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Article

Glycerol/Hypophosphorous Acid and PhSeSePh: An Efficient and Selective System for Reactions in the Carbon-Carbon Double Bond of (*E*)-Chalcones

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Este trabalho descreve nossos resultados para a reação entre benzenosselenol, gerado *in situ* pela reação entre disseleneto de difenila com H_3PO_2, com uma série de (*E*)-chalconas utilizando glicerol como solvente. Utilizando as condições de reação otimizadas, uma variedade de produtos de redução 1,4-quimiosseletivas podem ser obtidos em bons rendimentos. A mistura glicerol/H_3PO_2 pode ser facilmente recuperada e reutilizada em condições de reação de redução 1,4-quimiosseletivas por ciclos sucessivos sem perda de eficiência. Adicionalmente, sob condições de reação de redução 1,4-quimiosseletivas, o produto natural zingerona pode ser sintetizada em bom rendimento.

We describe herein our results for the reaction of benzeneselenol, generated *in situ* by reaction of diphenyl diselenide with H_3PO_2, with various (*E*)-chalcones using glycerol as solvent. Using our optimized reaction conditions, a range of chemoselective 1,4-reduction products could be obtained in good yields. The glycerol/H_3PO_2 system can be easily recovered and reused in chemoselective 1,4-reductions for successive cycles without loss of efficiency. Additionally, under 1,4-reducing reaction conditions, the natural product zingerone can be synthesized in good yield.

Keywords: chalcones, selenium, glycerol, reduction, zingerone

Introduction

Conjugate addition reactions of sulfur and selenium nucleophiles to electron-deficient olefins are a very useful method for new carbon-chalcogenium bond formation in organic synthesis. Several methods for the formation of C–S bond via thia-Michael addition were described using the readily available organylthiols.[1] However, the synthesis of β-selanylcarbonyl compounds was not extensively studied, since the generation and use of selenol analogs is not trivial.[2-13] Organoselenium compounds are attractive molecules due their selective reactions[14] and the interest in the synthesis of these compounds has increased in the last years because of their use in materials area,[15] as ionic liquids[16] in asymmetric catalysis,[17] and because of their interesting biological activities.[18]

β-Selanylcarbonyl compounds are particularly interesting synthons, because they can be used as intermediates in the synthesis of dihydromevinolin,[19] idesolide[20] and taxol.[21] Traditional methods for the synthesis of β-selanylcarbonyl compounds via Michael addition commonly make use of the already available benzeneselenol and some catalysts can be used.[3-5] Nevertheless, the use of air-sensitive, highly volatile, and unpleasant smelling benzeneselenol leads to serious ecological and safety problems. To overcome this problem, β-selanylcarbonyl compounds could be synthesized when the benzeneselenol was generated *in situ*.[6-11] Alternatively, Santi and co-workers described the synthesis of β-selanylcarbonyl compounds using PhSeZnCl in reactions of addition to unsaturated ketones.[12] Besides being scarce, in most cases these methods are limited to a few functional groups and long reaction times are necessary. Furthermore, there is still an attention in developing simple, efficient and catalyst-free methodologies to synthesize β-selanylcarbonyl compounds.

In this context, the development of methodologies employing green solvents (recyclable and environmentally friendly) has recently gained much attention, because of the extensive use of solvents in almost all chemical and pharmaceutical industries, and of the predicted disappearance of fossil oil.[22] Biodegradability, high availability, no flammability, being obtained from

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renewable sources are among the desirable characteristics for a green solvent.[23] Thus, the use of glycerol[24] and their eutetics[25] as a sustainable green solvent was recently reported and a great number of organic reactions were performed using this solvent.

More recently, glycerol proved to be an efficient and recyclable solvent for the synthesis of a range of organochalcogenium compounds.[26] For example, our research group described a methodology to synthesize 2-organylselanyl pyridines by reactions of 2-chloropyridines with organylselenols, generated *in situ* by reaction of diorganyl diselenides, using glycerol as solvent and hypophosphorous acid (H_3PO_2).[27] Using this methodology the products were obtained in high yields and the glycerol/H_3PO_2 system can be easily recovered and reused for five times without loss of efficiency.

In view of the explained above, we decided to examine the synthesis of β-selanylcarbonyl compounds via reaction of benzeneselenol, generated *in situ* by reaction of diphenyl diselenide with H_3PO_2, with (*E*)-chalcones using glycerol as solvent (Scheme 1).

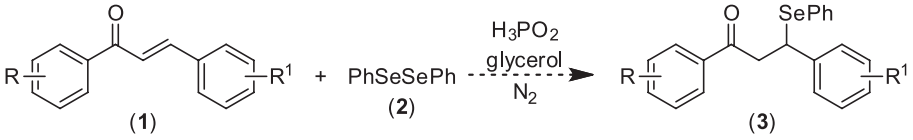
Results and Discussion

Initially, we chose (*E*)-1,3-diphenyl-prop-2-en-1-one **1a** and diphenyl diselenide **2** as model substrates to establish the best conditions for the reaction using glycerol and H_3PO_2 as the solvent-reducing agent system and some experiments were performed to synthesize compound **3a** (Scheme 2). Thus, a mixture of diphenyl diselenide **2** and 0.1 mL of H_3PO_2 (50 wt.% in H_2O) in glycerol (1.0 mL) was stirred at 90 ºC for 30 min under N_2 atmosphere to afford *in situ* benzeneselenol. After this time, (*E*)-chalcone **1a** (0.5 mmol) was added in the reaction vessel and the reaction remained at 90 ºC for additional 24 h.

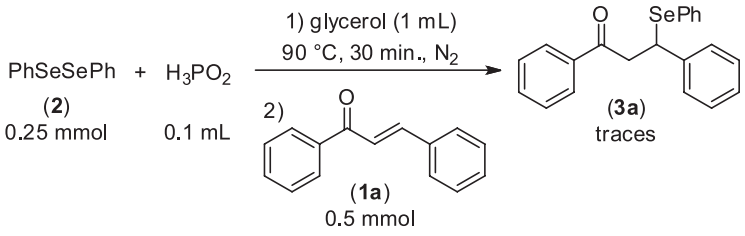
Unfortunately, under these reaction conditions, only traces of the product **3a** were formed and to our surprise, the 1,4-reduction product, 1,3-diphenyl-1-propanone **4a** was obtained in 42% yield (Table 1, entry 1). The chemoselective 1,4-reduction of α,β-unsaturated carbonyl compounds is an attractive and important tactic in organic synthesis.[28] A range of significant advances have been made toward the development of efficient protocols for the chemoselective 1,4-reduction of α,β-unsaturated carbonyl compounds, specially methodologies based on the use of transition metal catalysts.[29] For example, Kosal and Ashfeld described that a titanocene complex can be used as an efficient catalyst for the conjugate reduction of α,β-unsaturated carbonyl derivatives. A series of α,β-unsaturated aldehydes, ketones, esters, unsubstituted amides and ynones, underwent chemoselective conjugate reduction by utilizing a catalytic quantity of titanocene complex.[30] Additionally, selective reducing agents based on chalcogen atoms (Se and Te) were used for the 1,4-reduction of α,β-unsaturated carbonyl compounds.[31]

In view of this surprising result of 1,4-reduction reaction, we decided to explore these reaction conditions, firstly increasing the quantity of H_3PO_2 in the reaction (Table 1). Thus, when the reactions were performed increasing the quantity of H_3PO_2 from 0.2 to 0.5 mL, a mild increase in the yield of product **4a** was observed and only traces of product **3a** were observed (Table 1, entries 2 and 3).

In view of these moderate results, we decided to explore these reaction conditions to obtain reduced products of (*E*)-chalcones increasing the amount of PhSeSePh **2**. To our delight, when the reaction was carried out in the presence of 0.5 mmol of diphenyl diselenide **2** and 0.2 mL of H_3PO_2 the reduction product **4a** was obtained in 89% yield after 2 hours at 90 ºC under nitrogen atmosphere (Table 1, entry 4). Under these reaction



Scheme 1. General purpose of this work.



Scheme 2. Reaction conditions to synthesize **3a**.

Table 1. Optimization of reaction conditions[a]

entry	PhSeSePh / mmol	H_3PO_2 / mL	time / h	Yield **4a** / %
1	0.25	0.1	24	42
2	0.25	0.2	24	47
3	0.25	0.5	24	47
4	0.5	0.2	2	89
5	0.75	0.3	2	81
6[b]	1.0	0.4	2	82
7	0.5	–	24	–
8	–	0.2	24	–
9	0.5	0.2	2	89

[a]Reactions are performed using (*E*)-chalcone **1a** (0.5 mmol), PhSeSePh **2** and H_3PO_2 in glycerol (1 mL), at 90 °C under N_2 atmosphere; [b]reaction using 1.5 mL of glycerol.

conditions, only traces of the β-phenylselanyl adduct **3a** was observed and we recovered, after chromatographic column, PhSeSePh **2** in 78%. Using larger amounts of diphenyl diselenide **2**, the reactions gave the reduction product **4a** in lower yields comparable to reactions using 0.5 mmol of diphenyl diselenide **2** (Table 1, entries 5 and 6). Besides, when the reaction was carried out without H_3PO_2 or PhSeSePh **2** no reaction product **4a** was formed even after 24 h (Table 1, entries 7 and 8). Finally, when the reaction was performed without the preliminary 30 min of diphenyl diselenide cleavage, just stirring a mixture of (*E*)-chalcone **1a** (0.5 mmol), diphenyl diselenide **2** (0.5 mmol) and 0.2 mL of H_3PO_2 (50 wt.% in H_2O) in glycerol (1.0 mL) at 90 ºC under nitrogen atmosphere, the corresponding product **4a** was obtained in good yield (Table 1, entry 9).

Thus, in an optimized reaction, (*E*)-chalcone **1a** (0.5 mmol), diphenyl diselenide **2** (0.5 mmol) and H_3PO_2 (0.2 mL) were dissolved in glycerol (1.0 mL). The heterogeneous reaction mixture was stirred for 2 hours at 90 °C under nitrogen atmosphere affording 1,3-diphenyl-1-propanone **4a** in 89% yield (Table 1, entry 9).

After the reduction reaction optimization, a study regarding the recovery and reuse of glycerol was performed. Subsequent to the formation of product **4a**, the reaction mixture was diluted and extracted with a mixture of hexane/ethyl acetate 95:5 (3 × 5 mL). The upper phase was dried and the solvent evaporated. The inferior, glycerol phase, was dried under vacuum and directly reused in a new reaction with (*E*)-chalcone **1a** and diphenyl diselenide **2** at 90 °C without the addition of more H_3PO_2. To our satisfaction, after 2 h at this temperature the corresponding product **4a** was obtained in 86% yield. After this successful experiment, we speculate the possible reuse of the glycerol/H_3PO_2 system for additional cycles (Figure 1). It was observed that a good level of efficiency was maintained even after four reactions. These results showed that the 1,3-diphenyl-1-propanone **4a** was obtained in 89, 86, 82, 77 and 74% yields after successive cycles (Figure 1). It is important to note that in all reactions performed, PhSeSePh **2** was recovered after chromatographic column in a range of 64-78% yield.

