Palladium catalyzed C(sp<sup>2</sup>)-C(sp<sup>2</sup>) bond formation. A highly regio- and chemoselective dehydrogenative C-3 alkenylation of pyrones and pyridones

Hafiz Ul Lah, Faheem Rasool, and Syed Khalid Yousuf

Medicinal Chemistry Division, Indian Institute of Integrative Medicine, Sanatnagar-Srinagar-India-190005.

* Medicinal Chemistry Division, Indian Institute of Integrative Medicine, Sanatnagar-Srinagar-India-190005, Fax: +91-194244133; Tel: +91-1942431253/55; E-mail: khalidiiim@gmail.com.

General information  2-2
Experimental procedures and spectral analysis  2-13
Copies of <sup>1</sup>H, <sup>13</sup>C NMR and DEPT  12-43
General information

$^1$H and $^{13}$C NMR spectra were recorded on Bruker 400 MHz spectrometer with TMS as the internal standard. Chemical shifts are expressed in parts per million (δ ppm). Silica gel coated aluminium plates were used for TLC. The molecular formula of the compounds was analysed through HRMS with a QTOF analyser. Reagents used were mostly purchased from Sigma-Aldrich. The solvents used were mostly of LR grade.

Experimental procedures and spectral analysis.

Synthesis of 3-alkenylated -4-hydroxy-6-methyl-pyrones

**General procedure:** 3-alkenylated -4-hydroxy-6-methyl-pyrones. To a solution of the 4-Hydroxy-6-methyl-2-pyrone (0.4 mmol, 1.0 equiv.) in DMF:DMSO (8:2) 2ml, was added styrene (0.44 mmol, 1.1 equiv.), 5 mol \% Pd(OAc)$_2$ and 5 mol \% Cu(OTf)$_2$ in open air flask. The reaction mixture was allowed to stir at room temperature for 16 h. The completion of the reaction was monitored through TLC followed by extraction using ethyl acetate and water. The organic layer was concentrated in rotary evaporator and the crude mixture was subjected to column chromatography using DCM:CH$_3$OH as eluent to yield the desired product.
4-Hydroxy-6-methyl-3-styryl-pyran-2-one (3): The title compound was prepared by using general procedure using 4-hydroxy-6-methyl-2-pyrone (0.4 mmol, 50 mg) and styrene (0.44 mmol, 50 μl) to yield 3 as semisolid (70%, 62 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (60:40), Rf value 0.44. in 70:30 ethylacetate : hexane]. 1H NMR (400 MHz, MeOD) δ 7.60 (d, J = 16.5 Hz, 1H), 7.40 (d, J = 7.7 Hz, 2H), 7.25 (t, J = 7.6 Hz, 2H), 7.14 (dd, J = 14.7, 9.0 Hz, 2H), 6.03 (s, 1H), 2.20 (s, 3H). 13C NMR (101 MHz, MeOD), δ 168.1, 166.3, 162.3, 140.2, 131.3, 129.6 x 2, 128.0, 127.2 x 2, 119.0, 101.7, 101.3, 19.9. HRMS (ESI+) m/z calcd for C_{14}H_{12}NaO_3 (M+Na)^+ 251.0684, found; 251.0693.

3-[2-(2-Chloro-phenyl)-vinyl]-4-hydroxy-6-methyl-pyran-2-one (4): The title compound was prepared by the general procedure using 4-hydroxy-6-methyl-2-pyrene (0.4 mmol, 50 mg) and 3-chlorostyrene (0.44 mmol, 58 μl) to yield 4 as semisolid (67%, 71 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (60:40), Rf value 0.43. in 70:30 ethylacetate : hexane]. 1H NMR (400 MHz, MeOD) δ 8.05 (d, J = 16.4Hz, 1H), 7.70 (t, J = 9.3 Hz, 1H), 7.35 (d, J = 7.9 Hz, 1H), 7.30 – 7.10 (m, 3H), 6.09 (s, 1H), 2.27 (s, 3H). 13C NMR (101 MHz, MeOD), δ 168.1, 166.0, 162.4, 137.9, 134.0, 130.4, 128.8, 127.7, 127.1, 126.9, 121.4, 101.5, 101.2, 20.0. HRMS (ESI+) m/z calcd for C_{14}H_{11}NaClO_3 (M+Na)^+ 285.0294, found; 285.0286.

