Supporting Information

Highly Efficient One-Pot Three-Component Mannich Reaction in Water Catalyzed by Heteropoly Acids

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Table 1. Direct Mannich Reaction Catalyzed by Heteropoly Acid in Different Solvents^a

Entry	Solvent	Catalyst	Yield [%] ^[b]	anti:syn ^[c]
1	Water	A	88	64:36
2	Water	B	86	65:35
3	MeOH	A	82	69:30
4	MeOH	B	60	64:36
5	EtOH	A	74	84:36
6	Toluene	A	54	63:37
7	Toluene	B	50	64:36
8	CH_3CN	A	68	64:36
9	CH_3CN	B	64	63:37
10	$\text{ClCH}_2\text{CH}_2\text{Cl}$	B	76	65:35
11	Diethyl ether	A	45	70:30
12 ^[d]	Water:Toluene	A	72	65:35
13 ^[e]	Water + SDS	B	78	64:36
14 ^[f]	Water + CTAB	B	68	60:40
15	Water	-	32	30:70

^a Reaction Conditions: 4-chlorobenzaldehyde (3 mmol), aniline (3.1 mmol), cyclohexanone (5 mmol) and catalyst (10 mg).

^b Yield of isolated product.

^c Diastereomeric ratio measured by NMR spectroscopic analysis of the crude reaction mixture.

^d Water: Toluene (2:2)

^e 0.07 gram SDS was used

^f 0.1 gram CTAB was used

Experimental Section

General. All chemicals were purchased and used without any further purification. NMR spectra were recorded at 500 MHz for proton and at 125.7 MHz for carbon nuclei in ($\text{CDCl}_3/\text{CCl}_4$) or ($\text{DMSO-d}_6/\text{CDCl}_3$). The products were purified by column chromatography carried out on silica gel by using ethyl acetate/ petroleum ether mixtures. Reactions were carried out room temperature, all aldehydes, ketones and amines were employed, are commercially available. All products obtained are known compound. $\text{H}_3\text{PMO}_{12}\text{O}_{40}$ and $\text{H}_3\text{PW}_{12}\text{O}_{40}$ used without further purification. Water distilled before used.

General Procedure for the Three-Component Mannich-Type Reactions in Water

aldehyde (3 mmol), amine (3.1 mmol) and cyclohexanone (5 mmol) was successively added to a solution of catalyst (10 mg) in water (5 ml) placed in a test tube and the reaction mixture was vigorous stirred at room temperature for 3-16 h, the reaction mixture was diluted with ethyl acetate, and the organic materials were extracted. The organic phases were combined and dried over Na_2SO_4 . The solvent was removed under reduced pressure to give desired products. The residual crude product was purified by column chromatography on neutral silica gel (ethyl acetate: petroleum ether 1:4) and in some cases crystallized from diethyl ether or ethanol to give a mixture of the Mannich adducts. The syn/anti ratio was determined by ^1H and ^{13}C NMR analysis.

T-115 1H NMR in CDCl3 at 298 K 84/7/3

Table 2 Entry 7

Current Data Parameters
NAME Torlian
EXPNO 26
PROCNO 1

F2 - Acquisition Parameters
Date_ 20050925
Time 16.17
INSTRUM spect
PROBHD 5 mm BBI 1H-BB
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 4
DS 2
SWH 10330.578 Hz
FIDRES 0.315264 Hz
AQ 1.5860566 sec
RG 114
DM 48.400 usec
DE 6.50 usec
TE 300.0 K
D1 3.00000000 sec
MCREST 0.00000000 sec
MCPRK 0.01500000 sec

***** CHANNEL f1 *****
NUC1 1H
P1 9.30 usec
PL1 3.00 dB
SF01 500.130085 MHz

F2 - Processing parameters
SI 32768
SF 500.130000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 18.00 cm
CY 8.31 cm
F1P 10.262 ppm
F1 5132.16 Hz
F2P -0.336 ppm
F2 -167.87 Hz
PPMCM 0.58974 ppm/cm
HZCM 294.44647 Hz/cm

