Supplementary Information for

Asymmetric Reformatsky-Type Reaction of Isatin-Derived $N$-Sulfinyl Ketimines: Efficient and Practical Synthesis of Enantiopure Chiral 2-Oxoindolinyl-$\beta^{3,3}$-Amino Acids

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1. General Remarks

$^1$H and $^{13}$C NMR spectra were determined on Varian-MERCURY Plus-300 and Bruker
ADVANCE III 500 instruments. Chemical shifts are reported in $\delta$ ppm referenced to an internal
SiMe$_4$ standard for $^1$H NMR and CDCl$_3$ ($\delta$ 77.0) for $^{13}$C NMR. Chiral HPLC was performed on a
JASCO 2000 instrument by using Daicel columns with 2-propanol / hexane as the eluent. HPLC
was performed on Waters 1525EF and Agilent Technologies 1260 series HPLC system. Mass
spectra and high-resolution mass spectra were measured on a Finnigan MAT-95 mass spectrometer.
All the solvents were freshly distilled. Ethyl bromoacetate and ethyl 2-bromoisobutyrate were also
distilled before used. The Znic powder and CuCl were activated. The reaction is air- and
moisture-sensitive so all reactions were performed under an argon atmosphere with oven-dried
glassware.
2. Copies of $^1$H and $^{13}$C NMR Spectra

Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-2-oxo-1-tritylindolin-3-yl)acetate (2a)
Ethyl 2-((R)-3-(((R)-tert-butylsulfinyl)amino)-2-oxo-1-tritylindolin-3-yl)acetate (2a’)

[Chemical structures and spectra images]

4
Ethyl 2-((S)-4-bromo-3-(((R)-tert-butylsulfinyl)amino)-2-oxo-1-tritylindolin-3-yl)acetate (2b)
Ethyl 2-((S)-3-(((R)-tert-butylsulfanyl)amino)-5-fluoro-2-oxo-1-tritylindolin-3-yl)acetate (2c)
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-5-chloro-2-oxo-1-tritylindolin-3-yl)acetate (2d)
Ethyl 2-((S)-5-bromo-3-(((R)-tert-butylsulfinyl)amino)-2-oxo-1-tritylindolin-3-yl)acetate (2e)
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-5-methyl-2-oxo-1-tritylindolin-3-yl)acetate (2f)
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-5-methoxy-2-oxo-1-tritylindolin-3-yl)acetate (2g)
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-5-isopropyl-2-oxo-1-tritylindolin-3-yl)acetate (2h)
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-6-chloro-2-oxo-1-tritylindolin-3-yl)acetate (2i)
Ethyl 2-((S)-6-bromo-3-(((R)-tert-butylsulfinyl)amino)-2-oxo-1-tritylindolin-3-yl)acetate (2j)
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-7-fluoro-2-oxo-1-tritylindolin-3-yl)acetate (2k)
Ethyl 2-(((S)-3-(((R)-tert-butylsulfinyl)amino)-5-fluoro-6-methoxy-2-oxo-1-tritylindolin-3-yl)acetate (2l)
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-4,6-difluoro-2-oxo-1-tritylindolin-3-yl)acetate (2m)
Ethyl 2-((R)-3-(((R)-tert-butylsulfinyl)amino)-2-oxo-1-tritylindolin-3-yl)-2-methylpropanoate (2n)
Ethyl (S)-2-(3-amino-2-oxo-1-tritylindolin-3-yl)acetate (3)
Ethyl (S)-2-(3-amino-2-oxoindolin-3-yl)acetate (4)
(S)-2-(3-amino-2-oxoindolin-3-yl)acetic acid (5)

(S)-spiro[azetidine-2,3'-indoline]-2',4-dione (6)
(3aS, 8aR)-8-trityl-2,3,8a-tetrahydro-3aH-furo[2,3-b]indol-3a-amine (7)
3. Copies of HPLC Spectra

Ethyl 2-((S)-3-(((R)-tert-butylsulfanyl)amino)-2-oxo-1-tritylindolin-3-yl)acetate (2a)

\[
\begin{align*}
\text{HPLC: Agilent Eclipse Plus-C18 4.6*250 mm; detected at 254 nm; methanol / water = 72 / 28; flow rate = 1 mL / min; Retention time: 19.7 min (minor), 21.4 min (major).}
\end{align*}
\]

Reaction system before worked up

Major product: 21.4 min

Minor product: 19.7 min
Ethyl 2-((S)-4-bromo-3-(((R)-tert-butylsulfanyl)amino)-2-oxo-1-tritylindolin-3-yl)acetate (2b)

98:2 dr

HPLC (of its sulfonyl derivative): Chiralpak AD-H Column (250 mm); detected at 224 nm; n-hexane / i-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 7.3 min (major), 10.2 min (minor).
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-5-fluoro-2-oxo-1-tritylindolin-3-yl)acetate (2c)

94:6 dr
HPLC: Agilent Eclipse Plus-C18 4.6*250 mm; detected at 254 nm; methanol / water = 75 / 25; flow rate = 1 mL / min; Retention time: 13.9 min (minor), 15.9 min (major).

Reaction system before worked up

Major product: 16.3 min

Minor product: 14.3 min
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-5-chloro-2-oxo-1-tritylindolin-3-yl)acetate (2d)

95:5 dr

HPLC: Agilent Eclipse Plus-C18 4.6*250 mm; detected at 254 nm; methanol / water = 75 / 25; flow rate = 1 mL / min; Retention time: 19.5 min (minor), 24.6 min (major).

