Asymmetric *syn*-selective direct aldol reaction of protected hydroxyacetone catalyzed by primary amino acid derived bifunctional organocatalysts in the presence of water

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Supporting Information

Table of Contents

1. NMR spectra (¹ H and ¹³ C) of organocatalysts	3-10
2. NMR spectra (¹ H and ¹³ C) of aldol addition products	11-33
3. HPLC Chromatograms of aldol addition products	34-53

1. NMR spectra (¹H and ¹³C) of organocatalysts

Organocatalyst 1a: (2S,3S)-N-butyl-3-methylpentane-1,2-diamine. Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz)



Organocatalyst 1j. (S)-2-amino-1-morpholino-3-phenylpropane. Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 125MHz (Bruker Avance 500 MHz)

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Oragnocatalyst 1f. (2*S*,3*S*) 2-amino-3-methyl-1-(pyrrolidin-1-yl)pentane Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 75 MHz (Jeol AL-300).



Oragnocatalyst 1i. (S)-2-amino-3-methyl-1-morpholinobutane. Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 75 MHz (Jeol AL-300).



Oragnocatalyst 1h. (S)-2-amino-4-methyl-1-morpholinopentane. Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).



Oragnocatalyst 1g. (S)-2-amino-3-methyl-1-morpholinopentane. Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 75 MHz (Jeol AL-300).

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Oragnocatalyst 1d. (2*S*,3*S*)-3methyl- \dot{N} , \dot{N} -dioctylpentane-1,2-diamine. Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 75 MHz (Jeol AL-300).

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Oragnocatalyst 1e. (2*S*,3*S*)-2-amino-3-methyl-1-(pyrrolidin-1-yl)pentane. Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 75 MHz (Jeol AL-300).

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2. NMR spectra (¹H and ¹³C) of aldol addition products







(3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(3 -nitrophenyl)butan-2-one (4f). Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz) (3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2 -nitrophenyl)butan-2-one (4g). Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4 -trifluoromethylphenyl)butan-2-one (**4h**). Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(3 -tifluoromethylphenyl)butan-2-one (4i). Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2 -trifluoromethylphenyl)butan-2-one (**4j**). Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4 -cyanophenyl)butan-2-one (4k). Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4 -chlorophenyl)butan-2-one (**4m**). Spectra: ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4 -bromophenyl)butan-2-one (4n). Spectra: ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4 -fluorophenyl)butan-2-one (4I). Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2 -chlorophenyl)butan-2-one (4p). Spectra; ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2⁻-fluorophenyl)butan-2-one (40). ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3R,4S)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4 -methylphenyl)butan-2-one (4t). Spectra: ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2 -methoxyphenyl)butan-2-one (**4u**).

Spectra: $^1\mathrm{H}$ NMR at 400 MHz (Bruker Avance 400 MHz) and $^{13}\mathrm{C}$ at 100 MHz (Bruker Avance 400 MHz).

(3*R*,4*S*)-4-Acetoxy-1,3-bis(*tert*-butyldimethylsiloxy)-4-(4'-nitrophenyl)butan-2-one (4**Z**)

Spectra: 1 H NMR at 400 MHz (Bruker Avance 400 MHz) and 13 C at 100 MHz (Bruker Avance 400 MHz).

(3*R*,4*S*)-4-Acetoxy-1,3-bis(benzyloxy)-4-(4'-nitrophenyl)butan-2-one (4y).

Spectra: 1 H NMR at 400 MHz (Bruker Avance 400 MHz) and 13 C at 100 MHz (Bruker Avance 400 MHz).

(3R,4S)-3-(*tert*-butyldiphenylsilyloxy)-4-hydroxy-4-(4 -nitrophenyl)butan-2-one (4c). Spectra: ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

(3R,4S)-3-(benzyloxy)-4-hydroxy-4-(4 -nitrophenyl)butan-2-one (4e). Spectra: ¹H NMR at 300 MHz (Jeol AL-300) and ¹³C at 100 MHz (Bruker Avance 500 MHz).

