H), 7.70-7.72 (m, 2H), 7.82 (d, 1H, *J*=16 Hz), 8.10 (d, 1H, *J*=16 Hz)

(*E*)-3-(4-methoxyphenyl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (**1b**)



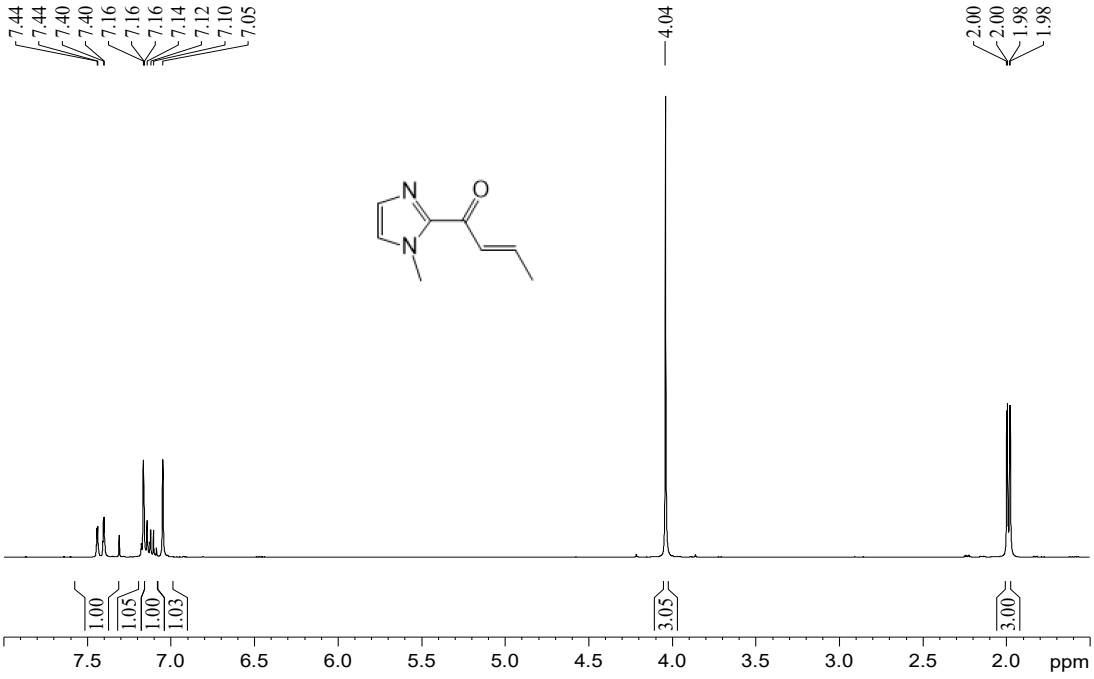
^{1}H-NMR(400MHz, $CDCl_3$) δ/ppm=3.84 (s, 3H), 4.09 (s, 3H), 6.92 (d, 2H, *J* = 8.8 Hz), 7.07 (s, 1H), 7.21 (s, 1H), 7.65 (d, 2H, *J* = 8.8 Hz), 7.80 (d, 1H, *J* = 16.0 Hz), 7.95 (d, 1H, *J* = 16.0 Hz)

(*E*)-3-(2-bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (**1c**)



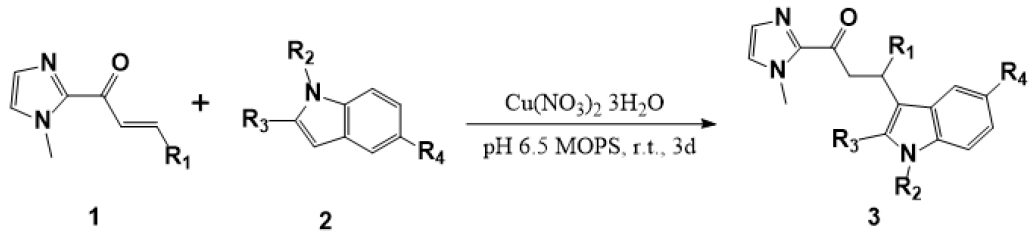
^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm=3.96 (s, 3H), 7.16 (s, 1H), 7.34 (m, 1H), 7.42 (m, 1H), 7.53 (s, 1H), 7.66 (dd, 1H, J = 1.1 Hz, J = 6.9 Hz), 7.90 (dd, 1H, J = 1.2 Hz, J = 6.4 Hz), 7.95 (d, 1H, J = 15.5 Hz).

(*E*)-1-(1-methyl-1*H*-imidazol-2-yl)but-2-en-1-one (**1d**)



^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm=1.99 (dd, 3H, J = 8.0 Hz, J = 8.0 Hz), 4.04 (s, 3H), 7.05 (s, 1H), 7.12 (dq, 1H), 7.16 (dq, 1H), 7.43 (dd, 1H, J = 16.0 Hz, J = 16.0 Hz).

Preparation and characteristics of racemic Friedel-Crafts alkylation products 3a-3g



1

1a: R_1=Ph
1b: R_1=*p*-$MeOC_6H_4$
1c: R_1=*o*-BrC_6H_4
1d: R_1=Me

2

2a: R_2=Me, R_3=H, R_4=H
2b: R_2=H, R_3=H, R_4=MeO
2c: R_2=H, R_3=H, R_4=H
2d: R_2=H, R_3=H, R_4=Cl

3

3a: R_1=Ph, R_2=Me, R_3=H, R_4=H
3b: R_1=*p*-$MeOC_6H_4$, R_2=H, R_3=H, R_4=MeO
3c: R_1=*o*-BrC_6H_4, R_2=Me, R_3=H, R_4=H
3d: R_1=Me, R_2=H, R_3=H, R_4=MeO
3e: R_1=Me, R_2=H, R_3=H, R_4=H
3f: R_1=Me, R_2=Me, R_3=H, R_4=H
3g: R_1=Me, R_2=H, R_3=H, R_4=Cl

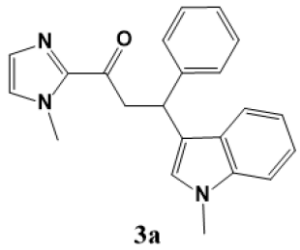
Preparation of a 500 mL 30 mM MOPS buffer (pH 6.5)

3.1389 g (15 mmol) of 3-(*N*-morpholino) propanesulfonic acid (MOPS, MW = 209.26 g/mol) were dissolved in 100 mL of ultrapure water which is tracked by pH meter. A 0.1 M solution of NaOH (MW = 40.00 g/mol) in ultrapure water was added to adjust pH value to 6.5. Transfer this solution to a 500 mM volumetric flask, then dilute with ultrapure water to volume and mix.

General procedure A

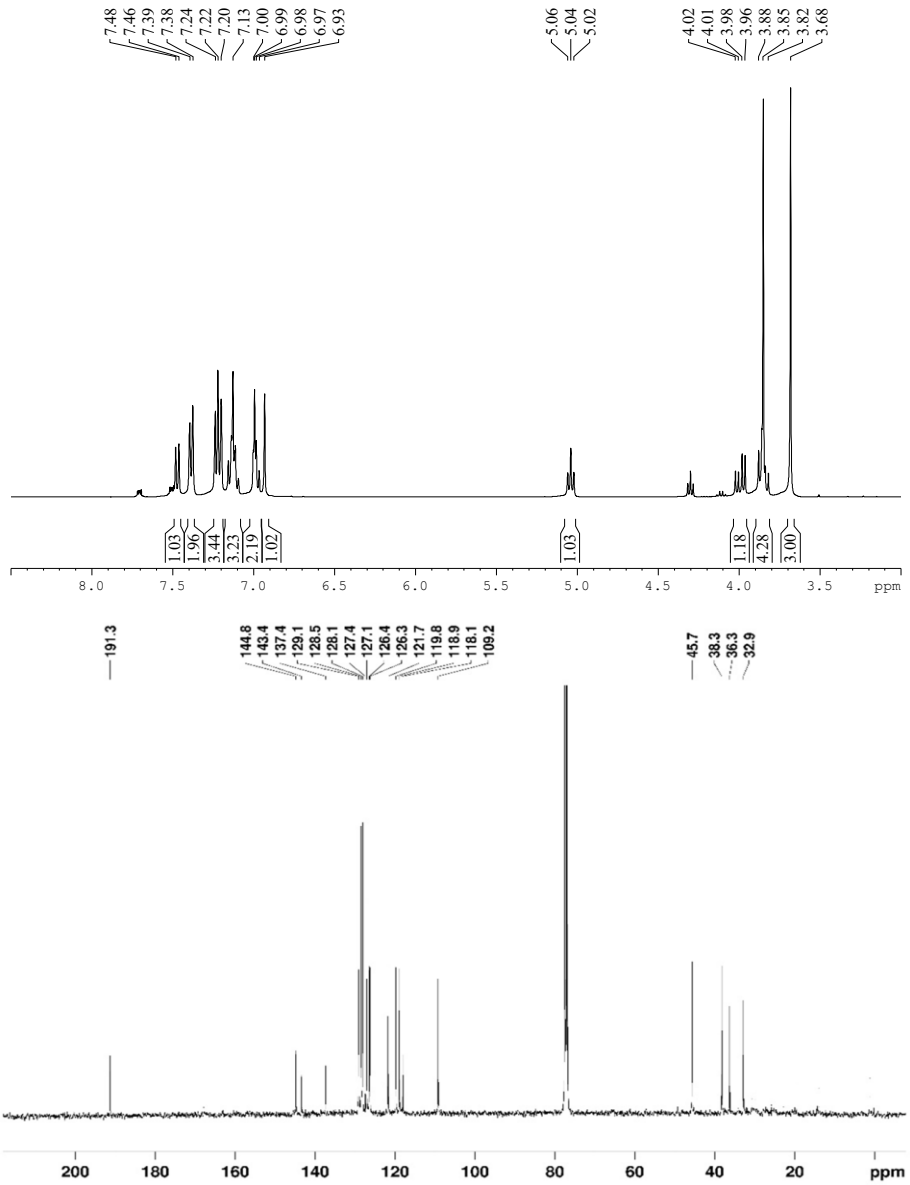
An oven-dried 500 mL round-bottomed flask was charged with $Cu(NO_3)_2 \cdot 3H_2O$ (0.8 mmol, 2.0 equiv) in 50 mL pH = 6.5 MOPS buffer. Then the *α, β*-unsaturated substrate (0.40 mmol, 1.0 equiv) and the desired indole (2.0 mmol, 5 equiv) were added. The solution was stirred at r.t. for 3 d. The reaction was eventually extracted with Et_2O (3 x 25 mL). The combined organic layer dried over anhydrous Na_2SO_4, gravity filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel.

