Supporting Information for

Diastereoocontrol in the Synthesis of 2,3,4-Trisubstituted Pyrrolidines and Tetrahydrofurans via a Pd(II)-Catalyzed Three-Component Coupling Reaction

Sandeep Raiker, Benoy Kumar Pal and Helena C. Malinakova*

Department of Chemistry, University of Kansas, 1251 Wescoe Hall Drive, Lawrence, Kansas 66045
and Center of Excellence in Chemical Methodologies and Library Development, University of Kansas, 2034 Becker Drive, Shankel Structural Biology Center, West Campus, Lawrence, Kansas 66047

*Corresponding author Tel.: 1 785-864-4743; fax: 1 785-864-5396; E-mail: hmalina@ku.edu.

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1. Analytical data for amines 5 (a, b, d and e) and the monotosylated diol:

(±)-(1R,2R)-1-amino-2-hexyl-1-(p-methoxycarbonylphenyl)-3-(p-methoxycarbonylphenyl)-3-butene (5a). \( R_f = 0.35 \) (MeOH/DCM 1 : 19); \(^1\)H NMR (500 MHz, CDCl₃) \( \delta \) 7.99 (d, \( J = 7.0 \) Hz, 2H), 7.97 (d, \( J = 8.0 \) Hz, 2H), 7.48 (d, \( J = 8.5 \) Hz, 2H), 7.42 (d, \( J = 8.5 \) Hz, 2H), 5.52 (s, 1H), 5.29 (s, 1H), 4.00 (d, \( J = 9.0 \) Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 2.83-2.72 (m, 1H), 2.29 (s br, 2H), 1.34-1.01 (m, 10H), 0.77 (t, \( J = 7.0 \) Hz, 3H); \(^{13}\)C NMR (125 MHz, CDCl₃) \( \delta \) 13.9, 22.5, 27.1, 29.2, 29.7, 31.6, 32.4, 52.1, 52.7, 60.3, 116.2, 126.8 (2C), 127.5 (2C), 128.9, 129.2, 129.6 (2C), 129.7 (2C), 148.0, 149.6, 150.2, 166.92, 166.98; IR (neat, cm\(^{-1}\)) 3377, 3336, 1724, 1716;

(±)-(1R,2R)-1-amino-1-(p-nitrophenyl)-2-(hexyl)-3-(p-methoxycarbonylphenyl)-3-butene (5b). \( R_f = 0.40 \) (MeOH/DCM 1 : 19); \(^1\)H NMR (500 MHz, CDCl₃) \( \delta \) 8.15 (d, \( J = 8.5 \) Hz, 2H), 7.99 (d, \( J = 8.5 \) Hz, 2H), 7.52 (d, \( J = 8.5 \) Hz, 2H), 7.47 (d, \( J = 8.5 \) Hz, 2H), 5.54 (s, 1H), 5.29 (s, 1H), 4.08 (d, \( J = 8.5 \) Hz, 1H), 3.92 (s, 3H), 2.79 (td, \( J = 9.0 \) Hz, 3.0 Hz, 1H), 1.90-1.69 (m, 2H), 1.34-1.05 (m, 10H), 0.78 (t, \( J = 7.0 \) Hz, 3H); \(^{13}\)C NMR (125 MHz, CDCl₃) \( \delta \) 13.9, 22.5, 27.1, 29.2, 31.6, 32.2, 52.2, 52.6, 59.9, 116.5, 123.5 (2C), 126.8 (2C), 128.4 (2C), 129.1, 129.7 (2C), 147.2, 147.7, 149.6, 151.8, 166.8; IR (neat, cm\(^{-1}\)) 3380, 3321, 1720;

(±)-(1R,2R)-1-amino-1-(p-methoxycarbonylphenyl)-2-(2-ethyl-1-hexyl)-3-(2-naphthyl)-3-butene amine (5c). Amine 5c was not characterized.

(±)-(1R,2R)-1-amino-1-(p-methoxycarbonylphenyl)-2-(2-ethyl-1-hexyl)-3-(p-methoxycarbonylphenyl)-3-butene (5d): \( R_f = 0.30 \) (MeOH/DCM 1 : 19); \(^1\)H NMR (500 MHz, CDCl₃): d = 7.99 (t, \( J = 8.0 \) Hz, 4 H); 7.52 (dd, \( J = 8.5 \) Hz, 2.0 Hz, 2 H), 7.45 (dd, \( J = 8.0 \) Hz, 1.5 Hz, 2 H), 5.54 (s, 1 H), 5.33 (s, 1 H), 4.00 (d, \( J = 9.0 \) Hz, 1 H), 3.92 (s, 3 H), 3.91 (s, 3 H), 2.93-2.87 (m, 1 H), 2.06-1.77 (m, 2 H), 1.36-0.94 (m, 9 H), 0.91-0.88 (m, 2 H), 0.80 (t, \( J = 7.5 \) Hz, 1.5 H), 0.72 (t, \( J = 7.5 \) Hz, 1.5 H), 0.65 (t, \( J = 7.5 \) Hz, 1.5 H), 0.46 (t, \( J = 7.0 \) Hz, 3 H).
Hz, 1.5 H) (two diastereomers are arising from the stereocenter in the branched alkyl substituent).

