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Phosphine-Mediated Enantioselective [1+4] Annulation of Morita-Baylis-Hillman Carbonates with 2-Enoylpyridines

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Supporting Information

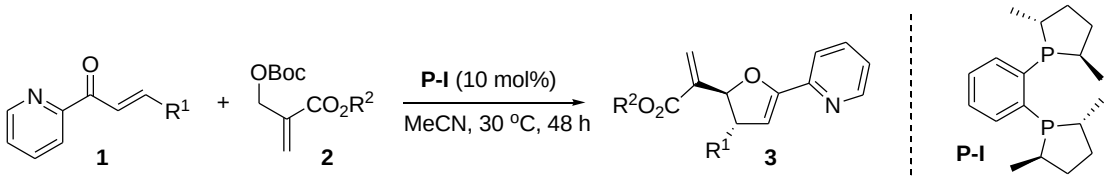
Contents

Experimental section

General

All reactions were carried out with dry, freshly distilled solvents in anhydrous conditions. Toluene and THF were distilled from sodium, while dichloromethane was distilled from CaH_2 immediately prior to use. All chemicals were used without further purification as commercially available unless otherwise noted. All reactions were performed under an atmosphere of dry nitrogen. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 and 365 nm). Flash chromatography was conducted on silica gel (300–400 mesh). NMR (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) spectra were recorded in $CDCl_3$ with TMS as the internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Data for ^{1}H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quarter; m, multiplet), coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High resolution mass spectral (HRMS) analyses were measured using ESI techniques.

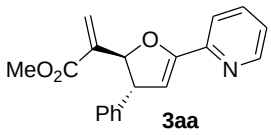
General procedure for the asymmetric [1+4] annulation between Morita-Baylis-Hillman Carbonates 2 with 2-Enoylpyridines 1



Under nitrogen atmosphere, a mixture of 2-enoylpyridines **1** (0.20 mmol), MBH carbonate **2** (0.24 mmol), **P-I** (0.02 mmol) in MeCN (1.0 mL) was stirred at 30 ^{o}C in a sealed tube for 48 h. After removal of the solvent, the crude residue was purified by column chromatography (petroleum ether/ethyl acetate) on silica gel to give the corresponding products **3**.

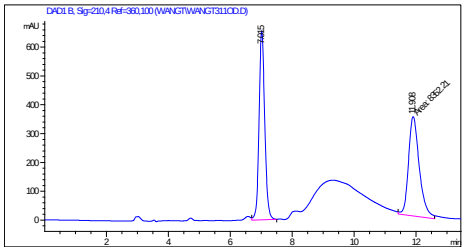
Compounds characterization

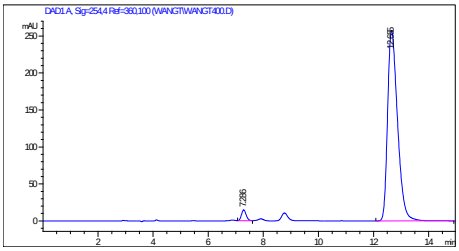
methyl 2-((2S,3R)-2,3-dihydro-3-phenyl-5-(pyridin-2-yl)furan-2-yl)acrylate (3aa)



3aa

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.65-8.63 (m, 1H), 7.77-7.73 (m, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.36-7.31 (m, 4H), 7.28-7.23 (m, 2H), 6.34 (s, 1H), 5.91-5.90 (m, 2H), 5.39-5.37 (m, 1H), 4.10-4.08 (m, 1H), 3.76 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 166.1, 155.5, 149.8, 143.4, 139.6, 136.8, 128.7, 127.8, 127.2, 124.7, 123.4, 120.3, 103.1, 87.1, 56.1, 52.0. HRMS: exact mass calculated for $[M+H]^+$ ($C_{19}H_{18}NO_3$) requires m/z 308.12812, found m/z 308.12759; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (minor) = 7.286 min, t_R (major) = 12.655 min, 95% ee.





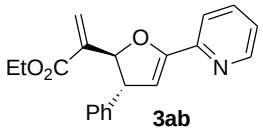
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	7.015	8345.5	655.9	0.1944	49.980	0.846
2	11.908	8352.2	344.3	0.4043	50.020	0.729

Chiral

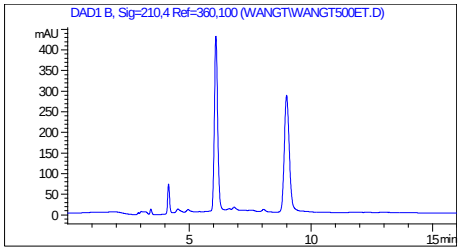
#	Time	Area	Height	Width	Area%	Symmetry
1	7.286	171.9	14.7	0.1825	2.596	0.846
2	12.655	6450.8	257.3	0.3865	97.404	0.625

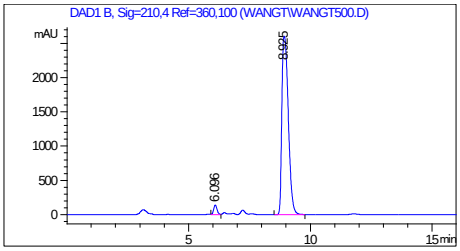
ethyl 2-((2S,3R)-2,3-dihydro-3-phenyl-5-(pyridin-2-yl)furan-2-yl)acrylate (3ab)



3ab

^{1}H NMR (400 Hz, CDCl3): δ (ppm) 8.63-8.62 (m, 1H), 7.75-7.71 (m, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.36-7.22 (m, 6H), 6.33 (s, 1H), 5.91-5.87 (m, 2H), 5.41-5.39 (m, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.10-4.08 (m, 1H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 165.6, 155.4, 149.7, 143.4, 139.9, 136.7, 128.6, 127.7, 127.1, 124.4, 123.3, 120.2, 103.2, 87.1, 60.9, 56.1, 14.2. HRMS: exact mass calculated for $[M+H]^+$ ($C_{20}H_{20}NO_3$) requires m/z 322.14377, found m/z 322.14325; HPLC conditions: Daicel Chiralpak OD-H column, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 210 nm, retention time: t_R (minor) = 6.096 min, t_R (major) = 8.925 min, 94% ee.





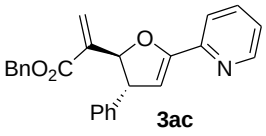
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	6.095	4058.8	425	0.1454	49.337	0.826
2	8.999	4167.9	283.4	0.2256	50.663	0.771

Chiral

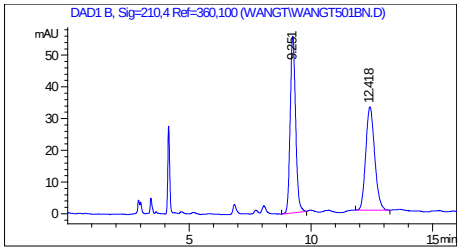
#	Time	Area	Height	Width	Area%	Symmetry
1	6.096	1351	142.1	0.1469	2.740	0.858
2	8.925	47958.2	2606.5	0.2907	97.260	0.541

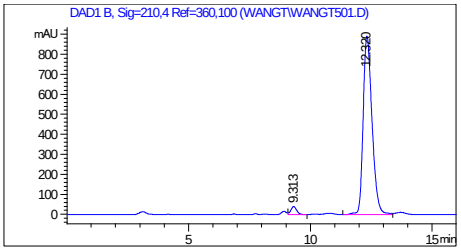
benzyl 2-((2S,3R)-2,3-dihydro-3-phenyl-5-(pyridin-2-yl)furan-2-yl)acrylate (3ac)



3ac

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.64-8.63 (m, 1H), 7.76-7.71 (m, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.33-7.22 (m, 11H), 6.39 (s, 1H), 5.91-5.90 (m, 2H), 5.43-5.42 (m, 1H), 5.23 (s, 2H), 4.12-4.10 (m, 1H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 165.4, 155.4, 149.8, 149.3, 143.2, 139.6, 136.7, 135.7, 128.7, 128.6, 128.4, 127.7, 127.1, 125.2, 123.4, 120.2, 103.2, 87.1, 66.7, 56.0. HRMS: exact mass calculated for $[M+H]^+$ ($C_{25}H_{22}NO_3$) requires m/z 384.15942, found m/z 384.15915; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 210 nm, retention time: t_R (minor) = 9.313 min, t_R (major) = 12.32 min, 94% ee.





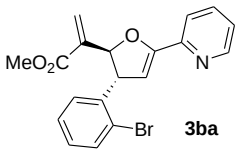
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	9.251	858.3	55.7	0.2377	50.826	0.856
2	12.418	830.4	32.6	0.3956	49.174	0.834

Chiral

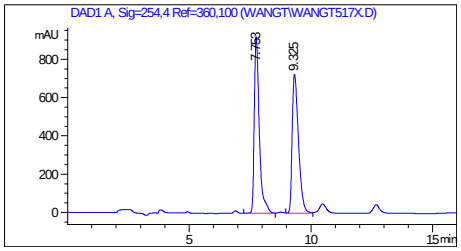
#	Time	Area	Height	Width	Area%	Symmetry
1	9.313	665.4	40.1	0.2555	2.850	0.904
2	12.32	22682.7	892.7	0.3904	97.150	0.695

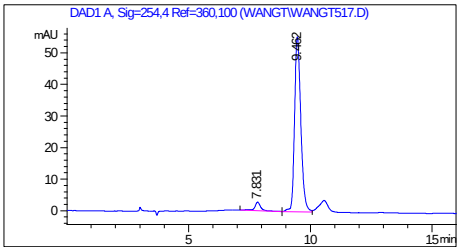
methyl 2-((2S,3R)-3-(2-bromophenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl)acrylate (3ba)



3ba

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.62 (d, *J* = 4.4 Hz, 1H), 7.75-7.71 (m, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.55-7.53 (m, 1H), 7.48-7.46 (m, 1H), 7.32-7.23 (m, 2H), 7.11-7.07 (m, 1H), 6.38 (s, 1H), 5.96 (s, 1H), 5.86 (d, *J* = 2.8 Hz, 1H), 5.46 (d, *J* = 5.6 Hz, 1H), 4.70 (q, *J* = 2.8 Hz, 1H), 3.71 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 165.9, 155.6, 149.8, 149.2, 142.8, 139.7, 136.7, 132.7, 129.4, 128.6, 128.3, 125.0, 123.7, 123.5, 120.3, 103.2, 86.7, 54.9, 52.1. HRMS: exact mass calculated for $[M+Na]^+$ ($C_{19}H_{16}NO_3BrNa$) requires m/z 408.02058, found m/z 408.02008; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (minor) = 7.831 min, t_R (major) = 9.462 min, 91% ee.





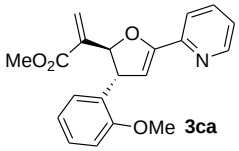
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	7.753	13231	921.3	0.2195	50.305	0.578
2	9.325	13070.5	725.8	0.2781	49.695	0.55

Chiral

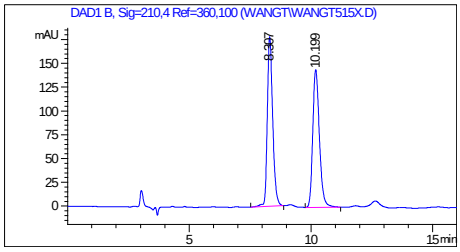
#	Time	Area	Height	Width	Area%	Symmetry
1	7.831	45.3	2.7	0.248	4.383	0.91
2	9.462	989.1	55.4	0.2722	95.617	0.756

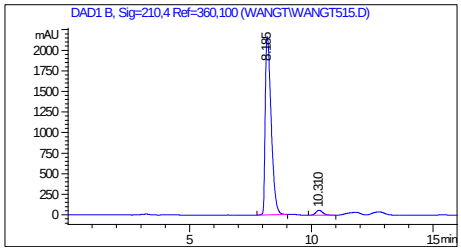
methyl 2-((2S,3R)-2,3-dihydro-3-(2-methoxyphenyl)-5-(pyridin-2-yl)furan-2-yl)acrylate (3ca)



3ca

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.62 (d, *J* = 4.4 Hz, 1H), 7.74-7.69 (m, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.38-7.35 (m, 1H), 7.26-7.20 (m, 2H), 6.94 (t, *J* = 7.2 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.33 (s, 1H), 5.94 (s, 1H), 5.85 (d, *J* = 3.2 Hz, 1H), 5.40 (d, *J* = 6.4 Hz, 1H), 4.62 (q, *J* = 3.2 Hz, 1H), 3.78 (s, 3H), 3.69 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 166.3, 156.7, 155.2, 149.7, 149.6, 140.7, 136.7, 131.7, 128.4, 128.0, 124.6, 123.2, 121.1, 120.2, 110.4, 103.2, 86.5, 55.4, 51.8, 48.9. HRMS: exact mass calculated for $[M+H]^+$ ($C_{20}H_{20}NO_4$) requires m/z 338.13868, found m/z 338.13834; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 210 nm, retention time: t_R (major) = 8.158 min, t_R (minor) = 10.31 min, 94% ee.

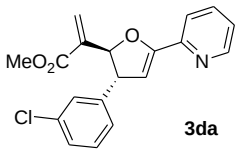




Racemic Chiral

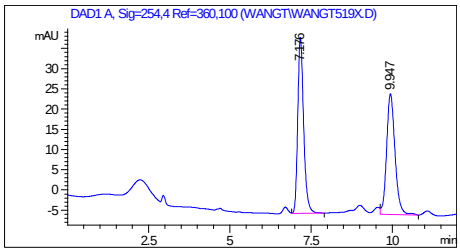
#	Time	Area	Height	Width	Area%	Symmetry	#	Time	Area	Height	Width	Area%	Symmetry
1	8.307	2733.4	178.3	0.2349	49.979	0.746	1	8.185	36697.8	2165.8	0.2617	96.993	0.469
2	10.199	2735.8	144.8	0.2924	50.021	0.754	2	10.31	1137.7	59.6	0.2947	3.007	0.799

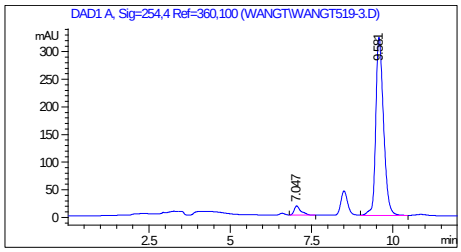
(4R,5S)-tert-butyl 5-(1-(methoxycarbonyl)vinyl)-4,5-dihydro-4-phenylfuran-2-carboxylate (3da)



3da

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.62-8.61 (m, 1H), 7.75-7.71 (m, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.48-7.45 (m, 1H), 7.36-7.34 (m, 1H), 7.27-7.23 (m, 2H), 7.19-7.15 (m, 1H), 6.37 (s, 1H), 5.95 (s, 1H), 5.85 (d, *J* = 3.2 Hz, 1H), 5.45 (d, *J* = 5.6 Hz, 1H), 4.71-4.68 (m, 1H), 3.70 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 165.9, 155.6, 149.8, 149.2, 141.0, 139.8, 136.7, 133.1, 129.4, 129.3, 128.2, 127.6, 124.9, 123.5, 120.3, 102.9, 86.6, 52.1. HRMS: exact mass calculated for $[M+H]^+$ ($C_{19}H_{17}ClNO_3$) requires m/z 342.08915, found m/z 342.08887; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (minor) = 7.047 min, t_R (major) = 9.58 min, 91% ee.

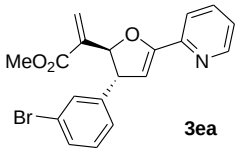




Racemic Chiral

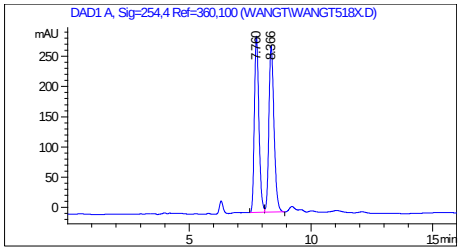
#	Time	Area	Height	Width	Area%	Symmetry	#	Time	Area	Height	Width	Area%	Symmetry
1	7.176	548.6	43.6	0.1949	50.470	0.755	1	7.047	241.6	16.7	0.2111	4.326	0.557
2	9.947	538.3	29.9	0.2743	49.530	0.794	2	9.58	5343.8	322.1	0.2536	95.674	0.692

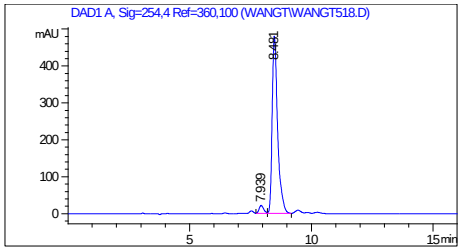
methyl 2-((2S,3R)-3-(3-bromophenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl)acrylate (3ea)



3ea

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.64 (d, *J* = 4.8 Hz, 1H), 7.77-7.73 (m, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.49 (s, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.29-7.25 (m, 2H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.34 (s, 1H), 5.90-5.87 (m, 2H), 5.35 (d, *J* = 4.8 Hz, 1H), 4.05-4.03 (m, 1H), 3.77 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 165.9, 156.0, 149.8, 149.0, 145.8, 139.3, 136.8, 130.8, 130.2, 126.5, 124.9, 123.6, 122.8, 120.3, 102.3, 86.9, 55.7, 52.0. HRMS: exact mass calculated for $[M+H]^+$ ($C_{19}H_{17}BrNO_3$) requires m/z 386.03863, found m/z 386.03827; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (minor) = 7.939 min, t_R (major) = 8.481 min, 92% ee.





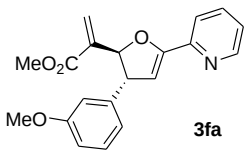
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	7.76	3776.6	292	0.1989	48.298	0.774
2	8.366	4042.9	274.9	0.2276	51.702	0.759

Chiral

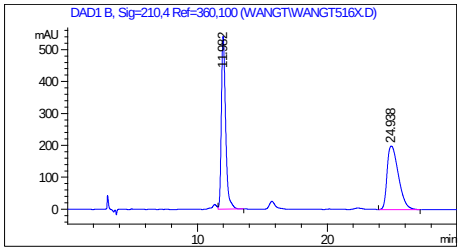
#	Time	Area	Height	Width	Area%	Symmetry
1	7.939	289.4	21.8	0.2026	3.726	0.773
2	8.481	7476.5	480.3	0.2376	96.274	0.621

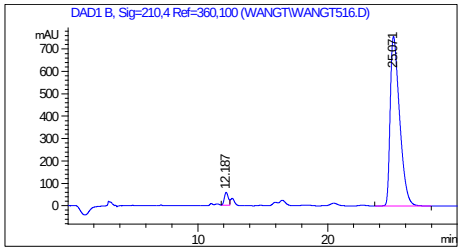
methyl 2-((2S,3R)-2,3-dihydro-3-(3-methoxyphenyl)-5-(pyridin-2-yl)furan-2-yl)acrylate (3fa)



3fa

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.63 (d, *J* = 4.8 Hz, 1H), 7.76-7.71 (m, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.27-7.23 (m, 2H), 6.94-6.89 (m, 2H), 6.81-6.79 (m, 1H), 6.33 (s, 1H), 5.89-5.88 (m, 2H), 5.38 (d, *J* = 5.2 Hz, 1H), 4.08-4.06 (m, 1H), 3.79 (s, 3H), 3.76 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 166.0, 160.0, 155.6, 149.8, 145.1, 139.6, 136.7, 129.7, 124.8, 123.4, 120.3, 120.2, 113.6, 112.4, 103.0, 87.1, 56.1, 55.4, 51.9. HRMS: exact mass calculated for $[M+H]^+$ ($C_{20}H_{20}NO_4$) requires m/z 338.13868, found m/z 338.13831; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 210 nm, retention time: t_R (minor) = 12.187 min, t_R (major) = 25.071 min, 94% ee.