1-(1-methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropan-1-one (3a)

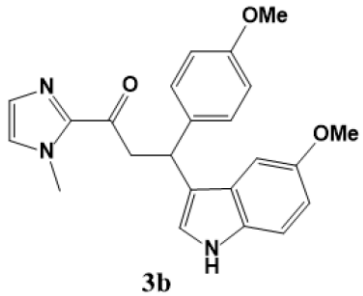


3a

Following the general procedure A: **1a** (84.9 mg, 0.40 mmol), **2a** (262.4 mg, 2.0 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (193 mg, 0.80 mmol). The title compound (molecular formula: $C_{22}H_{21}N_3O$, MW = 343.43 g/mol, 110 mg) was isolated as a brown solid in 80% yield. ^{1}H NMR (CD_3OD, 400 MHz): δ/ppm=3.68 (s, 3H), 3.82-3.88 (m, 4H), 4.00 (dd, J = 15.9 Hz, J = 7.5 Hz,1H), 5.04 (t, J = 7.8 Hz, 1H), 6.93 (s, 1H), 6.96-7.00 (m, 2H), 7.13 (s, 3H), 7.22 (t, J =8.0 Hz, 3H), 7.38 (d, J =7.3 Hz, 2H), 7.47 (d, J =7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ/ppm= 32.9 (q), 36.3 (q), 38.3 (d), 45.7 (t), 109.2 (d), 118.1 (s), 118.9 (d), 119.8 (d), 121.7 (d), 126.3 (d), 126.4 (d), 127.1 (d), 128.1 (s), 128.5 (d), 129.1 (d), 137.4 (s), 143.4 (s), 144.8 (s), 191.3 (s). HRMS (ESI) calcd. for $C_{22}H_{22}N_3O$: 344.1763 $([M+H])^+$, found 344.1759 $([M+H])^+$.

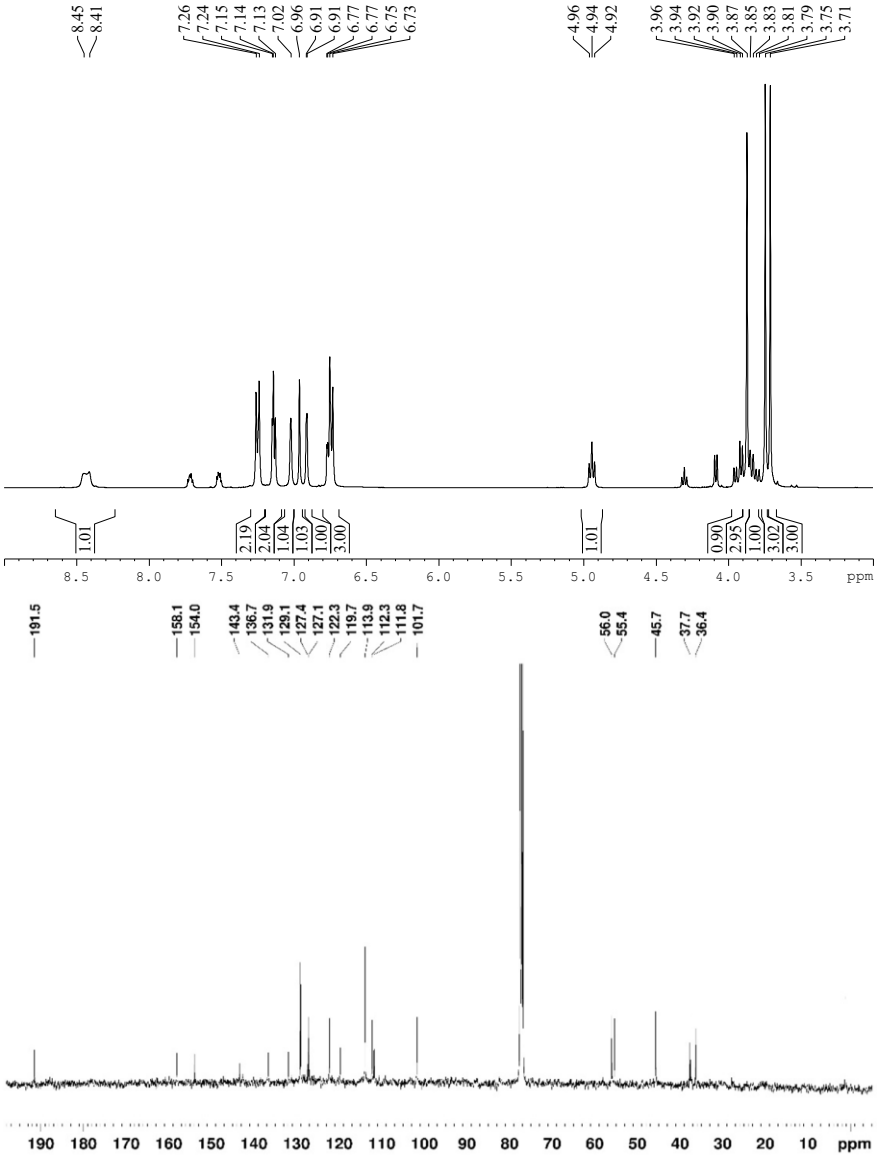


3-(5-methoxy-1*H*-indol-3-yl)-3-(4-methoxyphenyl)-1-(1-methyl-1*H*-imidazol-2-yl)propan-1-one (3b)

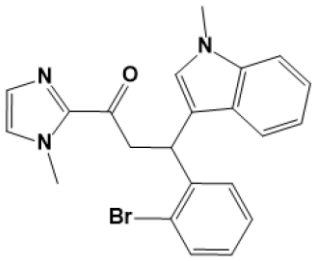


3b

Following the general procedure A: **1b** (96.9 mg, 0.40 mmol), **2b** (294.4 mg, 2.0 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (193 mg, 0.80 mmol). The title compound (molecular formula: $C_{23}H_{23}N_3O_3$, MW = 389.46 g/mol, 133.0 mg) was isolated as a brown solid in 85% yield. ^{1}H NMR ($CDCl_3$, 400 MHz)：δ/ppm=3.70 (s, 3H), 3.75 (s, 3H), 3.82 (dd, J =8.3Hz, J =8.1Hz, 1H), 3.87 (s, 3H), 3.93 (dd, J = 15.7 Hz, J = 7.6 Hz, 1H), 4.94(t, J =7.5 Hz, 1H), 6.73-6.77 (m, 3H), 6.91 (s, 1H), 6.96 (s, 1H), 7.02 (s, 1H), 7.13-7.15 (m, 2H), 7.25(d, J = 8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ/ppm= 36.4 (q), 37.7 (d), 45.7 (t), 55.4 (q), 56.0 (q), 101.7 (d), 111.8 (d), 112.3 (d), 113.9 (d), 119.7 (s), 122.3 (d), 127.1 (s), 127.4 (d), 129.1 (d), 131.9 (s), 136.7 (s), 143.4 (s), 154.0 (s), 158.1 (s), 191.5 (s). HRMS (ESI) calcd. for $C_{23}H_{24}N_3O_3$: 390.1818 $([M+H])^+$, found 390.1809 $([M+H])^+$.

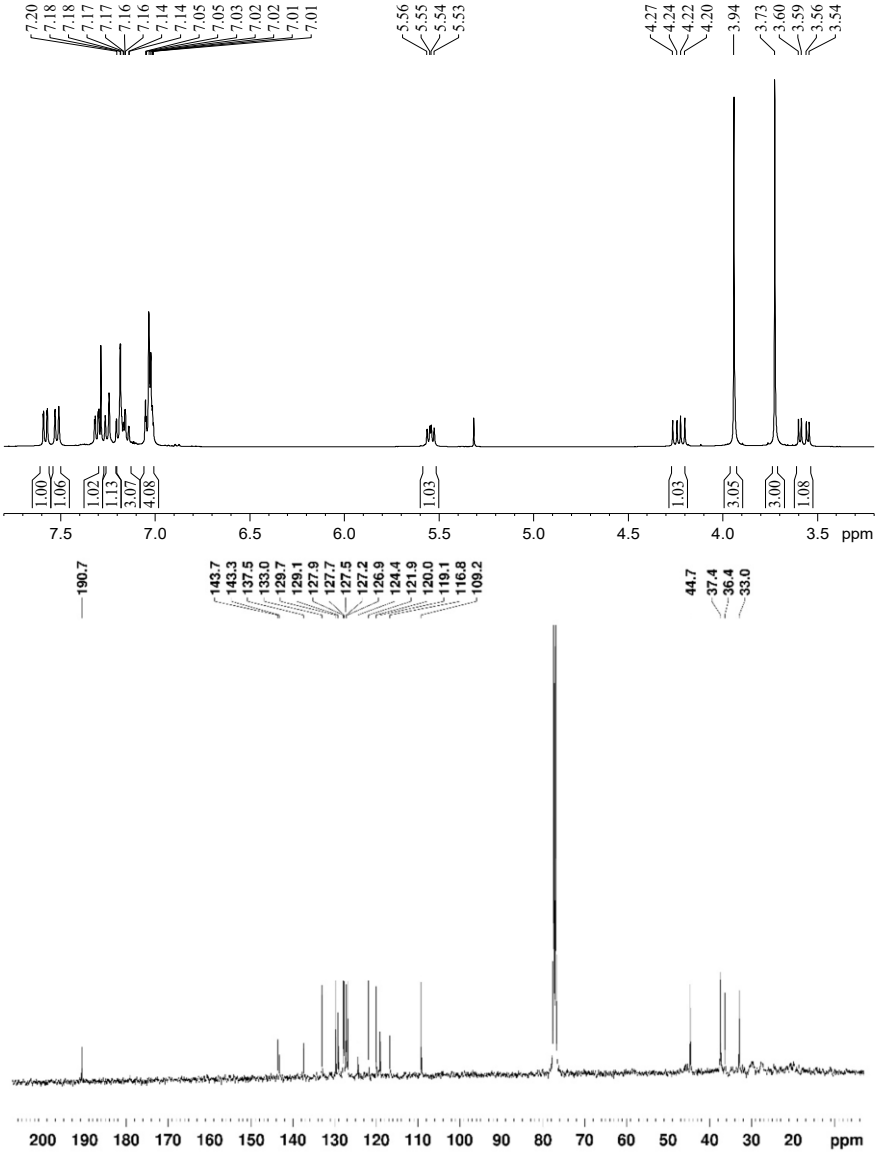


3-(2-Bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3yl)propan-1-one (3c)

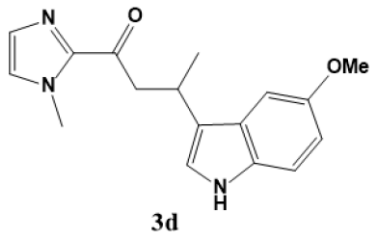


3c

Following the general procedure A: **1c** (116.5 mg, 0.40 mmol), **2a** (262.4 mg, 2.0 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (193 mg, 0.80 mmol). The title compound (molecular formula: $C_{22}H_{20}N_3OBr$, MW = 422.33 g/mol, 93.0 mg) was isolated as a brown solid in 55% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ/ppm=3.57 (dd, J = 5.6 Hz, J = 10.6 Hz, 1H), 3.72 (s, 3H), 3.94 (s, 3H), 4.23 (dd, J = 9.0 Hz, J = 7.6 Hz, 1H), 5.54 (dd, J = 6.0 Hz, J = 2.8 Hz, 1H), 7.02 (m, 4H), 7.14 (m, 3H), 7.24 (m, 1H), 7.28 (m, 1H), 7.52 (d, J = 7.9 Hz, 2H), 7.58 (dd, J = 1.2 Hz, J = 1.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ/ppm= 33.0 (q), 36.4 (q), 37.4 (t),44.7 (d), 109.2 (d), 116.8 (s), 119.1 (d), 120.0 (d), 121.9 (d), 124.4 (s), 126.9 (d), 127.2(d), 127.5 (s), 127.7 (d), 127.9 (d), 129.1 (d), 129.7 (d),133.0 (d), 137.5 (s), 143.3 (s),143.7 (s), 190.7 (s). HRMS (ESI) calcd. for $C_{22}H_{21}N_3OBr$: 422.0868 ($[M+H]^+$, found 422.0865 ($[M+H]^+$.

