A facile approach for the synthesis of novel 1-oxa- and 1-aza-flavonyl-4-methyl-1H-
benzo[d][1,3]oxazin-2(4H)-ones by microwave enhanced Suzuki-Miyaura coupling
using bidentate chromen-4-one-based Pd(II)–diimine complex as catalyst

Sumit Kumar* and Naseem Ahmed*

Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee 247 667,
Uttarakhand, India.

*Corresponding author. Fax and Tel.: +91 1332 285745.

E-mail address: sumitdcy@iitr.ac.in; nasemfcy@iitr.ac.in

SUPPORTING INFORMATION

Table of Contents

General Information ................................................................. S2
General Procedures...............................................................S2
Characterization Data ............................................................ S3-S17
Reference..................................................................................S17

$^1$H, $^{13}$C and HRMS Spectra .................................................... S18-S47
**General Information**

Unless otherwise noted, chemicals were purchased from commercial suppliers at the highest purity grade available and were used without further purification. Solvents were distilled by standard methods. Thin layer chromatography was performed on Merck precoated 0.25 mm silica gel plates (60F-254) using UV light as visualizing agent and/or iodine as developing agent. Silica gel (100-200 mesh) was used for column chromatography. Melting points were performed with Ambassador® and Digital Melting point apparatus (Nutronics), Popular India. IR spectra were recorded on FT-IR spectrometer and expressed as wave numbers (cm⁻¹). ¹H and ¹³C NMR spectra were recorded on a Brüker Avance 500 & Jeol Resonance ECX 400 spectrometer. Spectra were referenced internally to the residual proton resonance in CDCl₃ (δ 7.26 ppm) or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Spectra were processed using Bruker Topspin® 3.0.b.8. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ¹³C NMR spectra were referenced to CDCl₃ (δ 77.23 ppm, the middle peak). Coupling constants are expressed in Hz. The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were obtained on a Brüker micrOTOF™-Q II mass spectrometer (ESIMS).

**General procedure for synthesis of Heteroarylboronic acids (3a-3c).**

The synthesis followed the literature procedure.

![Chemical Structure](image)

**General procedure for synthesis of compounds (4a-r, 5a-c, 6a-c):** To a G-4 process vial capped with Teflon septum was added 3-bromo flavone (1 mmol), boronic acid (1.1 mmol),
Pd-complex C (0.3 mol%, 1.6 mg), TBAB (0.25 mmol), K$_2$CO$_3$ (2.5 mmol) and 6 ml of ethanol. After a pre-stirring for one minute, the vial was subjected to microwave irradiation time of 18-20 minute at 60 °C. It was then cooled to room temperature, diluted with water, and extracted with EtOAc for three times. The organic phase was dried with Na$_2$SO$_4$ and concentrated to yield the product. The crude material was chromatographed on a silica gel column eluting with a mixture of ethyl acetate and hexane. (The purified products were identified by FTIR, NMR and HRMS spectra).

Characterization Data

3,3'-(1E,1'E)-(naphthalene-1,2-diylbis(azanylylidene))bis(methanylylidene))bis(4H-chromen-4-one) (L)

Yield: 85% as yellow solid. $^1$H NMR (500 MHz, CDCl$_3$, ppm): δ 8.44-8.35 (m, 1H), 8.28-8.20 (m, 2H), 7.98-7.96 (m, 1H), 7.83-7.73 (m, 2H), 7.56-7.55 (m, 1H), 7.52-7.47 (m, 3H), 7.43-7.40 (m, 2H), 7.33-7.26 (m, 2H), 7.25-7.21 (m, 2H), 7.15-7.13 (m, 1H), 6.82 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm): δ 178.3, 161.8, 154.7, 151.8, 143.1, 137.4, 136.4, 134.8, 127.6, 126.3, 126.0, 125.1, 124.6, 121.9, 120.3, 118.2, 113.2, 108.8. FTIR (KBr, $\nu$ = cm$^{-1}$): 1715, 1645, 1624. Anal. Calcd (in %) for C$_{30}$H$_{18}$N$_2$O$_4$: C, 76.59; H, 3.86; N, 5.95. Found: C, 76.43; H, 3.72; N, 5.79. HRMS (ESI+): m/z calcd for C$_{30}$H$_{18}$N$_2$O$_4$[M+Na]$^+$: 493.1158, found: 493.1158.

(4-methyl-2-oxo-4-vinyl-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)boronic acid (3a)

Yield: 81% as white solid; $^1$H NMR (500 MHz, DMSO-d$_6$, ppm): δ 10.29 (s, 1H, D$_2$O exchangeable), 7.97 (s, 2H, D$_2$O exchangeable), 7.68 (d, $J$ = 10Hz, 2H), 6.83 (d, $J$ = 8Hz, 1H), 6.01 (dd, $J$ = 10.5, 18Hz, 1H), 5.16 (d, $J$ = 10.5Hz, 1H), 4.98 (d, $J$ = 17Hz, 1H), 1.73 (s, 3H). $^{13}$C NMR (100 MHz, DMSO-d$_6$, ppm): δ 153.4, 140.6, 137.4, 136.5, 131.4, 128.9, 123.9, 116.2, 115.0, 85.1,
26.3. FTIR (KBr, \( v = \text{cm}^{-1} \)): 3408, 3279, 2978, 2930, 1718, 1645, 1513, 1355, 1248, 1088, 925. HRMS (ESI+): m/z calcd for C_{11}H_{13}BNO_{4} [M+H]^+ : 234.0932 found: 234.0930.