**(+)-(2R,3R)-Ethyl-3-(1-hexyl)-4-(phenyl)-2-(amino)-4-pentenoate (5e):** \( R_f = 0.25 \) (EtOAc/hexane 1 : 2); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.44-7.23 (m, 5H), 5.45 (s, 0.1H), 5.40 (s, 0.9H), 5.17 (s, 0.9H), 5.14 (s, 0.1H), 3.83-3.75 (m, 1H), 3.53 (d, \( J = 5.2 \) Hz, 1H), 3.52-3.45 (m, 1H), 3.15 (quintet, \( J = 5.6 \) Hz, 1H), 2.36 (br s, 2H), 1.75-1.60 (m, 2H), 1.55-1.10 (m, 8H), 1.04 (t, \( J = 7.2 \) Hz, 3H), 0.90 (t, \( J = 6.8 \) Hz, 3H).

![Chemical Structure](image)

**Analytical data for the monotosyldiol:** \( R_f = 0.5 \) (EtOAc/hexane 1 : 7); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.62 (d, \( J = 8.4 \) Hz, 2 H), 7.31-7.23 (m, 4.0 H), 7.20 (t, \( J = 7.2 \) Hz, 3.0 H), 7.13 (d, \( J = 8.8 \) Hz, 2 H), 6.83 (d, \( J = 8.8 \) Hz, 2 H), 4.58 (d, \( J = 2.4 \) Hz, 1.0 H), 4.34 (dd, \( J = 9.6 \) Hz, \( J = 4.8 \) Hz, 1.0 H), 4.25 (dd, \( J = 9.6 \) Hz, \( J = 7.6 \) Hz, 1.0 H), 3.82 (s, 3.0 H), 3.06 (sextet, \( J = 4.4 \) Hz, 1.0 H), 2.35 (s, 3.0 H), 1.94-1.89 (m, 1.0 H), 1.64-1.48 (br, 1 H), 1.50-1.39 (m, 2 H), 1.23-1.12 (m, 4 H), 1.09-0.86 (m, 4 H), 0.82 (t, \( J = 7.2 \) Hz, 3.0 H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 13.9, 21.6, 25.5, 28.4, 29.4, 31.4, 45.8, 47.1, 55.2, 72.3, 73.12, 114.1 (2C), 125.3 (2C), 126.8, 127.8 (2C), 128.1 (2C), 129.1 (2C), 129.6 (2C), 132.2, 132.7, 143.7, 144.5, 158.5; IR (neat, cm\(^{-1}\)) 3413 (w br), 1512 (s), 1176 (s); HRMS (ES\(^+\)) calcd for C\(_{30}\)H\(_{38}\)O\(_5\)SNa\(^{M+Na^+}\), 533.2338, found 533.2341.
2a. Preparation of tetrahydrofuran 12a by Mitsunobu conditions:

(±)-(2R,3S,4R)-2-phenyl-3-(1-hexyl)-4-(p-methoxyphenyl)-tetrahydrofuran (12a). To a solution of diol 11a (0.03 g, 0.084 mmol, 1 equiv) in dry THF (3.0 ml) at 0°C under argon was added triphenylphosphine (0.022 g, 0.084 mmol, 1 equiv) and DEAD (13 μL, 0.084 mmol, 1.0 equiv). The solution was stirred at 0°C for 2.5 h. The reaction mixture was directly loaded on silica and purified using flash column chromatography eluting with EtOAc/hexane (1 : 10) to afford an inseparable mixture of diastereomeric furans 12a (0.024 g, 85%) as a colorless oil. The ratio of diastereomers was measured by GC (dr 9 : 1) as described below.

**Analytical data for 12a** (dr 9 : 1 by GC): R<sub>f</sub> = 0.7 (EtOAc/hexane 1 : 7); ¹H NMR (400 MHz, CDCl₃) δ 7.37-7.27 (m, 5H), 7.23 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 5.30 (d, J = 8.0 Hz, 1H), 4.48 (t, J = 8.4 Hz, 1H), 3.92 (t, J = 8.8 Hz, 1H), 3.83 (s, 3H), 3.18 (q, J = 8.8 Hz, 1H), 2.48 (quintet, J = 7.2 Hz, 1H), 1.19-0.96 (m, 8H), 0.93-0.85 (m, 2H), 0.80 (t, J = 7.2 Hz, 3H).