3-[2-(4-Chloro-phenyl)-vinyl]-4-hydroxy-6-methyl-pyran-2-one (5): The title compound was prepared by the general procedure using 4-hydroxy-6-methyl-2-pyrene (0.4 mmol, 50 mg) and 4-chlorostyrene (0.44 mmol, 54 μl) to yield 5 as semisolid (68%, 72 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (60:40), Rf
value 0.43 in 70:30 ethylacetate : hexane. $^1$H NMR (400 MHz, DMSO-$d_6$) δ 7.56 (d, $J$ = 16.4 Hz, 1H), 7.46 (d, $J$ = 8.5 Hz, 2H), 7.36 (d, $J$ = 8.5 Hz, 2H), 7.15 (d, $J$ = 16.4 Hz, 1H), 6.13 (s, 1H), 2.21 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 166.5, 162.4, 161.6, 137.3, 131.1, 128.6 x 2, 127.4 x 2, 126.8, 119.4, 100.0, 98.6, 19.5. HRMS (ESI$^+$) m/z calcd for C$_{14}$H$_{11}$NaClO$_3$ (M+Na)$^+$ 285.0294, found; 285.0283.

3-[(2-(4-Bromo-phenyl)-vinyl]-4-hydroxy-6-methyl-pyran-2-one (6): The title compound was prepared by the general procedure using 4-hydroxy-6-methyl-2-pyrone (0.4 mmol, 50 mg) and 4-bromostyrene (0.57 mmol, 75 µl) to yield 6 as semisolid (64%, 79 mg). The product was purified using column chromatography [eluent: hexane : ethylacetate (60:40), R$_f$ value 0.43 in 70:30 ethylacetate : hexane]. $^1$H NMR (400 MHz, MeOD) δ 7.56 (d, $J$ = 16.4 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.31 (d, $J$ = 8.5 Hz, 2H), 7.19 (d, $J$ = 16.4 Hz, 1H), 6.03 (s, 1H), 2.21 (s, 3H). $^{13}$C NMR (101 MHz, MeOD), δ 168.4, 166.2, 163.0, 139.5, 132.8 x 2, 130.0, 129.0 x 2, 121.6, 120.0, 101.6, 19.9. HRMS (ESI$^+$) m/z calcd for C$_{14}$H$_{11}$NaBrO$_3$ (M+Na)$^+$ 328.9789, found; 328.9796.

3-[(2-(4-Fluoro-phenyl)-vinyl]-4-hydroxy-6-methyl-pyran-2-one (7): The title compound was prepared by the general procedure using 4-hydroxy-6-methyl-2-pyrone (0.4 mmol, 50 mg) and 4-fluorostyrene (0.44 mmol, 56 µl) to yield 7 as semisolid (70%, 69 mg). The product was purified using column chromatography [eluent: hexane : ethylacetate (60:40), R$_f$ value 0.43 in 70:30 ethylacetate : hexane]. $^1$H NMR (400 MHz, DMSO) δ 7.58 (d, $J$ = 16.4 Hz, 1H), 7.48 (dd, $J$ = 8.6, 5.6 Hz, 2H), 7.17 – 7.05 (m, 3H), 6.12 (s, 1H), 2.23 (m, 3H). $^{13}$C NMR (101 MHz, DMSO) δ 166.22, 162.59, 162.54, 161.31, 160.12, 135.03, 135.00, 127.68, 127.61, 127.21, 118.51, 118.49, 115.67, 115.45, 100.07, 98.81, 19.4. HRMS (ESI$^+$) m/z calcd for C$_{14}$H$_{11}$NaFO$_3$ (M+Na)$^+$ 269.0590, found; 269.0597.
4-Hydroxy-6-methyl-3-(2-o-tolyl-vinyl)-pyran-2-one (8): The title compound was prepared by the general procedure using 4-hydroxy-6-methyl-2-pyrone (0.4 mmol, 50 mg) and 2-methylstyrene (0.44 mmol, 47 μl) to yield 8 as semisolid (70%). The product was purified using column chromatography [eluent; hexane : ethylacetate (60:40), Rf value 0.43. in 70:30 ethylacetate : hexane]. $^1$H NMR (400 MHz, DMSO) $\delta$ 7.82 (d, J = 16.2 Hz, 1H), 7.50 (d, J = 7.7 Hz, 1H), 7.20 – 7.09 (m, 3H), 7.03 (d, J = 16.2 Hz, 1H), 6.13 (s, 1H), 2.30 (s, 2H), 2.21 (s, 3H). $^{13}$C NMR (101 MHz, DMSO) $\delta$ 166.16, 162.64, 161.28, 137.32, 134.83, 130.28, 126.85, 126.25, 126.06, 124.20, 119.47, 100.04, 99.18, 19.51, 19.51. HRMS (ESI$^+$) m/z calcd for C_{15}H_{14}NaO_3 (M+Na)$^+$ 265.0841, found; 265.0849.