(4-allyl-4-methyl-2-oxo-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)boronic acid (3b)

Yield: 80% as white solid; \(^1\)H NMR (500 MHz, DMSO-d_6, ppm): \(\delta\) 10.16 (s, 1H, D_2O exchangeable), 7.92 (s, 2H, D_2O, exchangeable), 7.61 (t, \( J = 3.5 \text{Hz} \), 2H), 6.77 (d, \( J = 8.5 \text{Hz} \), 1H), 5.62-5.56 (m, 1H), 5.07-5.02 (m, 2H), 2.66-2.62 (m, 1H), 2.55-2.51 (m, 1H), 1.55 (s, 3H).

\(^{13}\)C NMR (100 MHz, DMSO-d_6, ppm): \(\delta\) 153.2, 137.3, 136.1, 132.8, 131.2, 128.7, 124.6, 121.2, 114.9, 85.9, 45.1, 27.7. FTIR (KBr, \( v = \text{cm}^{-1} \)): 3430, 3158, 2978, 2934, 1720, 1656, 1383, 1342, 1257, 1109, 1042. HRMS (ESI+): m/z calcd for C_{12}H_{16}BNO_{4} [M+H]^+ : 248.1088 found: 248.1087.

(4-methyl-2-oxo-4-pentyl-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)boronic acid (3c)

Yield: 95% as yellow solid; \(^1\)H NMR (500 MHz, CDCl_3, ppm): \(\delta\) 9.76 (s, 1H, D_2O exchangeable), 7.41 (d, \( J = 8.5 \text{Hz} \), 1H), 7.18 (s, 1H), 6.86 (d, \( J = 8.5 \text{Hz} \), 1H), 2.03-1.98 (m, 2H), 1.75 (s, 3H), 1.49-1.35 (m, 6H), 0.94 (t, \( J = 7 \text{Hz} \), 3H). \(^{13}\)C NMR (125 MHz, CDCl_3, ppm): \(\delta\) 153.0, 133.6, 131.8, 127.0, 126.9, 116.5, 115.8, 85.5, 41.1, 31.9, 27.2, 23.3, 22.6, 14.8. HRMS (ESI+): m/z calcd. for C_{14}H_{21}BNO_{4} [M+H]^+ : 278.1558.

6-(2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4a)

Yield: 95% as brown solid, mp 160-168 \(^\circ\)C; \(^1\)H NMR (500 MHz, CDCl_3, ppm): \(\delta\) 9.08 (s, 1H, D_2O exchangeable), 8.27 (d, \( J = 8\text{Hz} \), 1H), 7.80 (d, \( J = 9\text{Hz} \), 1H), 7.7 (t, \( J = 8.5 \text{Hz} \), 1H), 7.48 (d, \( J = 8 \text{Hz} \), 1H), 7.44 (t, \( J = 7.5 \text{Hz} \), 1H), 7.37 (dd, \( J = 1.5 \), 8.5 Hz, 1H), 7.13 (d, \( J = 8\text{Hz} \), 1H), 7.08-7.02 (m, 3H), 6.87 (d, \( J = 8\text{Hz} \), 1H), 6.06-5.97 (m, 1H), 5.26-5.06 (m, 2H), 3.90 (s, 3H), 1.82 (s, 3H). \(^{13}\)C NMR (125 MHz, CDCl_3, ppm): \(\delta\) 174.8, 164.5, 161.8, 155.9, 153.0, 139.4, 134.2, 132.3, 131.5, 129.4, 127.5, 127.3, 126.8, 125.9, 124.5, 123.6, 120.0, 117.7, 115.7, 114.8, 113.8.
113.7, 87.7, 55.6, 25.7. FTIR (KBr, v = cm⁻¹): 3256, 2955, 1709, 1655, 1615, 1587, 1505, 1463, 1345, 1333, 1306. HRMS (ESI+): m/z calcd. for C_{27}H_{22}NO_{5} [M+H]^+ : 440.1492 found : 440.1495.

6-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4b)

Yield: 91% as brown solid, mp 139-143 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 8.93 (s, 1H, D₂O exchangeable), 8.28 (d, J = 8 Hz, 1H), 7.70 (t, J = 8 Hz, 1H), 7.51 (t, J = 8Hz, 2H), 7.46 (d, J = 7.5 Hz, 1H), 7.35 (dd, J = 1.5, 8 Hz, 1H), 7.13 (d, J = 7.5 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 6.87 (d, J = 7.5 Hz, 1H), 6.05-5.96 (m, 1H), 5.25-5.05 (m, 2H), 3.95 (s, 6H), 1.81 (s, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 173.4, 161.9, 155.7, 151.6, 148.6, 139.4, 134.6, 134.2, 132.3, 129.4, 127.5, 126.7, 125.8, 125.2, 124.5, 123.8, 123.5, 123.3, 121.9, 117.9, 114.8, 112.6, 110.7, 108.7, 83.8, 56.2, 25.7. FTIR (KBr, v = cm⁻¹): 3267, 2975, 1713, 1652, 1611, 1557, 1505, 1463, 1350, 1328, 1306. HRMS (ESI+): m/z calcd. for C_{28}H_{23}NNaO₆ [M+Na]^+ :492.1417 found : 492.1431.

