A Sustainable Strategy for the Straightforward Preparation of 2H-azirines and Highly Functionalized NH-aziridines from Vinyl Azides

Using a Single Solvent Flow-Batch Approach

Michael Andresini, Leonardo Degennaro, Renzo Luisi

"Flow Chemistry and Microreactor Technology FLAME-Lab
Department of Pharmacy – Drug Sciences, University of Bari ‘A. Moro’ Via E. Orabona 4, Bari, I-70125

SUPPORTING INFORMATION
Table of Contents

1. General methods S2
2. General Procedure A for the preparation of vinyl azides S3
   Characterization data for compounds 1a-l S3
3. General Procedure B for the preparation of 2H-azirines S7
   Characterization data for compounds 2a-l S7
4. General Procedure C for the preparation of NH-aziridines S11
5. Characterization data for compounds 3a-l S12
6. Copies of 1H, 13C, 19F, NOESY NMR spectra S17
7. References S47
1. General methods

All reagents were purchased from Sigma-Aldrich, TCI, Alfa Aesar and Fluorochem, and used without previous purification. Thin Layer Chromatography (TLC) was performed on a 0.25 mm precoated silica gel thick plates 60F254 (Merck); the spots were visualized under UV light ($\lambda = 254$ nm) and/or KMnO$_4$ (aq). Flash chromatography was performed using 230-400 mesh silica and a mobile phase as indicated for each entry, according to standard techniques. HRMS spectra were recorded on Agilent 6530 accurate mass Q-TOF instrument using electrospray ion source (ESI), operating in positive and negative ion mode, as described for each entry. Infrared spectra ($\nu_{\text{max}}$, FT-IR/ATR) were recorded in reciprocal centimeters (cm$^{-1}$) using a PerkinElmer 283 Spectrometer (FT-IR) or a PerkinElmer Spectrum Two Spectrometer with a 2x2 mm diamond crystal (ATR). Nuclear magnetic resonance spectra were recorded using an Agilent 500 spectrometer (500 MHz for $^1$H, 125 MHz for $^{13}$C, 470 MHz for $^{19}$F), and a Varian Mercury 300 spectrometer (300 MHz for $^1$H, 75 MHz for $^{13}$C, 282 MHz for $^{19}$F). The peak of the (residual) solvent signal was used as an internal standard, related to TMS, with $\delta$ 7.26 ppm ($^1$H in CDCl$_3$), $\delta$ 77.00 ppm ($^{13}$C in CDCl$_3$). For $^{19}$F spectra, absolute referencing was used. Spin-spin coupling constants ($J$) are given in Hz. Assignment of the resonances was performed by combined application of standard NMR techniques (HSQC, COSY). Assignment of relative stereochemistry for compounds 3k and 3l was performed by NOESY experiments.

Flow equipment: Solutions of the reagents were introduced into the flow microreactor system using a Harvard PHD 2000 syringe pump, equipped with gastight syringe purchased from SGE (Harvard PHD 2000). A Volcano reactor (Syrris, stainless steel tubular reactor, 4mL) was employed. Connections were obtained using stainless steel and PTFE microtubes with an inner diameter of 500μL. Microtubes were connected to the reactor by with stainless steel fittings (GL Sciences, 1/16 OUW).
2. General Procedure A for the preparation of vinyl azides

Vinyl azides 1a-l were prepared according to the reported procedures with slight modification, starting from alkenes.\(^1\),\(^2\)

\[
\begin{array}{c}
\text{R}^1\text{=C=CR}^2
\end{array}
\xrightarrow[\text{NaN}_3 (2.0 \text{ equiv.}), \text{I}_2 (1.5 \text{ equiv.})]{\text{MeOH/H}_2\text{O, r.t., 3 h}}
\begin{array}{c}
\text{R}^1\text{=C=CR}^2
\end{array}
\xrightarrow[\text{BuOK (1.2 equiv.)}]{\text{Et}_2\text{O, 0°C, 1.5 h}}
\begin{array}{c}
\text{N}_3\\\text{N}_3
\end{array}
\]

To a solution of alkene (8.5 mmol, 1.0 equiv.) in 18 mL of solvent (MeOH/H\(_2\)O = 5:1), sodium azide (17.0 mmol, 2.0 equiv.) was added in one portion at 25°C, then iodine (12.8 mmol, 1.5 equiv.) was added, and the solution was stirred for 3 h. Subsequently, CH\(_2\)Cl\(_2\) (90 mL) and H\(_2\)O (50 mL) were added, the organic layer separated and washed with an aqueous solution of Na\(_2\)S\(_2\)O\(_5\) (5%) until the organic phase appeared colourless. The organic layer was washed twice with H\(_2\)O (2 x 35 mL), dried over Na\(_2\)SO\(_4\), the solvent was evaporated under reduced pressure and the product was immediately used for the next synthetic step without further purification. To a solution of the obtained beta-iodo azide in Et\(_2\)O (17 mL), t-BuOK (10.2 mmol, 1.2 equiv.) was added at 0°C and the reaction mixture was stirred at the same temperature for 1.5 h. Subsequently, the mixture was filtered through a pad of diatomaceous earth, and the solvent evaporated under reduced pressure. Purification by column chromatography afforded vinyl azides 1a–m as reported for each entry.

Characterization data for vinyl azides 1a–l

1-(1-azidovinyl)-4-methylbenzene (1a)

Prepared according General Procedure A. The product was purified by column chromatography (SiO\(_2\), R\(_f\) 0.9, Hexane) to afford vinyl azide 1a as a pale yellow oil (812 mg, 60%). \(^1\)H NMR (300 MHz, CDCl\(_3\), ppm) \(\delta\) 7.51 (d, \(J = 8.0\) Hz, 2H, Ar\(_i\) H), 7.21 (d, \(J = 8.0\) Hz, 2H, Ar\(_i\) H), 5.43 (d, \(J = 2.2\) Hz, 1H), 4.96 (d, \(J = 2.2\) Hz, 1H), 2.41 (s, 3H, CH\(_3\)). Analytical data (NMR) in agreement with those reported in the literature.\(^3\)