After that, the versatility of our reduction methodology was evaluated, by reacting other (*E*)-chalcones **1b-k** with

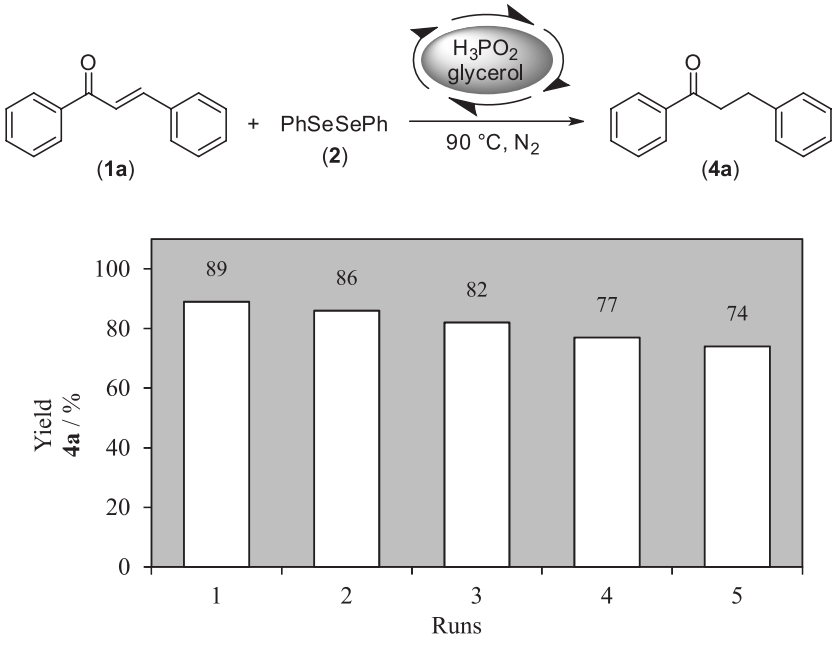
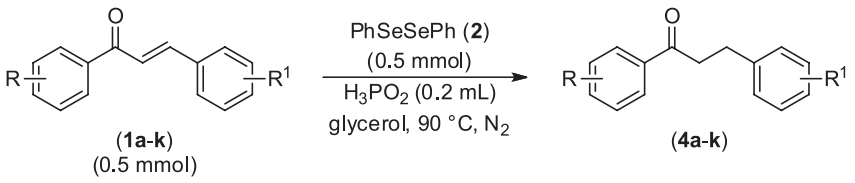


Figure 1. Reuse of solvent-reducing agent glycerol/H_3PO_2 system.

Table 2. Scope and variability of chemoselective 1,4-reduction reaction[a]



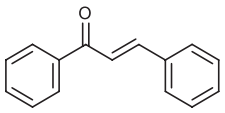
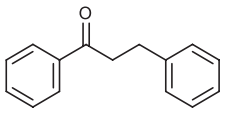
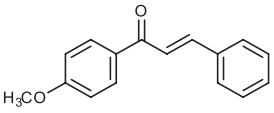
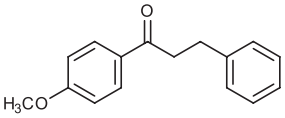
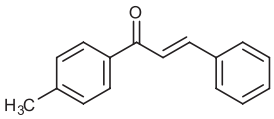
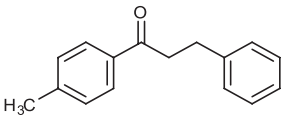
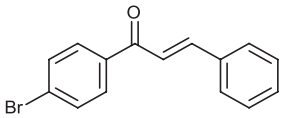
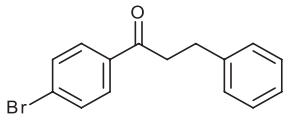
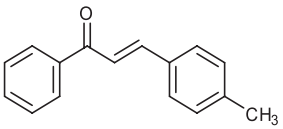
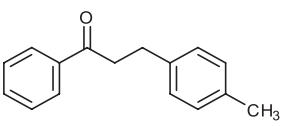
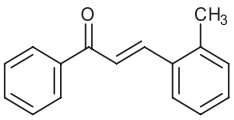
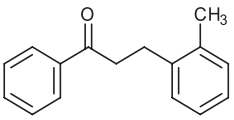
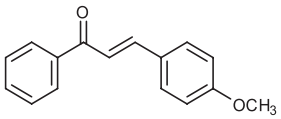
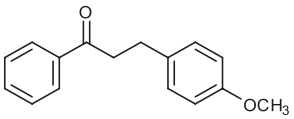
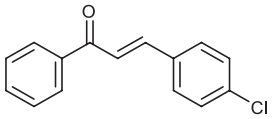
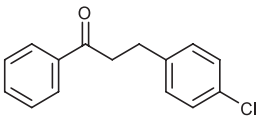
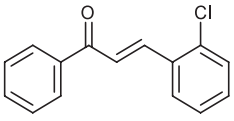
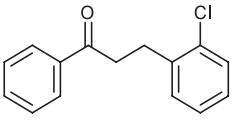
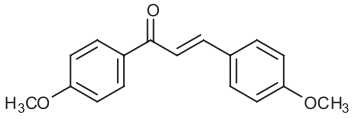
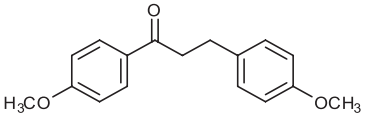
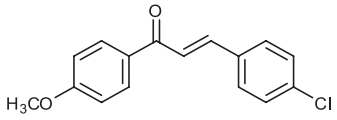
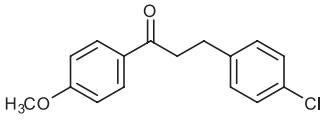
entry	(*E*)-Chalcone (**1**)	time / h	Product (**4**)	Yield / %[b]
1	 **1a**	2.0	 **4a**	89
2	 **1b**	2.0	 **4b**	72
3	 **1c**	2.0	 **4c**	80
4	 **1d**	2.0	 **4d**	74
5	 **1e**	2.0	 **4e**	87
6	 **1f**	2.0	 **4f**	78
7	 **1g**	3.0	 **4g**	75
8	 **1h**	2.0	 **4h**	70
9	 **1i**	2.5	 **4i**	74

Table 2. continuation

entry	(*E*)-Chalcone (**1**)	time / h	Product (**4**)	Yield / %[b]
10	 **1j**	2.0	 **4j**	80
11	 **1k**	2.5	 **4k**	87

[a]Reactions are performed in the presence of the appropriate (*E*)-chalcone (**1a**-**k**) (0.5 mmol), PhSeSePh (**2**) (0.5 mmol) and H_3PO_2 (0.2 mL; 50 wt.% in H_2O) in glycerol (1 mL), at 90 °C under N_2 atmosphere; [b]yields are given for isolated products.

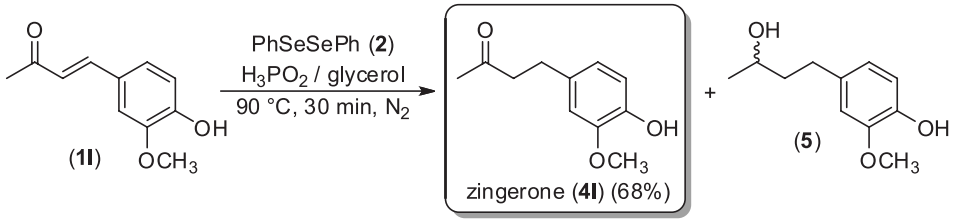
diphenyl diselenide **2** under the optimized reduction reaction conditions (Table 2). The obtained results reveal that the reaction worked well with a range of (*E*)-chalcones tested, affording good yields of the products **3b**-**k** (Table 2, entries 2-11). According to these results, the reactions are not sensitive to electronic effects in the aromatic ring of the chalcone. Therefore, (*E*)-chalcones containing either electron-donating (OMe, Me) or electron-withdrawing groups (Br, Cl) in different parts of the molecules gave good yields of the desired reduction products (Table 2, entries 2-11). The position of the substituted groups did not considerably affect reactivity.

Additionally, this reducing reaction condition was utilized in the synthesis of zingerone, a natural product. Zingerone [4-(4-hydroxy-3-methoxyphenyl)-2-butanone] is a vanillinoid compound and one of the pungent components of ginger (rizhome of *Zingiber officinale* Roscoe),[32] and this compound is a likely active constituent responsible for the antidiarrheal activity of ginger.[33] To synthesize the desired natural product, 2-methoxy-4-(3-oxo-1-butenyl) phenol **1l** (0.5 mmol) was reacted with PhSeSePh **2** (0.5 mmol) and H_3PO_2 (0.2 mL) in glycerol (1.0 mL) at 90 °C under N_2 atmosphere for 30 minutes (Scheme 3). Under these reaction conditions, the desired zingerone **4l** was obtained in 68% and unfortunately, 2-methoxy-4-(3-hydroxybutyl)phenol **5** was formed as by-product in 19% yield. The formation of this side product **5** proves that the chemoselectivity in the reduction reactions seems to be strongly correlated to the presence of both aromatic substituents in the α,β-unsaturated carbonyl compounds, and when an aliphatic moiety is present, the reduction of the keto group could occur.

Experimental

General remarks

The reactions were monitored by thin layer chromatography (TLC) carried out on Merck silica gel (60 F_{254}) by using UV light as visualizing agent and 5% vanillin in 10% H_2SO_4 and heat as developing agents. Baker silica gel (particle size 0.040-0.063 mm) was used for flash chromatography. Proton nuclear magnetic resonance (^{1}H NMR) spectra were obtained at 300 MHz on a Varian Gemini NMR and at 400 MHz on Bruker DPX 400 spectrometers. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts (δ) are reported in ppm, referenced to tetramethylsilane (TMS) as the external reference. Coupling constants (*J*) are reported in Hz. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were obtained at 75 MHz on a Varian Gemini NMR and at 100 MHz on Bruker DPX 400 spectrometers. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$. Low-resolution mass spectra were obtained with a Shimadzu GC-MS-QP2010 mass spectrometer.



Scheme 3. Synthesis of zingerone.

Procedure for the reduction of α,β-unsaturated ketones using PhSeSePh/glycerol/H_3PO_2

Glycerol (1.0 mL) was added to a 5 mL round-bottomed flask containing α,β-unsaturated ketones **1a-l** (0.5 mmol), diphenyl diselenide **2** (0.5 mmol) and H_3PO_2 (0.2 mL). The reaction mixture was stirred at 90 °C under nitrogen atmosphere for the time indicated in Table 2. After that, the reaction mixture was received in water (20 mL), extracted with ethyl acetate (3 × 5 mL), dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using ethyl acetate/hexane as the eluent.

1,3-Diphenyl-1-propanone (**4a**):[34] Yield: 0.093 g (89%); white solid; m.p.: 73-75 °C; MS: *m/z* (rel. int.) 210 (31), 105 (100), 91 (12), 77 (48); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.96-7.91 (m, 2H, Ph–H), 7.55-7.49 (m, 1H, Ph–H), 7.44-7.39 (m, 2H, Ph–H), 7.31-7.15 (m, 5H, Ph–H), 3.27 (t, 2H, *J* 8.0 Hz, CH_2), 3.05 (t, 2H, *J* 8.0 Hz, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 199.0, 141.2, 136.7, 132.9, 128.5, 128.4, 128.3, 127.9, 126.1, 40.3, 30.0.