4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl)-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4c)

Yield: 89% as brown solid, mp 140-145 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 8.95 (s, 1H, D₂O exchangeable), 8.28 (d, J = 8Hz, 1H), 7.72-7.68 (m, 1H), 7.51 (s, 1H), 7.36 (dd, J = 2, 8.5 Hz, 1H), 7.12 (d, J = 7.5 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 6.87 (d, J = 8 Hz, 1H), 6.04-5.96 (m, 1H), 5.25-5.05 (m, 2H), 3.96 (s, 3H), 3.95 (s, 6H), 1.81 (s, 3H). ¹³C NMR (100 MHz, CDCl₃, ppm): δ 173.3, 161.9, 155.6, 153.1, 139.4, 134.4, 132.3, 129.4, 127.9, 127.5, 126.7, 125.9, 124.5, 123.5, 118.0, 115.7, 114.7, 107.1, 82.4, 61.2, 56.5, 25.7. FTIR (KBr, v = cm⁻¹): 3269,
2959, 1713, 1690, 1652, 1621, 1555, 1513, 1473, 1359, 1336, 1321. HRMS (ESI+): m/z calcd. for C_{29}H_{26}NO_{7} [M+H]^+ : 522.1523 found : 522.1501.

4-allyl-6-(2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4d)

Yield: 94% as brown solid, mp 124-125 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ9.74 (s, 1H, D₂O exchangeable), 8.27 (d, J = 8 Hz, 1H), 7.72 (s, 1H), 7.53-7.50 (m, 1H), 7.46-7.42 (m, 1H), 7.31 (d, J = 8.5 Hz, 2H), 7.17 (s, 1H), 7.01 (s, 2H), 7.00 (d, J = 8.5 Hz, 1H), 6.78 (d, J = 8.5 Hz, 1H), 5.75-5.66 (m, 1H), 5.13-5.01 (m, 2H), 3.9 (s, 3H), 2.69-2.60 (m, 2H), 1.67 (s, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ173.5, 162.0, 155.7, 152.5, 151.6, 148.6, 135.2, 134.3, 133.7, 132.0, 131.1, 127.1, 125.9, 123.3, 121.8, 120.5, 117.9, 116.4, 115.7, 112.5, 110.6, 108.6, 84.3, 56.3, 45.5, 26.3. FTIR (KBr, v = cm⁻¹): 3267, 2975, 1713, 1692, 1652, 1557, 1505, 1463, 1350, 1328, 1306. HRMS (ESI+): m/z calcd. for C_{28}H_{24}NO_{5} [M+H]^+ : 454.1648 found : 454.1636.

4-allyl-6-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4e)

Yield: 92% as brown solid, mp 117-119 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ9.40 (s, 1H, D₂O exchangeable), 8.29 (d, J = 8Hz, 1H), 7.91 (s, 1H), 7.27 (t, J = 8 Hz, 1H), 7.53-7.45 (m, 2H), 7.32 (d, J = 8 Hz, 1H), 7.18 (s, 1H), 7.10 (d, J = 18 Hz, 2H), 6.79 (d, J = 8.5 Hz, 1H), 5.73-5.65 (m, 1H), 5.14-5.09 (m, 2H), 3.93 (d, 6H), 2.67-2.63 (m, 2H), 1.68 (s, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ173.5, 162.0, 155.7, 152.6, 151.6, 148.6, 135.2, 134.3, 133.7, 132.0, 131.1, 127.1, 125.9, 123.3, 121.8, 120.5, 117.9, 116.4, 115.7, 112.5, 110.6, 108.6, 84.3, 56.3, 45.5, 26.3. FTIR (KBr, v = cm⁻¹): 3267, 2975, 1713, 1692, 1652, 1557, 1505, 1463, 1350, 1328, 1306.
4-allyl-4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl)-1H-
benzo[d][1,3]oxazin-2(4H)-one (4f)

Yield: 88% as brown solid, mp 118-120 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 10.08 (s, 1H, D₂O exchangeable), 8.19 (dd, J = 8 Hz, 1H), 7.75 (s, 1H), 7.69-7.64 (m, 1H), 7.55-7.47 (m, 1H), 7.43-7.35 (m, 1H), 7.12-7.10 (m, 2H), 7.04 (s, 1H), 6.80-6.78 (m, 1H), 5.68-5.60 (m, 1H), 5.08-5.04 (m, 2H), 3.90 (s, 6H), 3.8 (s, 3H), 2.64-2.54 (m, 2H), 1.62 (s, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 173.4, 162.0, 153.1, 152.4, 140.6, 135.0, 134.4, 133.7, 132.0, 131.1, 127.9, 127.2, 126.7, 126.6, 126.0, 121.8, 121.4, 120.5, 118.0, 116.4, 115.7, 107.2, 84.4, 61.2, 56.6, 45.5, 26.3. FTIR (KBr, ν = cm⁻¹): 3235, 2934, 1716, 1686, 1463, 1406. HRMS (ESI+): m/z calcd. for C₂₉H₂₅NNaO₆ [M+Na]⁺ : 506.1574 found : 506.1575.