Table 2 Entry 7

T-115 ¹HNMR in CDCl₃ at 298 K B4/7/3

ppm
4.84717
4.83799
4.70822
4.69710

4.09132
4.07705
4.06284
4.04853

2.89344
2.88259
2.87169
2.86111
2.85085
2.83574
2.35485
2.32793
2.32055
2.29715
2.28409
2.27071
1.99305
1.83725
1.82482
1.81270
1.79976
1.68022
1.67179
1.66549
1.65648
1.64928
1.63195
1.57547
1.55779
1.23124
1.21691
1.20265

Current Data Parameters
NAME TorKian
EXPNO 26
PROCNO 1

F2 - Acquisition Parameters
Date_ 20050925
Time 16.17
INSTRUM spect
PROBHD 5 mm BBI 1H-BB
PULPROG zg30
TD 32768
SOLVENT CDCl₃
NS 4
DS 2
SWH 10330.578 Hz
FIDRES 0.315264 Hz
AQ 1.5860696 sec
RG 114
DM 48.400 usec
DE 6.50 usec
TE 300.0 K
D1 3.00000000 sec
MCREST 0.00000000 sec
MONRK 0.01500000 sec

===== CHANNEL f1 =====
NUC1 ¹H
P1 9.30 usec
PL1 3.00 dB
SFO1 500.133085 MHz

F2 - Processing parameters
SI 32768
SF 500.130000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 18.00 cm
CY 8.31 cm
FIP 4.884 ppm
F1 2442.48 Hz
F2P 1.119 ppm
F2 559.44 Hz
PPMCK 0.20917 ppm/cm
HZCM 104.61311 Hz/cm

T-111 1H NMR in CDCl3 at 300 K 84/6/27

ppm

Table 2 Entry 14

61.39

Current Data Parameters
NAME Torjian
EXPNO 18
PROCNO 1

F2 - Acquisition Parameters
Date_ 20050918
Time 9.21
INSTRUM spect
PROBHD 5 mm BBI 1H-89
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 4
DS 2
SMH 10330.578 Hz
FIDRES 0.315264 Hz
AQ 1.5860596 sec
RG 40.3
DM 48.400 usec
DE 6.50 usec
TE 293.6 K
O1 3.00000000 sec
MCHEST 0.00000000 sec
NMRK 0.01500000 sec

===== CHANNEL f1 =====
NUC1 1H
P1 9.30 usec
PL1 3.00 dB
SF01 500.1330885 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
KDM EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 18.00 cm
CY 9.30 cm
F1P 10.127 ppm
F1 5054.79 Hz
F2P -0.515 ppm
F2 -257.70 Hz
PCN/CN 0.59123 ppm/cm
HZCM 295.65409 Hz/cm

T-111 1H NMR in CDCl₃ at 300 K 04/6/27

Table 2 Entry 14

ppm

7.45853
7.44172
7.36402
7.34314
7.32963
7.29437

7.16746
7.09562
7.08181
7.06843
7.02570
7.00139
6.99207
6.98493
6.97498

6.57196

6.28923
6.27172
6.23781
6.22021

Current Data Parameters
NAME Turkjam
EXPNO 18
PROCNO 1

F2 - Acquisition Parameters
Date_ 20050918
Time 9.21
INSTRUM spect
PROBHD 5 mm BBI 1H-BB
PULPROG zg30
TD 32768
SOLVENT CDCl₃
NS 4
DS 2
SWH 10330.578 Hz
FIDRES 0.315264 Hz
AQ 1.5860696 sec
RG 40.3
DK 48.400 usec
DE 6.50 usec
TE 293.6 K
D1 3.00000000 sec
MCREST 0.00000000 sec
MCNMR 0.01500000 sec

***** CHANNEL f1 *****
NUC1 1H
P1 9.30 usec
PL1 3.00 dB
SFO1 500.1330895 MHz

F2 - Processing Parameters
SI 32768
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 18.00 cm
CY 9.30 cm
F1P 7.814 ppm
F1 3908.21 Hz
F2P 6.041 ppm
F2 3021.13 Hz
PPMCM 0.09854 ppm/cm
HZCM 49.28235 Hz/cm