1-(4-Methoxyphenyl)-3-phenylpropan-1-one (**4b**):[34] Yield: 0.086 g (72%); white solid; m.p.: 96-98 °C; MS: *m/z* (rel. int.) 240 (18), 136 (9), 135 (100), 107 (11), 92 (12), 77 (25), 64 (6), 51 (2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.93 (d, 2H, *J* 8.9 Hz, Ar–H), 7.32-7.19 (m, 5H, Ph–H), 6.92 (d, 2H, *J* 8.9 Hz, Ar–H), 3.85 (s, 3H, OCH_3), 3.27-3.21 (m, 2H, CH_2), 3.05 (t, 2H, *J* 8.0 Hz, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.8, 163.4, 141.4, 130.3, 129.9, 128.5, 128.4, 126.0, 113.7, 55.4, 40.1, 30.3.

3-Phenyl-1-(*p*-tolyl)propan-1-one (**4c**):[34] Yield: 0.090 g (80%); colorless liquid; MS: *m/z* (rel. int.) 224 (15), 209 (27), 120 (9), 119 (100), 105 (6), 91 (46), 77 (6), 65 (19), 51 (4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.84 (d, 2H, *J* 8.1 Hz, Ar–H), 7.30-7.18 (m, 7H, Ph–H and Ar–H), 3.25 (t, 2H, *J* 8.0 Hz, CH_2), 3.05 (t, 2H, *J* 8.0 Hz, CH_2), 2.38 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.8, 143.7, 141.4, 134.4, 129.2, 128.5, 128.4, 128.1, 126.0, 40.3, 30.2, 21.5.

1-(4-Bromophenyl)-3-phenylpropan-1-one (**4d**):[34] Yield: 0.107 g (74%); white solid; m.p.: 98-100 °C; MS: *m/z* (rel. int.) 288 (24), 209 (31), 185 (94), 183 (100), 157 (20), 155 (21), 105 (37), 91 (29), 77 (17), 65 (10), 51 (9); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.80 (d, 2H, *J* 8.7 Hz, Ar–H), 7.57 (d, 2H, *J* 8.7 Hz, Ar–H), 7.32-7.17 (m, 5H, Ph–H), 3.28-3.22 (m, 2H, CH_2), 3.05 (t, 2H, *J* 8.0 Hz, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 198.1, 141.0, 135.5, 131.9, 129.5, 128.5, 128.4, 128.2, 126.2, 40.3, 30.0.

1-Phenyl-3-(*p*-tolyl)propan-1-one (**4e**):[34] Yield: 0.097 g (87%); colorless liquid; MS: *m/z* (rel. int.) 225 (5), 224 (30), 209 (7), 119 (16), 105 (100), 91 (8), 77 (37), 51 (7); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.95-7.93 (m, 2H, Ph–H), 7.53 (t, 1H, *J* 7.2 Hz, Ph–H), 7.45-7.41 (m, 2H, Ph–H), 7.13 (d, 2H, *J* 8.0 Hz, Ar–H), 7.09 (d, 2H, *J* 8.0 Hz, Ar–H), 3.26 (t, 2H, *J* 8.0 Hz, CH_2), 3.02 (t, 2H, *J* 8.0 Hz, CH_2), 2.31 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.3, 138.2, 136.9, 135.6, 132.9, 129.2, 128.5, 128.2, 128.0, 40.5, 29.7, 20.9.

1-Phenyl-3-(*o*-tolyl)propan-1-one (**4f**):[34] Yield: 0.087 g (78%); colorless liquid; MS: *m/z* (rel. int.) 224 (9), 206 (30), 119 (11), 105 (100), 104 (24), 91 (10), 77 (38), 51 (7); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.97-7.94 (m, 2H, Ph–H), 7.57-7.51 (m, 1H, Ph–H), 7.46-7.41 (m, 2H, Ar–H), 7.20-7.12 (m, 4H, Ph–H and Ar–H), 3.26-3.21 (m, 2H, CH_2), 3.07-3.02 (m, 2H, CH_2), 2.34 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 199.3, 139.3, 136.8, 135.9, 133.0, 130.3, 128.7, 128.5, 128.0, 126.3, 126.1, 39.0, 27.4, 19.3.

3-(4-Methoxyphenyl)-1-phenylpropan-1-one (**4g**):[34] Yield: 0.090 g (75%); pale yellow solid; m.p.: 65-67 °C; MS: *m/z* (rel. int.) 240 (31), 135 (12), 121 (100), 108 (21), 105 (47), 91 (11), 77 (45), 65 (5), 51 (10); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (d, 2H, *J* 7.6 Hz, Ph–H), 7.53 (t, 1H, *J* 7.1 Hz, Ph–H), 7.42 (t, 2H, *J* 7.5 Hz, Ph–H), 7.15 (d, 2H, *J* 8.2 Hz, Ar–H), 6.83 (d, 2H, *J* 8.2 Hz, Ar–H), 3.76 (s, 3H, OCH_3), 3.24 (t, 2H, *J* 7.8 Hz, CH_2), 3.00 (t, 2H, *J* 7.8 Hz, CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.3, 158.0, 136.9, 133.3, 132.9, 129.3, 128.5, 128.0, 113.9, 55.2, 40.6, 29.3.

3-(4-Chlorophenyl)-1-phenylpropan-1-one (**4h**):[34] Yield: 0.085 g (70%); pale yellow solid; m.p.: 55-57 °C; MS: *m/z* (rel. int.) 244 (18), 125 (8), 105 (100), 77 (47), 51 (12); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.95-7.92 (m, 2H, Ph–H), 7.57-7.52 (m, 1H, Ph–H), 7.46-7.41 (m, 2H, Ph–H), 7.23 (d, 2H, *J* 8.6 Hz, Ar–H), 7.16 (d, 2H, *J* 8.6 Hz, Ar–H), 3.29-3.23 (m, 2H, CH_2), 3.05-3.00 (m, 2H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 198.7, 139.7, 136.7, 133.1, 131.8, 129.8, 128.6, 128.5, 127.9, 40.2, 29.3.

3-(2-Chlorophenyl)-1-phenylpropan-1-one (**4i**):[34] Yield: 0.090 g (74%); colorless liquid; MS: *m/z* (rel. int.) 243 (1), 210 (13), 209 (79), 105 (100), 103 (7), 77 (54), 51 (12); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.97-7.94 (m, 2H, Ph–H), 7.57-7.51 (m, 1H, Ph–H), 7.46-7.41 (m, 2H, Ph–H), 7.36-7.28 (m, 2H, Ar–H); 7.21-7.12 (m, 2H, Ar–H), 3.33-3.27 (m, 2H, CH_2), 3.20-3.14 (m, 2H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 198.9, 138.8, 136.7, 133.9, 133.1, 130.7, 129.5, 128.5, 128.0, 127.7, 126.9, 38.4, 28.3.

1,3-Bis(4-methoxyphenyl)propan-1-one (**4j**):[34] Yield: 0.108 g (80%); colorless liquid; MS: *m/z* (rel. int.) 270 (29), 135 (100), 134 (13), 121 (54), 108 (9), 107 (9), 91 (6), 77 (20); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.91 (d, 2H, *J* 8.9 Hz, Ar–H), 7.15 (d, 2H, *J* 8.7 Hz, Ar–H), 6.90 (d, 2H, *J* 8.9 Hz, Ar–H), 6.83 (d, 2H, *J* 8.7 Hz, Ar–H), 3.82 (s, 3H, CH_3), 3.75 (s, 3H, CH_3), 3.22-3.16 (m, 2H, CH_2), 3.00-2.95 (m, 2H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.8, 163.3, 157.8, 133.3, 130.1, 129.8, 129.2, 113.8, 113.6, 55.3, 55.1, 40.2, 29.3.

3-(4-Chlorophenyl)-1-(4-methoxyphenyl)propan-1-one (**4k**):[35] Yield: 0.119 g (87%); white solid; m.p.: 69-71 °C; MS: *m/z* (rel. int.) 274 (11), 135 (100), 107 (11), 92 (11), 77 (20); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.92 (d, 2H, *J* 8.9 Hz, Ar–H), 7.24 (d, 2H, *J* 8.5 Hz, Ar–H), 7.16 (d, 2H, *J* 8.5 Hz, Ar–H), 6.91 (d, 2H, *J* 8.9 Hz, Ar–H), 3.84 (s, 3H, CH_3), 3.21 (t, 2H, *J* 7.7 Hz, CH_2), 3.01 (t, 2H, *J* 7.7 Hz, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.3, 163.4, 139.8, 131.7, 130.2, 129.7 (2C), 128.4, 113.7, 55.6, 39.6, 29.4.

General procedure for the synthesis of zingerone using PhSeSePh/glycerol/H_3PO_2

Glycerol (1.0 mL) was added to a 5 mL round-bottomed flask containing 2-methoxy-4-(3-oxo-1-butenyl)phenol **1l** (0.5 mmol), diphenyl diselenide **2** (0.5 mmol) and H_3PO_2 (0.2 mL). The reaction mixture was stirred at 90 °C under nitrogen atmosphere for 30 min. After that, the reaction mixture was received in water (20 mL), extracted with ethyl acetate (3 × 5 mL), dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using ethyl acetate/hexane (10:90) as the eluent.

4-(4-Hydroxy-3-methoxyphenyl)-2-butanone (**4l**):[36] Yield: 0.066 g (68%); colorless needles; m.p.: 36-37 °C; MS: *m/z* (rel. int.) 194 (M^+, 43), 151 (12), 137 (100), 119 (24), 91 (23), 77 (10), 43 (27); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.81 (d, 1H, *J* 8.0 Hz, Ar–H), 6.70-6.64 (m, 2H, Ar–H), 5.73 (br, 1H, Ar–O<u>H</u>), 3.85 (s, 3H, OCH_3), 2.85-2.80 (m, 2H, CH_2), 2.75-2.70 (m, 2H, CH_2), 2.13 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 208.3, 146.3, 143.8, 132.7, 120.6, 114.3, 111.0, 55.7, 45.4, 30.0, 29.3.

Conclusion

In summary, we described here our results for the reaction of benzeneselenol, generated *in situ* by reaction of diphenyl diselenide with H_3PO_2, with various (*E*)-chalcones using glycerol as solvent at 90 °C under nitrogen atmosphere. Using our optimized reaction conditions, a range of chemoselective 1,4-reduction products were obtained in good yields and a range of chalcones containing electron-donating or electron-withdrawing groups were employed as substrates. In addition, the glycerol/H_3PO_2 system can be easily recovered and reused in chemoselective 1,4-reductions for successive cycles without loss of efficiency. Under 1,4-reducing reaction conditions, zingerone was synthesized in good yield.

Supplementary Information

Supplementary data are available free of charge at http://jbcs.sbq.org.br as PDF file.

