RICE STRAW ASH EXTRACT/GLYCEROL: AN EFFICIENT SUSTAINABLE APPROACH FOR KNOEVENAGEL CONDENSATION

Diego Seckler,[a,c] Camila M. Dea,[a] Elise Ane Maluf Rios,[a] Marcelo Godoi,[b] Daniel da Silveira Rampon,[a] Marcelo Gonçalves Montes D'Oca,[c] and Caroline Da Ros Montes D'Oca*[a]

[a] Laboratory of Polymers and Catalysis (LAPOCA), Department of Chemistry, Federal University of Paraná–UFPR, P. O. Box 19032, Curitiba, PR, 81531-990, Brazil.

[b] Food and Chemistry School, Federal University of Rio Grande – FURG, RS 95500-000, Brazil, PR, 81070-190, Brazil.

[c] Kolbe's Laboratory of Organic Synthesis, Department of Chemistry, Federal University of Paraná–UFPR, P. O. Box 19032, Curitiba, PR, 81531-990, Brazil.

Phone/fax: +55 (41)3361-3396, e-mail: carolinedoca@ufpr.br

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1 *EXPERIMENTAL SECTION*

1.1 *General Information*

All commercially available reagents were used without further purification. The solvents employed in extraction and purification (hexane and ethyl acetate) were distilled prior to use. The reactions were monitored by TLC (thin-layer chromatography) using pre-coated silica gel 60 F254 plates. The visualization was accomplished with UV light, stained with iodine, or by the mixture between 5.0% vanillin in 10% of H_2SO_4 and heat as developing agents. Flash chromatography was performed using Merck silica gel pore size 60 Å, 230-400 mesh with the indicated eluent system. The NMR spectra (^1H and ^{13}C) were obtained on a Bruker Nuclear Ascend 400 spectrometer. The spectra were obtained either in $CDCl_3$ or DMSO-*d6* solutions. The chemical shifts (δ) are reported in ppm, referenced to tetramethylsilane (TMS) as the internal standard. The coupling constants (*J*) are reported in Hertz (Hz). Hydrogen coupling patterns are described as singlet (s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet triplets (dt), triplet (t), triplet of doublets (td), doublet of quartets (dq), quartet (q), quintet (quint), sextet (sext), broad signal (br) and multiplet (m). Low-resolution mass spectra were obtained with a Shimadzu GC-MS-QP2010 Plus mass spectrometer. The melting point measuring for some representative compounds were obtained on a MP90 Melting Point System.

1.2 *General procedure for optimization of the reaction conditions*

The yields of the product **3a** depicted on the optimization tables (Table 1 on the manuscript) were obtained using the principle of the internal standard (IS) in GC-MS analysis.[71] Anthracene was chosen as IS. The first step of this procedure was the calibration curve plot of the average area ratio of the analyte (**3a**) relative to the average area ratio of the IS (anthracene) and the average mass ratio of the analyte (**3a**) relative to the average area ratio of the IS, in order to identify the linearity of the relationship with R^2.

In this way, two stock solutions of IS (0.0201 mol L^{-1}) *and* **3a** (0.0203 mol L^{-1}) in ethyl acetate were quickly prepared in a volumetric flask (25 mL). The solutions were storage in closed flasks into the refrigerator at 5 ºC, before their use on the same day. The vials (total volume of 1.5 mL) for the 10 calibration points were prepared by the addition of a constant amount of the stock IS solution (500 μL) and a gradient amount of **3a** (50 μL to 500 μL), and the elution bands of **3a** and SI and the area ratio of **3a** relative to the area ratio of the IS were determined (Table 1, 2 and 3). The average of triplicate data are shown in the Table 4.

On these tables, the column described by F/G which means the ratio of analyte area and SI area. RR*F* is relative response factor, which is described by FRR in the tables, as well as w_i, as described above. The slope of table 1, 2, 3, and 4 describes the relationship of ratio of analyte area/ standard area *vs* [analyte] in mol L^{-1}. The method employed in all the GC-MS analysis is described as follows: **GC**: column

oven temp: 150 ºC for 5.0 min; initial injection temp: 250 ºC; helium carrier gas; pressure 92.4 kPa; total flow 54 mL min^{-1}; column flow 1.0 mL min^{-1}; linear velocity 38 cm s^{-1}; purge flow 3.0 mL min^{-1}; split ratio of 50. **MS**: ion source temperature: 200 ºC; interface temperature: 260 ºC; solvent cut time 3.0 min. Under this method, the retention time of IS was 11.031 min and the retention time of **3a** was 7.348 min.

Table 1. Calibration Curve

vial	*analyte (µL)*	*standard (µL)*	*[analyte] (mol/L)*	*[stand] (mol/L)*	*Analyte area*	*Standard area*	*F/G*	*Standard mass(g)*	*Analyte Mass(g)*	*FRR*	*Wi*	*Average Wi*	*J/I*	*F2/G2*
1	50	500	6,767E-04	6,663E-03	313978	9809300	0,03200820	0,00178200	0,00019080	3,34510280	0,00954000	0,00645025	0,107070707	0,032008196
2	100	500	1,353E-03	6,663E-03	721294	9628255	0,07491430	0,00178200	0,00038160	2,85848509	0,01908000	0,01509663	0,214141414	0,074914302
3	150	500	2,030E-03	6,663E-03	1253777	9445174	0,13274260	0,00178200	0,00057240	2,41981180	0,02862000	0,02675012	0,321212121	0,132742605
4	200	500	2,707E-03	6,663E-03	1887487	9631008	0,19598021	0,00178200	0,00076320	2,18533709	0,03816000	0,03949368	0,428282828	0,195980213
5	250	500	3,383E-03	6,663E-03	2474389	9627443	0,25701414	0,00178200	0,00095400	2,08297307	0,04770000	0,05179316	0,535353535	0,257014142
6	300	500	4,060E-03	6,663E-03	3087630	9583838	0,32217051	0,00178200	0,00114480	1,99405041	0,05724000	0,06492339	0,642424242	0,322170512
7	350	500	4,737E-03	6,663E-03	3610583	9864189	0,36602938	0,00178200	0,00133560	2,04763603	0,06678000	0,07376177	0,749494949	0,366029382
8	400	500	5,413E-03	6,663E-03	4430012	9722305	0,45565450	0,00178200	0,00152640	1,87985779	0,07632000	0,09182291	0,856565657	0,455654498
9	450	500	6,090E-03	6,663E-03	4856158	9639791	0,50376175	0,00178200	0,00171720	1,91288116	0,08586000	0,10151742	0,963636364	0,503761752
10	500	500	6,767E-03	6,663E-03	5665160	10005389	0,56621087	0,00178200	0,00190800	1,89100409	0,09540000	0,11410208	1,070707071	0,566210869
Stoke Solution Standard (mol/L)		**0,019996**	**Stoke Solution Analyte (mol/L)**	**0,020273**	**2830046,8**	**9695669,2**	**0,290648647**	**0,001782000**	**0,001049400**	**2,2617**	**0,05247**	**0,05857**	**0,58889**	**0,29065**

Table 2. Calibration Curve

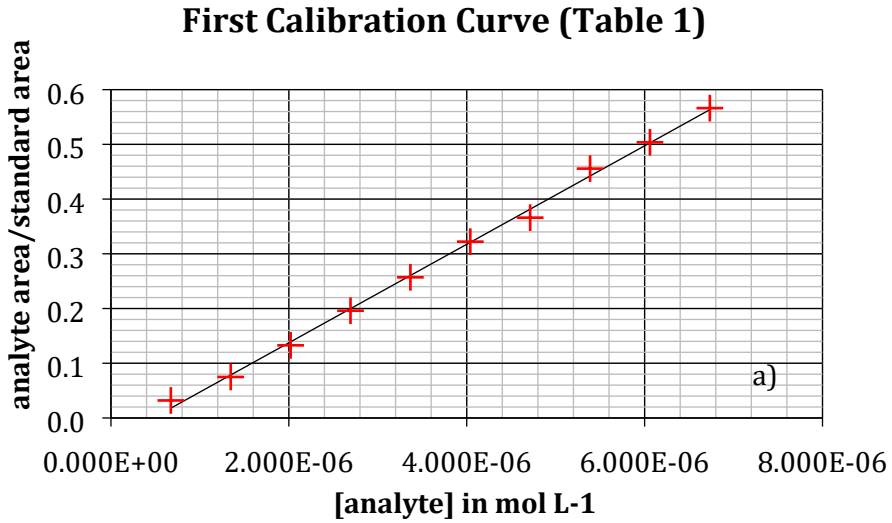
vial	*analyte (µL)*	*standard (µL)*	*[analyte] (mol/L)*	*[standard] (mol/L)*	*Analyte area*	*Standard area*	*F/G*	*Standard mass*	*Analyte Mass*	*FRR*	*Wi*	*Average Wi*	*J/I*	*F2/G2*
1	50	500	6,767E-04	6,633E-03	221977	9514467	0,023330471	44,55850000	0,00019300	0,00018565	0,00000039	0,00916364		0,023330471
2	100	500	1,353E-03	6,633E-03	710315	9448530	0,075177303	0,00177800	0,00038600	2,88781128	0,01934342	0,01202365	0,217097863	0,075177303
3	150	500	2,030E-03	6,633E-03	1348435	9428079	0,143023303	0,00177800	0,00057900	2,27687927	0,02901513	0,02287476	0,325646794	0,143023303
4	200	500	2,707E-03	6,633E-03	2185222	10339176	0,211353593	0,00177800	0,00077200	2,05435696	0,03868684	0,03380332	0,434195726	0,211353593
5	250	500	3,383E-03	6,633E-03	2578075	9379199	0,274871554	0,00177800	0,00096500	1,97453920	0,04835855	0,04396221	0,542744657	0,274871554
6	300	500	4,060E-03	6,633E-03	3112220	9135079	0,340688898	0,00177800	0,00115800	1,91169595	0,05803026	0,05448886	0,651293588	0,340688898
7	350	500	4,737E-03	6,633E-03	3864174	9561206	0,404151317	0,00177800	0,00135100	1,88009413	0,06770197	0,06463886	0,75984252	0,404151317
8	400	500	5,413E-03	6,633E-03	4382700	10003624	0,438111228	0,00177800	0,00154400	1,98212553	0,07737368	0,07007032	0,868391451	0,438111228
9	450	500	6,090E-03	6,633E-03	4975738	8469743	0,587472135	0,00177800	0,00173700	1,66295612	0,08704539	0,09395870	0,976940382	0,587472135
10	500	500	6,767E-03	6,633E-03	5592976	6799583	0,822546912	0,00177800	0,00193000	1,31966858	0,09671710	0,13155592	1,085489314	0,822546912
Stoke Solution Standard (mol/L)		**0,019951**	**Stoke Solution Analyte (mol/L)**	**0,020507**	**2897183,2**	**9207868,6**	**0,332072671**	**4,457450200**	**0,001061500**	**1,79503**	**0,05223**	**0,05365**	**0,65129**	**0,33207**

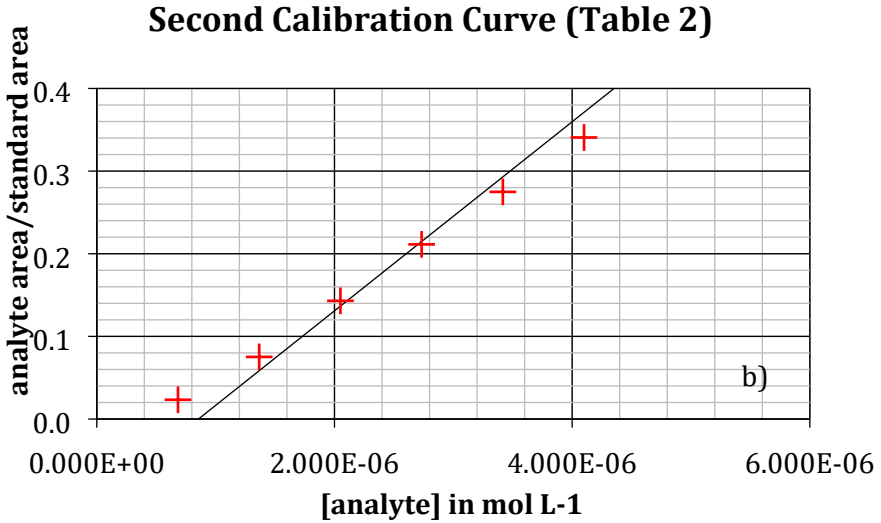
Table 3. Calibration Curve

vial	*analyte (µL)*	*standard (µL)*	*[analyte] (mol/L)*	*[standard] (mol/L)*	*Analyte area*	*Standard area*	*F2/G2*	*Standard mass*	*Analyte Mass*	*FRR*	*Wi*	*Average Wi*	*J/I*	*F2/G2*
1	50	500	6,767E-04	6,633E-03	227888	9402187	0,024237765	0,00178200	0,00019040	4,40825463	0,00952000	0,00517580	0,10684624	0,024237765
2	100	500	1,353E-03	6,633E-03	582608	9066855	0,064256901	0,00178200	0,00038080	3,32559583	0,01904000	0,01372160	0,21369248	0,064256901
3	150	500	2,030E-03	6,633E-03	1281349	9467909	0,135336007	0,00178200	0,00057120	2,36846592	0,02856000	0,02890004	0,320538721	0,135336007
4	200	500	2,707E-03	6,633E-03	1872776	9213839	0,203256862	0,00178200	0,00076160	2,10268405	0,03808000	0,04340405	0,427384961	0,203256862
5	250	500	3,383E-03	6,633E-03	2262716	9743720	0,232223011	0,00178200	0,00095200	2,30050932	0,04760000	0,04958957	0,534231201	0,232223011
6	300	500	4,060E-03	6,633E-03	2988741	9178525	0,325623235	0,00178200	0,00114240	1,96877057	0,05712000	0,06953452	0,641077441	0,325623235
7	350	500	4,737E-03	6,633E-03	3545177	9038501	0,392230636	0,00178200	0,00133280	1,90684667	0,06664000	0,08375805	0,747923681	0,392230636
8	400	500	5,413E-03	6,633E-03	3986995	9299198	0,428746113	0,00178200	0,00152320	1,99365054	0,07616000	0,09155567	0,854769921	0,428746113
9	450	500	6,090E-03	6,633E-03	5149363	9495881	0,542273329	0,00178200	0,00171360	1,77330529	0,08568000	0,11579860	0,961616162	0,542273329
10	500	500	6,767E-03	6,633E-03	5389486	9173133	0,587529473	0,00178200	0,00190400	1,81856817	0,09520000	0,12546272	1,068462402	0,587529473
Stoke Solution Standard (mol/L)		**0,019996**	**Stoke Solution Analyte (mol/L)**	**0,020230569**	**2728710**	**9307975**	**0,293571333**	**0,001782000**	**0,001047200**	**2,3967**	**0,0524**	**0,0627**	**0,5877**	**0,2936**

