Supporting Information
for DOI: 10.1055/s-0037-1610110
© Georg Thieme Verlag KG Stuttgart · New York 2018
Supporting Information

α-Alkylation of N-C Axially Chiral Quinazolinone Derivatives bearing Various \textit{ortho}-Substituted Phenyl Groups: Relation between Diastereoselectivity and \textit{ortho}-Substituent

Mizuki Matsuoka, Asumi Iida, and Osamu Kitagawa*

†Department of Applied Chemistry, Shibaura Institute of Technology, 3-7-5 Toyosu, Kohto-ku, Tokyo, 135-8548, Japan.

The Contents of Supporting Information. Experimental procedures and characterization data for synthesis of new compounds, copies of $^1$H-NMR and $^{13}$C-NMR spectra of all compounds.

(Contents)
Experimental procedures and characterization data S2-S13

Copies of $^1$H- and $^{13}$C-NMR chart of all compounds S14-S43
Experimental Section

Melting points were uncorrected. $^1$H and $^{13}$C NMR spectra were recorded on a 400 MHz spectrometer. In $^1$H and $^{13}$C NMR spectra, chemical shifts were expressed in $\delta$ (ppm) downfield from CHCl$_3$ (7.26 ppm) and CDCl$_3$ (77.0 ppm), respectively. HRMS were recorded on a double focusing magnetic sector mass spectrometer using electron impact ionization. Column chromatography was performed on silica gel (75-150 µm). Medium-pressure liquid chromatography (MPLC) was performed on a 25 x 4 cm i. d. prepacked column (silica gel, 10 µm) with a UV detector.

3-(2-Fluorophenyl)-2-ethylquinazolin-4(3H)-one (1a). Under N$_2$ atmosphere, to 2-fluoroaniline (278 mg, 2.5 mmol) and N-propionyl anthranilic acid (386 mg, 2.0 mmol) in toluene (6.0 mL) was added PCl$_3$ (412 mg, 3.0 mmol), and the reaction mixture was stirred for 30 min at rt and for 7 h at 130 °C. The mixture was poured into water and extracted with AcOEt. The AcOEt extracts were washed with brine, dried over MgSO$_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave 1a (499 mg, 93%). 1a: white solid; mp 85-86 °C; IR (neat) 1697 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$: 8.28 (1H, dd, $J = 1.6$, 8.0 Hz), 7.72-7.80 (2H, m), 7.45-7.54 (2H, m), 7.28-7.35 (3H, m), 2.47 (2H, q, $J = 7.2$ Hz), 1.24 (3H, t, $J = 7.2$ Hz); $^{13}$C NMR (CDCl$_3$) $\delta$: 161.8, 158.9, 157.3, 156.4, 147.4, 134.6, 131.3 (d, $J_{C-F} = 7.6$ Hz), 130.1, 127.0 (d, $J_{C-F} = 11.5$ Hz), 126.6, 125.1 (d, $J_{C-F} = 4.2$ Hz), 124.8 (d, $J_{C-F} = 14.3$ Hz) 118.6 (d, $J_{C-F} = 361.3$ Hz), 117.0, 28.7, 10.8; MS (m/z) 291 (MNa$^+$); HRMS. Calcd for C$_{16}$H$_{13}$FN$_2$NaO (MNa$^+$) 291.09096. Found: 291.08878.

3-(2-Chlorophenyl)-2-ethylquinazolin-4(3H)-one (1b). 1b was prepared from 2-chloroaniline (319 mg, 2.5 mmol) and N-propionyl anthranilic acid (386 mg, 2.0 mmol) in accordance with the procedure for the synthesis of 1a. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave 1b (467 mg, 82%). 1b: white solid; mp 123-126 °C; IR (neat) 1682 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$: 8.29 (1H, dd, $J = 1.6$, 8.0 Hz), 7.74-7.81 (2H, m), 7.62 (1H, m), 7.44-7.50 (3H, m), 7.33 (1H, m), 2.44 (1H, qd, $J = 7.6$, 16.4 Hz), 2.36 (1H, qd, $J = 7.6$, 16.4 Hz),
1.25 (3H, t, J = 7.6 Hz); $^{13}$C NMR (CDCl$_3$) δ: 161.6, 157.2, 147.5, 135.1, 134.7, 132.8, 130.7, 130.1, 128.2, 127.12, 127.10, 126.7, 120.6, 28.7, 10.8; MS (m/z) 307 (MNa$^+$, $^{35}$Cl); HRMS. Calcd for C$_{16}$H$_{13}$N$_2$NaO (MNa$^+$) 307.06141. Found: 307.06243.

3-(2-Bromophenyl)-2-ethylquinazolin-4(3H)-one (1c). 1c was prepared from 2-bromoaniline (559 mg, 3.25 mmol) and N-propionyl anthranilic acid (483 mg, 2.5 mmol) in accordance with the procedure for the synthesis of 1a. Purification of the residue by column chromatography (hexane/AcOEt = 3) gave 1c (611 mg, 74%). 1c: white solid; mp 142-143 °C; IR (neat) 1682 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ: 8.29 (1H, dd, J = 1.2, 8.0 Hz), 7.73-7.81 (3H, m), 7.46-7.54 (2H, m), 7.40 (1H, dt, J = 1.6, 7.6 Hz), 7.35 (1H, dd, J = 1.2, 7.6 Hz), 2.42 (1H, qd, J = 7.6, 16.4 Hz), 2.35 (1H, qd, J = 7.6, 16.4 Hz), 1.26 (3H, t, J = 7.6 Hz); $^{13}$C NMR (CDCl$_3$) δ: 161.6, 157.0, 147.6, 136.7, 134.6, 133.9, 130.8, 130.1, 128.9, 127.2, 127.1, 126.6, 123.2, 120.7, 28.8, 10.8; MS (m/z) 307 (MNa$^+$, $^{79}$Br); HRMS. Calcd for C$_{16}$H$_{14}$BrN$_2$O (MH$^+$) 329.02859. Found: 329.03065.

