The Decarboxylative Blaise Reaction

Jae Hoon Lee, Bo Seung Choi, Jay Hyok Chang, Hee Bong Lee, Joo-Yong Yoon, Jaeick Lee, and Hyunik Shin*

Chemical Development Division, LG Life Sciences Ltd/R&D, 104-1, Moonji-dong, Yusong-gu, Daejeon 305-380, Korea.

hisin@lgls.com

Contents

1. General Methods
2. Characterization Data
3. ¹H and ¹³C spectra of 3a
4. ¹H and ¹³C spectra of 3b
5. ¹H and ¹³C spectra of 3d
6. ¹H and ¹³C spectra of 3f
7. ¹H and ¹³C spectra of 3g
8. ¹H and ¹³C spectra of 3h
9. ¹H and ¹³C spectra of 3i
10. ¹H and ¹³C spectra of 3j
11. ¹H and ¹³C spectra of 3k

S-1
1. General Methods

All reactions were performed under nitrogen atmosphere. All commercially available reagents and solvents were used without further purification unless otherwise noted. Column chromatography was performed with silica gel (0.063-0.2 mm). The combined organic layers were dried over MgSO4. Solvents were evaporated under reduced pressure. All yields given refer to as isolated yields. NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts (delta) are reported in ppm downfield from tetramethylsilane. Coupling constants (J values) are reported in Hertz. HRMS experiments were performed on a hybrid quadrupole time-of-flight mass spectrometer. LC-MS experiments were performed using a single-quadrupole mass spectrometer equipped with HPLC system.

2. Characterization Data

(Z)-3-Amino-3-phenyl-acrylic acid ethyl ester (3a):\(^1\) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.45-7.38 (m, 2 H), 7.33-7.24 (m, 3 H), 4.85 (s, 1 H), 4.05 (q, \(J = 7.1\) Hz, 2 H), 1.18 (t, \(J = 7.1\) Hz, 3 H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.4, 160.5, 137.72, 130.2, 128.8, 126.1, 84.5, 58.9, 14.6; LC-MS (ESI) m/z: 192.2 (M+1).

(Z)-3-Amino-3-(4-bromo-phenyl)-acrylic acid ethyl ester (3b): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.54 (d, \(J = 8.5\) Hz, 2 H), 7.41 (d, \(J = 8.5\) Hz, 2 H), 4.93 (s, 1 H), 4.16 (q, \(J = 7.1\) Hz, 2 H), 1.29 (t, \(J = 7.1\) Hz, 3 H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.1, 159.1, 136.6, 132.0, 127.7, 124.4, 85.1, 50.0, 14.6; LC-MS (ESI) m/z: 270.0 (M+1), 272.1 (M+1); HRMS (ESI) Calcd for C\(_{11}\)H\(_{13}\)BrNO\(_2\): 270.0124. Found 270.0123 (M+H\(^+\)).

(Z)-3-Amino-3-p-tolyl-acrylic acid ethyl ester (3d): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.50 (m, 2 H), 6.92 (m, 2 H), 4.93 (s, 1 H), 4.16 (q, \(J = 7.1\) Hz, 2 H), 3.83 (s, 3 H), 1.29 (t, \(J = 7.1\) Hz, 3 H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 161.1, 160.1, 129.7, 127.4, 114.0, 83.5, 58.7, 55.3, 14.5; LC-MS (ESI) m/z: 206.2 (M+1).

(Z)-3-Amino-3-(4-methoxy-phenyl)-acrylic acid ethyl ester (3f): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.42 (d, \(J = 7.9\) Hz, 2 H), 7.19 (d, \(J = 7.9\) Hz, 2 H), 4.94 (s, 1 H), 4.16 (q, \(J = 7.1\) Hz, 2 H), 2.36 (s, 3 H), 1.29 (t, \(J = 7.1\) Hz, 3 H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.3, 160.4, 140.3, 134.5, 129.3, 125.9, 83.8, 58.7, 21.1, 14.4; LC-MS (ESI) m/z: 222.1 (M+1); HRMS (ESI) Calcd for C\(_{12}\)H\(_{16}\)NO\(_3\): 222.1124. Found 222.1122 (M+H\(^+\)).

(Z)-3-Amino-3-pyridin-2-yl-acrylic acid ethyl ester (3i): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.62 (d, 1 H), 7.74 (m, 2 H), 7.34 (m, 1 H), 5.34 (s, 1 H), 4.20 (q, \(J = 7.1\) Hz, 2 H), 1.31 (t, \(J = 7.1\) Hz, 3 H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.5, 155.4, 151.2, 148.6, 136.7, 124.6, 120.1, 82.2, 58.9, 14.5; LC-MS (ESI) m/z: 193.1 (M+1), 194.1 (M+2); HRMS (ESI) Calcd for C\(_{9}\)H\(_{13}\)N\(_2\)O\(_2\): 193.0971. Found 193.0977 (M+H\(^+\)).

(Z)-3-Amino-3-furan-3-yl-acrylic acid ethyl ester (3j): $^1$H MNR (400 MHz, CDCl$_3$) $\delta$ 7.73 (m, 1 H), 7.44 (m, 1 H), 6.55 (m, 1 H), 4.94 (s, 1 H), 4.15 (q, $J = 7.1$ Hz, 2 H), 1.29 (t, $J = 7.1$ Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.3, 152.3, 143.9, 140.6, 124.0, 107.9, 83.7, 58.8, 14.5; LC-MS (ESI) m/z: 182.1 (M+1); HRMS (ESI) Calcd for C$_9$H$_{12}$NO$_3$: 182.0811. Found 182.0815 (M+H$^+$).

(Z)-3-Amino-3-cyclopropyl-acrylic acid ethyl ester (3k): $^1$H MNR (400 MHz, CDCl$_3$) $\delta$ 4.43 (s, 1 H), 4.06 (q, $J = 7.1$ Hz, 2 H), 1.39 (m, 1 H), 1.23 (t, $J = 7.1$ Hz, 3 H), 0.84 (m, 2 H), 0.71 (m, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.3, 165.1, 152.3, 143.9, 140.6, 124.0, 107.9, 80.5, 58.4, 15.7, 14.5, 7.0; LC-MS (ESI) m/z: 156.1 (M+1); HRMS (ESI) Calcd for C$_8$H$_{14}$NO$_2$: 156.1019. Found 156.1020 (M+H$^+$).

---

3. $^1$H and $^{13}$C spectra of 3a
4. $^1\text{H}$ and $^{13}\text{C}$ spectra of 3b
5. $^1$H and $^{13}$C spectra of 3d
6. $^1$H and $^{13}$C spectra of 3f
7. $^1$H and $^{13}$C spectra of 3g
8. $^1$H and $^{13}$C spectra of 3h
9. $^1$H and $^{13}$C spectra of 3i
10. $^1$H and $^{13}$C spectra of 3j
11. $^1$H and $^{13}$C spectra of 3k