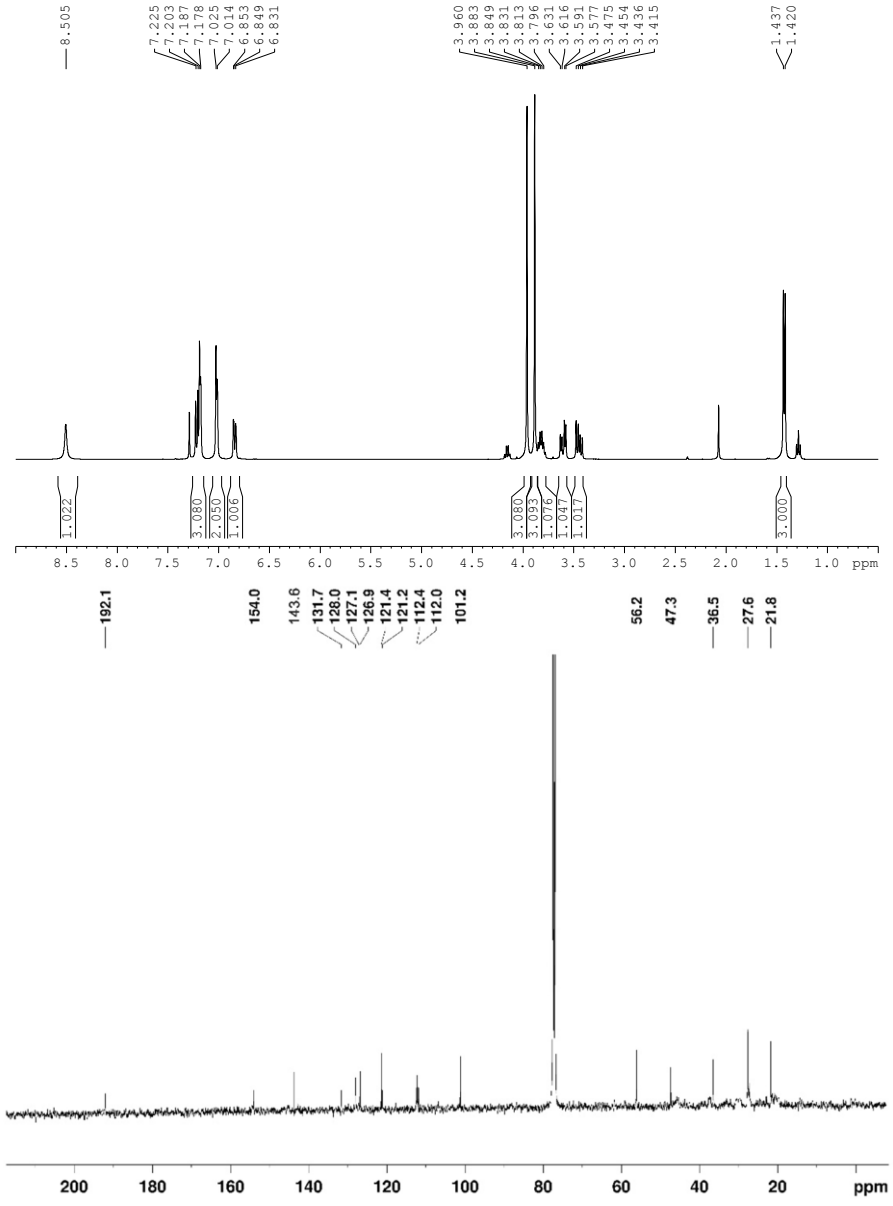


3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (3d)

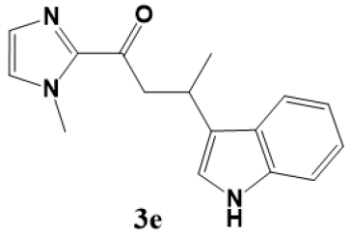


3d

Following the general procedure A: **1d** (60.0 mg, 0.40 mmol), **2b** (294.4 mg, 2.0 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (193 mg, 0.80 mmol).The title compound (molecular formula: $C_{17}H_{19}N_3O_2$, MW = 297.36 g/mol, 107.0 mg) was isolated as a brown solid in 90% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ/ppm=1.42 (d, J = 6.9 Hz, 3H), 3.41 (dd, J = 8.3 Hz, J = 15.6 Hz, 1H), 3.58 (dd, J = 6.2, J = 15.6 Hz, 1H), 3.77 – 3.83 (m, 1H), 3.88 (s, 3H), 3.95 (s, 3H), 6.83 (dd, J = 2.5 Hz, J = 8.8 Hz, 1H), 7.00 (s, 1H), 7.18-7.22 (m, 3H), 8.50 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ/ppm= 21.8 (q), 27.6 (q), 36.5 (d), 47.3 (q), 56.2 (t), 101.2 (d), 112.0 (d), 112.4 (d), 121.2 (d), 121.4 (d), 126.9 (s), 127.1 (d), 128.0 (s), 131.7 (s), 142.6 (s), 154.0 (s), 192.1 (s). HRMS (ESI) calcd. for $C_{17}H_{20}N_3O_2$: 298.1556 $([M+H])^+$, found 298.1559 $([M+H])^+$.

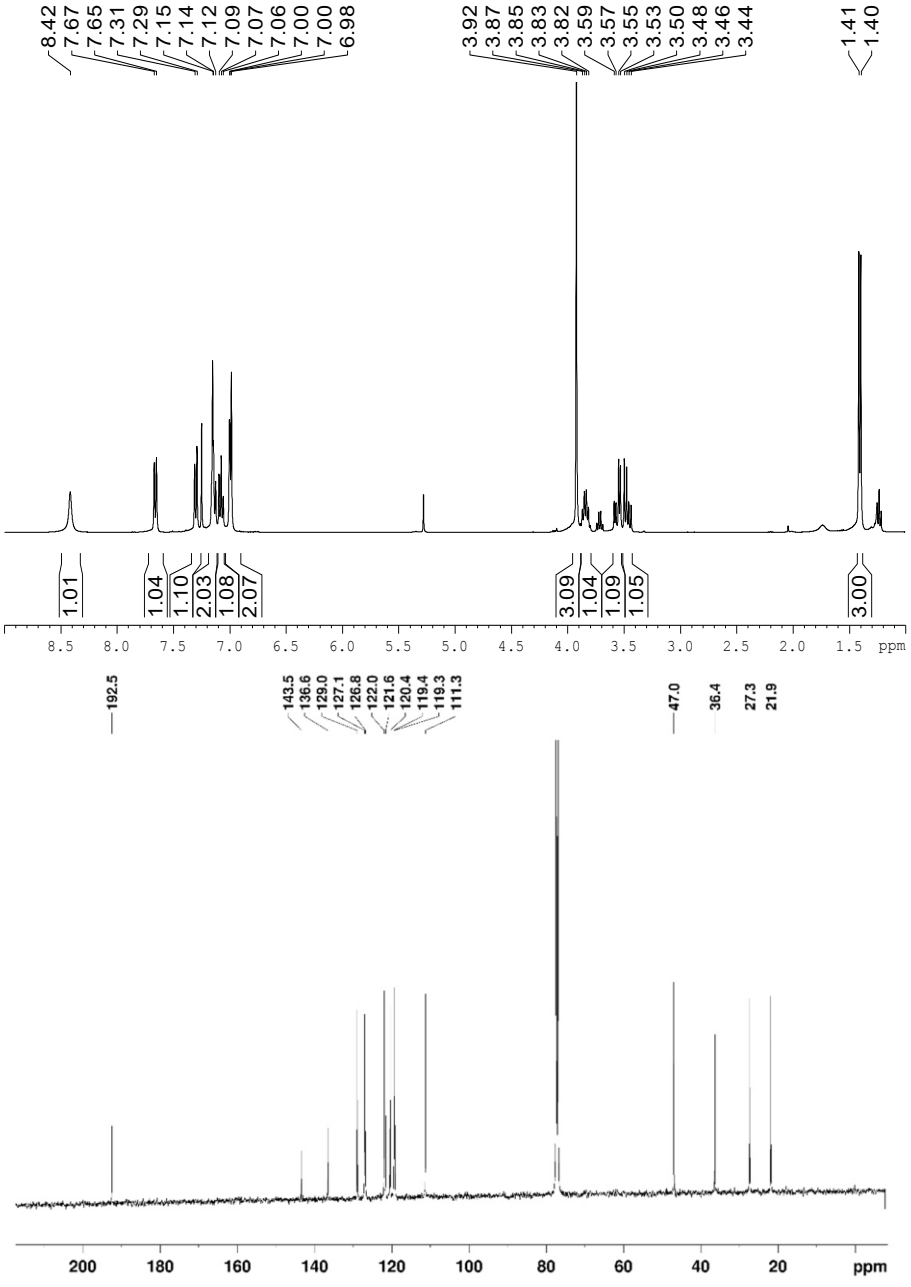


3-(1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (3e)

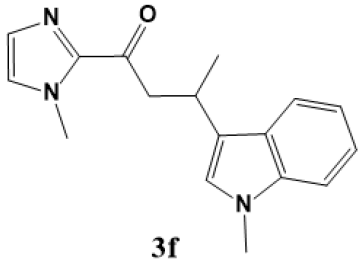


3e

Following the general procedure A: **1d** (60.0 mg, 0.40 mmol), **2c** (234.3 mg, 2.0 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (193 mg, 0.80 mmol). The title compound (molecular formula: $C_{16}H_{17}N_3O$, MW = 267.33 g/mol, 80.0 mg) was isolated as a brown solid in 74% yield. ^1H NMR ($CDCl_3$, 400 MHz): δ/ppm=1.40 (d, J = 6.9 Hz, 3H), 3.51 (m, 2H), 3.84 (m, 1H), 3.92 (s, 3H), 7.00 (t, J = 7.1 Hz, 2H), 7.07 (t, J = 8.2 Hz, 1H), 7.14(m, 2H), 7.30 (d, J = 8.1 Hz, 1H), 7.66 (d, J = 7.9 Hz, 1H), 8.42(s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ/ppm= 21.9 (q), 27.3 (t), 36.4 (d), 47.0 (q), 111.3 (d), 119.3 (d), 119.4 (d), 120.4 (d), 121.6 (s), 122.0 (d), 126.8 (s), 127.1 (d), 129.0 (d), 136.6 (s), 143.5 (s), 192.5 (s). HRMS (ESI) calcd. for $C_{16}H_{18}N_3O$: 268.1450 $([M+H])^+$, found 268.1451 $([M+H])^+$.