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Supplementary Information

Glycerol/Hypophosphorous Acid and PhSeSePh: An Efficient and Selective System for Reactions in the Carbon-Carbon Double Bond of (*E*)-Chalcones

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Selected spectra

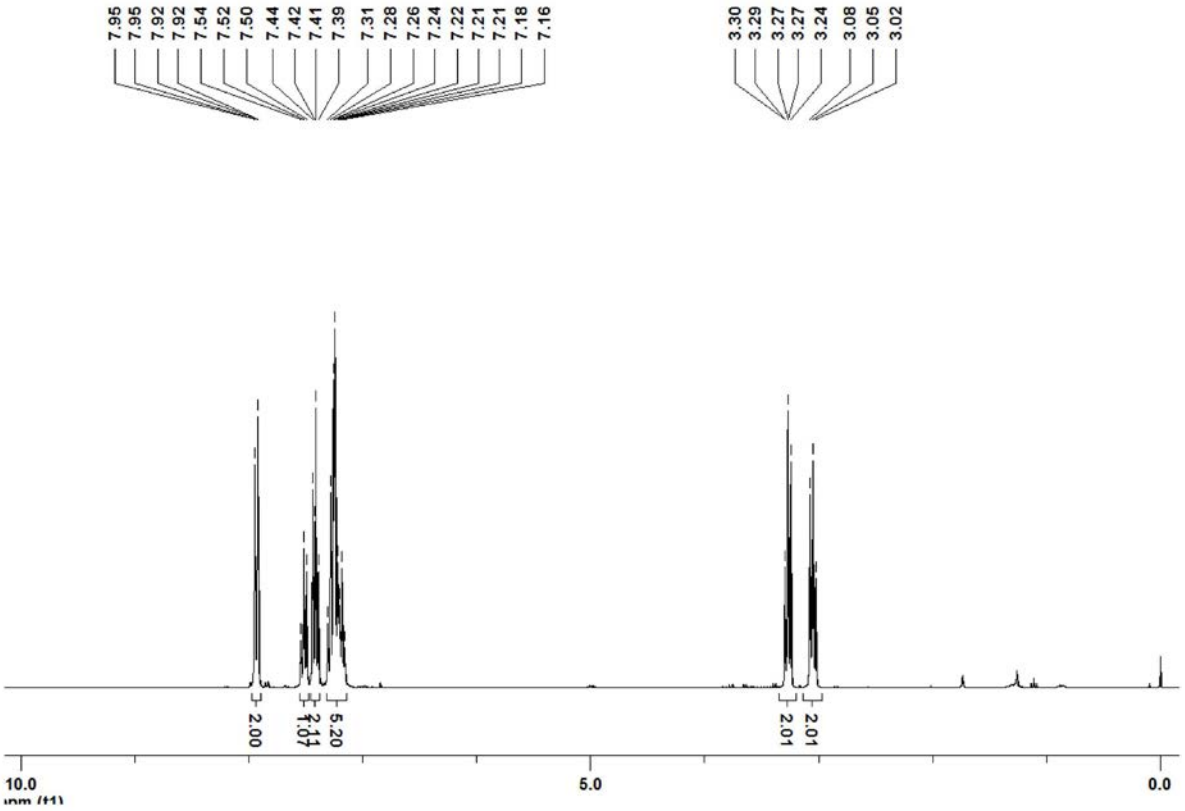

Figure S1. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of 1,3-diphenyl-1-propanone (**4a**).

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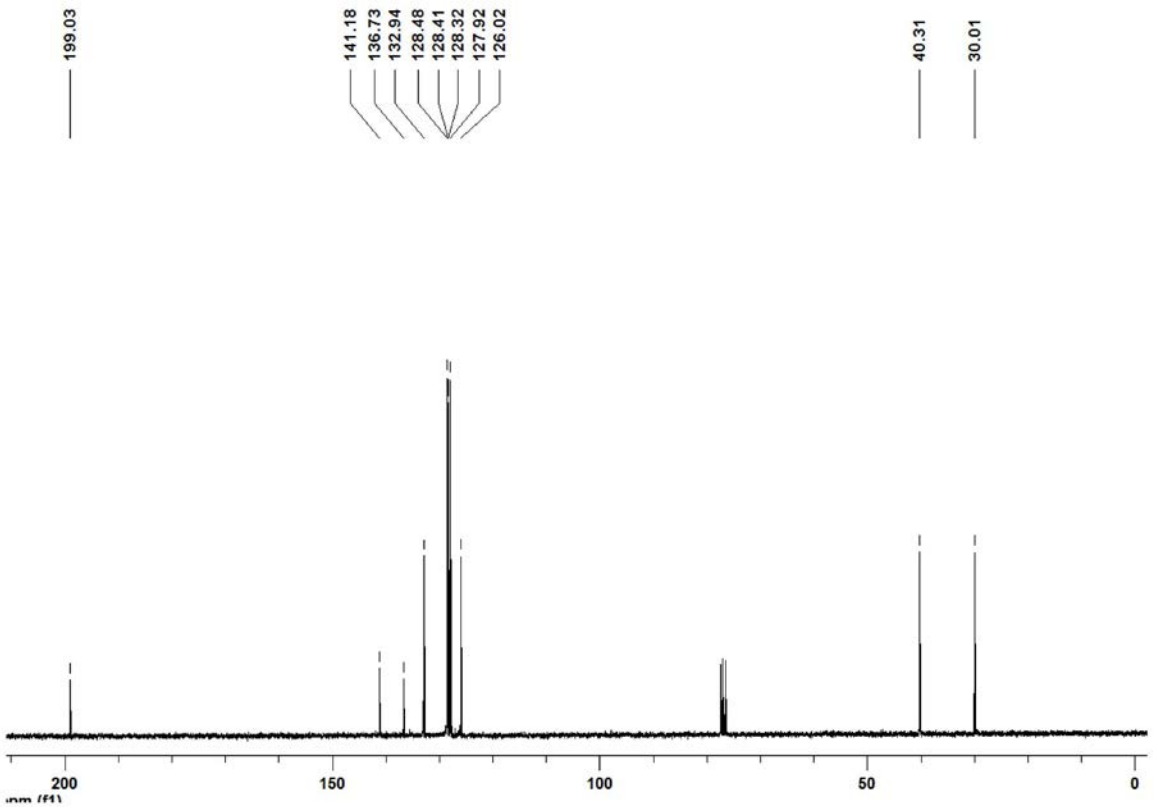

Figure S2. ^{13}C NMR ($CDCl_3$, 75 MHz) spectrum of 1,3-diphenyl-1-propanone (**4a**).

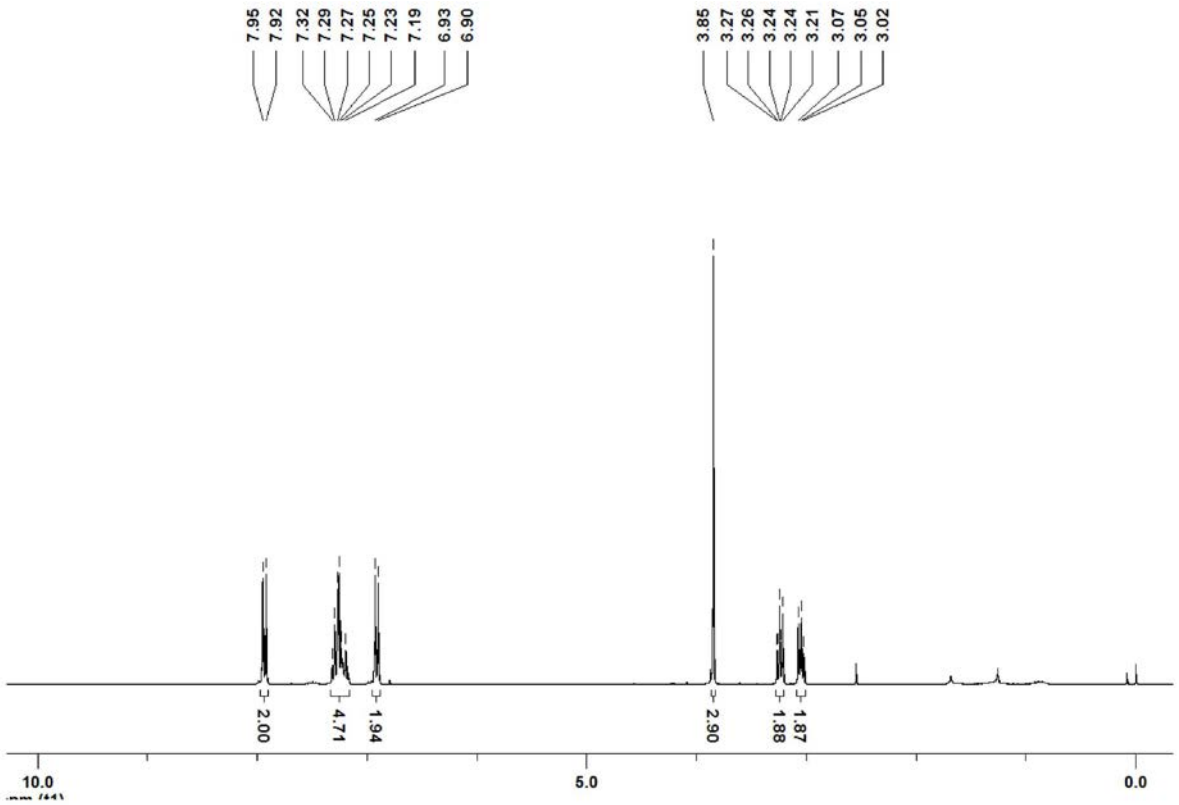

Figure S3. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of 1-(4-methoxyphenyl)-3-phenylpropan-1-one (**4b**).

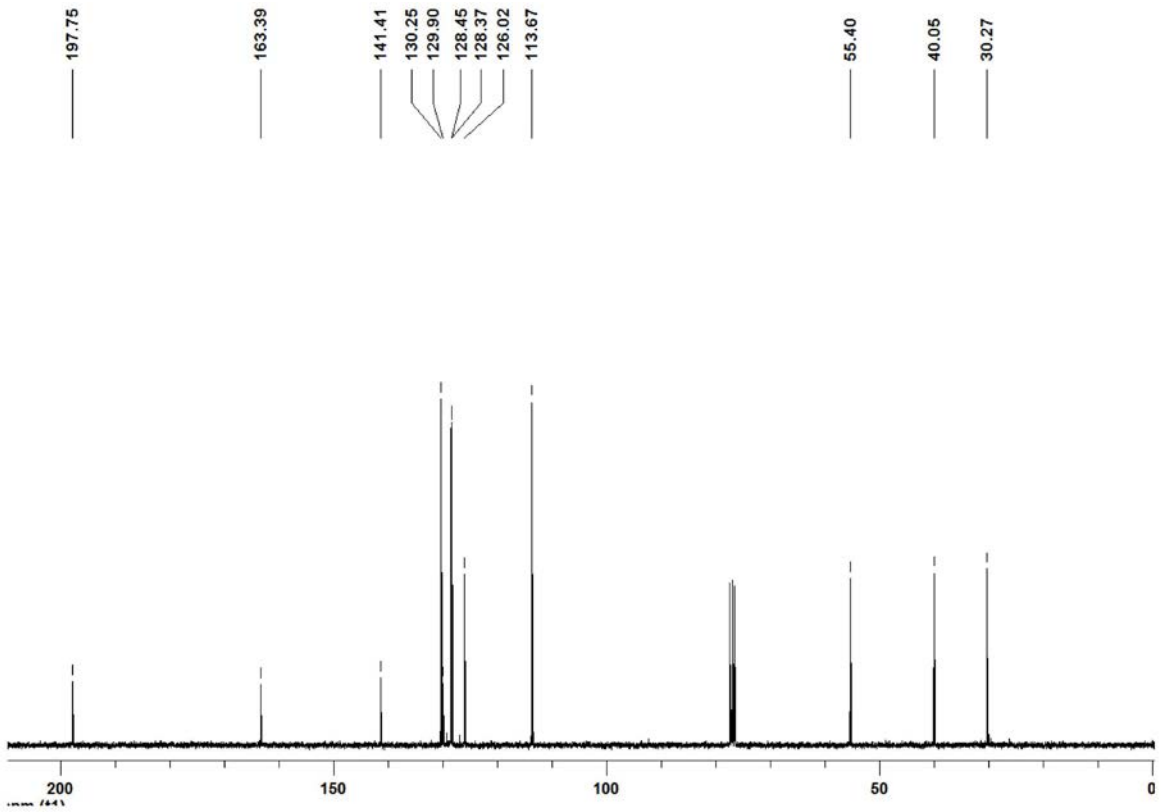

Figure S4. ^{13}C NMR ($CDCl_3$, 75 MHz) spectrum of 1-(4-methoxyphenyl)-3-phenylpropan-1-one (**4b**).