1-(1-azidovinyl)-4-chlorobenzene (1b)
Prepared according General Procedure A. The product was purified by column chromatography (SiO$_2$, R$_f$ 0.9, Hexane) to afford vinyl azide 1b as a pale yellow oil (1068 mg, 70%). $^1$H NMR (500 MHz, CDCl$_3$, ppm) δ 7.50–7.48 (m, 2H, Ar$^\ominus$ H), 7.34–7.31 (m, 2H, Ar$^\ominus$ H), 5.43 (d, J = 2.6 Hz, 1H), 4.97 (d, J = 2.6 Hz, 1H). Analytical data (NMR) in agreement with those reported in the literature.$^3$

1-(1-azidovinyl)-4-fluorobenzene (1c)

Prepared according General Procedure A. The product was purified by column chromatography (SiO$_2$, R$_f$ 0.9, Hexane) to afford vinyl azide 1c as a pale yellow oil (651 mg, 47%). $^1$H NMR (500 MHz, CDCl$_3$, ppm) δ 7.57–7.50 (m, 2H, Ar$^\ominus$ H), 7.08–7.00 (m, 2H, Ar$^\ominus$ H), 5.37 (d, J = 2.6 Hz, 1H), 4.94 (d, J = 2.6 Hz, 1H). $^{19}$F NMR (282 MHz, CDCl$_3$, ppm) δ -112.31 (ddd, J = 13.6, 8.5, 5.3 Hz). Analytical data (NMR) in agreement with those reported in the literature.$^3$

1-(1-azidovinyl)-2-methylbenzene (1d)

Prepared according General Procedure A. The product was purified by column chromatography (SiO$_2$, R$_f$ 0.9, Hexane) to afford vinyl azide 1f as a pale yellow oil (730 mg, 54%). $^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 7.28–7.18 (m, 5H, Ar$^\ominus$ H), 5.05 (s, 1H), 4.74 (s, 1H), 2.39 (s, 3H, CH$_3$). Analytical data (NMR) in agreement with those reported in the literature.$^3$

1-(1-azidovinyl)-3-bromobenzene (1e)

Prepared according General Procedure A. The product was purified by column chromatography (SiO$_2$, R$_f$ 0.9, Hexane) to afford vinyl azide 1d as a brown oil (952 mg, 50%). $^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 7.72–7.70 (m, 1H, Ar$^\ominus$ H), 7.50–7.45 (m, 2H, Ar$^\ominus$ H), 7.22 (t, J = 7.9 Hz, 1H, Ar$^\ominus$ H), 5.45 (d, J = 2.7 Hz, 1H), 4.98 (d, J = 2.7 Hz, 1H). Analytical data (NMR) in agreement with those reported in the literature.$^4$
1–(1–azidovinyl)–2–bromobenzene (1f)

Prepared according General Procedure A. The product was purified by column chromatography (SiO₂, Rf 0.9, Hexane) to afford vinyl azide 1f as a brown oil (1257 mg, 66%). ¹H NMR (300 MHz, CDCl₃, ppm) δ 7.62 (d, J = 7.7 Hz, 1H, Arᵢ H), 7.36–7.32 (m, 2H, Arᵢ H), 7.26–7.23 (m, 1H, Arᵢ H), 5.12 (d, J = 1.2 Hz, 1H), 4.85 (d, J = 1.2 Hz, 1H). Analytical data (NMR) in agreement with those reported in the literature.³

1–(1–azidovinyl)–4–bromobenzene (1g)

Prepared according General Procedure A. The product was purified by column chromatography (SiO₂, Rf 0.9, Hexane) to afford vinyl azide 1g as a brown oil (1714 mg, 90%). ¹H NMR (300 MHz, CDCl₃, ppm) δ 7.49–7.47 (m, 2H, Arᵢ H), 7.44–7.42 (m, 2H, Arᵢ H), 5.44 (d, J = 2.4 Hz, 1H), 4.98 (d, J = 2.4 Hz, 1H). Analytical data (NMR) in agreement with those reported in the literature.³

2–azidodec–1–ene (1h)

Prepared according General Procedure A. The product was purified by column chromatography (SiO₂, Rf 0.95, Hexane) to afford azide 1i as a colourless oil (478 mg, 31%). ¹H NMR (300 MHz, CDCl₃, ppm) δ 4.62 (broad signal, 2H, C=CH₂), 2.07 (t, J = 7.5 Hz, 2H), 1.51–1.42 (m, 2H), 1.37–1.26 (m, 10H), 0.88 (t, J = 6.8 Hz, 3H). Analytical data (NMR) in agreement with those reported in the literature.⁵

2–azidododec–1–ene (1i)

Prepared according General Procedure A. The product was purified by column chromatography (SiO₂, Rf 0.95, Hexane) to afford azide 1j as a colourless oil (961 mg, 54%). ¹H NMR (300 MHz, CDCl₃, ppm) δ 4.62 (broad signal, 2H, C=CH₂), 2.06 (t, J = 7.5 Hz, 2H),
1.49 ÷ 1.44 (m, 2H), 1.38 ÷ 1.23 (m, 14H), 0.88 (t, J = 6.8 Hz, 3H). Analytical data (NMR) in agreement with those reported in the literature.6

2-azidotetradec-1-ene (1j)

Prepared according General Procedure A. The product was purified by column chromatography (SiO₂, Rf 0.95, Hexane) to afford azide 1k as a colourless oil (1190 mg, 59%). ¹H NMR (300 MHz, CDCl₃, ppm) ù 4.62 (d, J = 0.8 Hz, 2H, C=CH₂), 2.06 (t, J = 7.5 Hz, 2H), 1.49 ÷ 1.43 (m, 2H), 1.36 ÷ 1.24 (broad signal, 18H), 0.88 (t, J = 6.6 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃, ppm) ù 147.0 (N₃C=CH₂), 98.1 (N₃C=CH₂), 33.8 (CH₂), 32.1 (CH₂), 29.8 (3 × CH₂), 29.7 (CH₂), 29.5 (2 × CH₂), 29.0 (CH₂), 27.5 (CH₂), 22.8 (CH₂), 14.2 (CH₃). IR (ATR, neat)/cm⁻¹ 2955, 2853, 2104, 1626, 1466, 1274. HRMS (ESI) m/z (M–H)⁻ calcd for C₁₄H₂₇N₃ 236.2132; found 236.2125.

