Amine-Catalyzed Direct Aldol Additions

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Experimental Procedures and Characterization of the Products

Aldehydes were freshly distilled before use. ^1H -NMR und ^{13}C -NMR spectra were recorded at 300 and 75 MHz in CDCl_3 (if not stated otherwise), respectively using a AC-300 spectrometer. Chemical shifts are given in ppm. Purification of products was accomplished by flash chromatography. Thin layer chromatography was performed with Merck Silica Gel 60 F₂₅₄ TLC plates.

General Procedure of aldol addition:

In a typical experiment 0.5 mmol of tertiary amine was carefully added to a mixture of 10 mmol of corresponding ketones and 20 mmol aldehyde at 0°C. The reaction mixture was stirred at room temperature and monitored by TLC. After completion the reaction-mixture was absorbed by Celite® and purified by column chromatography.

Using eluent hexane / ethylacetate 8/2 for compounds **2a-2d** and

hexane / ethylacetate 6/4 for compounds **3a-c** and **4**

rac-(3*S*,4*R*)-3,4-Dihydroxy-5-methylhexan-2-one (*syn*-**2a**) ^{1,2}

¹H-NMR (CDCl₃, 300 MHz): δ = 4.11-4.16 (1H, m), 3.89 (1H, d, *J* = 4.2, OH), 3.38-3.45 (1H, m), 2.85 (1H, d, *J* = 9.4, OH), 2.14 (3H, s), 1.78 (1H, ds, *J* = 6.6, 8.9), 0.93 (3H, d, *J* = 6.8), 0.87 (3H, d, *J* = 6.8).

¹³C-NMR (75 MHz): δ = 209.2, 77.6, 77.2, 31.1, 25.0, 19.0, 18.8.

rac-(3*R*,4*R*)-3,4-Dihydroxy-5-methylhexan-2-one (*anti*-**2a**)^{1,2}

¹H-NMR (CDCl₃, 300 MHz): δ = 4.22 (1H, m), 3.77 (m, 1H), 2.23 (3H, s), 1.81-1.98 (1H, m), 1.03 (3H, d, *J* = 6.7), 0.97 (3H, d, *J* = 6.7).

¹³C-NMR (75 MHz): δ = 210.7, 78.3, 77.6, 29.6, 27.4, 19.2, 16.7.

rac-(3*S*,4*R*)-3,4-Dihydroxy-6-phenylhexan-2-one (*syn*-**2b**)^{3,4,5}

¹H-NMR (CDCl₃, 300 MHz): δ = 7.1-7.4 (5H, m), 3.82-4.10 (3H, m), 2.60-2.98 (3H, m), 2.21 (3H, s), 1.92-2.2 (2H, m),

¹³C-NMR (75 MHz): δ = 208.4, 141.2, 128.3, 128.2, 125.8, 79.3, 70.9, 35.4, 31.8, 25.3.

X-ray-structure analysis of *syn-2b* ⁶

rac-(3*S*,4*R*)-3,4-Dihydroxy-6-phenylhexan-2-one (*anti-2b*) ^{5,6,7}

¹H-NMR (CDCl₃, 300 MHz): δ = 7.12-7.39 (5H, m), 4.25 (1H, m), 3.82-4.02 (1H, m), 2.55-2.93 (2H, m), 2.18-2.41 (1H, m), 2.12 (3H, s), 1.45-1.62 (1H, m).

¹³C-NMR (75 MHz): δ = 208.4, 141.3, 128.3, 128.2, 125.8, 80.5, 71.5, 33.17, 31.5, 26.6.

rac-(3*S*,4*R*)-4-cyclohexyl-3,4-dihydroxybutan-2-one (*syn*-**2c**)^{7,8}

¹H-NMR (CDCl₃, 300 MHz): δ = 4.05 (dd, *J* = 4.9, 1.3 Hz, 1H), 3.81 (d, *J* = 4.9, 1H), 3.40 (m, 1H), 2.87 (d, *J* = 9.1, 1H), 2.04 (s, 3H), 1.82-1.93 (m, 1H), 1.34-1.67 (m, 6H), 0.72-1.18 (m, 4H).