3-(2-Iodophenyl)-2-ethylquinazolin-4(3H)-one (1d). 1d was prepared from 2-iodoaniline (438 mg, 2.5 mmol) and N-propionyl anthranilic acid (386 mg, 2.0 mmol) in accordance with the procedure for the synthesis of 1a. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave 1d (564 mg, 75%). 1d: white solid; mp 171-174 °C; IR (neat) 1682 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ: 8.30 (1H, dd, J = 1.2, 8.4 Hz), 8.02 (1H, dd, J = 0.8, 7.6 Hz), 7.75-7.81 (2H, m), 7.55 (1H, dt, J = 1.2, 7.6 Hz), 7.48 (1H, ddd, J = 1.6, 6.4, 8.0 Hz), 7.33 (1H, dd, J = 1.6, 8.0 Hz), 7.22 (1H, dt, J = 1.2, 8.0 Hz), 2.41 (1H, qd, J = 7.6, 16.8 Hz), 2.31 (1H, qd, J = 7.6, 16.8 Hz), 1.27 (3H, t, J = 7.2 Hz); $^{13}$C NMR (CDCl$_3$) δ: 161.6, 156.9, 147.5, 140.3, 140.2, 134.6, 130.7, 129.9, 129.4, 127.21, 127.15, 126.6, 120.8, 99.4, 29.1, 10.9; MS (m/z) 399 (MNa$^+$); HRMS. Calcd for C$_{16}$H$_{13}$I$^+$N$_2$NaO (MNa$^+$) 398.99703 Found: 398.99450.

3-(2-Methylphenyl)-2-ethylquinazolin-4(3H)-one (1e). 1e was prepared from 2-methylaniline (268 mg, 2.5 mmol) and N-propionyl anthranilic acid (386 mg, 2.5 mmol) in accordance with the procedure for the synthesis of 1e. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave 1e (465 mg, 88%). 1e: white solid; mp 88-93 °C; IR
(neat) 1678 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.29 (1H, dd, J = 0.8, 6.8 Hz), 7.75-7.80 (2H, m), 7.48 (1H, m), 7.35-7.42 (3H, m), 7.16 (1H, d, J = 7.6 Hz), 2.39-2.48 (2H, m), 2.11 (3H, s), 1.23 (3H, t, J = 7.2 Hz); ¹³C NMR (CDCl₃) δ: 161.8, 157.9, 147.7, 136.4, 135.6, 134.5, 131.5, 129.5, 128.2, 127.5, 127.1, 127.0, 126.5, 120.7, 28.9, 17.5, 11.0; MS (m/z) 287 (MNa⁺); HRMS. Calcd for C₁₇H₁₆N₂NaO (MNa⁺) 287.11603 Found: 287.11570.

3-(2-Ethylphenyl)-2-ethylquinazolin-4(3H)-one (1f). 1f was prepared from 2-ethylaniline (303 mg, 2.5 mmol) and N-propionyl anthranilic acid (386 mg, 2.0 mmol) in accordance with the procedure for the synthesis of 1a. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave 1f (523 mg, 94%). 1f: white solid; mp 128-132 °C; IR (neat) 1678 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.28 (1H, d, J = 8.0 Hz), 7.73 (2H, d, J = 3.6 Hz), 7.40-7.44 (3H, m), 7.34 (1H, m), 7.13 (1H, d, J = 7.6 Hz), 2.26-2.43 (4H, m), 1.22 (3H, t, J = 7.2 Hz), 1.15 (3H, t, J = 7.2 Hz); ¹³C NMR (CDCl₃) δ: 162.1, 158.0, 147.7, 140.9, 135.8, 134.4, 129.7, 129.3, 128.3, 127.3, 127.1, 127.0, 126.5, 120.7, 28.9, 23.6, 13.5, 11.0; MS (m/z) 301 (MNa⁺); HRMS. Calcd for C₁₈H₁₈N₂NaO (MNa⁺) 301.13168 Found: 301.13116.

3-(2-Isopropylphenyl)-2-ethylquinazolin-4(3H)-one (1g). 1g was prepared from 2-isopropylaniline (338 mg, 2.5 mmol) and N-propionyl anthranilic acid (386 mg, 2.0 mmol) in accordance with the procedure for the synthesis of 1a. Purification of the residue by column chromatography (hexane/AcOEt = 6) gave 1g (374 mg, 64%). 1g: white solid; mp 178-182 °C; IR (neat) 1674 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.29 (1H, dd, J = 1.6, 8.4 Hz), 7.73-7.80 (2H, m), 7.45-7.53 (3H, m), 7.35 (1H, m), 7.11 (1H, d, J = 8.4 Hz), 2.63 (1H, sept, J = 6.8 Hz), 2.15 (1H, qd, J = 7.2, 16.0 Hz), 2.07 (1H, qd, J = 7.2, 16.0 Hz), 1.25 (3H, t, J = 7.2 Hz), 1.19 (3H, d, J = 6.8 Hz), 1.16 (3H, d, J = 6.8 Hz); ¹³C NMR (CDCl₃) δ: 162.2, 158.1, 147.6, 145.8, 143.8, 134.4, 129.9 128.2, 127.2, 127.1, 127.0, 126.5, 120.7, 29.0, 28.2, 24.2, 23.0, 11.0; MS (m/z) 315 (MNa⁺); HRMS. Calcd for C₁₉H₂₀N₂NaO (MNa⁺) 315.14733 Found: 315.14490.