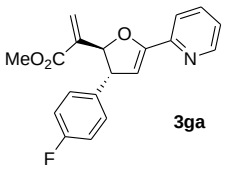
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	11.982	12370	541.7	0.3504	50.744	0.658
2	24.938	12007.4	199.2	0.9453	49.256	0.57

Chiral

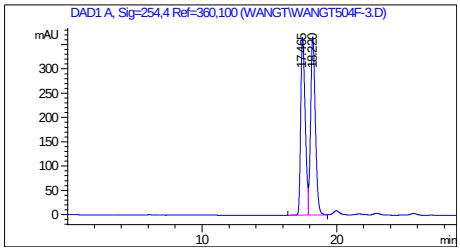
#	Time	Area	Height	Width	Area%	Symmetry
1	12.187	1215.8	57.7	0.3257	3.085	0.818
2	25.071	38193.6	758.9	0.7712	96.915	0.502

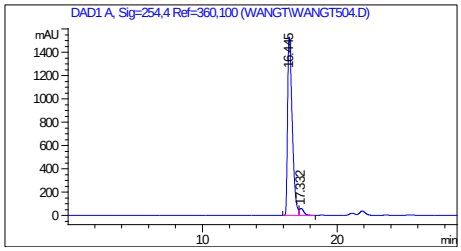
methyl 2-((2S,3R)-3-(4-fluorophenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl)acrylate (3ga)



3ga

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.63-8.61(m, 1H), 7.75-7.71 (m, 1H), 7.67-7.65 (m, 1H), 7.32-7.27 (m, 2H), 7.26-7.23 (m, 1H), 7.03-6.97 (m, 2H), 6.32 (s, 1H), 5.89-5.87 (m, 2H), 5.32-5.30 (m, 1H), 4.06-4.04 (m, 1H), 3.75 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 166.0, 163.3, 160.8, 155.6, 149.8, 149.1, 139.4, 139.1, 136.8, 129.3, 129.2, 124.6, 123.5, 120.2, 115.5, 115.3, 102.8, 87.1, 55.3, 51.9. ^{19}F NMR: δ (ppm) -116.1. HRMS: exact mass calculated for $[M+H]^+$ ($C_{19}H_{17}FNO_3$) requires m/z 326.11870, found m/z 326.11786; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.5 mL/min, λ = 254 nm, retention time: t_R (major) = 16.445 min, t_R (minor) = 17.332 min, 93% ee.





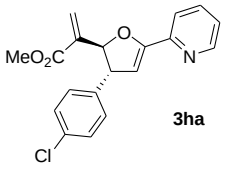
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	17.465	8516.5	366.1	0.3594	48.651	0.665
2	18.22	8989	366.6	0.3781	51.349	0.757

Chiral

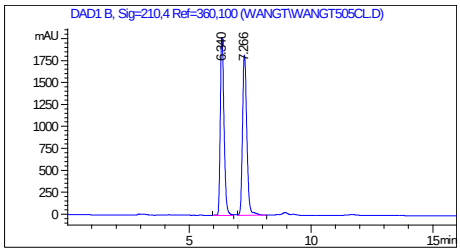
#	Time	Area	Height	Width	Area%	Symmetry
1	16.445	36769.6	1533	0.3678	96.390	0.504
2	17.332	1376.9	59.6	0.3434	3.610	0.612

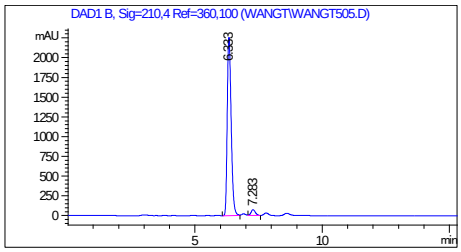
methyl 2-((2S,3R)-3-(4-chlorophenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl)acrylate (3ha)



3ha

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.63-8.61(m, 1H), 7.76-7.71 (m, 1H), 7.67-7.65 (m, 1H), 7.30-7.23 (m, 5H), 6.32 (s, 1H), 5.88-5.86 (m, 2H), 5.31-5.30 (m, 1H), 4.05-4.03 (m, 1H), 3.75 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 165.9, 155.8, 149.8, 149.0, 141.9, 139.3, 136.8, 132.8, 129.1, 128.8, 124.7, 123.5, 120.3, 102.5, 86.9, 55.4, 52.0. HRMS: exact mass calculated for $[M+H]^+$ ($C_{19}H_{17}ClNO_3$) requires m/z 342.08915, found m/z 342.08859; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 210 nm, retention time: t_R (major) = 6.333 min, t_R (minor) = 7.283 min, 96% ee.





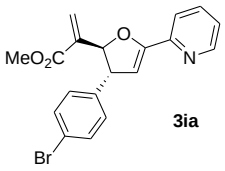
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	6.34	21637.3	2029.2	0.1664	48.921	0.705
2	7.266	22592	1826.3	0.1923	51.079	0.753

Chiral

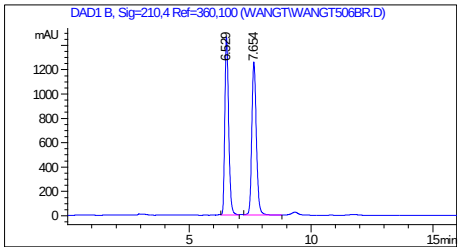
#	Time	Area	Height	Width	Area%	Symmetry
1	6.333	24684.6	2259	0.1715	96.554	0.695
2	7.283	881.1	74.4	0.1822	3.446	0.896

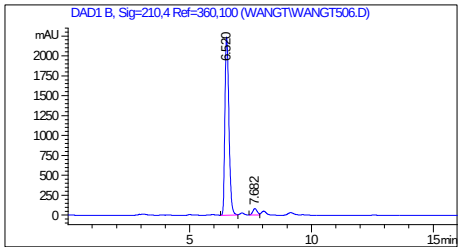
methyl 2-((2S,3R)-3-(4-bromophenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl)acrylate (3ia)



3ia

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.64-8.62(m, 1H), 7.76-7.72 (m, 1H), 7.67-7.65 (m, 1H), 7.46-7.42 (m, 2H), 7.27-7.20 (m, 3H), 6.33 (s, 1H), 5.89 (t, *J* = 1.2 Hz, 1H), 5.86 (d, J = 3.2 Hz, 1H), 5.32-5.30 (m, 1H), 4.04-4.02 (m, 1H), 3.76 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 165.9, 155.9, 149.8, 149.0, 142.4, 139.3, 136.8, 131.7, 129.5, 124.7, 123.6, 121.0, 120.3, 102.4, 86.9, 55.5, 52.0. HRMS: exact mass calculated for $[M+H]^+$ ($C_{19}H_{17}BrNO_3$) requires m/z 386.03863, found m/z 386.03787; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 210 nm, retention time: t_R (major) = 6.52 min, t_R (minor) = 7.682 min, 92% ee.





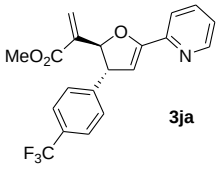
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	6.529	16090.3	1464.9	0.1701	49.304	0.717
2	7.654	16544.7	1259.4	0.2013	50.696	0.792

Chiral

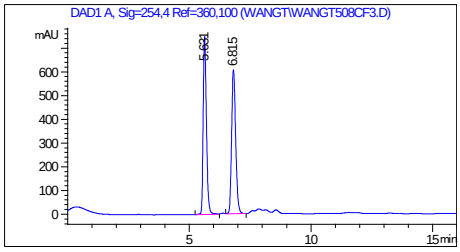
#	Time	Area	Height	Width	Area%	Symmetry
1	6.52	25718.4	2239.1	0.18	96.202	0.69
2	7.682	1015.3	80.5	0.1971	3.798	0.862

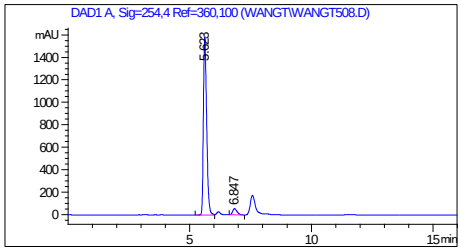
methyl 2-((2S,3R)-3-(4-(trifluoromethyl)phenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl) acrylate (3ja)



3ja

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.65-8.64 (m, 1H), 7.78-7.74 (m, 1H), 7.70-7.68 (m, 1H), 7.60-7.58 (m, 2H), 7.49-7.47 (m, 2H), 7.29-7.26 (m, 1H), 6.36 (s, 1H), 5.93-5.90 (m, 2H), 5.38-5.36 (m, 1H), 4.14-4.12 (m, 1H), 3.77 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 163.9, 154.1, 147.9, 147.0, 145.5, 137.2, 134.8, 126.2, 123.7, 123.6, 122.9, 121.7, 118.3, 100.2, 84.8, 53.9, 50.0, 23.5. ^{19}F NMR: δ (ppm) -62.4. HRMS: exact mass calculated for $[M+H]^+$ ($C_{20}H_{17}F_3NO_3$) requires m/z 376.11550, found m/z 376.11533; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (major) = 5.623 min, t_R (minor) = 6.847 min, 91% ee.





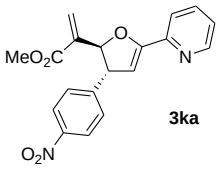
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	5.631	6957	750.5	0.1441	49.751	0.725
2	6.815	7026.6	607.7	0.1789	50.249	0.779

Chiral

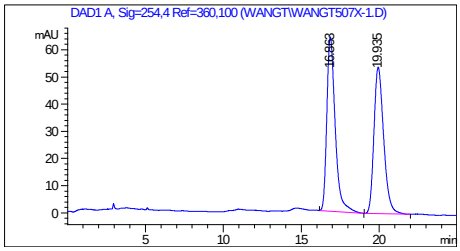
#	Time	Area	Height	Width	Area%	Symmetry
1	5.623	14766.4	1589.1	0.1424	95.540	0.682
2	6.847	689.3	55	0.1942	4.460	0.731

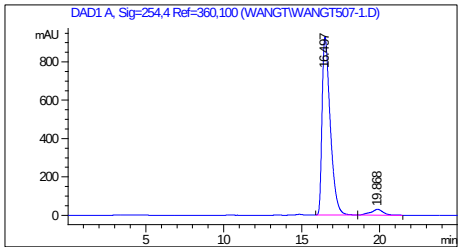
methyl 2-((2S,3R)-2,3-dihydro-3-(4-nitrophenyl)-5-(pyridin-2-yl)furan-2-yl)acrylate (3ka)



3ka

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.64-8.63 (m, 1H), 8.21-8.17 (m, 2H), 7.79-7.74 (m, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.53-7.51 (m, 2H), 7.30-7.26 (m, 1H), 6.35 (s, 1H), 5.93 (s, 1H), 5.89 (d, *J* = 3.2 Hz, 1H), 5.35-5.34 (m, 1H), 4.17-4.15 (m, 1H), 3.77 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 165.9, 156.5, 150.9, 149.9, 148.7, 147.2, 138.9, 136.9, 128.7, 125.0, 124.0, 123.8, 120.4, 101.7, 86.5, 55.8, 52.1. HRMS: exact mass calculated for $[M+H]^+$ ($C_{19}H_{17}N_2O_5$) requires m/z 353.11320, found m/z 353.11298; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (major) = 16.497 min, t_R (minor) = 19.868 min, 91% ee.





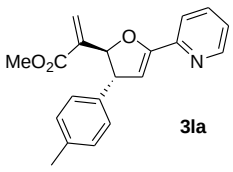
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	16.863	2401.4	64.1	0.5649	50.754	0.65
2	19.935	2330.1	53.9	0.6524	49.246	0.725

Chiral

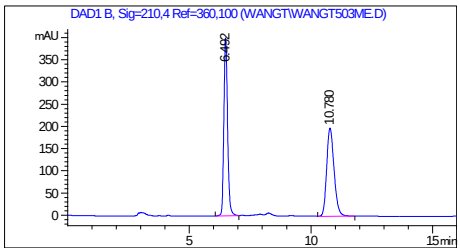
#	Time	Area	Height	Width	Area%	Symmetry
1	16.497	33930.9	929.8	0.5537	95.487	0.515
2	19.868	1603.8	29.8	0.782	4.513	1.217

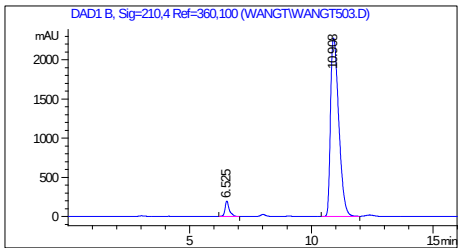
methyl 2-((2S,3R)-2,3-dihydro-5-(pyridin-2-yl)-3-p-tolylfuran-2-yl)acrylate (3la)



3la

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.64-8.62 (m, 1H), 7.75-7.71 (m, 1H), 7.67-7.65 (m, 1H), 7.26-7.22 (m, 3H), 7.15-7.13 (m, 2H), 6.33 (s, 1H), 5.89-5.88 (m, 2H), 5.35-5.33 (m, 1H), 4.07-4.05 (m, 1H), 3.76 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 166.0, 155.3, 149.7, 149.3, 140.4, 139.6, 136.7, 129.4, 127.6, 124.6, 123.3, 120.2, 103.2, 87.2, 55.7, 51.9, 21.2. HRMS: exact mass calculated for $[M+H]^+$ ($C_{20}H_{20}NO_3$) requires m/z 322.14377, found m/z 322.14349; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 210 nm, retention time: t_R (minor) = 6.525 min, t_R (major) = 10.908 min, 92% ee.





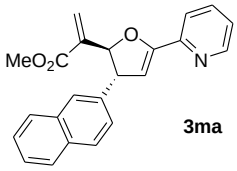
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	6.492	4255.2	400.6	0.1639	50.419	0.811
2	10.78	4184.5	198.6	0.3259	49.581	0.768

Chiral

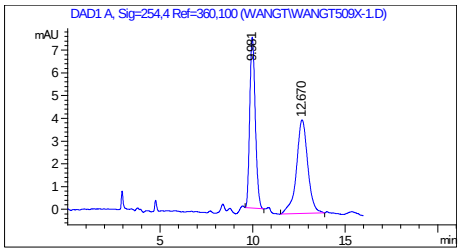
#	Time	Area	Height	Width	Area%	Symmetry
1	6.525	2404.2	197	0.1824	4.288	0.678
2	10.908	53667.3	2280.1	0.3646	95.712	0.543

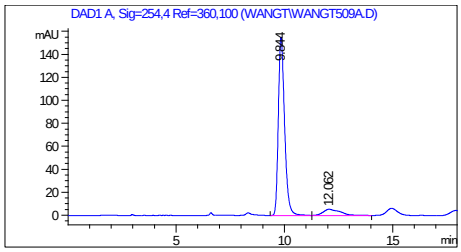
methyl 2-((2S,3R)-2,3-dihydro-3-(naphthalen-2-yl)-5-(pyridin-2-yl)furan-2-yl)acrylate (3ma)



3ma

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.63 (d, *J* = 4.4 Hz, 1H), 8.06-8.03 (m, 1H), 7.89-7.86 (m, 1H), 7.78-7.72 (m, 2H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 6.4 Hz, 1H), 7.51-7.44 (m, 3H), 7.25-7.23 (m, 1H), 6.42 (s, 1H), 6.00-5.99 (m, 2H), 5.58 (d, *J* = 6.0 Hz, 1H), 5.00-4.98 (m, 1H), 3.50 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 166.0, 155.2, 149.7, 149.3, 140.1, 139.3, 136.6, 133.9, 131.3, 128.9, 127.6, 126.0, 125.8, 125.5, 125.3, 123.3, 123.2, 120.2, 103.9, 86.8, 51.8, 51.5. HRMS: exact mass calculated for $[M+H]^+$ ($C_{23}H_{20}NO_3$) requires m/z 358.14377, found m/z 358.14334; HPLC conditions: Daicel Chiralpak OD-H column, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (major) = 9.844 min, t_R (minor) = 12.062 min, 83% ee.





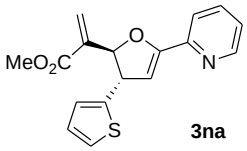
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	9.981	156.8	7.5	0.3231	47.251	0.792
2	12.67	175.1	4.1	0.6254	52.749	0.978

Chiral

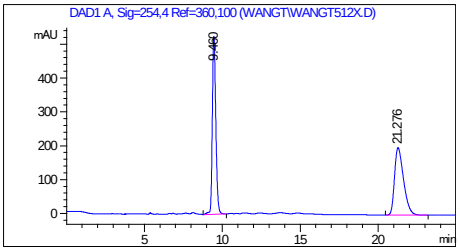
#	Time	Area	Height	Width	Area%	Symmetry
1	9.844	3124.5	155.2	0.3089	91.356	0.699
2	12.062	295.6	5.4	0.7263	8.644	0.502

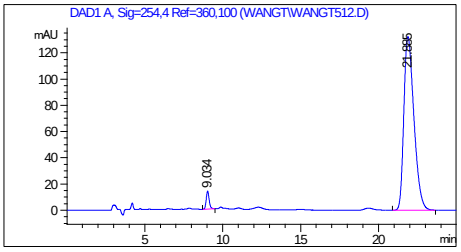
methyl 2-((2S,3S)-2,3-dihydro-5-(pyridin-2-yl)-3-(thiophen-2-yl)furan-2-yl)acrylate (3na)



3na

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.57-8.56 (m, 1H), 7.68-7.58 (m, 2H), 7.19-7.12 (m, 2H), 6.93-6.88 (m, 2H), 6.27 (s, 1H), 5.90-5.80 (m, 2H), 5.34-5.33 (m, 1H), 4.33-4.31 (m, 1H), 3.74 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 166.0, 155.9, 149.8, 149.1, 147.1, 139.0, 136.7, 127.0, 125.1, 124.5, 124.4, 123.6, 120.3, 102.0, 87.2, 52.0, 50.7. HRMS: exact mass calculated for $[M+H]^+$ ($C_{17}H_{16}NO_3S$) requires m/z 314.08454, found m/z 314.08408; HPLC conditions: Daicel Chiralpak OD-H column, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (minor) = 9.034 min, t_R (major) = 21.885 min, 94% ee.





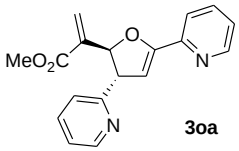
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	9.46	8170.8	525.2	0.2395	50.562	0.77
2	21.276	7989.2	198.9	0.6187	49.438	0.605

Chiral

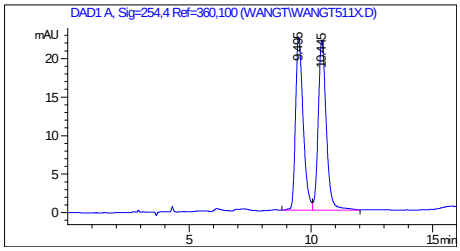
#	Time	Area	Height	Width	Area%	Symmetry
1	9.034	178.8	13.7	0.2007	2.923	0.833
2	21.885	5938.8	132.4	0.6954	97.077	0.63

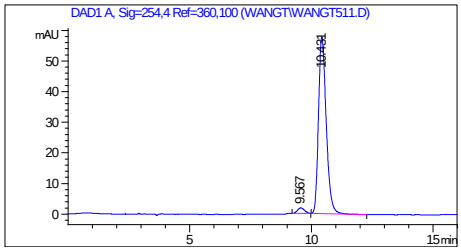
methyl 2-((2S,3R)-2,3-dihydro-3,5-di(pyridin-2-yl)furan-2-yl)acrylate (3oa)



3oa

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.58-8.57 (m, 2H), 7.73-7.62 (m, 3H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.23-7.20 (m, 1H), 7.17-7.13 (m, 1H), 6.35 (s, 1H), 5.97-5.91 (m, 2H), 5.76 (d, *J* = 5.6 Hz, 1H), 4.29-4.27 (m, 1H), 3.68 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 165.9, 162.3, 155.6, 149.65, 149.59, 149.2, 139.7, 136.8, 136.7, 124.9, 123.4, 122.3, 122.1, 120.4, 102.5, 85.2, 58.4, 51.9. HRMS: exact mass calculated for $[M+H]^+$ ($C_{18}H_{17}N_2O_3$) requires m/z 309.12337, found m/z 309.12314; HPLC conditions: Daicel Chiralpak OD-H column, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (minor) = 9.567 min, t_R (major) = 10.431 min, 94% ee.