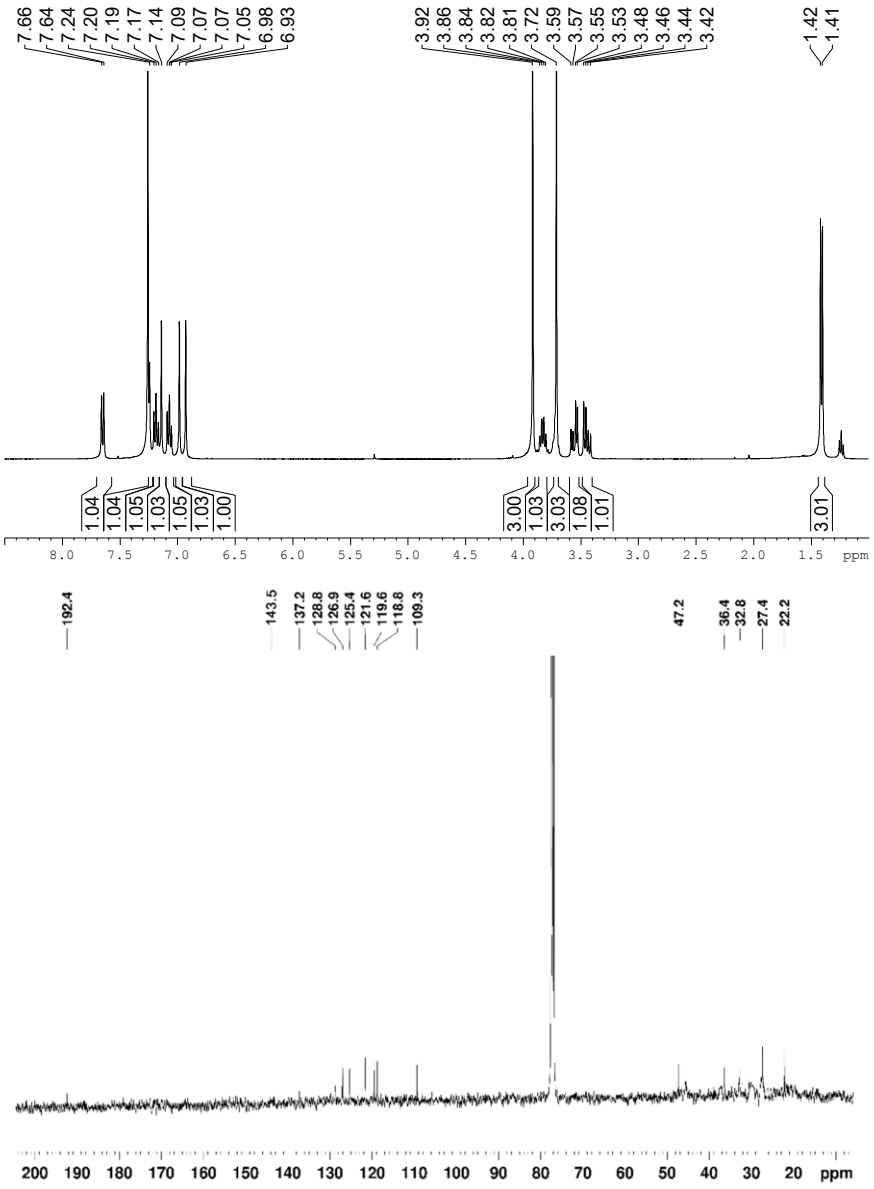


1-(1-methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)butan-1-one (3f)

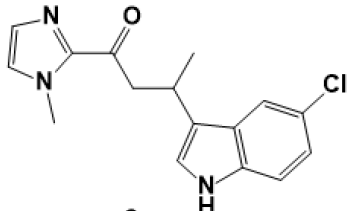


3f

Following the general procedure A: **1d** (60.0 mg, 0.40 mmol), **2a** (262.4 mg, 2.0 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (193 mg, 0.80 mmol). The title compound (molecular formula: $C_{17}H_{19}N_3O$, MW = 281.36 g/mol, 99.0 mg) was isolated as a brown solid in 88% yield. ^1H NMR ($CDCl_3$, 400 MHz): δ/ppm=1.41 (d, J = 6.9, 3H), 3.45 (dd, J = 2.2 Hz, J = 8.00 Hz, 1H), 3.60 (dd, J = 6.5 Hz, 1H), 3.72 (s, 3H), 3.83 (dd, J = 7.0 Hz, J = 7.2 Hz, 1H), 3.92 (s, 3H), 6.93 (s, 1H), 6.98 (s, 1H), 7.27 (s, 1H), 7.07 (m, 1H), 7.14 (s, 1H), 7.19 (t , J = 7.0 Hz, 1H), 7.24 (s, 1H), 7.65(d , J = 7.7 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ/ppm= 22.2 (q), 27.4 (d), 32.8 (q), 36.4 (q), 47.2 (t), 109.3 (d), 118.8 (d), 119.6 (d), 121.6 (d), 125.4 (d), 126.9 (d), 128.8 (d),137.2 (s), 143.5 (s), 192.4 (s). HRMS (ESI) calcd. for $C_{17}H_{20}N_3O$: 282.1606 ($[M+H]^+$, found 282.1601 ($[M+H]^+$.

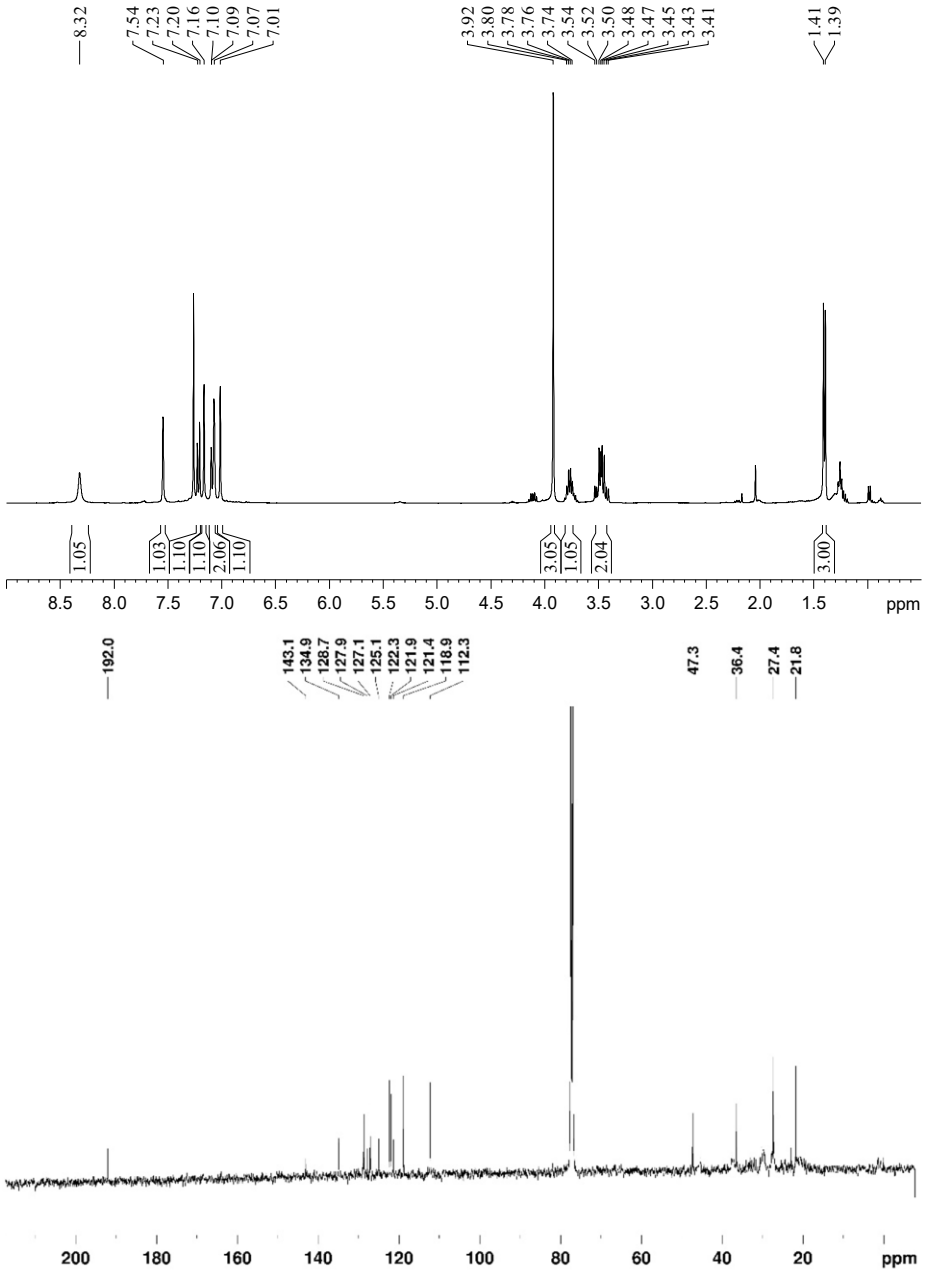


3-(5-chloro-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (3g)

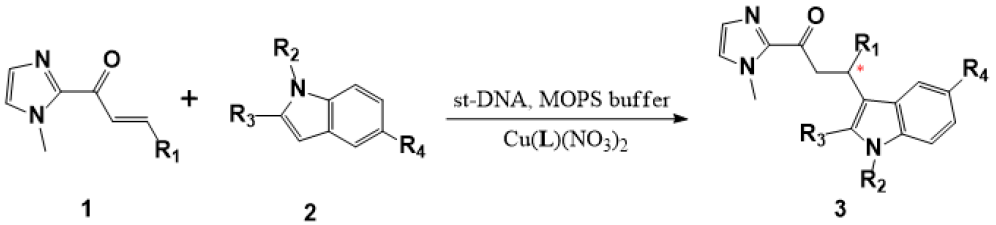


3g

Following the general procedure A: **1d** (60.0 mg, 0.40 mmol), **2d** (303.2 mg, 2.0 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (193 mg, 0.80 mmol). The title compound (molecular formula: $C_{17}H_{18}ClN_3O$, MW = 315.80 g/mol, 91.0 mg) was isolated as a brown solid in 72% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ/ppm=1.40 (d, J = 6.9 Hz, 3H), 3.47 (m, 2H), 3.77 (m, 1H), 3.92 (s, 3H), 7.01 (s, 1H), 7.08(d, J = 9.5 Hz, 2H), 7.16 (s, 1H), 7.21 (d, J = 8.6Hz, 2H), 7.54 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ/ppm= 21.8 (q), 27.4 (d), 36.4 (q), 47.3 (t), 112.3 (d), 118.9 (d), 121.4 (s), 121.9 (d), 122.3 (d), 125.1 (s), 127.1 (d), 127.9 (s), 128.7 (d), 134.9 (s), 143.1 (s), 192.0 (s). HRMS (ESI) calcd. for $C_{17}H_{19}ClN_3O$: 302.1060 ($[M+H]^+$, found 302.1056 ($[M+H]^+$.



