Supporting Information for the Letter entitled

HMPA Promotes Retro-Aldol Reaction, Resulting in Syn-Selective Addition of Lithiated 1-Naphthylacetonitrile to Aromatic Aldehydes

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General

All reactions were performed in oven-dried (120 °C, overnight) glassware under a nitrogen atmosphere. THF was distilled from Na/benzophenone immediately prior to use. HMPA was distilled from CaH_2 under reduced pressure and stored over molecular sieves. Lithium diisopropylamide (2.0 M in THF), nitriles **1**, **3**, **4** , and aldehydes **5a-j** were purchased from Aldrich. Mesitylacetonitrile **2** was prepared according to the literature method,[1] substituting mono(bromomethyl)mesitylene[2] for the chloro derivative. Full characterization data for aldols *anti*-**6a**,[3] *syn*-**6a**,[3] *anti*-**8a**,[4] *anti*-**9a**,[4] and *anti*-**9h**[4] have been published previously. Selected coupling constant and chemical shift data for the corresponding *syn*-aldols has also been reported.[4] ^{1}H NMR spectra (400 or 300 MHz) and ^{13}C NMR spectra (100.75 or 75.48 MHz) were internally referenced and recorded in $CDCl_3$, unless otherwise noted. Elemental analysis was performed at the Shanghai Institute of Organic Chemistry (Chinese Academy of Sciences, P. R. C.)

Aldol Reaction Procedures

Aldol reactions were typically performed with 1-3 mmol of nitrile, 1.0 equivalents of LDA, and 1.0 - 1.1 equivalents of aldehyde, at a lithium concentration of 0.025 M, as described

previously.[4] For aldol reactions in the presence of HMPA the following modification was made. After deprotonation of the nitrile with LDA at -78 °C, HMPA was added and the temperature maintained at -78 °C for 30 minutes, after which the aldehyde was added. After an additional 30 minutes at -78 °C the reaction was quenched with saturated NH_4Cl (aq.) and worked up as described previously. For most reactions in the absence of HMPA, anti:syn ratios and yield were determined on the crude products by ^1H NMR analysis. For HMPA-mediated reactions, the anti:syn ratio and yields of the pure aldols after chromatography are reported. The two diastereomers generally have very similar R_f values, and for these experiments care was taken not to cause fractionation; in this way the anti:syn selectivities reported accurately reflect the reaction selectivity. A summary of the salient ^1H NMR data for the aldols is provided in Table S1.

Table S1. Summary of Vicinal Coupling Constants and Chemical Shift Data for Aldols[a]

			vicinal coupling constant		α-CN proton	
aldol	Ar	R	J(anti)	J(syn)	δ(anti)	δ(syn)
6a	Ph	Ph	5.8	6.8	4.06	4.14
7a	Mesityl	Ph	9.3[b]	8.8	4.32	4.41
8a	2-Naphth	Ph	5.4	6.8	4.19	4.26
9a	1-Naphth	Ph	4.2	6.1	4.84	5.06
9b	"	1-Naphth	3.9	5.6	5.81	6.09
9c	"	2-Naphth	3.9	6.0	5.28	5.38
9d	"	2-Me-Ph	5.1	6.1	5.35	5.52
9e	"	4-Me-Ph	3.9	6.2	5.12	5.17
9f	"	4-Cl-Ph	4.1	5.9	5.13	5.21
9g	"	4-MeO-Ph	4.1	6.0	5.12	5.18
9h	"	*t*-Bu	<1	na[c]	4.90	na[c]
9i	"	*c*-C_6H_{11}	2.6	8.8	4.97	4.66
9j	"	*i*-Pr	3.0	8.8	4.93	4.59

[a]NMR data measured in $CDCl_3$ at room temperature. [b]*anti*-**7a** coupling constant anomalously high; stereochemistry confirmed by x-ray crystallography. [c]Not available (syn-**9h** not detected).