4-Hydroxy-6-methyl-3-(2-m-tolyl-vinyl)-pyran-2-one (9): The title compound was prepared by the general procedure using 4-hydroxy-6-methyl-2-pyrene (0.4 mmol, 50 mg) and 3-methylstyrene (0.44 mmol, 47 μl) to yield 9 as semisolid (70%). The product was purified using column chromatography [eluent; hexane : ethylacetate (60:40), Rf value 0.44. in 70:30 ethylacetate : hexane]. $^1$H NMR (400 MHz, DMSO) $\delta$ 7.56 (d, J = 16.4 Hz, 1H), 7.27 – 7.18 (m, 3H), 7.16 – 7.10 (m, 1H), 7.02 (d, J = 4.1 Hz, 1H), 6.13 (s, 1H), 2.30 (s, 3H), 2.20 (s, 3H). $^{13}$C NMR (101 MHz, DMSO) $\delta$ 166.14, 162.64, 161.24, 138.37, 137.81, 128.65, 128.57, 127.76, 126.35, 123.22, 118.31, 100.07, 98.94, 21.04, 19.50. HRMS (ESI$^+$) m/z calcd for C_{15}H_{14}NaO_3 (M+Na)$^+$ 265.0840, found; 265.0840.

4.2.1.6. 4-Hydroxy-6-methyl-3-(2-m-tolyl-vinyl)-pyran-2-one (10): Prepared by the general procedure 1 using 4-hydroxy-6-methyl-2-pyrene (0.4 mmol, 50 mg) and 3-methylstyrene (0.44 mmol, 47μl) to yield 10 as semisolid (69%, 67 mg). The product was
purified using column chromatography [eluent; hexane : ethylacetate (60:40), \( R_f \) value 0.45. in 70:30 ethylacetate : hexane]. \(^1\)H NMR (400 MHz, DMSO) \( \delta \) 7.56 (d, \( J = 16.3 \) Hz, 1H), 7.25 (d, \( J = 16.8 \) Hz, 3H), 7.18 – 6.98 (m, 2H), 6.14 (s, 1H), 2.51 (s, 3H), 2.22 (s, 3H). HRMS (ESI\(^+\)) m/z calcd for C\(_{15}\)H\(_{14}\)NaO\(_3\) (M+Na\(^+\)) 265.0841, found; 265.0845.

**4-Hydroxy-3-[2-(4-methoxy-phenyl)-vinyl]-6-methyl-pyran-2-one (11):** The title compound was prepared by the general procedure using 4-hydroxy-6-methyl-2-pyrone (0.4 mmol, 50 mg) and 4-methoxystyrene (0.44mmol, 59\( \mu \)l) to yield 11 as semisolid (70%, 73 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (60:40), \( R_f \) value 0.45. in 70:30 ethylacetate : hexane]. \(^1\)H NMR (400 MHz, MeOD) \( \delta \) 7.65 (d, \( J = 16.5 \) Hz, 1H), 7.45 (d, \( J = 8.6 \) Hz, 2H), 7.13-7.05 (m, 1H), 7.91 (d, \( J = 8.6 \) Hz, 2H), 6.09 (s, 1H), 3.85 (bs, 3H), 2.21 (s, 3H).\(^{13}\)C NMR (101 MHz, MeOD), \( \delta \) 167.0, 166.2, 161.3, 160.0, 132.6, 130.9, 128.2 x 2, 116.6, 114.8 x 2, 101.5, 98.8, 55.7, 19.9. HRMS (ESI\(^+\)) m/z calcd for C\(_{15}\)H\(_{14}\)NaO\(_4\) (M+Na\(^+\)) 281.0790, found; 281.0798.