6-(2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-pentyl-1H-benzo
[d][1,3]oxazin-2(4H)-one (4g)

Yield: 90% as white solid, mp 113-114 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 9.90 (s, 1H, D₂O exchangeable), 8.14 (dd, J = 8 Hz, 1H), 7.78 (d, J = 8.5 Hz, 1H), 7.67 (t, J = 8 Hz, 1H), 7.42 (m, 2H), 7.28 (d, J = 8.5 Hz, 1H), 7.15 (s, 2H), 6.99 (d, J = 8.5 Hz, 2H), 6.79 (d, J = 8 Hz, 1H), 3.86 (s, 3H), 1.91-1.87 (m, 2H), 1.64 (s, 3H), 1.37-1.24 (m, 6H), 0.82 (t, J = 8 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 178.0, 155.9, 155.4, 152.8, 146.4, 146.0, 133.9, 133.7, 131.7, 127.0, 126.9, 125.8, 125.3, 124.2, 118.0, 116.5, 115.7, 113.3, 112.6, 105.5, 85.4, 41.0, 31.8, 27.1, 23.2, 22.5, 14.1. FTIR (KBr, ν = cm⁻¹): 3228, 2934, 2869, 1705, 1687, 1615,
6-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4h)

Yield: 89% as white solid, mp 109-110 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ9.61 (s, 1H, D₂O exchangeable), 7.80-7.69 (m, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.46-7.41 (m, 1H), 7.31 (d, J = 8.5 Hz, 1H), 7.15 (s, 1H), 6.78 (d, J = 8 Hz, 1H), 3.95-3.96 (d, 6H), 1.92-1.88 (m, 2H), 1.65 (s, 3H), 1.37-1.28 (m, 8H), 0.84 (t, J = 8 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ173.4, 161.9, 152.7, 152.9, 151.6, 148.6, 134.2, 133.6, 131.8, 127.0, 126.9, 126.7, 125.8, 125.2, 123.3, 121.8, 117.9, 116.5, 115.8, 112.6, 110.7, 108.7, 85.5, 56.3, 56.2, 41.0, 31.9, 27.2, 23.3, 22.5, 14.1. HRMS (ESI+): m/z calcd. for C₃₁H₃₁NNaO₆ [M+Na]⁺: 536.2043 found: 536.2034.

6-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl)-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4i)

Yield: 87% as white solid, mp 155-158 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ9.63 (s, 1H, D₂O exchangeable), 8.28 (d, J = 8Hz, 1H), 7.72 (t, J = 8 Hz, 1H), 7.52-7.44 (m, 2H), 7.31 (d, J = 8.5 Hz, 1H), 7.16 (s, 1H), 7.09 (s, 2H), 6.79 (d, J = 8 Hz, 1H), 3.93 (d, 9H), 1.92-1.89 (m, 2H), 1.65 (s, 3H), 1.31-1.23 (m, 6H), 0.83 (t, J = 7 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ173.3, 161.9, 155.6, 153.1, 152.9, 140.6, 134.4, 133.6, 131.8, 127.9, 127.0, 126.9, 126.7, 126.0, 121.8, 118.0, 116.5, 115.8, 109.1, 107.2, 85.5, 61.1, 56.5, 41.0, 31.8, 27.2, 23.2, 22.5, 14.1. HRMS (ESI+): m/z calcd. for C₃₂H₃₃NNaO₇ [M+Na]⁺: 566.2149 found: 566.2151.

6-(2-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4j)
Yield: 86% as brown solid, mp 159-161 °C; $^1$H NMR (500 MHz, CDCl$_3$, ppm): δ 9.49 (s, 1H, D$_2$O exchangeable), 9.08 (s, 1H, D$_2$O exchangeable), 8.28 (d, J = 8 Hz, 1H), 7.79 (d, J = 9Hz, 1H), 7.70 (t, J = 8.5 Hz, 1H), 7.37 (dd, J = 1.5, 8.5 Hz, 1H), 7.13 (d, J = 8 Hz, 1H), 7.08-7.02 (m, 2H), 6.87 (d, J = 8Hz, 1H), 6.84 (d, J = 8 Hz, 1H), 6.06-6.00 (m, 1H), 5.26-5.06 (m, 2H), 3.90 (s, 3H), 1.82 (t, J = 8Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm): δ 174.8, 164.5, 161.8, 155.9, 139.4, 138.7, 134.6, 134.2, 132.3, 131.5, 129.4, 127.5, 123.6, 120.0, 117.7, 115.7, 114.8, 113.7, 87.7, 55.6, 25.7. FTIR (KBr, ν = cm$^{-1}$): 3305, 3267, 2975, 1714, 1692, 1641, 1557, 1505, 1463. HRMS (ESI+): m/z calcd. for C$_{27}$H$_{22}$N$_2$NaO$_4$ [M+Na]$^+$ : 461.1471 found : 461.1467.