Preparation and HPLC analysis of enantioselective Friedel-Crafts alkylation products 3a-3g



1

1a: R_1=Ph
1b: R_1=*p*-MeOC$_6$H$_4$
1c: R_1=*o*-BrC$_6$H$_4$
1d: R_1=Me

2

2a: R_2=Me, R_3=H, R_4=H
2b: R_2=H, R_3=H, R_4=MeO
2c: R_2=H, R_3=H, R_4=H
2d: R_2=H, R_3=H, R_4=Cl

3

3a: R_1=Ph, R_2=Me, R_3=H, R_4=H
3b: R_1=*p*-MeOC$_6$H$_4$, R_2=H, R_3=H, R_4=MeO
3c: R_1=*o*-BrC$_6$H$_4$, R_2=Me, R_3=H, R_4=H
3d: R_1=Me, R_2=H, R_3=H, R_4=MeO
3e: R_1=Me, R_2=H, R_3=H, R_4=H
3f: R_1=Me, R_2=Me, R_3=H, R_4=H
3g: R_1=Me, R_2=H, R_3=H, R_4=Cl

Preparation of a 0.9 mM stock solution of [Py$_4$-dmbpy-Cu^{2+}]

To a solution of **Py$_4$-dmbpy** (294.5 mg, 0.41 mmol) in methanol was added $Cu(NO_3)_2{\cdot}3H_2O$ (100.0 mg, 0.41 mmol), dissolved in methanol. The solution was stirred for 24 h. The bright green solid was filtered and washed with methanol. Yield: 213.43 mg, 59%.

General procedure B

To a 3 mM base pair solution of DNA in a 30 mM MOPS buffer (10 mL, prepared 24 h in advance) was added a 0.9 mM solution of **Py$_4$-dmbpy-Cu^{II}** or **dmbpy-Cu^{II}** in a 5 mL ultrapure water. The resulting DNA solution (2 mM base pair, 15 mL) was cooled to 5 °C. To the cold mixture was added a 0.75 M solution of enone in DMSO (20 μL), followed by a 3.75 M solution of substituted indole in DMSO (20 μL). The reaction was stirred at 5 °C. After 10 h, the mixture was warmed to r.t. and extracted with Et_2O (3×15 mL). The combined organic layers were dried over Na_2SO_4, filtered through a plug of silica gel and concentrated under reduced pressure, to give the crude product which was subjected to HPLC analysis without further purification.

HPLC figure caption

(a) standard sample of start materials **1**.
(b) racemic products **3** catalyzed by $Cu(NO_3)_2$, were purified as standards.
(c) Friedel-Crafts reaction catalyzed by st-DNA/**Py$_4$-dmbpy-Cu^{II}**.

Calculation formula of the conversion

Conversions of **1** were calculated using the following formula[1,2]:

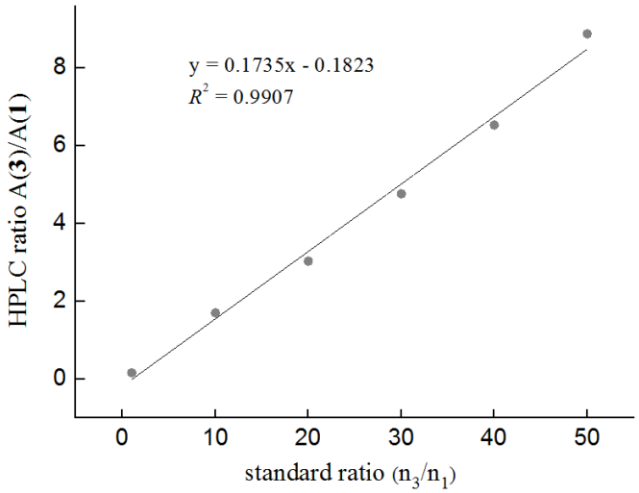
$$\text{Conv.}(\%) = \frac{\text{A}(3)}{A(3) + A(1) \times f} \times 100\%$$

Where **A(3)** is the total peak area of the products of the reaction, **A(1)** is the peak area of the starting material (α, β-unsaturated substrates) and ***f*** is the correction factor determined from a calibration curve, and the results are shown in Table S1.

Table S1. The correction factor ***f*** of products **3a-g.**

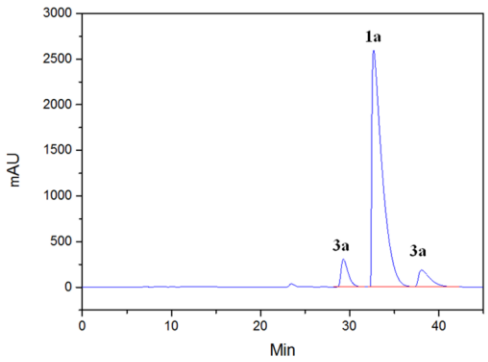
Entry	Starting materials	Products	*f*	R^2
1	**1a**	**3a**	0.1735	0.9907
2	**1b**	**3b**	0.3849	0.9945
3	**1c**	**3c**	1.4153	0.9521
4	**1d**	**3d**	0.8735	0.9807
5	**1d**	**3e**	0.3180	0.9946
6	**1d**	**3f**	0.6593	0.9895
7	**1d**	**3g**	0.5201	0.9937

Take the correction factor ***f*** of **3a** as an example:



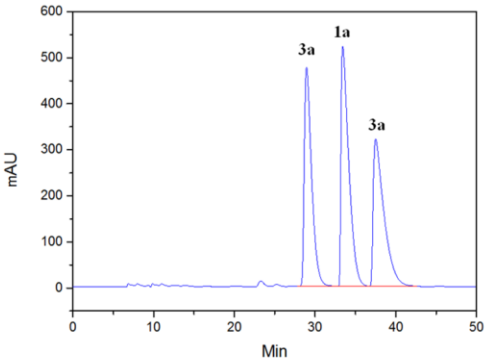
The HPLC ratios of peak areas **A(3)/A(1)** were determined with the standard molar ratios (n_3/n_1) of 1, 10, 20, 30, 40, 50. The correction factor (***f*** = 0.1735) was estimated from the fitting curve (R^2 = 0.9907). The HPLC chromatograms of the various molar ratios (n_3/n_1) are shown below.

1:1 mixture of products **3a** and substrate **1a**



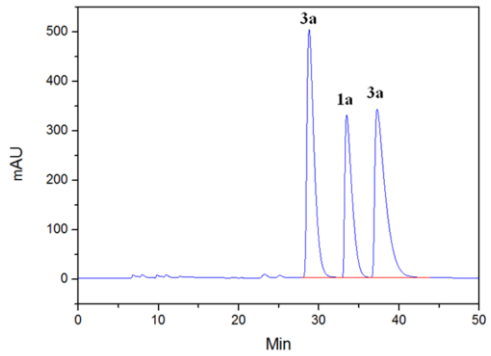
Index	Name	Time (min)	Area (%)
1	**3a**	29.302	7.044
2	**1a**	32.690	85.919
3	**3a**	38.066	7.037
Total			100

10:1 mixture of products **3a** and substrate **1a**



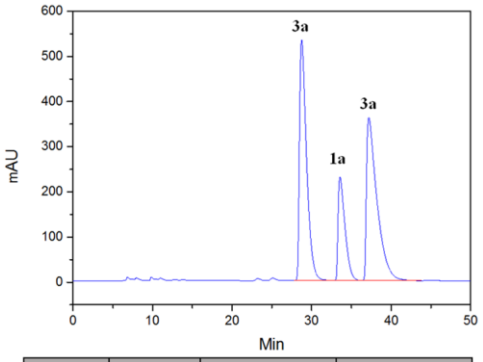
Index	Name	Time (min)	Area (%)
1	**3a**	28.946	31.742
2	**1a**	33.426	36.911
3	**3a**	37.509	31.346
Total			100

20:1 mixture of products **3a** and substrate **1a**



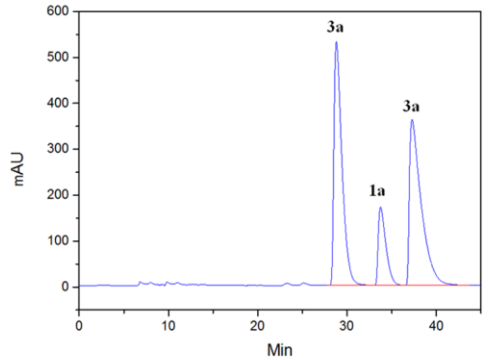
Index	Name	Time (min)	Area (%)
1	**3a**	28.817	37.622
2	**1a**	33.468	24.766
3	**3a**	37.302	37.612
Total			100

30:1 mixture of products **3a** and substrate **1a**



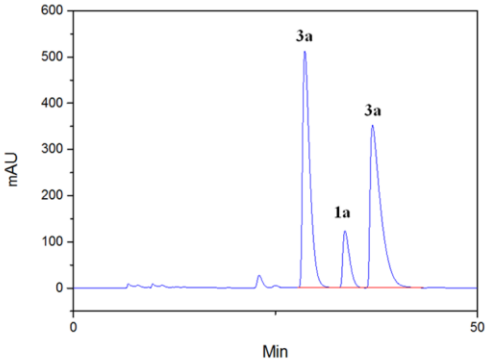
Index	Name	Time (min)	Area (%)
1	**3a**	28.750	41.304
2	**1a**	33.571	17.340
3	**3a**	37.200	41.357
Total			100

40:1 mixture of products **3a** and substrate **1a**



Index	Name	Time (min)	Area (%)
1	**3a**	28.812	43.320
2	**1a**	33.752	13.270
3	**3a**	37.286	43.410
Total			100

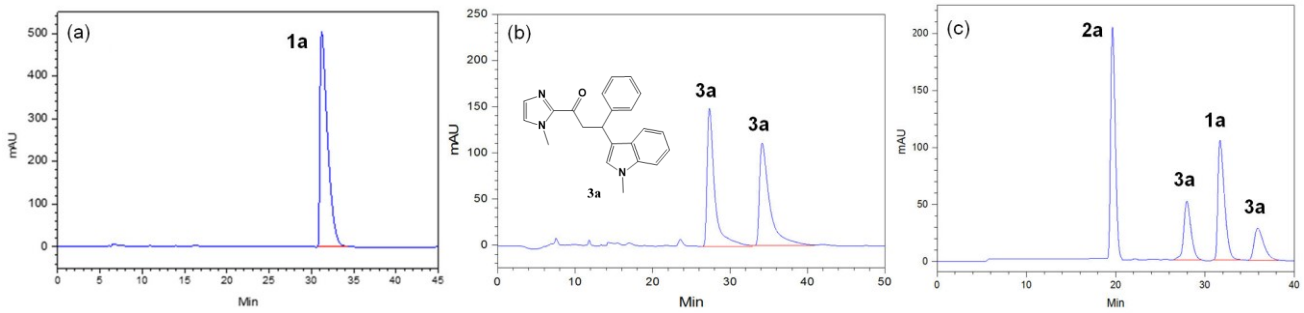
50:1 mixture of products **3a** and substrate **1a**



Index	Name	Time (min)	Area (%)
1	**3a**	28.635	44.891
2	**1a**	33.602	10.118
3	**3a**	37.014	44.991
Total			100

1-(1-methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropan-1-one (3a)