**4-Hydroxy-6-methyl-3-[2-(3-nitro-phenyl)-vinyl]-pyran-2-one (12):** Prepared by the general procedure 1 using 4-hydroxy-6-methyl-2-pyrone (0.4 mmol, 50 mg) and 3-nitrostyrene (0.44 mmol, 66\( \mu \)l) to yield 12 as semisolid (69%, 76 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (50:50), \( R_f \) value 0.38. in 70:30 ethylacetate : hexane]. \(^1\)H NMR (400 MHz, DMSO) \( \delta \) 8.21 (s, 1H), 8.03 (dd, \( J = 8.1, 1.1 \) Hz, 1H), 7.89 (d, \( J = 7.8 \) Hz, 1H), 7.73 – 7.55 (m, 2H), 7.30 (d, \( J = 16.3 \) Hz, 1H), 6.15 (s, 1H), 2.22 (s, 3H).\(^{13}\)C NMR (101 MHz, MeOD), \( \delta \) 167.2, 162.3, 162.1, 148.4, 140.3, 132.2, 130.1, 125.7, 121.4, 121.2, 119.6, 100.0, 98.3, 19.5. HRMS (ESI\(^+\)) m/z calcd for C\(_{14}\)H\(_{11}\)NaNO\(_5\) (M+Na\(^+\)) 296.0535, found; 296.0542.
4-Hydroxy-6-methyl-3-(2-phenyl-propenyl)-pyran-2-one (13): The title compound was prepared by general procedure using 4-hydroxy-6-methyl-2-pyrones (0.4 mmol, 50 mg) and alpha methyl styrene (1.1 equiv.) to yield 13 as semisolid (70 %). The product was purified using column chromatography [eluent: hexane : ethylacetate (60:40), Rf value 0.50. in 70:30 ethylacetate : hexane]. 1H NMR (400 MHz, DMSO) δ 7.54 – 7.46 (m, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.27 (t, J = 7.3 Hz, 1H), 6.27 (s, 1H), 6.10 (s, 1H), 2.20 (s, 1H), 1.91 (s, 1H). 13C NMR (101 MHz, DMSO) δ 165.48, 162.98, 161.25, 142.35, 138.02, 128.31, 127.13, 125.57, 117.44, 99.99, 99.33, 19.38, 18.14. HRMS (ESI+) m/z calcd for C14H15NaO3 (M+Na)+ 265.2699, found; 265.2693. Anal cal. for C14H15O3; C, 74.36, H, 5.82; observed C, 74.30, H, 5.89.

4-Hydroxy-3-[3-(4-methoxy-phenyl)-propenyl]-6-methyl-pyran-2-one (14): The title compound was prepared by general procedure using 4-hydroxy-6-methyl-2-pyrones (0.4 mmol, 50 mg) and 4-methoxy allyl benzene (1.1 equiv.) to afford 14 as semisolid in 70 % yield. The product was purified using column chromatography [eluent: hexane : ethylacetate (60:40), Rf value 0.48. in 70:30 ethylacetate : hexane]. 1H NMR (400 MHz, DMSO) δ 7.56 (d, J = 16.4 Hz, 1H), 7.27 – 7.18 (m, 3H), 7.16 – 7.10 (m, 1H), 7.02 (d, J = 4.1 Hz, 1H), 6.13 (s, 1H), 2.30 (s, 3H), 2.20 (s, 3H). 13C NMR (101 MHz, DMSO) δ 166.14, 162.98, 161.24, 138.37, 137.81, 128.65, 128.57, 127.76, 126.35, 123.22, 118.31, 100.07, 98.94, 21.04, 19.50. HRMS (ESI+) m/z calcd for C16H16NaO4 (M+Na)+ 295.2958, found; 295.2951.

Synthesis of 3-alkenylated 4-hydroxy-6-methyl-pyridones.

General procedure (2): To a solution of the 4-Hydroxy-6-methyl-2-pyridone/4-chloro-6-methyl-2-pyrene/4-methoxy-6-methyl-2-pyrene (0.4 mmol, 1.0 equiv.) in DMF:DMSO (8:2) 2ml, was added styrene (0.44 mmol, 1.1 equiv.), 5 mole % Pd(OAc)2 and 5 mole % Cu(OTf)2 in open air flask. The reaction mixture was stirred at 80 °C for 16h. The completion of the reaction was monitored through TLC followed by extraction with ethyl acetate and water. The organic layer was concentrated in rotary evaporator and the crude
mixture was subjected to column chromatography using DCM:CH$_3$OH in case of 4-Hydroxy-6-methyl-2-pyridone and Hexane: Ethyl acetate in case of 4-chloro-6-methyl-2-pyrone and 4-methoxy-6-methyl-2-pyrone as eluent to yield the desired product.