Table 4. Average of data from tables 1, 2 and 3

vial	analyte (µL)	standard (µL)	[analyte] (mol/L)	[standard] (mol/L)	Analyte area	Standard area	F2/G2	Standard mass	Analyte Mass	FRR	Wi	Average Wi	J/I	F2/G2
1	50	500	1,584E-06	6,718E-06	254614	9575318	0,0265255	14,85402133	0,00019140	2,58451436	0,00635346	0,00692990	1,28854E-05	0,026590692
2	100	500	1,356E-06	6,718E-06	671406	9381213	0,0714495	0,00178067	0,00038280	3,02396406	0,01915447	0,01361396	0,214975665	0,071569172
3	150	500	2,033E-06	6,718E-06	1294520	9447054	0,1370340	0,00178067	0,00057420	2,35505233	0,02873171	0,02617497	0,322463497	0,137028997
4	200	500	2,711E-06	6,718E-06	1981828	9728008	0,2035302	0,00178067	0,00076560	2,11412603	0,03830895	0,03890035	0,429951329	0,203723969
5	250	500	3,389E-06	6,718E-06	2438393	9583454	0,2547029	0,00178067	0,00095700	2,11934053	0,04788618	0,04844831	0,537439161	0,25443784
6	300	500	4,067E-06	6,718E-06	3062864	9299147	0,3294942	0,00178067	0,00114840	1,95817231	0,05746342	0,06298225	0,644926994	0,329370377
7	350	500	4,744E-06	6,718E-06	3673311	9487965	0,3874704	0,00178067	0,00133980	1,94485894	0,06704066	0,07405290	0,752414826	0,387154801
8	400	500	5,422E-06	6,718E-06	4266569	9675042	0,4408373	0,00178067	0,00153120	1,95187795	0,07661789	0,08448297	0,859902658	0,440987114
9	450	500	6,100E-06	6,718E-06	4993753	9201805	0,5445024	0,00178067	0,00172260	1,78304752	0,08619513	0,10375824	0,96739049	0,542692765
10	500	500	6,778E-06	6,718E-06	5549207	8659368	0,6587624	0,00178067	0,00191400	1,67641362	0,09577237	0,12370691	1,074878323	0,640832809
Stoke Solution Standard (mol/L)		**0,019981**	**Stoke Solution Analyte (mol/L)**	**0,020337**	**2818647**	**9403838**	**0,305430884**	**1,487004733**	**0,001052700**	**2,151136766**	**0,052352424**	**0,058305076**	**0,5804**	**0,3034**





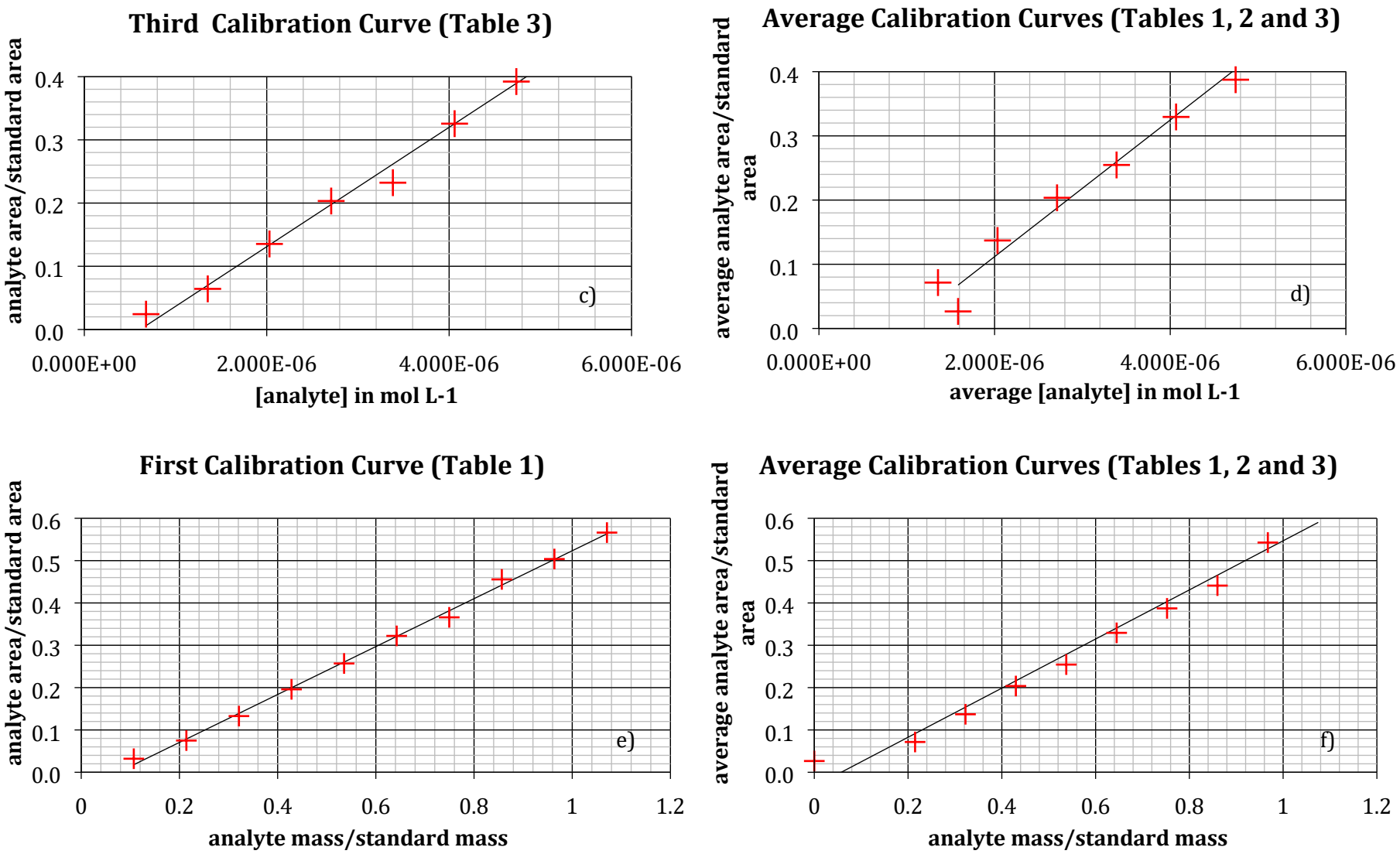
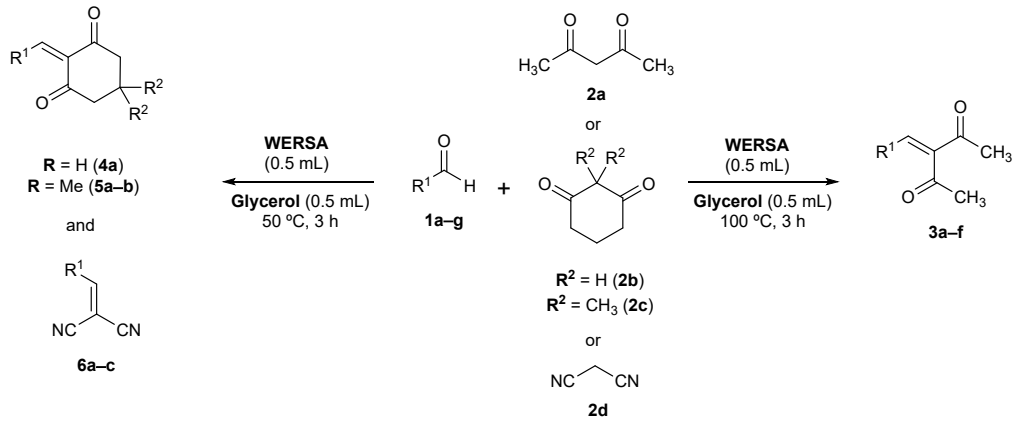


FIG. S1. The slope of line describes the relationship of ratio of PA by SA vs [analyte] mol L^{-1}. The same behavior of slope of line describes the relationship of ratio of PA by SA vs ratio of AM by SM. PA = Product area; AS = Standard area; AM = Analyte mass; SM = Standard mass.

1.3 *PROCEDURE FOR OPTIMIZATION OF THE REACTION CONDITIONS*

As described above, the reaction optimization was based on the yields of **3a** obtained in the experiments of the Table 1 of the manuscript. In these reactions, acetylacetone (**2a**), benzaldehyde (**1a**), WERSA, and co-solvent were added into the 5 mL tube reaction. After the proper time and temperature of the experiments (Tables 1 of the manuscript), the quenching of reaction was done as follows: the crude of reaction was added into the 50 mL becker flask and then 25 mL of ethyl acetate was added. In a second one 25 mL becker flask of a freshly prepared stock solution of IS (anthracene, 0.0200 mol L^{-1}). After that, an aliquot of 500 μL of stock solution of IS was took and added to the sample vial, followed by addition of 300 μL of crude product along with 1500 μL of ethyl acetate. Based on the chromatogram of the sample, the area ratio of **3a**/IS and the mass ratio of **3a**/IS were obtained, which allowed the yield determination of **3a**. In an experiment (Table 1, entry 17), the organic layer containing **3a** and IS was concentrated under vacuum. The product **3a** was obtained as red oil (91 mg, 97% yield) after purification by flash chromatography using hexane and ethyl acetate (100:0; 95:5 93:7 and 90:10, v:v) as eluent.

1.4 *GENERAL PROCEDURE FOR KNOEVENAGEL CONDENSATION*



SCHEME S1. The condensation reaction of aldehydes with 1, 3-dicarbonyl compounds, and malononitrile.

The aldehydes **1a-g** (1.5 mmol, 3.0 equiv.) and 1,3-dicarbonyl compound **2a-c** (0.5 mmol, 1.0 equiv.) were added into 5 mL tube reaction, followed by the addition of WERSA (0.5 mL) and glycerol (0.5 mL). The mixture was coupled in a condenser and heated at 100 °C for 3 h for **2a** and at 50 ºC for **2b-c** for the appropriate time as described at table 2 (Manuscript). After the completion of the reaction (the progress of the reaction was monitored by TLC (10% EtOAc/hexane) and/or GC) ethyl acetate (1 mL) was added into the flask reaction and the organic layer was extracted, dried over anhydrous $MgSO_4$ and the crude product was purified by column chromatography using silica gel 60 (230–400 mesh particle size, 40-63 μm), employing hexane/ethyl acetate with increasing polarity. The desired products **3a-f**, **4a**, **5a-c**, **and 6a-c** were identified by GC–MS, ^{1}H NMR, and ^{13}C NMR spectroscopy when required.

3-(Phenylbenzylidene)-2,4-pentanedione (**3a**).[72] The product was isolated as a red oil (91.3 mg, 97%) by flash chromatography employing a mixture of hexane and ethyl acetate (100:0, 90:10, 80:20, 70:30; v:v) as eluent. **^{1}H NMR** (400 MHz, $CDCl_3$) δ7.50 (s, 1H), 7.39 (m, 5H), 2.41 (s, 3H), 2.27 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 205.4, 196.5, 142.8, 139.8, 132.9, 130.6, 129.7, 129.0, 31.6, 26.4. **MS:** *m/z* (*Rel. Int.)*: 187 (M^+, 100), 43 (96).