1-(1-azidovinyl)-2,3,4,5,6-pentafluorobenzene (1k)

Prepared according General Procedure A. The product was purified by column chromatography (SiO₂, Rf 0.9, Hexane) to afford vinyl azide 1l as a pale yellow oil (700 mg, 35%). ¹H NMR (300 MHz, CDCl₃, ppm) ù 5.40 (d, J = 2.3 Hz, 1H), 5.12 (d, J = 2.3 Hz, 1H). ¹⁹F NMR (282 MHz, CDCl₃, ppm) ù -138.69 ÷ -141.44 (m), -152.16 (tt, J = 21.0, 2.4 Hz), -158.59 ÷ -162.86 (m). ¹³C NMR (125 MHz, CDCl₃, ppm) ù 144.6 (m, C F), 141.8 (m, C F), 137.8 (m, C F), 132.0 (N₃C=CH₂), 110.5 (m, Ar C), 108.3 (N₃C=CH₂). IR (ATR, neat)/cm⁻¹ 2151, 2102, 1493, 1327, 989, 707. HRMS (ESI) m/z (M–H)⁻ calcd for C₈H₃F₅N₃ 234.0096; found 234.0110.

(Z)-(1-azidoethene-1,2-diyl)dibenzene (1l)

Prepared according General Procedure A. The product was purified by column chromatography (SiO₂, Rf 0.9, Hexane) to afford azide 1m as a colourless oil (564 mg, 30%). ¹H NMR (300 MHz, CDCl₃, ppm) ù 7.72 (d, J = 7.8 Hz, 2H), 7.54 ÷ 7.42 (m, 7H), 7.28 ÷ 7.26 (m, 1H), 6.03 (s, 1H). Analytical data (NMR) in agreement with those reported in the literature.6
3. General Procedure B

The process can be executed using a PHD ULTRA® Syringe Pump (Harvard Apparatus), a Volcano reactor (4 mL, Syrris) and a back–pressure regulator of 8 bar. A solution of vinyl azide (1.0 mmol) in CPME (4 mL, 0.25 M) was introduced by syringe pump into the pre–heated reactor (130°C, probe feedback control) with a flow rate of 250 μL/min. Subsequently, fresh solvent (CPME) was fluxed in the reactor upon the same conditions, and the outgoing solution was collected in a round bottom flask. The solvent was evaporated under reduced pressure and the products were obtained after chromatography or without any further purification as indicated for each entry.

Characterization data for azirines 2a–l

3–(p–tolyl)–2H–azirine (2a)

Prepared according General Procedure B using vinyl azide 1a (159 mg). The product was obtained without any further purification as a yellow oil (131 mg, 99%). $^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 7.80 (d, $J = 8.0$ Hz, 2H, Ar–H), 7.36 (d, $J = 8.0$ Hz, 2H, Ar–H), 2.46 (s, 3H, Ar–CH$_3$), 1.76 (s, 2H, NCH$_2$). Analytical data (NMR) in agreement with those reported in the literature.$^7$

3–(4–chlorophenyl)–2H–azirine (2b)

Prepared according General Procedure B using vinyl azide 1b (180 mg). The product was obtained without further purification as a yellow oil (150 mg, 99%). $^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 7.86i 7.83 (m, 2H, Ar–H), 7.56i 7.53 (m, 2H, Ar–H), 1.75 (s, 2H, NCH$_2$). Analytical data (NMR) in agreement with those reported in the literature.$^7$
3-(4-fluorophenyl)-2H-azirine (2c)

Prepared according General Procedure B using vinyl azide 1c (163 mg). The product was obtained without further purification as a yellow oil (134 mg, 99%). $^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 7.94–7.90 (m, 2H, Ar–H), 7.28–7.24 (m overlapping CDCl$_3$, 2H, Ar–H), 1.80 (s, 2H, NCH$_2$). $^{19}$F NMR (470 MHz, CDCl$_3$, ppm) δ -104.79 (m, 1F) Analytical data (NMR) in agreement with those reported in the literature.

3- (o-tolyl)-2H-azirine (2d)

Prepared according General Procedure B using vinyl azide 1d (159 mg). The product was obtained without further purification as a yellow oil (131 mg, 99%). $^1$H NMR (500 MHz, CDCl$_3$, ppm) δ 7.75 (d, J = 7.5 Hz, 1H, Ar–H), 7.47 (t, J = 7.5 Hz, 1H, Ar–H), 7.39 (t, J = 7.5 Hz, 1H, Ar–H), 7.35 (d, J = 7.6 Hz, 1H, Ar–H) 2.70 (s, 3H, Ar–CH$_3$), 1.69 (s, 2H, NCH$_2$). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) δ 165.1 (C=N), 140.9 (Ar), 132.5 (Ar), 130.9 (Ar), 126.3 (Ar), 124.0 (Ar), 19.9 (NCH$_2$), 17.9 (Ar–CH$_3$). IR (ATR, neat)/cm$^{-1}$ 3042, 2976, 2924, 1734, 1488, 981, 759, 669. HRMS (ESI-TOF) m/z (M+H)$^+$ calcd for C$_9$H$_{10}$N 132,0813; found 132,0807.

3-(3-bromophenyl)-2H-azirine (2e)

Prepared according General Procedure B using vinyl azide 1e (224 mg). The product was obtained without further purification as a brown oil (195 mg, 99%). $^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 8.05 (t, J = 1.7 Hz, 1H, Ar–H), 7.90–7.81 (m, 2H, Ar–H), 7.72 (ddd, J = 8.0, 1.7, 1.0 Hz, 1H, Ar–H), 7.44 (t, J = 8.0 Hz, 1H, Ar–H), 1.82 (s, 2H, C=NCH$_2$). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) δ 165.5 (C=N), 135.9 (Ar), 132.5 (Ar), 130.77 (Ar), 128.1 (Ar), 127.6 (Ar), 123.2 (Ar), 20.4 (NCH$_2$). IR (film)/cm$^{-1}$ 3052, 2978, 2101, 1742, 1566, 1291, 993, 787. HRMS (ESI-TOF) m/z (M+H)$^+$ calcd for C$_9$H$_7$BrN 195,9762; found 195,9753.
3–(2-bromophenyl)–2H–azirine (2f)