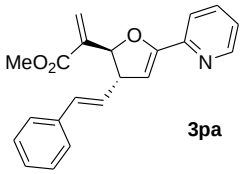
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	9.495	489.1	22.5	0.3336	49.065	0.668
2	10.445	507.7	22.1	0.3505	50.935	0.75

Chiral

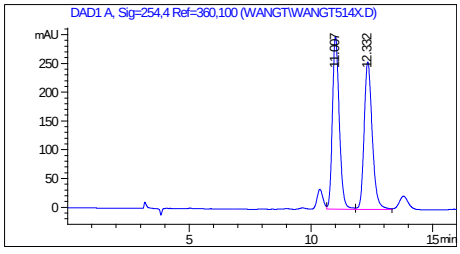
#	Time	Area	Height	Width	Area%	Symmetry
1	9.567	37.2	1.8	0.3171	2.837	0.87
2	10.431	1273.2	57.8	0.3392	97.163	0.719

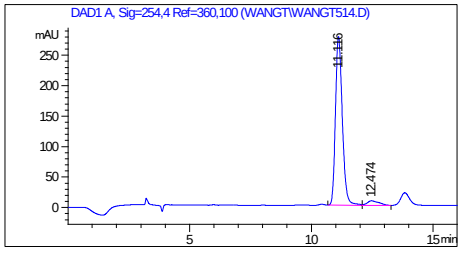
methyl 2-((2S,3S)-2,3-dihydro-5-(pyridin-2-yl)-3-styrylfuran-2-yl)acrylate (3pa)



3pa

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.64-8.62 (m, 1H), 7.75-7.71 (m, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.40-7.38 (m, 2H), 7.30 (m, 2H), 7.26-7.19 (m, 2H), 6.51 (d, *J* = 16.0 Hz, 1H), 6.42-6.37 (m, 1H), 6.33 (s, 1H), 5.90-5.89 (m, 1H), 5.82 (d, *J* = 2.8 Hz, 1H), 5.33 (d, *J* = 5.6 Hz, 1H), 3.80 (s, 3H), 3.75-3.71 (m, 1H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 166.1, 155.3, 149.8, 139.5, 137.3, 136.7, 131.0, 130.8, 128.6, 127.5, 126.5, 124.7, 123.4, 120.2, 101.6, 84.9, 53.7, 52.0. HRMS: exact mass calculated for $[M+H]^+$ ($C_{21}H_{20}NO_3$) requires m/z 334.14377, found m/z 334.14337; HPLC conditions: Daicel Chiralpak OD-H column, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (major) = 11.116 min, t_R (minor) = 12.474 min, 92% ee.





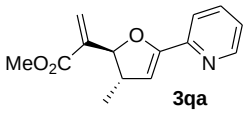
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	11.007	5875.3	299.9	0.3025	49.805	0.761
2	12.332	5921.2	256.3	0.3555	50.195	0.761

Chiral

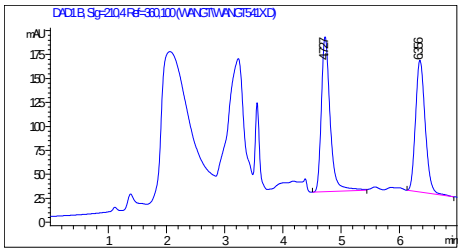
#	Time	Area	Height	Width	Area%	Symmetry
1	11.116	5405.1	276.9	0.2998	95.710	0.755
2	12.474	242.3	7.4	0.4623	4.290	0.579

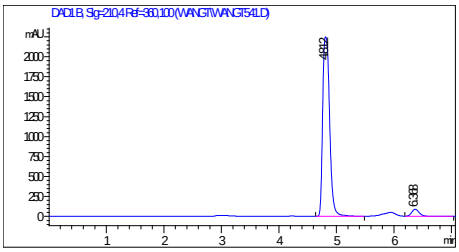
methyl 2-((2S,3S)-2,3-dihydro-3-methyl-5-(pyridin-2-yl)furan-2-yl)acrylate (3qa)



3qa

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.59-8.58 (m, 1H), 7.72-7.68 (m, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.22-7.19 (m, 1H), 6.26 (s, 1H), 5.84 (s, 1H), 5.76 (d, *J* = 3.2 Hz, 1H), 5.09 (d, *J* = 4.8 Hz, 1H), 3.80 (s, 3H), 2.99-2.92 (m, 1H), 1.33 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 166.4, 154.0, 149.7, 149.6, 140.0, 136.7, 123.9, 123.1, 120.0, 104.9, 86.0, 52.0, 45.6, 21.2. HRMS: exact mass calculated for $[M+H]^+$ ($C_{14}H_{16}NO_3$) requires m/z 246.11247, found m/z 246.11223; HPLC conditions: Daicel Chiralpak OD-H column, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 210 nm, retention time: t_R (major) = 4.812 min, t_R (minor) = 6.368 min, 92% ee.





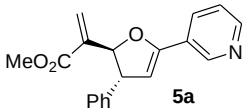
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	4.727	1703.6	161.9	0.1607	51.817	0.669
2	6.356	1584.2	137.7	0.1782	48.183	0.793

Chiral

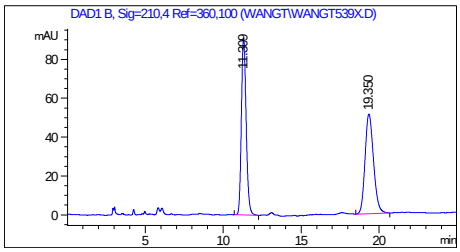
#	Time	Area	Height	Width	Area%	Symmetry
1	4.812	18741.6	2251.8	0.1331	95.817	0.689
2	6.368	818.1	87.8	0.1427	4.183	0.813

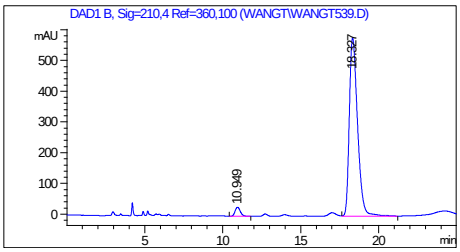
methyl 2-((2S,3R)-2,3-dihydro-3-phenyl-5-(pyridin-3-yl)furan-2-yl)acrylate (5a)



5a

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8.91 (s, 1H), 8.56-8.54 (m, 1H), 7.95-7.93 (m, 1H), 7.36-7.28 (m, 6H), 6.33 (s, 1H), 5.85 (s, 1H), 5.55-5.54 (m, 1H), 5.34-5.33 (m, 1H), 4.06-4.05 (m, 1H), 3.75 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 166.0, 153.1, 149.6, 146.9, 143.4, 139.6, 132.7, 128.8, 127.6, 127.3, 126.5, 124.5, 123.5, 100.9, 86.8, 56.2, 52.0. HRMS: exact mass calculated for $[M+H]^+$ ($C_{19}H_{18}NO_3$) requires m/z 308.12812, found m/z 308.12759; HPLC conditions: Daicel Chiralpak AS-H column, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 210 nm, retention time: t_R (minor) = 10.949 min, t_R (major) = 18.327 min, 94% ee.





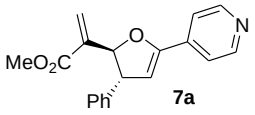
Racemic

#	Time	Area	Height	Width	Area%	Symmetry
1	11.309	1940.6	91.3	0.3301	49.967	0.813
2	19.35	1943.2	51.3	0.5776	50.033	0.803

Chiral

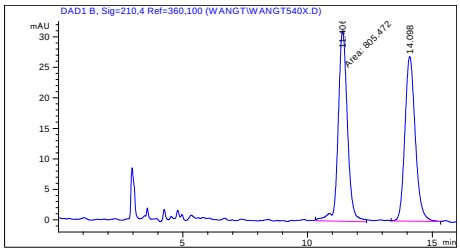
#	Time	Area	Height	Width	Area%	Symmetry
1	10.949	695.1	29.6	0.3681	3.162	0.83
2	18.327	21289.5	580.3	0.56	96.838	0.622

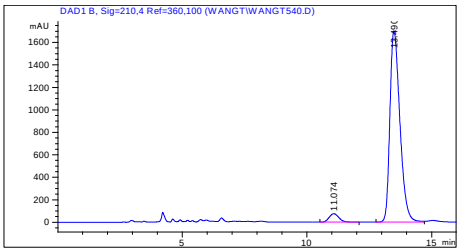
methyl 2-((2S,3R)-2,3-dihydro-3-phenyl-5-(pyridin-4-yl)furan-2-yl)acrylate (7a)



7a

^{1}H NMR (400 Hz, $CDCl_3$): δ (ppm) 8. 63 (d, *J* = 5.2 Hz, 2H), 7.52-7.51 (m, 2H), 7.36-7.24 (m, 5H), 6.33 (s, 1H), 5.84 (s, 1H), 5.69 (d, *J* = 3.2 Hz, 1H), 5.34 (d, *J* = 3.2 Hz, 1H), 4.07-4.05 (m, 1H), 3.75 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$): δ (ppm) 165.8, 153.6, 150.2, 143.0, 139.4, 137.4, 128.8, 127.6, 127.3, 124.6, 119.5, 103.5, 86.9, 56.1, 51.9. HRMS: exact mass calculated for $[M+H]^+$ ($C_{19}H_{18}NO_3$) requires m/z 308.12812, found m/z 308.12778; HPLC conditions: Daicel Chiralpak OD-H column, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 210 nm, retention time: t_R (minor) = 11.074 min, t_R (major) = 13.49 min, 92% ee.





Racemic

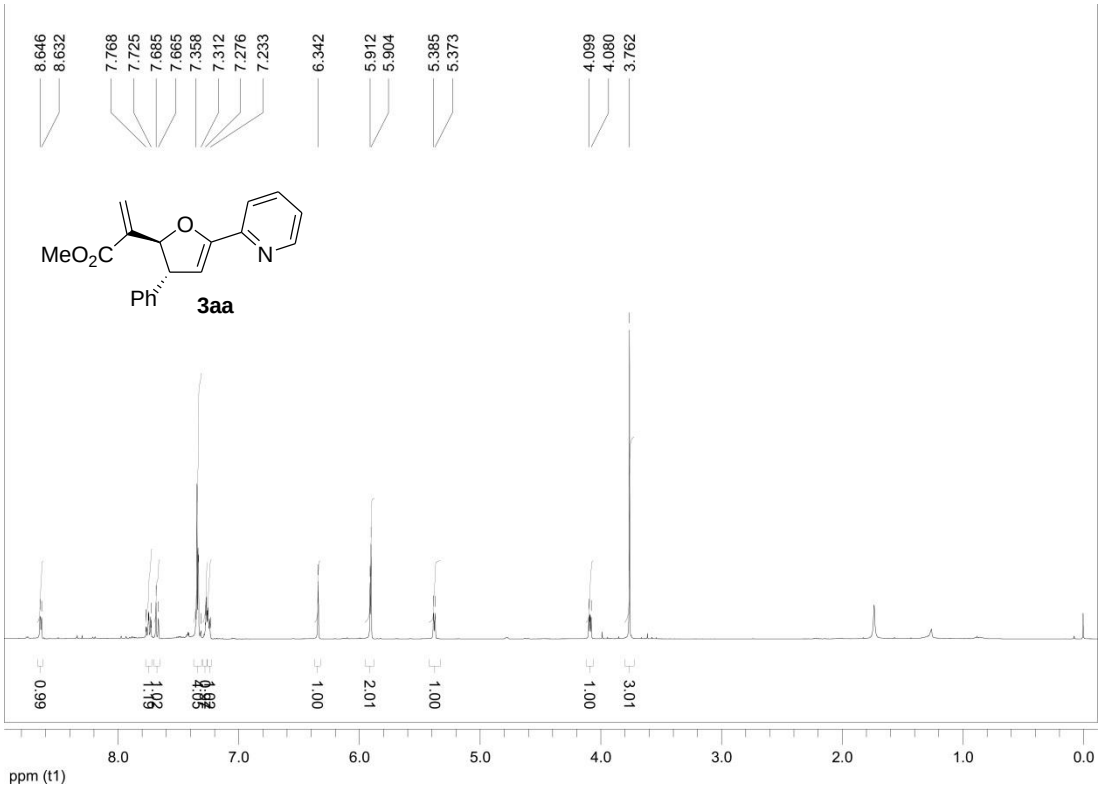
#	Time	Area	Height	Width	Area%	Symmetry
1	11.406	805.5	31.2	0.4298	50.797	0.89
2	14.098	780.2	27	0.445	49.203	0.825

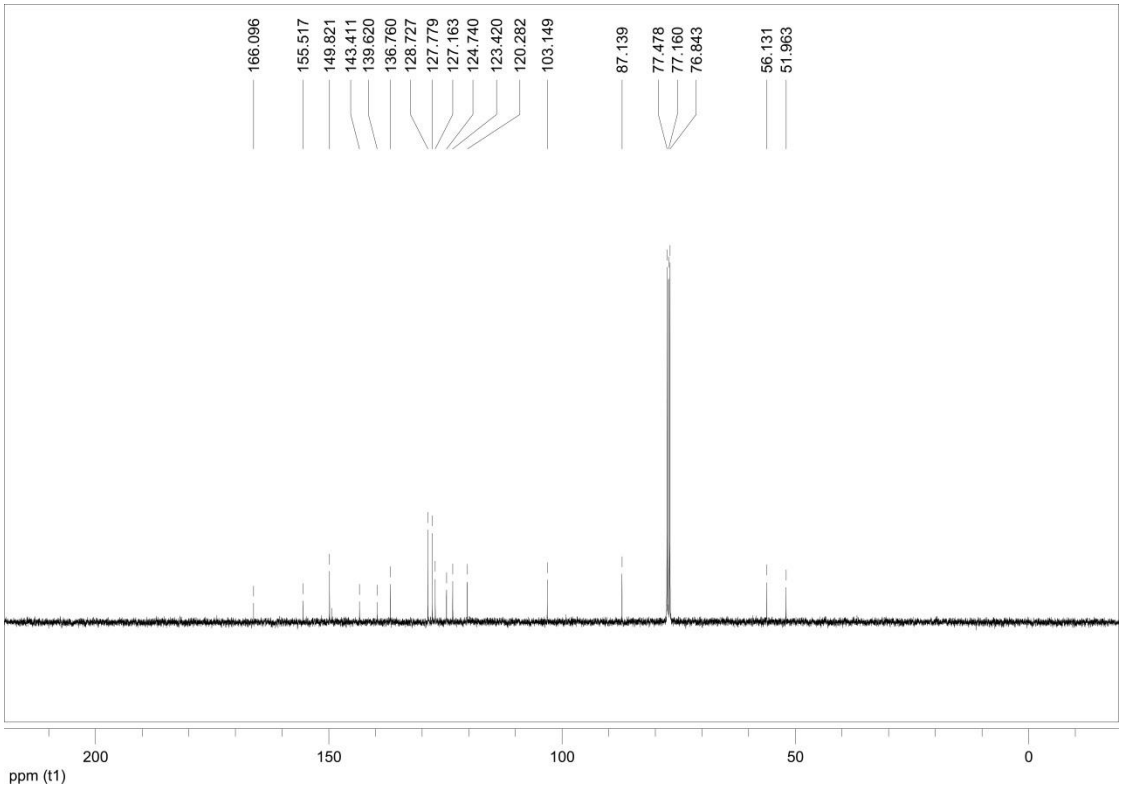
Chiral

#	Time	Area	Height	Width	Area%	Symmetry
1	11.074	2026.3	74.8	0.434	4.091	0.86
2	13.49	47507.8	1702.7	0.4295	95.909	0.644

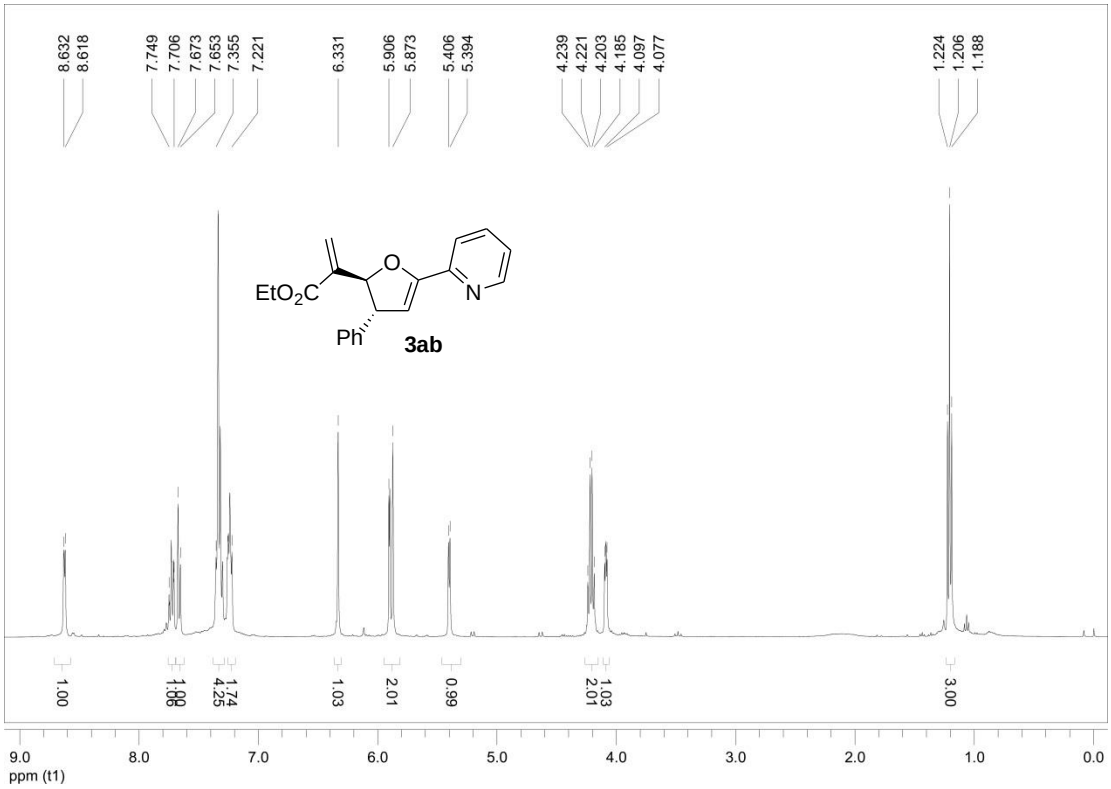
Copies of NMR spectra

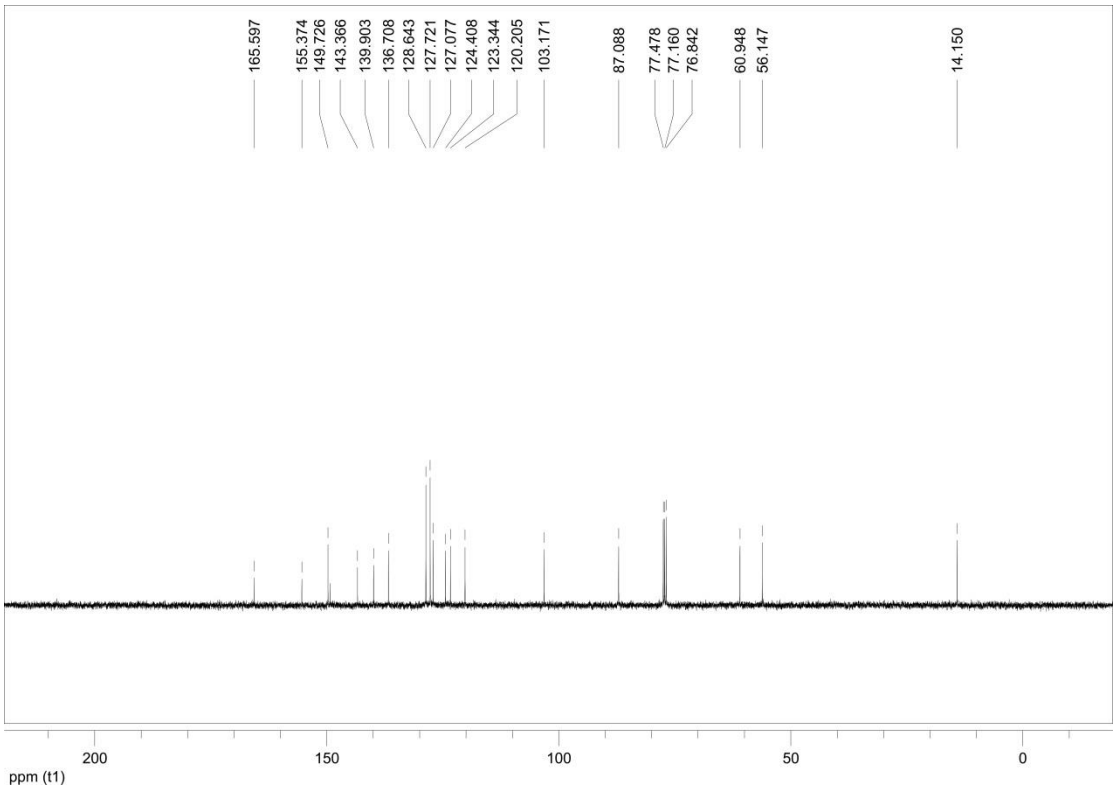
methyl 2-((2S,3R)-2,3-dihydro-3-phenyl-5-(pyridin-2-yl)furan-2-yl)acrylate (3aa)