213 1H NMR in CDCl3 at 298 K 84/9/22

Current Data Parameters

NAME	Az121
EXPNO	131
PROCNO	1

F2 - Acquisition Parameters

Date_	20051213
Time	12.56
INSTRUM	spect
PROBHD	5 mm BBI 1H-BB
PULPROG	zg
TD	32768
SOLVENT	DMSO
NS	12
DS	0
SMH	10000.000 Hz
FIDRES	0.305176 Hz
AQ	1.6385000 sec
RG	3.2
DM	50.000 usec
DE	6.50 usec
TE	292.5 K
D1	3.00000000 sec
MCREST	0.00000000 sec
MCORR	0.01500000 sec

===== CHANNEL f1 =====

NUC1	1H
P1	10.30 usec
PL1	2.00 dB
SFO1	500.1300885 MHz

F2 - Processing parameters

S1	32768
SF	500.1300000 MHz
KOH	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	18.00 cm
CY	16.16 cm
F1p	10.038 ppm
F1	5020.33 Hz
F2p	-0.141 ppm
F2	-70.58 Hz
PPMCK	0.56551 ppm/cm
HZCK	282.82828 Hz/cm

213 ¹³CNMR in CDCl₃ at 298 K 84/9/22

Table 2 Entry 19

Current Data Parameters
NAME A2171
EXPNO 132
PROCNO 1
F2 - Acquisition Parameters
Date_ 20051213
Time 12:59
INSTRUM spect
PROBHD 5 mm BBI 1H-BB
PULPROG zgpg30
TD 65536
SOLVENT CDCl₃
NS 27
DS 2
SWH 40000.000 Hz
FIDRES 0.610352 Hz
AQ 0.6192625 sec
RG 2560.3
DM 12.500 usec
DE 6.50 usec
TE 292.8 K
D1 3.00000000 sec
D11 0.03000000 sec
DELTA 2.90000010 sec
MCREST 0.00000000 sec
MCRRK 0.01500000 sec
===== CHANNEL f1 =====
NUC1 ¹³C
P1 10.50 usec
PL1 0.00 dB
SF01 125.7703143 MHz
===== CHANNEL f2 =====
PROBHD 5 mm BBI 1H-BB
NUC2 ¹H
PCPD2 87.00 usec
PL2 -6.00 dB
PL12 12.00 dB
PL13 12.00 dB
SF02 500.132005 MHz
F2 - Processing parameters
SI 32768
SF 125.7577399 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
ID NMR plot parameters
CX 20.00 cm
CY 12.55 cm
F1P 227.548 ppm
F1 200.65.20 Hz
F2P -2.293 ppm
F2 -200.35 Hz

Table 2 Entry 24

126 ¹H NMR in CDCl₃ at 298 K 84/8/4

Current Data Parameters

NAME	A2121
EXPNO	32
PROCNO	1

F2 - Acquisition Parameters

Date_	20051026
Time	11.17
INSTRUM	spect
PROBHD	5 mm BBI 1H-BB
PULPROG	zg
TD	32768
SOLVENT	CDCl ₃
NS	4
DS	2
SWH	10000.000 Hz
FIDRES	0.305176 Hz
AQ	1.638500 sec
RG	11.3
DM	50.000 usec
DE	6.50 usec
TE	291.7 K
D1	3.00000000 sec
MCREST	0.00000000 sec
MCNRF	0.01500000 sec

===== CHANNEL f1 =====

NUC1	¹ H
P1	10.30 usec
PL1	2.00 dB
SFO1	500.1330885 MHz

F2 - Processing parameters

SI	32768
SF	500.1300000 MHz
MDM	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	18.00 cm
CY	9.00 cm
F1P	10.044 ppm
F1	5023.29 Hz
F2P	-0.236 ppm
F2	-118.02 Hz
PPMCM	0.57111 ppm/cm
HZCM	285.62805 Hz/cm

26 ¹HNMR in CDCl₃ at 298 K 84/8/4

ppm
212.102
211.457

146.633
146.344
146.247
145.589
129.406
127.076
126.971
125.996
125.366
124.954
124.759
123.120
115.749
115.479

77.819
77.566
77.312

57.726
56.440
55.079
54.789
42.717
42.618
31.640
30.119
28.102
27.202
25.199
24.670