6-(2-(3,4-dimethoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4k)

Yield: 85% as Brown solid, mp 147-150 °C; $^1$H NMR (500 MHz, CDCl$_3$, ppm): δ 9.31 (s, 1H, D$_2$O exchangeable), 8.93 (s, 1H, D$_2$O exchangeable), 8.28 (d, J = 8Hz, 1H), 7.70 (t, J = 8 Hz, 1H), 7.51 (t, J = 8.5 Hz, 2H), 7.46 (d, J = 8Hz, 1H), 7.36 (dd, J = 1.5, 8.5 Hz, 1H), 7.13 (d, J = 7.5 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 6.99 (d, J = 8.5 Hz, 1H), 6.87 (d, J = 7.5 Hz, 1H), 6.05-5.98 (m, 1H), 5.20-5.05 (m, 2H), 3.95 (s, 6H), 1.81 (t, J = 8 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm): δ 174.8, 164.5, 161.8, 156.0, 153.2, 139.4, 138.7, 134.6, 134.2, 133.8, 132.3, 131.5, 129.4, 127.5, 125.9, 124.5, 123.6, 120.1, 117.7, 115.8, 114.8, 113.7, 84.3, 55.8, 25.8. HRMS (ESI+): m/z calcd. for C$_{28}$H$_{24}$N$_2$NaO$_5$ [M+Na]$^+$ : 491.1577 found : 491.1572.
4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-1,4-dihydroquinolin-3-yl)-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4l)

Yield: 85% as Brown solid, mp 112-115 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ9.31 (s, 1H, D₂O exchangeable), 8.93 (s, 1H, D₂O exchangeable), 8.26 (d, J = 8Hz, 1H), 7.70-7.68 (m, 1H), 7.50 (s, 1H), 7.34 (dd, J = 2, 8.5 Hz, 1H), 7.11 (d, J = 7.5 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 8.5 Hz, 1H), 6.86(d, J = 8 Hz, 1H), 6.03-5.94 (m, 1H), 5.23-5.03 (m, 2H), 3.95 (s, 3H), 3.94 (s, 6H), 1.79 (s, 3H).

¹³C NMR (125 MHz, CDCl₃, ppm): δ174.7, 164.1, 161.5, 156.5, 153.6, 139.1, 138.5, 134.1, 134.0, 133.6, 132.2, 131.4, 129.3, 127.4, 126.8, 125.4, 124.2, 123.7, 123.5, 120.1, 117.5, 115.7, 84.3, 60.5, 55.8, 25.7. HRMS (ESI+): m/z calcd. for C₂₉H₂₆N₂O₆[M+Na]⁺ : 521.1683 found : 521.1682.

4-allyl-6-(2-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4m)

Yield: 86% as Brown solid, mp 138-141 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ9.61 (s, 1H, D₂O exchangeable), 8.26 (dd, J = 1, 8 Hz, 1H), 7.80 (d, J = 8.5 Hz, 2H), 7.68 (t, J = 7.5 Hz, 1H), 7.48 (d, J = 8.5 Hz, 1H), 7.43 (t, J = 7 Hz, 1H), 7.32 (dd, J = 1.5, 8.5 Hz, 1H), 7.18 (s, 1H), 7.02 (d, J = 8.5 Hz, 2H), 6.77 (d, J = 8.5 Hz, 1H), 6.23 (s, 1H, D₂O exchangeable), 5.72-5.65 (m, 1H), 5.14-5.09 (m, 2H), 3.89 (s, 3H), 2.70-2.62 (m, 2H), 1.68 (s, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ175.0, 164.6, 161.8, 155.9, 152.5, 134.3, 133.7, 132.0, 131.9, 131.5, 131.1, 127.2, 127.1, 126.8, 126.6, 125.9, 120.5, 120.0, 117.7, 116.6, 115.7, 113.7, 84.3, 55.6, 45.5, 26.3. FTIR (KBr, v = cm⁻¹): 3394, 3293, 2957, 2930, 1712, 1686, 1646, 1610, 1572, 1355. HRMS (ESI+): m/z calcd. for C₂₈H₂₈N₂NaO₄[M+Na]⁺ : 475.1628 found : 475.1631.
4-allyl-6-(2-(3,4-dimethoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4n)

Yield: 85% as Brown solid, mp 160-165 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ9.66 (s, 1H, D₂O exchangeable), 8.28 (dd, J = 1, 8 Hz, 1H), 7.74-7.71 (m, 2H), 7.52 (d, J = 8 Hz, 1H), 7.46 (t, J = 7 Hz, 1H), 7.31 (dd, J = 1.5, 8 Hz, 1H), 7.17 (d, J = 1.5 Hz, 1H), 7.09 (s, 2H), 6.78 (d, J = 8.5 Hz, 1H), 5.71-5.67 (m, 1H), 5.52 (s, 1H, D₂O exchangeable), 5.13-5.09 (m, 2H), 3.94 (s, 3H), 2.69-2.60 (m, 2H), 1.67 (s, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ174.1, 152.4, 150.5, 150.3, 148.5, 139.4, 135.2, 133.7, 132.2, 132.0, 131.1, 127.2, 126.6, 124.4, 123.5, 122.3, 121.9, 120.5, 116.4, 115.7, 112.6, 110.6, 84.3, 56.1, 56.0, 45.5, 26.3. FTIR (KBr, v = cm⁻¹): 3375, 3290, 2987, 2927, 1713, 1677, 1648, 1601, 1407, 1352. HRMS (ESI⁺): m/z calcd. for C₂₉H₂₆N₂NaO₅ [M+Na]⁺: 505.1733 found: 505.1733.