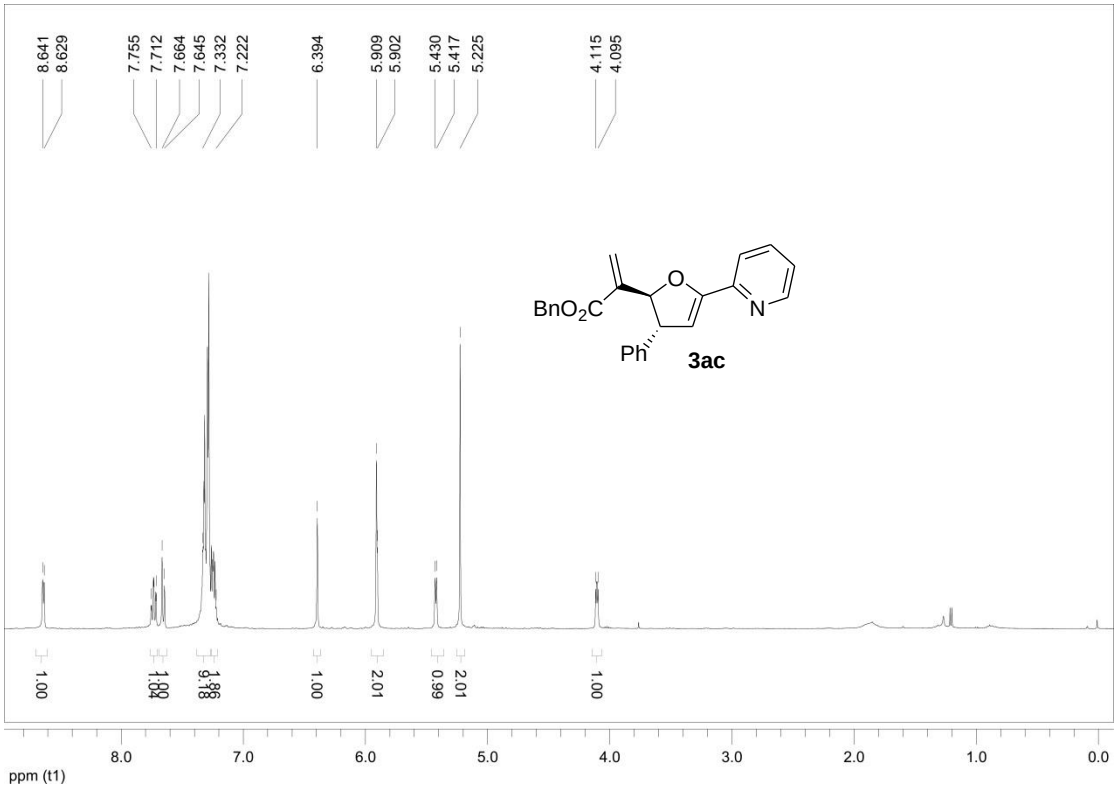


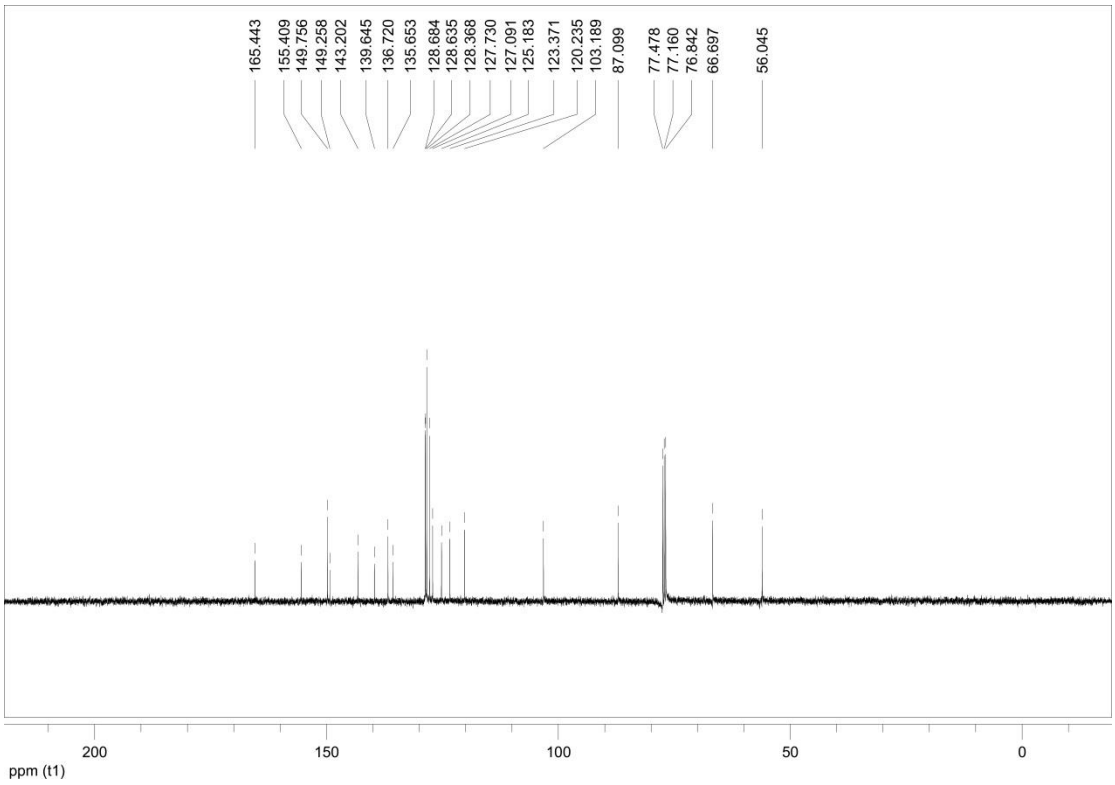
ethyl 2-((2S,3R)-2,3-dihydro-3-phenyl-5-(pyridin-2-yl)furan-2-yl)acrylate (3ab)



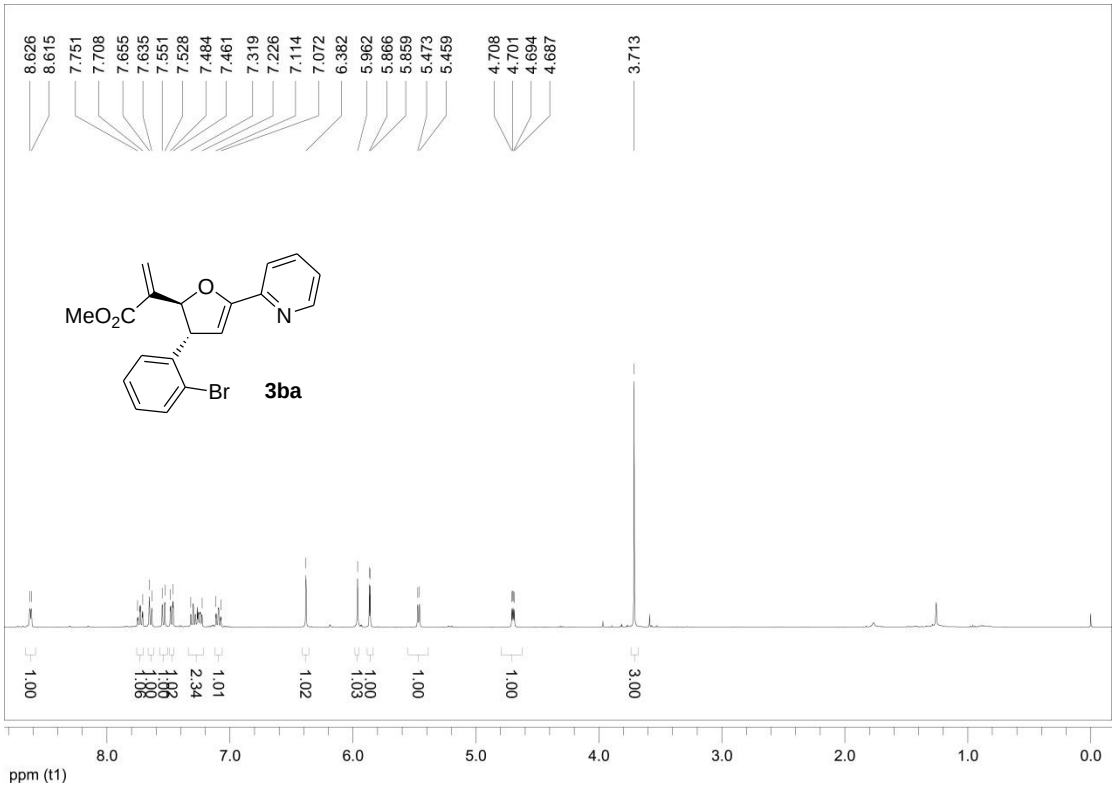


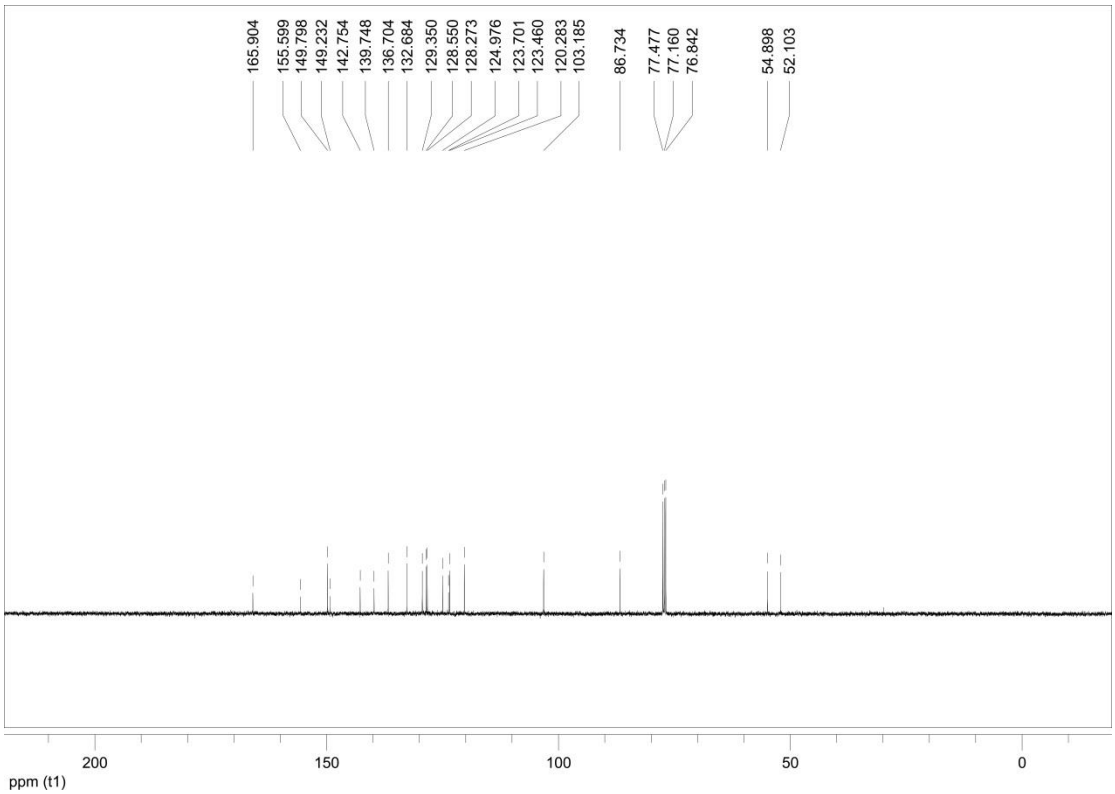
benzyl 2-((2S,3R)-2,3-dihydro-3-phenyl-5-(pyridin-2-yl)furan-2-yl)acrylate (3ac)



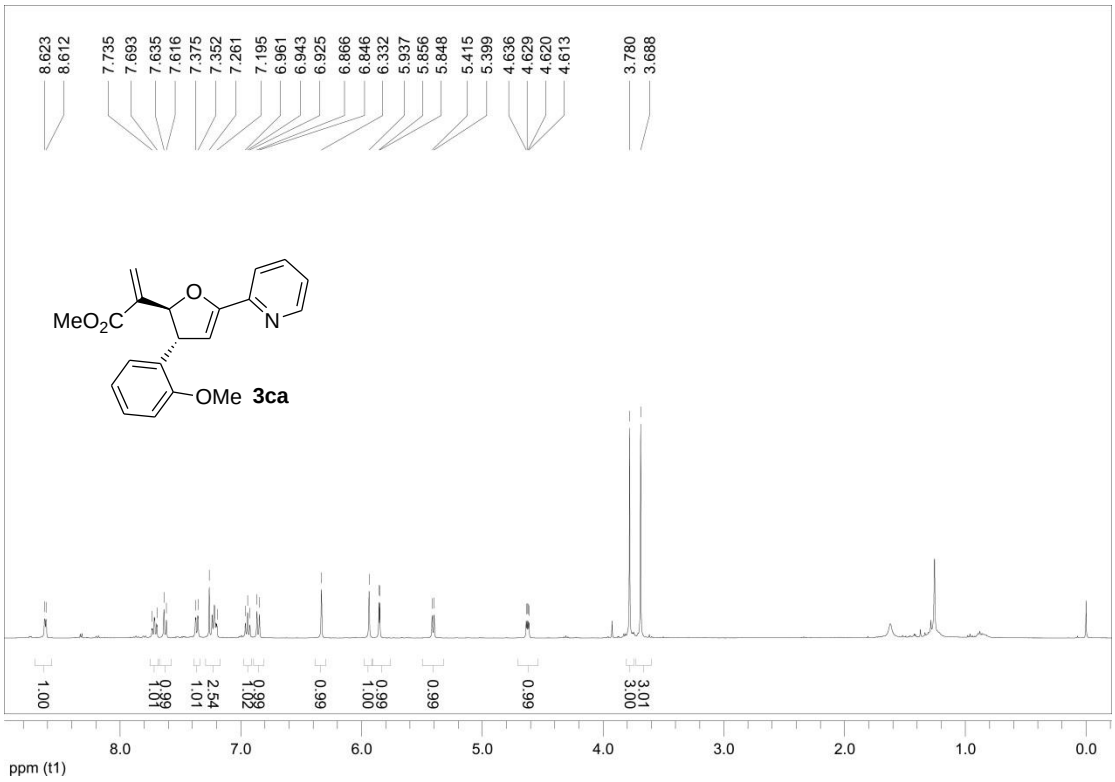


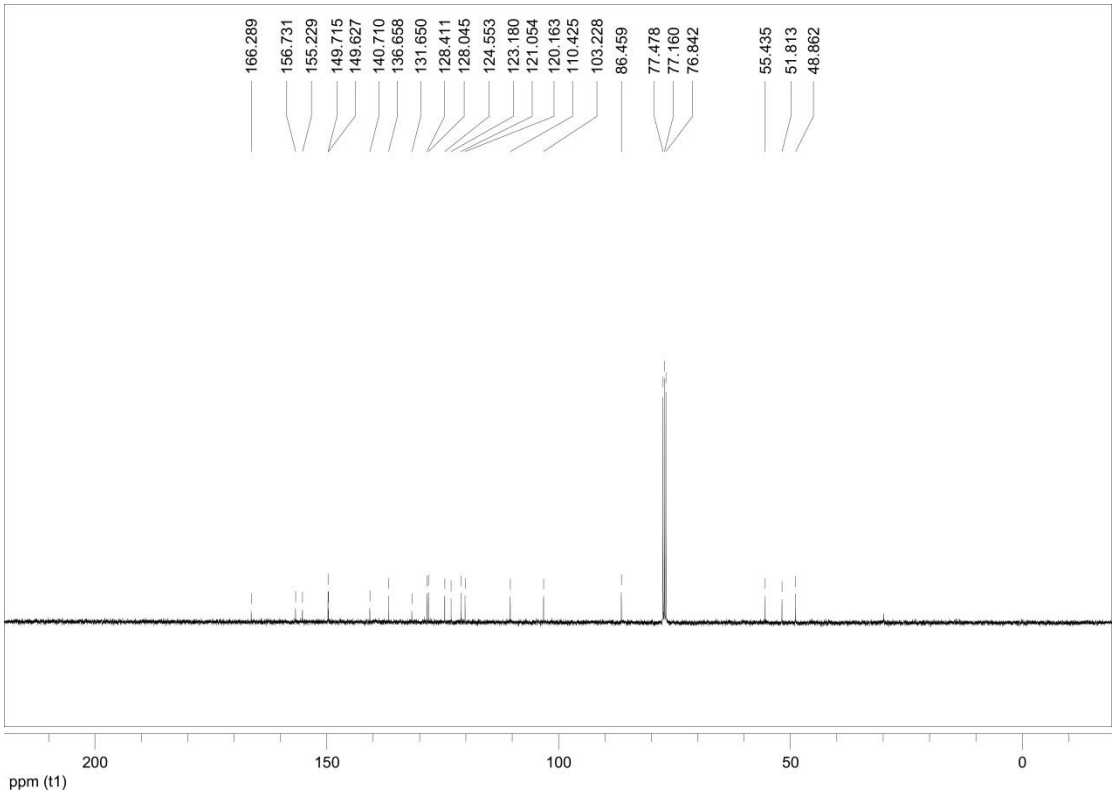
methyl 2-((2S,3R)-3-(2-bromophenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl)acrylate (3ba)



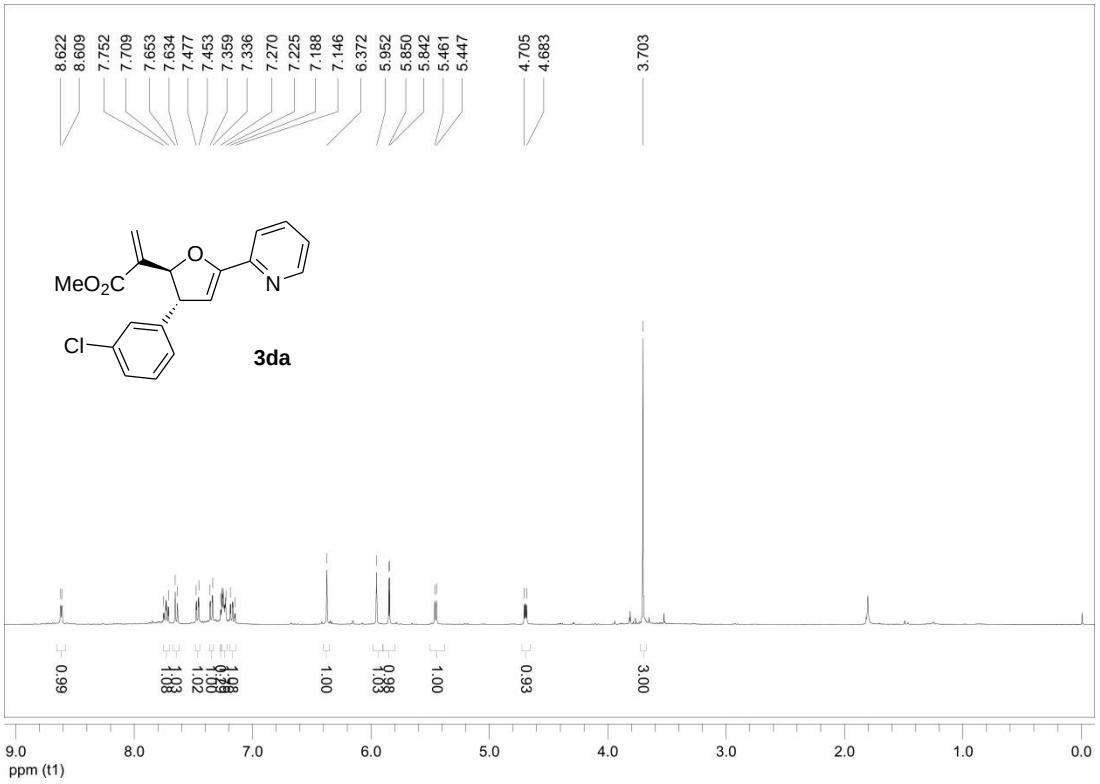


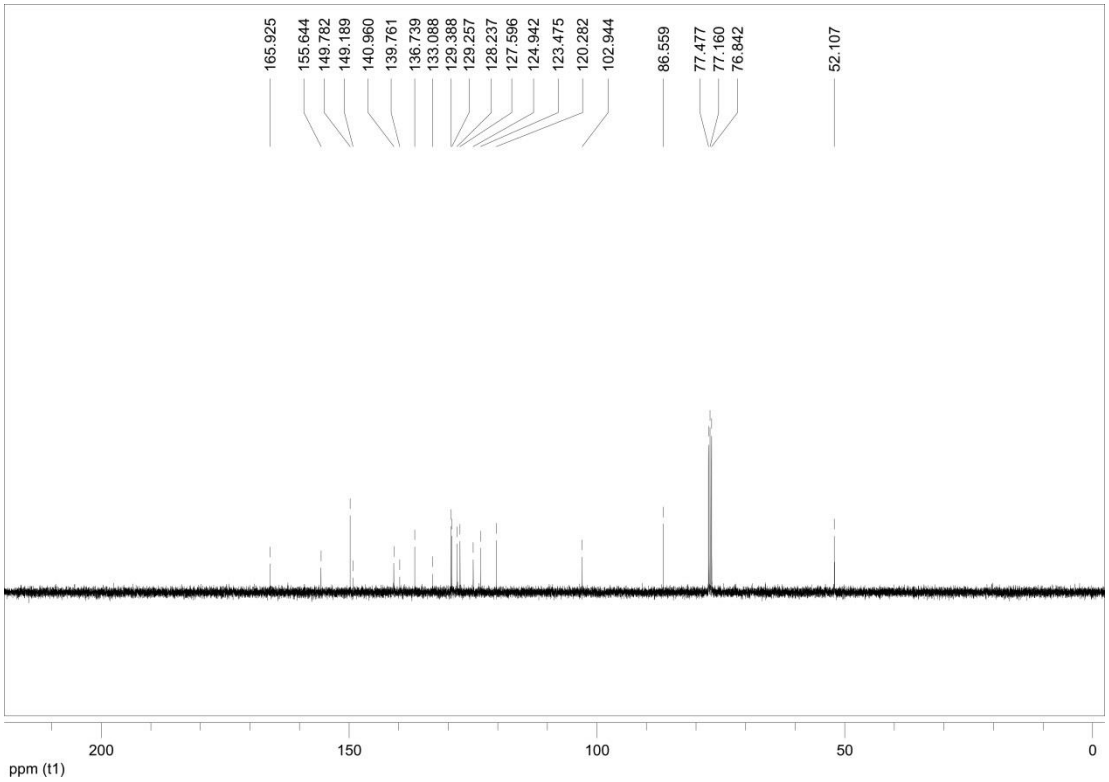
methyl 2-((2S,3R)-2,3-dihydro-3-(2-methoxyphenyl)-5-(pyridin-2-yl)furan-2-yl)acrylate (3ca)