4-Hydroxy-6-methyl-3-styryl-1H-pyridin-2-one (15): Prepared by the general procedure 2 using 4-hydroxy-6-methyl-2-pyridone (0.4 mmol, 50 mg) and styrene (0.44 mmol, 50 μl) to yield 11 as semisolid (70%, 62 mg) The product was purified using column chromatography [eluent; DCM : MeOH (98:2), R$_f$ value 0.50. in 90:10 DCM:MeOH]. $^1$H NMR (400 MHz, MeOH) δ 7.71 (d, $J = 16.5$ Hz, 1H), 7.41 (d, $J = 7.7$ Hz, 2H), 7.25 (dd, $J = 13.9, 6.4$ Hz, 2H), 7.11 (t, $J = 7.3$ Hz, 1H), 5.89 (s, 1H), 2.20 (s, 3H). HRMS (ESI$^+$) m/z calcd for C$_{14}$H$_{13}$NaNO$_2$ (M+Na)$^+$ 250.0844, found; 250.0849.

3-[2-(4-Chloro-phenyl)-vinyl]-4-hydroxy-6-methyl-1H-pyridin-2-one (16): Prepared by the general procedure 2 using 4-hydroxy-6-methyl-2-pyridone (0.4 mmol, 50 mg) and 4-chlorostyrene (0.44 mmol, 54 μl) to yield 16 as semisolid (65%, 68 mg). The product was purified using column chromatography [eluent; DCM : MeOH (98:2), R$_f$ value 0.48. in 90:10 DCM:MeOH]. $^1$H NMR (400 MHz, DMSO) δ 7.56 (d, $J = 16.4$ Hz, 1H), 7.46 (d, $J = 8.5$ Hz, 2H), 7.36 (d, $J = 8.5$ Hz, 2H), 7.15 (d, $J = 16.4$ Hz, 1H), 6.13 (s, 1H), 2.21 (s, 3H). $^{13}$C NMR (101 MHz, DMSO) δ 166.5, 162.4, 161.6, 137.3, 131.1, 128.6 x 2, 127.4 x 2, 126.8, 119.4, 100.0, 98.6, 19.5. HRMS (ESI$^+$) m/z calcd for C$_{14}$H$_{12}$NaClNO$_2$ (M+Na)$^+$ 284.0454, found; 284.0448.
3-[2-(2-Chloro-phenyl)-vinyl]-4-hydroxy-6-methyl-1H-pyridin-2-one (17): Prepared by the general procedure 2 using 4-hydroxy-6-methyl-2-pyridone (0.4 mmol, 50mg) and 3-chlorostyrene (0.44mmol, 58μl) to yield 17 as semisolid (67%, 70 mg). The product was purified using column chromatography [eluent; DCM : MeOH (98:2), R_f value 0.48. in 90:10 DCM:MeOH]. ¹H NMR (400 MHz, DMSO) δ 8.14 (d, J = 16.3 Hz, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.40 (d, J = 7.9 Hz, 1H), 7.29 (dd, J = 12.1, 4.1 Hz, 2H), 7.18 (dd, J = 11.1, 4.1 Hz, 1H), 5.81 (s, 1H), 2.14 (s, 3H). ¹³C NMR (101 MHz, DMSO) δ 164.8, 163.2, 144.9, 137.2, 131.6, 129.5, 127.6, 127.4, 125.6, 123.3, 122.6, 104.8, 97.9, 18.5. HRMS (ESI⁺) m/z calcd for C_{14}H_{12}NaClNO₂ (M+Na)⁺ 284.0454, found; 284.0459.