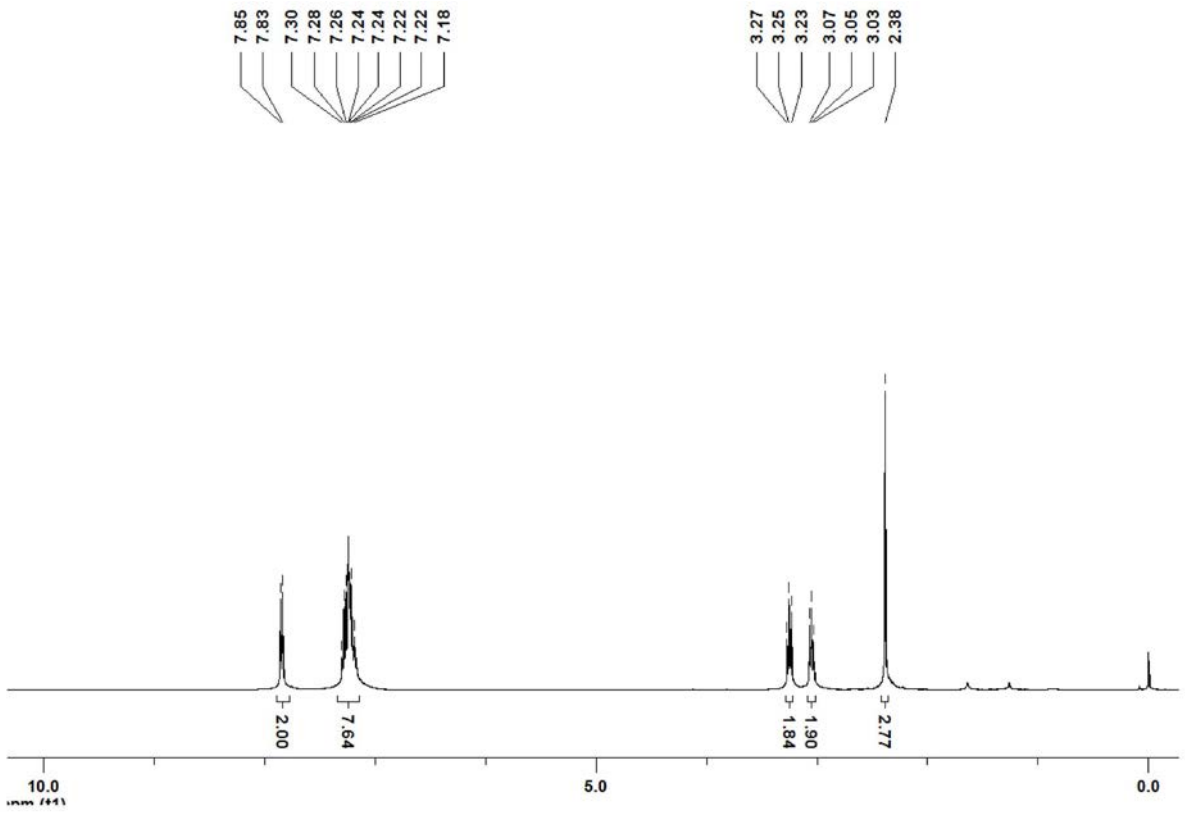

Figure S5. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 3-phenyl-1-(*p*-tolyl)propan-1-one (**4c**).

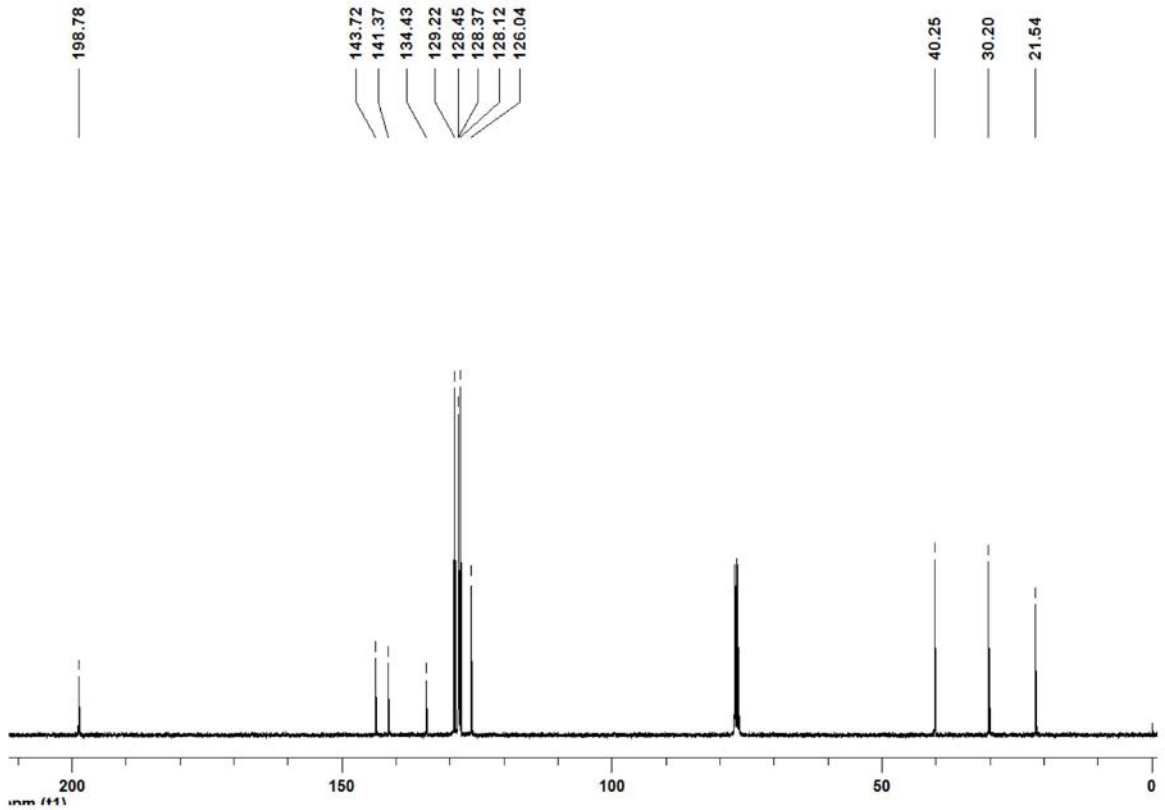

Figure S6. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 3-phenyl-1-(*p*-tolyl)propan-1-one (**4c**).

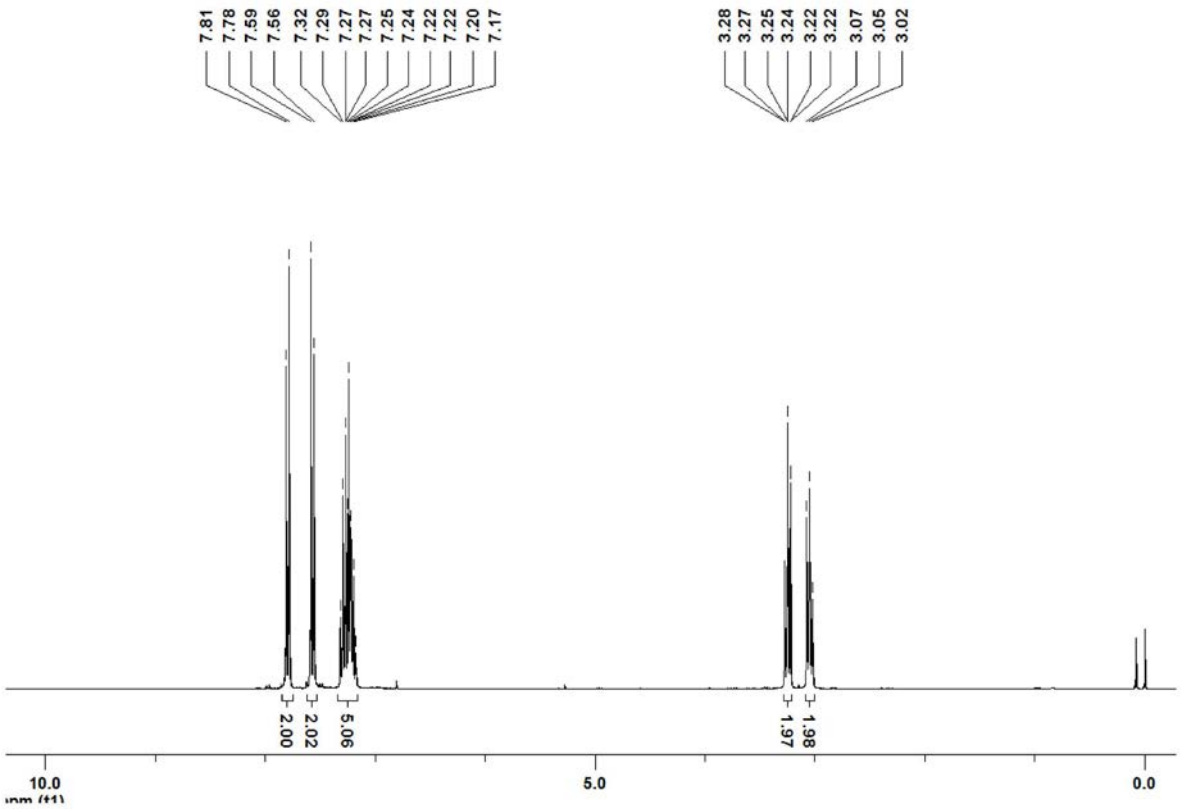

Figure S7. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of 1-(4-bromophenyl)-3-phenylpropan-1-one (**4d**).