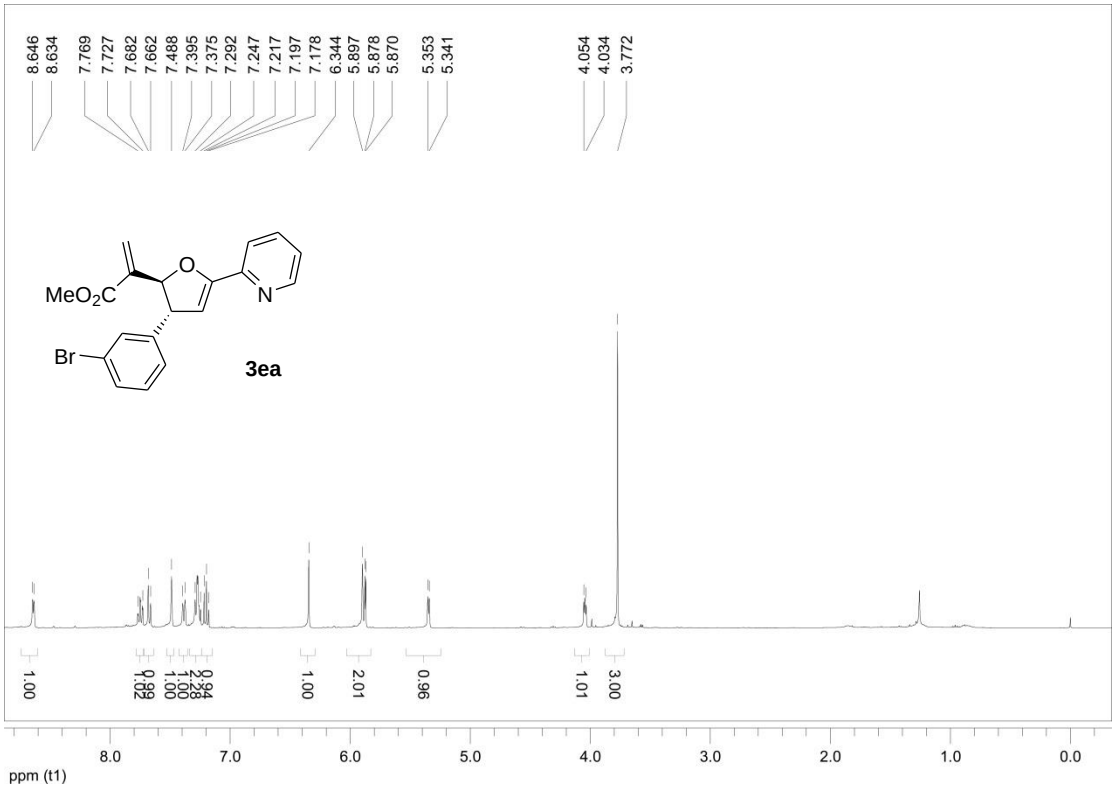


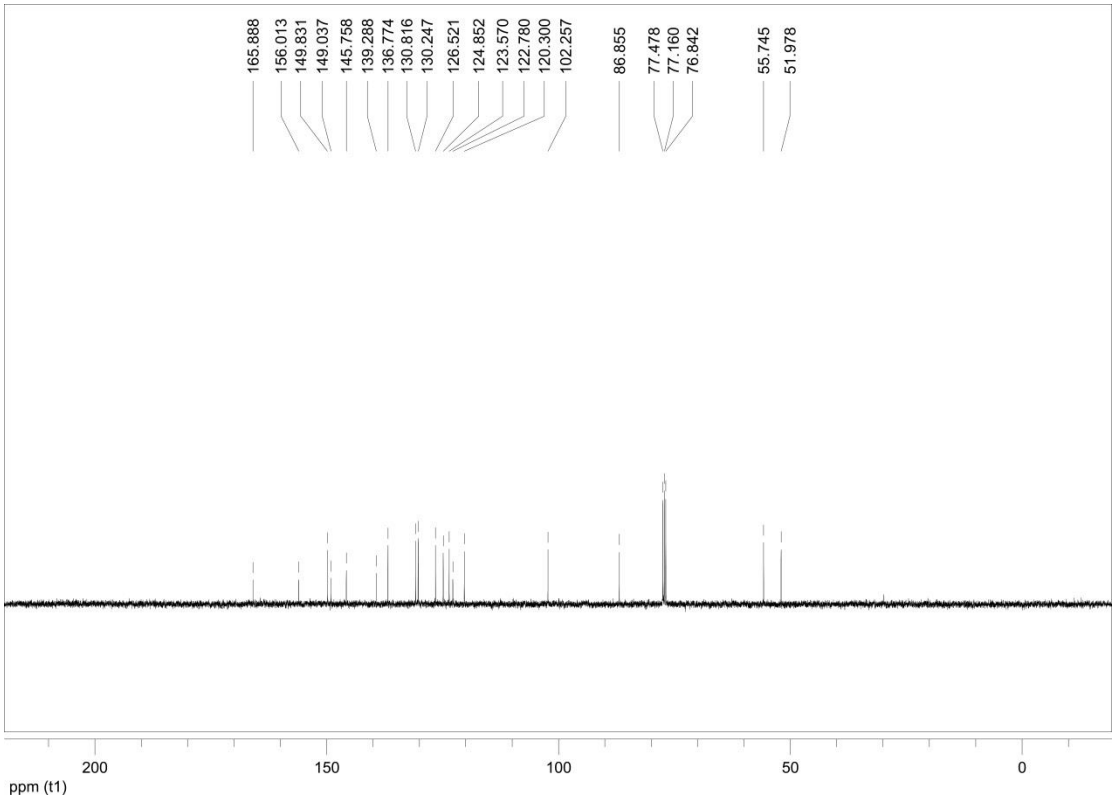
(4R,5S)-tert-butyl 5-(1-(methoxycarbonyl)vinyl)-4,5-dihydro-4-phenylfuran-2-carboxylate (3da)



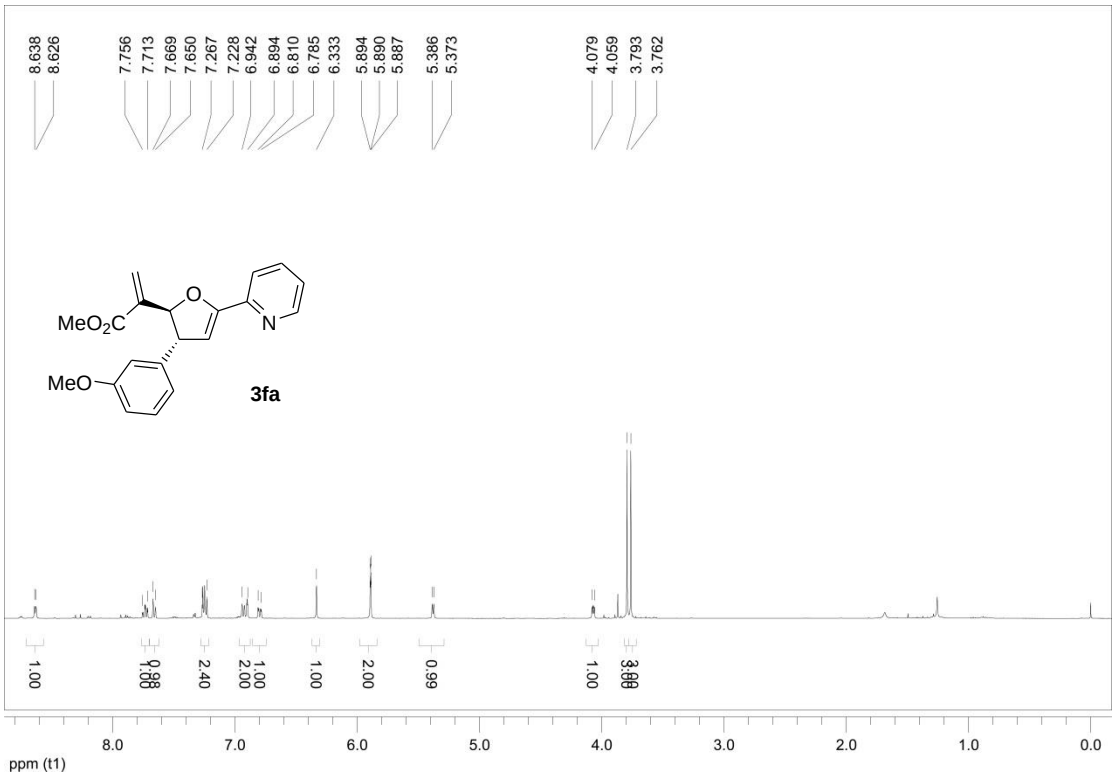


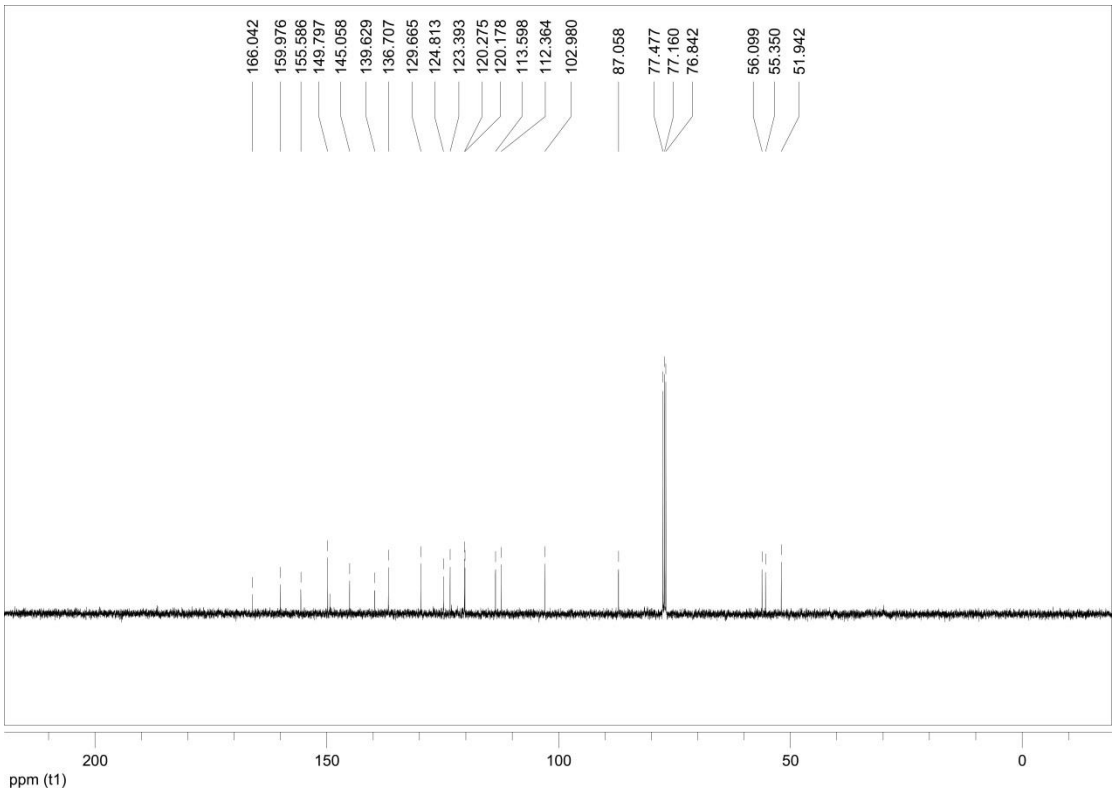
methyl 2-((2S,3R)-3-(3-bromophenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl)acrylate (3ea)



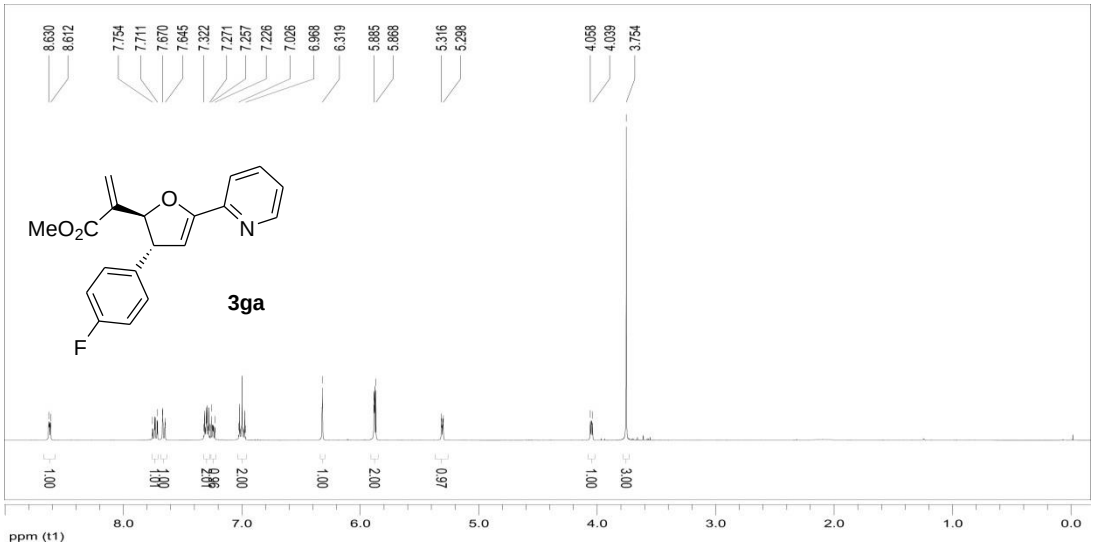


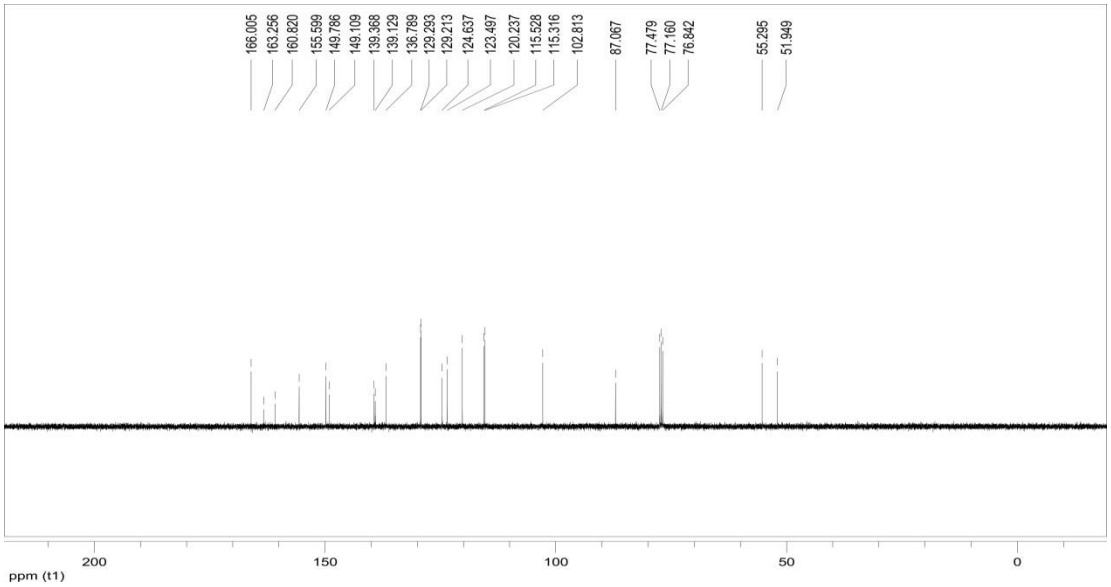
methyl 2-((2S,3R)-2,3-dihydro-3-(3-methoxyphenyl)-5-(pyridin-2-yl)furan-2-yl)acrylate (3fa)

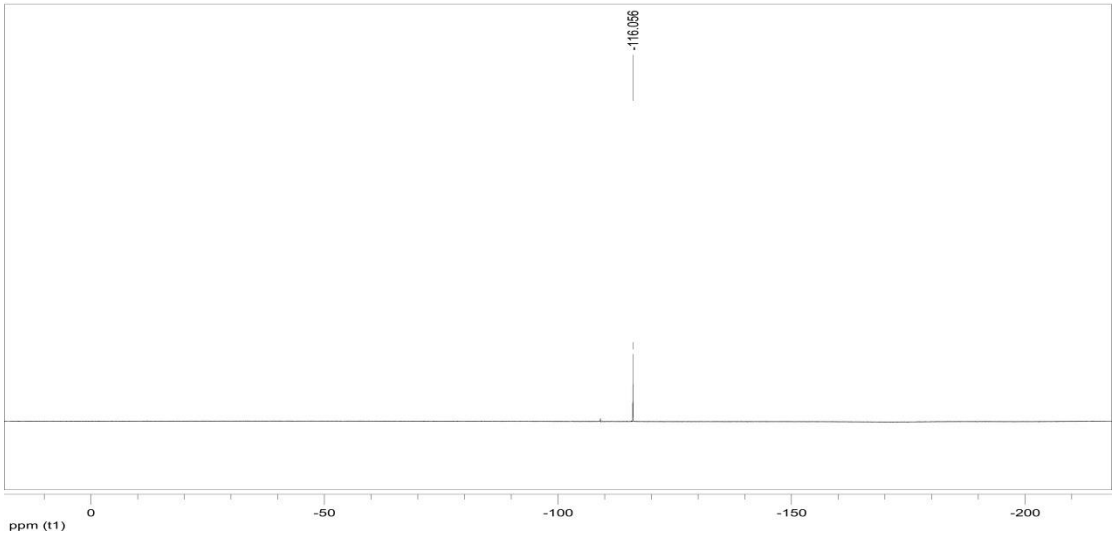




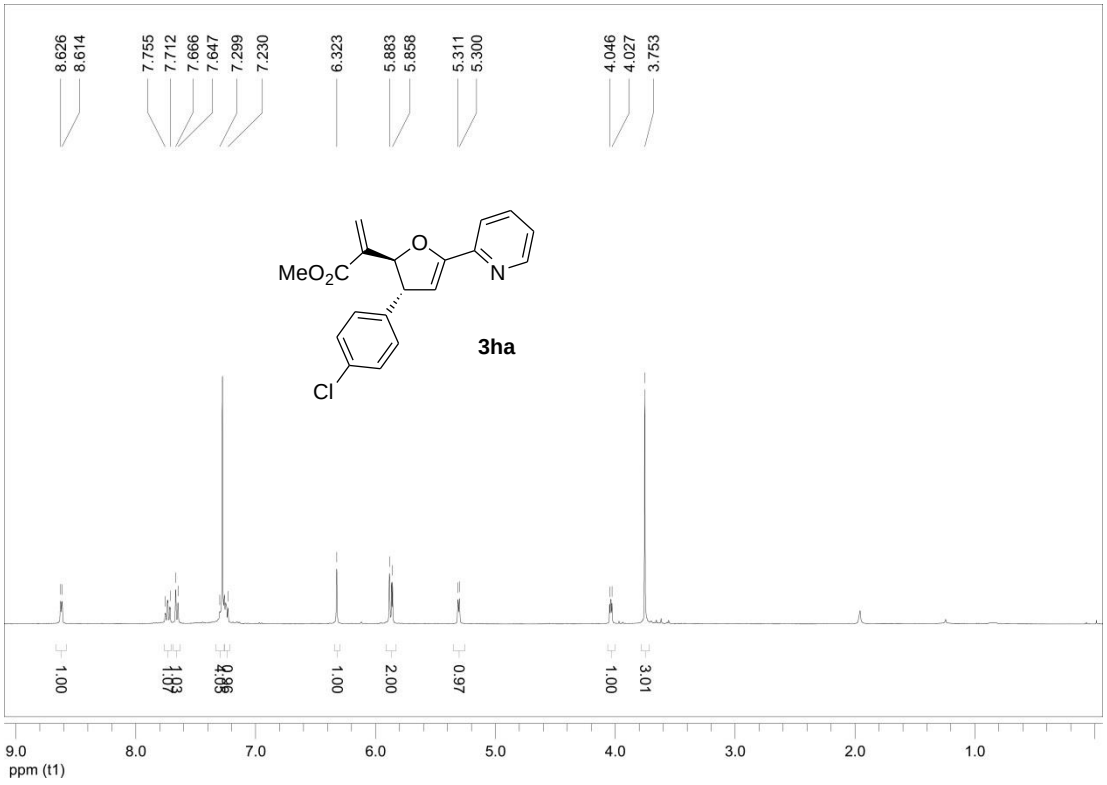
methyl 2-((2S,3R)-3-(4-fluorophenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl)acrylate (3ga)