4-allyl-4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-1,4-dihydroquinolin-3-yl)-1H-benzo[d][1,3]oxazin-2(4H)-one (4o)

Yield: 81% as Brown solid, mp 178-180 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 9.71 (s, 1H, D₂O exchangeable), 9.20 (s, 1H, D₂O exchangeable), 8.24 (d, J = 8 Hz, 1H), 7.83 (d, J = 8 Hz, 1H), 7.63-7.58 (m, 2H), 7.34-7.28 (m, 2H), 7.15 (s, 1H), 7.03 (s, 1H), 6.78 (d, J = 8.5 Hz, 1H), 5.71-5.63 (m, 1H), 5.12-5.07 (m, 2H), 3.77 (s, 9H), 2.67-2.58 (m, 2H), 1.65 (s, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 173.9, 152.8, 152.3, 150.5, 139.4, 138.9, 135.1, 133.7, 131.9, 131.1, 130.3, 127.1, 126.5, 126.0, 124.5, 123.4, 121.7, 120.4, 118.7, 116.4, 115.6, 106.8, 84.2, 60.9, 56.3, 45.5, 26.3. HRMS (ESI⁺): m/z calcd. for C₃₀H₂₈N₂NaO₆ [M+Na]⁺: 535.1839 found: 535.1841.
6-(2-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4p)

Yield: 83% as white solid, mp 145-148 °C; $^1$H NMR (500 MHz, CDCl$_3$, ppm): δ 9.90 (s, 1H, D$_2$O exchangeable), 8.24 (d, $J = 8$ Hz, 1H), 7.78 (d, $J = 8.5$ Hz, 1H), 7.65 (t, $J = 7.5$ Hz, 1H), 7.46-7.39 (m, 2H), 7.29 (d, $J = 8.5$ Hz, 1H), 7.15 (s, 2H), 7.00 (d, $J = 8.5$ Hz, 2H), 6.80 (d, $J = 8.5$ Hz, 1H), 5.82 (s, 1H, D$_2$O exchangeable), 3.86 (s, 3H), 1.92-1.87 (m, 2H), 1.64 (s, 3H), 1.37-1.29 (m, 6H), 0.82 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm): δ 174.9, 164.5, 161.8, 155.9, 153.0, 145.1, 134.2, 131.7, 131.5, 127.2, 127.0, 126.9, 126.8, 125.9, 120.0, 117.6, 116.5, 115.7, 113.7, 85.4, 55.6, 41.0, 31.8, 27.1, 23.2, 22.5, 14.0. FTIR (KBr, $\nu$ = cm$^{-1}$): 3375, 3290, 2987, 2927, 1710, 1677, 1643, 1407, 1352. HRMS (ESI+): m/z calcd. for C$_{30}$H$_{30}$N$_2$NaO$_4$ [M+Na]$^+$: 505.2097 found: 505.2096.

6-(2-(3,4-dimethoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4q)

Yield: 85% as white solid, mp 117-118 °C; $^1$H NMR (500 MHz, DMSO, ppm): δ 12.18, (s, 1H, D$_2$O exchangeable), 10.28 (s, 1H, D$_2$O exchangeable), 8.16 (d, $J = 8$ Hz, 1H), 7.68 (d, $J = 3.5$ Hz, 2H), 7.41-7.38 (m, 3H), 7.23-7.13 (m, 2H), 7.02 (s, 1H), 6.82 (d, $J = 8.5$ Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 1.91 (t, $J = 13$ Hz, 2H), 1.56 (s, 3H), 1.28-0.80 (m, 6H), 0.79 (t, $J = 7$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm): δ 173.4, 161.9, 155.6, 152.9, 151.6, 148.6, 134.2, 133.6, 131.8, 126.9, 126.6, 125.8, 125.2, 123.3, 121.8, 117.9, 116.5, 115.8, 112.5, 110.7, 108.7, 85.5, 56.3, 56.2, 41.0, 31.8, 27.2, 23.2, 22.5, 14.1. HRMS (ESI+): m/z calcd. for C$_{31}$H$_{32}$N$_2$NaO$_5$ [M+Na]$^+$: 535.2203 found: 535.2170.
4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-1,4-dihydroquinolin-3-yl)-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4r)

Yield: 84% as white solid, mp 110-113 °C; \(^1\)H NMR (500 MHz, DMSO, ppm): \(\delta\) 12.25 (s, 1H, D\(_2\)O exchangeable), 10.27 (s, 1H,D\(_2\)O exchangeable), 8.29-8.22 (m, 1H), 8.15 (t, \(J = 8\) Hz, 1H), 7.41-7.38 (m, 4H), 7.28 (s, 1H), 6.93 (d, \(J = 21.5\) Hz, 1H), 6.82 (d, \(J = 8.5\) Hz, 1H), 3.83 (s, 6H), 3.74 (s, 3H), 1.93-1.74 (m, 2H), 1.56 (s, 3H), 1.27-1.16 (m, 6H), 0.79 (t, \(J = 10\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm): \(\delta\) 173.3, 161.9, 155.6, 153.1, 152.9, 140.6, 134.4, 133.6, 131.8, 127.9, 127.0, 126.9, 126.7, 126.0, 121.8, 118.0, 116.5, 115.8, 109.1, 107.2, 85.5, 61.1, 56.5, 41.0, 31.8, 27.2, 23.2, 22.5, 14.1. HRMS (ESI+): m/z calcd. for C\(_{32}\)H\(_{34}\)N\(_2\)O\(_6\) [M+Na\(^+\)]: 565.2309 found : 565.2304.