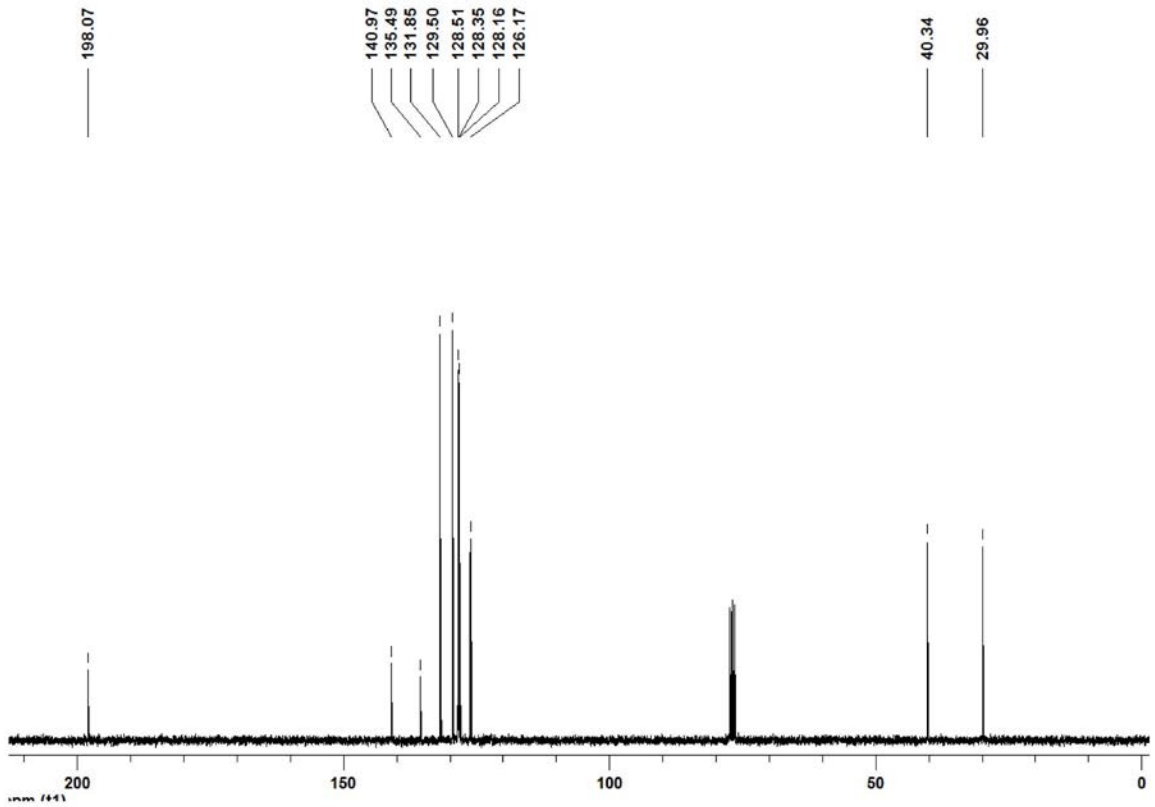

Figure S8. ^{13}C NMR ($CDCl_3$, 75 MHz) spectrum of 1-(4-bromophenyl)-3-phenylpropan-1-one (**4d**).

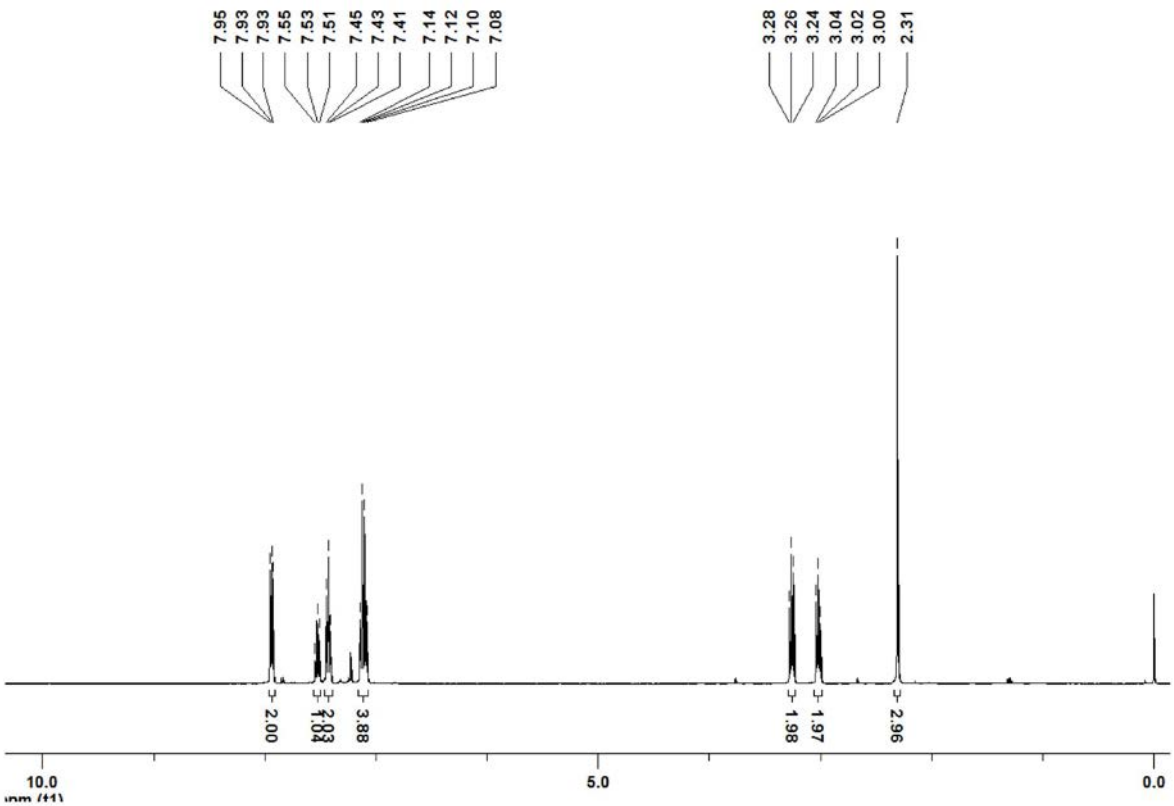

Figure S9. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 1-phenyl-3-(*p*-tolyl)propan-1-one (**4e**).

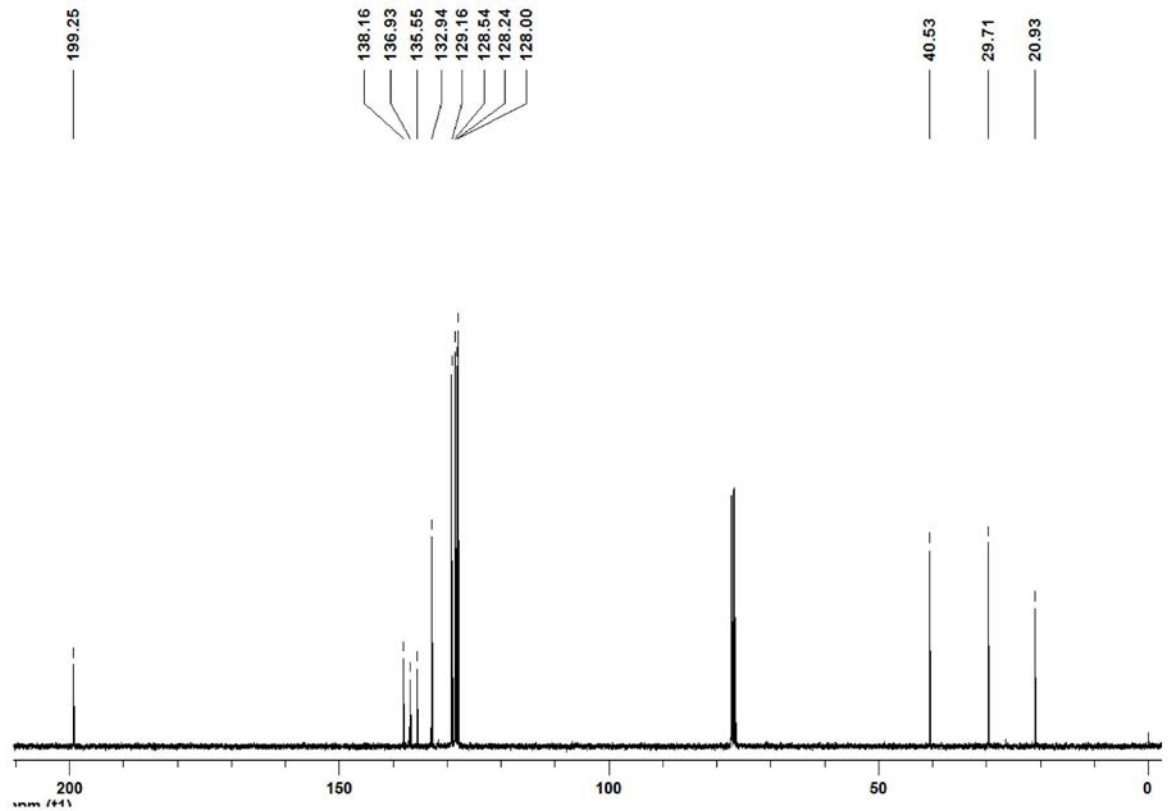

Figure S10. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 1-phenyl-3-(*p*-tolyl)propan-1-one (**4e**).

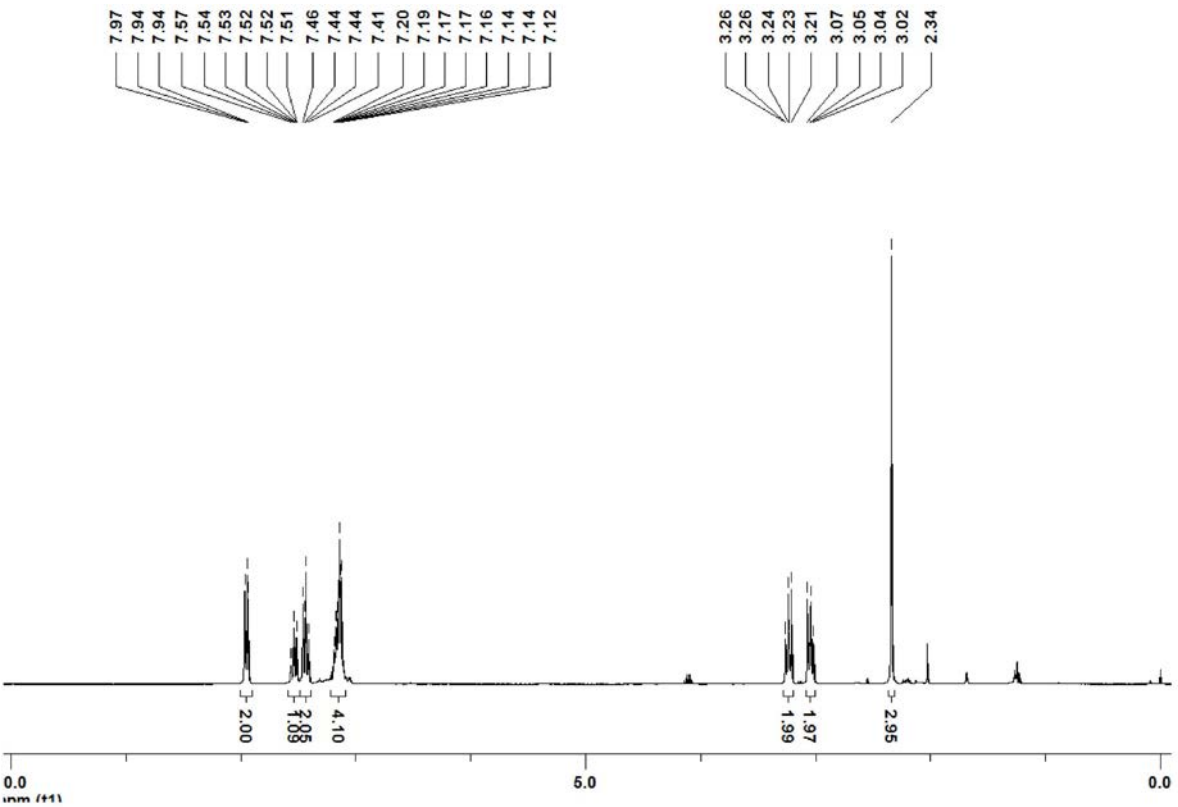

Figure S11. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of 1-phenyl-3-(*o*-tolyl)propan-1-one (**4f**).