Prepared according General Procedure B using vinyl azide 1f (224 mg). The product was obtained without further purification as a brown oil (195 mg, 99%). $^1$H NMR (300 MHz, CDCl$_3$, ppm) $\delta$ 7.84 (dd, $J = 7.6$, 1.7 Hz, 1H, Ar–H), 7.73 (dd, $J = 8.0$, 1.0 Hz, 1H, Ar–H), 7.50 (td, $J = 7.5$, 1.2 Hz, 1H), 7.43 (td, $J = 7.7$, 1.8 Hz, 1H), 1.88 (s, 2H, C=NCH$_2$). Analytical data (NMR) in agreement with those reported in the literature.}$^8$

3–(4-bromophenyl)–2H–azirine (2g)

Prepared according General Procedure B using vinyl azide 1g (224 mg). The product was obtained without further purification as a brown oil (192 mg, 98%). $^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 7.77 (d, $J = 8.4$ Hz, 2H, 2–Ar'H), 7.71 (d, $J = 8.4$ Hz, 2H, 2–Ar'H), 1.81 (s, 2H, C=NCH$_2$). Analytical data (NMR) in agreement with those reported in the literature.}$^7$

3–octyl–2H–azirine (2h)

Prepared according General Procedure B (twice) using vinyl azide 1i (181 mg). The product was obtained without further purification as a yellow oil (150 mg, 98%). $^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 2.78 (t, $J = 7.3$ Hz, 2H, C–H$_2$C=N), 1.74 (q, $J = 7.3$ Hz, 2H), 1.43–1.39 (m, 2H), 1.36 (s, 2H, C=NCH$_2$), 1.35–1.21 (broad signal, 8H), 0.88 (t, $J = 6.9$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 169.8 (CH$_2$C=N), 31.8, 29.2 (2–CH$_2$), 31.8, 29.2 (2–CH$_2$), 29.1, 28.4, 24.1, 22.6, 18.8, 14.0 (CH$_3$). IR (ATR, neat)/cm$^{-1}$ 2955, 2925, 2856, 1466, 1260, 725. HRMS (ESI TOF) m/z (M+H)$^+$ calcd for C$_{10}$H$_{20}$N 154, 1596; found 154, 1591.

3–decyl–2H–azirine (2i)

Prepared according General Procedure B using vinyl azide 1j (209 mg). The product was obtained without further purification as a brown oil (175 mg, 97%). $^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ $^1$H NMR (300 MHz, CDCl$_3$, ppm) $\delta$ 2.78 (t, $J = 7.3$ Hz, 2H, C–H$_2$C=N), 1.74 (q, $J = 7.3$ Hz, 2H), 1.43–1.20 (broad signal, 16H), 0.88 (t, $J = 6.9$ Hz, 3H). $^{13}$C NMR (125
MHz, CDCl$_3$, ppm) δ 169.9 (CH$_2$C=N), 32.0, 29.7, 29.6, 29.4 (2 νCH$_2$), 28.6, 24.3, 22.8, 18.9, 14.3 (CH$_3$). IR (ATR, neat)/cm$^{-1}$ 2956, 2926, 2856, 1672, 1460, 1378, 1261, 1035. HRMS (ESI-TOF) m/z (M+H)$^+$ calcd for C$_{12}$H$_{24}$N 182,1909; found 182,1909.

3–dodecyl–2H–azirine (2j)

Prepared according General Procedure B using vinyl azide 1k (237 mg). The product was obtained without further purification as a brown oil (203 mg, 97%). $^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 2.78 (t, $J = 7.3$ Hz, 2H, CH$_2$C=N), 1.74 (q, $J = 7.3$ Hz, 2H), 1.36–1.18 (broad signal, 20H), 0.88 (t, $J = 6.9$ Hz, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$, ppm) δ 169.9 (CH$_2$C=N), 34.0, 32.1, 29.8, 29.7, 29.6, 29.5, 29.4, 29.1, 28.6, 24.3, 22.8, 18.9, 14.2. IR (ATR, neat)/cm$^{-1}$ 2954, 2924, 2854, 1458, 986. HRMS (ESI-TOF) m/z (M+H)$^+$ calcd for C$_{14}$H$_{28}$N 210,2222; found 210,2218.

3–(perfluorophenyl)–2H–azirine (2k)

Prepared according General Procedure B. The product was obtained in mixture with vinyl azide 1l (1l:2l = 20:80). $^1$H NMR (500 MHz, CDCl$_3$, ppm) δ 1.85 (s, 2H, NCH$_2$). $^{19}$F NMR (282 MHz, CDCl$_3$, ppm) δ -136.90 – -137.06 (m, 2F), -144.63 (tt, $J = 20.6$, 5.1 Hz, 1F), -159.71 – -159.97 (m, 2F).

2,3–diphenyl–2H–azirine (2l)

Prepared according General Procedure B. The product was obtained without any further purification as a yellow oil (192 mg, 99%). $^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 7.72–7.69 (m, 2H, Ar H), 7.63i 7.51 (m, 3H, Ar H), 7.36 (t, $J = 7.7$ Hz, 1H), 7.30i 7.27 (m, 2H, Ar H), 7.17i 7.15 (m, 2H, Ar H), 3.33 (s, 1H, C=NCHPh). Analytical data (NMR) in agreement with those reported in the literature.\textsuperscript{7}

4. General Procedure C
The process can be executed using a PHD ULTRA™ Syringe Pump (Harvard Apparatus), a Volcano reactor (4 mL, Syrris) and a back–pressure regulator of 8 bar. A solution of vinyl azide (1.0 mmol) in CPME (4 mL, 0.25 M) was introduced by syringe pump into the pre–heated reactor (130°C, probe feedback control) with a flow rate of 250 μL/min. Subsequently, fresh solvent (CPME) was fluxed in the reactor upon the same conditions. The outgoing solution was collected in a closed round bottom flask with nitrogen atmosphere for 16 min, since the formation of nitrogen was observed. The stirred solution was cooled to -78°C and organolithium (1.2 equiv.) was added in one portion. After 5 min, H₂O (100 μL) was added, and the reaction mixture was stirred at room temperature. The solution was filtered on a Na₂SO₄ pad, the solvent was evaporated under reduced pressure, and the products were isolated through silica gel chromatography as described for each entry.