3-(2-Chlorophenylbenzylidene)-2,4-pentanedione (**3b**).[73] The product was isolated as a white solid (103.4 mg, 93%) by flash chromatography employing a mixture of hexane and ethyl acetate (100:0, 90:10, 80:20, 70:30 v:v) as eluent. **^{1}H NMR** (1H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.50 – 7.43 (m, 1H), 7.40 – 7.30 (m, 2H), 7.30 – 7.23 (m, 1H), 2.46 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ204.2, 196.3, 144.4, 136.5, 134.4, 131.7, 131.4, 130.2, 130.0, 127.2, 31.6, 26.7. **MS:** *m/z* (*Rel. Int.)*: 187 (M^+, 100), 43 (95.6).

3-(2-Fluorophenylbenzylidene)-2,4-pentanedione (**3c**).[73] The product was isolated as an uncoloured liquid (97.0 mg, 94%) by flash chromatography employing a mixture of hexane and ethyl acetate (70:30; v:v) as eluent. **^{1}H NMR** (400 MHz, $CDCl_3$)δ 7.64 (s, 1H), 7.44 – 7.39 (m, 1H), 7.39 – 7.33 (m, 1H), 7.18 – 7.09 (m, 2H), 2.45 (s, 3H), 2.29 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$)δ204.5, 196.5, 160.6 (d, *J* = 252.5 Hz), 144.1, 132.5 (d, *J* = 8.7 Hz), 132.0 (d, *J* = 4.9 Hz), 130.0, 124.6 (d, *J* = 3.2 Hz), 121.2 (d, *J* = 12.4 Hz), 116.0 (d, *J* = 21.7 Hz), 31.4, 26.5. **MS:** *m/z* (*Rel. Int.)*: 206 (M^+, 33.7), 149 (71.4), 43 (100).

3-(2-Thienylmethylene)-2,4-pentanedione (**3d**).**[72]** The product was isolated as an yellow liquid (89.4 mg, 92%) by flash chromatography employing a mixture of hexane and ethyl acetate (70:30; v:v) as eluent. **^{1}H NMR** (400 MHz, $CDCl_3$)δ7.55 (dd, *J* = 5.1, and 0.4 Hz, 1H), 7.53 (s, 2H), 7.34 (dd, *J* = 3.7, and 0.5 Hz, 1H), 7.10 (dd, *J* = 5.1, and 3.7 Hz, 1H), 2.44 (s, 4H), 2.41 (s, 5H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ205.0, 196.3, 139.3, 140.0, 134.1, 132.4, 132.1, 128.2, 31.3, 26.1. **MS:** *m/z* (*Rel. Int.)*: 194 (M^+, 41), 179 (20), 151 (21), 137 (85), 109 (21), 43 (100).

3-(2-Furanylbenzylidene)-2,4-pentanedione (**3e**).[74] The product was isolated as an uncoloured liquid (79.3 mg, 89%) by flash chromatography employing a mixture of hexane and ethyl acetate (100:0, 90:10, 80:20; v:v) as eluent.**^{1}H NMR** (400 MHz, $CDCl_3$) δ7.55 (d, *J* = 1.8 Hz, 1H), 7.17 (s, 1H), 6.78 (d, *J* = 3.7 Hz, 1H), 6.52 (dd, *J* = 3.5, and 1.8 Hz, 1H), 2.44 (s, 3H), 2.37 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ204.3, 195.8, 149.0, 146.5, 138.4, 125.0, 118.3, 113.0, 31.5, 26.1. **MS:** *m/z* (*Rel. Int.)*: 178 (M^+, 33.5), 121 (85.3), 43 (100).

3-(2-Hydroxymethylfurylbenzylidene)-2,4-pentanedione (**3f**).[74] The product was isolated as an brown liquid (102.1 mg, 98%) by flash chromatography employing a mixture of hexane and ethyl acetate (100:0, 90:10, 80:20; v:v) as eluent. **^{1}H NMR** (400 MHz, $CDCl_3$)δ7.13 (s, 1H), 6.73 (d, *J* = 3.4 Hz, 1H), 6.40 (d, *J* = 3.4 Hz, 1H), 4.58 (s, 2H), 3.15 (br, 1H), 2.43 (s, 3H), 2.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ205.1, 195.9, 159.1, 148.3, 138.0, 125.1, 119.3, 110.6, 57.2, 31.4, 26.0. **MS:** *m/z* (*Rel. Int.)*: 177 (M^+, 28.4), 135 (24.8), 43 (100).

2-Benzylidenecyclohexane-1,3-dione (**4a**).[75] The product was isolated as white solid (87.8 mg, 88%) by flash chromatography employing a mixture of hexane and ethyl acetate

(100:0, 90:10, 80:20; v:v) as eluent. **^{1}H NMR (**400 MHz, DMSO-d_6) δ7.21 – 7.0 (m, 5H), 6.89 (s, 1H), 2.57 – 2.23 (m, 2H), 2.21 – 2.01 (m, 2H), 1.93 – 1.54 (m, 2H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 169.5, 167.8, 145.6, 144.7, 128.9, 125.6, 125.2, 116.2, 39.4, 36.1, 20.2. **MS:** *m/z* (*Rel. Int.)*: 200 (M^+, 69.6), 199 (100), 102 (43).

2-(2-Thyenilmethylene)-5,5-dimethyl-1,3-cyclohexanedione (**5a**).[76] The product was obtained as yellow liquid (104.2 mg, 89%) by flash chromatography employing a mixture of hexane and ethyl acetate (100:0, 90:10, 80:20) as eluent. **^{1}H NMR** (400 MHz, $CDCl_3$) δ8.35 (s, 1H), 7.93 – 7.75 (m, 2H), 7.23 (dd, *J* = 5.1, and 3.9 Hz, 1H), 2.58 (d, *J* = 11.1 Hz, 3H), 1.09 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ197.8, 197.7, 145.0, 143.6, 139.6, 128.2, 53.4, 52.3, 28.6. **MS:** *m/z* (*Rel. Int.)*: 234 (M^+,100), 219 (13), 191 (21), 122 (64), 150 (30).

2-(2-Furanylmethylene)-5,5-dimethyl-1,3-cyclohexanedione (**5b**).[76] The product was obtained as brown liquid (98.9 mg, 91%) by flash chromatography employing a mixture of hexane and ethyl acetate (100:0, 90:10, 80:20) as eluent. **^{1}H NMR** (400 MHz, $CDCl_3$) δ7.45 – 6.79 (m, 1H), 6.28 (dd, *J* = 3.2, and 1,2 Hz, 1H), 6.06 – 5.79 (m, 1H), 5.38 (s, 1H), 2.33 (br, 4H), 1.17 – 1.13 (br, 3H), 1.12 – 1.05 (br, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ189.4, 151.7, 141.0, 114.2, 110.1, 106.3, 46.8, 46.3, 31.4, 29.2. **MS:** *m/z* (*Rel. Int.)*: 218 (M^+,100), 190 (34.9), 162 (77.1), 106 (75.2).

2-(4-Methoxybenzylidene)-5,5-dimethyl-1,3-cyclohexanedione (**5c**).[77] The product was obtained as yellow solid (107.5 mg, 83%) by flash chromatography employing a mixture of hexane and ethyl acetate (100:0, 90:10, 80:20)· **^{1}H NMR** (400 MHz, $CDCl_3$)δ7.05 – 6.72 (m, 5H), 3.76 (s, 3H), 2.37 (s, 4H), 1.22 (s, 3H), 1.09 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ190.3, 189.3, 132.0, 130.0, 127.8, 115.8, 46.5, 32.1, 31.4, 29.6, 27.0. **MS:** *m/z* (*Rel. Int.)*: 258 (M+, 82.7), 257 (100), 227 (76.2).

2-Benzylidenemalononitrile (**5a**).[78] The product was obtained as white solid (73.4 mg, 95%) by flash chromatography employing a mixture of hexane and ethyl acetate (100:0, 90:10, 80:20) as eluent. **^{1}H NMR** (400 MHz, $CDCl_3$) δ7.92 – 7.88 (m, 2H), 7.78 (s, 1H), 7.63 (m, 1H), 7.58 – 7.49 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ160.0, 134.6, 130.7, 129.6, 113.7, 112.6, 82.9. **MS:** *m/z* (*Rel. Int.)*: 154 (M^+,100), 127 (86), 103 (58).

2-(4-Methoxybenzylidene)malononitrile (**5b**).[78] The product was obtained as white solid (89.9 mg, 98%) by flash chromatography employing a mixture of hexane and ethyl acetate (100:0, 90:10, 80:20) as eluent. **^{1}H NMR** (400 MHz, $CDCl_3$) δ7.91 (d, *J* = 9.0 Hz, 2H), 7.65 (s, 1H), 7.01 (d, *J* = 8.9 Hz, 2H), 3.91 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ164.9, 158.8, 133.4, 124.1, 115.2, 114.4, 113.3, 77.0, 55.8. **MS:** *m/z* (*Rel. Int.)*: 114 (38.8), 141 (26.7), 184 (M^+,100).

(2-Furanylbenzylidene)malononitrile (**5c**).[78-79] The product was obtained as brown solid (68.4 mg, 95%) by flash chromatography employing a mixture of hexane and ethyl acetate (100:0, 90:10, 80:20) as eluent. **^{1}H NMR** (400 MHz, $CDCl_3$) δ7.81 (d, *J* = 1.7 Hz, 1H), 7.53 (s, 1H), 7.37 (d, *J* = 4.0 Hz, 1H), 6.73 (dd, *J* = 4.0, and 1.7 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$)δ 149.6, 148.1, 143.1, 123.5, 114.4, 113.8, 112.6. **MS:** *m/z* (*Rel. Int.)*: 89 (30.4), 115 (40.5), 144 (M^+,100).

1.5 *GENERAL PROCEDURE FOR TANDEM KNOEVENAGEL-MICHAEL ADDITION-CYCLIZATION REACTION*

(SCHEME 2) of Manuscript: The benzaldehyde (**1a**) (0.5 mmol, 1.0 equiv., 51 μL), 1,3-cyclohexanedione (**2b**) (1.0 mmol, 56.1 mg, 1.0 equiv.) were added into 5 mL tube reaction, followed by the addition of WERSA (0.5 mL) and glycerol (0.5 mL). The mixture was coupled in a condenser and heated at 100 °C for 3 h. After the completion of the reaction (the progress of the reaction was monitored by TLC (10% EtOAc/hexane) and/or GC) ethyl acetate (2 mL) was added into the flask reaction and the organic layer was extracted, dried over anhydrous $MgSO_4$ and the solvent was removed by vacuum. The brown solid obtained was them washed with EtOAc (3x 15 mL) with immediate precipitation of the white solid that was collected by filtration without further purification. The desired products **7a**, **8a** were identified by GC–MS, ^{1}H NMR and by comparation of melting point.

9-phenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (8a).[80] The product was obtained as white solid (121.9 mg, 83%) by filtration as described above. **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 7.68 – 6.47 (m, 5H), 3.92 (s, 1H), 2.65 – 2.26 (m, 4H), 2.12 (m, 4H), 1.99 – 1.48 (m, 4H). Mp (ºC): found 203–207, Ref: 203-205. **MS:** *m/z* (*Rel. Int.)*: 294 (M^+, 50), 217 (100).

1.6 *SELECTED SPECTRA OF REPRESENTATIVE COMPOUNDS*

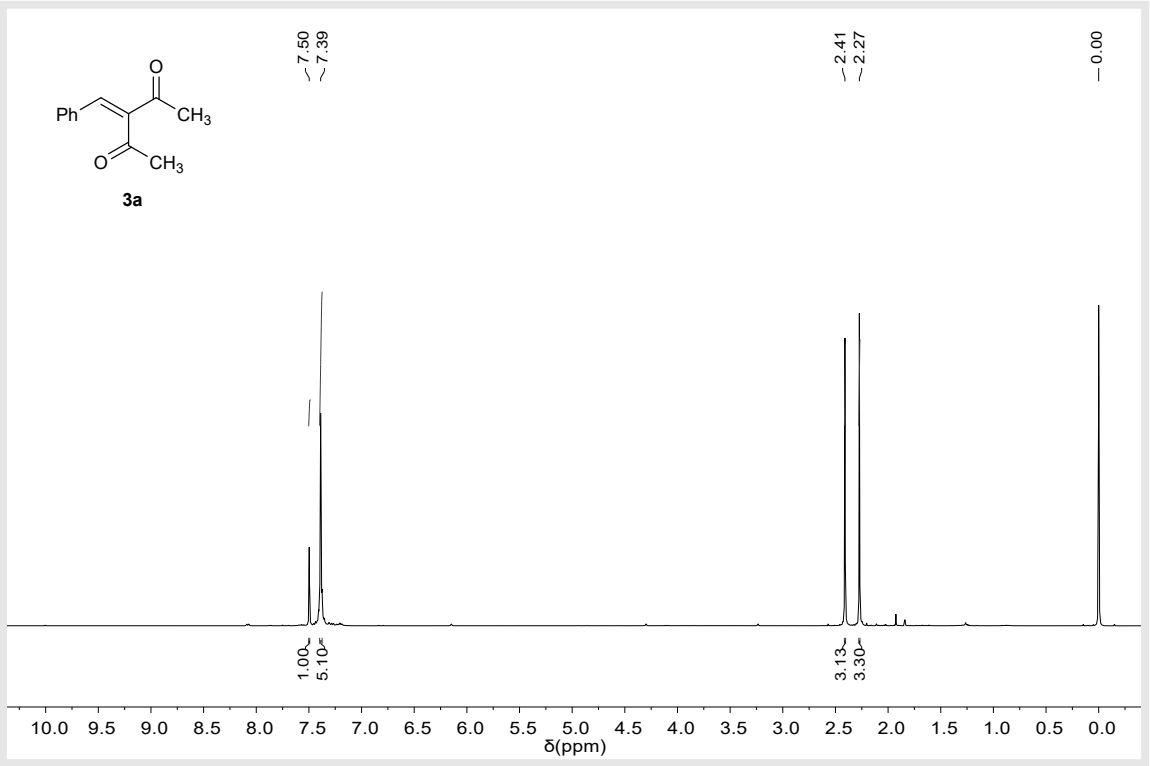


Figure S1. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3a**.