¹³C-NMR (75 MHz): δ = 209.3, 77.1, 75.9, 40.0, 29.2, 28.7, 25.9, 25.5, 25.4, 21.9.

rac-(3*S*,4*S*)-4-cyclohexyl-3,4-dihydroxybutan-2-one (*anti*-**2c**)

¹H-NMR (CDCl₃, 300 MHz): δ = 4.22 (m, 1H), 3.78 (m, 1H), 3.55 (m, 1H), 2.22 (s, 3H), 1.98-2.09 (m, 1H), 1.62-1.78 (m, 6H), 1.18-1.28 (m, 4H).

¹³C-NMR (75 MHz): δ = 209.0, 77.2, 76.2, 40.7, 29.5, 29.1, 26.2, 25.8, 25.7, 25.0.

hemiketal of *rac*-(3*S*,4*R*)-4-cyclohexyl-3,4-dihydroxybutan-2-one

¹H-NMR (CDCl₃, 300 MHz): δ = 4.75 (1H, d, *J* = 5.9, CH), 3.61 (1H, dd, *J* = 1.1, 9.6, CH), 3.17 (1H, dd, *J* = 1.1, 11.5, CH), 2.93 (1H, d, *J* = 11.5, OH), 2.84 (1H, s, OH), 1.96-1.58 (14 H, m, 2 CH, 6 CH₂), 1.39 (3H, s, CH₃), 1.32-0.84 (8H, m, 4 CH₂).

¹³C-NMR (75 MHz): δ = 98.6, 98.0, 80.7, 68.6, 43.3, 38.7, 30.8, 28.8, 28.6, 28.5, 27.8, 27.7, 27.0, 26.9, 26.7.

HRMS (ESI) calc. For C₃₄H₆₀O₈ + Na: 619.4180. found: 619.4191.

rac-(3*S*,4*R*)-3,4-dihydroxy-4-phenylbutanon (*syn*-**2d**)⁹

¹H-NMR (CDCl₃, 300 MHz): δ = 7.32-7.45 (5H, m), 5.03 (1H, dd, *J* = 2.5, 6.2), 4.33 (1H, d, *J* = 6.4), 4.25-4.30 (2H, m), 2.18 (3H, s).

¹³C-NMR (75 MHz): δ = 26.3, 73.9, 80.6, 128.1, 128.3, 128.5, 139.9, 208.1.

rac-(3*S*,4*S*)-3,4-dihydroxy-4-phenylbutanon (*anti*-**2d**)

¹H-NMR (CDCl₃, 300 MHz): δ = 7.32-7.45 (5H, m), 4.97 (1H, dd, J = 4.4, 4.5), 4.48 (1H, d, J = 4.5), 4.44 (1H, dd, J = 4.4, 5.8), 4.36 (1H, d, J = 5.8), 1.92 (3H, s).

¹³C-NMR (75 MHz): δ = 27.6, 74.8, 81.0, 126.1, 126.2, 126.5, 139.0, 208.2.

rac-4-Hydroxymethyl-(2*R*,6*R*)-2,6-diisopropyl-(1,3)dioxane-(4*S*,5*S*)-4,5-diol (**3a**)

m.p.: 79°C decomposition

¹H-NMR (CDCl₃, 300 MHz): δ = 4.88 (1H, d, J = 5.3, CH), 3.85 (1H, d, J = 11.7, CH₂), 3.58 (1H, d, J = 11.7, CH₂), 3.53 (1H, dd, J = 1.0, 10.2, CH), 3.42 (1H, d, J = 1.0, CH), 1.91 (1H, ds, J = 6.6, 10.2, CH), 1.79 (1H, ds, J = 5.3, 6.8, CH), 1.1 (3H, d, J = 6.6, CH₃), 0.95 (3H, d, J = 6.6, CH₃), 0.92 (3H, d, J = 6.8, CH₃), 0.89 (3H, d, J = 6.8, CH₃).