**Combined flow-batch system**
Characterization data for aziridines 4a-l

2-phenyl-2-(p-tolyl)aziridine (4a)

Prepared according General Procedure C using azirine 2a. The product was purified by column chromatography (SiO₂, Rf 0.30, Hexane/Ethyl Acetate/Triethylamine 80:19:1) to afford aziridine 4a as a brown waxy solid (102 mg, 49%). ¹H NMR (500 MHz, CDCl₃, ppm) δ 7.37–7.28 (m, 5H, Ar–H), 7.24 (d, J = 8.0 Hz, 2H, Ar–H), 7.13 (d, J = 8.0 Hz, 2H, Ar–H), 2.38 and 2.34 (2 × s, 2H, 2 × C=NCH₂), 2.34 (s, 3H, CH₃). ¹³C NMR (125 MHz, CDCl₃, ppm) δ 142.99 (Ar–Cq), 139.82 (Ar–Cq), 137.01 (Ar–Cq), 129.24 (Ar), 127.85 (Ar), 127.17 (Ar), 43.89 (Cq), 35.55 (NCH₂), 21.21 (Ar–CH₃).

IR (ATR, neat)/cm⁻¹ 3293, 3026, 2920, 1657, 1446, 808, 698. HRMS (ESI-TOF) m/z (M+H)⁺ calcd for C₁₅H₁₆N₂ 210.1283; found 210.1286.

2-hexyl-2-(p-tolyl)aziridine (4b)

Prepared according General Procedure C using azirine 2a. The product was purified by column chromatography (SiO₂, Rf 0.45, Hexane/Ethyl Acetate/Triethylamine 70:29:1) to afford aziridine 4b as a brown waxy solid (109 mg, 50%). ¹H NMR (500 MHz, CDCl₃, ppm) δ 7.25 (d, J = 8.0 Hz, 2H, Ar–H), 7.12 (d, J = 8.0 Hz, 2H, Ar–H), 2.33 (s, 3H, Ar–CH₃), 1.91 and 1.85 (2 × s, 2H, 2 × C=NCH₂), 1.81–1.75 (m, 1H), 1.72–1.67 (m, 1H), 1.29–1.21 (m, 8H), 0.84 (t, J = 6.9 Hz, 3H, CH₂CH₃). ¹³C NMR (125 MHz, CDCl₃, ppm) δ 139.7 (Ar–Cq), 136.7 (Ar–Cq), 129.1 (2 × Ar), 127.6 (2 × Ar), 41.7 (Cq), 39.6 (CH₂C=NCH₂), 33.1 (CH₂C=NCH₂), 31.9 (CH₂), 29.5 (CH₂), 26.3 (CH₂), 22.7(CH₂), 21.2 (Ar–CH₃), 14.2 (CH₃). IR (ATR, neat)/cm⁻¹ 3291, 2954, 2856, 1676, 1464, 815. HRMS (ESI-TOF) m/z (M+H)⁺ calcd for C₁₅H₂₄N₂ 218,1909; found 218,1914.

2-butyl-2-(p-tolyl)aziridine (4c)
Prepared according General Procedure C using azirine 2a. The product was purified by column chromatography (SiO2, Rf 0.30 Hexane/Ethyl Acetate/Triethylamine 70:29:1) to afford aziridine 4c as a brown waxy solid (87 mg, 46%). 1H NMR (500 MHz, CDCl3, ppm) δ 7.26 (d, J = 7.6 Hz, 2H, Arı H), 7.12 (d, J = 7.6 Hz, 2H, Arı H), 2.33 (s, 3H, Arı CH3), 1.92 and 1.85 (2 ´s, 2H, 2 ´C=NCH2H), 1.80i 1.77 (m, 1H), 1.73i 1.69(m, 1H), 1.28i 1.26 (m, 4H), 0.84 (t, J = 6.9 Hz, 3H, CH2CH3). 13C NMR (125 MHz, CDCl3, ppm) δ 139.7 (Arı C), 136.7 (Arı C), 129.1 (2 ´Ar), 127.6 (2 ´Ar), 41.7 (Cq), 39.3 (CH2C=NCH2), 33.0 (CH2C=NCH2), 28.5 (CH2), 22.9 (CH2), 21.2 (Arı CH3), 14.2 (CH3). IR (ATR, neat)/cm⁻¹ 3296, 2956, 2928, 2859, 1517, 1458, 817, 561. HRMS (ESITOF) m/z (M+H)+ calcd for C13H20N 190,1596; found 190,1596.

2–isobutyl–2–(p–tolyl)aziridine (4d)

Prepared according General Procedure C using azirine 2a. The product was purified by column chromatography (SiO2, Rf 0.45 Hexane/Ethyl Acetate/Triethylamine 50:49:1) to afford aziridine 4d as a brown waxy solid (89 mg, 47%). 1H NMR (300 MHz, CDCl3, ppm) δ 7.29 (d, J = 8.0 Hz, 2H, Arı H), 7.12 (d, J = 8.0 Hz, 2H, Arı H), 2.33 (s, 3H, Arı CH3), 1.95 and 1.84 (2 ´s, 2H, 2 ´C=NCH2H), 1.69i 1.67 (m, 2H), 1.52 (ept, J= 6.7 Hz, 1H, CH(CH3)2), 1.07 (broad signal,1H, NH), 0.89 and 0.88 (2 ´d, J = 6.5 Hz, 6H, 2 ´CH(CH3)). 13C NMR (75 MHz, CDCl3, ppm) δ 139.6 (Arı C), 136.6 (Arı C), 129.1 (2 ´Ar), 127.6 (2 ´Ar), 48.9 (Cq), 40.6 (CH2C=NCH2), 32.8 (CH2C=NCH2), 26.2 (CH2), 23.3 (CHCH3), 22.9 (CHCH3) 21.2 (Arı CH3). IR (ATR, neat)/cm⁻¹ 3293, 3052, 2953, 2868, 1517, 1467, 813, 804, 560. HRMS (ESITOF) m/z (M+H)+ calcd for C13H20N 190,1596; found 190,1596.