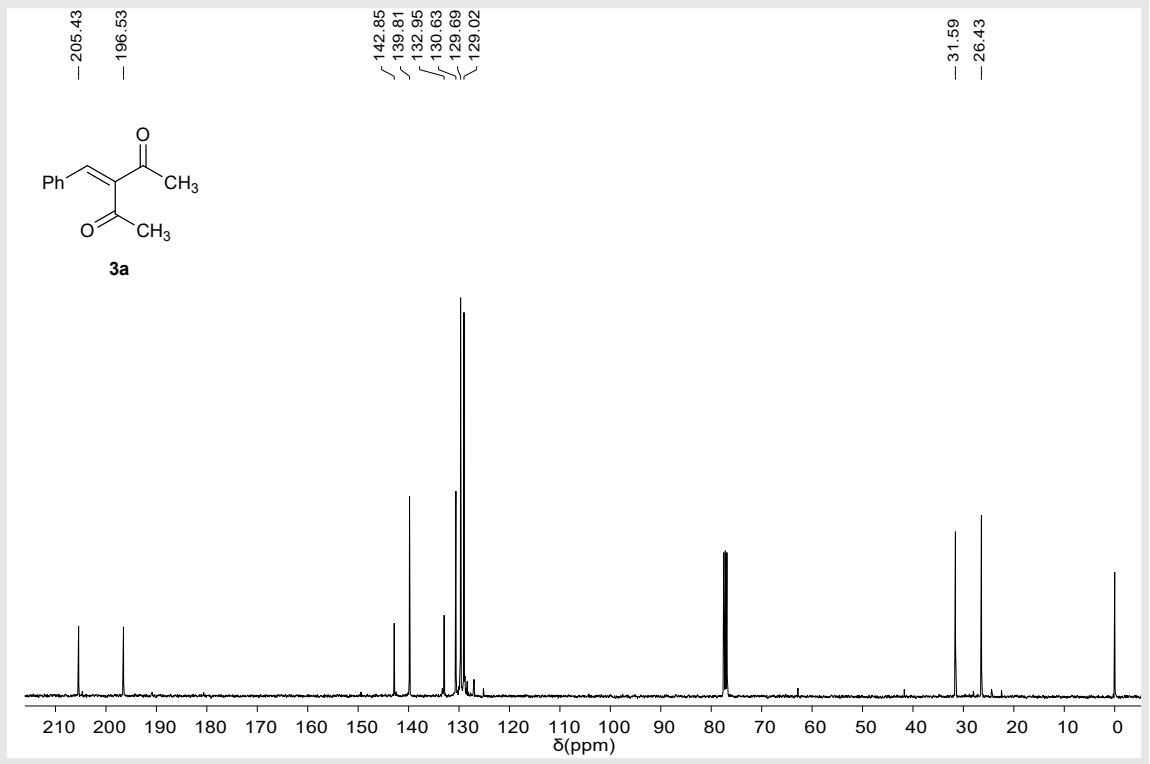


Figure S2. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3a**.

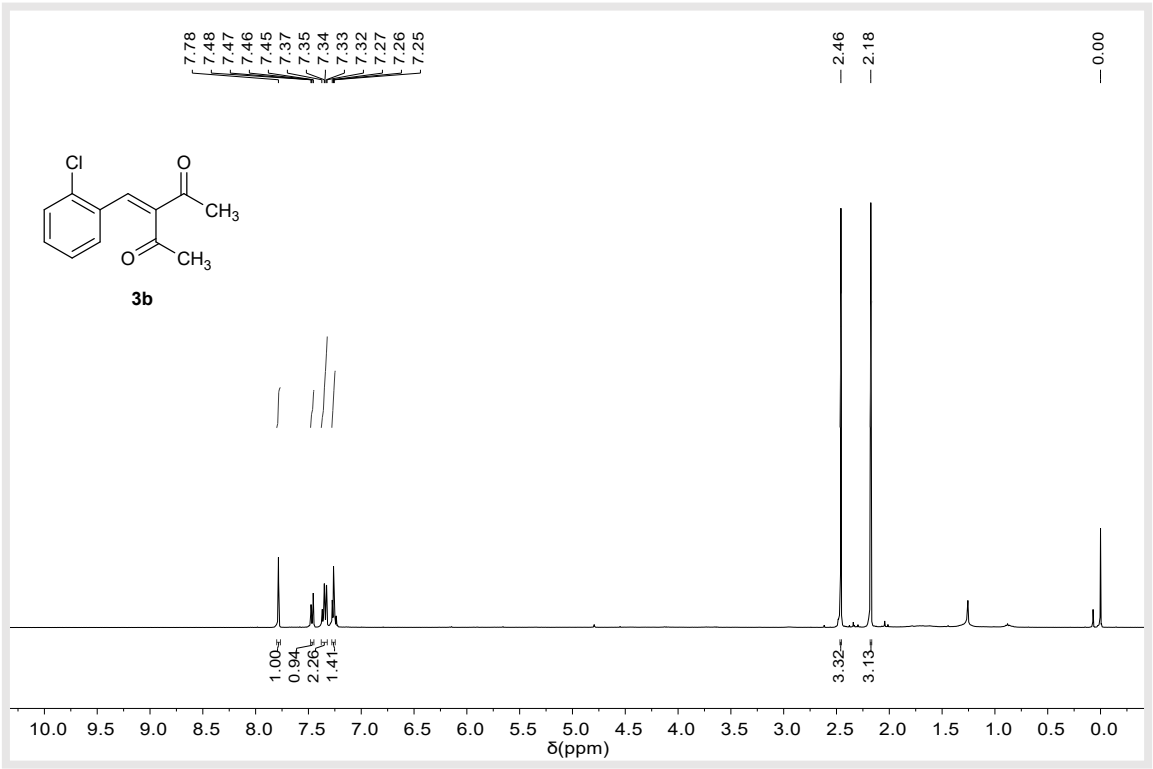


Figure S3. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3b**.

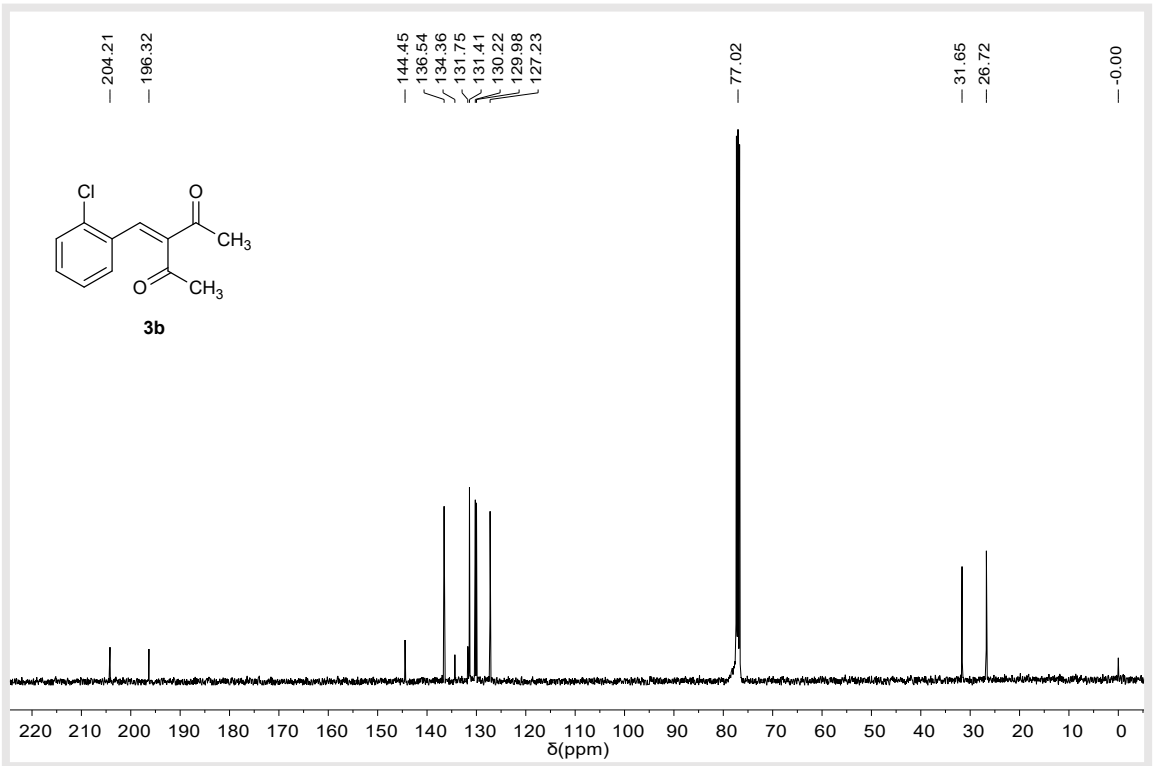


Figure S4. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3b**.