Aldolate Equilibration Experiment Procedures

Aldolate equilibration experiments were performed by treating a 0.025M solution of the desired aldol in THF at -78 °C with 1.0 equivalents of LDA, in the presence or absence of HMPA. After 30 minutes, the reaction was quenched and worked up as for the aldol reaction, and samples were directly analyzed by ^{1}H NMR. The highly enriched samples of *syn*-**7a**, *syn*-**8a**, *syn*-**9c** used in the aldolate equilibration experiments were obtained by careful chromatographic separation of anti- and syn-diastereomers. Pure *anti*-**7a**, *anti*-**8a** and *anti*-**9c** were obtained by crystallization of anti:syn mixtures obtained from HMPA-free aldol reactions.

(2*RS*, 3*RS*)-3-Hydroxy-3-phenyl-2-(2',4',6'-trimethylphenyl)-propionitrile (*anti*-7a) and (2*RS*, 3*SR*)-3-Hydroxy-3-2-(2',4',6'-trimethylphenyl)-phenylpropanenitrile (*syn*-7a)

Mesitylacetonitrile **2** (336 mg, 2.1 mmol) and benzaldehyde **5a** (206 mg, 1.94 mmol) were combined as above *without addition of HMPA*, to yield after workup and chromatography 289 mg (56%) of predominantly *anti*-**7a** (anti:syn = 88:12). Careful column chromatography (85/15 CH_2Cl_2/hexanes) allowed the pure anti- and syn-diastereomers to be isolated.

anti-**7a**

^{1}H NMR: δ 2.20 (s, v br baseline, 9H), 3.154 (s, br, 1H), 4.322 (d, J = 9.3 Hz, 1H), 5.179 (d, J = 8.3 Hz, 1H), 6.74 (br, 2H), 7.0-7.25 (m, 5H);

^{13}C NMR (50 °C): δ 20.61, 20.76, 41.35, 73.39, 119.31, 125.80, 126.11, 128.20, 128.49, 130.25, 137.10, 138.04, 139.99;

IR (KBr): 3452 (s, br), 2244 (w) cm^{-1};

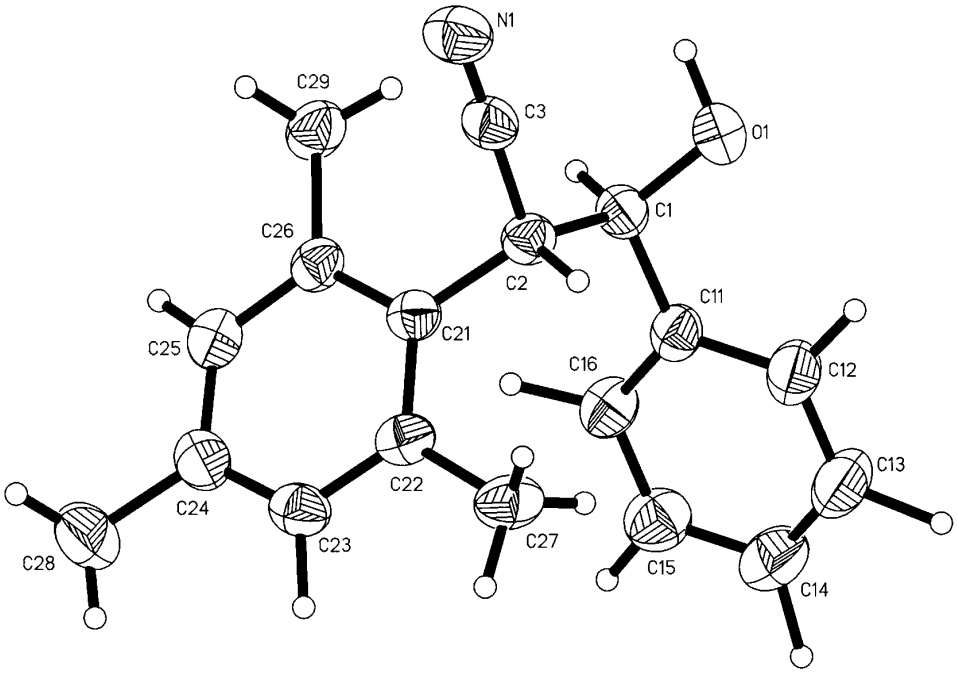
MS (CI$^+$(NH_3)): 283.2 (m+NH_4^+);

mp: 100.3-100.9 °C;

Analysis: Calcd for $C_{18}H_{19}NO$: C, 81.48; H, 7.22; N, 5.28. Found: C, 81.27; H, 7.14; N, 5.34.