¹³C-NMR (75 MHz): δ = 99.1, 96.3, 81.0, 66.7, 66.1, 32.3, 27.9, 17.4, 17.3, 16.6.

HRMS (ESI) calc. For C₁₁H₂₂O₅ + Na: 257.1359. found: 257.1363.

rac-4-Hydroxymethyl-(2*R*,6*R*)-2,6-diphenethyl-(1,3)dioxane-(4*S*,5*S*)-4,5-diol (**3b**)

m.p.: 103°C decomposition

¹H-NMR (D₆-DMSO, 300 MHz): δ = 7.35-7.12 (10H, m, CH_{ar}), 5.61 (1H, s, OH), 5.01 (1H, dd, *J* = 1.1, 5.7, 5.7, CH), 4.62 (1H, dd, *J* = 5.9, 6.3, OH), 4.52 (1H, d, *J* = 8.5, OH), 3.83 (1H, ddd, *J* = 1.1, 5.3, 7.9, CH), 3.59 (1H, dd, *J* = 6.8, 10.8, CH₂), 3.33 (1H, dd, *J* = 5.7, 10.8, CH₂), 3.1 (1H, dd, *J* = 1.1, 8.5, CH), 2.72-2.58 (4H, m, 2 CH₂), 1.98-1.62 (4H, m, 2 CH₂).

¹³C-NMR (75 MHz) : δ = 142.5, 142.1, 128.8, 128.8, 126.2, 126.2, 97.3, 93.4, 74.4, 66.5, 64.9, 36.1, 32.8, 31.1, 30.4.

calcd. For C₂₁H₂₆O₅: C: 70.37, H 7.31; found C: 69.71, H 7.37

HRMS (ESI) calc. For C₂₁H₂₆O₅: 358.17802. found: 358.

rac-(2*R*, 6*R*)-2,6-Dicyclohexyl-4-hydroxymethyl-(1,3)dioxane-(4*S*,5*S*)-4,5-diol (**3c**)

m.p.: 103°C decomposition

X-ray-structure analysis of **3c**:

¹H-NMR (D₆-DMSO, 300 MHz): δ = 4.61 (1H, d, J = 6.4, CH), 3.51 (1H, d, J = 11.2, CH₂), 3.38 (1H, dd, J = 0.7, 9.4, CH), 3.19 (1H, d, J = 11.2, CH₂), 3.19 (1H, d, J = 0.7, CH), 1.97 – 0.70 (22H, m, 2 CH, 10 CH₂).

¹³C-NMR (75 MHz): δ = 97.0, 97.0, 79.6, 64.9, 64.3, 41.9, 37.1, 29.6, 27.9, 27.5, 27.4, 26.7, 26.5, 25.8, 25.8, 25.7.

HRMS (ESI) calc. for C₁₇H₃₀O₅: 314.20932. found: 314.20933

rac-(3*S*,4*R*)-1.3.4-Trihydroxy-6-phenyl-hexan-2-one (*syn*-**4b**)¹⁰

m.p.: 52-54 °C

¹H-NMR (CDCl₃, 300 MHz): δ = 7.32-7.23 (5H, m, CH_{ar}), 4.52 (1H, d, *J* = 19.3, CH₂), 4.36 (1H, d, *J* = 16.3, CH₂), 4.18 (1H, d, *J* = 1.9, CH), 3.84 (1H, ddd, *J* = 1.9, 5.5.3, 7.7), 2.73-2.48 (2H, m, CH₂), 1.93-1.75 (2H, m, CH₂).

¹³C-NMR (75 MHz): δ = 212.1, 141.2, 128.4, 128.3, 128.3, 126.0, 77.9, 71.7, 66.4, 34.7, 31.8.