4-Hydroxy-6-methyl-3-[2-(3-nitro-phenyl)-vinyl]-1H-pyridin-2-one (18): Prepared by the general procedure 2 using 4-hydroxy-6-methyl-2-pyridone (0.4 mmol, 50 mg) and 3-nitrostyrene (0.44 mmol, 66μl) to yield 18 as semisolid (67%, 72 mg). The product was purified using column chromatography [eluent; DCM : MeOH (97:3), R_f value 0.40. in 90:10 DCM:MeOH]. ¹H NMR (400 MHz, DMSO) δ 8.21 (d, J = 10.5 Hz, 1H), 8.04 (d, J = 7.5 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 16.4 Hz, 1H), 7.61 (t, J = 8.0 Hz, 1H), 7.32 (d, J = 16.3 Hz, 1H), 6.15 (s, 1H), 2.23 (s, 3H). ¹³C NMR (101 MHz, DMSO) δ 167.3, 162.4, 162.1, 148.4, 140.3, 132.2, 130.1, 125.6, 121.5, 121.2, 119.5, 100.1, 98.1, 19.5. HRMS (ESI⁺) m/z calcd for C_{14}H_{12}NaClNO_4 (M+Na)⁺ 295.0695, found; 295.0689. Anal cal. for C_{14}H_{12}N_2O_4; C, 61.76, H, 4.44, N, 10.29; observed C, 61.70, H, 4.48, N, 10.32.
4-Methoxy-6-methyl-3-styryl-pyran-2-one (20): To a solution of 4-methoxy-6-methyl-2-pyrone (0.4 mmol, 1.0 equiv.) in DMF:DMSO (8:2) 2ml, was added styrene (0.44 mmol, 1.1 equiv.), 5 mole % Pd(OAc)$_2$ and 5 mole % Cu(OTf)$_2$ in open air flask. The reaction mixture was stirred at 80 °C for 10h. The completion of the reaction was monitored through TLC followed by usual procedure to obtain 20 as semisolid (71%, 61 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (93:7), R$_f$ value 0.52. in 50:50 hexane : ethylacetate]. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.85 (d, $J$ = 16.4 Hz, 1H), 7.57 (d, $J$ = 7.5 Hz, 2H), 7.38 (t, $J$ = 7.6 Hz, 2H), 7.33 (s, 1H), 7.25 (d, $J$ = 5.7 Hz, 1H), 6.15 (s, 1H), 4.03 (s, 3H), 2.37 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 166.0, 163.4, 161.8, 138.8, 131.9, 128.8 x 2, 127.4, 126.8 x 2, 117.7, 102.6, 95.3, 56.7, 20.7. HRMS (ESI$^+$) m/z calcd for C$_{15}$H$_{14}$NaO$_3$ (M+Na)$^+$ 265.0841, found; 265.0848.

Synthesis of 3-alkenylated -4-Chloro-6-methyl-pyridones.

General procedure (3): To a solution of 4-chloro-6-methyl-2-pyrene (0.4 mmol, 1.0 equiv.) in DMF:DMSO (8:2) 2ml, was added styrene (0.44 mmol, 1.1 equiv.), 5 mol % Pd(OAc)$_2$ and 5 mol % Cu(OTf)$_2$ in open air flask. The reaction mixture was stirred at 80 °C for 16h. The completion of the reaction was monitored through TLC followed by extraction with ethyl acetate and water. The organic layer was concentrated in rotary evaporator and the crude mixture was subjected to column chromatography using Hexane : Ethyl acetate as eluent to yield the desired product.

4-Chloro-6-methyl-3-styryl-pyran-2-one (22): Prepared by the general procedure 3 using 4-chloro-6-methyl-2-pyrene (0.35mmol, 50 mg) and styrene (0.39 mmol, 44µl) to yield 22 as semisolid (65%, 54 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (96:4), R$_f$ value 0.55. in 20:80 hexane : ethylacetate]. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.47 – 7.44 (m, 2H), 7.40 – 7.35 (m, 2H), 7.32 – 7.30 (m, 1H), 6.75 (d, $J$ = 16.3 Hz, 1H), 6.62 (d, $J$ = 16.3 Hz, 1H), 6.37 (s, 1H), 2.43 (s, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 160.3, 160.0, 153.4, 137.0, 136.2, 129.0, 128.9, 126.8, 119.4, 115.3, 112.2, 111.2, 106.3, 19.6. HRMS (ESI$^+$) m/z calcd for C$_{14}$H$_{11}$ClO$_2$ (M+Na)$^+$ 269.0345, found; 269.0349. Anal cal. for C$_{14}$H$_{11}$ClO$_2$: C, 68.16, H, 4.49; observed C, 68.11, H, 4.43.
4-Chloro-3-[2-(4-chloro-phenyl)-vinyl]-6-methyl-pyran-2-one (23): Prepared by the general procedure 3 using 4-chloro-6-methyl-2-pyronone (0.35 mmol, 50 mg) and 4-chlorostyrene (0.39 mmol, 48µl) to yield 23 as semisolid (64%, 63 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (96:4), R$_f$ value 0.54. in 20:80 hexane : ethylacetate]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40 – 7.31 (m, 4H), 6.78 – 6.68 (m, 1H), 6.58 (d, $J$ = 16.3 Hz, 1H), 6.37 (s, 1H), 2.42 (s, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 160.0, 159.4, 147.2, 136.1, 134.3, 132.4, 130.1, 129.3, 127.0, 126.9, 121.7, 118.1), 107.7, 19.8. HRMS (ESI$^+$) m/z calcd for C$_{14}$H$_{10}$NaCl$_2$O$_2$ (M+Na)$^+$ 302.9956, found; 302.9959. Anal cal. for C$_{14}$H$_{10}$Cl$_2$O$_3$: C, 59.81, H, 3.59; observed C, 59.87, H, 3.53.