3-(2-Trifluoromethylphenyl)-2-ethylquinazolin-4(3H)-one (1h). 1h was prepared from 2-trifluoromethylaniline (403 mg, 2.5 mmol) and N-propionyl anthranilic acid (386 mg, 2.0 mmol) in
accordance with the procedure for the synthesis of 1a. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave 1h (495 mg, 78%). 1h: white solid; mp 172-177 °C; IR (neat) 1684 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.27 (1H, dd, J = 1.6, 8.0 Hz), 7.89 (1H, d, J = 6.8 Hz), 7.77-7.81 (3H, m), 7.67 (1H, t, J = 7.6 Hz), 7.48 (1H, ddd, J = 1.2, 6.8, 8.0 Hz), 7.37 (1H, d, J = 7.6 Hz), 2.39 (1H, qd, J = 7.2, 16.4 Hz), 2.30 (1H, qd, J = 7.2, 16.4 Hz), 1.26 (3H, t, J = 7.2 Hz); ¹³C NMR (CDCl₃) δ: 162.3, 157.1, 147.4, 135.3, 134.7, 133.5, 130.9, 129.9, 127.90 (q, J_C-F = 30.5 Hz), 127.86 (q, J_C-F = 5.8 Hz), 127.1, 127.0, 126.7, 122.8 (q, J_C-F = 272.6 Hz), 120.3, 28.8, 10.8; MS (m/z) 341 (MNa⁺); HRMS. Calcd for C₁₇H₁₃F₃N₂NaO (MNa⁺) 341.08777. Found: 341.08992.

(P*•S*) and (P*•R*) 3-(2-Bromophenyl)-2-(pent-4-en-2-yl)quinazolin-4(3H)-one (2c and 2c'). Under N₂ atmosphere, to the solution of rac-1c (99 mg, 0.3 mmol) in THF (2.0 mL) was added THF solution of LiN(SiMe₃)₂ (1.3 M, 0.346 mL, 0.45 mmol) at -20 °C, and the mixture was stirred for 30 min at -20 °C. Allyl bromide (54 mg, 0.45 mmol) was added to the mixture at -20 °C. After being stirred for 30 min at -20 °C, the mixture was poured into NH₄Cl aq and extracted with AcOEt. The AcOEt extracts were washed with brine, dried over MgSO₄, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave the mixtures of 2c and 2c' (94 mg, 85 %). The diastereomer ratio of 2c and 2c' (7.5:1) was determined on the basis of ¹H-NMR analysis. 2c and 2c' were completely separated by medium pressure liquid chromatography (MPLC, eluent: hexan/AcOEt = 8) to give diastereomerically pure 2c and 2c' (82 mg and 12 mg). 2c: white solid; mp 114-116 °C; IR (neat) 1684 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.29 (1H, dd, J = 0.8, 7.6 Hz), 7.73-7.80 (3H, m), 7.51 (1H, dt, J = 1.6, 7.6 Hz), 7.47 (1H, ddd, J = 2.0, 6.8, 7.6 Hz), 7.39 (1H, dt, J = 1.6, 8.0 Hz), 7.33 (1H, d, J = 1.6, 7.6 Hz), 5.57 (1H, tdd, J = 6.8, 10.8, 16.0 Hz), 4.94 (1H, d, J = 10.8 Hz), 4.94 (1H, d, J = 16.0 Hz), 2.41-2.56 (2H, m), 2.20 (1H, td, J = 6.8, 13.6 Hz), 1.33 (3H, d, J = 6.8 Hz); ¹³C NMR (CDCl₃) δ: 161.8, 159.8, 147.7, 136.7, 135.5, 134.6, 133.8, 130.7, 128.6, 127.3, 127.0, 126.5, 123.3, 120.6, 117.2, 40.4, 37.9, 18.9; MS (m/z) 391 (MNa⁺, ⁷⁹Br); HRMS. Calcd for C₁₉H₁₅⁷⁹BrN₂ONa (MNa⁺) 391.04220. Found: 391.04207. 2c': white solid; mp 78-80 °C; IR (neat) 1680 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.28 (1H, dd, J = 1.6, 8.0 Hz),
7.73-7.81 (3H, m), 7.51 (1H, dt, $J = 1.2$, 7.2 Hz), 7.47 (1H, ddd, $J = 1.2$, 7.2, 8.4 Hz), 7.40 (1H, dt, $J = 2.0$, 8.0 Hz), 7.35 (1H, dd, $J = 2.0$, 8.0 Hz), 5.71 (1H, m), 5.04 (1H, d, $J = 17.2$ Hz), 4.97 (1H, d, $J = 10.0$ Hz), 2.75 (1H, m), 2.31-2.40 (2H, m), 1.17 (3H, d, $J = 6.4$ Hz); $^{13}$C NMR (CDCl$_3$) δ: 161.8, 160.0, 147.6, 136.6, 136.2, 134.6, 133.9, 130.8, 130.2, 128.7, 127.3, 127.1, 126.6, 123.3, 120.6, 117.0, 39.1, 38.0, 19.4; MS ($m/z$) 391 (MNa$^+$, $^{79}$Br); HRMS. Calcd for C$_{19}$H$_{17}$$^{79}$BrN$_2$ONa (MNa$^+$) 391.04220. Found: 391.04071.