The relative stereochemistry of *anti*-**7a** was confirmed by single crystal X-ray crystallography

Ortep of (±)-*anti*-7a



Crystallographic information for this structure has been submitted to *Organic Letters* in CIF format. Tables of the relevant structure factors may be obtained from the author.

syn-**7a**

^{1}H NMR: δ 2.167 (s, 1H), 2.264 (s, 3H), 2.440 (br, 6H), 4.408 (d, J = 8.8 Hz, 1H), 5.070 (d, J = 8.8 Hz, 1H), 6.902 (s, 2H), 7.35-7.50 (m, 5H);

^{13}C NMR: δ 20.76 (br), 40.85, 73.91, 118.19, 125.65, 126.38, 128.72, 128.96, 130 (v br), 137 (v br), 138.36, 140.08;

IR (KBr): 3456 (s, br), 2246 (w) cm^{-1};

MS (CI^{+}(NH_3)): 283.2 (m+NH_4^{+});

mp: 103.7-105.5 °C;

Analysis: Calcd for $C_{18}H_{19}NO$: C, 81.48; H, 7.22; N, 5.28. Found: C, 81.19; H, 7.16; N, 5.20.

(2*RS*,3*SR*)-3-hydroxy-2-(2'-naphthyl)-3-phenylpropionitrile (*syn*-8a)

2-naphthylacetonitrile **3** (505.9 mg, 3.03 mmol) and **5a** (321 mg, 3.03 mmol) were combined as above *with addition of* HMPA to yield after workup and chromatography 677 mg (82%) of predominantly *syn*-aldol (*anti*:*syn* = 36:64). A second reaction was performed and allowed to proceed for 24 hours (instead of 30 minutes) before addition of the quench. This modification improved the anti:syn ratio to 29:71, with an NMR yield of 93%. A syn-enriched sample (anti:syn = 4:96) was prepared by careful chromatography, and was used for the aldolate equilibration experiments, melting point determination, and elemental analysis.

^{1}H NMR ($CDCl_3$): δ 2.33 (d, *J* = 3.3Hz, 1H), 4.31 (d, *J* = 6.6Hz, 1H), 5.10 (dd, *J* = 3.3, 6.6 Hz, 1H), 7.29-7.35 (m, 6H), 7.49-7.55 (m, 2H), 7.71 (s, 1H), 7.78-7.86 (m, 3H);

^{13}C NMR ($CDCl_3$): δ 46.83, 76.12, 118.62, 125.69, 126.51, 126.61, 126.63, 127.60, 127.84, 128.15, 128.40, 128.64, 128.85, 129.14, 132.89, 132.93, 138.68;

MS ($CI^+(NH_3)$): 273 (m);

mp: 106.2-108.6 °C (anti:syn = 4:96)

Analysis: Calcd for $C_{19}H_{15}NO\cdot 0.2H_2O$: C 82.40%, H 5.61%, N 5.06% : Found: C 82.12%, H 5.34%, N 4.94%

(2*RS*,3*SR*)-3-hydroxy-2-(1'-naphthyl)-3-phenylpropionitrile (*syn*-9a)

1-naphthylacetonitrile **4** (170 mg, 1.02 mmol) and **5a** (110 mg, 1.02 mmol) were combined as above for *syn*-**8a** to yield after workup and chromatography 210 mg (76%) of predominantly *syn*-aldol **9a** (*anti*:*syn* = 8:92).