4-Chloro-3-[2-(2-chloro-phenyl)-vinyl]-6-methyl-pyran-2-one (24): Prepared by the general procedure 3 using 4-chloro-6-methyl-2-pyronone (0.35 mmol, 50 mg) and 2-chlorostyrene (0.39 mmol, 51µl) to yield 24 as semisolid (65%, 64 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (96:4), R$_f$ value 0.55. in 20:80 hexane : ethylacetate]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.36 (d, $J$ = 16.1 Hz, 1H), 7.63 (d, $J$ = 7.7 Hz, 1H), 7.37 (d, $J$ = 4.5 Hz, 1H), 7.27 – 7.18 (m, 2H), 7.15-7.10 (m, 1H), 6.16 (s, 1H), 2.27 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 160.1, 159.5, 147.3, 136.1, 134.5, 133.3, 132.4, 130.2, 129.4, 127.0, 121.7, 107.9, 20.0. HRMS (ESI$^+$) m/z calcd for C$_{14}$H$_{10}$NaCl$_2$O$_2$ (M+Na)$^+$ 302.9956, found; 302.9949.

3-[2-(4-Bromo-phenyl)-vinyl]-4-chloro-6-methyl-pyran-2-one (25): Prepared by the general procedure 3 using 4-chloro-6-methyl-2-pyronone (0.35 mmol, 50 mg) and 4-bromostyrene (0.46mmol, 60µl) to yield 25 as semisolid (60%, 67 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (96:4), R$_f$ value 0.55. in 20:80 hexane : ethylacetate]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.49 (d, $J$ = 8.4 Hz, 2H), 7.31 (d, $J$ = 8.4 Hz, 2H), 6.74 (d, $J$ = 16.3 Hz, 1H), 6.60 (d, $J$ = 16.3 Hz, 1H), 6.37 (s, 1H), 2.42 (s,
\( ^{13}C \) NMR (101 MHz, CDCl\(_3\)) \( \delta \) 160.2, 153.3, 135.8, 135.0, 132.1, 129.5, 128.2, 120.2, 115.2, 112.2, 19.8. HRMS (ESI\(^+\)) m/z calcd for C\(_{14}\)H\(_{10}\)NaBrClO\(_2\) (M+Na\(^+\)) 346.9450, found; 346.9457. Anal cal. for C\(_{14}\)H\(_{10}\)BrClO\(_2\); C, 51.65, H, 3.10; observed C, 51.60, H, 3.15.

4-Chloro-3-[2-(4-fluoro-phenyl)-vinyl]-6-methyl-pyran-2-one (26): Prepared by the general procedure 3 using 4-chloro-6-methyl-2-pyrone (0.35 mmol, 50 mg) and 4-bromostyrene (0.39 mmol, 48 \( \mu l \)) to yield 26 as semisolid (61%, 57 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (96:4), \( R_f \) value 0.55. in 20:80 hexane : ethylacetate]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.42 (dd, \( J = 8.5, 5.5 \) Hz, 2H), 7.06 (t, \( J = 8.6 \) Hz, 2H), 6.62 (dd, \( J = 33.7, 16.3 \) Hz, 2H), 6.37 (s, 1H), 2.42 (s, 3H). HRMS (ESI\(^+\)) m/z calcd for C\(_{14}\)H\(_{10}\)NaFClO\(_2\) (M+Na\(^+\)) 346.9451, found; 346.9458.