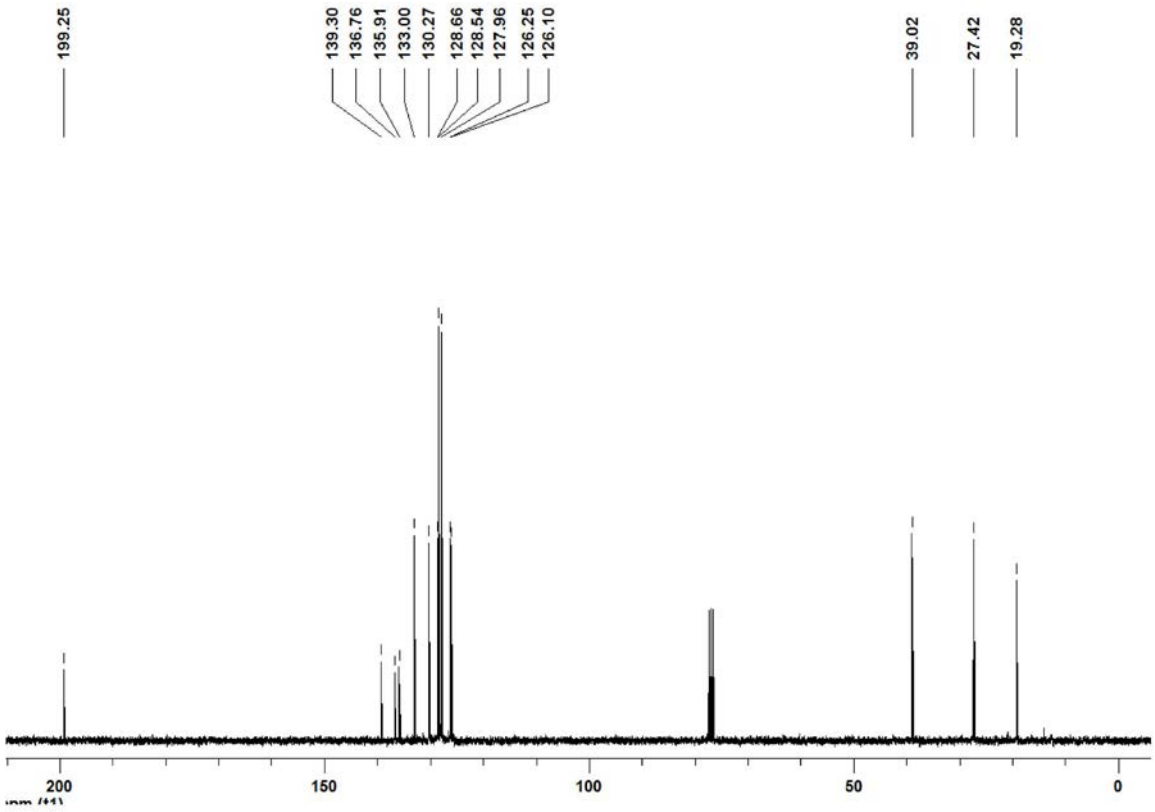

Figure S12. ^{13}C NMR ($CDCl_3$, 75 MHz) spectrum of 1-phenyl-3-(*o*-tolyl)propan-1-one (**4f**).

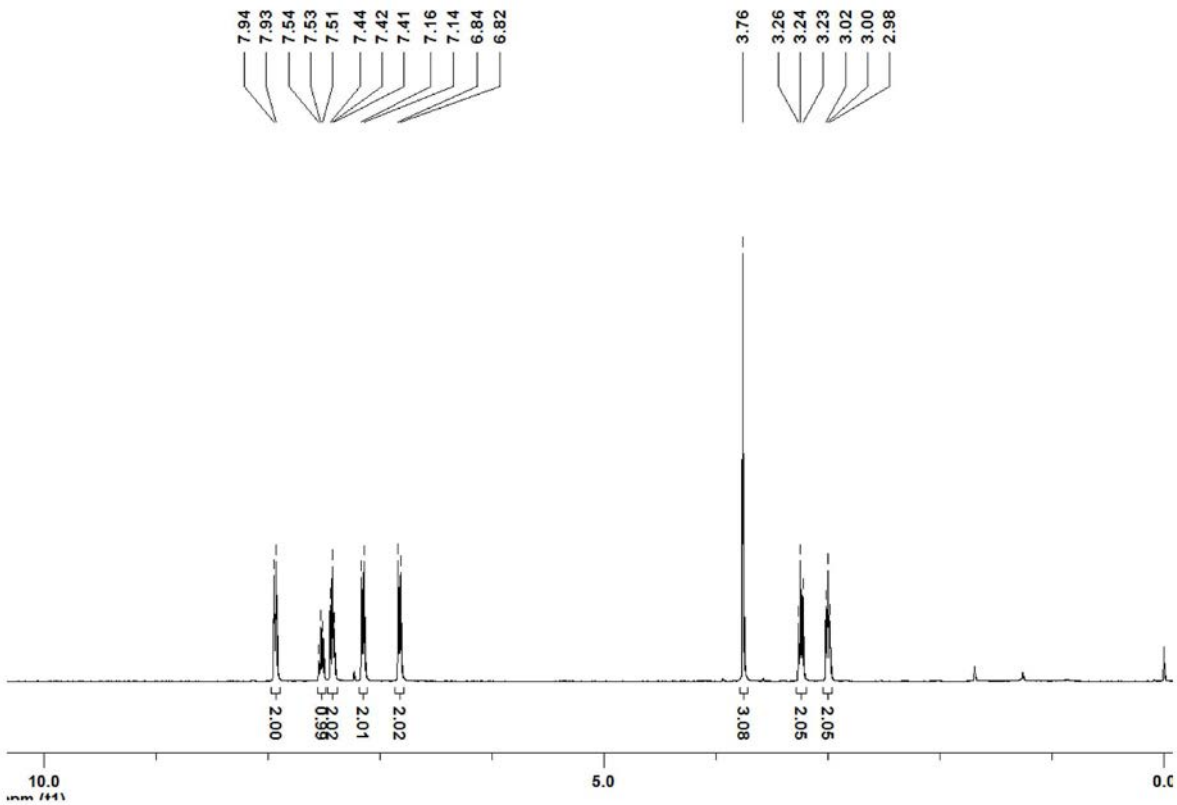

Figure S13. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 3-(4-methoxyphenyl)-1-phenylpropan-1-one (**4g**).

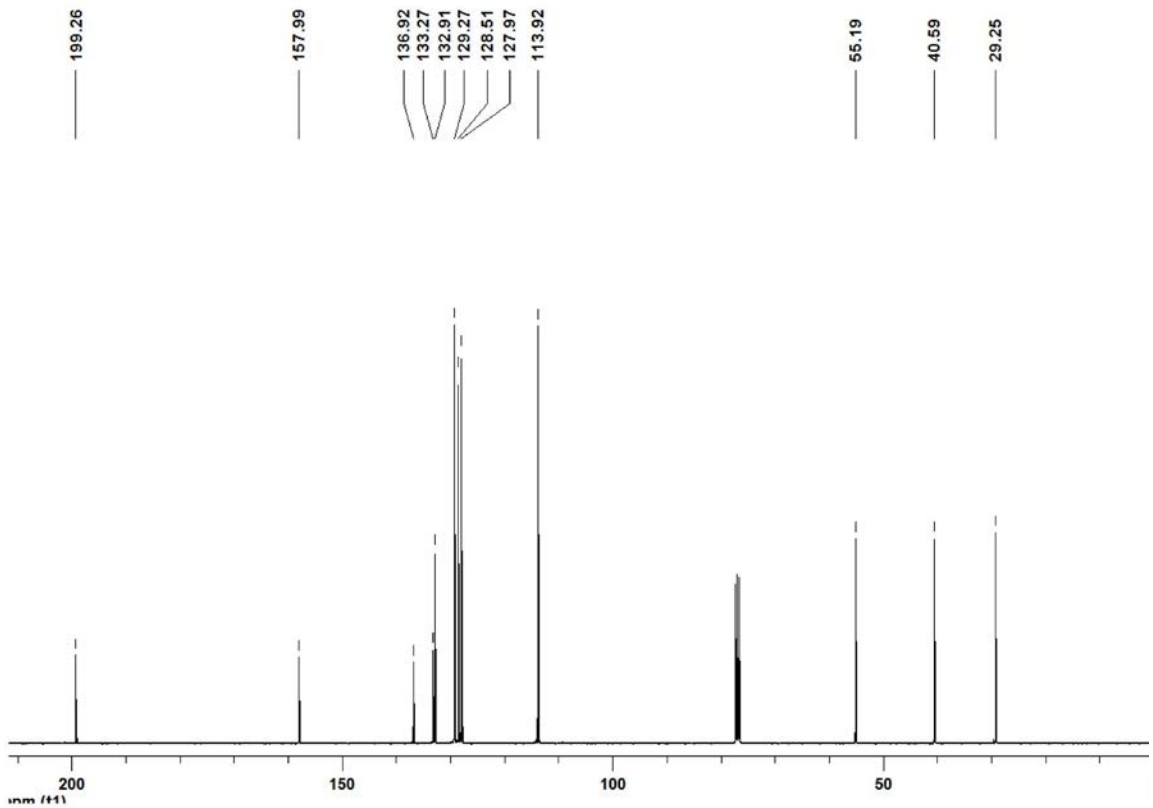

Figure S14. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 3-(4-methoxyphenyl)-1-phenylpropan-1-one (**4g**).