HRMS (ESI) calc. for C₁₂H₁₆O₄: 224.10486. found: 224.10484.

(S)-2-(tert-Butyldimethylsilyloxy)propanal (5) ¹¹

TBDMS-protected lactaldehyde **5** was prepared by formation of the TBDMS-ether of (S)-ethyl lactate followed by reduction with DIBAL.

¹H NMR (CDCl₃) δ = 0.10 (s, 6 H), 0.92 (s, 9 H), 1.27 (d, *J* = 7.0 Hz, 3H), 4.09 (dq, *J* = 1.3, 7.0 Hz, 1H), 9.60 (d, *J* = 1.3 Hz, 1H).

2.6-Bis-(1-(tertbutyl-dimethylsilyloxy)-ethyl)-4-hydroxymethyl-(1.3)dioxane-4.5-diol

Acetal was isolated as a byproduct yields < 3%.

¹H-NMR (CDCl₃, 300 MHz): δ = 4.85 (1H, d, *J* = 4.3, CH), 3.97 (1H, m, CH), 3.82-3.69 (4H, m, 3 CH, CH₂), 1.17 (3H, d, *J* = 6.2, CH₃), 1.16 (3H, d, *J* = 6.2, CH₃), 0.87 (18H, s, 6 CH₃), 0.07 (3H, s, CH₃), 0.06 (3H, s, CH₃), 0.05 (6H, s, 2 CH₃).

¹³C-NMR (75 MHz): δ = 97.5, 96.2, 80.2, 69.6, 68.7, 66.8, 66.2, 25.8, 18.0, -4.7, -4.7.

HRMS (ESI) calc. for C₂₁H₄₆O₇Si₂+H: 467.2860. found: 467.2861.

calc. for C₂₁H₄₆O₇Si₂+Na: 489.2674. found: 489.2671

(5S)-5-(*tert*-Butyl-dimethylsilyloxy)-(3S,4S)-1,3,4-trihydroxy-hexan-2-one (6) and
(5S)-5-(*tert*-Butyl-dimethylsilyloxy)-(3R,4R)-1,3,4-trihydroxy-hexan-2-one (7)

The main fraction (~ 95%) obtained after column chromatography consists of an inseparable mixture (1:1) of (3S, 4S)-ketone **6** and (3R, 4R)-ketone **7**.

¹H-NMR (CDCl₃, 300 MHz): δ = 4.58 (1H, d, *J* = 19.3, CH₂), 4.57 (1H, d, *J* = 19.2, CH₂), 4.54 (1H, m, CH), 4.44 (1H, d, *J* = 19.8, CH₂), 4.44 (1H, d, *J* = 19.6, CH₂), 4.25 (1H, d, *J* = 2.5, CH₂), 4.05-3.91 (2H, m, 2 CH), 3.65 (1H, dd, *J* = 2.6, 5.7, CH), 3.64 (1H, dd, *J* = 1.1, 5.7), 1.24 (3H, d, *J* = 7.0, CH₃), 1.21 (3H, d, *J* = 7.0, CH₃), 0.88 (9H, s, 3 CH₃), 0.88 (9H, s, 3 CH₃), 0.09 (12 H, s, 4 CH₃).

¹³C-NMR (75 MHz): δ = 212.3, 211.3, 75.8, 75.6, 75.5, 75.4, 70.3, 69.4, 66.7, 66.6, 25.7, 25.7, 17.9, 17.8, -4.2, -4.5, -4.9, -5.2.