Reaction system before worked up

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Major product: 24.4 min

Minor product: 20.2 min
Ethyl 2-((S)-5-bromo-3-(((R)-tert-butylsulfinyl)amino)-2-oxo-1-tritylindolin-3-yl)acetate (2e)

96:4 dr

HPLC: Agilent Eclipse Plus-C18 4.6*250 mm; detected at 254 nm; methanol / water = 75 / 25; flow rate = 1 mL / min; Retention time: 21.4 min (minor), 27.2 min (major).

Reaction system before worked up

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Major product: 27.8 min

Minor product: 21.7 min
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-5-methyl-2-oxo-1-tritylindolin-3-yl)acetate (2f)

93:7 dr
HPLC: Agilent Eclipse Plus-C18 4.6*250 mm; detected at 254 nm; methanol / water = 75 / 25; flow rate = 1 mL / min; Retention time: 17.6 min (minor), 19.0 min (major).

Reaction system before worked up

Major product: 19.8 min

Minor product: 17.5 min
Ethyl 2-((S)-3-((R)-tert-butylsulfinyl)amino)-5-methoxy-2-oxo-1-tritylindolin-3-yl)acetate (2g)

92:8 dr

HPLC on Waters 1525EF with Denali C18 reversed-phase column (4.6 × 250 mm); detected at 254 nm; acetonitrile / water = 60 / 40; flow rate = 1 mL / min; Retention time: 16.4 min (minor), 18.6 min (major).

Reaction system before worked up

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Major product: 18.6 min

Minor product: 16.4 min
Ethyl 2-\(((S)-3-(((R\text{-}\text{tert-buty)sulfinyl})\text{amino})-5\text{-isopropyl-2-oxo-1-}\text{tritylindol}in-3\text{-yl})\text{acetate (2h)}\

96:4 dr

HPLC: column, Athena C18-WP, 2.1 × 50 mm; solvent system, acetonitrile-0.2% HCOOH with gradient elution; flow rate, 0.3 mL/min; UV detection, 254 nm; Shimadzu LC-MS-2020, Shimadzu Corporation, Kyoto, Japan. Retention time: 10.3 min (minor), 10.5 min (major).

Retention system before worked up

Mass spectrum under both positive and negative ionization modes confirmed that the peak with retention time of 10.3 min is the minor product.
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-6-chloro-2-oxo-1-tritylindolin-3-yl)acetate (2i)

90:10 dr

HPLC: Agilent Eclipse Plus-C18 4.6*250 mm; detected at 254 nm; methanol / water = 75 / 25; flow rate = 1 mL / min; Retention time: 17.4 min (minor), 19.0 min (major).

Reaction system before worked up

<table>
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<tr>
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Major product: 18.8 min

Minor product: 17.1 min
Ethyl 2-((S)-6-bromo-3-(((R)-tert-butylsulfanyl)amino)-2-oxo-1-tritylindolin-3-yl)acetate (2j)

88:12 dr

HPLC: Agilent Eclipse Plus-C18 4.6*250 mm; detected at 254 nm; methanol / water = 75 / 25; flow rate = 1 mL / min; Retention time: 18.5 min (minor), 20.2 min (major).

Reaction system before worked up

![HPLC graph](image)

<table>
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<th>#</th>
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Major product: 20.3 min

![HPLC graph](image)

Minor product: 18.5 min

![HPLC graph](image)
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-7-fluoro-2-oxo-1-tritylindolin-3-yl)acetate (2k)

[Chemical structure image]

93:7 dr

HPLC on Waters 1525EF with Denali C18 reversed-phase column (4.6 × 250 mm); detected at 254 nm; acetonitrile / water = 65 / 35; flow rate = 1 mL / min;

Retention time: 17.8 min (minor), 20.8 min (major).

Reaction system before worked up

![HPLC graph with retention times]

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Major product: 20.6 min

Minor product: 17.9 min
Ethyl 2-((S)-3-(((R)-tert-butylsulfinyl)amino)-5-fluoro-6-methoxy-2-oxo-1-tritylindolin-3-yl)acetate (2l)

86:14 dr
HPLC: Agilent Eclipse Plus-C18 4.6*250 mm; detected at 254 nm; methanol / water = 70 / 30; flow rate = 1 mL / min; Retention time: 23.0 min (minor), 26.1 min (major).

Reaction system before worked up

Major product: 26.0 min

Minor product: 23.0 min
Ethyl 2-(((S)-3-(((R)-tert-butylsulfinyl)amino)-4,6-difluoro-2-oxo-1-tritylindolin-3-yl)acetate (2m)

85:15 dr

HPLC (of its sulfonyl derivative): Chiralpak AD-H Column (250 mm); detected at 224 nm; n-hexane / i-propanol = 95 / 5; flow = 0.7 mL / min; Retention time: 12.3 min (major), 25.0 min (minor).
Ethyl 2-((R)-3-(((R)-tert-butylsulfinyl)amino)-2-oxo-1-tritylindolin-3-yl)-2-methylpropanoate (2n)

83:17 dr

HPLC on Waters 1525EF with Denali C18 reversed-phase column (4.6 × 250 mm); detected at 254 nm; acetonitrile / water = 70 / 30; flow rate = 1 mL / min;
Retention time: 17.3 min (minor), 26.9 min (major).

Reaction system before worked up

<table>
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<tr>
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Major product: 26.8 min

Minor product: 17.2 min