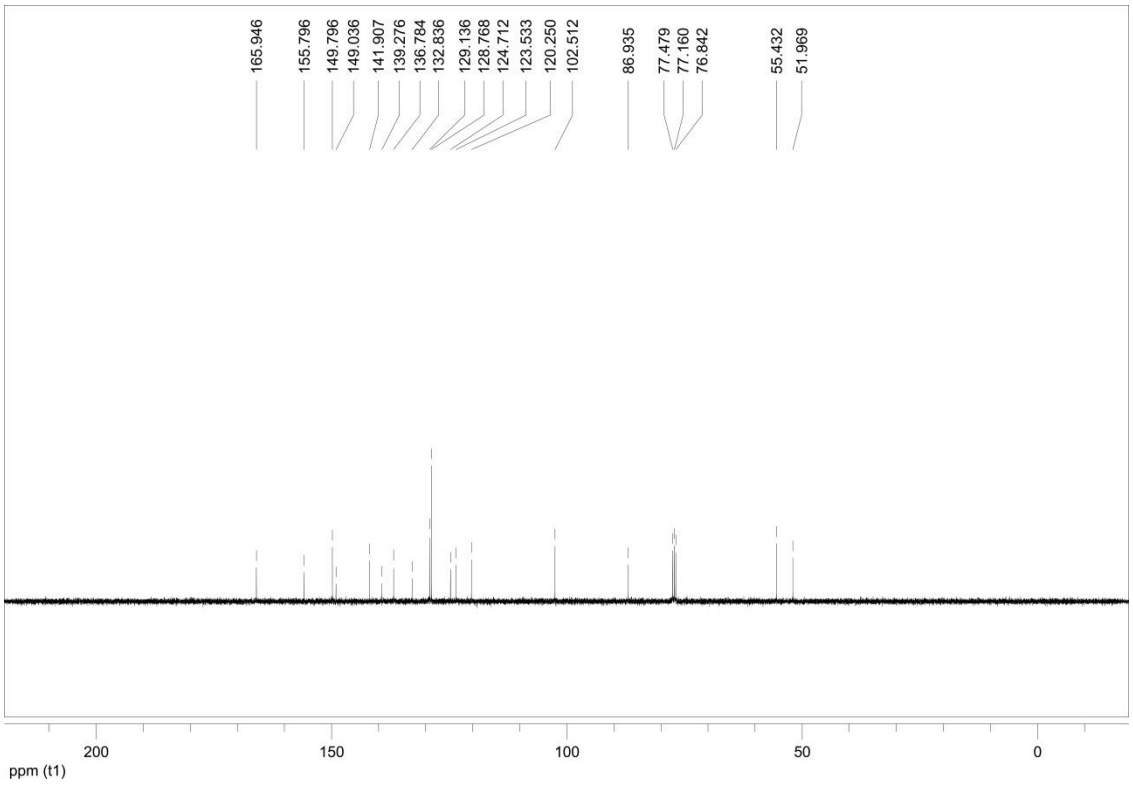




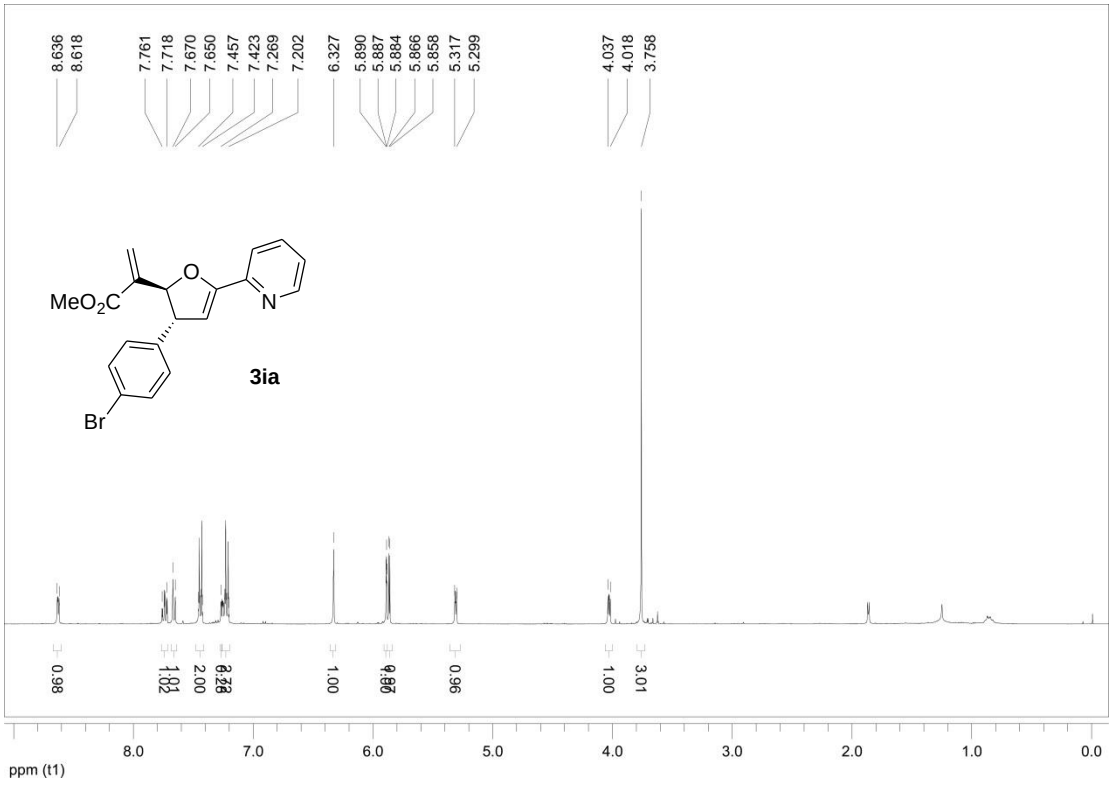


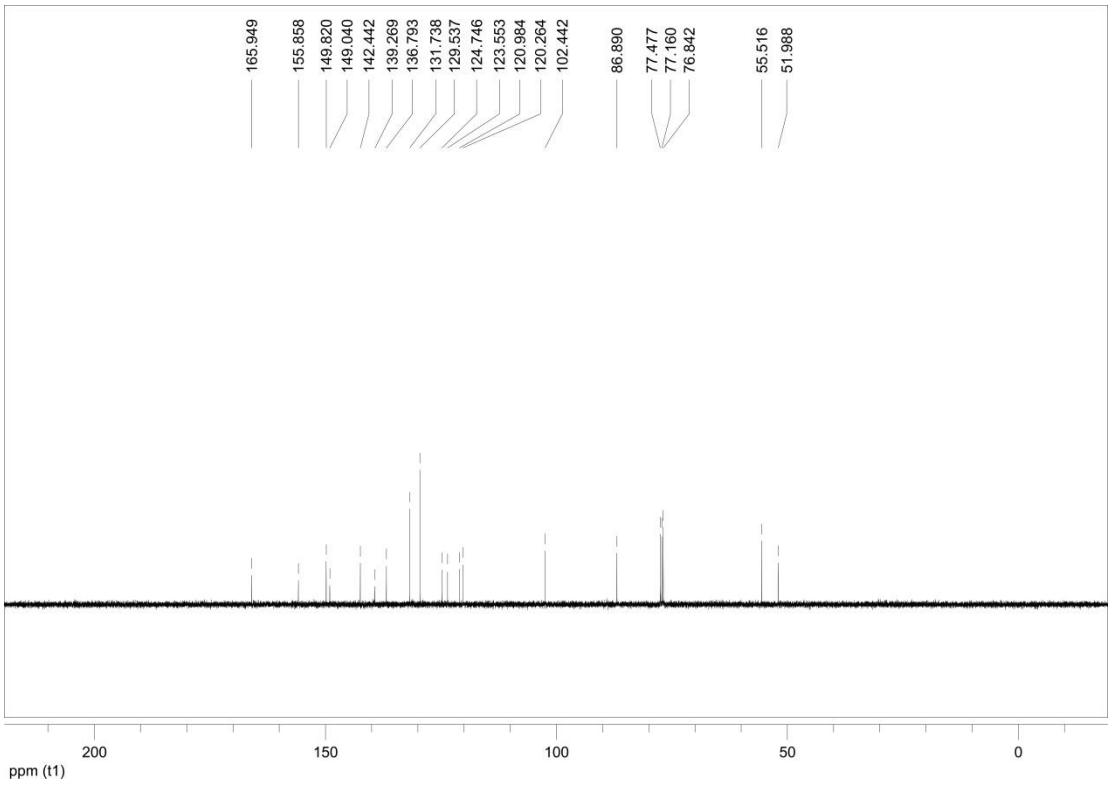
methyl 2-((2S,3R)-3-(4-chlorophenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl)acrylate (3ha)



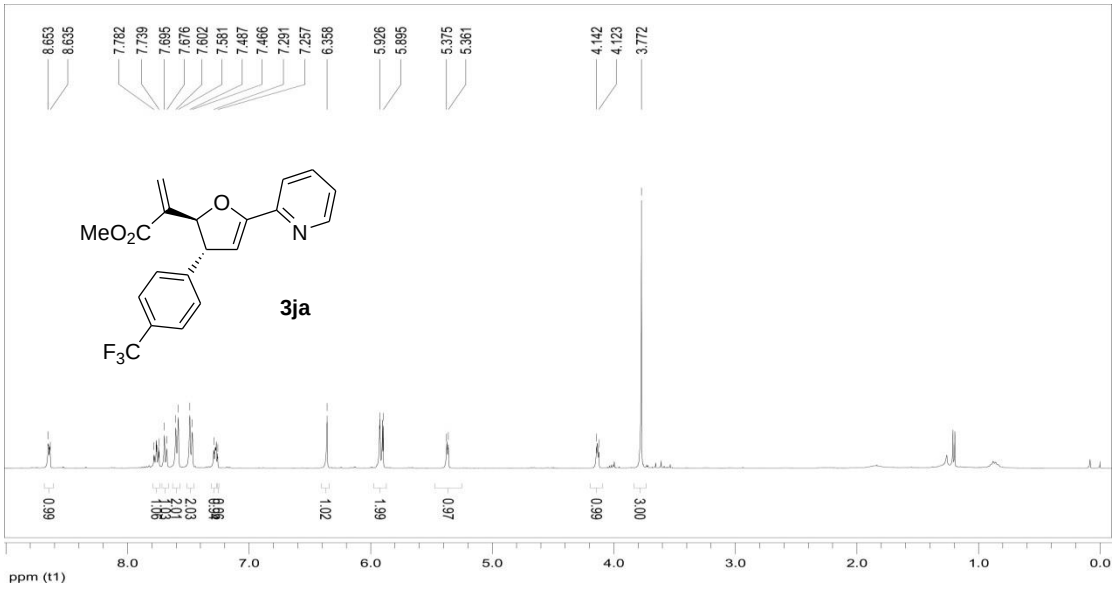


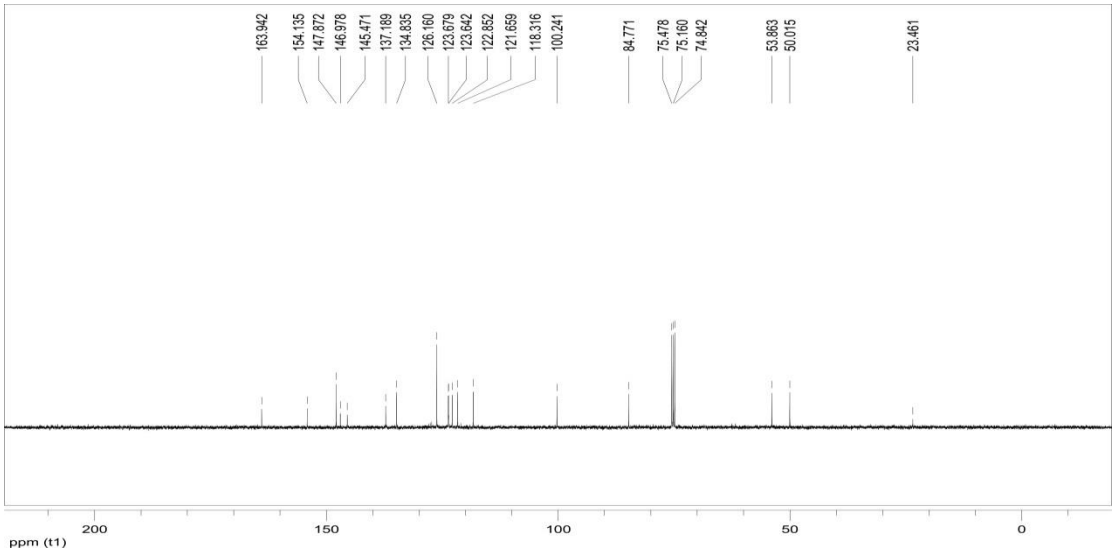
methyl 2-((2S,3R)-3-(4-bromophenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl)acrylate (3ia)

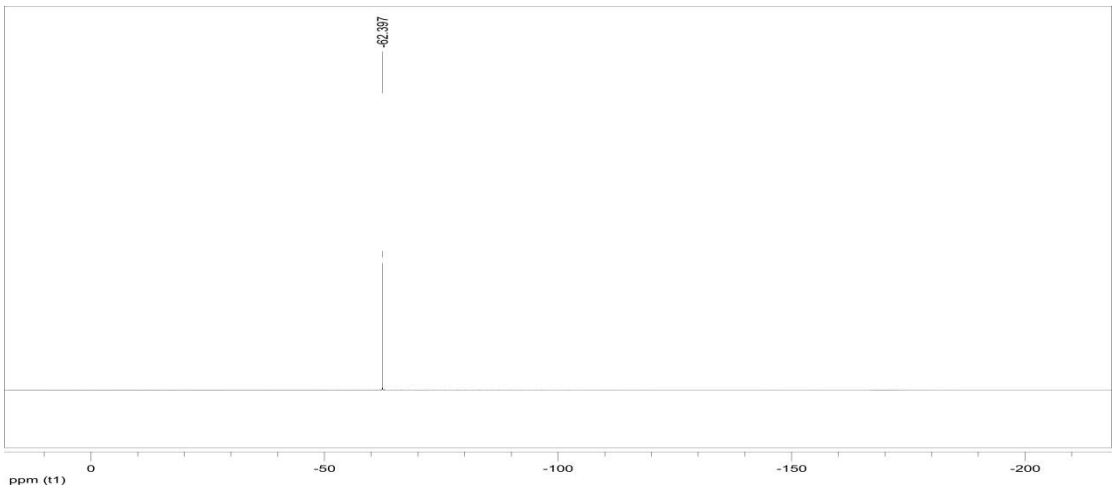




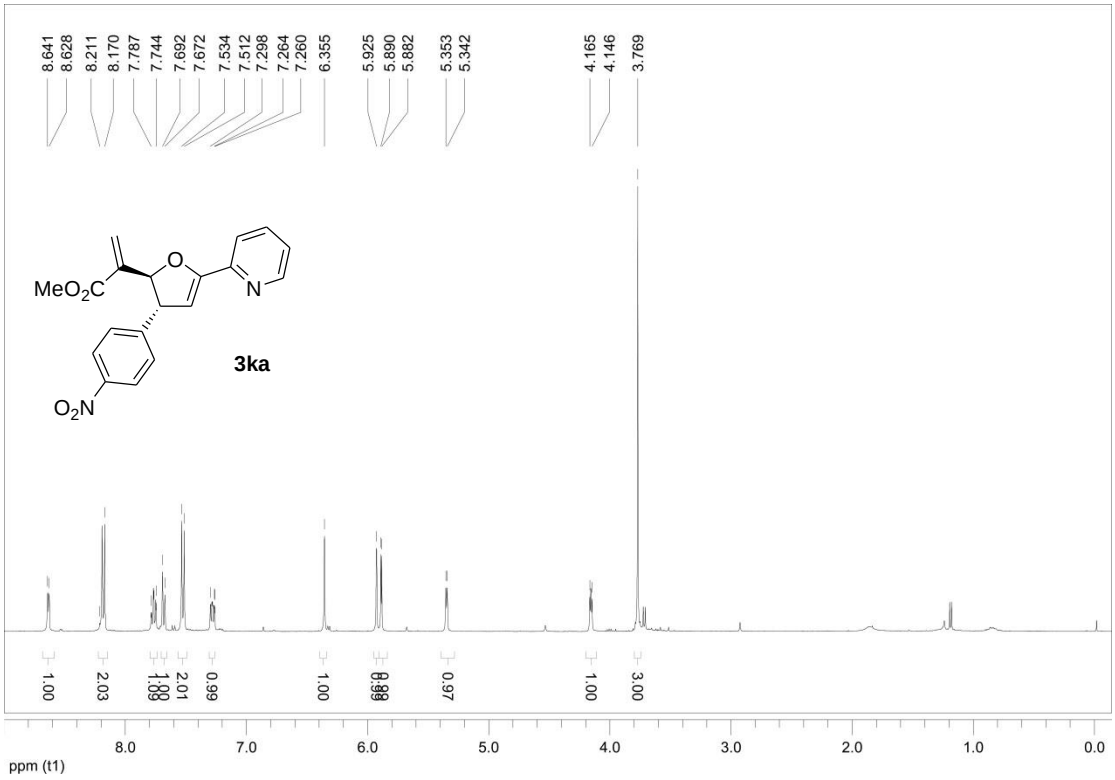
methyl 2-((2S,3R)-3-(4-(trifluoromethyl)phenyl)-2,3-dihydro-5-(pyridin-2-yl)furan-2-yl) acrylate (3ja)