HRMS (ESI) calc. for C₁₂H₂₆O₅Si+H: 279.1622. found: 279.1621.
 C₁₂H₂₆O₅Si+NH₄ 296.1888. found: 296.1886.
 C₁₂H₂₆O₅Si+Na: 301.1441 found: 301.1442.
 C₁₂H₂₆O₅Si+K: 317.1180 found: 317.1181

1-Mosher-ester of mixture of **6** and **7**:

¹H-NMR (CDCl₃, 300 MHz): δ = 7.63-7.32 (10 H, m, 10 CH), 5.29 (1H, d, *J* = 17.6, CH₂), 5.18 (1H, d, *J* = 17.6, CH₂), 4.97 (1H, d, *J* = 17.0, CH₂), 4.87 (1H, d, *J* = 17.0, CH₂), 4.79 (1H, d, *J* = 1.3, CH), 4.58 (1H, d, *J* = 1.3, CH), 4.42-4.06 (4H, m, 4 CH), 3.68 (3H, q, *J* = 1.3, OMe), 3.67 (3H, q, *J* = 1.3, OMe), 1.28 (3H, d, *J* = 6.2, CH₃), 1.25 (3H, d, *J* = 6.4, CH₃), 0.92 (9 H, s, 3 CH₃), 0.91 (9 H, s, 3 CH₃), 0.09 (6H, s, 2CH₃), 0.08 (6H, s, 2 CH₃).

Deprotection of TBDMS-group of **6** and **7** was achieved by TBAF in THF. The resulting 1:1 mixture of rhamnulofuranose **8** and deoxy-sorbose **9** could be successfully separated by column chromatography (CHCl₃/MeOH/ H₂O – 5.5 / 3.5 / 0.5). These conditions of separation by chromatography were adopted from a separation of deoxy-D-fructose and deoxy-L-sorbose.¹⁵

β -L-Rhamnulofuranose (8)¹²

$[\alpha]_D^{25} = + 5.8^\circ$ ($c = 0.4$ g/100ml, DMSO)

major anomer:

$^1\text{H-NMR}$ (D_2O , 300 MHz): $\delta = 3.95$ (1H, d, $J = 8.1$, CH), 3.77 (1H, dd, $J = 8.1$, CH), 3.68 (dq, $J = 6.2, 8.1$, CH), 3.45 (1H, d, $J = 12.1$, CH), 3.37 (1H, d, $J = 12.1$, CH), 1.21 (3H, d, $J = 6.2$, CH_3).

$^{13}\text{C-NMR}$ (75 MHz): $\delta = 102.1, 80.4, 77.4, 76.2, 63.8, 20.0$.

minor anomer:

$^1\text{H-NMR}$ (D_2O , 300 MHz): $\delta = 3.61$ (1H, dd, $J = 6.0, 7.7$), 3.52 (1H, d, $J = 13.2$, CH), 3.50 (1H, d, $J = 13.2$, CH), 1.09 (3H, d, $J = 6.0$, CH_3).

$^{13}\text{C-NMR}$ (75 MHz): $\delta = 104.9, 83.5, 82.2, 76.1, 63.9, 18.4$.

α -6-Deoxy-L-sorbose (9)^{13,14,15,16}

For comments to assignment of α - and β -anomers see reference 12.

$[\alpha]_D^{25} = + 2.5^\circ$ ($c = 0.7$ g/100ml, DMSO)

major anomer:

$^1\text{H-NMR}$ (D_2O , 300 MHz): $\delta = 4.29$ (1H, dq, $J = 5.3, 6.6$, CH), 4.09 (1H, dd, $J = 4.5, 5.3$, CH), 3.96 (1H, d, $J = 4.5$, CH), 3.50 (1H, d, $J = 12.1$, CH_2), 3.43 (1H, d, $J = 12.1$, CH_2), 1.07 (3H, d, $J = 6.6$, CH_3).

$^{13}\text{C-NMR}$ (75 MHz): $\delta = 104.5, 79.3, 79.2, 77.5, 66.0, 16.6$.

minor

¹H-NMR (D₂O, 300 MHz): δ = 4.06 (1H, d, J = 2.85), 4.02 (1H, dd, J = 2.85, 4.75), 1.18 (3H, d, J = 6.6)

¹³C-NMR (75 MHz): δ = 109.4, 82.0, 80.7, 77.7, 65.4, 17.5.