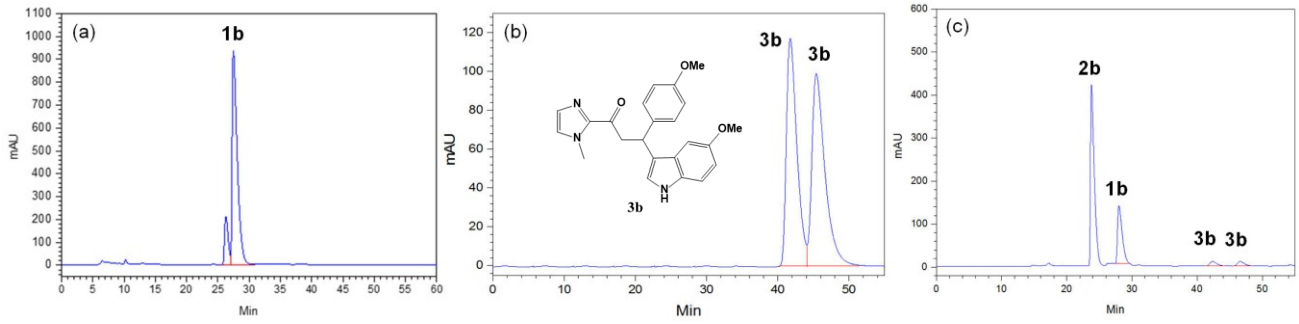
Following the general procedure B: st-DNA (2 mM base pair), **1a** (1 mM), **2a** (5 mM), **Py$_4$-dmbpy-Cu^{II}** (0.3 mM) and MOPS buffer (20 mM, pH 6.5); HPLC analysis of the crude residue indicated an enantiomeric excess of (+)17%. Daicel Chiralcel OD-H column; hexane/iPrOH 85:15, flow: 0.5 mL/min.; λ = 254 nm]. Retention times: major enantiomer t_R = 27.963 min; minor enantiomer t_R = 35.901 min.



Index	Retention time (min)	Compound	Area	*ee* (%)	Conversion (%)
1	27.963	**3a**	2989.6		
2	31.688	**1a**	5402.4	17	84
3	35.901	**3a**	2104.5		

3-(5-methoxy-1*H*-indol-3-yl)-3-(4-methoxyphenyl)-1-(1-methyl-1*H*-imidazol-2-yl) propan-1-one (3b)

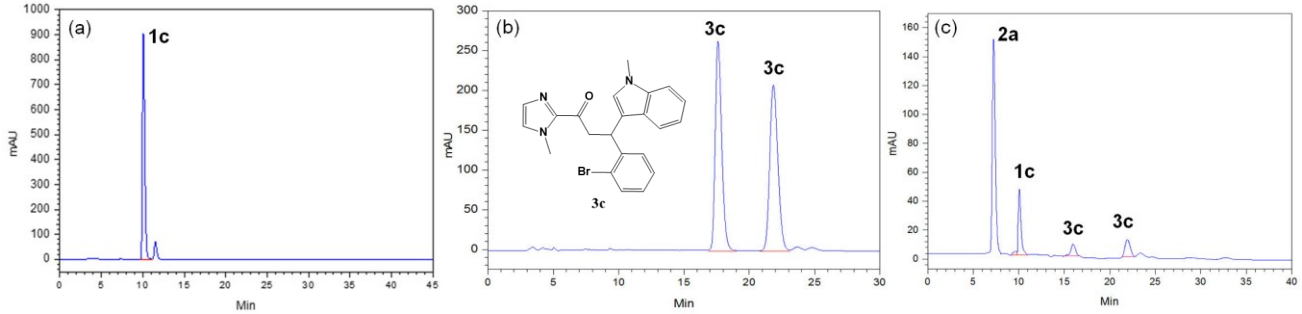
Following the general procedure B: st-DNA (2 mM base pair), **1b** (1 mM), **2b** (5 mM), **Py$_4$-dmbpy-Cu^{II}** (0.3 mM) and MOPS buffer (20 mM, pH 6.5); HPLC analysis of the crude residue indicated an enantiomeric excess of (-)8.0%. Daicel Chiralcel OD-H column; hexane/iPrOH 80:20, flow: 0.5 mL/min.; λ = 254 nm. Retention times: major enantiomer t_R = 45.581 min; minor enantiomer t_R = 41.917 min.



Index	Retention time(min)	Compound	Area	*ee* (%)	Conversion(%)
1	28.009	**1b**	17280.5		
2	41.917	**3b**	1052.3	-8	26
3	45.581	**3b**	1235.5		

3-(2-Bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl) propan-1-one (3c)

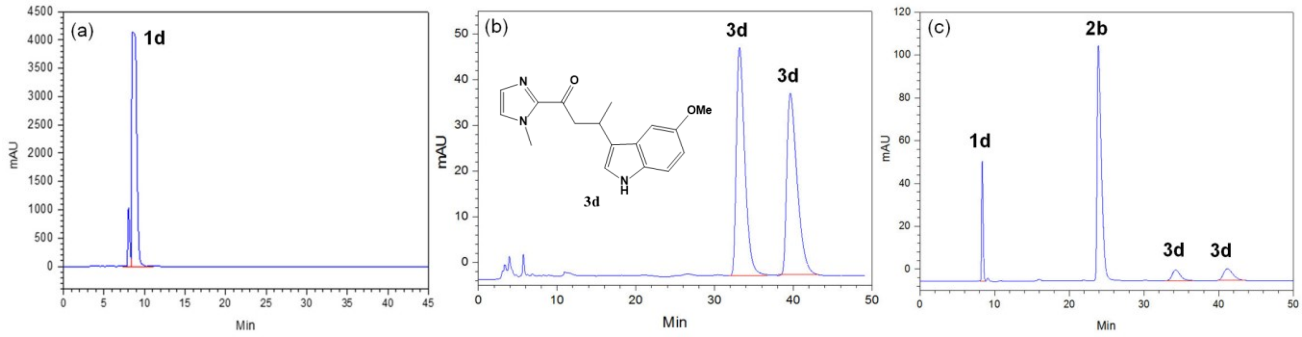
Following the general procedure B: st-DNA (2 mM base pair), **1c** (1 mM), **2a** (5 mM), **Py$_4$-dmbpy-Cu^{II}** (0.3 mM) and MOPS buffer (20 mM, pH 6.5); HPLC analysis of the crude residue indicated an enantiomeric excess of (-)32%. Daicel Chiralcel AD-H column; hexane/iPrOH 90:10, flow: 1.0 mL/min.; λ = 254 nm. Retention times: major enantiomer t_R = 21.938 min; minor enantiomer t_R = 16.937 min.



Index	Retention time(min)	Compound	Area	*ee* (%)	Conversion(%)
1	10.072	**1c**	1114.6		
2	16.937	**3c**	283.5	-32	34
3	21.938	**3c**	545.1		

3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl) butan-1-one (3d)

Following the general procedure B: st-DNA (2 mM base pair), **1d** (1 mM), **2b** (5 mM), **Py$_4$-dmbpy-Cu^{II}** (0.3 mM) and MOPS buffer (20 mM, pH 6.5); HPLC analysis of the crude residue indicated an enantiomeric excess of (-)15.0%. Daicel Chiralcel OD-H column; hexane/iPrOH 90:10, flow: 1.0 mL/min.; λ = 254 nm. Retention times: major enantiomer t_R = 41.177 min; minor enantiomer t_R = 34.240 min.

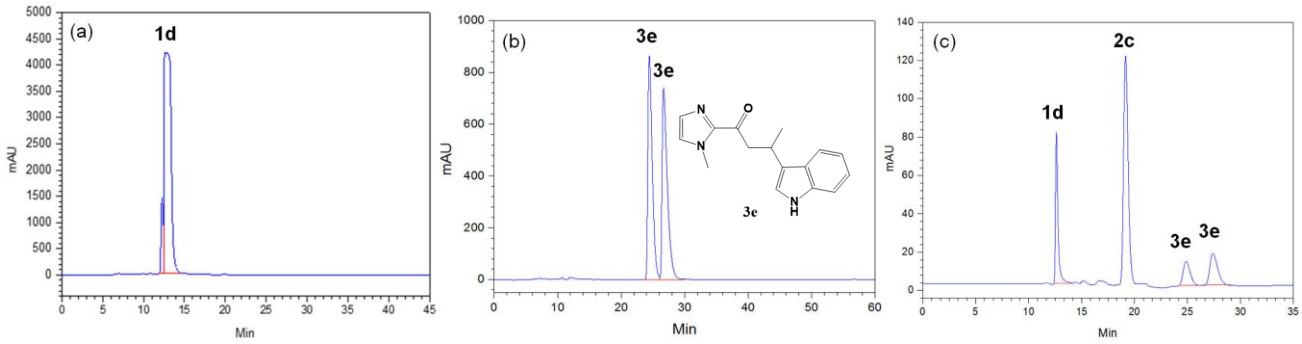


Index	Retention time(min)	Compound	Area	*ee* (%)	Conversion(%)

1	8.355	**1d**	792.6		
2	34.240	**3d**	358.0	-15	55
3	41.177	**3d**	480.4		

3-(1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (3e)

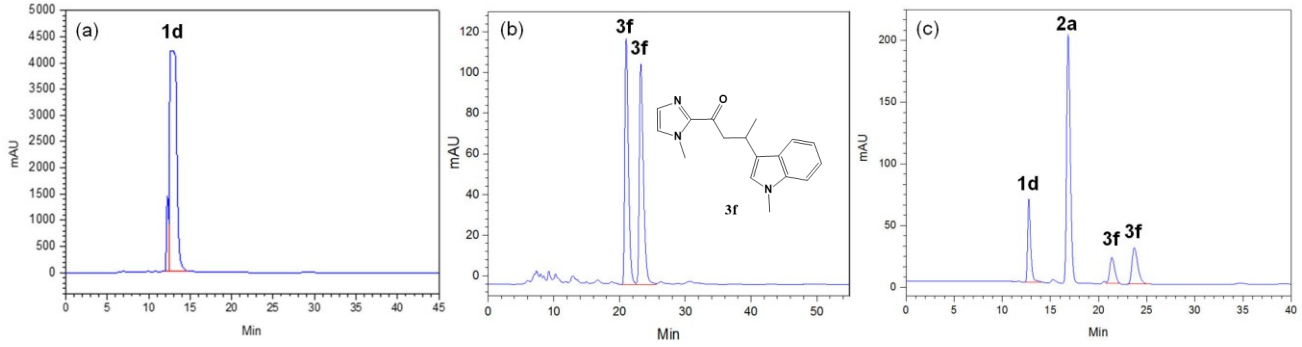
Following the general procedure B: st-DNA (2 mM base pair), **1d** (1 mM), **2c** (5 mM), **Py$_4$-dmbpy-Cu^{II}** (0.3 mM) and MOPS buffer (20 mM, pH 6.5); HPLC analysis of the crude residue indicated an enantiomeric excess of (-)17%. Daicel Chiralcel OD-H column; hexane/iPrOH 80:20, flow: 0.5 mL/min.; λ = 254 nm. Retention times: major enantiomer t_R = 27.409 min; minor enantiomer t_R = 24.884 min.