3. HPLC Chromatograms of aldol addition products

Peak	Name	Ret. Time	Area %
1	RT33.055	33.055	2.7935
2	RT35.359	35.359	46.5166
3	RT38.766	38.766	3.9958
4	RT48.694	48.694	46.6941

Peak	Name	Ret. Time	Area %
1	RT33.908	33.908	4.1185
2	RT36.429	36.429	1.9602
3	RT39.593	39.593	4.3389
4	RT48.989	48.989	89.5824

Peak	Name	Ret. Time	Area %
1	RT16.760	16.760	49.6854
2	RT17.914	17.914	48.0272
3	RT19.008	19.008	0.4049
4	RT20.364	20.364	1.8825

Peak	Name	Ret. Time	Area %
1	RT16.604	16.604	92.2896
2	RT18.116	18.116	1.3159
3	RT19.080	19.080	4.5392
4	RT20.344	20.344	1.8553

Peak	Name	Ret. Time	Area %
1	RT10.311	10.311	44.4803
2	RT11.660	11.660	43.0224
3	RT13.746	13.746	5.9476
4	RT20.173	20.173	6.5497

Peak	Name	Ret. Time	Area %
1	RT10.279	10.279	82.9391
2	RT11.751	11.751	3.0467
3	RT13.803	13.803	7.2474
4	RT20.300	20.300	6.7668

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Peak	Name	Ret. Time	Area %
1	RT14.674	14.674	44.0190
2	RT16.804	16.804	5.9458
3	RT21.638	21.638	44.1025
4	RT25.227	25.227	5.9327

Peak	Name	Ret. Time	Area %
1	RT15.548	15.548	2.9145
2	RT17.330	17.330	7.8837
3	RT21.851	21.851	83.6665
4	RT25.158	25.158	5.5353

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Peak	Name	Ret. Time	Area %
1	RT4.159	4.159	37.5190
2	RT4.845	4.845	23.8698
3	RT6.164	6.164	38.6112

Peak	Name	Ret. Time	Area %
1	RT4.166	4.166	61.1756
2	RT4.842	4.842	32.9709
3	RT6.242	6.242	5.8535

Peak	Name	Ret. Time	Area %
1	RT9.416	9.416	29.9809
2	RT12.654	12.654	38.6616
3	RT15.636	15.636	31.3575

Peak	Name	Ret. Time	Area %
1	RT9.005	9.005	86.7521
2	RT12.215	12.215	11.2645
3	RT15.267	15.267	1.9834

Peak	Name	Ret. Time	Area %
1	RT18.986	18.986	47.1202
2	RT19.977	19.977	49.1191
3	RT22.991	22.991	1.9918
4	RT24.703	24.703	1.7688

Peak	Name	Ret. Time	Area %
1	RT19.766	19.766	3.4996
2	RT20.839	20.839	85.9012
3	RT24.555	24.555	5.9566
4	RT26.552	26.552	4.6426

Peak	Name	Ret. Time	Area %
1	RT21.208	21.208	45.1515
2	RT22.151	22.151	47.8955
3	RT25.000	25.000	3.2591
4	RT27.094	27.094	3.6939

Peak	Name	Ret. Time	Area %
1	RT20.437	20.437	0.9285
2	RT21.328	21.328	92.4193
3	RT24.240	24.240	3.1067
4	RT26.360	26.360	3.5455

Peak	Name	Ret. Time	Area %
1	RT12.476	12.476	14.8530
2	RT13.323	13.323	42.3449
3	RT13.966	13.966	42.8021

Peak	Name	Ret. Time	Area %
1	RT12.520	12.520	20.7252
2	RT13.385	13.385	3.1170
3	RT14.004	14.004	76.1577

Peak	Name	Ret. Time	Area %
1	RT7.947	7.947	41.0591
2	RT11.043	11.043	8.8968
3	RT12.563	12.563	8.7406
4	RT14.686	14.686	41.3035

Peak	Name	Ret. Time	Area %
1	RT7.749	7.749	84.3458
2	RT10.618	10.618	8.9350
3	RT12.061	12.061	4.7339
4	RT13.997	13.997	1.9854