($P^*, S^*$) and ($P^*, R^*$) 3-(2-Fluorophenyl)-2-(pent-4-en-2-yl)quinazolin-4(3H)-one (2a and 2a$'$). 2a and 2a$'$ were prepared from rac-1a (80 mg, 0.3 mmol) and allyl bromide (54 mg, 0.45 mmol) in accordance with the procedure for synthesis of 2c and 2c$'$. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave the mixtures of 2a and 2a$'$ (85 mg, 96%). 2a and 2a$'$ were completely separated by MPLC (hexane/AcOEt = 7) to give diastereomerically pure 2a and 2a$'$ (40 mg and 41 mg). The diastereomer ratio of 2a and 2a$'$ (1:1) was determined on the basis of the isolated yield. The stereochemistries of 2a and 2a$'$ could not be determined. 2a or 2a$'$: white solid; mp 77-80 °C; IR (neat) 1692 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ: 8.27 (1H, dd, $J = 1.2$, 7.6 Hz), 7.73-7.80 (2H, m), 7.44-7.54 (2H, m), 7.24-7.35 (3H, m), 5.62 (1H, m), 4.98 (1H, dd, $J = 1.2$, 16.8 Hz), 4.94 (1H, dd, $J = 2.0$, 10.0 Hz), 2.57-2.68 (2H, m), 2.23 (1H, m), 1.23 (3H, d, $J = 6.4$ Hz); $^{13}$C NMR (CDCl$_3$) δ: 162.0, 159.9, 159.2, 156.7, 147.6, 135.7, 134.6, 131.2 (d, $J_{C-F} = 7.7$ Hz), 130.7, 127.1 (d, $J_{C-F} = 25.8$ Hz), 126.6, 125.0 (d, $J_{C-F} = 3.8$ Hz), 124.8 (d, $J_{C-F} = 13.4$ Hz), 118.6 (d, $J_{C-F} = 362.3$ Hz) 117.1, 117.0, 39.8, 37.9, 19.1; MS ($m/z$) 331 (MNa$^+$); HRMS. Calcd for C$_{19}$H$_{17}$FN$_2$NaO (MNa$^+$) 331.12226. Found: 331.12033. 2a or 2a$'$: white solid; mp 86-88 °C; IR (neat) 1694 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ: 8.26 (1H, dd, $J = 1.2$, 7.6 Hz), 7.72-7.80 (2H, m), 7.52 (1H, m), 7.46 (1H, ddd, $J = 1.2$, 6.8, 7.6 Hz), 7.27-7.35 (3H, m), 5.62 (1H, m), 4.97 (1H, d, $J = 17.2$ Hz), 4.94 (1H, d, $J = 10.0$ Hz), 2.65 (1H, td, $J = 6.4$, 13.6 Hz), 2.55 (1H, sext, $J = 6.4$ Hz), 2.34 (1H, td, $J = 6.8$, 13.6 Hz), 1.23 (3H, d, $J = 6.4$ Hz); $^{13}$C NMR (CDCl$_3$) δ: 162.0, 159.9, 159.0, 156.5, 147.6, 135.6, 134.6, 131.3 (d, $J_{C-F} = 7.7$ Hz), 130.1, 127.1 (d, $J_{C-F} = 25.8$ Hz), 126.6, 125.1 (d, $J_{C-F} = 3.8$ Hz), 124.9 (d, $J_{C-F} =
The diastereomer ratio of chromatography (hexane/AcOEt = 4) gave the mixtures of accordance with the procedure for synthesis of (M130.1.
m(1H, 347.09271 117.2 159.9, 147.7, 5.59 δ
and 2b) were completely separated by MPLC (hexane/AcOEt = 7) to give diastereomerically pure 2b and 2b' (77 mg and 15 mg). 2b: white solid; mp 99-101 °C; IR (neat) 1684 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.29 (1H, dd, J = 1.2, 7.6 Hz), 7.74-7.80 (2H, m), 7.61 (1H, m), 7.43-7.50 (3H, m), 7.32 (1H, m), 5.59 (1H, m), 4.95 (1H, d, J = 15.6 Hz), 4.94 (1H, d, J = 11.2 Hz), 2.56 (1H, td, J = 6.8, 13.2 Hz), 2.48 (1H, m), 2.21 (1H, td, J = 7.2, 13.2 Hz), 1.30 (3H, d, J = 7.2 Hz); ¹³C NMR (CDCl₃) δ: 161.8, 159.9, 147.7, 135.6, 135.1, 134.6, 133.0, 130.8, 130.7, 130.6, 128.0, 127.3, 127.0, 126.5, 120.6, 117.2, 40.3, 37.9, 19.0; MS (m/z) 347 (MNa⁺, ³⁵Cl); HRMS. Calcd for C₁₉H₁₇²⁵Cl₂NaO(MNa⁺) 347.09271. Found: 347.09023. 2b': colorless oil; IR (neat) 1682 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.28 (1H, td, J = 0.8, 7.6 Hz), 7.73-7.78 (2H, m), 7.62 (1H, m), 7.44-7.51 (3H, m), 7.34 (1H, m), 5.68 (1H, m), 5.02 (1H, qd, J = 2.0, 16.8 Hz), 4.95 (1H, td, J = 0.8, 10.4 Hz), 2.73 (1H, m), 2.28-2.42 (2H, m), 1.18 (3H, d, J = 6.4 Hz); ¹³C NMR (CDCl₃) δ: 161.8, 159.9, 147.7, 136.1, 135.0, 134.6, 132.9, 130.70, 130.68, 130.2, 128.1, 127.3, 127.0, 126.6, 120.6, 116.9, 39.1, 38.0, 19.4; MS (m/z) 347 (MNa⁺, ³⁵Cl); HRMS. Calcd for C₁₉H₁₇²⁵Cl₂NaO(MNa⁺) 347.09271. Found: 347.09105.