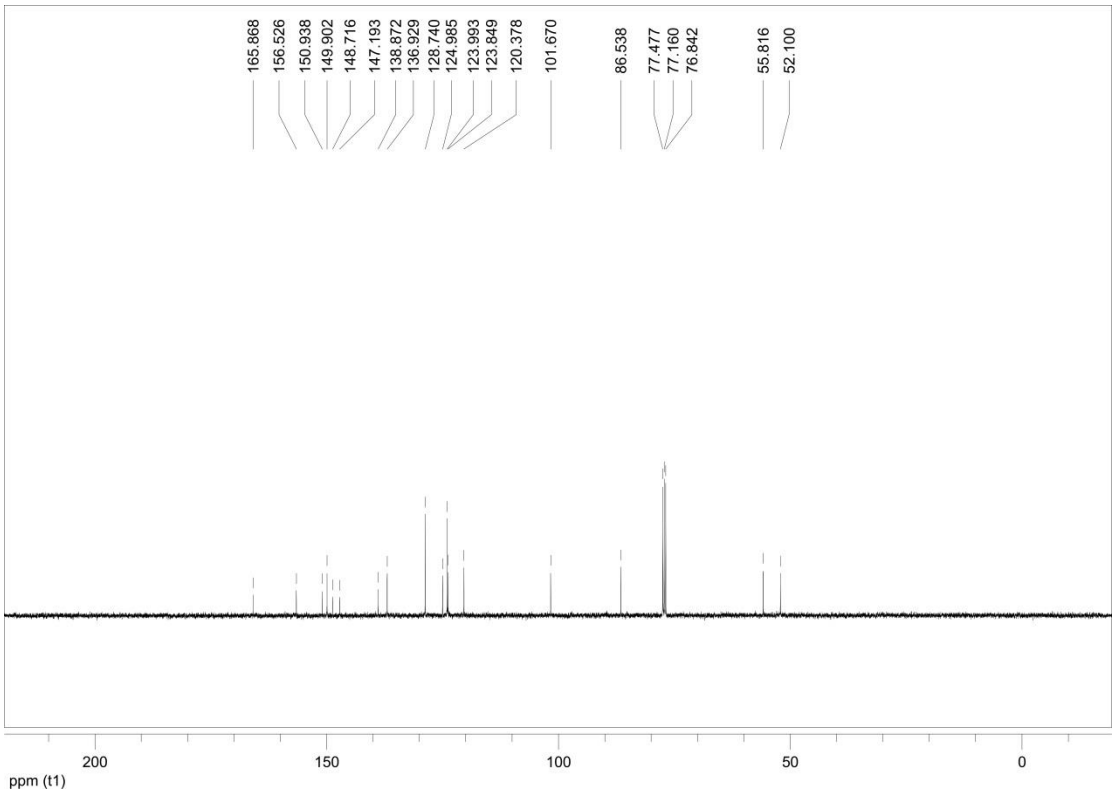




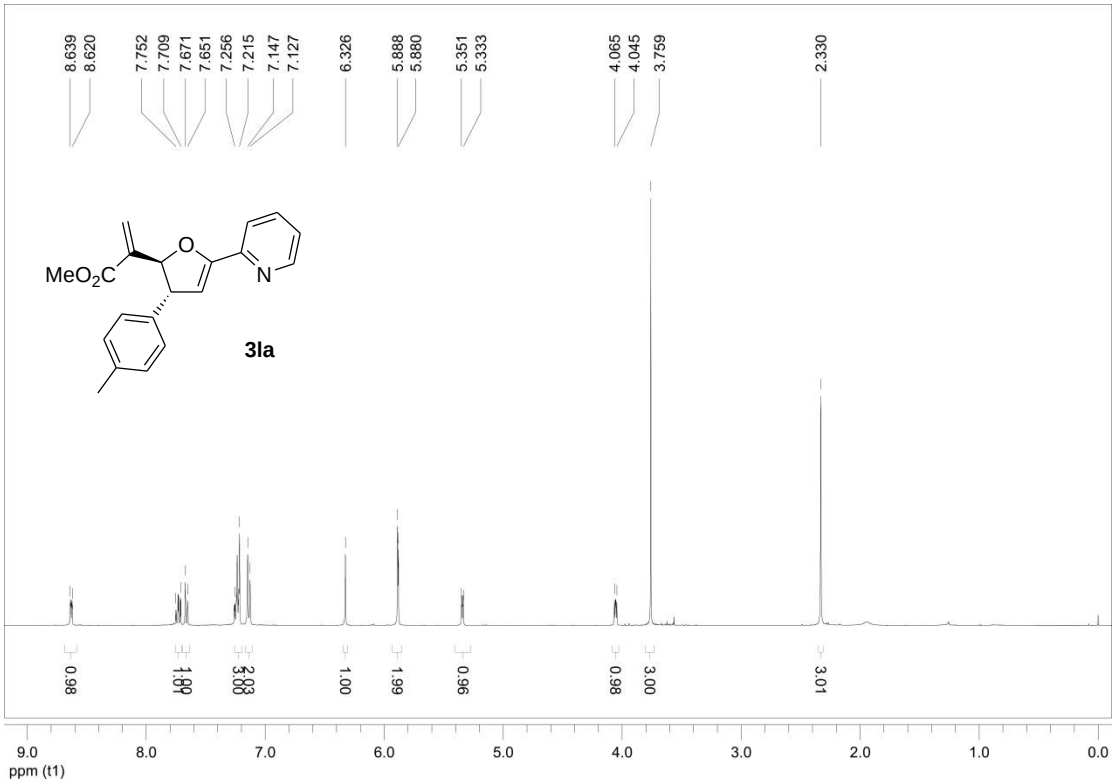


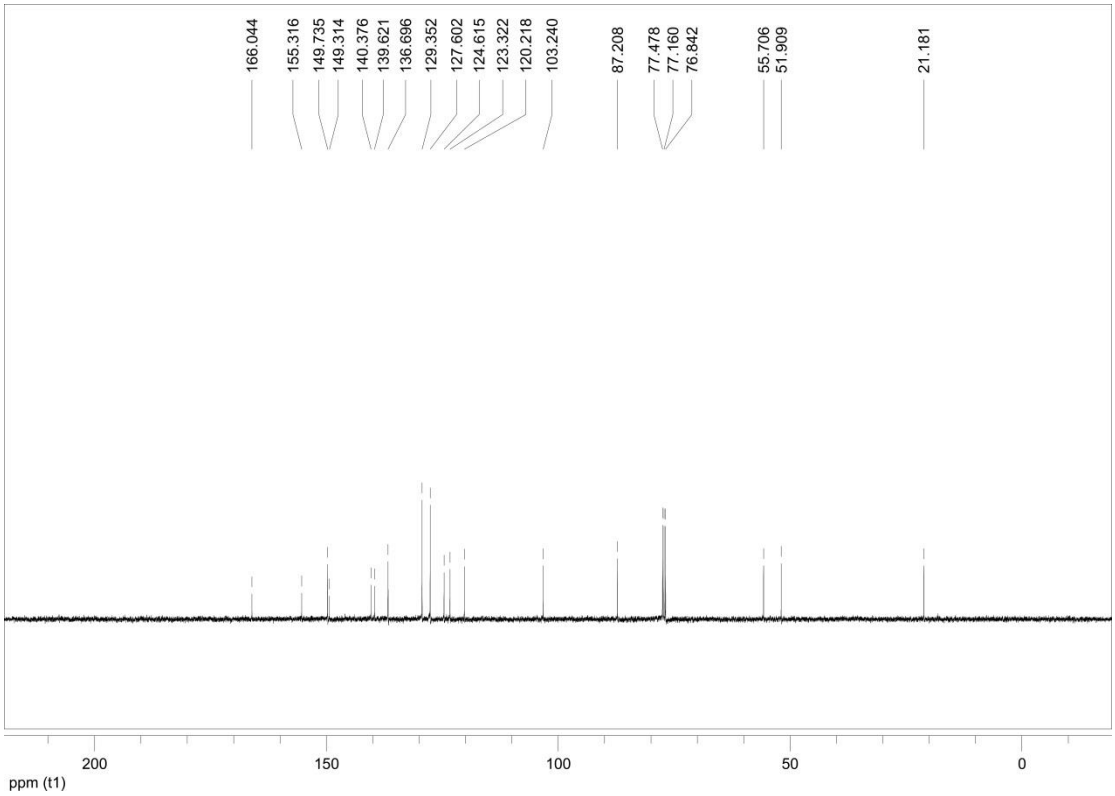
methyl 2-((2S,3R)-2,3-dihydro-3-(4-nitrophenyl)-5-(pyridin-2-yl)furan-2-yl)acrylate (3ka)



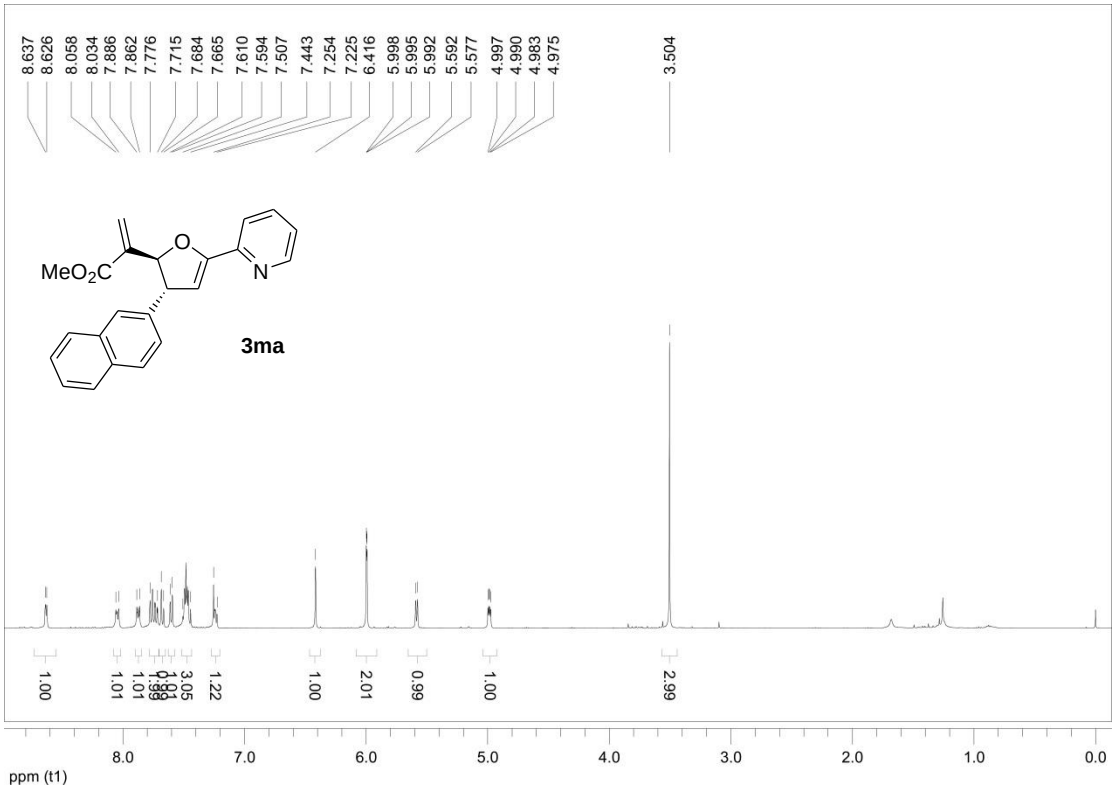


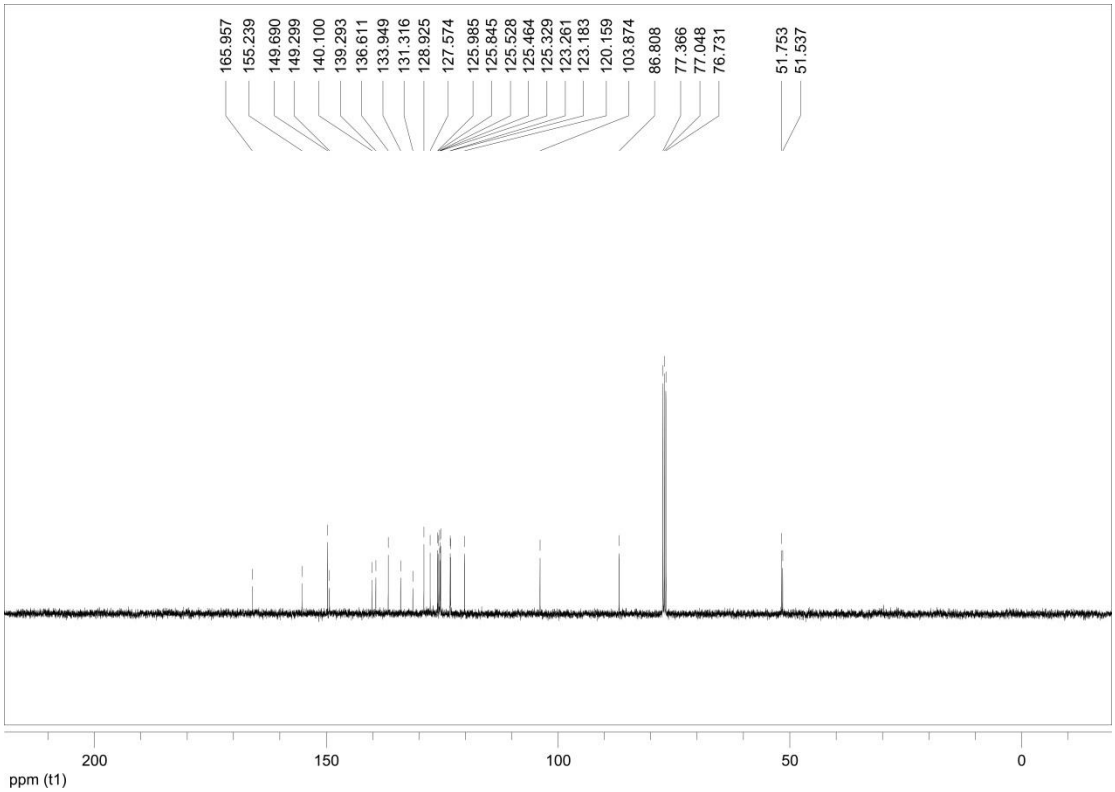
methyl 2-((2S,3R)-2,3-dihydro-5-(pyridin-2-yl)-3-p-tolylfuran-2-yl)acrylate (3la)



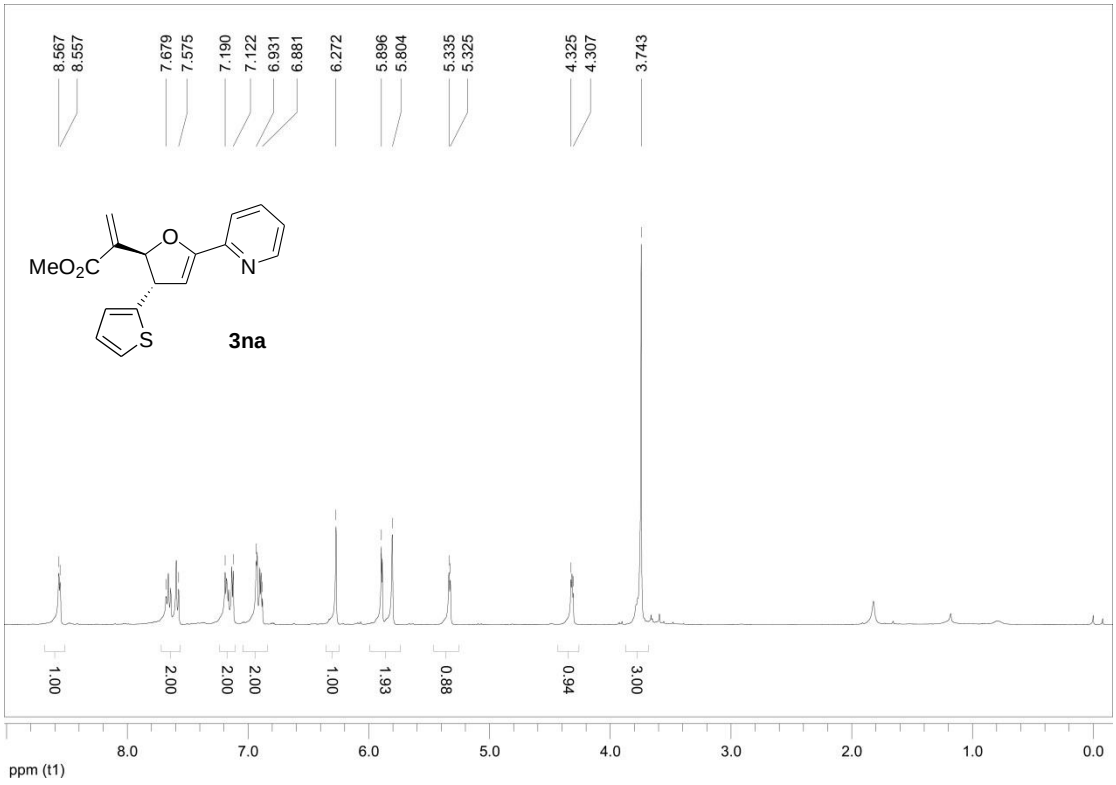


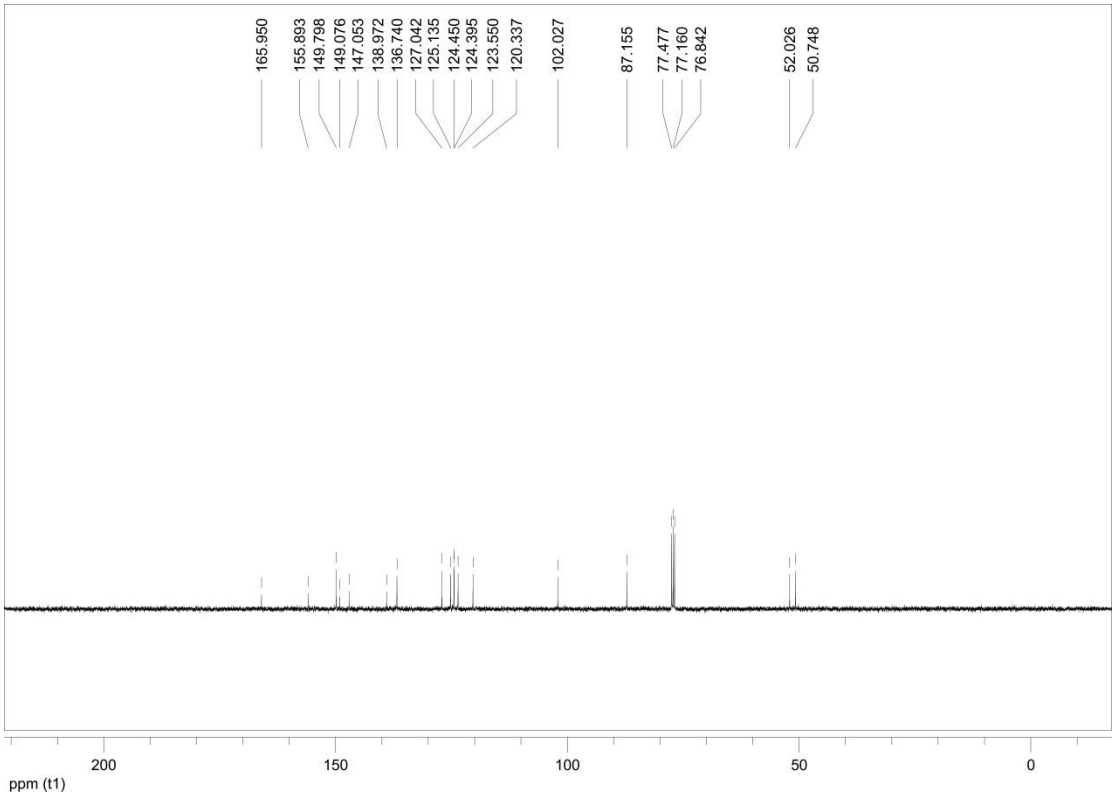
methyl 2-((2S,3R)-2,3-dihydro-3-(naphthalen-2-yl)-5-(pyridin-2-yl)furan-2-yl)acrylate (3ma)