2–phenyl–2–(o–tolyl)aziridine (4e)

Prepared according General Procedure C using azirine 2d. The product was purified by column chromatography (SiO2, Rf 0.55 Hexane/Ethyl Acetate/Triethylamine 50:49:1) to afford aziridine 4e as a brown oil (109 mg, 52%). 1H NMR (500 MHz, CDCl3, ppm) δ 7.52i 7.51 (m, 1H, Arı H), 7.27i 7.23 (m, 4H, Arı H), 7.21i 7.15 (m, 4H, Arı H), 2.45 and 2.34 (2 ´s, 2H, 2 x C=NCH2H), 2.24 (s, 3H, Arı CH3). 13C NMR (125 MHz, CDCl3, ppm) δ 142.3 (Arı Cq), 140.1 (Arı Cq), 138.1 (Arı Cq), 130.5 (Ar), 129.5 (Ar), 128.3 (Ar), 127.8 (Ar), 126.6 (Ar), 125.9 (Ar), 125.8 (Ar), 42.8 (Cq), 36.5, 19.6 (Arı CH3). IR (ATR, neat)/cm⁻¹ 3280, 3060, 2854, 1639, 1494, 755, 698. HRMS (ESITOF) m/z (M+H)+ calcd for C15H16N 210,1283; found 210,1281.
2-hexyl-2-\((\text{o-toly})\)aziridine (4f)

Prepared according General Procedure C using azirine 2d. The product was purified by column chromatography (SiO\(_2\), R\(_f\) 0.35 Hexane/Ethyl Acetate/Triethylamine 70:29:1) to afford aziridine 4f as a brown waxy solid (134 mg, 62%). \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 7.29\(\text{i}\) 7.26 (m, 1H, Ar\(_i\) H), 7.18\(\text{i}\) 7.12 (m, 3H, Ar\(_i\) H), 2.43 (s, 3H, Ar\(_i\) CH\(_3\)), 1.93 and 1.89 (2 \(\gamma\)s, 2H, 2 \(\gamma\)C=NCH\(_2\)), 1.74\(\text{i}\) 1.79 (m, 1H, CH\(_{CHC}NCH\_2\)), 1.64\(\text{i}\) 1.59 (m, 1H, CH\(_{CHC}NCH\_2\)), 1.31\(\text{i}\) 1.21 (broad signal, 8H), 0.84 (t, \(J = 6.9\) Hz, 3H, CH\(_2\)CH\(_3\)) . \(^13\)C NMR (125 MHz, CDCl\(_3\), ppm) \(\delta\) 140.8 (Ar\(_i\) C\(_q\)), 136.7 (Ar\(_i\) C\(_q\)), 130.4 (Ar), 129.4 (Ar), 127.2 (Ar), 125.6 (Ar), 41.7 (C\(_q\)), 38.6 (CH\(_2\)C=NCH\(_2\)), 32.7 (CH\(_2\)C=NCH\(_2\)), 31.9 (CH\(_2\)), 29.5 (CH\(_2\)), 26.2 (CH\(_2\)), 22.7 (CH\(_2\)), 19.3 (Ar\(_i\) CH\(_3\)), 14.2 (CH\(_3\)) . IR (ATR, neat)/cm\(^{-1}\) 3282, 3058, 2927, 1687, 1457, 878, 760, 729. HRMS (ESITOF) m/z (M+H)\(^{+}\) calcd for C\(_{15}\)H\(_{24}\)N 218,1909; found 218,1907.

2-butyl-2-\((\text{o-toly})\)aziridine (4g)

Prepared according General Procedure C using azirine 2d. The product was purified by column chromatography (SiO\(_2\), R\(_f\) 0.35 Hexane/Ethyl Acetate/Triethylamine 60:39:1) to afford aziridine 4g as a brown waxy solid (97 mg, 51%). \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 7.30\(\text{i}\) 7.26 (m, 1H, Ar\(_i\) H), 7.18\(\text{i}\) 7.13 (m, 3H, Ar\(_i\) H), 2.43 (s, 3H, Ar\(_i\) CH\(_3\)), 1.93 and 1.89 (2 \(\gamma\)s, 2H, 2 \(\gamma\)C=NCH\(_2\)), 1.76\(\text{i}\) 1.62 (m, 2H), 1.33\(\text{i}\) 1.21 (m, 4H), 0.83 (t, \(J = 6.9\) Hz, 3H, CH\(_2\)CH\(_3\)) . \(^13\)C NMR (125 MHz, CDCl\(_3\), ppm) \(\delta\) 140.8 (Ar\(_i\) C\(_q\)), 136.8 (Ar\(_i\) C\(_q\)), 130.4 (Ar), 129.5 (Ar), 127.2 (Ar), 125.6 (Ar), 41.7 (C\(_q\)), 38.4 (CH\(_2\)C=NCH\(_2\)), 32.7 (CH\(_2\)C=NCH\(_2\)), 28.4 (CH\(_2\)) , 23.0 (CH\(_2\)), 19.3 (Ar\(_i\) CH\(_3\)) , 14.2 (CH\(_3\)) . IR (ATR, neat)/cm\(^{-1}\) 3298, 2956, 2930, 2858, 1491, 1458, 862, 761, 730. HRMS (ESITOF) m/z (M+H)\(^{+}\) calcd for C\(_{13}\)H\(_{20}\)N 190,1596; found 190,1591.