(P⁺,S⁺) and (P⁺,R⁺) 3-(2-Iodophenyl)-2-(pent-4-en-2-yl)quinazolin-4(3H)-one (2d and 2d'). 2d and 2d' were prepared from rac-1d (113 mg, 0.3 mmol) and allyl bromide (54 mg, 0.45 mmol) in accordance with the procedure for synthesis of 2c and 2c'. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave the mixtures of 2d and 2d' (106 mg, 85 %). The diastereomer ratio of 2d and 2d' (17.9:1) was determined on the basis of ¹H-NMR analysis. 2d and 2d' were completely separated by MPLC (hexane/AcOEt = 7) to give diastereomerically pure 2d
and 2d’ (100 mg and 5 mg). 2d: white solid; mp 135-137 °C; IR (neat) 1684 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.29 (1H, dd, J = 1.2, 7.6 Hz), 8.02 (1H, dd, J = 1.2, 7.6 Hz), 7.74-7.80 (2H, m), 7.54 (1H, dt, J = 1.2, 7.6 Hz), 7.47 (1H, ddd, J = 1.6, 6.4, 8.0 Hz), 7.33 (1H, dd, J = 1.2, 7.6 Hz), 7.21 (1H, dt, J = 2.0, 8.0 Hz), 5.55 (1H, m), 4.94 (1H, d, J = 9.6 Hz), 4.93 (1H, d, J = 16.0 Hz), 2.37-2.53 (2H, m), 2.22 (1H, td, J = 7.2, 13.6 Hz), 1.37 (3H, d, J = 6.4 Hz); ¹³C NMR (CDCl₃) δ: 161.7, 159.6, 147.6, 140.2, 140.1, 135.4, 134.5, 130.6, 130.0, 129.5, 127.3, 127.0, 126.5, 120.7, 117.2, 99.5, 40.3, 37.9, 18.9; MS (m/z) 439 (MNa⁺); HRMS. Calcd for C₁₉H₁₇IN₂ONa (MNa⁺) 439.02833. Found: 439.02796. 2d’: white solid; mp 117-120 °C; IR (neat) 1682 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.29 (1H, dd, J = 0.8, 8.8 Hz), 8.04 (1H, dd, J = 1.2, 8.0 Hz), 7.74-7.81 (2H, m), 7.54 (1H, dt, J = 1.2, 8.0 Hz), 7.47 (1H, ddd, J = 2.0, 6.8, 8.0 Hz), 7.34 (1H, dd, J = 1.6, 8.0 Hz), 7.22 (1H, dt, J = 1.2, 7.6 Hz), 5.76 (1H, m), 5.07 (1H, qd, J = 2.0, 17.2 Hz), 4.99 (1H, td, J = 0.8, 10.0 Hz), 2.79 (1H, td, J = 6.4, 14.0 Hz), 2.42 (1H, td, J = 8.0, 14.0 Hz), 2.31 (1H, m), 1.15 (3H, d, J = 6.4 Hz); ¹³C NMR (CDCl₃) δ: 161.7, 159.9, 147.7, 140.22, 140.17, 136.4, 134.6, 130.7, 129.7, 129.5, 127.3, 127.1, 126.6, 120.8, 117.0, 99.6, 39.2, 38.1, 19.3; MS (m/z) 417 (MH⁺); HRMS. Calcd for C₁₉H₁₈IN₂O (MH⁺) 417.04638. Found: 417.04603.

(P⁺,S⁺) and (P⁺,R⁺) 3-(2-Methylphenyl)-2-(pent-4-en-2-yl)quinazolin-4(3H)-one (2e and 2e’). 2e and 2e’ were prepared from rac-1e (79 mg, 0.3 mmol) and allyl bromide (54 mg, 0.45 mmol) in accordance with the procedure for synthesis of 2e and 2e’. Purification of the residue by column chromatography (hexane/AcOEt = 5) gave the mixtures of 2e and 2e’ (81 mg, 89 %). The diastereomer ratio of 2e and 2e’ (6:1:1) was determined on the basis of ¹H-NMR analysis. 2e and 2e’ were separated by MPLC (hexane/AcOEt = 15) to give 2e (32 mg), 2e’ (5 mg) and the mixture of 2e and 2e’. 2e: white solid; mp 76-80 °C; IR (neat) 1682 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.29 (1H, dd, J = 1.6, 8.0 Hz), 7.74-7.80 (2H, m), 7.46 (1H, ddd, J = 1.6, 6.4, 8.0 Hz), 7.26-7.42 (3H, m), 7.16 (1H, d, J = 7.6 Hz), 5.59 (1H, tdd, J = 6.8, 10.0, 16.8 Hz), 4.96 (1H, d, J = 16.8 Hz), 4.95 (1H, d, J = 10.0 Hz), 2.48-2.61 (2H, m), 2.18 (1H, td, J = 7.2, 13.2 Hz), 2.12 (3H, s), 1.23 (3H, d, J = 6.4 Hz); ¹³C NMR (CDCl₃) δ: 162.0, 160.4, 147.8, 136.3, 135.8, 135.6, 134.4, 131.4, 129.4, 128.8, 127.21,
127.17, 127.0, 126.4, 120.7, 117.1, 40.2, 37.5, 18.8, 17.6; MS (m/z) 327 (MNa⁺); HRMS. Calcd for C_{20}H_{20}N_{2}O_{4}Na (MNa⁺) 327.14733. Found: 327.14478. 2e': colorless oil; IR (neat) 1682 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.28 (1H, dd, J = 0.8, 8.0 Hz), 7.73-7.80 (2H, m), 7.46 (1H, ddd, J = 2.0, 7.2, 8.4 Hz), 7.34-7.42 (3H, m), 7.16 (1H, d, J = 8.0 Hz), 5.64 (1H, tdd, J = 6.8, 10.0, 16.8 Hz), 5.01 (1H, dd, J = 2.0, 16.8 Hz), 4.94 (1H, td, J = 0.8, 10.0 Hz), 2.71 (1H, td, J = 6.8, 13.2 Hz), 2.39 (1H, m), 2.25 (1H, td, J = 7.2, 13.2 Hz), 2.10 (3H, s), 1.19 (3H, d, J = 6.4 Hz); ¹³C NMR (CDCl₃) δ: 162.0, 160.4, 147.8, 136.2, 135.8, 134.4, 131.4, 129.4, 128.2, 127.23, 127.18, 127.0, 126.4, 120.7, 117.1, 39.3, 38.2, 20.0, 17.8; MS (m/z) 327 (MNa⁺); HRMS. Calcd for C_{20}H_{20}N_{2}O_{4}Na (MNa⁺) 327.14733. Found: 327.14722.