^{1}H NMR ($CDCl_3$): δ 2.38 (broad s, 1H), 5.06 (d, *J* = 6.1 Hz, 1H), 5.23 (d, *J* = 6.1 Hz, 1H), 7.17-7.19 (m, 2H), 7.27-7.42 (m, 5H), 7.53-7.63 (m, 2H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 7.7 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 1H);

^{13}C NMR ($CDCl_3$):δ 43.3, 75.3, 118.8, 122.1, 125.3, 125.8, 126.2, 126.7, 127.1, 127.5, 127.8, 128.3, 128.9, 129.3, 129.4, 130.7, 133.8, 138.7;

MS ($CI^+(NH_3)$): 291 ($m+NH_4^+$);

mp: semi-solid

Anal. (as acetate) Calcd for $C_{21}H_{17}NO_2$: C 79.98%, H 5.43%, N 4.44% : Found: C 79.77%, H 5.34%, N 4.42%

(2*RS*,3*SR*)-3-hydroxy-2-(1'-naphthyl)-3-(1"-naphthyl)-propionitrile (*syn*-9b)

4 (333 mg, 1.99 mmol) and 1-naphthaldehyde **5b** (311 mg, 1.99 mmol) were combined as above for *syn*-**8a** to yield after workup and chromatography 514 mg (80%) of predominantly *syn*-aldol **9b** (*anti*:*syn* = 8:92).

^{1}H NMR ($CDCl_3$): δ 2.53(d, *J* = 3.5 Hz, 1H) , 5.28 (d, *J* = 5.6 Hz, 1H), 6.09 (dd, *J* = 3.5, 5.6 Hz, 1H), 7.15-7.26 (m, 2H), 7.35-7.47 (m, 6H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.72-7.86 (m, 5H);

^{13}C NMR ($CDCl_3$): δ 42.0, 71.3, 119.3, 121.9, 122.0, 124.8, 125.1, 125.1, 125.5, 126.0, 126.1, 126.8, 127.6, 127.7, 128.9, 129.1, 129.3, 129.3, 130.6, 131.0, 133.3, 133.6, 134.7;

MS ($CI^+(NH_3)$): 341 ($m+NH_4^+$);

mp: semi solid

Anal. Calcd for $C_{25}H_{19}NO_2$: C 82.17%, H 5.24%, N 3.83% : Found: : C 82.19%, H 5.24%, N 3.85%

(2*RS*,3*SR*)-3-hydroxy-2-(1'-naphthyl)-3-(2"-naphthyl)-propionitrile (*syn*-9c)

4 (172 mg, 1.03 mmol) and 2-naphthaldehyde **5c** (162 mg, 1.07 mmol) were combined as above for *syn*-**8a** to yield after workup and chromatography 245 mg (73%) of predominantly *syn*-aldol **9c** (*anti*:*syn* = 5:95).

^{1}H NMR ($CDCl_3$): δ 2.53 (s, broad, 1H), 5.14 (d, *J* = 6.0 Hz, 1H), 5.38 (d, *J* = 6.0 Hz, 1H), 7.21-7.25 (m, 1H), 7.29-7.36 (m, 2H), 7.45-7.65 (m, 4H), 7.68 (s, 1H), 7.73-7.87 (m, 4H), 7.94 (d, *J* = 8.3 Hz, 1H), 8.1 (d, *J* = 8.3 Hz, 1H);

^{13}C NMR ($CDCl_3$): δ43.4, 75.4, 118.8, 122.1, 124.1, 125.3, 126.1, 126.2, 126.3, 126.4, 127.1, 127.6, 127.7, 127.8, 128.0, 128.2, 129.3, 129.5, 130.6, 132.8, 133.5, 133.8, 136.2;

MS (CI^+ (NH_3)): 341 (m+NH_4^+);

mp: 110.2-111.5 °C

Anal. Calcd for $C_{25}H_{19}NO_2$: C 82.17.%, H 5.24%, N 3.83% : Found: : C 82.06.%, H 5.24%, N 3.98%

(2*RS*,3*SR*)-3-hydroxy-3-(2'-methylphenyl)-2-(1"-naphthyl)-propionitrile (*syn*-9d)

4 (173 mg, 1.03 mmol) and 2-methylbenzaldehyde **5d** (127 mg, 1.06 mmol) were combined as above for *syn*-**8a** to yield after workup and chromatography 241mg (81%) of predominantly *syn*-aldol **9d** (*anti*:*syn* = 7:93).