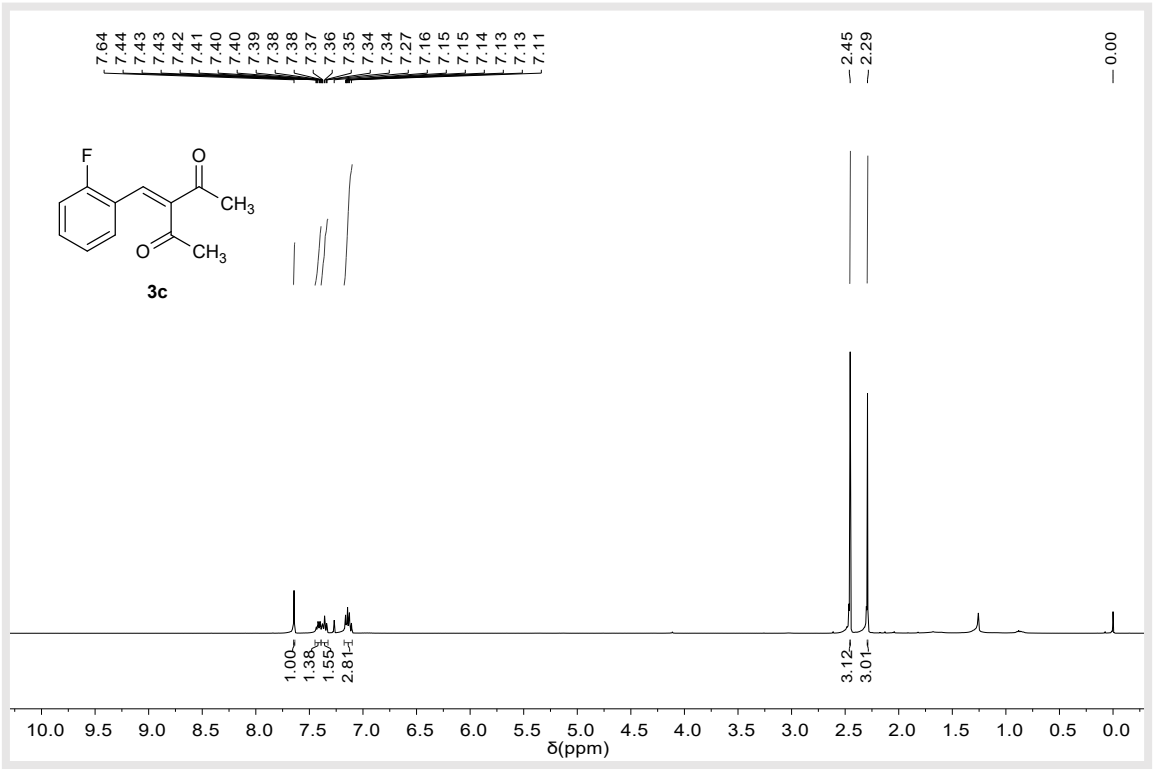


Figure S5. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3c.**

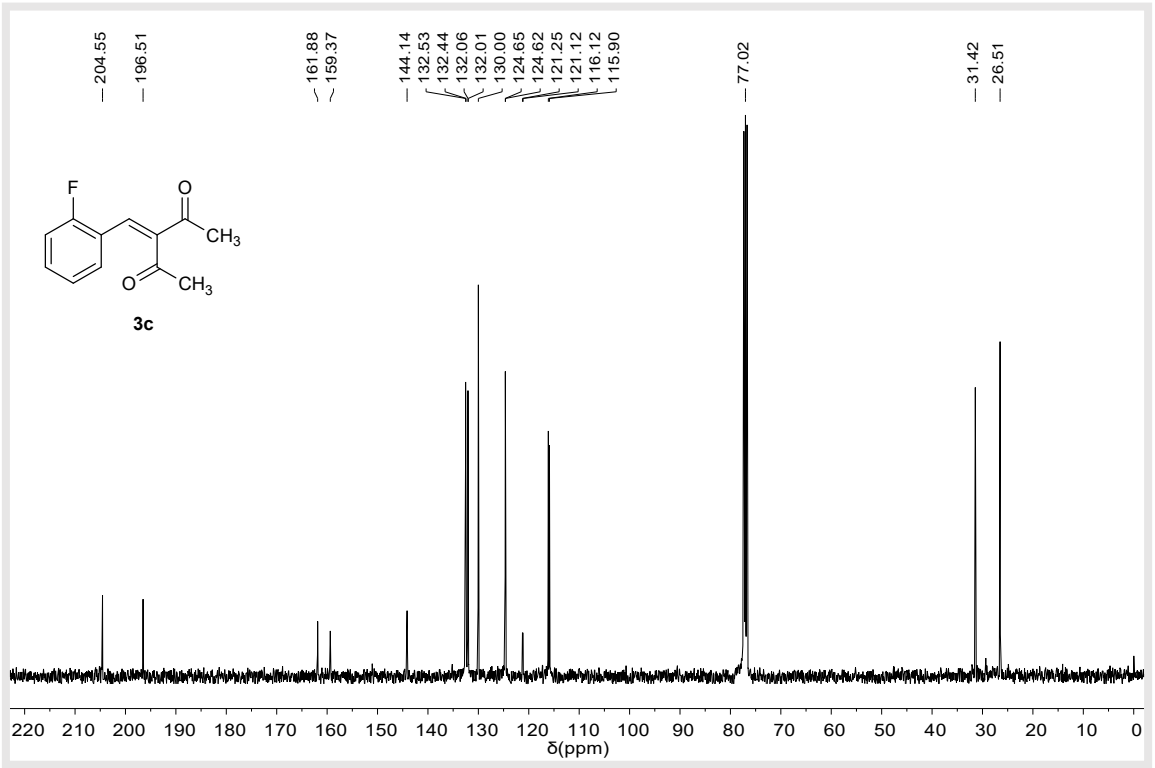


Figure S6. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3c**.

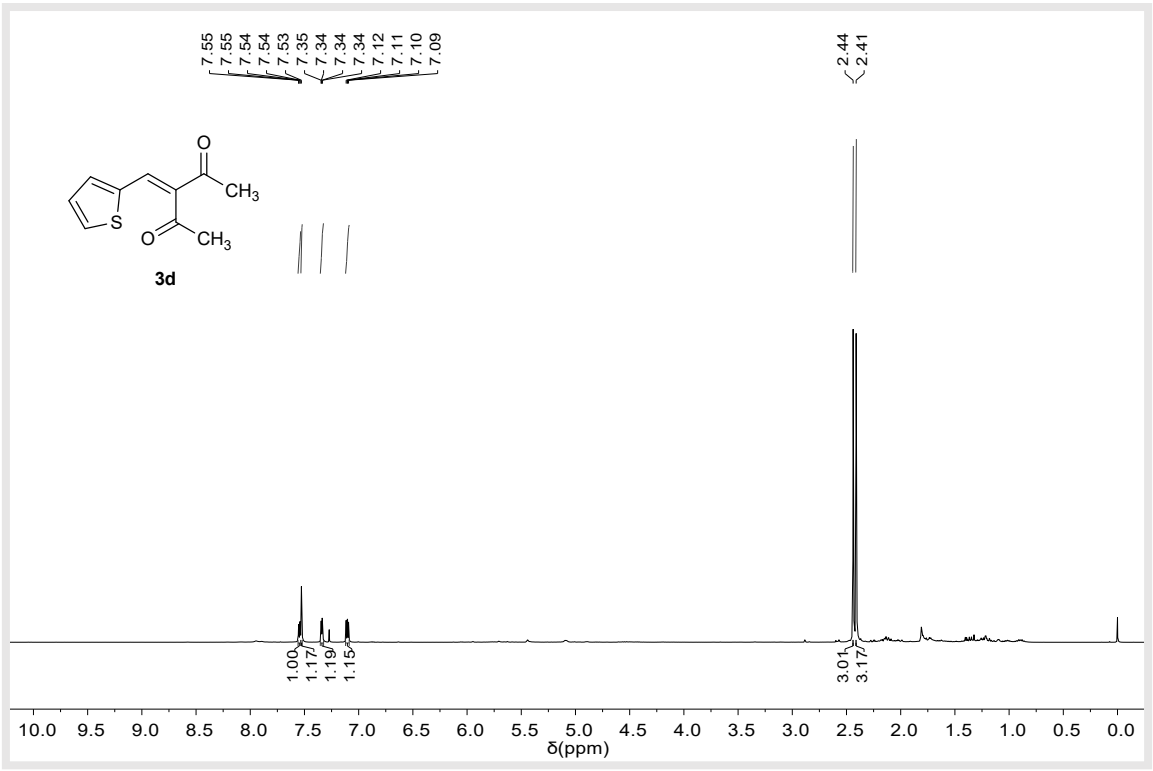


Figure S7. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3d.**

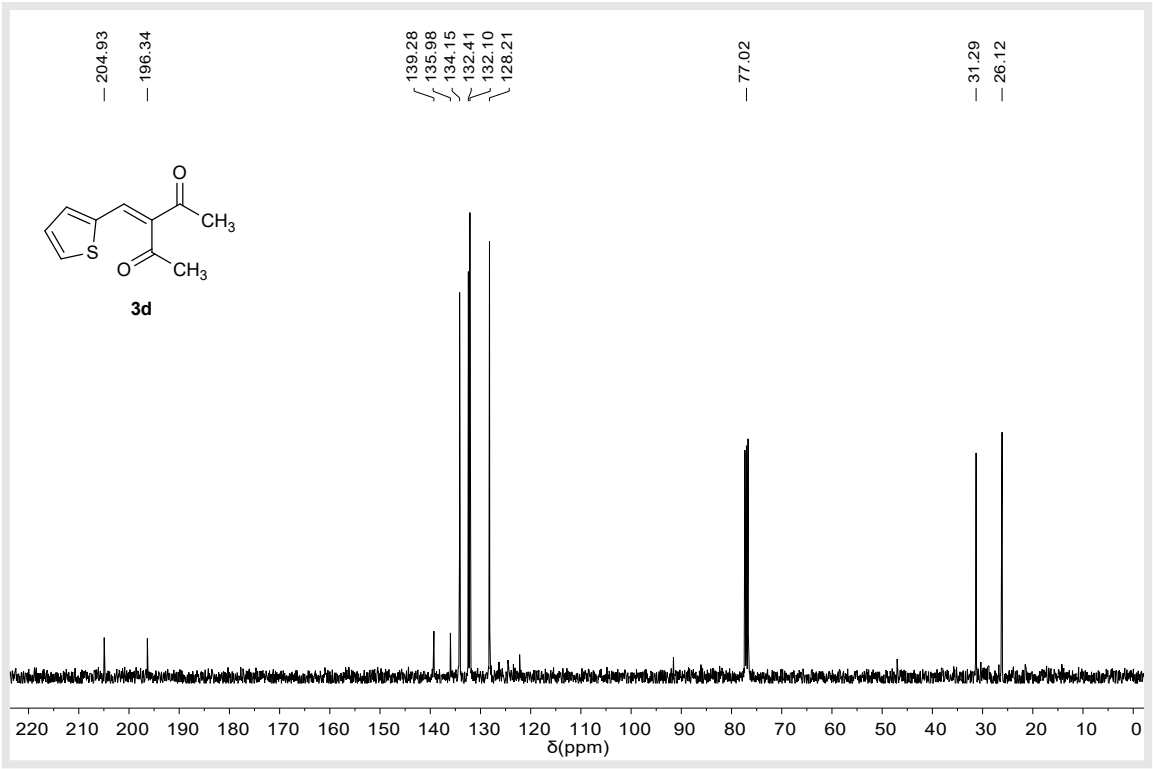


Figure S8. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3d**.

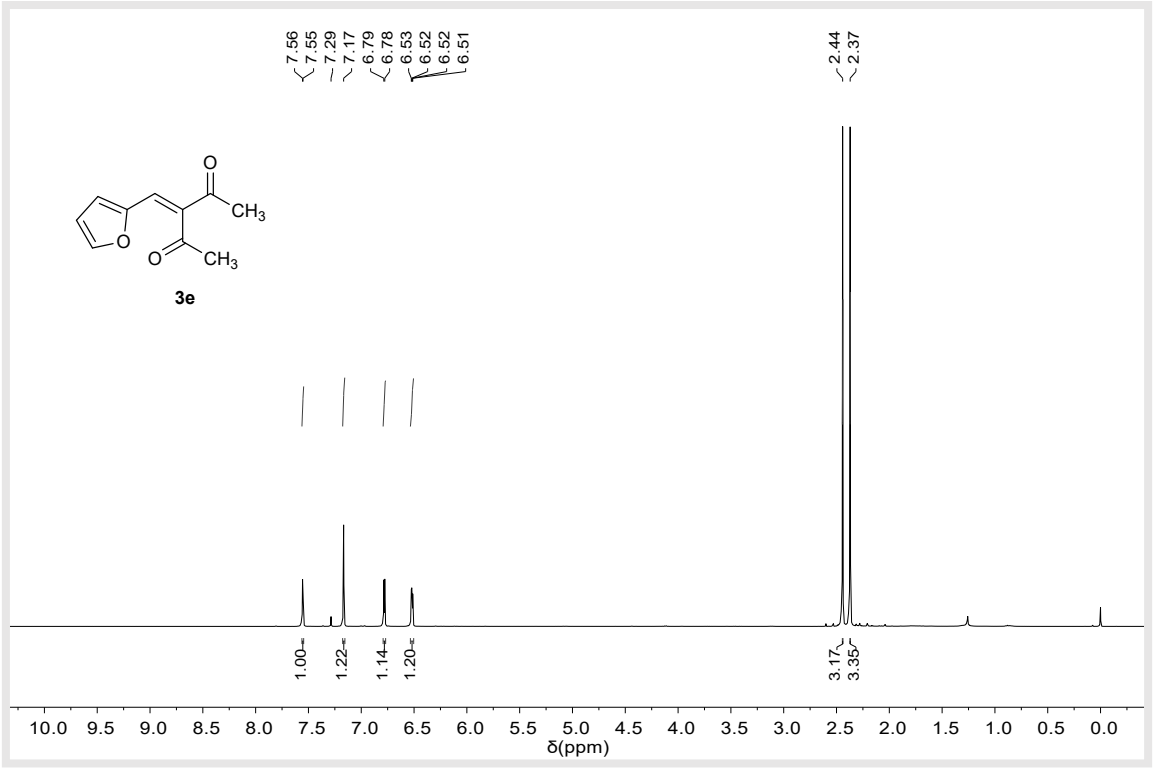


Figure S9. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3e**.

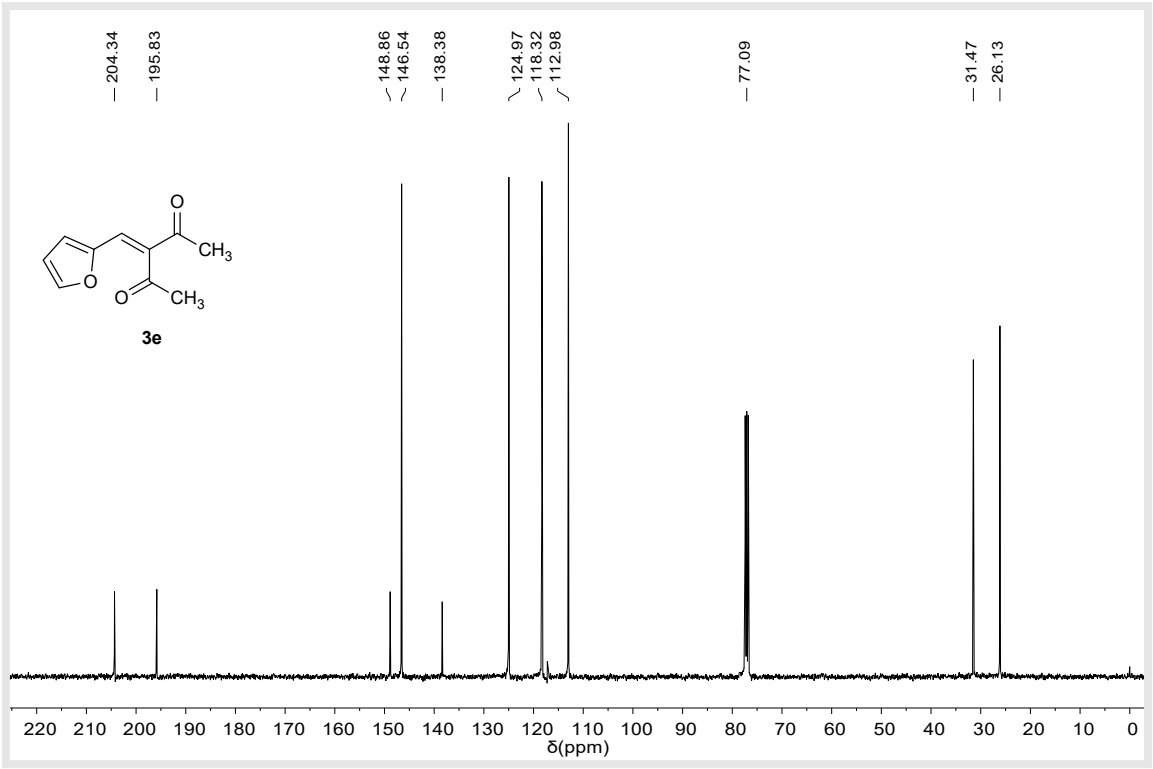


Figure S10. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3e**.