2-decyl-2-phenylaziridine (4h)

Prepared according General Procedure C using azirine 2i. The product was purified by column chromatography (SiO\(_2\), R\(_f\) 0.45 Hexane/Ethyl Acetate/Triethylamine 60:39:1) to
afford aziridine 4h as a yellow waxy solid (116 mg, 45%). \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 7.37 (d, \(J = 7.1\) Hz, 2H, Ar\(\text{I H}\)), 7.31 (t, \(J = 7.5\) Hz, 2H, Ar\(\text{I H}\)), 7.24 (t, \(J = 7.3\) Hz, 2H, Ar\(\text{I H}\)), 1.94 and 1.90 (2 \(\text{ s}, 2\) H, 2 \(\text{ sNCHH}\)), 1.84\(\text{i}\) 1.79 (m, 1H), 1.74\(\text{i}\) 1.68 (m, 1H), 1.29\(\text{i}\) 1.21 (broad signal, 16H), 0.87 (t, \(J = 6.5\) Hz, 3H, CH\(_2\)CH\(_3\)\). \(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm) \(\delta\) 142.6 (Ar\(\text{I} q\)C), 128.4 (Ar\(\text{I} C\)), 127.7 (Ar\(\text{I} C\)), 127.1 (Ar\(\text{I} C\)), 42.1 (C\(_q\)), 39.6 (CH\(_2\)C\(_q\)PhN), 32.0 (C\(_q\)NCH\(_2\)), 29.8 (CH\(_2\)), 29.7 (2 \(\text{ rCH}_2\)), 29.6 (2 \(\text{ rCH}_2\)), 29.4 (2 \(\text{ rCH}_2\)), 29.3 (CH\(_2\)), 14.3 (CH\(_3\)). IR (ATR, neat)/cm\(^{-1}\) 3298, 3059, 2923, 2852, 1465, 867, 698. HRMS (ESI-TOF) m/z (M+H\(^+\)) calcd for C\(_{18}\)H\(_{30}\)N 260,2378; found 260,2380.

2-dodecyl-2-isobutylaziridine (4i)

Prepared according General Procedure C using azirine 2j. The product was purified by column chromatography (SiO\(_2\), R\(f\) 0.30 Hexane/Ethyl Acetate/Triethylamine 50:49:1) to afford aziridine 4i as a yellow waxy solid (128 mg, 48%). \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 1.81\(\text{i}\) 1.73 (m, 1H), 1.52 and 1.51 (2 \(\text{ r}s, 2\) H, 2 \(\text{ rNCHH}\)), 1.47 and 1.14 (2 \(\text{ rdd}, J = 14.0, 8.0\) Hz, 2H, 2 \(\text{ rCH/CH(CH}_3\)_2\)), 1.34\(\text{i}\) 1.19 (broad signal, 22H), 0.94 and 0.92 (2 \(\text{ rdd}, J = 6.6\) Hz, 6H, 2 \(\text{ rCHCH}_3\)), 0.87 (t, \(J = 6.8\) Hz, 3H, CH\(_2\)CH\(_3\)\). \(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm) \(\delta\) 45.5, 37.0, 35.7, 32.4, 32.1, 30.0, 29.8 (3 \(\text{ rCH}_2\)), 29.5, 25.9, 25.8, 23.5, 22.9, 22.8, 14.3 (CH\(_3\)). IR (ATR, neat)/cm\(^{-1}\) 2954, 2923, 2853, 1466, 867, 698. HRMS (ESI-TOF) m/z (M+H\(^+\)) calcd for C\(_{18}\)H\(_{37}\)N 3004; found 3005.

2,2,3-triphenylaziridine (4j)

Prepared according General Procedure C using azirine 2i. The product was purified by column chromatography (SiO\(_2\), R\(f\) 0.60 Hexane/Ethyl Acetate/Triethylamine 90:10) to afford aziridine 4j as a white solid (168 mg, 62%). \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 7.41 (d, \(J = 7.4\) Hz, 2H, Ar\(\text{I H}\)), 7.35 (t, \(J = 7.5\) Hz, 2H, Ar\(\text{I H}\)), 7.28 (d, \(J = 7.4\) Hz, 1H, Ar\(\text{I H}\)), 7.25 (d, \(J = 7.0\) Hz, 2H, Ar\(\text{I H}\)), 7.16\(\text{i}\) 7.11 (m, 8H, Ar\(\text{I H}\)), 3.90 (s, 1H, NCHPh), 1.80 (NH). \(^{13}\)C NMR (75 MHz, CDCl\(_3\), ppm) \(\delta\) 144.4, 138.5, 137.2, 129.8, 128.8, 128.8, 127.8 (2 \(\text{ rAr}\)), 127.6, 127.4, 127.1, 126.8, (2 \(\text{ rAr}\)), 52.4, 47.0. Analytical data (NMR) in agreement with those reported in the literature.\(^9\)
(2S*,3R*)–2–hexyl–2,3–diphenylaziridine (4k)

Prepared according General Procedure C using azirine 2l. The product was purified by column chromatography (SiO₂, Rf 0.50 Hexane/Ethyl Acetate 80:20) to afford aziridine 4k as a pale yellow waxy solid (145 mg, 52%). ¹H NMR (500 MHz, CDCl₃, ppm) δ 7.17-7.12 (m, 4H, Ar-i H), 7.10-7.02 (m, 4H, Ar-i H), 6.96-6.94 (m, 2H, Ar-i H), 3.30 (s, 1H, C=NCHPh), 2.21-2.15 and 1.68-1.62 (2 × m, 2H, 2 × C=CH(CH₃)₂), 1.51 (broad signal, 1H, NH), 1.41-1.19 (broad signal, 8H), 0.86 (t, J = 7.0 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃, ppm) δ 138.7 (Ar-i C), 137.9 (Ar-i C), 129.3 (2 × Ar-i C), 127.7 (2 × Ar-i C), 127.2 (2 × Ar-i C), 126.5 (Ar-i C), 127.4 (Ar-i C), 50.8 (C₆), 45.6 (NCHPh), 42.9 (PhC(CH₂)₂), 31.9, 29.5, 26.2, 22.7, 14.2 (CH₃). IR (ATR, neat)/cm⁻¹ 3298, 3028, 2927, 2855, 1603, 1447, 752, 696. HRMS (ESI-TOF) m/z (M+H)+ calcd for C₂₀H₂₆N₂ 380.2065; found 380.2053.