^{1}H NMR ($CDCl_3$): δ 1.73 (s, 3H), 2.25 (broad s, 1H), 5.09 (d, *J* = 6.1 Hz, 1H), 5.52 (d, *J* = 6.1 Hz, 1H), 7.02 (d, *J* = 7.4 Hz, 1H), 7.19-7.31 (m, 2H), 7.36-7.43 (m, 2H), 7.51-7.61 (m, 2H), 7.71 (d, *J* = 7.4 Hz, 1H), 7.84-7.91 (m, 2H), 8.03 (d, *J* = 8.3 Hz, 1H);

^{13}C NMR ($CDCl_3$): δ 18.8, 42.5, 70.9, 119.0, 121.9, 125.4, 126.2, 126.2, 126.5, 127.1, 127.4, 127.9, 128.6, 129.2, 129.5, 130.3, 131.0, 133.7, 135.8, 137.4;

MS (CI^+(NH_3)): 305 (m+NH_4^+);

mp: 110.4-115.5 °C

Anal. Calcd for $C_{20}H_{17}NO$: C 83.60%, H 5.96%, N 4.87% : Found: C 83.64%, H 6.01%, N 5.04%

(2*RS*,3*SR*)-3-hydroxy-3-(4'-methylphenyl)-2-(1"-naphthyl)-propionitrile (*syn*-9e)

4 (175 mg, 1.04 mmol) and 4-methylbenzaldehyde **5e** (127 mg, 1.06 mmol) were combined as above for *syn*-**8a** to yield after workup and chromatography 215 mg (72%) of predominantly *syn*-aldol **9e** (*anti*:*syn* = 4:96).

^{1}H NMR ($CDCl_3$): δ 2.33 (s, 3H), 5.03 (d, *J* = 6.2 Hz, 1H), 5.17 (d, *J* = 6.2 Hz, 1H), 7.05-7.11(dd, *J* = 11.4, 8.4 Hz; 4H), 7.31-7.41 (m, 2H), 7.53-7.63 (m, 2H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H);

^{13}C NMR ($CDCl_3$): δ 21.2, 43.4, 75.3, 118.9, 122.2, 125.3, 126.1, 126.6, 127.0, 127.5, 128.0, 129.0, 129.3, 129.4, 130.7, 133.8, 135.8, 138.8;

MS ($CI^+(NH_3)$): 305 ($m+NH_4^+$);

mp: 80.6 – 82 °C

Anal. Calcd for $C_{20}H_{17}NO$: C 83.60%, H 5.96%, N 4.87% : Found C 83.61%, H 6.07%, N 5.03%

(2*RS*,3*SR*)-3-hydroxy-3-(4'-chlorophenyl)-2-(1"-naphthyl)-propionitrile (*syn*-9f)

4 (172 mg, 1.03 mmol) and 4-chlorobenzaldehyde **5f** (148 mg, 1.05 mmol) were combined as above for *syn*-**8a** to yield after workup and chromatography 237 mg (73%) of predominantly *syn*-aldol **9f** (*anti*:*syn* = 8:92).

^{1}H NMR ($CDCl_3$): δ 2.47 (s, broad, 1H), 5.05 (d, *J* = 5.9 Hz, 1H), 5.21 (d, *J* = 5.9 Hz, 1H), 7.07 (d, *J* = 8.5 Hz, 2H), 7.24-7.3 (m, 3H), 7.35-7.4 (dd, *J* = 7.4, 8.0 Hz, 1H), 7.54-7.65 (m, 2H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 1H), 8.02 (d, *J* = 8.3 Hz, 1H

^{13}C NMR ($CDCl_3$): δ43.4, 74.5, 118.5, 121.9, 125.3, 126.3, 127.2, 127.4, 127.5, 128.1, 128.4, 129.4, 129.6, 130.5, 133.8, 134.8, 137.1;

MS ($CI^+(NH_3)$): 325 ($m+NH_4^+$);

mp: 123.8-125.8 °C

Anal. Calcd for $C_{19}H_{14}NOCl$: C 74.15%, H 4.58%, N 4.55% : Found: C 74.28%, H 4.62%, N 4.67%

(2*RS*,3*SR*)-3-hydroxy-3-(4'-methoxyphenyl)-2-(1"-naphthyl)-propionitrile (*syn*-9g)

4 (178mg, 1.06 mmol) and 4-methoxybenzaldehyde **5g** (146mg, 1.07 mmol) were combined as above for *syn*-**8a** to yield after workup and chromatography 220mg (68%) of predominantly *syn*-aldol **9g** (*anti*:*syn* = 4:96).