Current Data Parameters
NAME Az121
EXPNO 33
PROCNO 1

F2 - Acquisition Parameters
Date_ 20051026
Time 11.19
INSTRUM spect
PROBHD 5 mm BB1 1H-BB
PULPROG zgpg30
TD 65536
SOLVENT CDCl₃
NS 64
DS 2
SWH 40000.000 Hz
FIDRES 0.610362 Hz
AQ 0.8192625 sec
RG 2560.3
DM 12.500 usec
DE 6.50 usec
TE 292.4 K
D1 3.00000000 sec
d11 0.03000000 sec
DELTA 2.90000010 sec
MCREST 0.00000000 sec
MCMK 0.01500000 sec

===== CHANNEL f1 =====
NUC1 ¹³C
P1 10.50 usec
PL1 0.00 dB
SFO1 125.7703143 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 ¹H
PCPD2 67.00 usec
PL2 -6.00 dB
PL12 12.00 dB
PL13 12.00 dB
SFO2 500.1320005 MHz

F2 - Processing parameters
SI 32768
SF 125.7577390 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

10 NMR plot parameters
CX 20.00 cm
CY 11.49 cm
F1P 225.842 ppm
F1 28401.38 Hz
F2P -3.031 ppm
F2 -381.23 Hz
PPMCM 11.44367 ppm/cm

146 ¹H NMR in CDCl₃ at 298 K 84/10/13

Table 3 Entry 4

ppm

7.94246
7.92724
7.63015
7.61663
7.60289
7.50611
7.49109
7.47605
7.44263
7.42253
7.40554
7.38905
7.33364
7.31737
7.30531
7.07617
7.05935
6.50061
6.48342
4.98295
4.97058
4.95854
3.48411
3.47687
3.46336

2.21002

Integral

1.0107
0.7065
1.1078
1.2661
1.1428
1.0589

1.0000

0.5709

0.9347

1.1294

ppm

10

8

6

4

2

0

Current Data Parameters
NAME AZ171
EXPNO 66
PROCNO 1

F2 - Acquisition Parameters
Date_ 20060104
Time 8.05

INSTRUM spect

PROBHD 5 mm BBI 1H-68

PULPROG zg30

TD 32768

SOLVENT CDCl₃

NS 0

DS 0

SWH 10330.578 Hz

FIDRES 0.315264 Hz

AQ 1.5860696 sec

RG 35.9

DN 48.400 usec

DE 6.50 usec

TE 299.9 K

D1 3.00000000 sec

MCREST 0.00000000 sec

MCNRC 0.01500000 sec

===== CHANNEL f1 =====

NUC1 ¹H

P1 10.30 usec

PL1 2.00 dB

SFO1 500.1330895 MHz

F2 - Processing parameters

SI 32768

SF 500.1300000 MHz

WDW EM

SSB 0

LB 0.30 Hz

GB 0

PC 1.00

1D NMR plot parameters

CX 18.00 cm

CY 11.64 cm

F1P 10.876 ppm

F1 5439.38 Hz

F2P -0.445 ppm

F2 -222.58 Hz

PPMK 0.62894 ppm/cm

HZCM 314.55289 Hz/cm

Table 3 Entry 4

146 13CNMR in CDCl3 at 298 K 84/10/13

Current Data Parameters
NAME Az121
EXPNO 57
PROCNO 1

F2 - Acquisition Parameters
Date_ 20050104
Time 8.08
INSTRUM spect
PROBHD 5 mm BBI 1H-BB
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 231
DS 2
SWH 40000.000 Hz
FIDRES 0.610352 Hz
AQ 0.8192625 sec
RG 2298.8
DM 12.500 usec
DE 6.50 usec
TE 294.9 K
D1 3.00000000 sec
D11 0.03000000 sec
DELTA 2.90000010 sec
WDECT 0.00000000 sec
MCMK 0.01500000 sec

===== CHANNEL f1 =====
NUC1 13C
P1 10.50 usec
PL1 0.00 dB
SF01 125.7703143 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 67.00 usec
PL2 -6.00 dB
PL12 12.00 dB
PL13 12.00 dB
SF02 500.1350000 MHz

F2 - Processing Parameters
SI 32768
SF 125.7577390 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