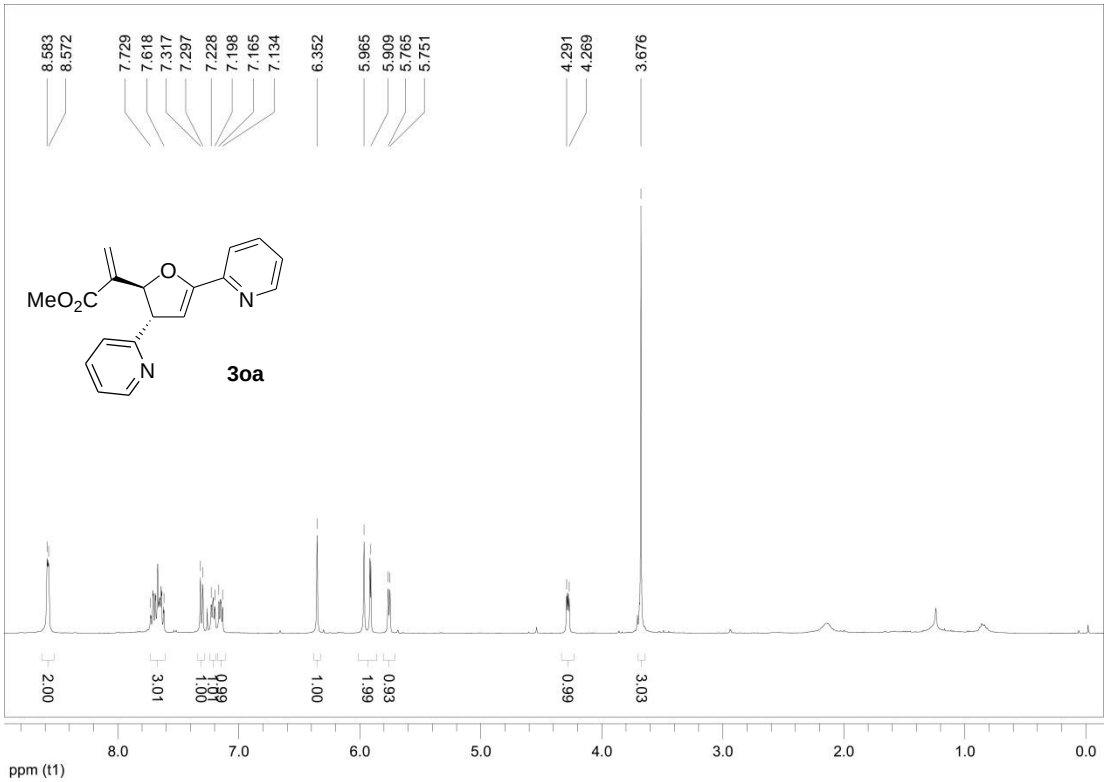


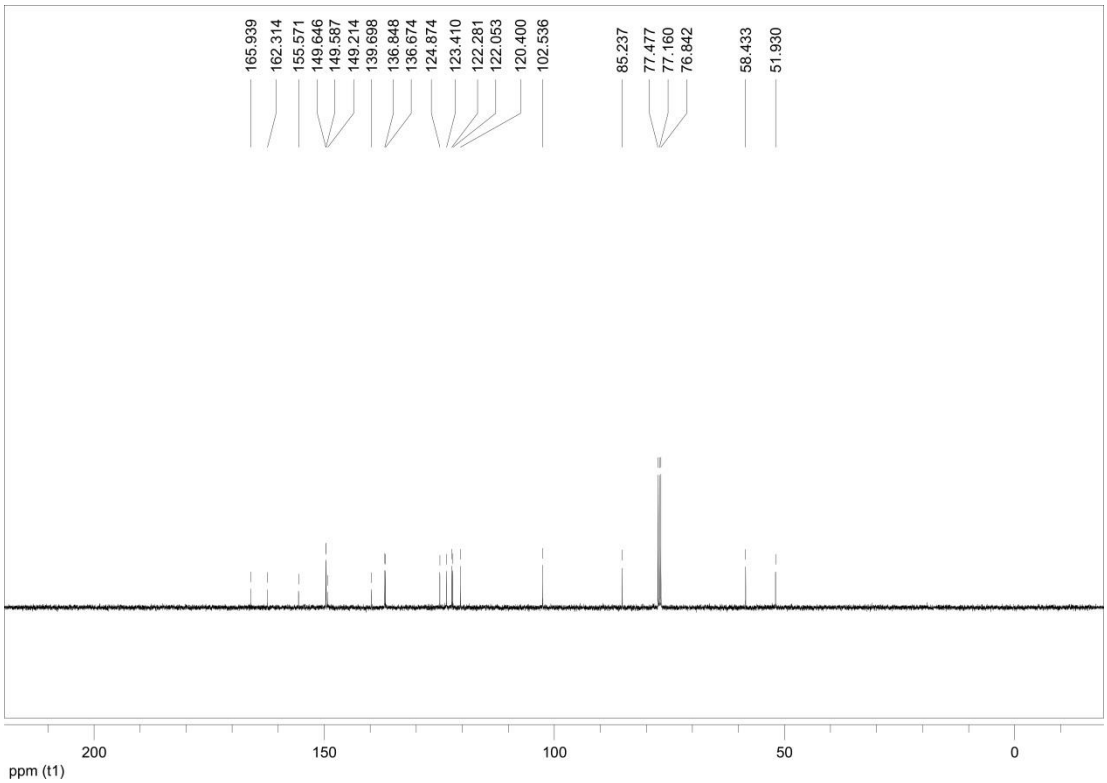
methyl 2-((2S,3S)-2,3-dihydro-5-(pyridin-2-yl)-3-(thiophen-2-yl)furan-2-yl)acrylate (3na)



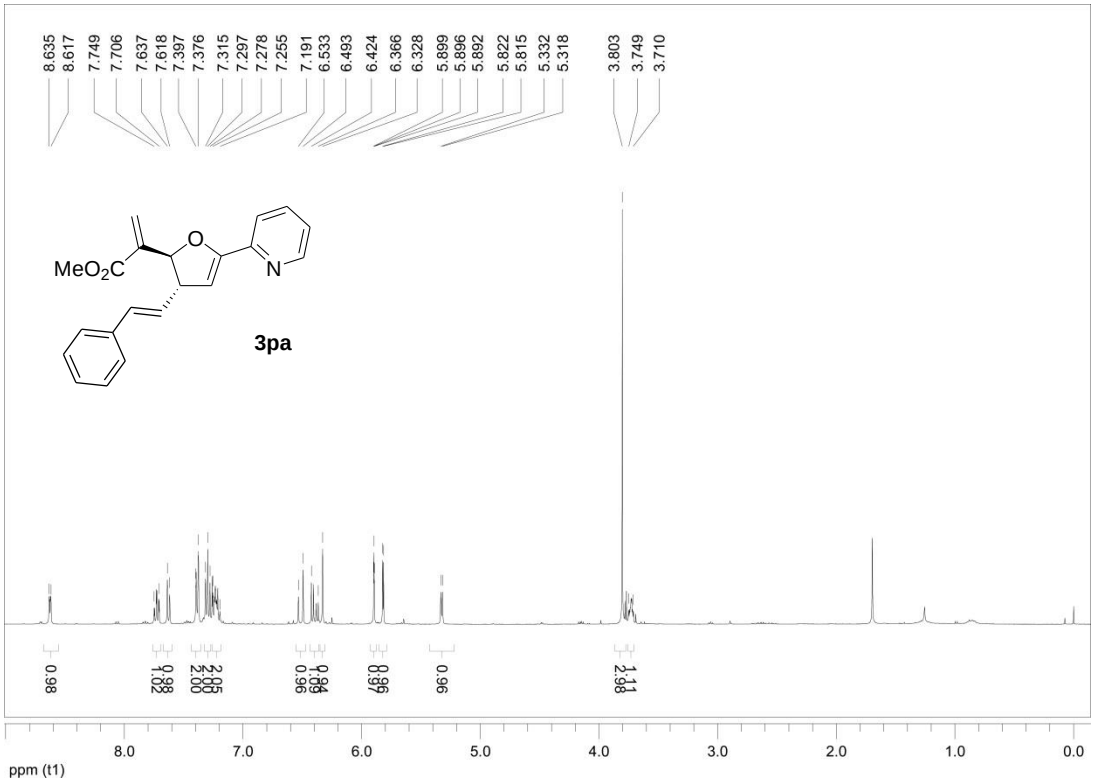


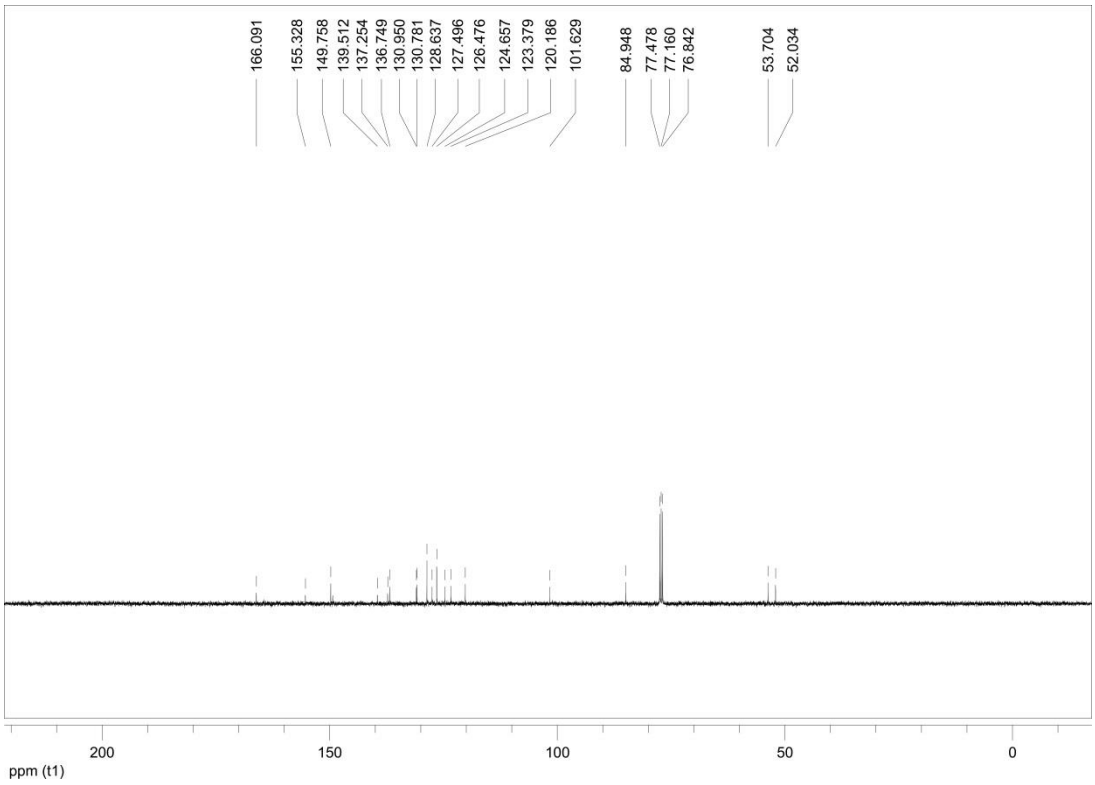
methyl 2-((2S,3R)-2,3-dihydro-3,5-di(pyridin-2-yl)furan-2-yl)acrylate (3oa)



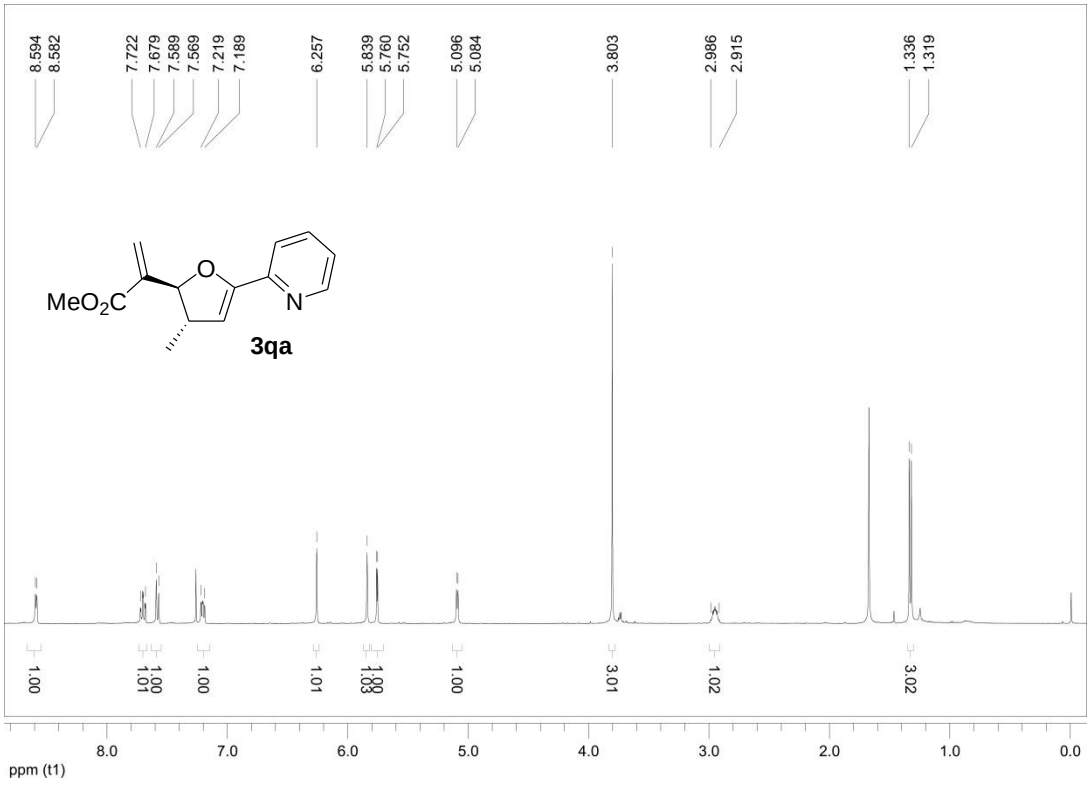


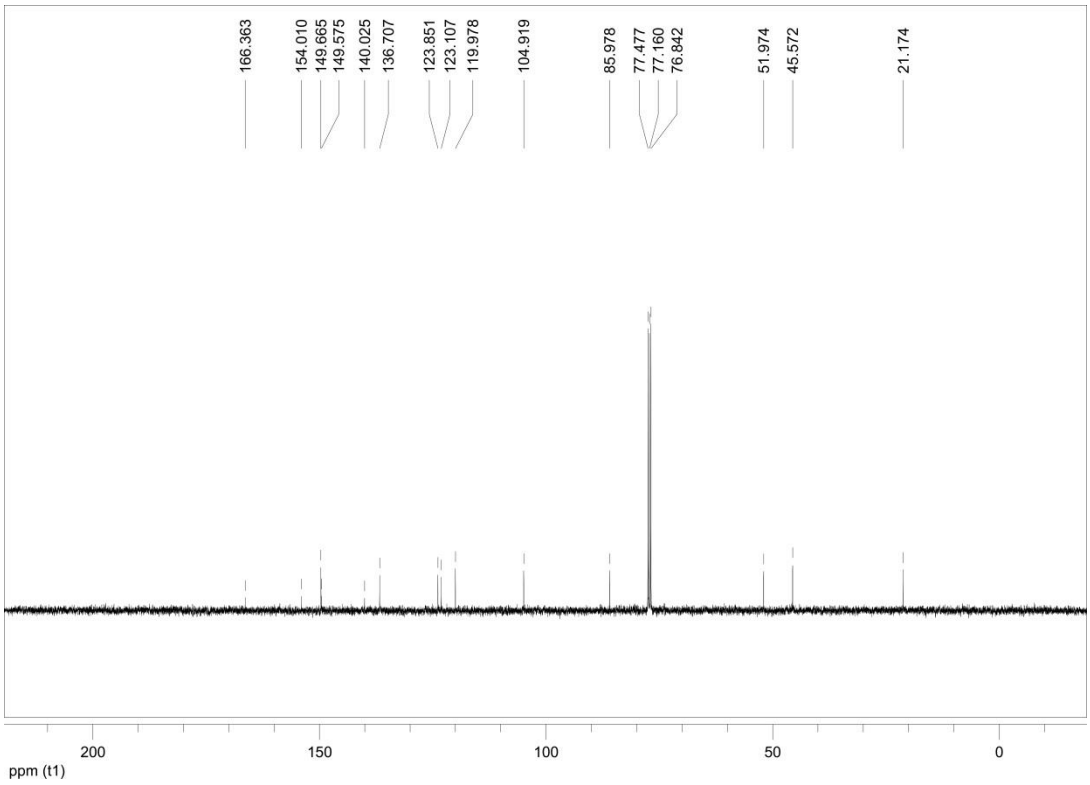
methyl 2-((2S,3S)-2,3-dihydro-5-(pyridin-2-yl)-3-styrylfuran-2-yl)acrylate (3pa)



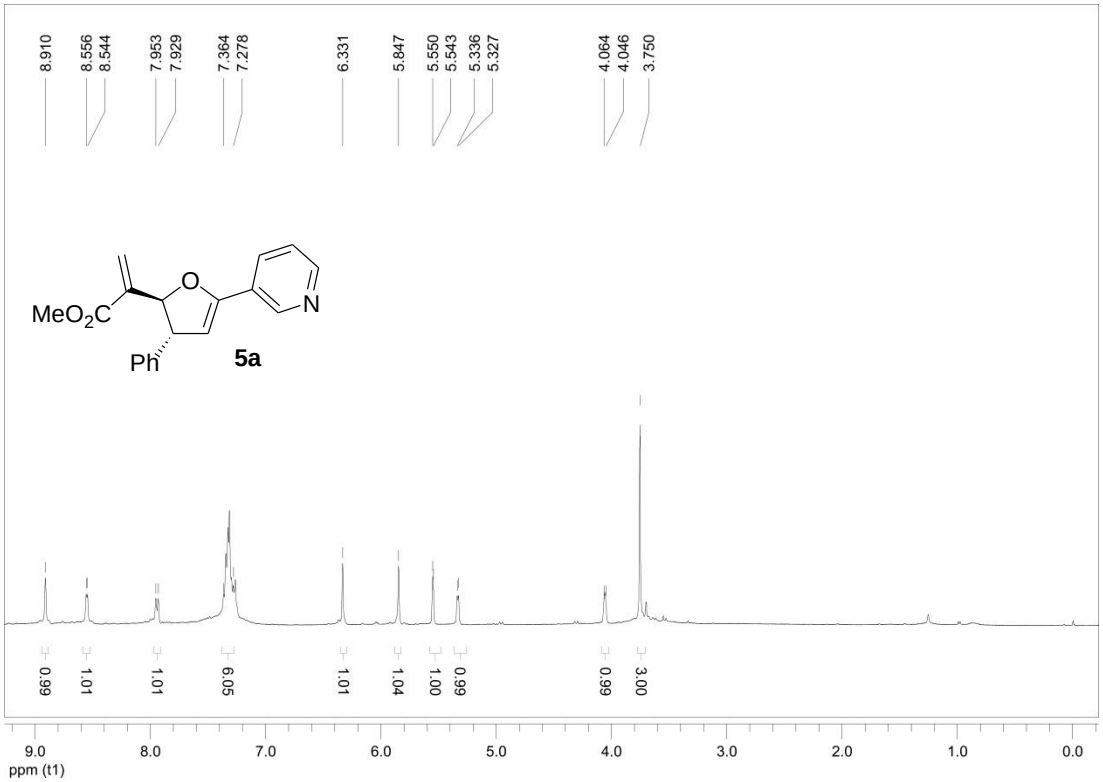


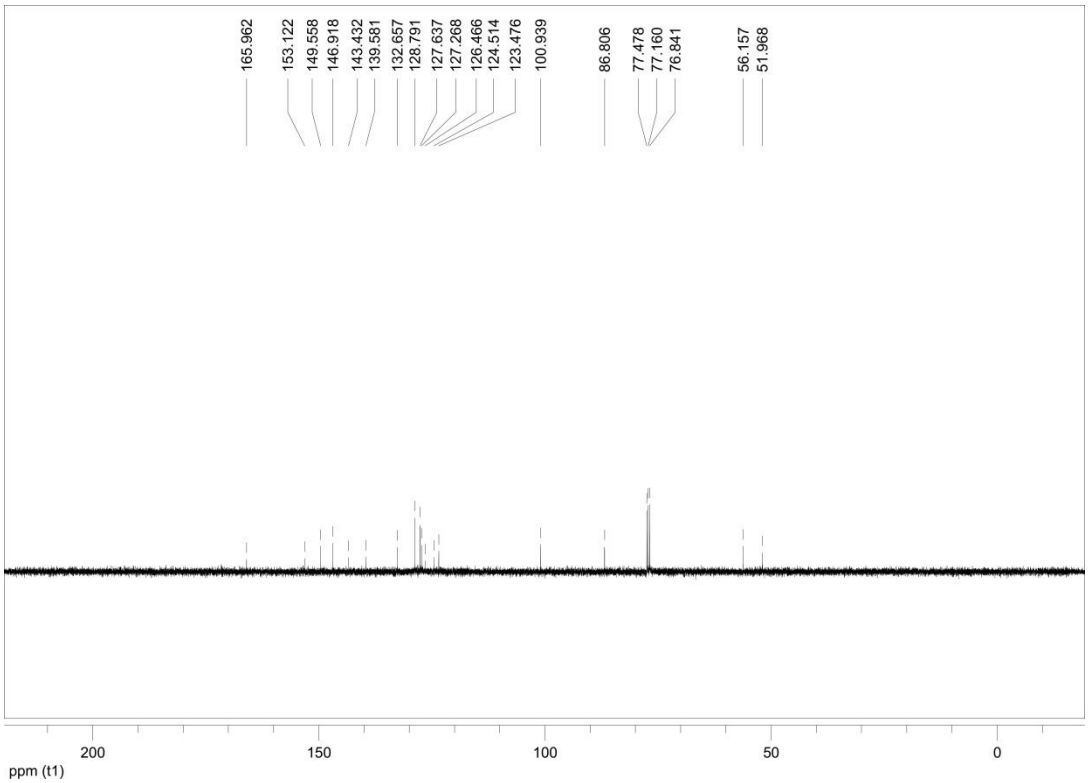
methyl 2-((2S,3S)-2,3-dihydro-3-methyl-5-(pyridin-2-yl)furan-2-yl)acrylate (3qa)





methyl 2-((2S,3R)-2,3-dihydro-3-phenyl-5-(pyridin-3-yl)furan-2-yl)acrylate (5a)





methyl 2-((2S,3R)-2,3-dihydro-3-phenyl-5-(pyridin-4-yl)furan-2-yl)acrylate (7a)