2,3-O-isopropylidene-D-glyceraldehyde (10)¹⁷

The protected glyceraldehydes was prepared by oxidative cleavage of 1,2:5,6-di-O-isopropylidene-D-mannitol¹⁸ with NaIO₄.

¹H NMR (CDCl₃) δ = 1.49 (s, 3H), 1.54 (s, 3H), 4.15 (m, 2H), 4.39 (m, 1H), 9.73 (d, 1H, J = 1.9 Hz, 1H).

5,6-Isopropylidene-D-fructose¹⁹

$[\alpha]_D^{25} = + 11.2^\circ$ (c = 8.3 g /100 ml, acetone)

¹H-NMR (D₆-acetone, 300 MHz): δ = 4.58-3.85 (7H, m, 3 CH, 2 CH₂), 1.37 (3H, s, CH₃), 1.28 (3H, s, CH₃).

¹³C-NMR (75 MHz) δ = 212.4, 100.9, 75.6, 75.0, 73.0, 66.8, 66.6, 24.8, 24.8.

HRMS (ESI) calc. for C₉H₁₆O₆+Na: 243.0836. found: 243.0836.

1-Mosher-ester of 5,6-isopropylidene-D-fructose:

¹H-NMR (CDCl₃, 300 MHz): δ = 7.58-7.52 (2H, m, 2 CH), 7.39-7.33 (3H, m, 3 CH), 5.19 (1H, d, J = 17.0, CH₂), 5.00 (1H, d, J = 17.0, CH₂), 4.44 (1H, d, J = 1.9, CH), 4.14-3.84 (7H, m, 2 CH, 1CH₂, 2 OH), 3.57 (3H, q, J = 1.3, OMe), 1.37 (3H, s, CH₃), 1.29 (3H, s, CH₃).

Removal of isopropylidene-group was achieved by DOWEX 50WX8 in methanol. Evaporation of solvent and subsequent purification of the resulting residue by column chromatography yield D-fructose in 71 %.

β -D-Fructose (11)

The assignment of the β -D-structure of fructose as the major anomer is based on comparison of corresponding signals in ^{13}C NMR spectra with those given in literature [20,21,22,23].

$$[\alpha]_{\text{D}}^{25} = -92.2^{\circ} (c = 1.3 \text{ g/100ml, H}_2\text{O})$$

$^1\text{H-NMR}$ (D_2O , 300MHz): $\delta = 3.41\text{--}4.00$ (7H, m, 3CH, 2CH₂).

$^{13}\text{C-NMR}$ (75 MHz): major anomer: $\delta = 99.1, 70.7, 70.2, 68.6, 64.9, 64.4$.
minor anomer: $\delta = 102.5, 81.7, 76.4, 75.4, 63.6, 63.4$.

Proof of configuration for compounds 3a-c

$\text{calc. } \phi = 60^\circ \rightarrow {}^3J_{ab} = 2\dots 5 \text{ Hz.}$ observed:

3a = 1.0 Hz
3b = 1.1 Hz
3c = 0.7 Hz

$$\text{calc } \phi = 180^\circ \rightarrow {}^3J_{ab} = 7 \dots 12 \text{ Hz}$$

Determination of diastereoselectivity of compounds **2a-d**

The diastereomer ratios of compounds **2a-d** were determined by integration of singletts (for -CO-CH₃) in the ¹H NMR spectra:

2a: 2.14 (syn), 2.23 (anti); **2b**: 2.21 (syn), 2.12(anti); **2c**: 2.04 (syn), 2.22 (anti); **2d**: 2.18 (syn), 1.92 (anti).

Proposed transition state explaining the *syn*-selectivity of ketales **3a-c**

The axial-position of the 5-OH group is fixed by hydrogen bonds to ring-oxygen atoms (1 and 3). Thus *syn*-configuration is provided.