(P⁺,S⁺) and (P⁺,R⁺) 3-(2-Ethylphenyl)-2-(pent-4-en-2-yl)quinazolin-4(3H)-one (2f and 2f'). 2f and 2f' were prepared from rac-1f (84 mg, 0.3 mmol) and allyl bromide (54 mg, 0.45 mmol) in accordance with the procedure for synthesis of 2c and 2c'. Purification of the residue by column chromatography (hexane/AcOEt = 5) gave the mixtures of 2f and 2f' (91 mg, 95 %). The diastereomer ratio of 2f and 2f' (10:1) was determined on the basis of ¹H-NMR analysis. 2f and 2f' were completely separated by MPLC (hexane/AcOEt = 10) to give diastereomerically pure 2f and 2f' (81 mg and 7 mg). 2f: white solid; mp 53-55 °C; IR (neat) 1678 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.28 (1H, dd, J = 1.2, 8.8 Hz), 7.75-7.78 (2H, m), 7.43-7.48 (3H, m), 7.38 (1H, m), 7.19 (1H, d, J = 8.0 Hz), 5.58 (1H, m), 4.96 (1H, d, J = 16.4 Hz), 4.95 (1H, d, J = 10.4 Hz), 2.51-2.61 (2H, m), 2.39-2.46 (2H, m), 2.22 (1H, m), 1.25 (3H, s), 1.20 (3H, t, J = 7.6 Hz); ¹³C NMR (CDCl₃) δ: 162.3, 160.6, 147.8, 141.1, 135.65, 135.60, 134.4, 129.6, 129.2, 128.8, 127.2, 127.0, 126.4, 120.7, 117.1, 40.3, 37.4, 23.5, 18.6, 13.5; MS (m/z) 341 (MNa⁺); HRMS. Calcd for C_{21}H_{22}N_{2}O_{4}Na (MNa⁺) 341.16298. Found: 341.16592. 2f': colorless oil; IR (neat) 1682 cm⁻¹; ¹H NMR (CDCl₃) δ: 8.28 (1H, dd, J = 1.2, 8.8 Hz), 7.72-7.80 (2H, m), 7.44-7.50 (3H, m), 7.36 (1H, dt, J = 2.8, 8.0 Hz), 7.15 (1H, d, J = 8.0 Hz), 5.65 (1H, m), 5.01 (1H, dd, J = 1.6, 17.2 Hz), 4.94 (1H, dd, J = 0.8, 11.2 Hz), 2.69 (1H, td, J = 6.8, 13.6 Hz), 2.35-2.43 (3H, m), 2.28 (1H, td, J = 7.2, 13.6 Hz), 1.174 (3H, t, J = 7.6 Hz), 1.172 (3H, d, J = 6.8 Hz); ¹³C NMR (CDCl₃) δ: 162.3, 160.6, 147.8, 141.0, 136.1, 135.6,
1.26 (1H, t, J = 6.4 Hz), 2.0 (1H, d, J = 6.4 Hz); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\): 162.4, 160.7, 147.7, 146.0, 135.5, 134.7, 134.3, 129.8, 128.7, 127.1, 126.9, 126.4, 120.7, 117.1, 40.4, 37.3, 28.1, 24.5, 22.8, 18.4; MS (\(m/z\)) 355 (M\(\text{Na}^+\)); HRMS. Calcd for C\(_{22}\)H\(_{24}\)N\(_2\)Na (M\(\text{Na}^+\)) 355.17863. Found: 355.17901.

**\((P{^a},S{^a})\)** 3-(2-Trifluoromethylphenyl)-2-(pent-4-en-2-yl)quinazolin-4(3H)-one (2h). 2h were prepared from rac-1h (96 mg, 0.3 mmol) and allyl bromide (54 mg, 0.45 mmol) in accordance with the procedure for synthesis of 2c and 2c'. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave 2h (105 mg, 98%). The minor diastereomer of 2h was not detected by \(^1\)H-NMR analysis. 2h: white solid; mp 98-101 °C; IR (neat) 1682 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 8.27 (1H, dd, J = 0.8, 7.6 Hz), 7.88 (1H, d, J = 8.0 Hz), 7.73-7.80 (3H, m), 7.65 (1H, t, J = 7.6 Hz), 7.46 (1H, ddd, J = 2.0, 6.4, 8.0 Hz), 7.41 (1H, d, J = 7.6 Hz), 5.58 (1H, m), 4.95 (1H, d, J = 15.6 Hz), 4.94 (1H, d, J = 11.2 Hz), 2.45 (1H, m), 2.37 (1H, m), 2.20 (1H, m), 1.29 (3H, d, J = 6.4 Hz); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\): 162.5, 159.8, 147.5, 135.2, 134.6, 133.2, 131.3, 127.94 (q, \(J_{\text{C-F}} = 30.5\) Hz), 127.87 (q, \(J_{\text{C-F}} = 4.8\) Hz), 127.2, 126.9, 126.6, 122.8 (q, \(J_{\text{C-F}} = 272.7\) Hz), 120.3, 117.3, 40.6, 37.9, 17.2; MS (\(m/z\)) 381 (M\(\text{Na}^+\)); HRMS. Calcd for C\(_{20}\)H\(_{17}\)F\(_3\)N\(_2\)Na (M\(\text{Na}^+\)) 381.11907. Found: 381.11744.
(P*,S*) and (P*,R*) 3-(2-Methylphenyl)-2-(sec-butyl)quinazolin-4(3H)-one (3e and 3e'). 3e and 3e' were prepared from rac-1e (79 mg, 0.3 mmol) and ethyl iodide (70 mg, 0.45 mmol) in accordance with the procedure for synthesis of 2c and 2e'. Purification of the residue by column chromatography (hexane/AcOEt = 5) gave the mixtures of 3e and 3e' (82 mg, 94%). The diastereomer ratio of 3e and 3e' (2.4:1) was determined on the basis of 1H-NMR analysis. 3e and 3e' were separated by MPLC (hexane/AcOEt = 15) to give 3e (24 mg), 3e' (6 mg) and the mixture of 3e and 3e'. 3e: white solid; mp 67-71 °C; IR (neat) 1682 cm⁻¹; ¹H-NMR (CDCl₃) δ: 8.29 (1H, dd, J = 1.2, 8.0 Hz), 7.72-7.79 (2H, m), 7.46 (1H, ddd, J = 1.2, 6.8, 8.0 Hz), 7.34-7.42 (3H, m), 7.14 (1H, d, J = 7.2 Hz), 2.36 (1H, m), 2.12 (3H, s), 1.85 (1H, m), 1.50 (1H, m), 1.22 (3H, d, J = 6.4 Hz), 0.79 (3H, t, J = 7.6 Hz); ¹³C-NMR (CDCl₃) δ:162.1, 161.2, 147.9, 136.4, 135.8, 134.3, 131.4, 129.3, 128.7, 127.21, 127.15, 127.0, 126.3, 120.6, 38.9, 29.1, 18.9, 17.6, 11.9; MS (m/z) 315 (MNa⁺); HRMS. Calcd for C₁₉H₂₆N₂NaO (MNa⁺) 315.14733. Found: 315.14520. 2e*: white solid; mp 91-94 °C; IR (neat) 1682 cm⁻¹; ¹H-NMR (CDCl₃) δ: 8.29 (1H, dd, J = 0.8, 8.0 Hz), 7.72-7.79 (2H, m), 7.46 (1H, ddd, J = 1.6, 6.4, 8.0 Hz), 7.34-7.42 (3H, m), 7.17 (1H, d, J = 7.2 Hz), 2.26 (1H, m), 2.13 (3H, s), 1.99 (1H, m), 1.53 (1H, m), 1.18 (3H, d, J = 6.4 Hz), 0.83 (3H, t, J = 7.6 Hz); ¹³C-NMR (CDCl₃) δ:162.0, 161.0, 147.9, 136.3, 135.7, 134.3, 131.3, 129.4, 128.2, 127.19, 127.15, 127.0, 126.3, 120.6, 39.6, 28.0, 20.1, 17.6, 12.4; MS (m/z) 315 (MNa⁺); HRMS. Calcd for C₁₉H₂₆N₂NaO (MNa⁺) 315.14733. Found: 315.14818.