6-(2-(furan-2-yl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (5a)

Yield: 90% as brown solid, mp 97-99 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm): \(\delta\) 8.75 (s, 1H, D\(_2\)O exchangeable), 8.19 (d, \(J = 7.5\) Hz, 1H), 7.65 (t, \(J = 8\) Hz, 1H), 7.61 (m, 2H), 7.48 (d, \(J = 8.5\) Hz, 2H), 7.38 (t, \(J = 7.5\) Hz, 1H), 7.12 (d, \(J = 2.5\) Hz, 1H), 6.78 (s, 1H), 6.59 (s, 1H), 6.04-5.96 (m, 1H), 5.24-5.05 (m, 2H), 1.81 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\), ppm): \(\delta\) 178.0, 155.9, 155.3, 145.9, 139.4, 138.7, 133.9, 132.2, 129.3, 127.4, 125.8, 125.3, 124.5, 123.5, 118.0, 116.5, 115.7, 114.7, 113.3, 112.7, 105.57, 84.2. FTIR (KBr, \(v = \text{cm}^{-1}\)): 3290, 2987, 1712, 1677, 1652, 1635, 1586, 1422, 1352. HRMS (ESI+): m/z calcd. for C\(_{24}\)H\(_{17}\)NNaO\(_5\) [M+Na\(^+\)]: 422.0998 found : 422.0995.
4-allyl-6-(2-(furan-2-yl)-4-oxo-4H-chromen-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (5b)

Yield: 91% as brown solid, mp 95-97 °C; $^1$H NMR (500 MHz, CDCl$_3$, ppm): $\delta$ 9.82 (s, 1H, D$_2$O exchangeable), 8.17 (d, $J = 8$ Hz, 1H), 7.76 (s, 1H), 7.65 (t, $J = 7.5$ Hz, 1H), 7.59 (s, 1H), 7.47 (d, $J = 8.5$ Hz, 1H), 7.37 (t, $J = 7$ Hz, 1H), 7.30 (d, $J = 8.5$ Hz, 1H), 7.16 (s, 1H), 7.12 (d, $J = 8.5$ Hz, 1H), 6.80 (d, $J = 8$ Hz, 1H), 5.73-5.65 (m, 1H), 5.13-5.08 (m, 2H), 2.66-2.62 (m, 2H), 1.66 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm): $\delta$ 178.2, 156.0, 155.5, 152.5, 146.5, 146.1, 134.0, 132.0, 131.2, 127.1, 126.6, 125.9, 125.4, 124.3, 121.8, 120.5, 118.1, 116.5, 115.7, 113.4, 112.8, 105.5, 84.3, 45.6, 26.3. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3284, 1713, 1697, 1609, 1556, 1372, 1303, 1236. HRMS (ESI+): m/z calcd. for C$_{25}$H$_{19}$NNaO$_5$ [M+Na]$^+$: 436.1155 found: 436.1161.

6-(2-(furan-2-yl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (5c)

Yield: 92% as brown solid, mp 96-99 °C; $^1$H NMR (500 MHz, CDCl$_3$, ppm): $\delta$ 9.69 (s, 1H, D$_2$O exchangeable), 8.17 (d, $J = 6.5$ Hz, 1H), 7.64-7.59 (m, 2H), 7.46 (d, $J = 7.5$ Hz, 1H), 7.36 (t, $J = 8$ Hz, 1H), 7.29 (d, $J = 7$ Hz, 1H), 7.12 (d, $J = 20$ Hz, 2H), 6.79 (d, $J = 8$ Hz, 1H), 6.58 (s, 1H), 1.91-1.86 (m, 2H), 1.64 (s, 3H), 1.37-1.23 (m, 6H), 0.82 (t, $J = 8$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm): $\delta$ 178.0, 155.9, 155.4, 152.8, 146.4, 146.0, 133.9, 133.7, 131.7, 127.0, 126.9, 125.8, 125.3, 124.2, 118.0, 116.5, 115.7, 113.3, 112.6, 105.5, 85.4, 41.0, 31.8, 27.1, 23.2, 22.5, 14.1. HRMS (ESI+): m/z calcd. for C$_{27}$H$_{23}$NNaO$_5$ [M+Na]$^+$: 466.1624 found: 466.1636.
6-(2-(furan-2-yl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (6a)

Yield: 89% as brown solid, mp 127-130 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm): \(\delta\) 9.17 (s, 1H, D\(_2\)O exchangeable), 8.75 (s, 1H, D\(_2\)O exchangeable), 8.19 (d, \(J = 9\) Hz, 1H), 7.66 (t, \(J = 7.5\) Hz, 1H), 7.61 (m, 2H), 7.48 (d, \(J = 8.5\) Hz, 2H), 7.38 (t, \(J = 7.5\) Hz, 1H), 7.12 (d, \(J = 2.5\) Hz, 1H), 6.78 (s, 1H), 6.59 (s, 1H), 6.04-5.96 (m, 1H), 5.24-5.05 (m, 2H), 1.81 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\), ppm): \(\delta\) 178.1, 155.8, 155.3, 145.9, 139.4, 138.7, 133.9, 132.2, 129.3, 127.4, 125.8, 125.3, 124.5, 123.5, 118.0, 116.5, 115.7, 114.7, 113.3, 112.7, 105.57, 84.2. FTIR (KBr, \(v = \text{ cm}^{-1}\)): 3486, 3229, 2869, 1717, 1693, 1645, 1546, 1462, 1341, 1259. HRMS (ESI+): m/z calcd. for C\(_{24}\)H\(_{18}\)N\(_2\)NaO\(_4\) [M+Na\(^+\)]: 421.1158 found : 421.1152.