In the case of equatorial configured 5-OH-group no hydrogen bonds are possible.

1.3-diaxial interactions

References

- ¹ Notz, W.; List, B. *J. Am. Chem. Soc.* **2000**, *122*, 7386-7387.
- ² Schetter, B.; Stosiek, C.; Ziemer, B.; Mahrwald, R. *Appl. Organometallic Chem.* **2007**, *21*, 139-145.
- ³ Miyoshi, N.; Fukuma, T.; Wada, M. *Chem. Letters* **1995**, 999-1000.
- ⁴ Miyoshi, N.; Takeuchi, S.; Ohgo, Y. *Chem. Letters* **1993**, 2129-2132.
- ⁵ Mukaiyama, T.; Tsuzuki, R.; Kato, J. *Chem. Letters* **1983**, 1825-1828.
- ⁶ Crystallographic data of compound *syn-2b* (CCDC 642381) and **3c** (CCDC 642382) have been deposited at the Cambridge Crystal Data Centre. This material can be obtained upon request to CCDC, 12 Union Road, Cambridge, 1EZ, UK (<http://www.ccdc.cam.ac.uk> email: deposit@ccdc.cam.ac.uk). The structure was refined with SHELX97 (Sheldrick, G.M.; programme for crystal structure refinement, Universität Göttingen.)
- ⁷ Sakthivel, K.; Notz, W.; Bui, T.; Barbas III, C.F. *J. Am. Chem. Soc.* **2001**, *123*, 5260-5267.
- ⁸ Chowdari, N. S.; Ramachary, D. B.; Barbas, C. F., III. *Synlett* **2003**, 1906-1909.
- ⁹ Walsh, P. J.; Sharpless, K. B. *Synlett* **1993**, 605
- ¹⁰ Fessner, W. D. *Ger.* **1992**, DE 4111971 C1.
- ¹¹ Hiram, M.; Shigemoto, T.; Ito, S. *J. Org. Chem.* **1987**, *52*, 3342-3346.
- ¹² Liu, K. K. C.; Kajimoto, T.; Chen, L.; Zhong, Z.; Ichikawa, Y.; Wong, C.-H. *J. Org. Chem.* **1991**, *56*, 6280-6389.
- ¹³ Wong, C.-H.; Mazenod, F. P.; Whitesides, G. M. *J. Org. Chem.* **1983**, *48*, 3493-3497.
- ¹⁴ Hecquet, L.; Bolte, J.; Demuynck, C. *Tetrahedron* **1996**, *52*, 8223-8232.
- ¹⁵ Hecquet, L.; Bolte, J.; Demuynck, C. *Tetrahedron* **1994**, *50*, 8677-84.
- ¹⁶ Peters, J.; Brockamp, H.-P.; Minuth, T.; Grothus, M.; Steigel, A.; Kula, M.-R., Elling, L. *Tetrahedron: Asym.* **1983**, *4*, 1173-1182.
- ¹⁷ Niu, C. S.; Petterson, M. J.; Miller, M. J. *J. Org. Chem.* **1996**, *61*, 1014-1022.
- ¹⁸ Dumont, R.; Pfander, H. *Helv. Chim. Acta* **1983**, *66*, 814-823.
- ¹⁹ Cordova, A.; Notz, W.; Barbas, C. F., III. *Chem. Comm.* **2002**, 3024-3025.
- ²⁰ Lawrence Jr., Q.; Gray, G. R. *Biochemistry* **1974**, *13*, 146-153.

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- ²¹ Thompson, J.; Robrish, S. A.; Pikis, A.; Brust, A.; Lichtenthaler, F. W. *Carb. Res.* **2001**, 331, 149-161.
- ²² Funcke, W.; Sonntag, von C.; Triantaphylides, C. *Carb. Res.* **1979**, 75, 305-309.
- ²³ Dais, P.; Perlin, A. S. *Carb. Res.* **1987**, 169, 159-69.