4-Chloro-3-[2-(4-methoxy-phenyl)-vinyl]-6-methyl-pyran-2-one (27): Prepared by the general procedure 3 using 4-chloro-6-methyl-2-pyrone (0.35 mmol, 50 mg) and 4-methoxystyrene (0.39 mmol, 52 \( \mu l \)) to yield 27 as semisolid (66%, 64 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (96:4), \( R_f \) value 0.56. in 20:80 hexane : ethylacetate]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.39 (d, \( J = 8.7 \) Hz, 2H), 6.90 (t, \( J = 5.9 \) Hz, 3H), 6.57 (d, \( J = 5.9 \) Hz, 1H), 6.35 (s, 1H), 3.82 (s, 3H), 2.41 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 160.4, 160.2, 159.8, 153.6, 136.5, 129.0, 128.1 x 2, 117.1, 115.6, 114.5 x 2, 112.2, 55.6, 19.6. HRMS (ESI\(^+\)) m/z calcd for C\(_{14}\)H\(_{10}\)NaBrClO\(_2\) (M+Na\(^+\)) 299.0451, found; 299.0458.
4-Chloro-6-methyl-3-[2-(3-nitro-phenyl)-vinyl]-pyran-2-one (28): Prepared by the general procedure 3 using 4-chloro-6-methyl-2-pyrrone (0.35 mmol, 50mg) and 3-nitro styrene (0.39 mmol, 56μl) to yield 28 as semisolid (64%, 65 mg). The product was purified using column chromatography [eluent; hexane : ethylacetate (93:7), Rf value 0.47. in 20:80 hexane : ethylacetate]. \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.30 (s, 1H), 8.15 (dd, \( J = 8.2, 1.2 \) Hz, 1H), 7.75 (d, \( J = 7.7 \) Hz, 1H), 7.56 (q, \( J = 7.9 \) Hz, 1H), 6.91 (d, \( J = 16.3 \) Hz, 1H), 6.75 – 6.66 (m, 1H), 6.40 (s, 1H), 2.45 (s, 3H). \( ^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 160.2, 159.9, 152.8, 148.8, 137.9, 134.4, 132.5, 130.0, 123.2, 122.7, 121.3, 114.5, 112.5, 19.7. HRMS (ESI\(^+\)) m/z calcd for C\(_{14}\)H\(_{10}\)NaClO\(_4\) (M+Na\(^+\)) 314.0196, found; 314.0189
Copies of $^1\text{H}$ and $^{13}\text{C}$ NMR.

$^1\text{H}$ NMR of compound 3.

$^{13}\text{C}$ NMR of compound 3:
Dept of compound 3:

\[ \text{H NMR of compound 4:} \]
$^{13}$C NMR of compound 4:

Dept of compound 4:
$^1$H NMR of compound 5.

$^{13}$C NMR of compound 5:
Dept of compound 5:

\[\text{H NMR of compound 6:}\]
\(^{13}\)C NMR of compound 6:

Dept of compound 6:
$^1$H NMR of compound 7:

$^{13}$C NMR of compound 7:
Dept of compound 7:

$^1$H NMR of compound 8:
$^{13}$C NMR of compound 8:

Dept of compound 8:
$^1$H NMR of compound 9:

$^{13}$C NMR of compound 9:
Dept of compound 9:

1H NMR of compound 12:
$^{13}$C NMR of compound 12:

Depth of compound 12:
$^1$H NMR of compound 13:

$^{13}$C NMR of compound 13:
Dept of compound 13:

\[
\text{H NMR of compound 14:}
\]

\[
\text{\textsuperscript{1}H NMR of compound 14:}
\]
$^{13}$C NMR of compound 14:

Dept of compound 14:
$^1$H NMR of compound 15:

$^1$H NMR of compound 16:
$^{13}$C NMR of compound 16:

Deuteron of compound 16:
$^1$H NMR of compound 17:

$^{13}$C NMR of compound 17:
Dept of compound 17:

\[ \text{Chemical structure of compound 17} \]

\[ \text{H NMR of compound 18:} \]

\[ \text{Chemical structure of compound 18} \]
\( ^{13}\text{C} \) NMR of compound 18:

\[ \text{Dept of compound 18:} \]
$^1$H NMR of compound 20:

$^{13}$C NMR of compound 20:
Dept of compound 20:

$^1$H NMR of compound 22:
$^{13}$C NMR of compound 22:

Dept of compound 22:
$^1$H NMR of compound 23:

$^{13}$C NMR of compound 23:
Dept of compound 23:

1H NMR of compound 24:
$^{13}$C NMR of compound 24:

Dept of compound 24:
\(^1\)H NMR of compound 25:

\[^{13}\text{C}\ NMR\ of\ compound\ 25:\]
Depth of compound 25:

[Image of H NMR spectrum for compound 25]

$^1$H NMR of compound 26:

[Image of H NMR spectrum for compound 26]
$^1$H NMR of compound 27:

$^{13}$C NMR of compound 27:
Dept of compound 27:

\[\text{Chemical structure of compound 27} \]

$^1$H NMR of compound 28:

\[\text{Chemical structure of compound 28} \]

\[\text{NMR spectrum of compound 28} \]
$^{13}$C NMR of compound 28: