Supporting Information

Reactions of Organolithiums with Dialkyl Oxalates. A Flow Microreactor Approach to Synthesis of Functionalized α-Keto Esters

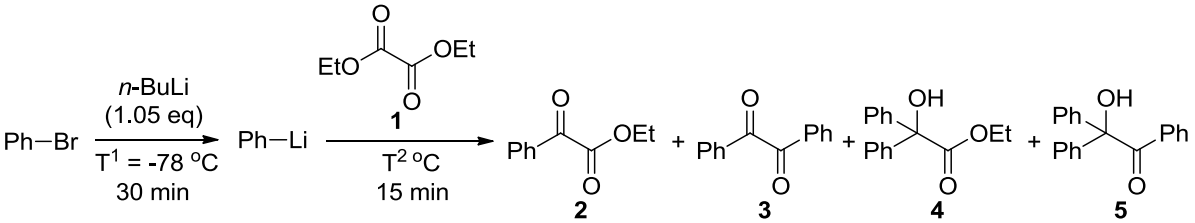
Aiichiro Nagaki, Daisuke Ichinari, and Jun-ichi Yoshida

General

GC analysis was performed on a SHIMADZU GC-2014 gas chromatograph equipped with a flame ionization detector using a fused silica capillary column (column, CBP1; 0.22 mm x 25 m). ^{1}H and ^{13}C NMR spectra were recorded on Varian MERCURYplus-400 (^{1}H 400 MHz and ^{13}C 100 MHz) spectrometer with Me_4Si or $CDCl_3$ as a standard in $CDCl_3$ unless otherwise noted. Gel permeation chromatography (GPC) was carried out on Japan Analytical Industry LC-908 and LC-9201. Diethyl ether and tetrahydrofuran was purchased from Kanto Chemical Co., Inc. as a dry solvent and used without further purification. Hexane was purchased from Wako, distilled before use, and stored over molecular sieves 4A. Bromobenzene, 2-bromoanisole, 3-bromoanisole, 4-bromoanisole, 2-iodonitrobenzene, 3-iodonitrobenzene, 4-iodonitrobenzene, ethyl 2-iodobenzoate, ethyl 3-iodobenzoate, ethyl 4-iodobenzoate, 2-bromobenzonitrile, 3-bromobenzonitrile, 4-bromobenzonitrile, *p*-dibromobenzene, 4,4'-dibromobiphenyl, *p*-diiodobenzene, mestiylbromide, diethyl oxalate, dimethyl oxalate, di-*t*-buthyl oxalate, phenyl lithium, *n*-BuLi, and acetic acid were commercially available.

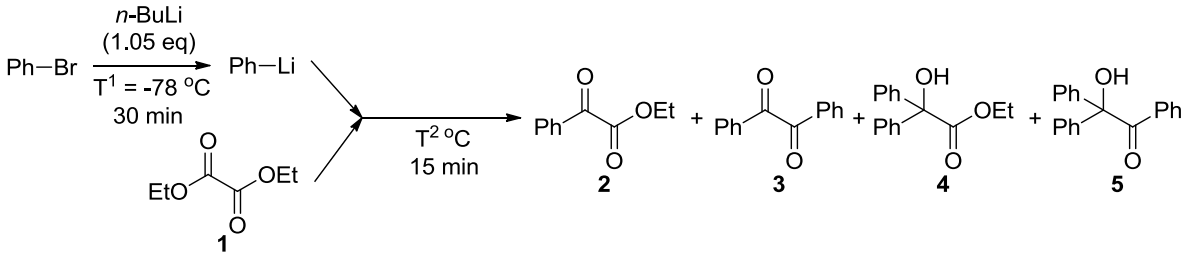
Stainless steel (SUS304) T-shaped micromixer with inner diameter of 250, 500 and 800 μm were manufactured by Sanko Seiki Co., Inc. Stainless steel (SUS316) microtube reactors with inner diameter of 1000 μm was purchased from GL Sciences. The micromixer and microtube reactors were connected with stainless steel fittings (GL Sciences, 1/16 OUW). The microflow system was dipped in a cooling bath to control the temperature. Solutions were introduced to the flow microreactor system using syringe pumps, Harvard Model 11, equipped with gastight syringes purchased from SGE.

General Procedure for Br-Li Exchange Reaction of Bromobenzene Followed by the Reaction with Diethyl Oxalate in a Macrobatch Systems (Method-A).



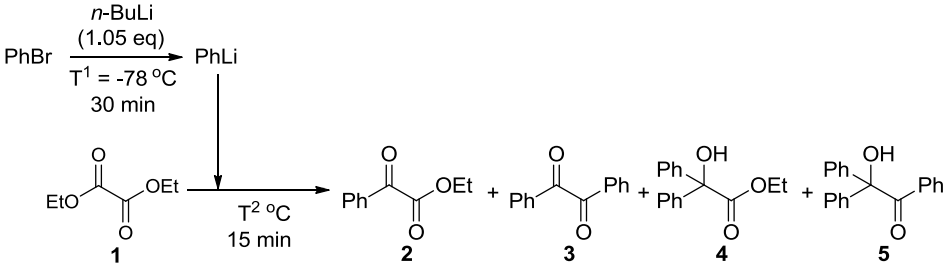
A solution of *n*-BuLi (0.42 M in *n*-hexane, 1.0 mL) was added to a mixture solution of bromobenzene (0.10 M in THF, 4.0 mL) at T^1 = -78 °C at regular pace for 1.0 min. After stirring for 30 min, a solution of diethyl oxalate (**1**) (0.20 M in THF, 2.0 mL) was added to this mixture at regular pace for 30 seconds. After stirring for 15 min, a solution of acetic acid (10% in water, 1.0 mL) was added into the reaction mixture. After stirring at T^2 °C for 5 min, a cooling bath was removed. When the reaction mixture reached room temperature, yields of ethyl 2-phenyl-2-oxoacetate (**2**), benzil (**3**), ethyl 2-hydroxy-2,2-diphenylacetate (**4**), and 2-hydroxy-1,2,2-triphenylethanone (**5**) were determined by GC analysis using an internal standard (dodecane). Dodecane as an internal standard was added to an aliquot of the product solution after work up. The results are summarized in Table S-1.

General Procedure for Br-Li Exchange Reaction of Bromobenzene Followed by the Reaction with Diethyl Oxalate in a Macrobatch Systems (Method-B).



A solution of *n*-BuLi (0.42 M in *n*-hexane, 1.0 mL) was added to a mixture solution of bromobenzene (0.10 M in THF, 4.0 mL) at T^1 = -78 °C at regular pace for 1.0 min. After stirring for 30 min, this solution and a solution of diethyl oxalate (**1**) (0.20 M in THF, 2.0 mL) was simultaneously added to the reaction vessel at regular pace for 30 seconds. After stirring for 15 min, a solution of acetic acid (10% in water, 1.0 mL) was added into the reaction mixture. After stirring at T^2 °C for 5 min, a cooling bath was removed. When the reaction mixture reached room temperature, yields of ethyl 2-phenyl-2-oxoacetate (**2**), benzil (**3**), ethyl 2-hydroxy-2,2-diphenylacetate (**4**), and 2-hydroxy-1,2,2-triphenylethanone (**5**) were determined by GC analysis using an internal standard (dodecane). Dodecane as an internal standard was added to an aliquot of the product solution after work up. The results are summarized in Table S-1.

General Procedure for Br-Li Exchange Reaction of Bromobenzene Followed by the Reaction with Diethyl Oxalate in a Macrobatch Systems (Method-C).

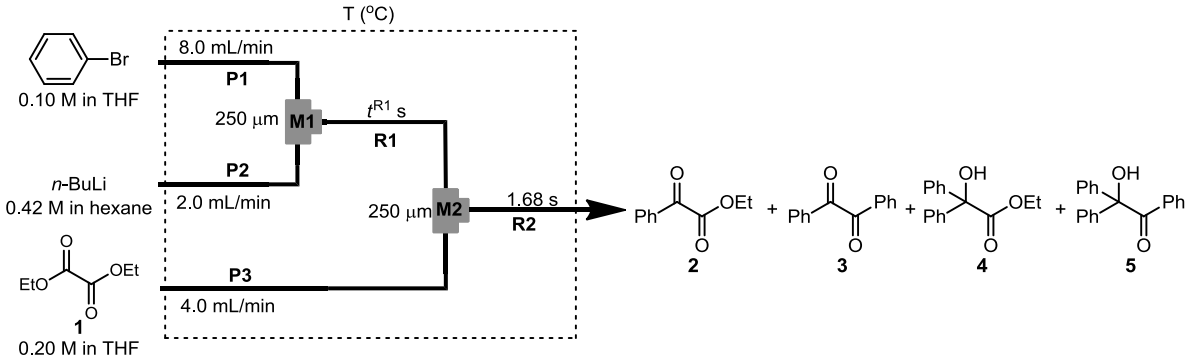


A solution of *n*-BuLi (0.42 M in *n*-hexane, 1.0 mL) was added to a mixture solution of bromobenzene (0.10 M in THF, 4.0 mL) at T^1 = -78 °C at regular pace for 1.0 min. After stirring for 30 min, this mixture was added to a solution of diethyl oxalate (**1**) (0.20 M in THF, 4.0 mL) at regular pace for 30 seconds. After stirring at T^2 °C for 15 min, a solution of acetic acid (10% in water, 1.0 mL) was added into the reaction mixture. After stirring at T^2 °C for 5 min, a cooling bath was removed. When the reaction mixture reached room temperature, yields of ethyl 2-phenyl-2-oxoacetate (**2**), benzil (**3**), ethyl 2-hydroxy-2,2-diphenylacetate (**4**), and 2-hydroxy-1,2,2-triphenylethanone (**5**) were determined by GC analysis using an internal standard (dodecane). Dodecane as an internal standard was added to an aliquot of the product solution after work up. The results are summarized in Table S-1.

Table S-1 Reaction of diethyl oxalate and phenyllithium using a conventional macro batch system

T^2 (°C)	method of addition	conversion of **1** (%)	yield (%)			
			2	**3**	**4**	**5**
-78	addition of **1** to PhLi (Method-A)	59	25	21	0	1
-78	simultaneous addition of **1** and PhLi (Method-B)	66	56	17	0	6
-78	addition of PhLi to **1** (Method-C)	70	63	9	0	7
-60	addition of PhLi to **1** (Method-C)	71	66	13	0	3
-40	addition of PhLi to **1** (Method-C)	81	62	15	0	5
-20	addition of PhLi to **1** (Method-C)	83	55	18	0	9
0	addition of PhLi to **1** (Method-C)	82	53	15	0	7
20	addition of PhLi to **1** (Method-C)	72	43	18	0	10

Effect of Temperature for Br-Li Exchange Reaction of Bromobenzene Followed by the Reaction with Diethyl Oxalate in the Flow Microreactor System

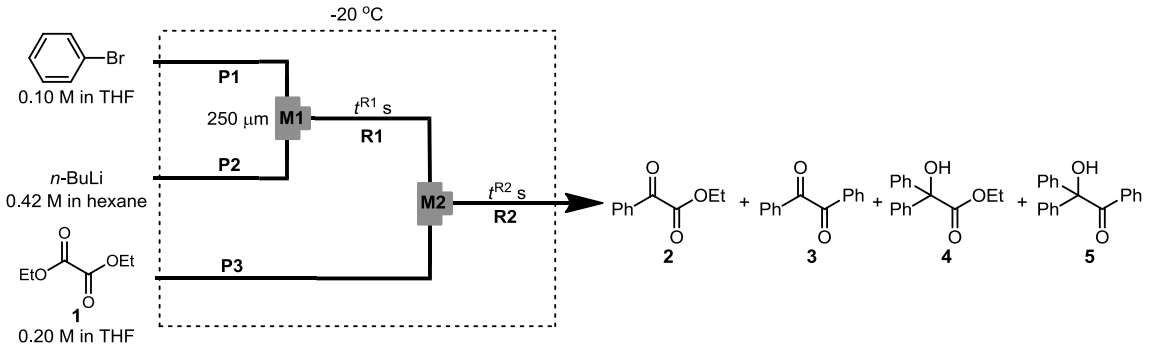


A flow microreactor system consisting of two T-shaped micromixers (**M1** and **M2**), two microtube reactors (**R1** and **R2**), and three tube pre-cooling units (**P1** (inner diameter ϕ = 1000 μm, length L = 100 cm), **P2** (ϕ = 1000 μm, L = 50 cm) and **P3** (ϕ = 1000 μm, L = 100 cm)) was used. A solution of bromobenzene (0.10 M in THF) (flow rate: 8.0 mL min^{-1}) and a solution of *n*-BuLi (0.42 M in hexane) (flow rate: 2.0 mL min^{-1}) were introduced to **M1** (ϕ = 250 μm) by syringe pumps. The resulting solution was passed through **R1** (ϕ = 1000 μm, L = 50 or 200 cm) and was mixed with a solution of diethyl oxalate (0.20 M in THF) (flow rate: 4.0 mL min^{-1}) in **M2** (ϕ = 250 μm). The resulting solution was passed through **R2** (ϕ = 1000 μm, L = 50 cm). After a steady state was reached, an aliquot of the product solution was collected for 30 s and was treated with 10% aqueous AcOH solution. Yields of ethyl 2-phenyl-2-oxoacetate (**2**), benzil (**3**), ethyl 2-hydroxy-2,2-diphenylacetate (**4**), and 2-hydroxy-1,2,2-triphenylethanone (**5**) were determined by GC analysis using an internal standard (dodecane). Dodecane as an internal standard was added to an aliquot of the product solution after work up. The results are summarized in Table S-2.

Table S-2 Reaction of diethyl oxalate with phenyllithium generated from bromobenzene using a flow microreactor system. The effect of the temperarure.

T (°C)	t^{R1} (s)	t^{R2} (s)	Conversion of **1** (%)	yield (%)			
				2	**3**	**4**	**5**
-78	9.42	1.68	96	87	3	0	0
-60	9.42	1.68	100	96	1	0	0
-40	2.35	1.68	100	96	2	0	0
-20	2.35	1.68	98	93	5	0	0
0	2.35	1.68	95	88	7	0	0
20	2.35	1.68	93	82	9	0	1

Effect of Mixing for Br-Li Exchange Reaction of Bromobenzene Followed by the Reaction with Diethyl Oxalate in the Flow Microreactor System



A flow microreactor system consisting of two T-shaped micromixers (**M1** and **M2**), two microtube reactors (**R1** and **R2**), and three tube pre-cooling units (**P1** (inner diameter ϕ = 1000 μm, length L = 100 cm), **P2** (ϕ = 1000 μm, L = 50 cm) and **P3** (ϕ = 1000 μm, L = 100 cm)) was used. A solution of bromobenzene (0.10 M in THF) and a solution of *n*-BuLi (0.42 M in hexane) were introduced to **M1** (ϕ = 250 μm) by syringe pumps. The resulting solution

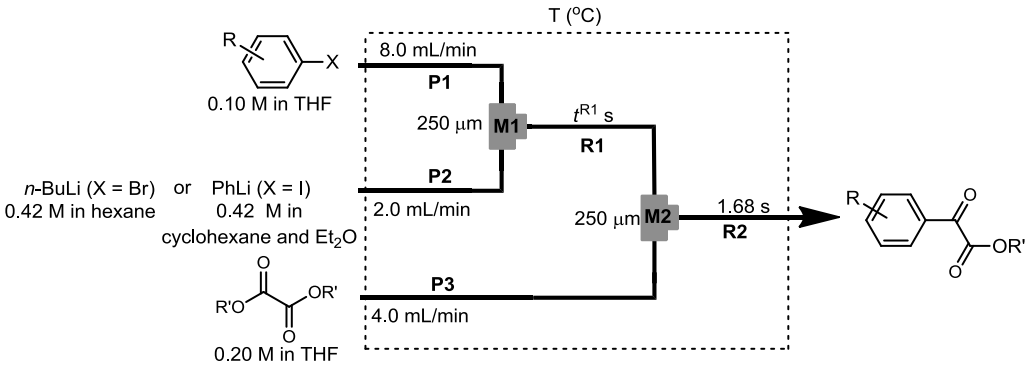
was passed through **R1** (ϕ = 1000 μm, L = 50 cm) and was mixed with a solution of diethyl oxalate (0.20 M in THF) (flow rate: 4.0 mL min^{-1}) in **M2**. The resulting solution was passed through **R2** (ϕ = 1000 μm, L = 50 cm). After a steady state was reached, an aliquot of the product solution was collected for 30 s and was treated with 10% aqueous AcOH solution. Yields of ethyl 2-phenyl-2-oxoacetate (**2**), benzil (**3**), ethyl 2-hydroxy-2,2-diphenylacetate (**4**), and 2-hydroxy-1,2,2-triphenylethanone (**5**) were determined by GC analysis using an internal standard (dodecane). Dodecane as an internal standard was added to an aliquot of the product solution after work up. The results are summarized in Table S-3.

Table S-3 Reaction of diethyl oxalate and phenyllithium generated from bromobenzene using a flow microreactor system. The effect of mixing.

inner diameter of **M2** (μm)	flow rate (mL/min)			t^{R1} (s)	t^{R2} (s)	conversion of **1** (%)	yield (%)			
	bromo benzene	*n*-BuLi	diethyl oxalate				**2**	**3**	**4**	**5**
250	10	2.5	5	1.89	1.35	98	95	5	0	0
250	8	2	4	2.35	1.68	98	93	5	0	0
250	6	1.5	3	3.14	2.24	96	90	5	0	0
250	4	1	2	4.71	3.37	92	80	8	0	2
250	2	0.5	1	7.85	6.73	60	29	10	0	5
500	8	2	4	2.35	1.68	88	77	17	0	2
800	8	2	4	2.35	1.68	72	47	22	0	8

The reactions were carried out at T = -20 °C

Typical Procedure for X-Li Exchange Reaction of Halobenzene Followed by the Reaction with Dialkyl Oxalate in the Flow Microreactor System



A flow microreactor system consisting of two T-shaped micromixers (**M1** and **M2**), two microtube reactors (**R1** and **R2**), and three tube pre-cooling units (**P1** (inner diameter ϕ = 1000 μm, length L = 100 cm), **P2** (ϕ = 1000 μm, L = 50 cm) and **P3** (ϕ = 1000 μm, L = 100 cm)) was used. A solution of halobenzene (0.10 M in THF) (flow rate: 8.0 mL min^{-1}) and a solution of *n*-BuLi (0.42 M in hexane) (flow rate: 2.0 mL min^{-1}) were introduced to **M1** (ϕ = 250 μm) by syringe pumps. The resulting solution was passed through **R1** and was mixed with a solution of diethyl oxalate (0.20 M in THF) (flow rate: 4.0 mL min^{-1}) in **M2** (ϕ = 250 μm). The resulting solution was passed through **R2** (ϕ = 1000 μm, L = 50 cm). After a steady state was reached, an aliquot of the product solution was collected for 30 s and was treated with 10% aqueous AcOH solution. A yield of desired product was determined by GC analysis using an internal standard or isolation by column chromatography. Dodecane as an internal standard was added to an aliquot of the product solution after work up.

Ethyl 2-phenyl-2-oxoacetate: Obtained in 93% yield (T = -20 °C, t^{R1} = 4.71 s (L = 100 cm, ϕ =1000 μm)) (GC ^{t}R 17.2 min). The spectral data were identical to those reported in the literature.[1]

Methyl 2-phenyl-2-oxoacetate: Obtained in 90% yield (T = -20 °C, t^{R1} = 4.71 s (L = 100 cm, ϕ =1000 μm)) (GC ^{t}R 16.8 min). The spectral data were identical to those reported in the literature.[2]

***t*-Butyl 2-phenyl-2-oxoacetate:** Obtained in 75% yield (T = -20 °C, t^{R1} = 4.71 s (L = 100 cm, ϕ =1000 μm)) (GC ^{t}R 18.5 min). The spectral data were identical to those reported in the literature.[2]

Ethyl 2-(4-methoxyphenyl)-2-oxoacetate: Obtained in 91% yield (T = -20 °C, t^{R1} = 2.35 s (L = 50 cm, ϕ =1000 μm)) (GC ^{t}R 21.2 min). The spectral data were identical to those reported in the literature.[1]

Ethyl 2-(3-methoxyphenyl)-2-oxoacetate: Obtained in 95% yield (T = -20 °C, t^{R1} = 2.35 s (L = 50 cm, ϕ =1000 μm)) (GC ^{t}R 20.5 min). The spectral data were identical to those reported in the literature.[3]

Ethyl 2-(2-methoxyphenyl)-2-oxoacetate: Obtained in 94% yield (T = -20 °C, t^{R1} = 2.35 s (L = 50 cm, ϕ =1000 μm)) (GC ^{t}R 20.5 min). The spectral data were identical to those reported in the literature.[1]

Ethyl 2-(4-cyanophenyl)-2-oxoacetate: Obtained in 75% yield (T = -20 °C, t^{R1} = 0.28 s (L = 6.0 cm, ϕ =1000 μm)) (GC ^{t}R 20.2 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 5/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (t, *J* = 7.6 Hz, 3H), 4.48 (q, *J* = 7.2 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 2H) , 8.16(d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 62.9, 117.5, 117.8, 130.4, 132.5, 135.5, 162.3, 184.3; HRMS (ESI) *m/z* calcd for $C_{11}H_{10}N_1O_3$ ($[M+H]^+$): 204.0651, found: 204.0655.

Ethyl 2-(3-cyanophenyl)-2-oxoacetate: Obtained in 87% yield (T = -20 °C, t^{R1} = 0.28 s (L = 6.0 cm, ϕ =1000 μm)) (GC ^{t}R 20.4 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 20/1 to 10/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (t, *J* = 7.2 Hz, 3H), 4.49 (q, *J* = 7.2 Hz, 2H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.94 (dt, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H), 8.31 (dt, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H),8.38 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 62.9, 113.5, 117.4, 129.9, 133.5, 133.7, 133.8, 137.4, 162.2, 183.6; HRMS (ESI) *m/z* calcd for $C_{11}H_{10}N_1O_3$ ($[M+H]^+$): 204.0651, found: 204.0655.

Ethyl 2-(2-cyanophenyl)-2-oxoacetate: Obtained in 63% yield (T = -20 °C, t^{R1} = 0.28 s (L = 6.0 cm, ϕ =1000 μm)), After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 20/1 to 10/1) (GC ^{t}R 20.0 min): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (t, *J* = 7.2 Hz, 3H), 4.49 (q, 7.2Hz, 2H), 7.79-7.76 (m, 2H), 7.89-7.87 (m, 1H), 8.05-8.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 63.1, 112.2, 116.6, 131.8, 132.7, 134.0, 134.8, 135.2, 162.2, 183.9; HRMS (ESI) *m/z* calcd for $C_{11}H_{10}$ N_1O_3 ($[M+H]^+$): 204.0655, found: 204.0653.

Ethyl 2-(4-nitrophenyl)-2-oxoacetate: Obtained in 89% yield (T = -20 °C, t^{R1} = 0.041 s (L = 3.5 cm, ϕ = 250 μm)) (GC ^{t}R 21.5 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 10/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (t, *J* = 7.2 Hz, 3H), 4.50(q, *J* = 7.2 Hz, 2H), 8.25 (d, *J* = 9.2 Hz, 1H) , 8.36(d, *J* = 9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 63.0, 123.9, 131.2, 137.0, 151.1, 162.2, 184.1; HRMS (ESI) *m/z* calcd for $C_{11}H_{10}N_1O_3$ ($[M+H]^+$): 224.0553, found: 224.0550.

Ethyl 2-(3-nitrophenyl)-2-oxoacetate: Obtained in 92% yield (T = -20 °C, t^{R1} = 0.041 s (L = 3.5 cm, ϕ = 250 μm)) (GC ^{t}R 21.6 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 10/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (t, *J* = 7.2 Hz, 3H), 4.51(q, *J* = 7.2 Hz, 2H), 7.77 (t, *J* = 8.0 Hz, 1H) , 8.41(dd, *J* = 8.0 Hz, *J* = 1.6 Hz, 1H) , 8.52(dd, *J* = 8.0 Hz, *J* = 2.0 Hz, 1H) , 8.91(d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 63.0, 125.0, 128.8, 130.2, 132.8, 135.4, 148.4, 162.1, 183.5; HRMS (ESI) *m/z* calcd for $C_{11}H_{10}N_1O_3$ ($[M+H]^+$): 224.0553, found: 224.0549.

Ethyl 2-(2-nitrophenyl)-2-oxoacetate: Obtained in 90% yield (T = -20 °C, t^{R1} = 0.041 s (L = 3.5 cm, ϕ = 250 μm)) (GC ^{t}R 21.1 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 10/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, *J* = 7.2 Hz, 3H), 4.34 (q, *J* = 7.2 Hz, 2H), 7.65 (dd, *J* = 7.2 Hz, *J* = 1.6 Hz, 1H) , 7.75(dt, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H) , 7.81(dt, *J* = 7.2 Hz, *J* = 1.2 Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ

13.8, 63.1, 123.9, 130.1, 132.4, 132.8, 134.8, 147.4, 159.5, 183.9; HRMS (ESI) *m/z* calcd for $C_{11}H_{10}N_1O_3$ ($[M+H]^+$): 224.0553, found: 224.0549.

Ethyl 2-(4-ethoxycarbonylphenyl)-2-oxoacetate: Obtained in 88% yield (T = -60 °C, t^{R1} = 0.041 s (L = 3.5 cm, ϕ = 250 μm)) (GC ^tR 23.2 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 10/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46-1. 38(m, 6H), 4.50-4.40(m, 4H), 8.09 (dd, *J* = 6.8 Hz, *J* = 1.6 Hz, 2H) , 8.17(dd, *J* = 6.8 Hz, *J* = 1.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.1, 61.6, 62.5, 129.7, 129.8, 135.4, 135.6, 163.0, 165.3, 185.5; HRMS (ESI) *m/z* calcd for $C_{13}H_{15}N_1O_5$ ($[M+H]^+$): 251.0911, found: 251.0914.

Ethyl 2-(3-ethoxycarbonylphenyl)-2-oxoacetate: Obtained in 83% yield (T = -60 °C, t^{R1} = 0.041 s (L = 3.5 cm, ϕ = 250 μm)) (GC ^tR 23.0 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 10/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47-1. 40(m, 6H), 4.51-4.40(m, 4H), 7.62 (t, *J* = 7.6 Hz, 1H), 8.21(dd, *J* = 7.6 Hz, *J* = 0.8 Hz, 1H), 8.33(dd, *J* = 7.6 Hz, *J* = 0.8 Hz, 1H), 8.67(m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 14.2, 61.5, 62.6, 129.1, 131.1, 131.4, 132.8, 133.8, 135.4, 163.2, 165.3, 185.4; HRMS (ESI) *m/z* calcd for $C_{13}H_{15}N_1O_5$ ($[M+H]^+$): 251.0906, found: 251.0914.

Ethyl 2-(2-ethoxycarbonylphenyl)-2-oxoacetate: Obtained in 89% yield (T = -60 °C, t^{R1} = 0.041 s (L = 3.5 cm, ϕ = 250 μm)) (GC ^tR 22.3 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 10/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39-1. 34(m, 6H), 4.37-4.30(m, 4H), 7.55 (dd, *J* = 8.0 Hz, *J* = 1.6 Hz, 1H), 7.67-7.60(m, 2H), 8.02(dd, *J* = 8.0 Hz, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.0, 62.1, 62.4, 128.9, 129.4, 130.2, 131.3, 132.8, 138.7, 150.3, 160.7, 166.3, 187.7; HRMS (ESI) *m/z* calcd for $C_{13}H_{15}N_1O_5$ ($[M+H]^+$): 251.0907, found: 251.0914.

Ethyl 2-(2,4,6-trimethylphenyl)-2-oxoacetate: Obtained in 73% yield (T = -20 °C, t^{R1} = 4.71 s (L = 100 cm, ϕ = 1000 μm)) (GC ^tR 20.3 min). The spectral data were identical to those reported in the literature.[1]

Ethyl 2-(4-bromophenyl)-2-oxoacetate: Obtained in 83% yield (T = -20 °C, t^{R1} = 2.35 s (L = 50 cm, ϕ = 1000 μm)) (GC ^tR 20.6 min). The spectral data were identical to those reported in the literature.[1]

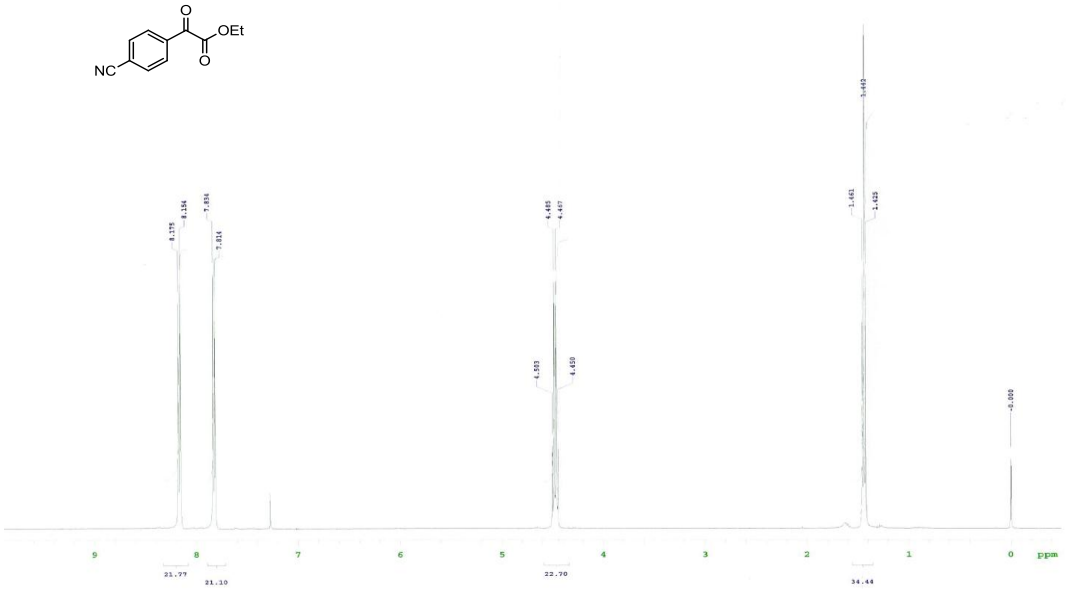
Ethyl 2-(4-iodophenyl)-2-oxoacetate: Obtained in 93% yield (T = -20 °C, t^{R1} = 0.28 s (L = 6.0 cm, ϕ = 1000 μm)) (GC ^tR 22.1 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 10/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (t, *J* = 7.2 Hz, 3H), 4.44(q, *J* = 7.6 Hz), 7.74 (dd, *J* = 3.6 Hz, *J* = 1.6 Hz, 1H) , 7.89(dd, *J* = 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 62.5, 103.7, 131.1, 131.8, 138.3, 163.1, 185.4; HRMS (ESI) *m/z* calcd for $C_{10}H_{10}I_1O_3$ ($[M+H]^+$): 304.9669, found: 304.9660.

***t*-Butyl 2-(4-iodophenyl)-2-oxoacetate:** Obtained in 75% yield (T = -40 °C, t^{R1} = 0.28 s (L = 6.0 cm, ϕ = 1000 μm)) (GC ^tR 23.2 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 100/1 to 20/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (s, 9H), 7.68 (d, *J* = 8.4 Hz, *2*H) , 7.88(d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0, 85.1, 103.3, 131.0, 131.8, 138.2, 163.0, 186.0; HRMS (ESI) *m/z* calcd for $C_{12}H_{13}I_1O_3$ ($[M+H]^+$): 332.9982, found: 332.9983.

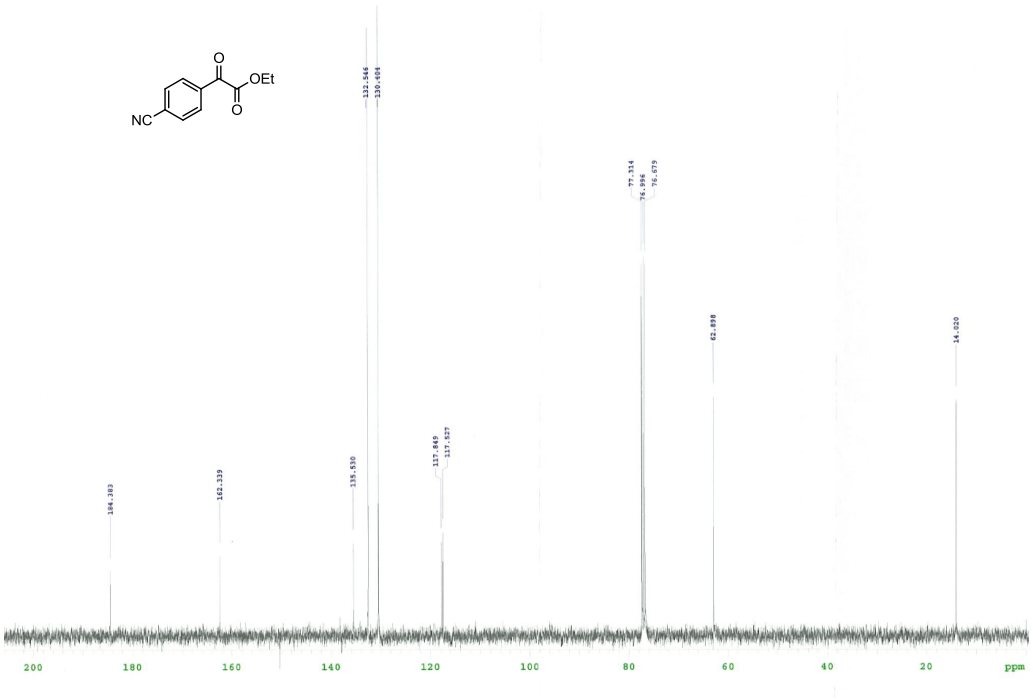
Ethyl 2-(4'-bromo-[1,1'-biphenyl]-4-yl)-2-oxoacetate: Obtained in 85% yield (T = -20 °C, t^{R1} = 2.35 s (L = 50 cm, ϕ = 1000 μm)) (GC ^tR 29.5 min). After extraction, the crude product was purified by column chromatography (hexane/ethyl acetate = 10/1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (t, *J* = 7.2 Hz, 3H), 4.47(q, *J* = 7.2 Hz), 7.49 (dd, *J* = 6.8 Hz, *J* = 2.0 Hz, 2H) , 7.57(dd, *J* = 6.4 Hz, *J* = 2.4 Hz, 2H), 7.69(dd, *J* = 6.8 Hz, *J* = 2.0Hz, 2H), 8.09(dd, *J* = 6.8 Hz, *J* = 2.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 62.4, 123.1, 127.2, 128.8, 130.7, 131.5, 132.2, 138.3, 146.2, 163.6, 185.7; HRMS (ESI) *m/z* calcd for $C_{10}H_{10}I_1O_3$ ($[M+H]^+$): 333.0121, found: 333.0114.

Reference

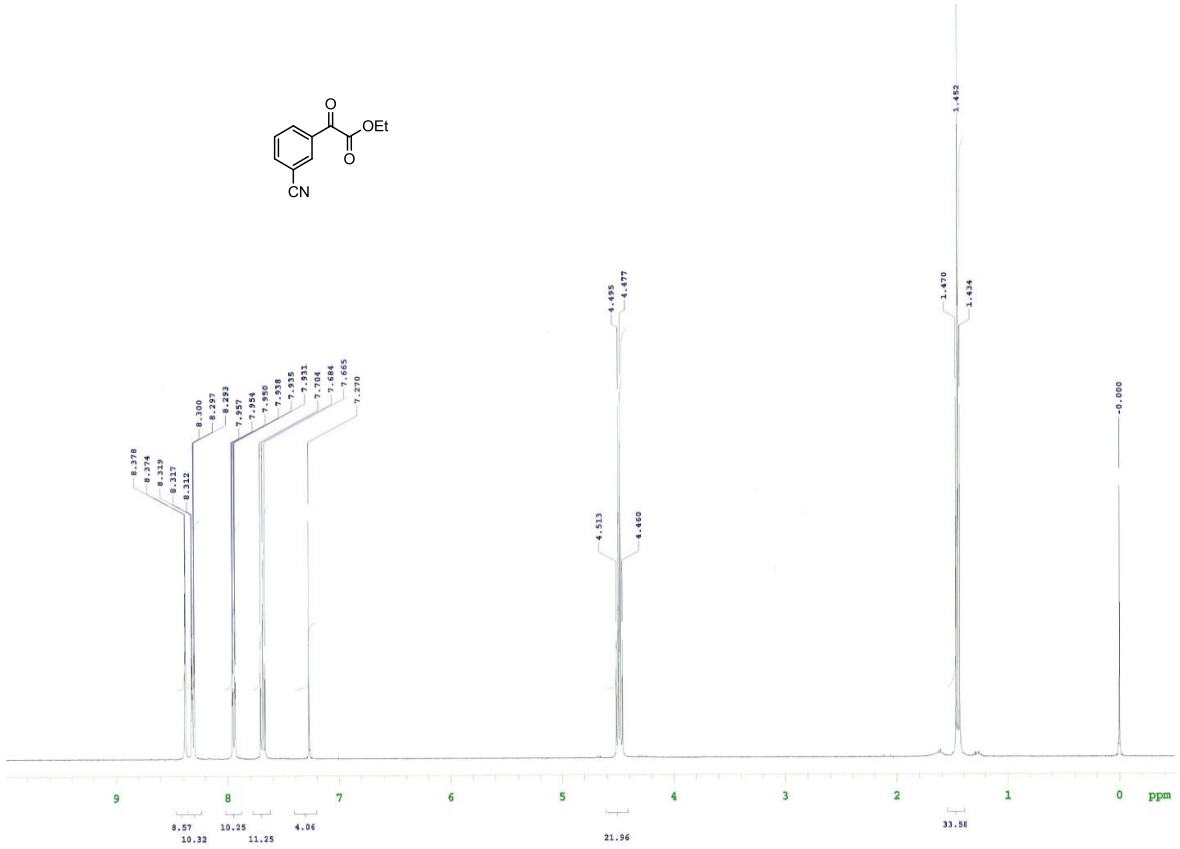
1. Q. Meng, Y. Sun, V. R. Vidal, J. P. Genêt and Z. Zhang, *J. Org. Chem.*, 2008, **73**, 3842.
2. S. K. Alamsetti and G. Sekar, *Chem. Commun.*, 2010, 7235.
3. H. Shimizu and M. Murakami, *Chem. Commun.*, 2007, 2855.



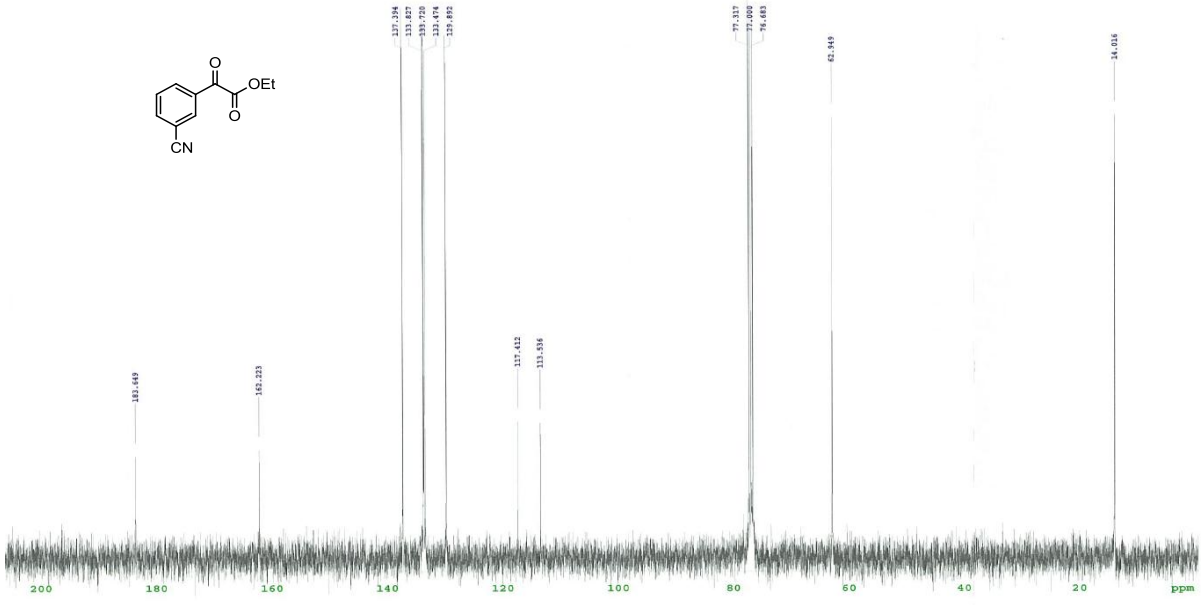
^{1}H NMR spectrum of ethyl 2-(4-cyanophenyl)-2-oxoacetate



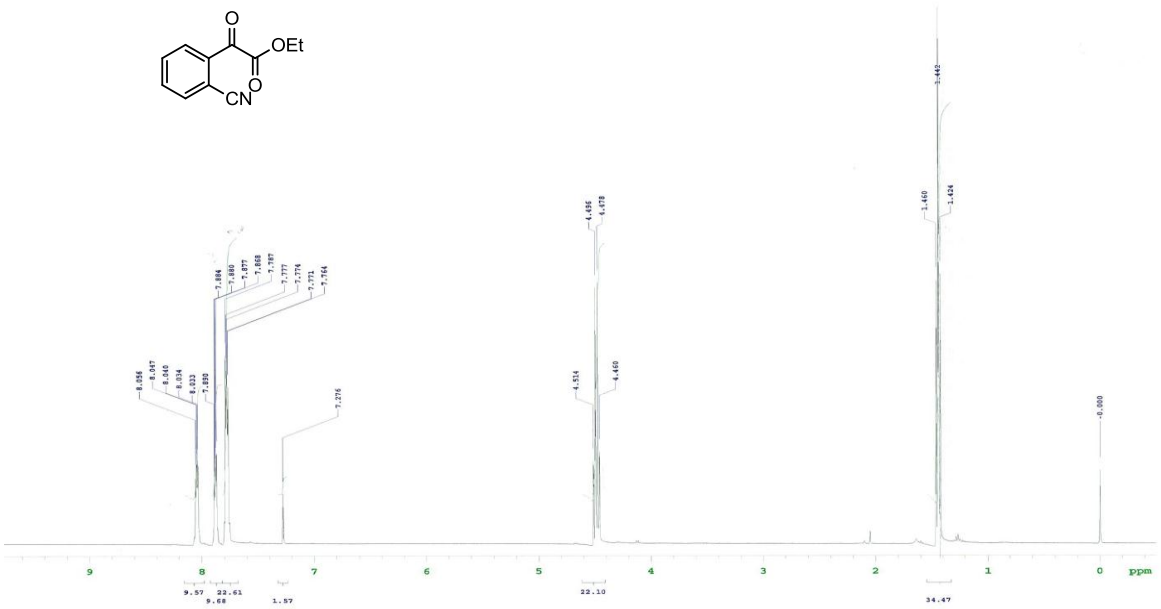
^{13}C NMR spectrum of ethyl 2-(4-cyanophenyl)-2-oxoacetate



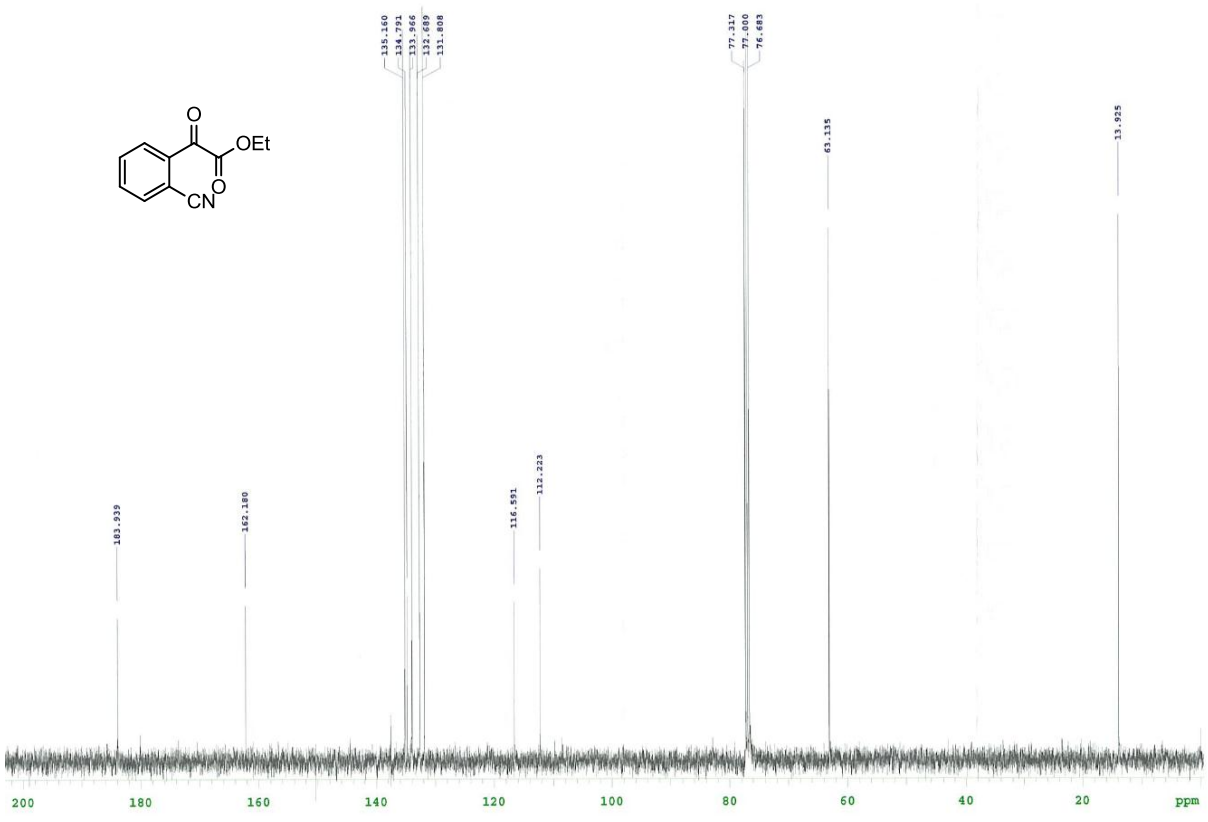
^{1}H NMR spectrum of ethyl 2-(3-cyanophenyl)-2-oxoacetate



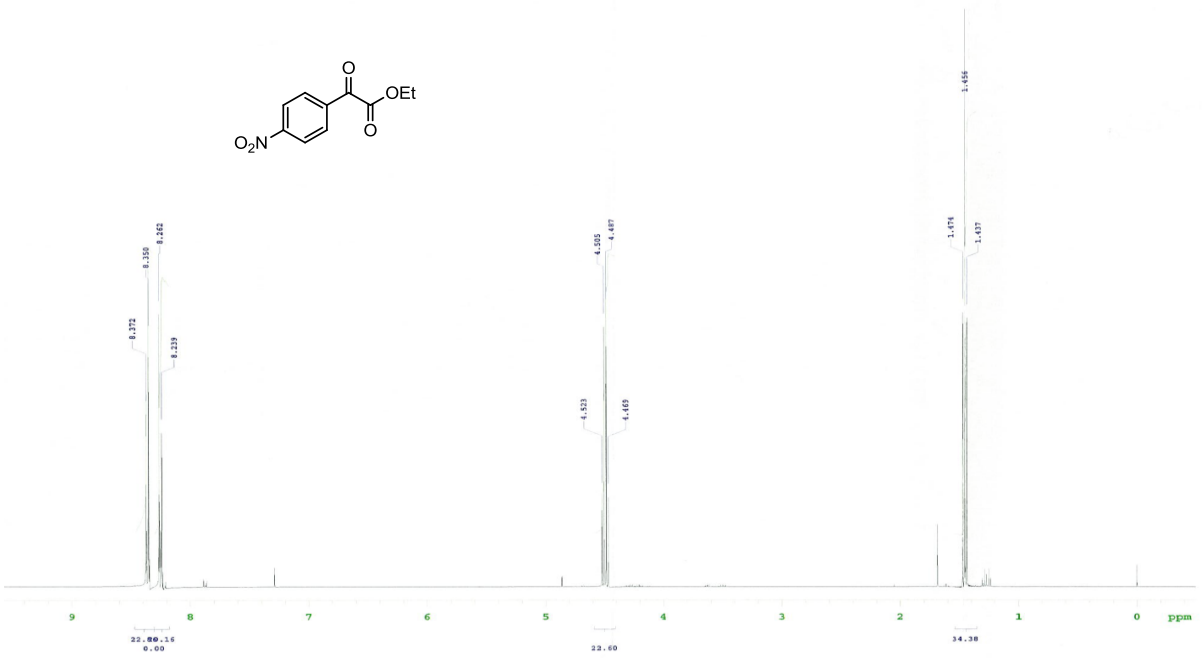
^{13}C NMR spectrum of ethyl 2-(3-cyanophenyl)-2-oxoacetate



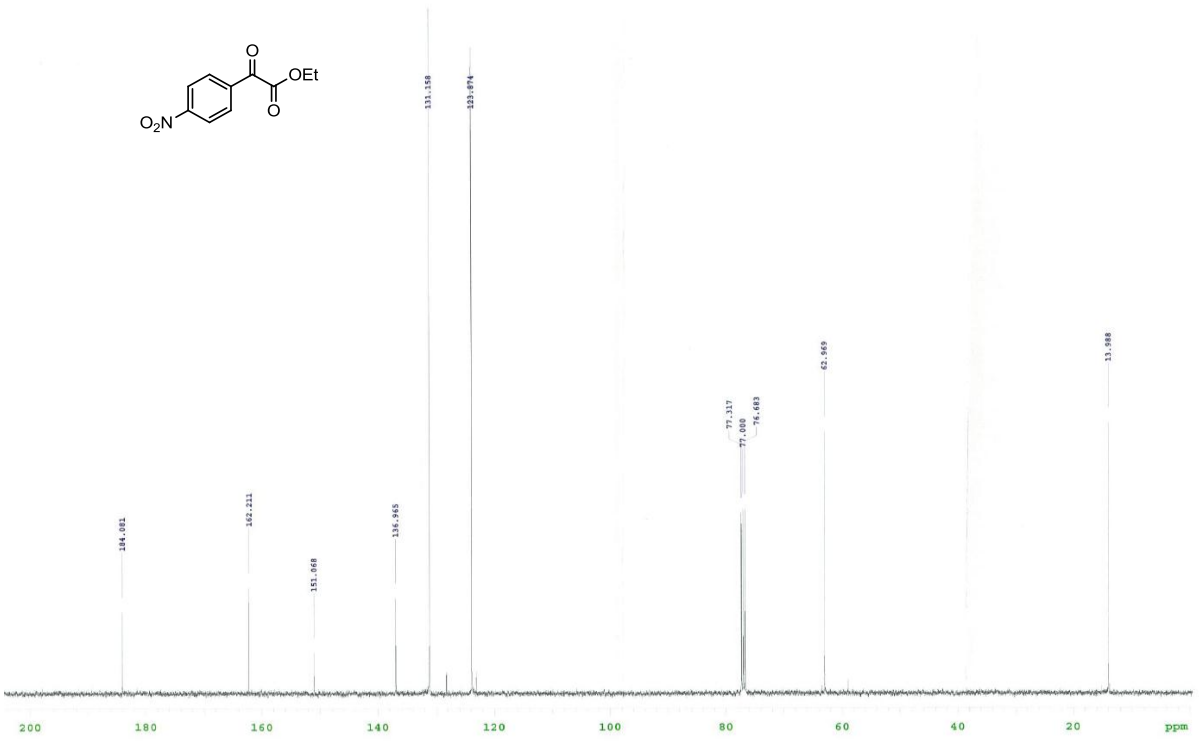
^{1}H NMR spectrum of ethyl 2-(2-cyanophenyl)-2-oxoacetate



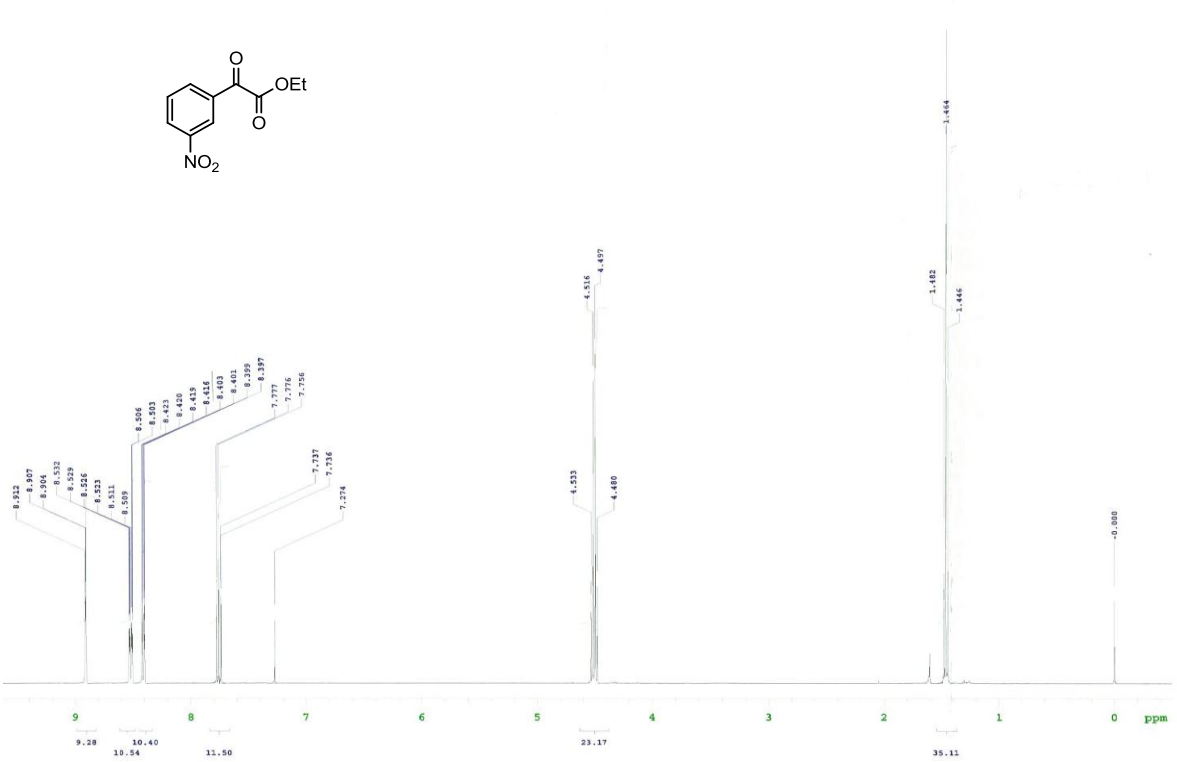
^{13}C NMR spectrum of ethyl 2-(2-cyanophenyl)-2-oxoacetate



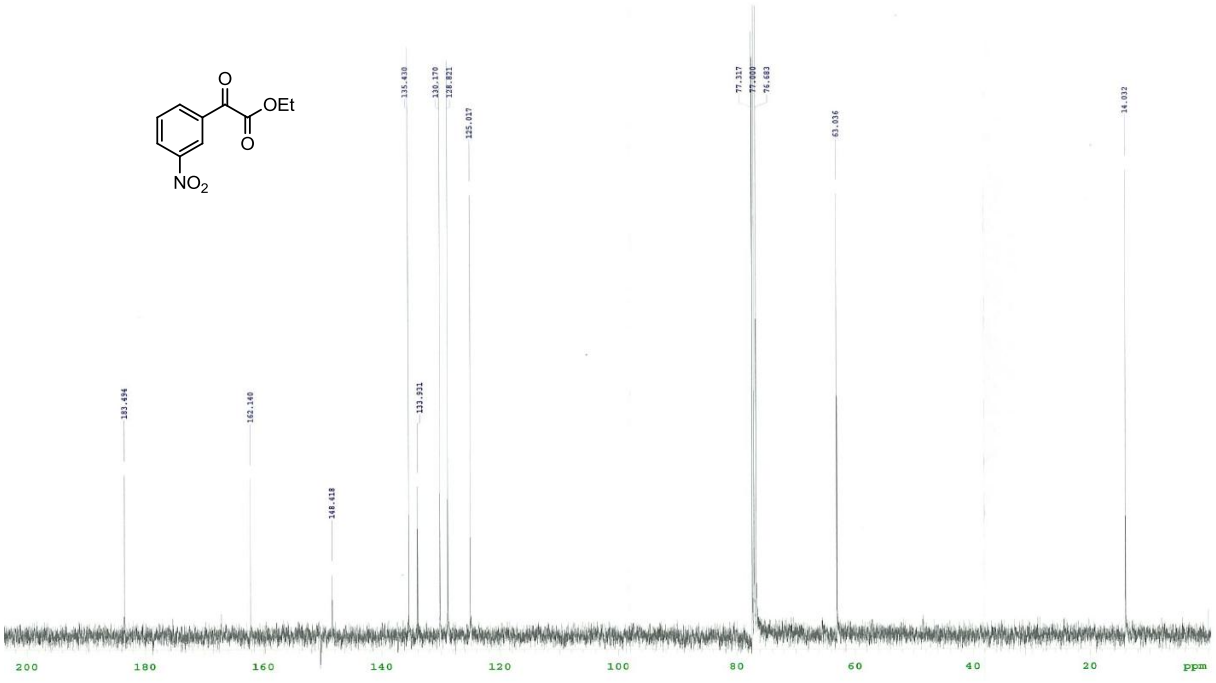
^{1}H NMR spectrum of ethyl 2-(4-nitrophenyl)-2-oxoacetate



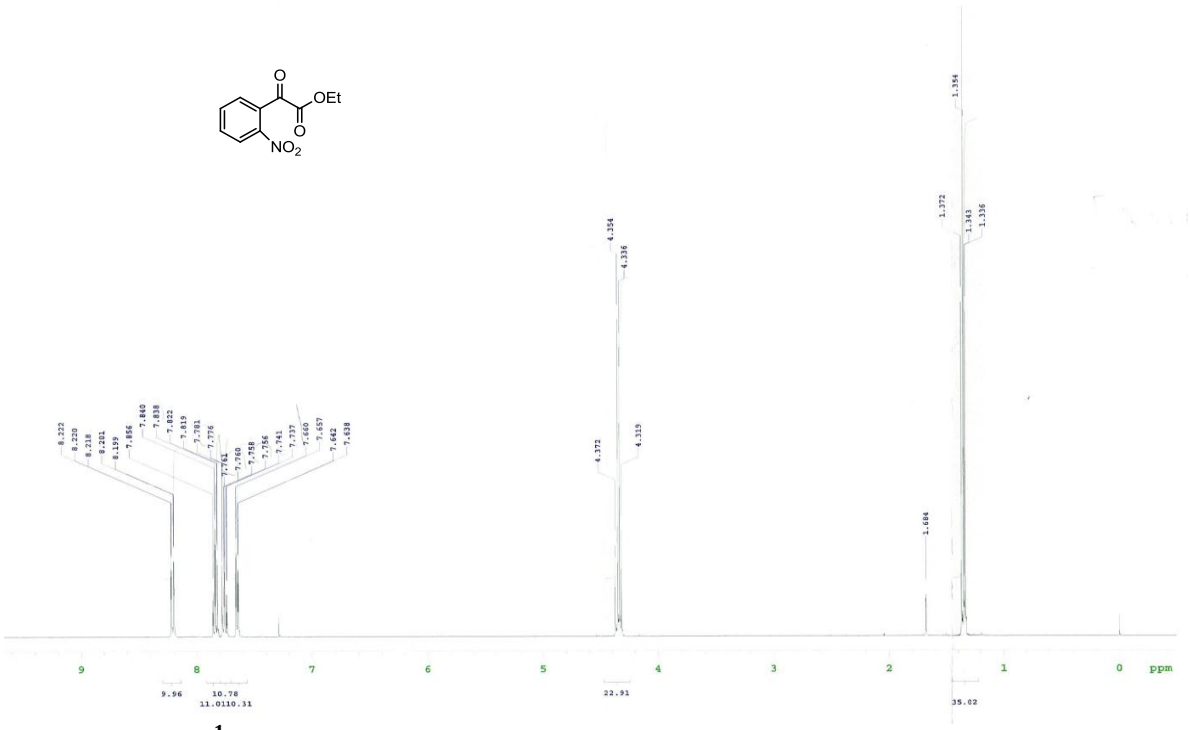
^{13}C NMR spectrum of ethyl 2-(4-nitrophenyl)-2-oxoacetate



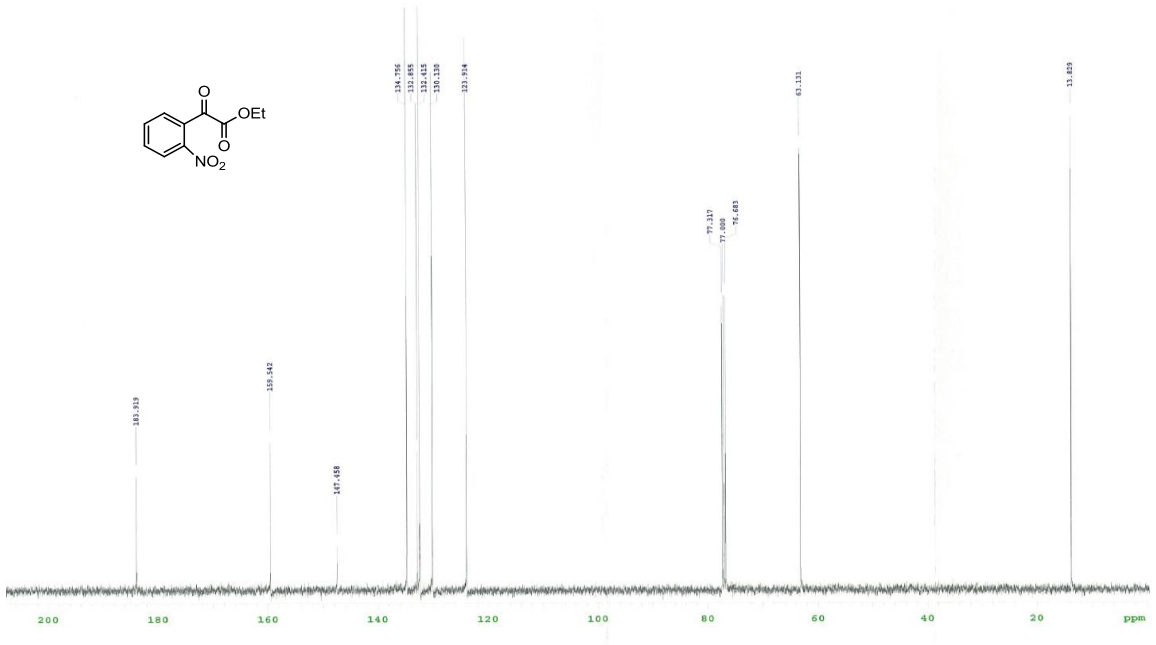
^{1}H NMR spectrum of ethyl 2-(3-nitrophenyl)-2-oxoacetate



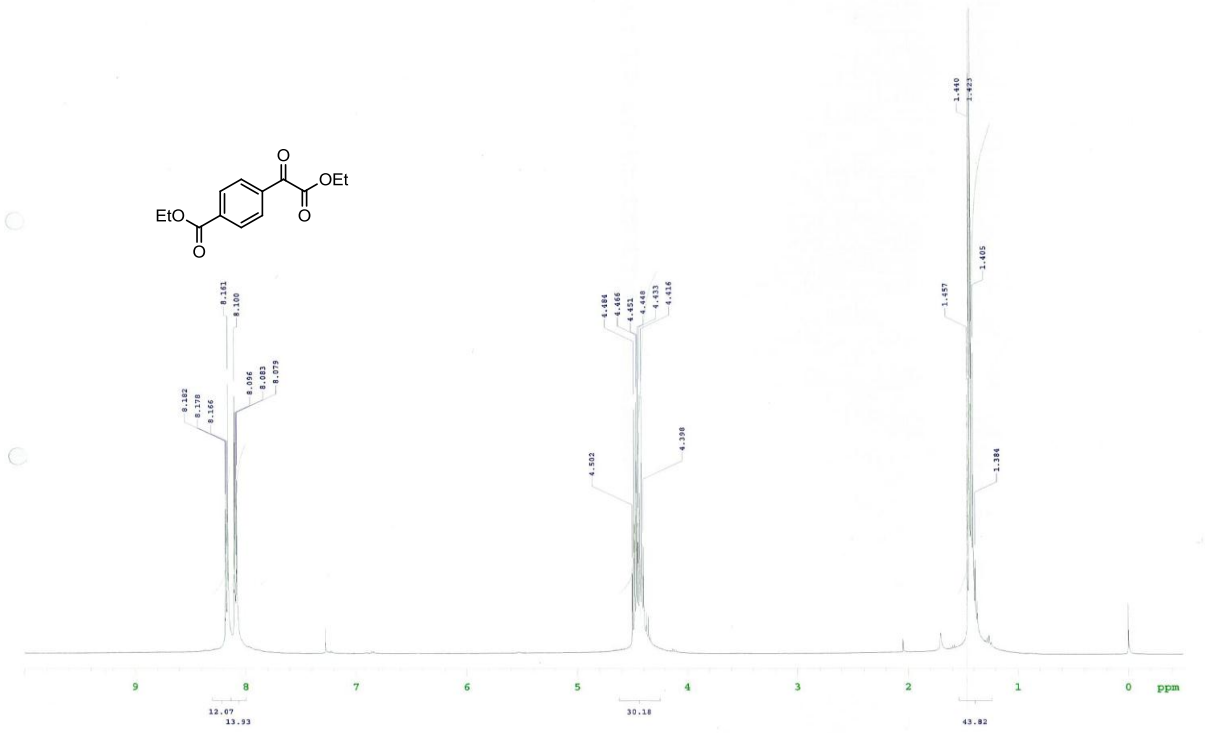
^{13}C NMR spectrum of ethyl 2-(3-nitrophenyl)-2-oxoacetate



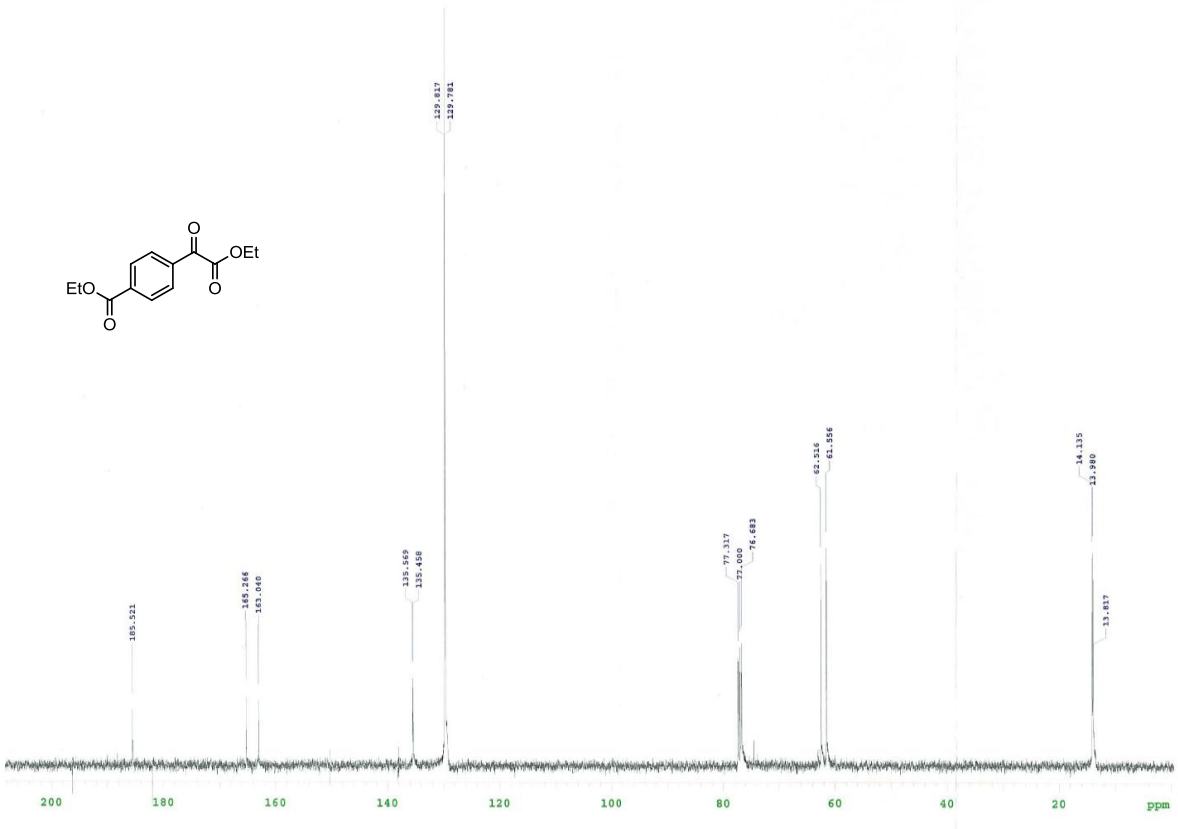
^{1}H NMR spectrum of ethyl 2-(2-nitrophenyl)-2-oxoacetate



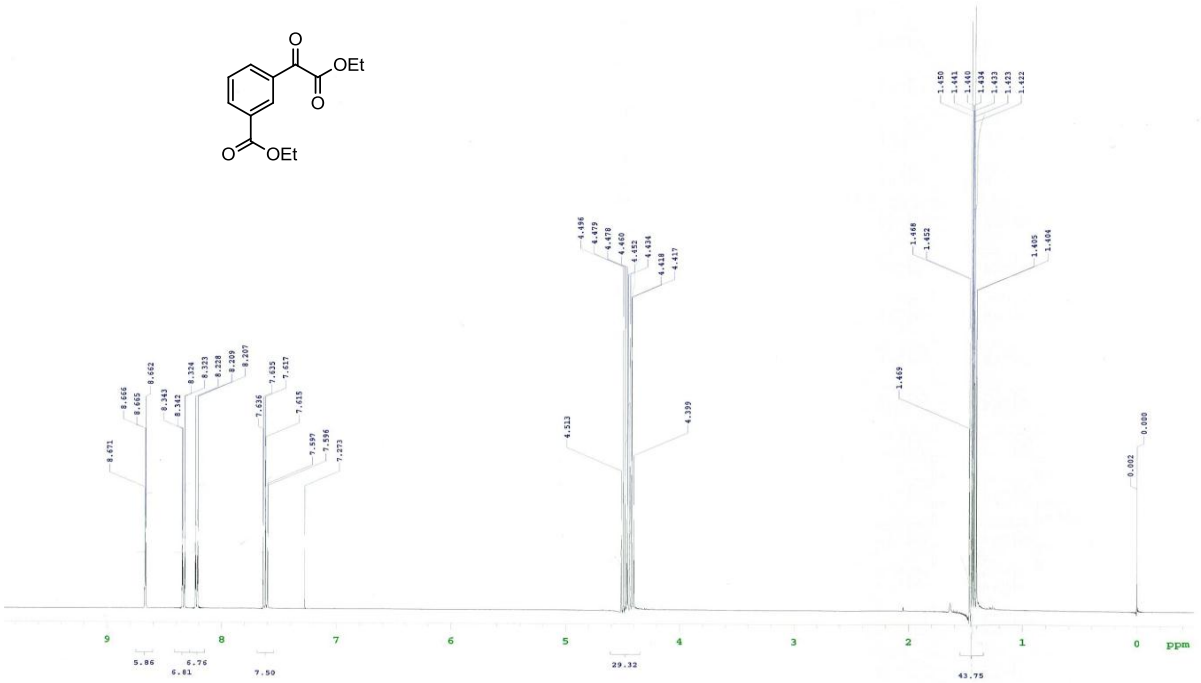
^{13}C NMR spectrum of ethyl 2-(2-nitrophenyl)-2-oxoacetate



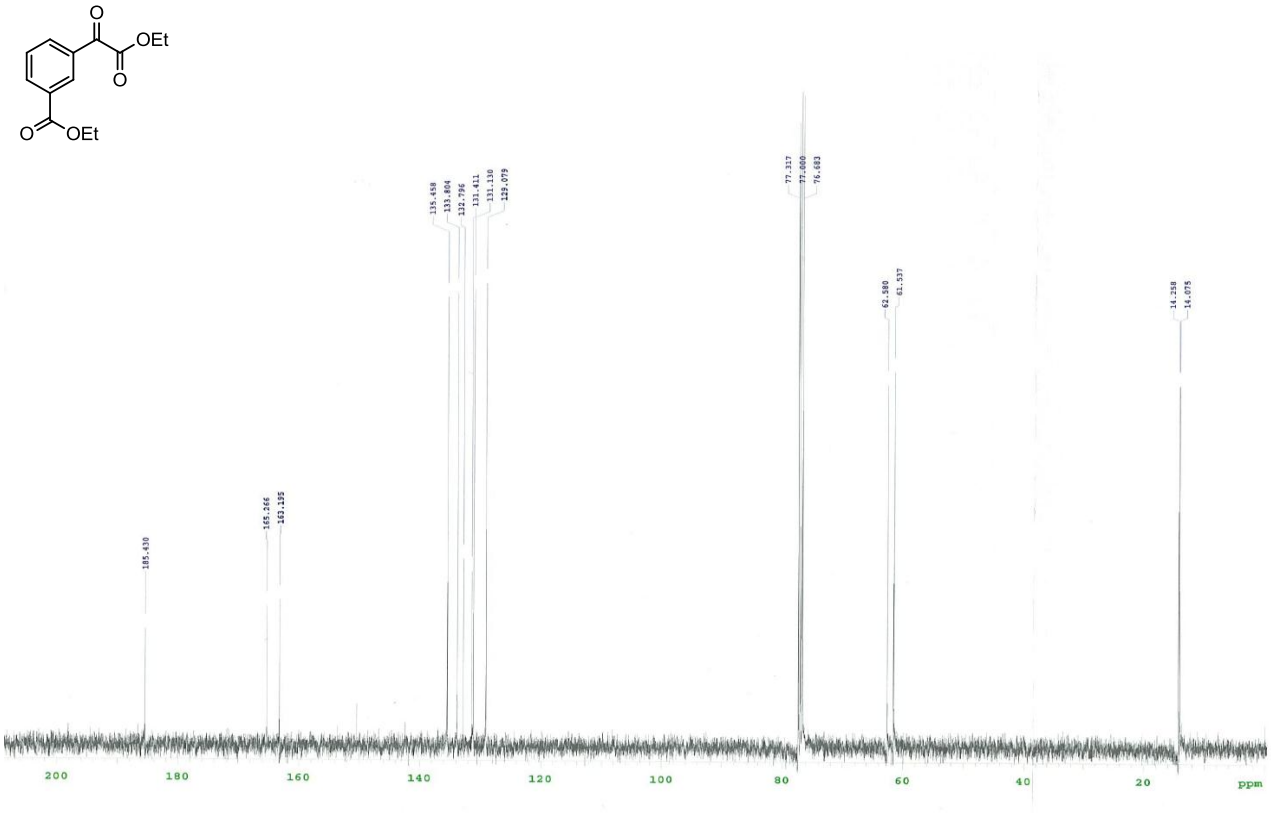
^{1}H NMR spectrum of ethyl 2-(4-ethoxycarbonylphenyl)-2-oxoacetate



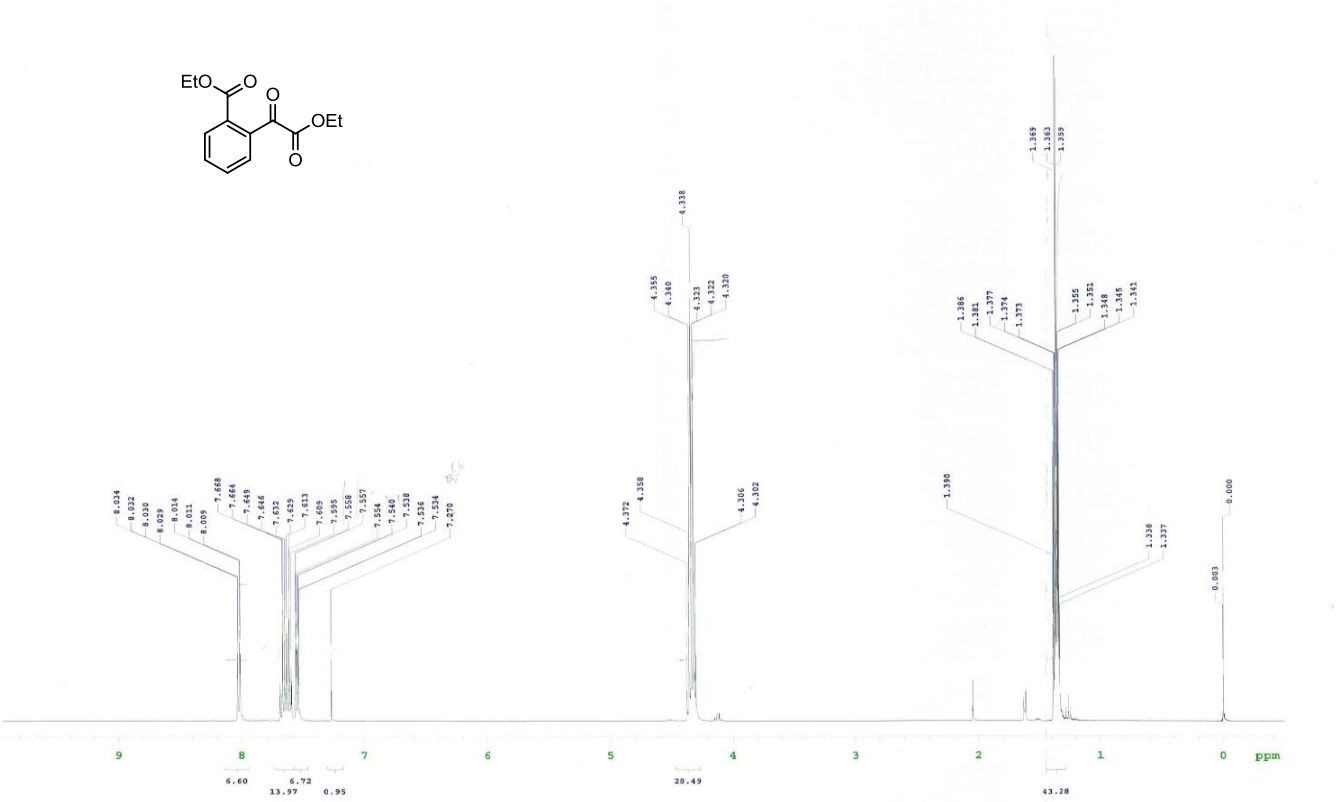
^{13}C NMR spectrum of ethyl 2-(4-ethoxycarbonylphenyl)-2-oxoacetate



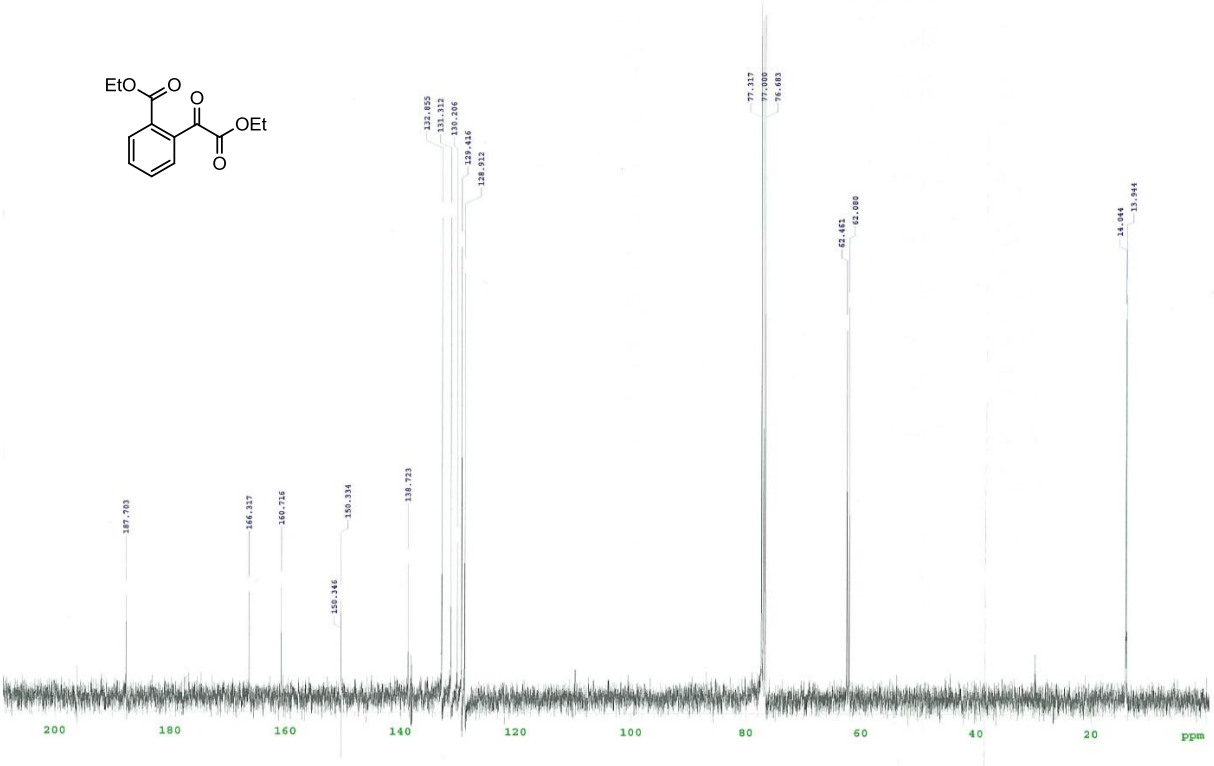
^{1}H NMR spectrum of ethyl 2-(3-ethoxycarbonylphenyl)-2-oxoacetate



^{13}C NMR spectrum of ethyl 2-(3-ethoxycarbonylphenyl)-2-oxoacetate

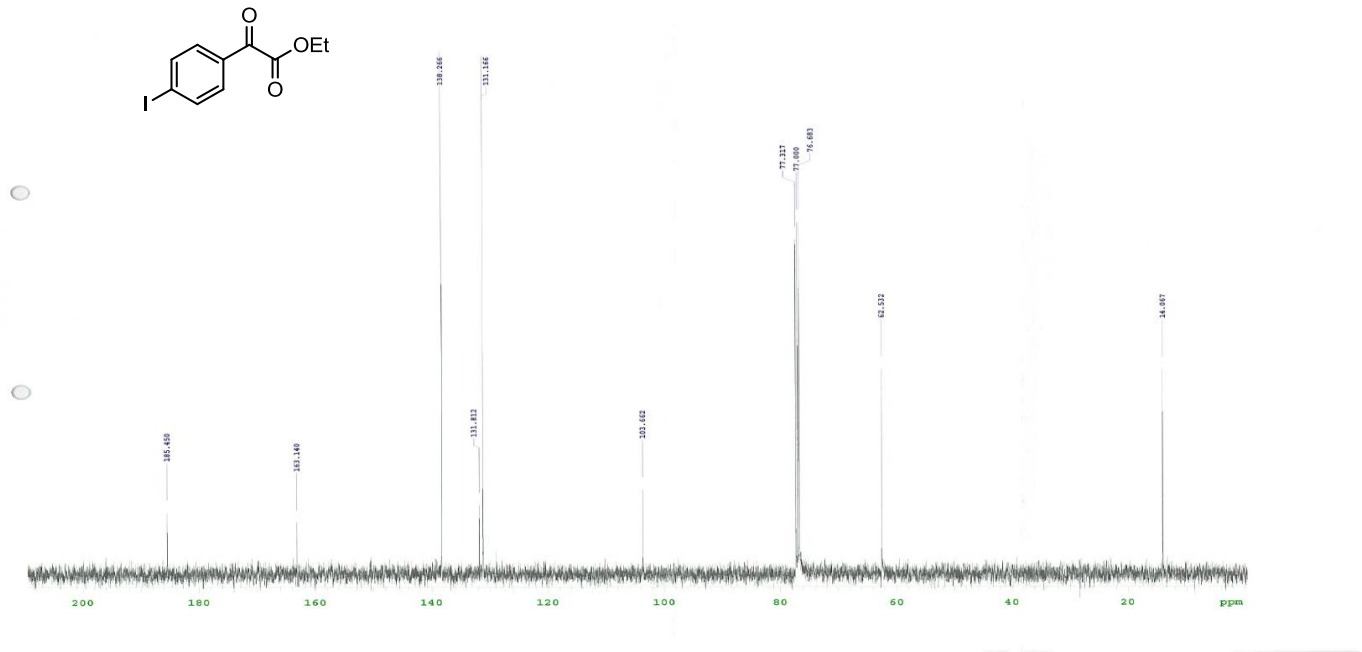


^{1}H NMR spectrum of ethyl 2-(2-ethoxycarbonylphenyl)-2-oxoacetate

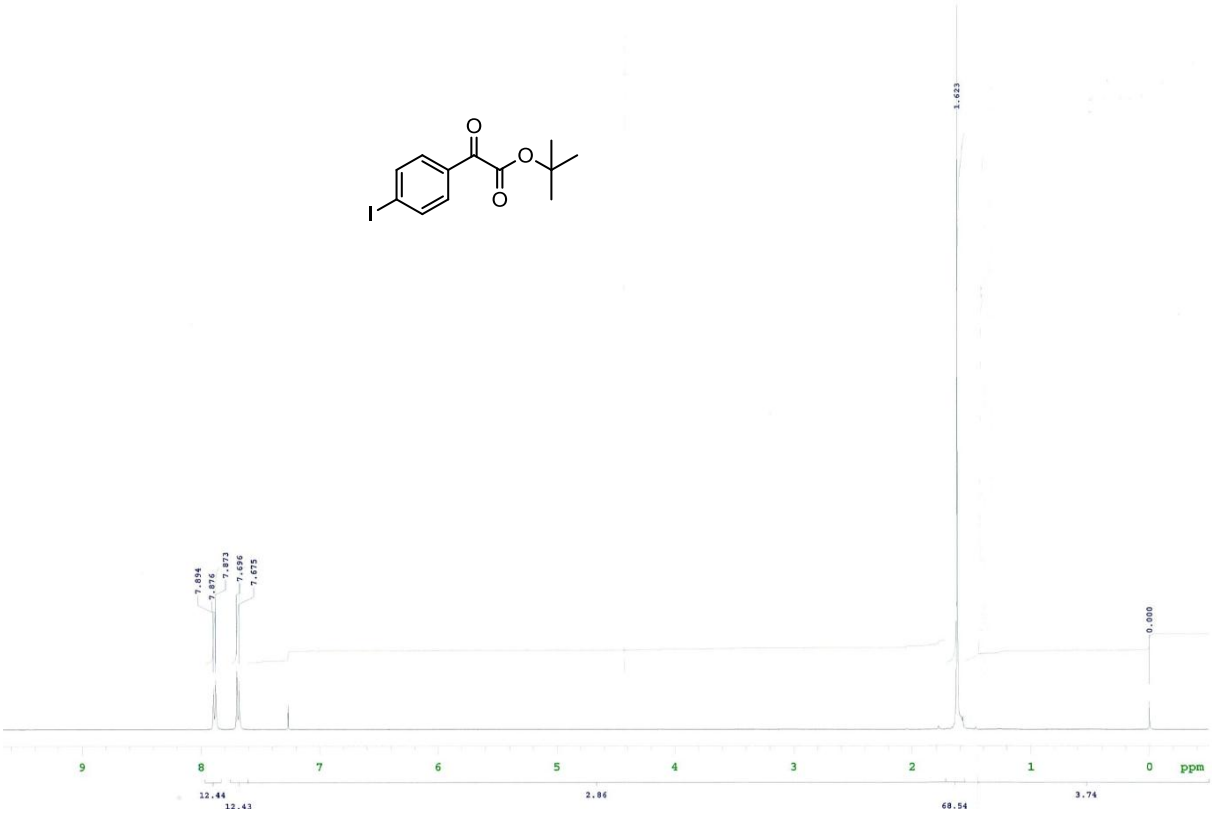


^{13}C NMR spectrum of ethyl 2-(2-ethoxycarbonylphenyl)-2-oxoacetate

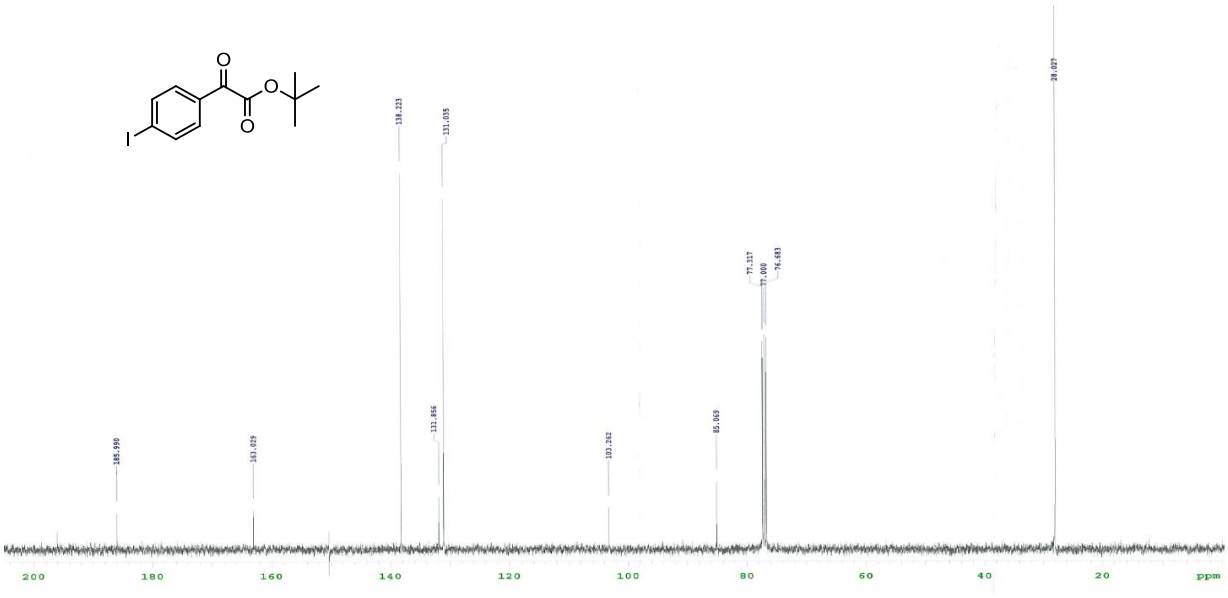
^{1}H NMR spectrum of ethyl 2-(4-iodophenyl)-2-oxoacetate



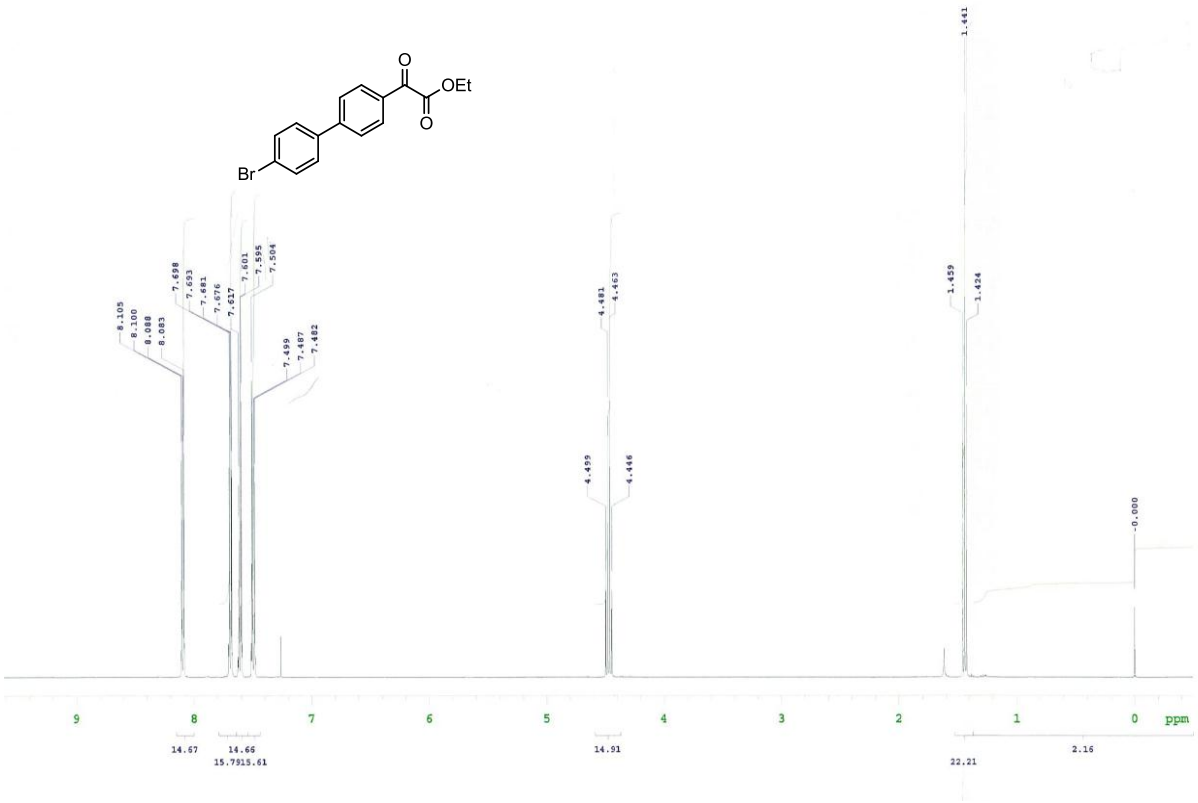
^{13}C NMR spectrum of ethyl 2-(4-iodophenyl)-2-oxoacetate



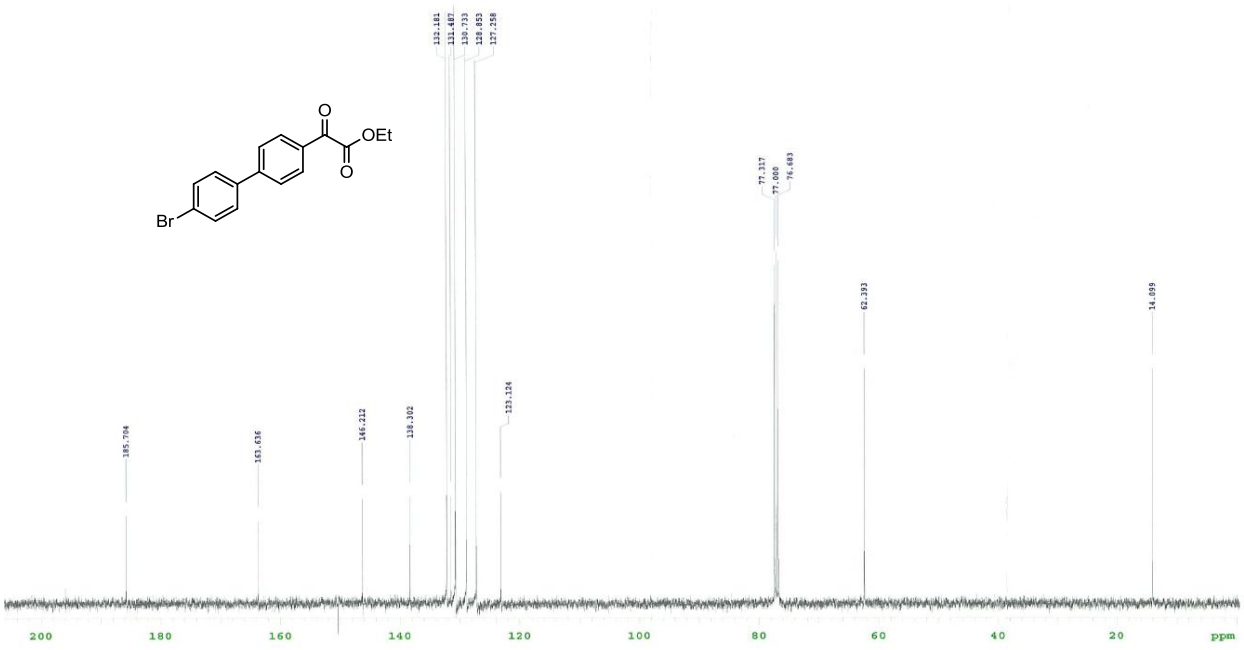
^{1}H NMR spectrum of *t*-Butyl 2-(4-iodophenyl)-2-oxoacetate



^{13}C NMR spectrum of *t*-Butyl 2-(4-iodophenyl)-2-oxoacetate



[1]H NMR spectrum of ethyl 2-(4'-bromo-[1,1'-biphenyl]-4-yl)-2-oxoacetate



[13]C NMR spectrum of ethyl 2-(4'-bromo-[1,1'-biphenyl]-4-yl)-2-oxoacetate