4-allyl-6-(2-(furan-2-yl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (6b)

Yield: 87% as brown solid, mp 146-148 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm): \(\delta\) 9.90 (s, 1H, D\(_2\)O exchangeable), 8.17 (dd, \(J = 2, 10\) Hz, 1H), 7.67-7.63 (m, 1H), 7.59 (d, \(J = 1\) Hz, 1H), 7.47 (d, \(J = 10\) Hz, 1H), 7.39-7.35 (m, 1H), 7.30-7.27 (m, 1H), 7.15 (d, \(J = 2.5\) Hz, 1H), 7.11 (d, \(J = 4.5\) Hz, 1H), 6.80 (d, \(J = 10.5\) Hz, 1H), 6.59-6.57 (m, 1H), 6.24 (s, 1H, D\(_2\)O exchangeable), 5.73-5.63 (m, 1H), 5.12-5.07 (m, 2H), 2.69-2.58 (m, 2H), 1.66 (s, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm): \(\delta\) 178.2, 156.1, 155.4, 152.5, 146.5, 146.1, 134.0, 132.0, 131.2, 127.1, 126.6, 125.9, 125.4, 124.3, 121.8, 120.5, 118.1, 116.5, 115.7, 113.4, 112.8, 105.5, 84.3, 45.6, 26.3. FTIR (KBr, \(v = \text{ cm}^{-1}\)): 3492, 3278, 2849, 1715, 1689, 1665, 1609, 1565, 1412, 1343, 1259. HRMS (ESI+): m/z calcd. for C\(_{25}\)H\(_{20}\)N\(_2\)NaO\(_4\) [M+Na\(^+\)]: 435.1315 found : 435.1314.
6-(2-(furan-2-yl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (6c)

Yield: 91% as brown solid, mp 153-157 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm): \(\delta\) 9.69 (s, 1H, D\(_2\)O exchangeable), 8.17 (d, \(J = 6.5\) Hz, 1H), 7.64-7.59 (m, 2H), 7.46 (d, \(J = 7.5\) Hz, 1H), 7.36 (t, \(J = 8\) Hz, 1H), 7.29 (d, \(J = 7\) Hz, 1H), 7.12 (d, \(J = 20\) Hz, 2H), 6.79 (d, \(J = 8\) Hz, 1H), 6.58 (s, 1H), 4.23 (s, 1H, D\(_2\)O exchangeable), 1.91-1.86 (m, 2H), 1.64 (s, 3H), 1.37-1.23 (m, 6H), 0.82 (t, \(J = 7\)Hz, 3H).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm): \(\delta\) 178.0, 155.9, 155.4, 152.8, 146.4, 146.0, 133.9, 133.7, 131.8, 127.1, 126.9, 125.8, 125.3, 124.3, 118.0, 116.5, 115.7, 113.3, 112.7, 105.5, 85.4, 41.0, 31.8, 27.2, 23.2, 22.5, 14.1. HRMS (ESI\(^+\)): m/z calcd. for C\(_{27}\)H\(_{26}\)N\(_2\)O\(_4\) [M+Na\(^+\)]: 465.1784 found : 465.1781.

6-(3-bromo-5-fluorophenyl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (6aa)

Yield: 94% as white solid; \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm): \(\delta\) 8.53 (s, 1H, D\(_2\)O exchangeable), 7.46 (s, 2H), 7.28 (s, 1H), 7.22 (d, \(J = 8\)Hz, 1H), 7.16 (d, \(J = 9.5\)Hz, 1H), 6.93 (d, \(J = 8.5\)Hz, 1H), 6.08 (dd, \(J = 10.5, 17\)Hz, 1H), 5.28 (d, \(J = 11\)Hz, 1H), 5.16 (d, \(J = 17\)Hz, 1H), 1.25 (s, 3H).\(^{13}\)C NMR (100 MHz, CDCl\(_3\), ppm): \(\delta\) 164.4, 161.9, 153.0, 144.0, 134.7, 134.1, 131.4, 128.0, 125.9, 125.3, 122.9, 120.5, 118.0, 115.5, 113.1, 85.1, 26.6. FTIR (KBr, \(v = \text{cm}^{-1}\)): 3142, 2912, 1701, 1656. HRMS (ESI\(^+\)): m/z calcd for C\(_{17}\)H\(_{26}\)BrFNO\(_2\) [M+H\(^+\)]: 362.0192 found: 362.0189.

4-allyl-6-(3-bromo-5-fluorophenyl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (7aa)

Yield: 94% as white solid; \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm): \(\delta\) 9.52 (s, 1H, D\(_2\)O exchangeable), 7.46 (t, \(J = 6.5\)Hz, 2H), 7.21 (s, 2H), 7.15 (d, \(J = 9\)Hz, 1H), 6.97 (d, \(J = 8.5\)Hz, 1H), 5.80-5.72 (m, 1H), 5.17-5.14 (m, 2H), 2.81-2.71 (m, 2H), 1.78 (s, 3H).\(^{13}\)C NMR (100 MHz, CDCl\(_3\), ppm): \(\delta\) 164.5, 161.9, 153.2, 144.2, 134.9, 134.2, 131.6, 128.1, 126.0, 125.4, 123.3, 120.6, 118.1, 115.7, 113.2,

Reference:
$^1$H and $^{13}$C Spectra

20_SKJ-Ligand H

20_SKJ-Ligand