Index	Retention time(min)	Compound	Area	*ee* (%)	Conversion(%)
1	12.622	**1d**	1944.8		
2	24.884	**3e**	618.2	-17.3	71
3	27.409	**3e**	876.9		

1-(1-methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl) butan-1-one (3f)

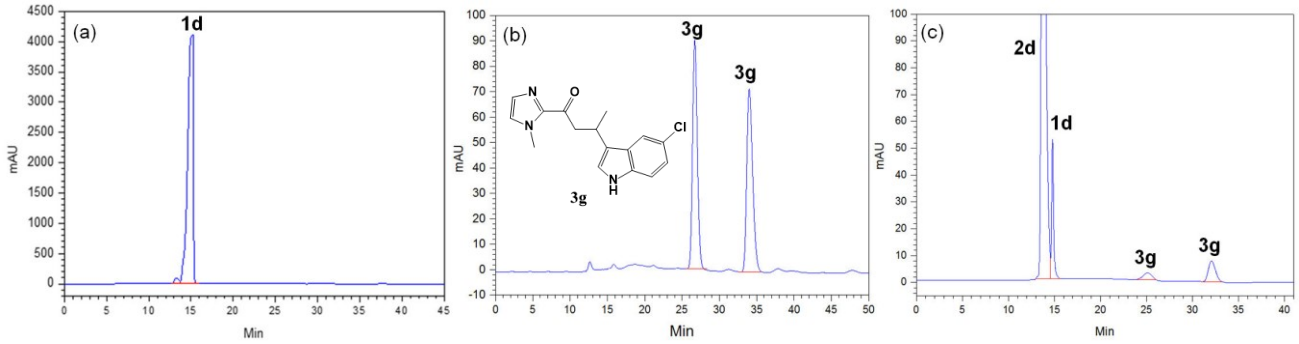
Following the general procedure B: st-DNA (2 mM base pair), **1d** (1 mM), **2a** (5 mM), **Py$_4$-dmbpy-Cu^{II}** (0.3 mM) and MOPS buffer (20 mM, pH 6.5); HPLC analysis of the crude residue indicated an enantiomeric excess of (-)21%. Daicel Chiralcel OD-H column; hexane/iPrOH 80:20, flow: 0.5 mL/min.; λ = 254 nm. Retention times: major enantiomer t_R = 23.709 min; minor enantiomer t_R = 21.838 min.



Index	Retention time(min)	Compound	Area	*ee* (%)	Conversion(%)
1	12.755	**1d**	1482.2		
2	21.838	**3f**	816.7	-21.4	68
3	23.709	**3f**	1262.4		

3-(5-chloro-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (3g)

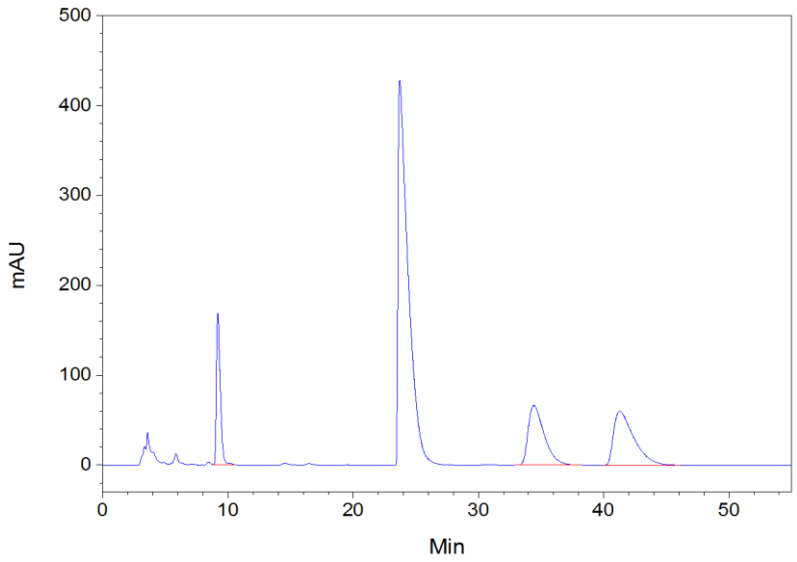
Following the general procedure B: st-DNA (2 mM base pair), **1d** (1 mM), **2d** (5 mM), **Py_4-dmbpy-Cu^{II}** (0.3 mM) and MOPS buffer (20 mM, pH 6.5); HPLC analysis of the crude residue indicated an enantiomeric excess of (-)32.0%. Daicel Chiralcel AD-H column; hexane/iPrOH 90:10, flow: 1.0 mL/min.; λ = 254 nm. Retention times: major enantiomer t_R = 33.066 min; minor enantiomer t_R = 25.090 min.



Index	Retention time(min)	Compound	Area	*ee* (%)	Conversion(%)
1	14.798	**1d**	822.9		
2	25.090	**3g**	224.6	-31.6	61
3	33.066	**3g**	432.3		

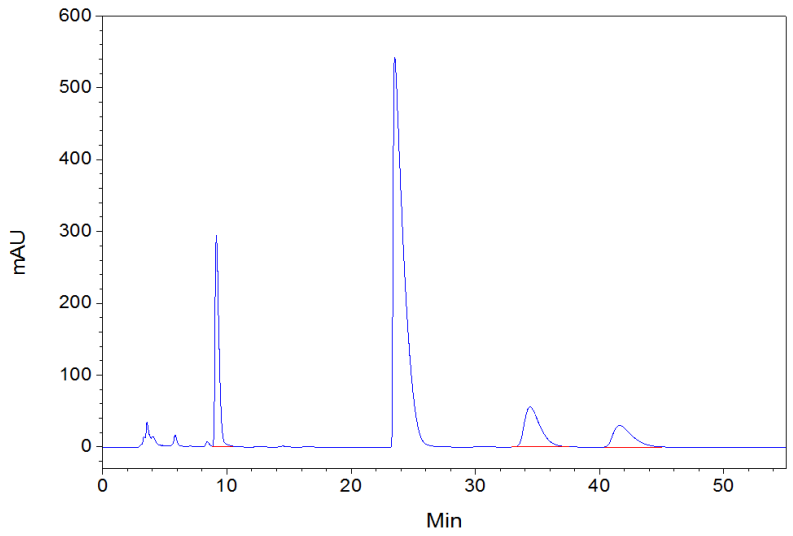
HPLC analysis of product 3d catalyzed by oligonucleotides/Py_4-dmbpy-Cu^{II}

ODN: d(GACTGACTAGTCAGTC)$_2$



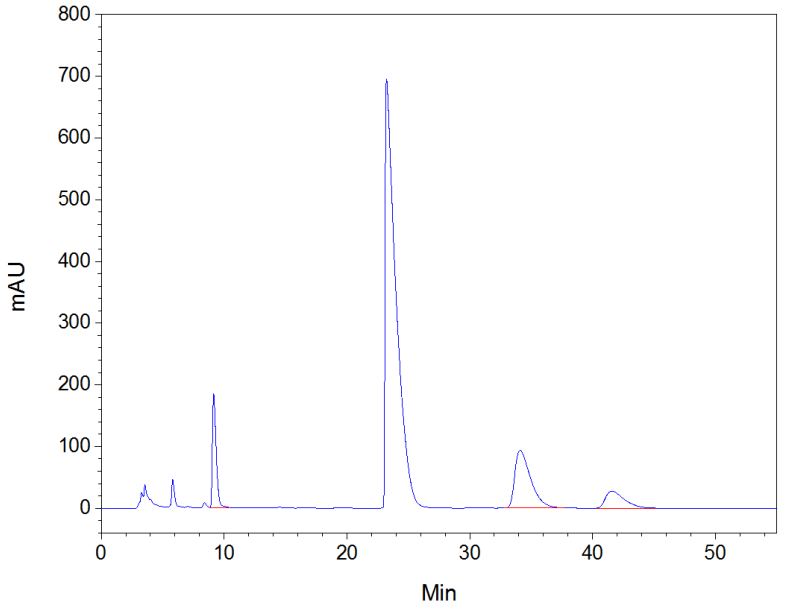
Index	Retention time (min)	Compound	Area	*ee* (%)	Conversion (%)
1	9.179	1d	3681.7		
2	34.417	3d	5840.9	-7	80
3	41.276	3d	6667.6		

ODN: d(TCAGGGCCCTGA)$_2$



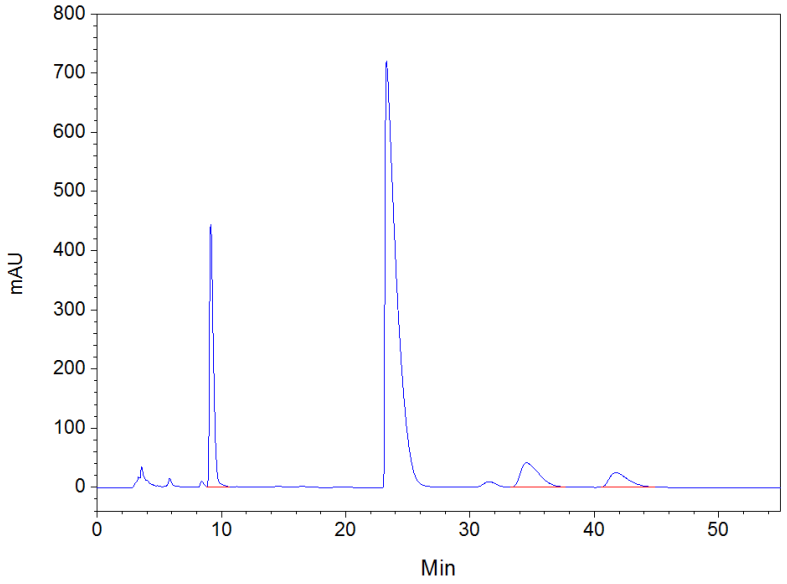
Index	Retention time (min)	Compound	Area	*ee* (%)	Conversion (%)
1	9.155	1d	6516.7		
2	34.395	3d	4917.9	20	57
3	41.602	3d	2651.9		

ODN: d(TCGGGGCCCCGA)$_2$



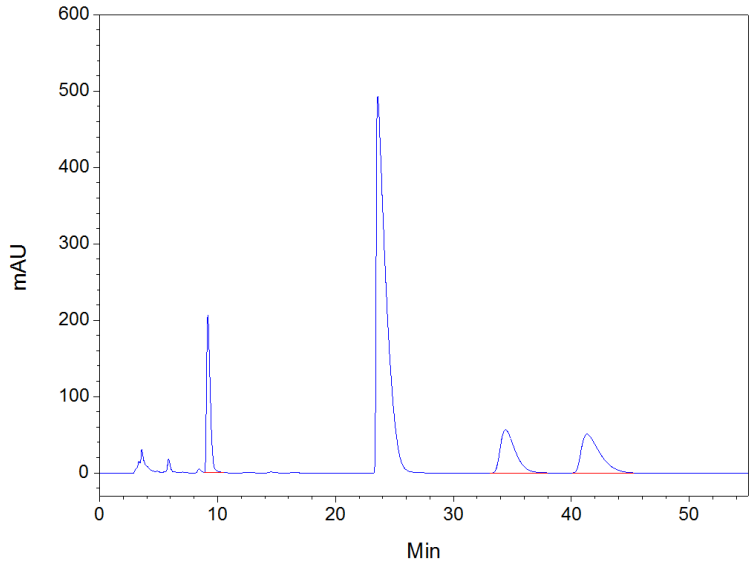
Index	Retention time (min)	Compound	Area	*ee* (%)	Conversion (%)
1	9.152	1d	4039.4		
2	34.101	3d	8275.5	48	76
3	41.567	3d	2913.3		