Peak	Name	Ret. Time	Area %
1	RT19.572	19.572	4.4845
2	RT19.798	19.798	4.2673
3	RT21.260	21.260	45.4395
4	RT22.877	22.877	45.8088

Peak	Name	Ret. Time	Area %
1	RT19.683	19.683	9.5807
2	RT19.978	19.978	5.9301
3	RT21.648	21.648	4.4763
4	RT23.275	23.275	80.0130

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Peak	Name	Ret. Time	Area %
1	RT9.125	9.126	44.8960
2	RT9.959	9.958	10.7918
3	RT11.582	11.578	44.3122

Peak	Name	Ret. Time	Area %
1	RT10.021	10.021	80.5295
2	RT10.228	10.228	15.8376
3	RT11.927	11.927	3.6330

Peak	Name	Ret. Time	Area %
1	RT10.899	10.899	34.4592
2	RT13.866	13.866	14.7458
3	RT14.665	14.665	15.0996
4	RT16.560	16.560	35.6954

Peak	Name	Ret. Time	Area %
1	RT11.116	11.116	81.6695
2	RT14.266	14.266	6.3819
3	RT15.059	15.059	7.7915
4	RT16.981	16.981	4.1570

Peak	Name	Ret. Time	Area %
1	RT14.149	14.149	36.9823
2	RT16.586	16.586	26.0470
3	RT27.486	27.486	36.9707

Peak	Name	Ret. Time	Area %
1	RT13.462	13.462	5.2323
2	RT16.291	16.291	36.3897
3	RT25.982	25.982	58.3781

Peak	Name	Ret. Time	Area %
1	RT15.185	15.183	44.2356
2	RT17.150	17.144	3.5784
3	RT18.021	18.018	3.7358
4	RT20.257	20.256	48.4501

Peak	Name	Ret. Time	Area %
1	RT15.183	15.183	82.5934
2	RT17.451	17.451	4.0181
3	RT17.964	17.964	9.5253
4	RT20.696	20.696	3.8632

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Peak	Name	Ret. Time	Area %
1	RT19.999	19.999	39.9519
2	RT24.449	24.449	19.9536
3	RT29.074	29.074	40.0945

Peak	Name	Ret. Time	Area %
1	RT24.399	24.399	2.8150
2	RT29.389	29.389	19.7909
3	RT33.388	33.388	77.3941

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Peak	Name	Ret. Time	Area %
1	RT48.479	48.479	44.9466
2	RT55.718	55.718	42.9199
3	RT70.492	70.492	12.1335

Peak	Name	Ret. Time	Area %
1	RT46.039	46.039	85.8244
2	RT53.942	53.942	8.4283
3	RT66.184	66.184	5.7473

Peak	Name	Ret. Time	Area %
1	RT21.862	21.862	6.5440
2	RT24.462	24.462	1.7573
3	RT28.845	28.845	4.2531
4	RT30.610	30.610	87.4456

Peak	Name	Ret. Time	Area %
1	RT16.639	16.639	66.8998
2	RT19.796	19.796	15.1993
3	RT22.450	22.450	16.0573
4	RT27.668	27.668	1.8435

Peak	Name	Ret. Time	Area %
1	RT19.995	19.995	41.5099
2	RT23.090	23.090	9.1902
3	RT31.868	31.868	40.4415
4	RT38.561	38.561	8.8584

Peak	Name	Ret. Time	Area %
1	RT18.823	18.823	75.6544
2	RT21.763	21.763	14.9253
3	RT30.395	30.395	5.6871
4	RT36.778	36.778	3.7332

Peak	Name	Ret. Time	Area %
1	RT11.971	11.971	7.5587
2	RT13.982	13.982	7.6894
3	RT20.825	20.825	44.2207
4	RT35.865	35.865	40.5312

Peak	Name	Ret. Time	Area %
1	RT11.707	11.707	4.2054
2	RT13.628	13.628	11.3763
3	RT19.974	19.974	82.3702
4	RT37.127	37.127	2.0480