^{1}H NMR ($CDCl_3$): δ 2.32 (s, broad, 1H), 3.8 (s, 3H), 5.04 (d, *J* = 6.0 Hz, 1H), 5.18 (d, *J* = 6.0 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 7.11 (d, *J* = 8.7 Hz, 2H), 7.31-7.42 (m, 2H), 7.53-7.64 (m, 2H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 1H)

^{13}C NMR ($CDCl_3$): δ 43.4, 55.3, 75.0, 113.7, 118.9, 122.1, 125.3, 126.1, 127.1, 127.5, 127.9, 129.3, 129.4, 130.6, 130.9, 133.8, 160.0;

MS): ($CI^+(NH_3)$) : 321 (m+NH_4^+);

mp: semi-solid

Anal. Calcd for $C_{20}H_{17}NO_2$: C 79.19%, H 5.65%, N 4.62%. Found C 78.86%, H 5.76%, N 4.46

(2*RS*,3*SR*)-3-hydroxy-3-cyclohexyl-2-(1'-naphthyl)-propionitrile (*anti*-9i)

4 (183.3 mg, 1.10 mmol) and cyclohexanecarboxaldehyde **5i** (125.0 mg, 1.11 mmol) were combined as above for *anti*-**7a** to yield after workup and chromatography 265.5 mg (87%) of predominantly *anti*-aldol (*anti*:*syn* = 95:5).

^{1}H NMR ($CDCl_3$): δ 1.00-1.10 (m, 1H), 1.15-1.45 (m, 1H), 1.70-1.95 (m, 5H), 2.05-2.20 (m, 2H), 3.62-3.67 (m, 1H), 4.97 (d, *J* = 2.6 Hz, 1H), 7.50-7.61 (m, 3H), 7.75-7.95 (m, 4H);

^{13}C NMR ($CDCl_3$): δ 25.60, 25.94, 26.20, 29.24, 29.40, 38.97, 41.84, 76.23, 118.58, 121.36, 125.31, 126.02, 126.91, 127.15, 128.85, 129.14, 129.37, 129.60, 133.93;

MS ($CI^+(CH_4)$: 280.1 (m+H);

mp: Semi-solid

Analysis: Calcd for $C_{19}H_{21}NO \cdot 0.3H_2O$: C 80.13%, H 7.64%, N 4.92% : Found: C 79.73%, H 7.29%, N 4.80%

(2*RS*,3*SR*)-3-hydroxy-4-methyl-2-(1'-naphthyl)-pentanenitrile (*anti*-9j)

4 (205.3 mg, 1.23 mmol) and isobutyraldehyde (91.3 mg, 1.27 mmol) were combined as above for *anti*-**7a** to yield after workup and chromatography 182.4 mg (62%) of predominantly *anti*-aldol (*anti*:*syn* = 94:6).

^{1}H NMR ($CDCl_3$): δ 1.11 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.85 (d, *J* = 4.8Hz, 1H), 2.02-2.14 (m, 1H), 3.61-3.66 (m, 1H), 4.92 (d, *J* = 3Hz, 1H), 7.51-7.62 (m, 3H), 7.80-7.90 (m, 4H);

^{13}C NMR ($CDCl_3$): δ 18.80, 19.40, 32.63, 39.51, 77.23, 118.62, 121.46, 125.37, 126.09, 126.98, 127.14, 128.82, 129.27, 129.43, 129.68, 134.00;

MS ($CI^+(CH_4)$): 240.0 (m+H);

mp: 72.6-74.3 °C

Analysis: Calcd for $C_{16}H_{17}NO \cdot 0.1H_2O$: C 79.70%, H 7.19%, N 5.81% : Found: C 79.67%, H 6.94%, N 5.69%

(5*RS*,6*SR*)-5-(1'-naphthyl)-6-(1"-naphthyl)-tetrahydro-1,3-oxazin-2-one (*cis*-10b)