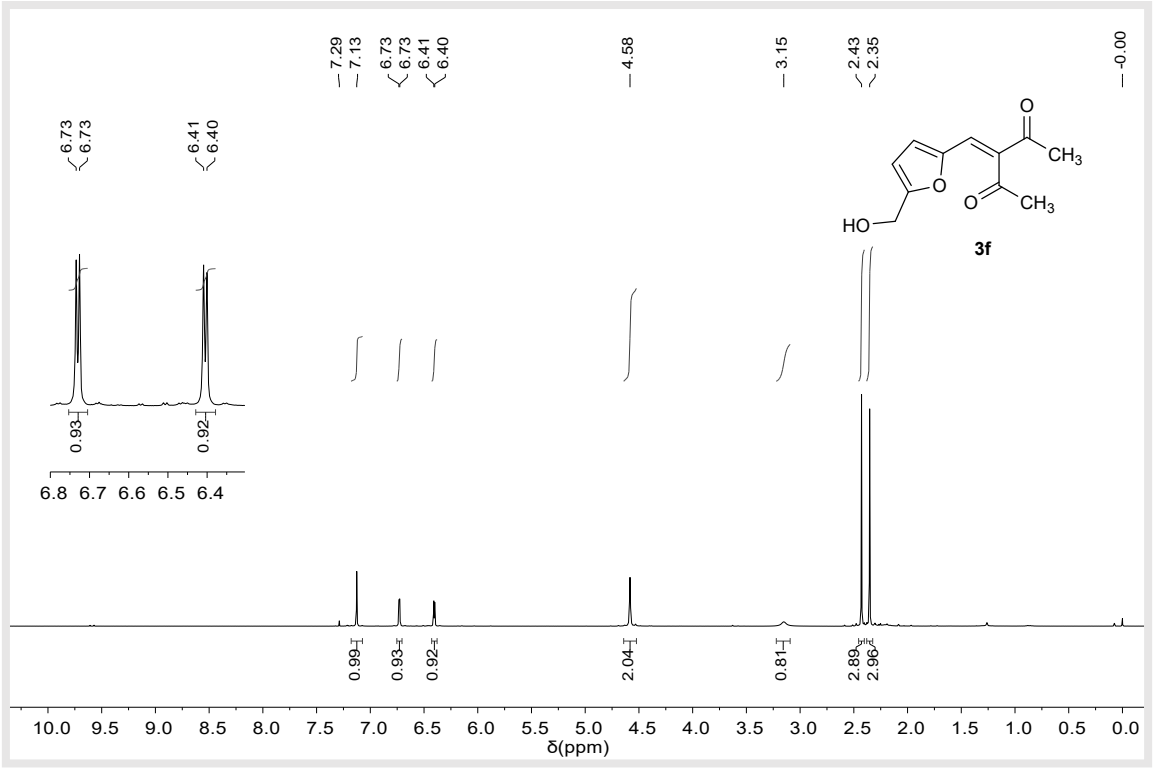


Figure S11. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3f**.

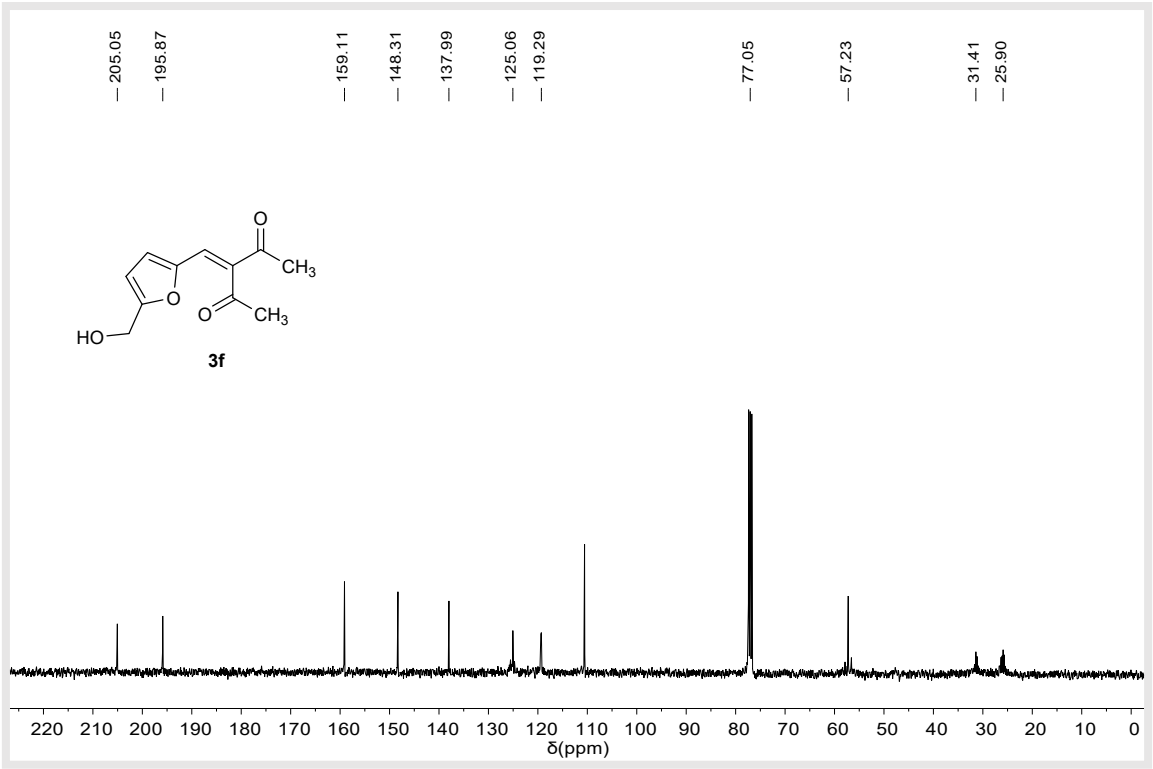


Figure S12. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3f**.

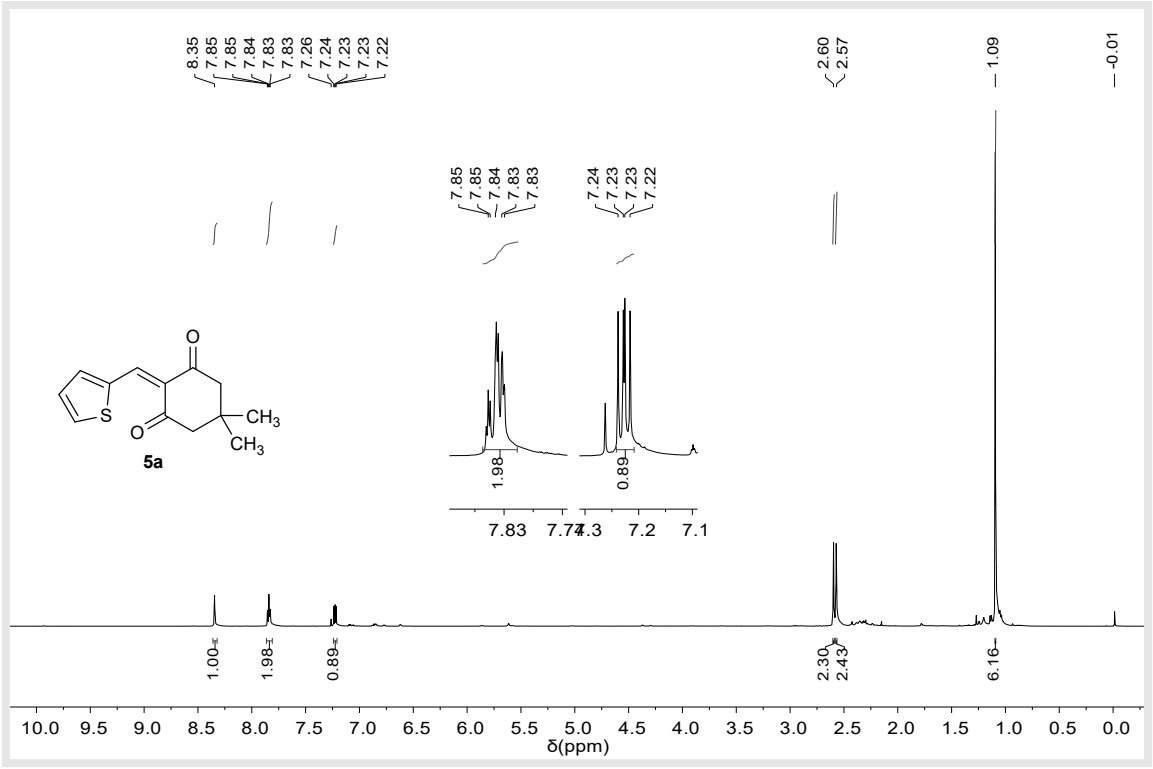


Figure S13. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **5a**.

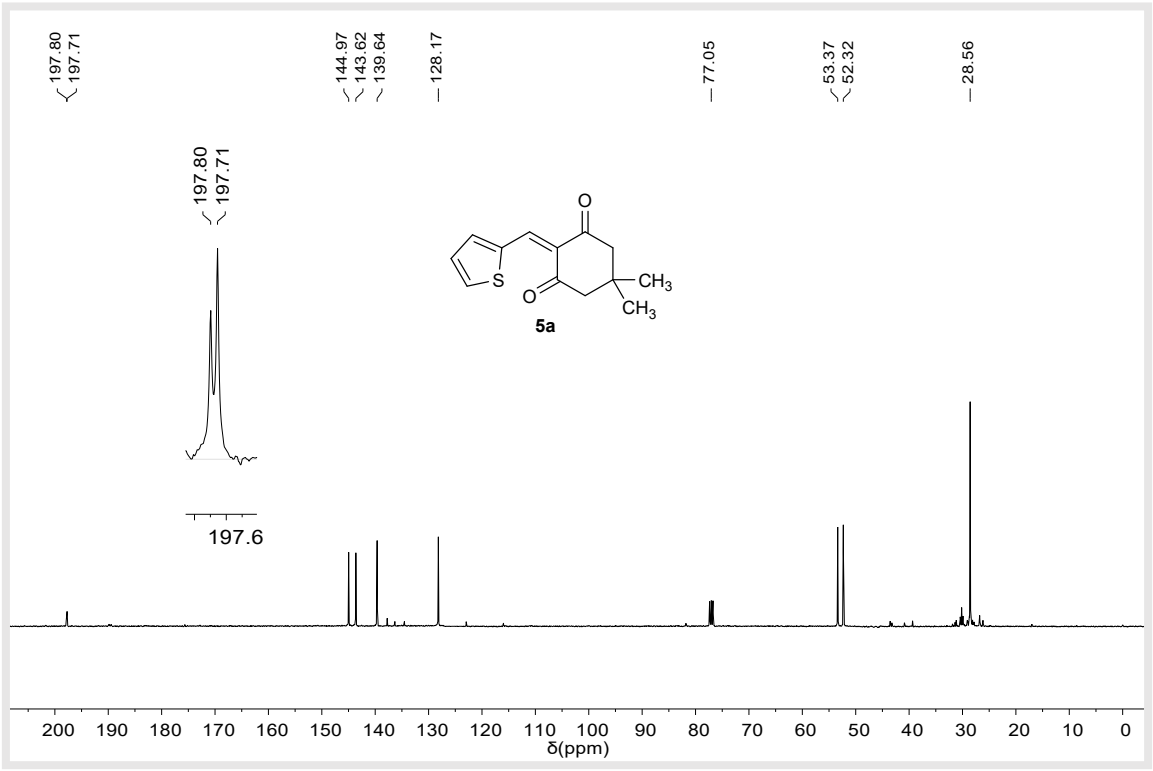


Figure S14. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **5a**.