(P*,S*) and (P*,R*) 3-(2-Ethylphenyl)-2-(sec-butyl)quinazolin-4(3H)-one (3f and 3f'). 3f and 3f' were prepared from rac-1f (84 mg, 0.3 mmol) and ethyl iodide (70 mg, 0.45 mmol) in accordance with the procedure for synthesis of 2c and 2e'. Purification of the residue by column chromatography (hexane/AcOEt = 5) gave the mixtures of 3f and 3f' (86 mg, 94%). The diastereomer ratio of 3f and 3f' (4.2:1) was determined on the basis of ¹H-NMR analysis. 3f and 3f' were completely separated by MPLC (hexane/AcOEt = 10) to give diastereomerically pure 3f and 3f' (67 mg and 17 mg). 3f: white solid; mp 94-97 °C; IR (neat) 1678 cm⁻¹; ¹H-NMR (CDCl₃)
δ: 8.29 (1H, dd, J = 1.2, 8.8 Hz), 7.72-7.79 (2H, m), 7.43-7.47 (3H, m), 7.38 (1H, m), 7.15 (1H, d, J = 8.0 Hz), 2.31-2.48 (3H, m), 1.82 (1H, m), 1.49 (1H, m), 1.22 (3H, d, J = 6.8 Hz), 1.18 (3H, t, J = 7.2 Hz), 0.78 (3H, t, J = 7.2 Hz); 13C-NMR (CDCl3) δ: 162.3, 161.4, 147.9, 141.1, 135.8, 134.3, 129.5, 129.1, 128.7, 127.2, 127.02, 127.00, 126.3, 120.7, 38.8, 29.3, 23.5, 18.6, 13.5, 11.9; MS (m/z) 329 (MNa+); HRMS. Calcd for C20H22N2NaO (MNa+) 329.16298. Found: 329.16286. 3f*: white solid; mp 87-90 °C; IR (neat) 1680 cm⁻¹; 1H-NMR (CDCl3) δ: 8.29 (1H, dd, J = 1.2, 8.4 Hz), 7.72-7.79 (2H, m), 7.44-7.47 (3H, m), 7.37 (1H, m), 7.16 (1H, d, J = 8.0 Hz), 2.40 (2H, dq, J = 2.0, 7.6 Hz), 2.25 (1H, m), 1.96 (1H, m), 1.56 (1H, m), 1.19 (3H, t, J = 7.6 Hz), 1.16 (3H, d, J = 7.2 Hz), 0.82 (3H, t, J = 7.6 Hz); 13C-NMR (CDCl3) δ: 162.4, 161.2, 147.9, 141.0, 135.7, 134.3, 129.5, 129.0, 128.3, 127.2, 127.04, 127.00, 126.3, 120.7, 39.5, 27.9, 23.4, 20.0, 13.4, 12.3; MS (m/z) 329 (MNa+); HRMS. Calcd for C20H22N2NaO (MNa+) 329.16298. Found: 329.16374.