ODN: d(TCGGAATTCCGA)$_2$



Index	Retention time (min)	Compound	Area	*ee* (%)	Conversion (%)
1	9.139	1d	9882.2		
2	34.533	3d	4271.0	23.3	45
3	41.736	3d	2651.9		

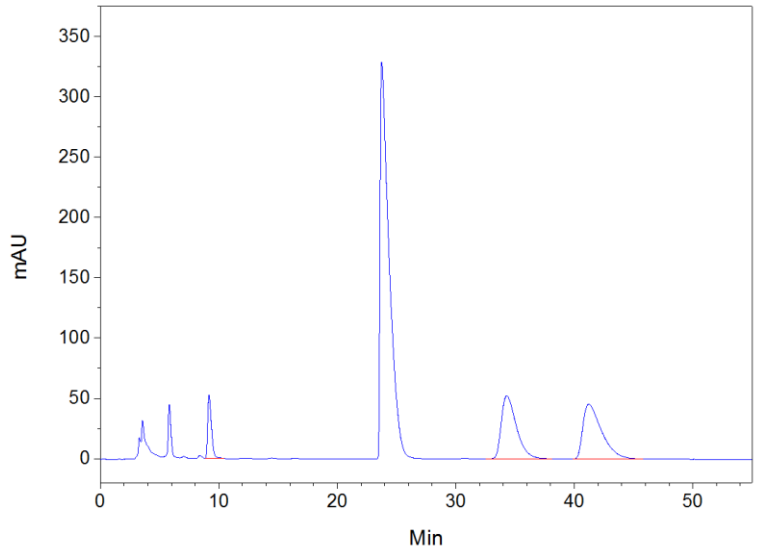
ODN: d(TCAGTGCACTGA)$_2$



Index	Retention time (min)	Compound	Area	*ee* (%)	Conversion (%)
1	9.165	1d	4475.0	6	73
2	34.416	3d	4907.4		

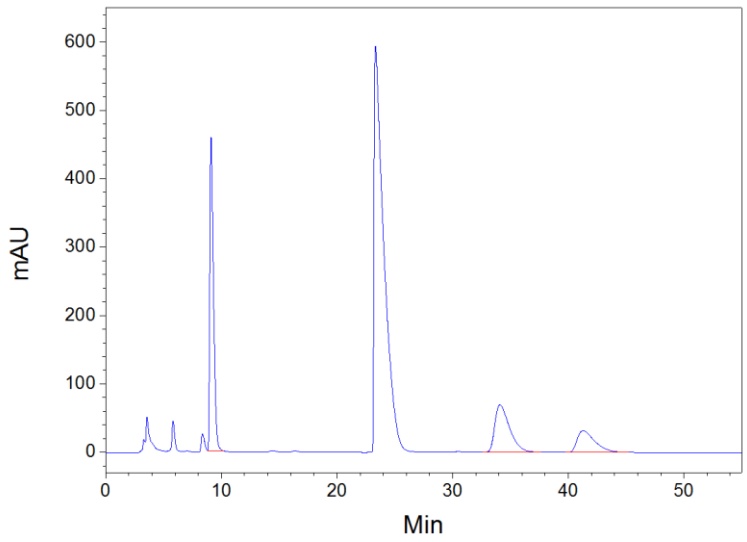
3	41.321	3d	5534.6		

ODN: d(GCATGATCATGC)$_2$



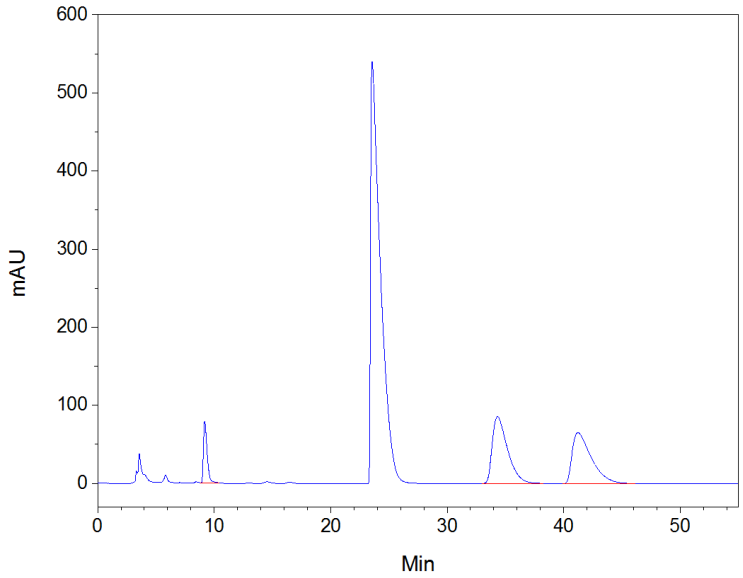
Index	Retention time (min)	Compound	Area	*ee* (%)	Conversion (%)
1	9.170	1d	1188.9		
2	34.293	3d	4135.4	-13	90
3	41.216	3d	5310.9		

ODN: d(GCGCGCGCGCGC)$_2$



Index	Retention time (min)	Compound	Area	*ee* (%)	Conversion (%)
1	9.101	1d	10359.1		
2	34.09	3d	6079.6	29.0	51
3	41.277	3d	3345.3		

ODN: d(ATATATATATAT)$_2$



Index	Retention time (min)	Compound	Area	*ee* (%)	Conversion (%)
1	9.185	1d	1792.1		
2	34.316	3d	7781.2	-2.5	91
3	41.222	3d	7397.7		

Basis spectra of SVD analysis

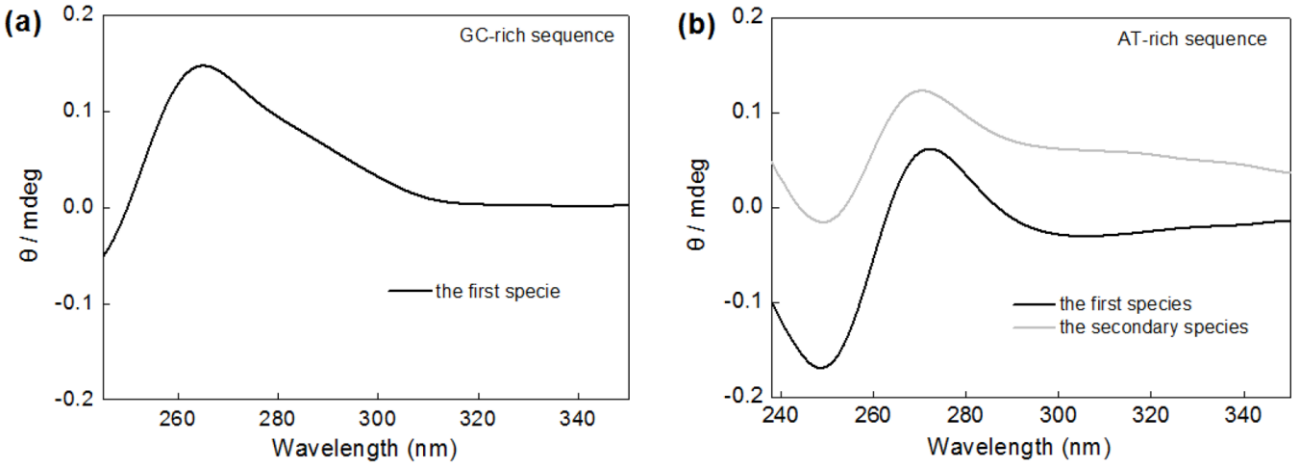


Fig. S1 Basis spectra produced by SVD analysis of (a) **Py$_4$-dmbpy-Cu^{II}**/GC-rich ODN d(TCGGGGCCCCGA)$_2$ and (B) **Py$_4$-dmbpy-Cu^{II}**/AT-rich ODN d(ATATATATATAT)$_2$ titrations that shown in Figure 2c-d. The most significant basis spectra, as judged by the magnitude of the singular values, correspond to spectral intensity.

UV-Vis titration spectra of Py$_4$-dmbpy-Cu^{II} with alternative oligonucleotides

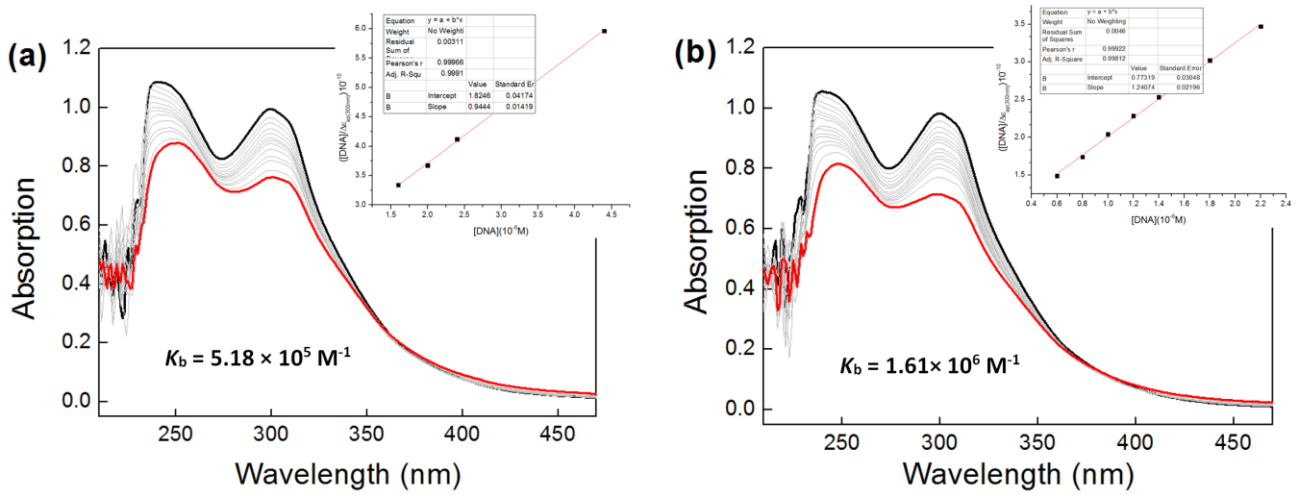


Fig. S2 UV-Vis titration spectra of **Py$_4$-dmbpy-Cu^{II}** with (a) AT-rich d(ATATATATATAT)$_2$ (r = 0-0.02 from black line to red line) and (b) GC-rich d(TCGGGGCCCCGA)$_2$ (r = 0-0.015 from black line to red line) sequences in MOPS buffer (20mM, pH=6.5). t = 25 ºC. The insert figure represents the least squares linear fit of the data. r = ODN/**Py$_4$-dmbpy-Cu^{II}**).

References

[1] N. S. Oltra, G. Roelfes, *Chem. Commun.* **2008**, 6039-6041.
[2] J. J. Marek, R. P. Singh, A. Heuer, U. Hennecke, *Chem. Eur. J.* **2017**, 23, 6004–6008.