2b. GC Analysis:

The GCMS data were collected on an Agilent 6890N gas chromatograph eluting into a Quattro Micro GC mass spectrometer (Micromass Ltd, Manchester UK). An HP-5MS, 15 meter column with a 0.25 ID was used. The carrier gas was Helium using constant flow control set to 1.5 ml per minute. 1.0μl of sample was injected into the column with a 20:1 split ratio. The injector port temperature was 240°C. The chromatographic conditions were as follows: The initial column temperature was 50°C with a 1 minute hold after which the temperature was increased 25°C/min to a final temperature of 300°C and held for 2 minutes. EI ionization was used with ion energy of 70V. The mass range was 45 to 400 m/z with a 0.3 scan time and an inter scan delay time of 0.07 seconds.

The first spectra is of the single diastereomer (12a) and second is of the 9:1 diastereomeric
3. HSQC $^{13}$C - $^1$H correlation data for 8a, 8e and 12a
8a Correlations found
All the values are in ppm

C₂ (69.1) - H² (4.42)
C₃ (55.8) - H³ (2.33)
C₄ (49.8) - H⁴ (2.80)
C₅ (56.2) - H⁵ and H⁶ (4.11 / 3.57)

8e Correlations found
All the values are in ppm

C₂ (66.0) - H² (4.05)
C₃ (51.6) - H³ (2.46)
C₄ (50.7) - H⁴ (2.70)
C₅ (55.3) - H⁵ and H⁶ (3.87 / 3.48)

12a Correlations found
All the values are in ppm

C₂ (84.14.0) - H² (5.30)
C₃ (51.5) - H³ (2.48)
C₄ (49.9) - H⁴ (3.19)
C₅ (75.0) - H⁵ and H⁶ (4.48 / 3.92)

HSQC (500 MHz, CDCl₃)
8e

HSGC (500 MHz, CDCl₃)

12a

HSGC (500 MHz CDCl₃)
4. Assignment of relative stereochemistry of compounds 8a, 8e and 12a using 1H NMR

NOE difference and HSQC $^{13}$C - $^1$H correlations

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<td>3.47</td>
<td>2.47</td>
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<table>
<thead>
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<td>2.48</td>
<td>7.24 5.30 3.92</td>
<td>$H^3$ - $H^2$ $H^3$ - $H^6$</td>
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</table>
5. X-ray structure of compound 8a

**Figure:** The thermal ellipsoids of compound 8a drawn at 50% probability level. The CCDC number is 858605
6. Copies of $^1$H NMR and $^{13}$C spectra for selected compounds
$^1$H NMR (125 MHz, CDCl$_3$)
$^{13}$C NMR (125 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

5b

MeOOC

NH$_2$
n-hexyl

NO$_2$
$^{13}$C NMR (125 MHz, CDCl$_3$)
$^{1}\text{H NMR (500 MHz, CDCl}_3)$
$^{1}$H NMR (400 MHz, CDCl$_3$)
\[6a\]

$^{13}$C NMR (125 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (125 MHz, CDCl$_3$)
$^{13}$C NMR (125 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$7_e$
$\text{HN-Ts}$

$\text{n-hexyl}$

$\text{COOEt}$

$\text{13C NMR (125 MHz, CDCl}_3\text{)}$

$T_e$
$^1\text{H NMR (500 MHz, CDCl}_3)$
$^{13}$C NMR (125 MHz, CDCl$_3$)
$^{13}$C NMR (125 MHz, CDCl$_3$)
\[ \text{S-57} \]

13C NMR (125 MHz, CDCl\textsubscript{3})
$^{1}{H}$ NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (125 MHz, CDCl$_3$)

dr 3:1

Additional peaks arising from dehydration in acid-contaminated CDCl$_3$ are present.
Sample lacking the dehydration byproducts; taken in CDCl₃ filtered through basic alumina
$^{1}H$ NMR (400 MHz, CDCl$_3$)
dr 3:1
$^{1}H$ NMR (400 MHz, CDCl$_3$)

dr 3:1
Additional peaks arising from dehydration in acid-contaminated CDCl₃ were present. Dehydration was still detected in basic alumina-filtered CDCl₃.
$^{13}$C NMR (125 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

12b

n-hexyl
$^1H$ NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (125 MHz, CDCl$_3$)

$\text{n-hexyl}$

12c
$^{1}H$ NMR (400 MHz, CDCl$_3$)