10 NMR plot parameters
CX 20.00 cm
CY 10.86 cm
FAP 215.195 ppm
F1 27062.47 Hz
F2P 1.100 ppm
F2 139.39 Hz
PRNOM 10.70424 ppm/1
HCDM 1346.15381 Hz/1

196 1H NMR in CDCl3 at 298 K 84/10/13

Current Data Parameters

NAME	Az121
EXPNO	58
PROCNO	1

F2 - Acquisition Parameters

Date_	20060103
Time	16.56
INSTRUM	spect
PROBHD	5 mm BBI 1H-BB
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	4
DS	0
SWH	10330.578 Hz
FIDRES	0.315264 Hz
AQ	1.5860696 sec
RG	25.4
DM	48.400 usec
DE	6.50 usec
TE	291.3 K
D1	2.00000000 sec
MDRES1	0.00000000 sec
MDPRK	0.01500000 sec

===== CHANNEL f1 =====

MU1	1H
P1	10.30 usec
PL1	2.00 dB
SFO1	500.130095 MHz

F2 - Processing parameters

SF	32768
SF	500.130000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	18.00 cm
CY	8.51 cm
F1P	11.163 ppm
F1	5582.86 Hz
F2P	0.283 ppm
F2	141.64 Hz
PPMCM	0.50442 ppm/cm
WIND	2700000 Hz/cm

196 13CNMR in CDCl3 at 298 K BA/10/13

- 147.220
- 142.045
- 137.151
- 133.931
- 133.399
- 129.591
- 129.368
- 129.167
- 128.586
- 128.310
- 118.512
- 114.358

- 77.764
- 77.509
- 77.254

- 54.652
- 46.527

Current Data Parameters
NAME AZ121
EXPNO 59
PROCNO 1

F2 - Acquisition Parameters

Date_ 20061003
Time 16:59
INSTRUM spect
PROBHD 5 mm BBI 1H-BB
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 87
DS 2
SWH 40000.000 Hz
FIDRES 0.810392 Hz
AQ 0.819825 sec
RG 2298.8
DM 12.500 usec
DE 6.50 usec
TE 292.2 K
D1 3.00000000 sec
D11 0.03000000 sec
DELTA 2.50000010 sec
WDECT 0.00000000 sec
WDMK 0.01500000 sec

***** CHANNEL f1 *****
NUC1 13C
P1 10.50 usec
PL1 0.00 dB
SFO1 125.7703143 MHz

***** CHANNEL f2 *****
CHOPRG2 waltz16
NUC2 1H
PCPD2 87.00 usec
PL2 -6.00 dB
PL12 12.00 dB
PL13 12.00 dB
SFO2 500.1360005 MHz

F2 - Processing Parameters
SI 32768
SF 125.7577290 MHz
MDM EX
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
CY 10.10 cm
F1P 226.749 ppm
F1 28515.46 Hz
F2P -1.950 ppm
F2 -245.22 Hz
PWCN 11.43496 ppm/cm
HZCN 1439.03418 Hz/cm

T-223 1H NMR in CDCl3 at 298K 84/9/28

Current Data Parameters

NAME Azizi

EXPNO 32

PROCNO 1

F2 - Acquisition Parameters

Date_ 20051220

Time 16:23

INSTRUM spect

PROBHD 5 mm BBI 1H-BB

PULPROG zgpg30

TD 32768

SOLVENT CDCl3

NS 8

DS 0

SWH 10330.578 Hz

FIDRES 0.315264 Hz

AQ 1.5980696 sec

RG 281.5

DE 48.400 usec

TE 293.1 K

D1 2.00000000 sec

MCREST 0.00000000 sec

MCWK 0.01500000 sec

===== CHANNEL f1 =====

NUC1 1H

P1 10.30 usec

PL1 2.00 dB

SFO1 500.1350985 MHz

F2 - Processing parameters

SF 500.1300000 MHz

KOM EM

SSB 0

LB 0.30 Hz

GB 0

PC 1.00

10 NMR plot parameters

CX 18.00 cm

CY 11.64 cm

F1p 10.279 ppm

F1 5140.79 Hz

F2p -0.256 ppm

F2 -128.27 Hz

PPMCK 0.58530 ppm/cm

HZCK 292.72534 Hz/cm