(2S*,3R*)–2–isobutyl–2,3–diphenylaziridine (4l)

Prepared according General Procedure C using azirine 2l. The product was purified by column chromatography (SiO₂, Rf 0.50 Hexane/AcOEt/Et₃N 90:9:1) to afford aziridine 4l as a pale yellow waxy solid (113 mg, 45%). ¹H NMR (300 MHz, CDCl₃, ppm) δ 7.47 (s, 1H, Ar-i H), 7.41-7.26 (m, 5H, Ar-i H), 7.25-7.17 (m, 4H, Ar-i H), 3.47 (s, PhCHN, 1H), 2.42 (dd, J = 13.0, 5.3 Hz, PhCC=CH(CH₂)₉, 1H), 1.84-1.67 (m, 2H), 1.19 and 1.15 (2 × t, J = 6.3 Hz, 2 × PhC(CH₂)₂(C=CH₂)). ¹³C NMR (75 MHz, CDCl₃, ppm) δ 138.3 (Ar-i C), 137.5 (Ar-i C), 129.1 (Ar), 127.5 (Ar), 127.4 (Ar), 127.1 (Ar), 126.3 (2 × Ar), 52.0 (PhC₆CH₂CH(CH₃)₂), 49.6 (PhC₆CH₂CH(C=CH₂)₂), 45.0 (PhCHN), 26.1 (PhC₆CH₂CH(CH₃)₂), 23.2 and 22.7 (2 × CH(CH₃)₂). IR (ATR, neat)/cm⁻¹ 3086, 3028, 2926, 2869, 1683, 1498, 871, 697, 607. HRMS (ESI-TOF) m/z (M+H)+ calcd for C₁₈H₂₂N₂ 252,1752; found 252,1756.
5. Copies of $^1$H, $^{13}$C, $^{19}$F, NOESY NMR spectra

(1) $^1$H NMR, 300 MHz, CDCl$_3$

(2) $^1$H NMR, 500 MHz, CDCl$_3$
(1c)

$^{1}H$ NMR, 500 MHz, CDCl$_3$

(1c)

$^{19}F$ NMR, 282 MHz, CDCl$_3$
(1H NMR, 300 MHz, CDCl₃)

(1H NMR, 300 MHz, CDCl₃)
(1H NMR, 500 MHz, CDCl₃)

1f

(1H NMR, 500 MHz, CDCl₃)

1g

(1H NMR, 500 MHz, CDCl₃)
$\text{C}_9\text{H}_7$ $\text{N}_3$

$1h$

($^1\text{H} \text{NMR, 300 MHz, CDCl}_3$)

$\text{C}_{17}\text{H}_{21}$ $\text{N}_3$

$1i$

($^1\text{H} \text{NMR, 300 MHz, CDCl}_3$)
$^{1}H$ NMR, 300 MHz, CDCl$_3$

$^{13}$C NMR, 75 MHz, CDCl$_3$
(1H NMR, 300 MHz, CDCl₃)

(19F NMR, 282 MHz, CDCl₃)
1k
($^{13}$C NMR, 125 MHz, CDCl$_3$)

1l
($^1$H NMR, 300 MHz, CDCl$_3$)
2a
({}^1H NMR, 300 MHz, CDCl$_3$)

2b
({}^1H NMR, 300 MHz, CDCl$_3$)
(1H NMR, 300 MHz, CDCl3)

(19F NMR, 470 MHz, CDCl3)
\( ^1\text{H NMR, 500 MHz, CDCl}_3 \)

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

(13C NMR, 125 MHz, CDCl$_3$)
(1H NMR, 500 MHz, CDCl₃)

2f

(1H NMR, 500 MHz, CDCl₃)

2g
$^{1}H$ NMR, 500 MHz, CDCl$_3$)

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

$^{13}C$ NMR, 125 MHz, CDCl$_3$
(1H NMR, 300 MHz, CDCl₃)

(13C NMR, 75 MHz, CDCl₃)
$^1$H NMR, 500 MHz, CDCl$_3$  

$^1$F NMR, 282 MHz, CDCl$_3$
(1H NMR, 500 MHz, CDCl₃)

(1H NMR, 500 MHz, CDCl₃)
\( ^{13}\text{C NMR, 125 MHz, CDCl}_3 \)

\( ^1\text{H NMR, 500 MHz, CDCl}_3 \)
$^{1}H$ NMR, 500 MHz, CDCl$_3$}

$^{13}C$ NMR, 125 MHz, CDCl$_3$
(1H NMR, 300 MHz, CDCl₃)

(13C NMR, 75 MHz, CDCl₃)
$^{1}H\text{ NMR, 500 MHz, CDCl}_3$

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

$^{13}C$ NMR, 125 MHz, CDCl$_3$)
$^3$g

($^1$H NMR, 500 MHz, CDCl$_3$)

$^{13}$g

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

$^{13}C$ NMR, 125 MHz, CDCl$_3$)
3i
($^1$H NMR, 500 MHz, CDCl$_3$)

3i
($^{13}$C NMR, 125 MHz, CDCl$_3$)
$^1$H NMR, 500 MHz, CDCl$_3$

$^{13}$C NMR, 75 MHz, CDCl$_3$
$3k$  
($^1$H NMR, 500 MHz, CDCl$_3$)

$3k$  
($^{13}$C NMR, 125 MHz, CDCl$_3$)
6. References

1. Terentiev, A. O.; Krylov, I. B.; Kokorekin, V. A.; Nikishin, G. I. Synthetic Communications 2008, 38 (21), 3797–3809.

2. Cen, J.; Li, J.; Zhang, Y.; Zhu, Z.; Yang, S.; Jiang, H. Org. Lett. 2018, 20 (15), 4434–4438.

3. Xiang, L.; Niu, Y.; Pang, X.; Yang, X.; Yan, R. Chem. Commun. 2015, 51 (30), 6598–6600.

4. Wu, S.-W.; Liu, F. Org. Lett. 2016, 18 (15), 3642–3645.

5. Li, Z.; Huo, T.; Li, L.; Feng, S.; Wang, Q.; Zhang, Z.; Pang, S.; Zhang, Z.; Wang, P.; Zhang, Z. Org. Lett. 2018, 20 (24), 7762–7766.

6. Li, X.; Liao, S.; Wang, Z.; Zhang, L. Org. Lett. 2017, 19 (14), 3687–3690.

7. Zhou, W.; Zhang, M.; Li, H.; Chen, W. Org. Lett. 2016, 19 (1), 106–109.

8. Khlebnikov, A. F.; Novikov, M. S.; Petrovskii, P. P.; Stoeckli-Evans, H. J. Org. Chem. 2011, 76 (13), 5384–5391.

9. Li, J.; Huang, W.; Chen, J.; He, L.; Cheng, X.; Li, G. Angew. Chem. Int. Ed. 2018, 57 (20), 5695–5698.