Aldol *syn*-**9b** was converted to the corresponding carbamate by our previously published two-step procedure.[4] Reduction of *syn*-**9b** (295 mg, 0.91 mmol) with $LiAlH_4/AlCl_3$ in diethyl ether, followed by chromatographic purification (2-10% methanol in CH_2Cl_2 + 0.7% conc. NH_4OH), afforded the corresponding *syn*-gamma-amino alcohol (168 mg, 56%). Reaction of the amino alcohol (73 mg, 0.22mmol) and triphosgene (40 mg, 0.60mmol) in the presence of triethylamine in methylene chloride, followed by chromatographic purification (75/25 ethyl acetate/hexane) afforded pure *cis*-**10b** (69 mg, 87%).

^{1}H NMR ($CDCl_3$): δ 4.03 (ddd, *J* = 2.4, 5.5, 11.7 Hz, 1H), 4.14 (ddd, *J* = 2.1, 5.6, 11.7 Hz, 1H), 4.77 (ddd, *J* = 3.7, 5.4, 5.5 Hz, 1H), 6.22 (d, *J* = 3.4 Hz, 1H), 6.80 (d, *J* = 3.5 Hz, 1H), 7.14-7.27 (m, 6H), 7.40-7.51 (m, 4H), 7.69-7.74 (m, 2H), 7.91 (dd, *J* = 4.6, 7.9 Hz, 2H);

^{13}C NMR ($CDCl_3$): δ 35.3, 44.0, 77.0, 121.3, 121.7, 124.5, 124.6, 124.7, 125.0, 125.1, 125.2, 125.9, 128.0, 128.4, 128.6, 128.7, 130.3, 131.4, 132.1, 132.3, 132.8, 133.1, 154.8;

MS ($CI^+(CH_4)$): 354 ($m+H^+$);

mp: 228.5-230.5 °C (dec)

Anal. Calcd for $C_{24}H_{19}NO_2 \bullet 0.2H_2O$: C 80.74%, H 5.48%, N 3.92% : Found: C 80.95%, H 5.48%, N 3.80%

(5*RS*,6*SR*)-5-(1'-naphthyl)-6-(2"-naphthyl)-tetrahydro-1,3-oxazin-2-one (*cis*-10c)

As described above for *cis*-**10b**, reduction of *syn*-**9c** (295 mg, 0.91 mmol) and chromatographic purification afforded the corresponding *syn*-gamma-amino alcohol mg (225 mg, 75%). Reaction of the amino alcohol (72 mg, 0.22mmol) and triphosgene (37 mg, 0.58mmol) and chromatographic purification afforded pure *cis*-**10c** (62 mg, 81%).

^{1}H NMR ($CDCl_3$): δ 3.64-3.7 (m, 1H), 3.80-3.87 (dd, J = 9.8, 10.6 Hz, 1H), 4.61 (ddd, J = 4.1, 4.7, 9.8 Hz, 1H), 5.70 (broad s, 1H), 6.11 (d, J = 4.1 Hz, 1H), 6.51 (dd, J = 1.8, 8.6 Hz, 1H), 6.71 (d, J = 7.2 Hz, 1H), 7.18 (dd, J = 7.6, 7.9 Hz, 1H), 7.38 (s, 1H), 7.41-7.47 (m, 2H), 7.49 (d, J =8.7 Hz, 1H), 7.51-7.61 (m, 2H), 7.63-7.77 (m, 2H), 7.78 (d, J =8.3 Hz, 1H), 7.92 (d, J = 7.8 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H);

^{13}CNMR ($CDCl_3$): δ 37.0, 41.4, 81.0, 122.2, 124.2, 125.0, 125.1, 125.4, 125.9, 126.2, 126.9, 127.1, 127.5, 128.0, 128.4, 129.3, 131.2, 131.5, 132.6, 132.8, 133.3, 133.8, 154.3

MS ($CI^+(CH_4)$):354 ($m+H^+$);

mp: 223.1-229.5 °C (dec)

Anal. Calcd for $C_{24}H_{19}NO_2$: C 81.56%, H 5.42%, N 3.96% : Found C 81.48%, H 5.44%, N 3.91%

References

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