(P*,S*) and (P*,R*) 3-(2-Iso-propylphenyl)-2-(sec-butyl)quinazolin-4(3H)-one (3g and 3g’). 3g and 3g’ were prepared from rac-1g (88 mg, 0.3 mmol) and ethyl iodide (70 mg, 0.45 mmol) in accordance with the procedure for synthesis of 2c and 2c’. Purification of the residue by column chromatography (hexane/AcOEt = 5) gave the mixtures of 3g and 3g’ (84 mg, 87%). The diastereomer ratio of 3g and 3g’ (14.7:1) was determined on the basis of 1H-NMR analysis. 3g and 3g’ were completely separated by MPLC (hexane/AcOEt = 9) to give diastereomerically pure 3g and 3g’ (77 mg and 6 mg). 3g: white solid; mp 104-106 °C; IR (neat) 1674 cm⁻¹; 1H-NMR (CDCl3) δ: 8.29 (1H, dd, J = 1.2, 8.4 Hz), 7.72-7.79 (2H, m), 7.49-7.52 (2H, m), 7.45 (1H, ddd, J = 2.0, 6.8, 8.4 Hz), 7.34 (1H, m), 7.12 (1H, d, J = 7.2 Hz), 2.64 (1H, sept, J = 6.8 Hz), 2.38 (1H, m), 1.80 (1H, m), 1.50 (1H, m), 1.24 (3H, d, J = 6.4 Hz), 1.22 (3H, d, J = 6.8 Hz), 1.15 (3H, d, J = 7.2 Hz), 0.77 (3H, t, J = 7.2 Hz); 13C-NMR (CDCl3) δ:162.11, 162.07, 146.9, 146.0, 134.54, 134.49, 129.8, 128.5, 127.1, 126.9, 126.6, 126.5, 120.4, 38.7, 29.2, 28.1, 24.4, 22.7, 18.3, 11.9; MS (m/z) 343 (MNa+); HRMS. Calcd for C21H24N2NaO (MNa+) 343.17863. Found: 343.17778. 3f*: white solid; mp 107-112 °C; IR (neat) 1670 cm⁻¹; 1H-NMR (CDCl3) δ: 8.28 (1H, dd, J = 1.6, 8.4 Hz),
7.71-7.79 (2H, m), 7.49-7.51 (2H, m), 7.45 (1H, ddd, J = 1.6, 6.8, 8.4 Hz), 7.34 (1H, m), 7.13 (1H, d, J = 7.6 Hz), 2.65 (1H, sept, J = 6.8 Hz), 2.28 (1H, m), 1.93 (1H, m), 1.63 (1H, m), 1.22 (3H, d, J = 6.8 Hz), 1.14 (3H, d, J = 6.8 Hz), 1.14 (3H, d, J = 6.8 Hz), 0.85 (3H, t, J = 7.6 Hz); \(^{13}\)C-NMR (CDCl\(_3\)) \(\delta\): 162.5, 161.5, 147.9, 146.0, 134.8, 134.3, 129.8, 128.4, 127.14, 127.07, 126.98, 126.93, 126.3, 120.7, 39.4, 28.2, 27.9, 24.6, 22.7, 19.7, 11.9; MS (m/z) 343 (M\(\text{Na}^+\)); HRMS. Calcd for C\(_{21}\)H\(_{24}\)N\(_2\)NaO (M\(\text{Na}^+\)) 343.17863. Found: 343.17804.

\((P^*S^*)\) and \((P^*R^*)\) 3-(2-Trifluoromethylphenyl)-2-(sec-butyl)quinazolin-4(3H)-one (3h and 3h'). 3h and 3h' were prepared from rac-1h (95 mg, 0.3 mmol) and ethyl iodide (70 mg, 0.45 mmol) in accordance with the procedure for synthesis of 2c and 2c'. Purification of the residue by column chromatography (hexane/AcOEt = 4) gave the mixtures of 3h and 3h' (89 mg, 85%). The diastereomer ratio of 3h and 3h' (20.3:1) was determined on the basis of \(^1\)H-NMR analysis. 3h and 3h' were completely separated by MPLC (hexane/AcOEt = 7) to give diastereomerically pure 3h and 3h' (82 mg and 5 mg). 3h: white solid; mp 114-117 °C; IR (neat) 1678 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 8.26 (1H, dd, J = 1.2, 8.0 Hz), 7.88 (1H, d, J = 6.8 Hz), 7.72-7.79 (3H, m), 7.66 (1H, t, J = 8.0 Hz), 7.45 (1H, ddd, J = 1.6, 6.8, 8.0 Hz), 7.38 (1H, d, J = 7.6 Hz), 2.22 (1H, m), 1.71 (1H, m), 1.48 (1H, m), 1.28 (3H, d, J = 6.4 Hz), 0.76 (3H, t, J = 7.2 Hz); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\): 162.4, 160.4, 147.4, 135.2, 134.4, 133.1, 131.0, 129.6, 127.69 (q, \(J_{\text{C-F}} = 30.5\) Hz), 127.67 (q, \(J_{\text{C-F}} = 4.8\) Hz), 127.1, 126.7, 126.4, 122.8 (q, \(J_{\text{C-F}} = 272.6\) Hz), 120.1, 39.0, 29.2, 16.6, 11.5; MS (m/z) 347 (MH\(^+\)); HRMS. Calcd for C\(_{10}\)H\(_{18}\)F\(_3\)N\(_2\)O (MH\(^+\)) 347.13712. Found: 347.13488.

3h': white solid; mp 89-92 °C; IR (neat) 1692 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 8.26 (1H, dd, J = 0.8, 7.2 Hz), 7.89 (1H, dd, J = 1.2, 7.6 Hz), 7.72-7.80 (3H, m), 7.67 (1H, t, J = 7.6 Hz), 7.46 (1H, ddd, J = 1.2, 6.8, 8.0 Hz), 7.38 (1H, d, J = 8.0 Hz), 2.13 (1H, m), 1.95 (1H, m), 1.70 (1H, m), 1.15 (3H, d, J = 6.4 Hz), 0.84 (3H, t, J = 7.6 Hz); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\): 162.6, 160.7, 147.7, 135.2, 134.6, 133.3, 131.0, 129.9, 128.2 (q, \(J_{\text{C-F}} = 31.4\) Hz), 128.0 (q, \(J_{\text{C-F}} = 4.8\) Hz), 127.3, 127.0, 126.6, 122.9 (q, \(J_{\text{C-F}} = 272.6\) Hz), 120.3, 39.7, 27.3, 19.7, 11.7; MS (m/z) 369 (MH\(^+\)); HRMS. Calcd for C\(_{10}\)H\(_{18}\)F\(_3\)N\(_2\)O (MH\(^+\)) 369.11907. Found: 369.11789.
Copies of $^1$H-NMR and $^{13}$C-NMR Chart of All Compounds
1d
3e’

Me

O

N

Me

Et

Me

O

N

Me

Et

3e’