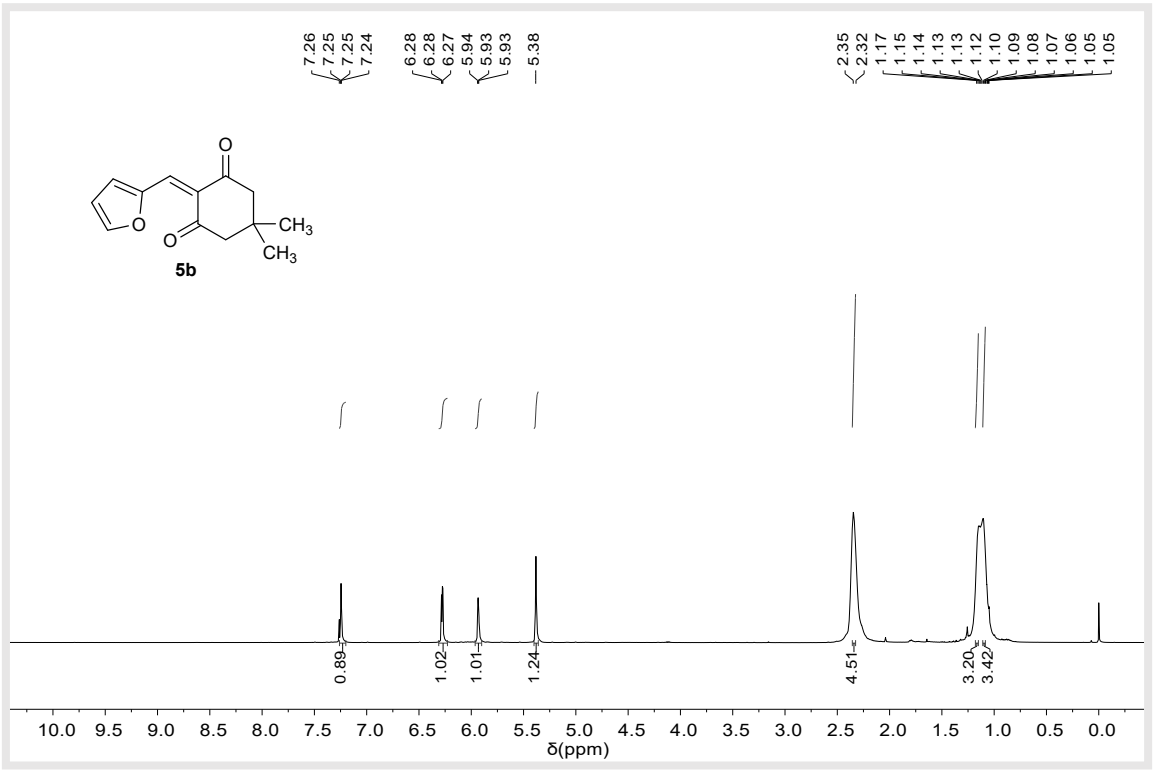


Figure S15. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 5**b**.

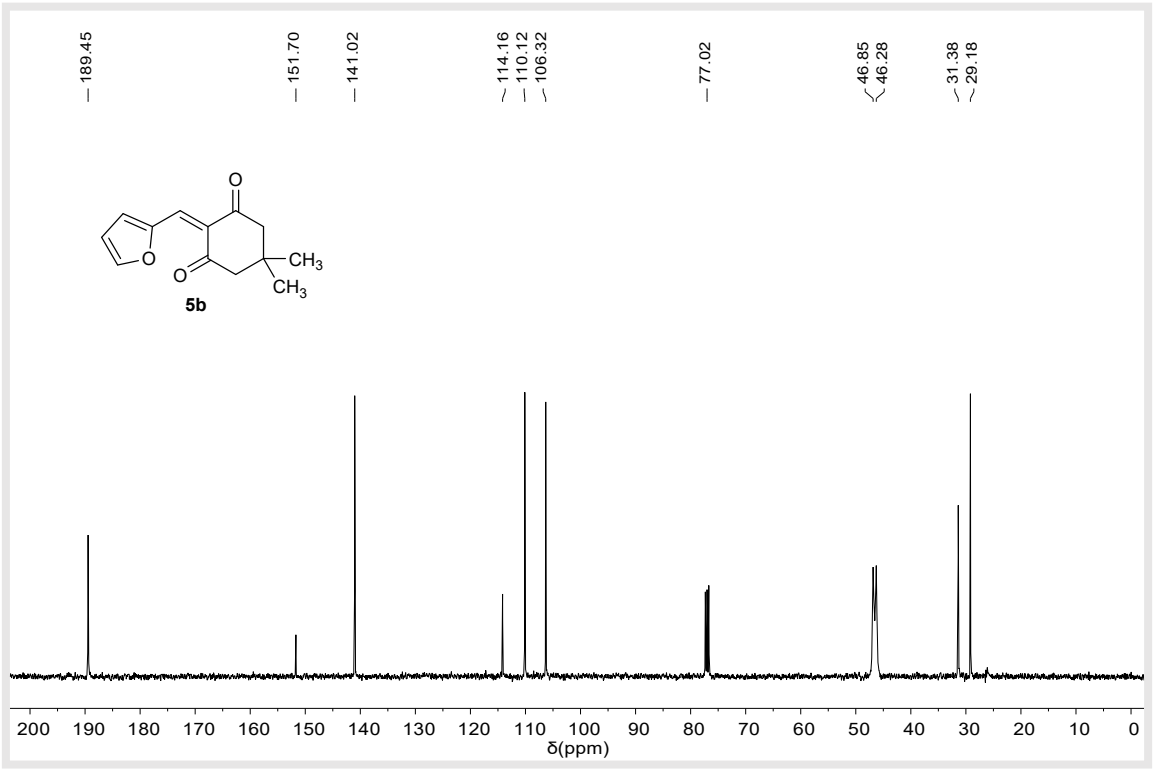


Figure S16. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 5**b**.

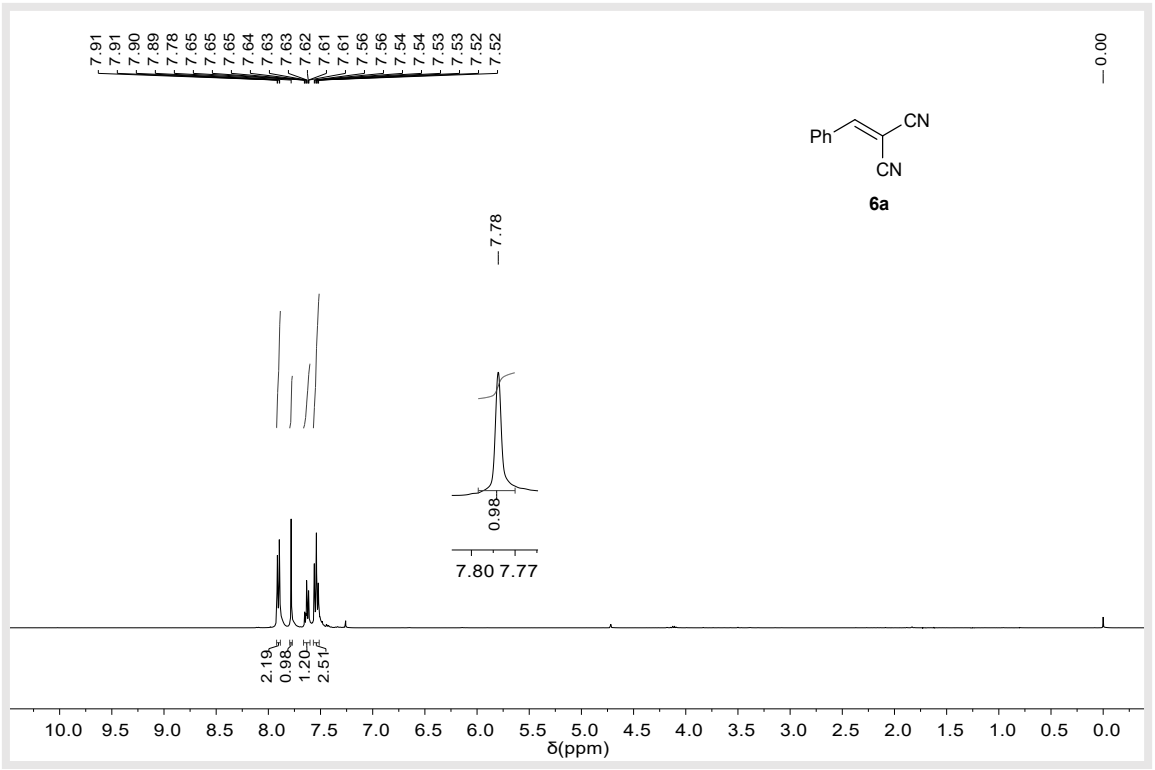


Figure S17. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **6a**.

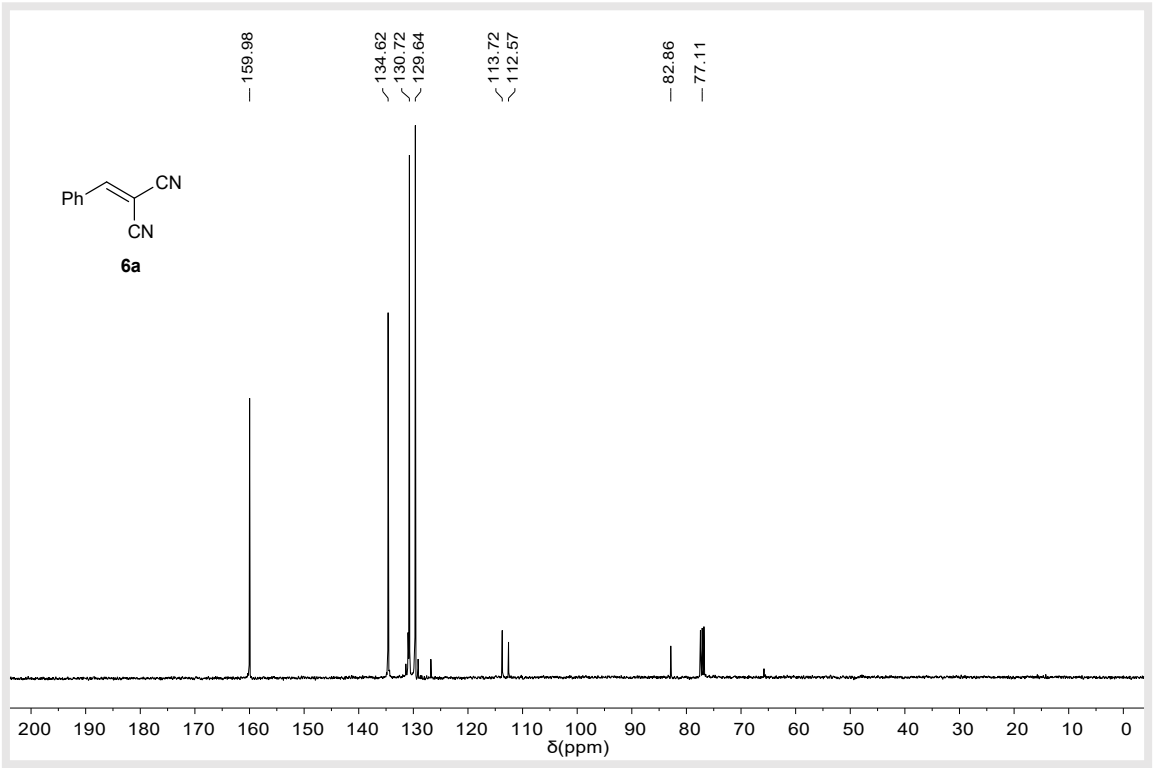


Figure S18. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **6a**.

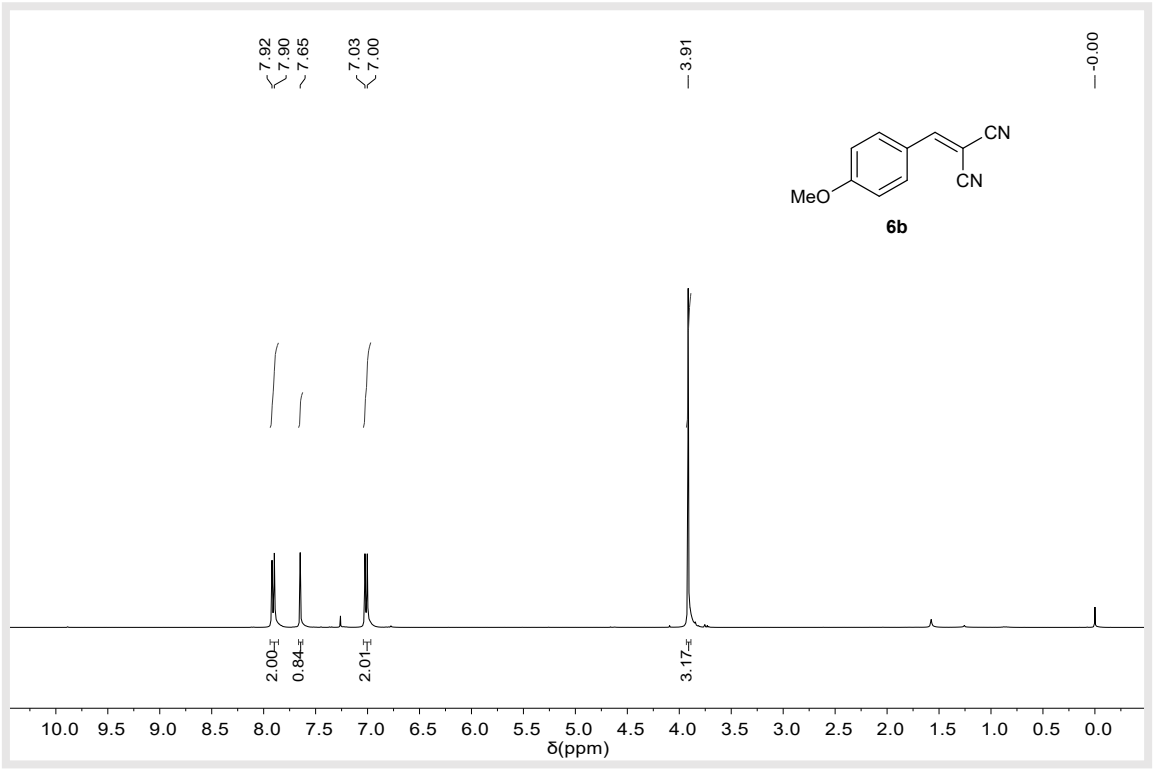


Figure S19. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **6b**.

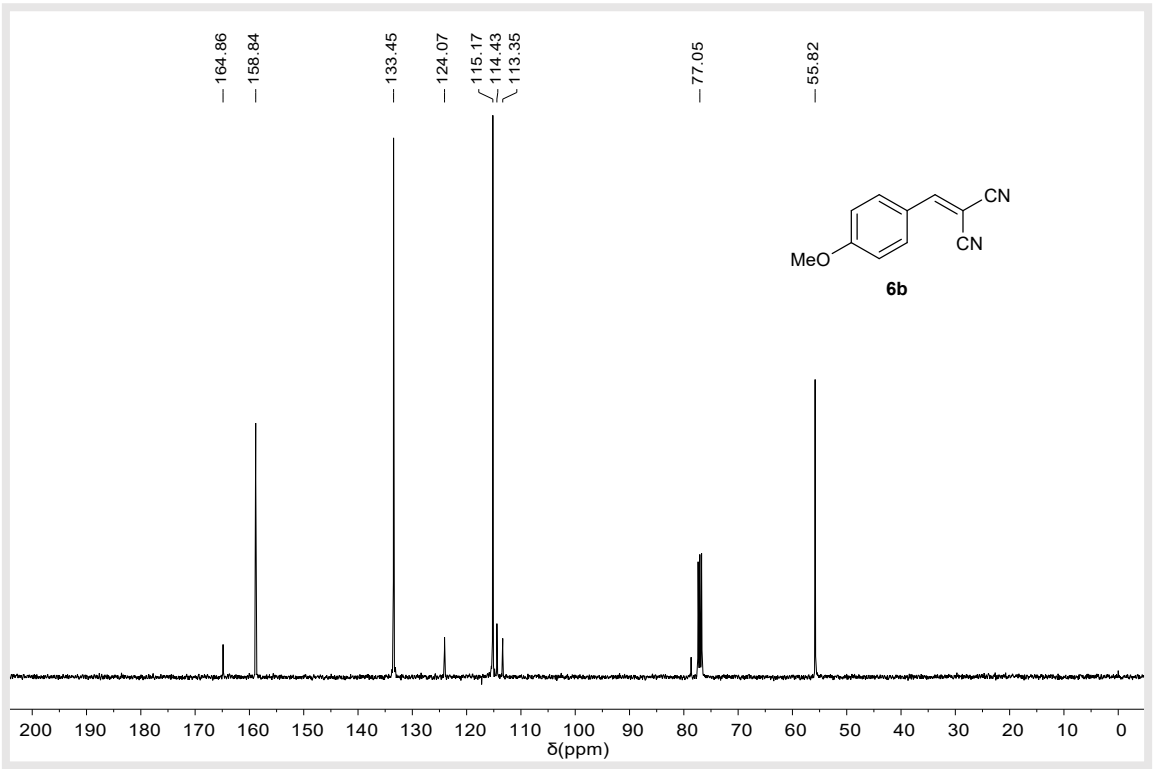


Figure S20. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 6**b**.

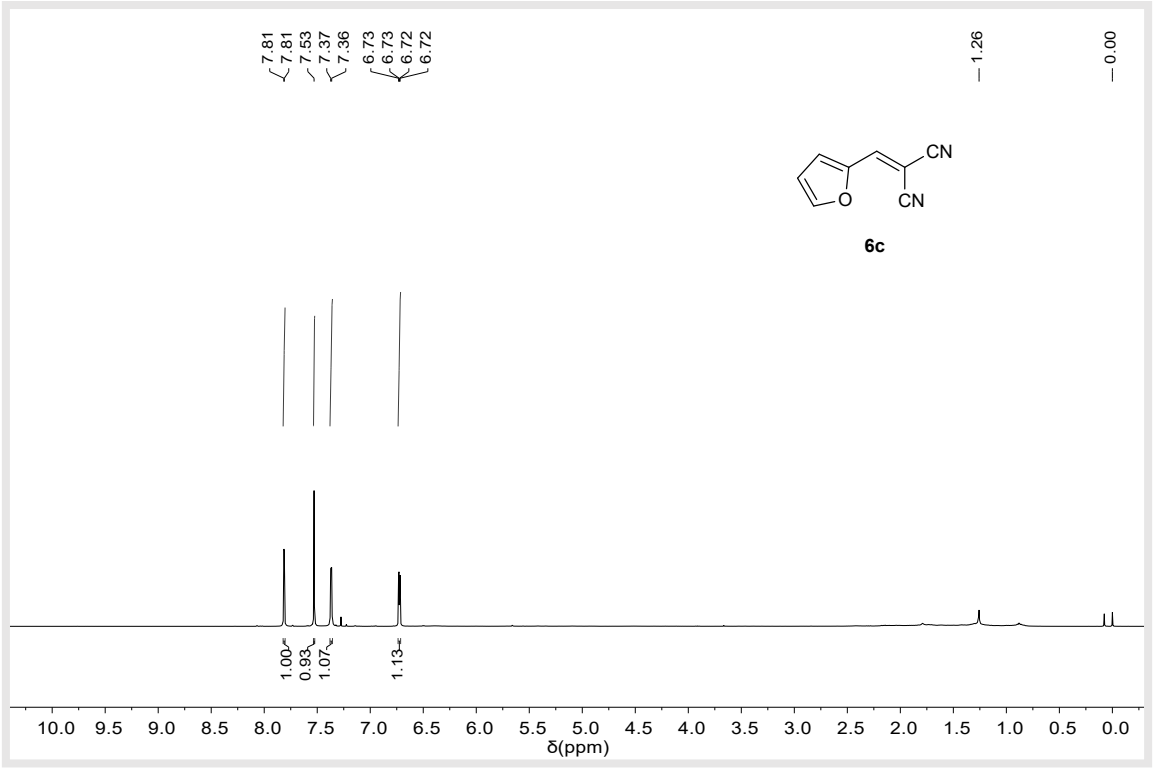


Figure S21. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **6c**.

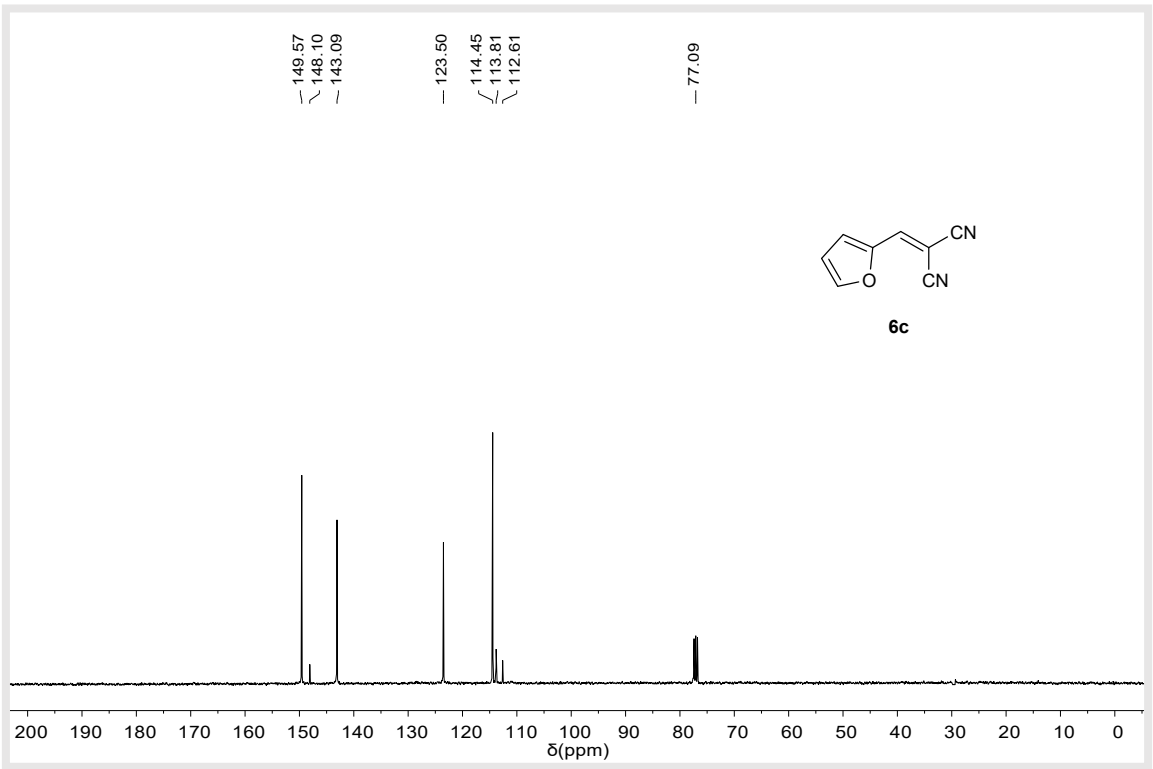


Figure S22. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **6c**.

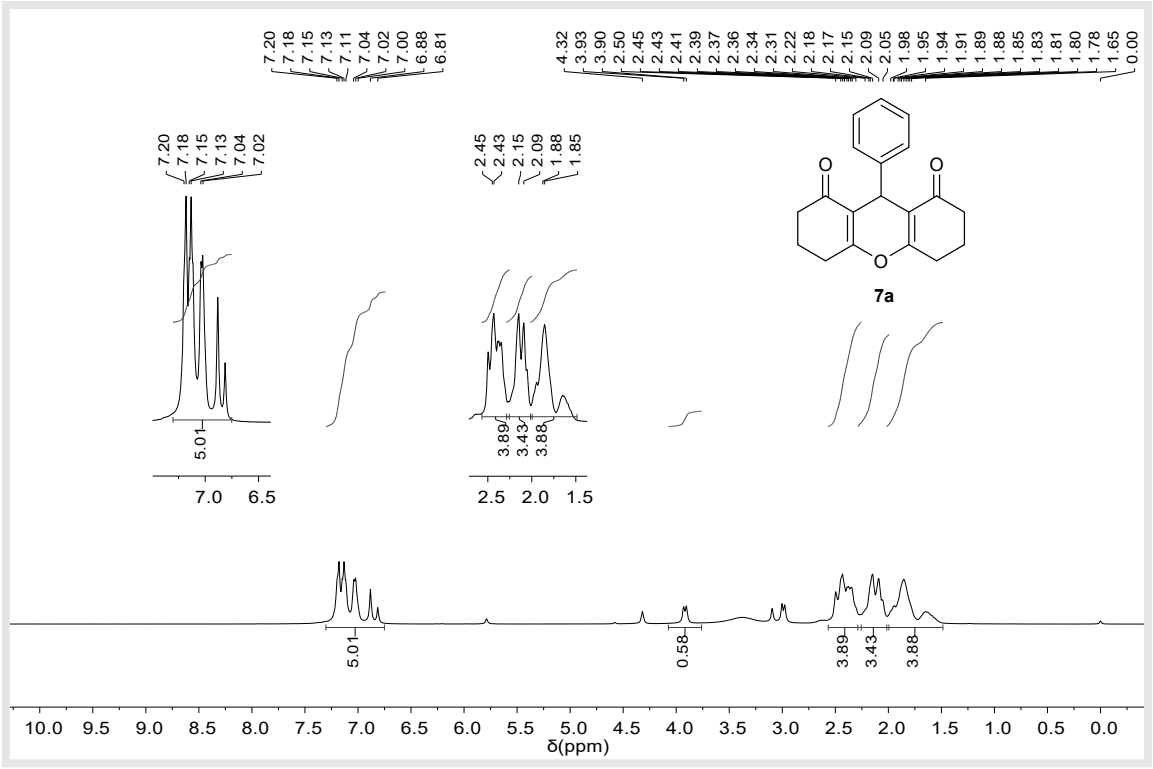


Figure S23. ^{1}H NMR (400 MHz, DMSO-*d6*) spectrum of **7a**.

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