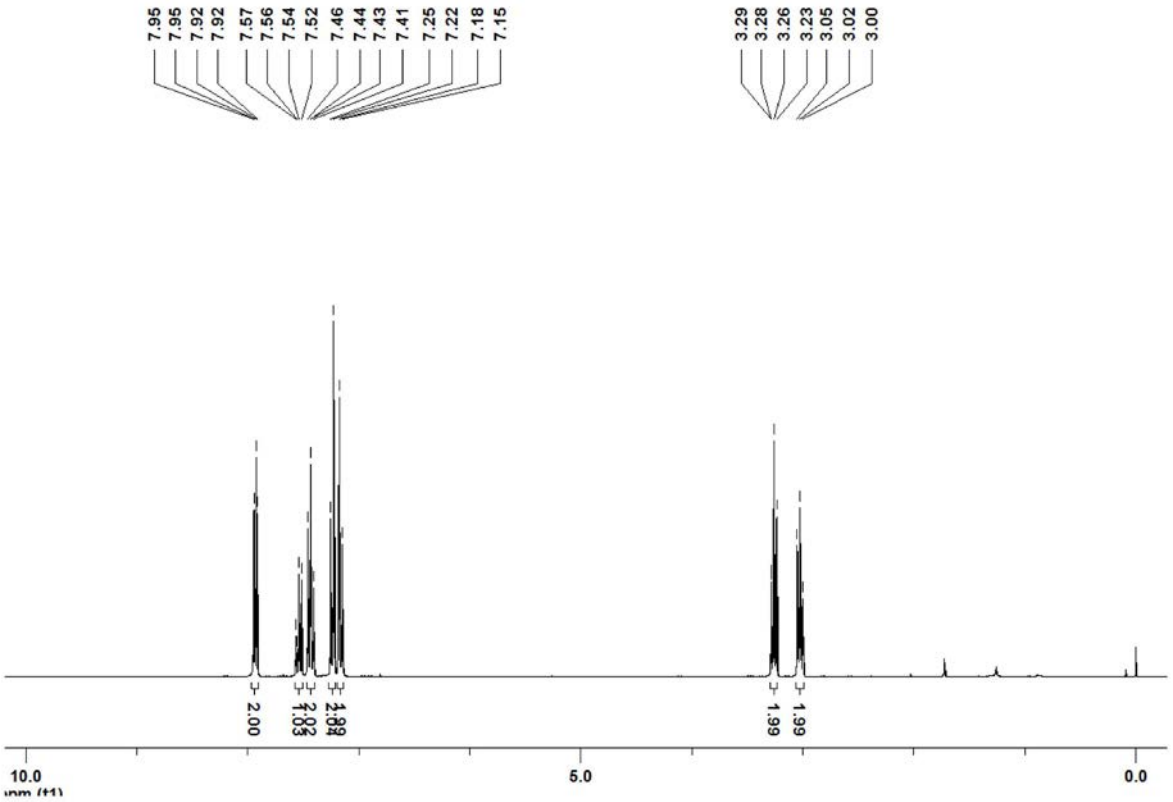

Figure S15. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of 3-(4-chlorophenyl)-1-phenylpropan-1-one (**4h**).

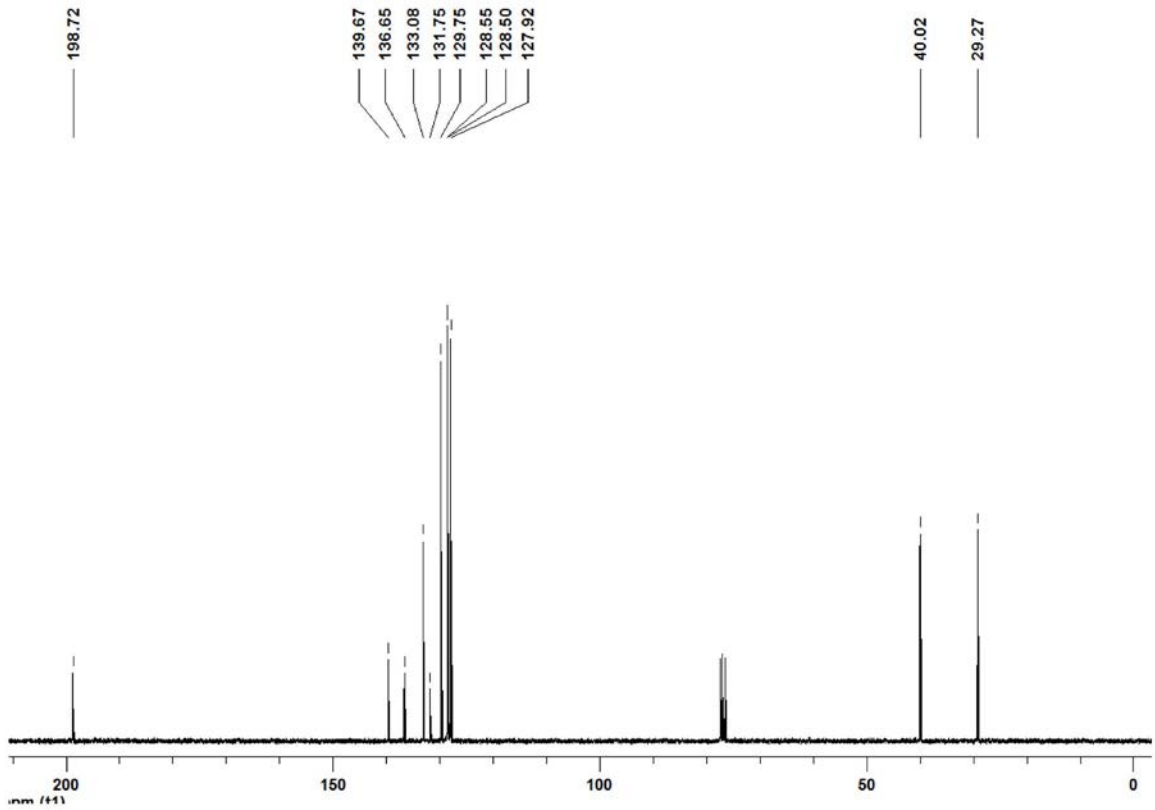

Figure S16. ^{13}C NMR ($CDCl_3$, 75 MHz) spectrum of 3-(4-chlorophenyl)-1-phenylpropan-1-one (**4h**).

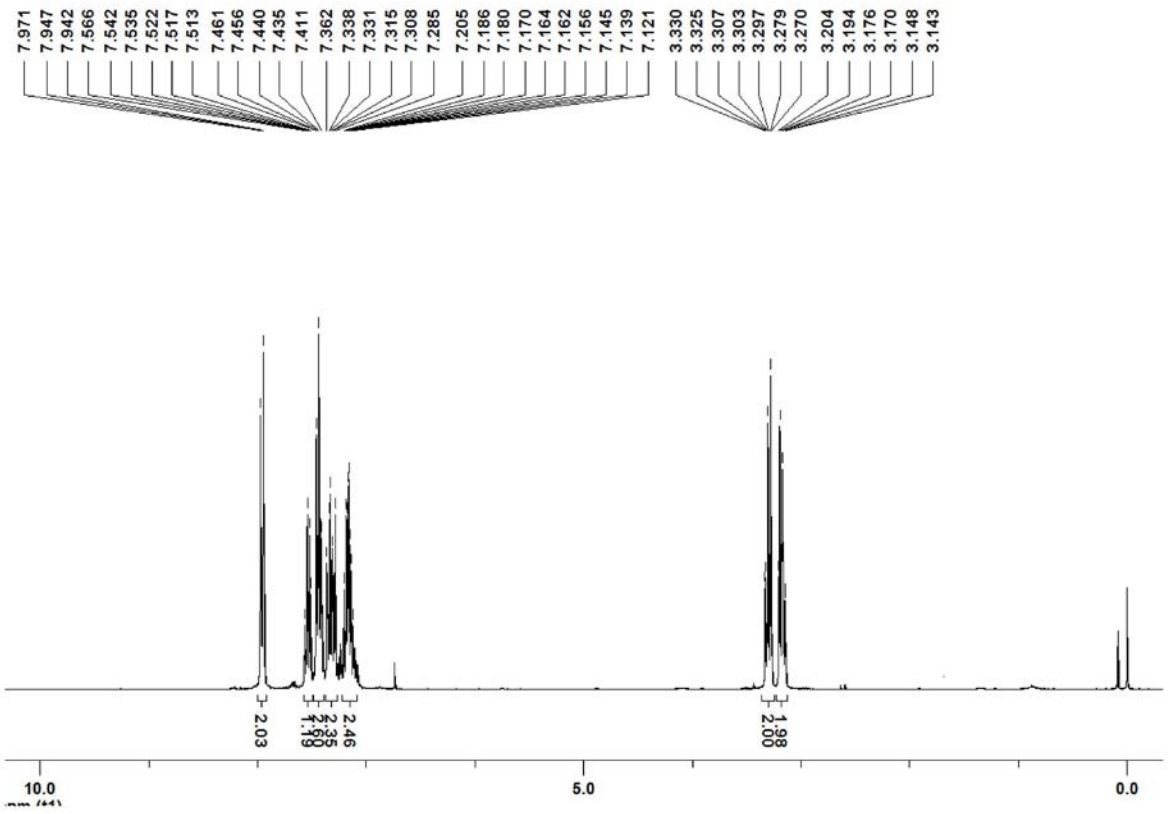

Figure S17. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of 3-(2-chlorophenyl)-1-phenylpropan-1-one (**4i**).

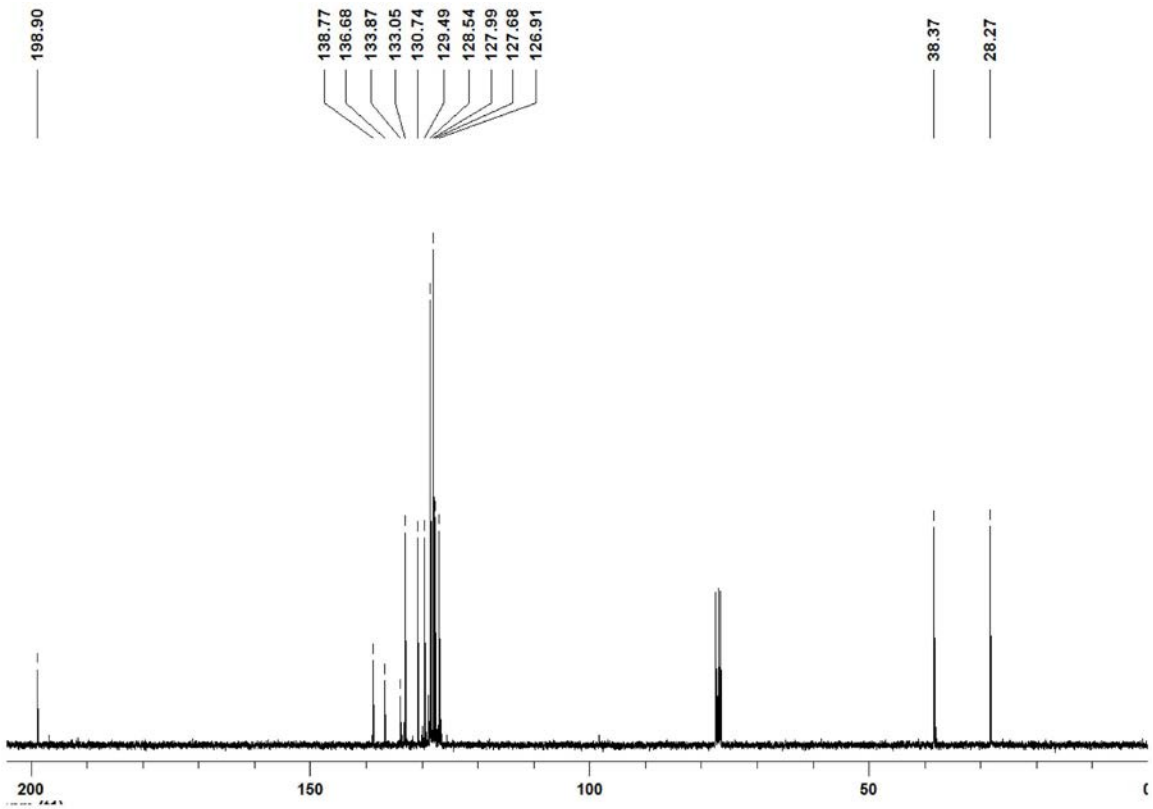

Figure S18. ^{13}C NMR ($CDCl_3$, 75 MHz) spectrum of 3-(2-chlorophenyl)-1-phenylpropan-1-one (**4i**).

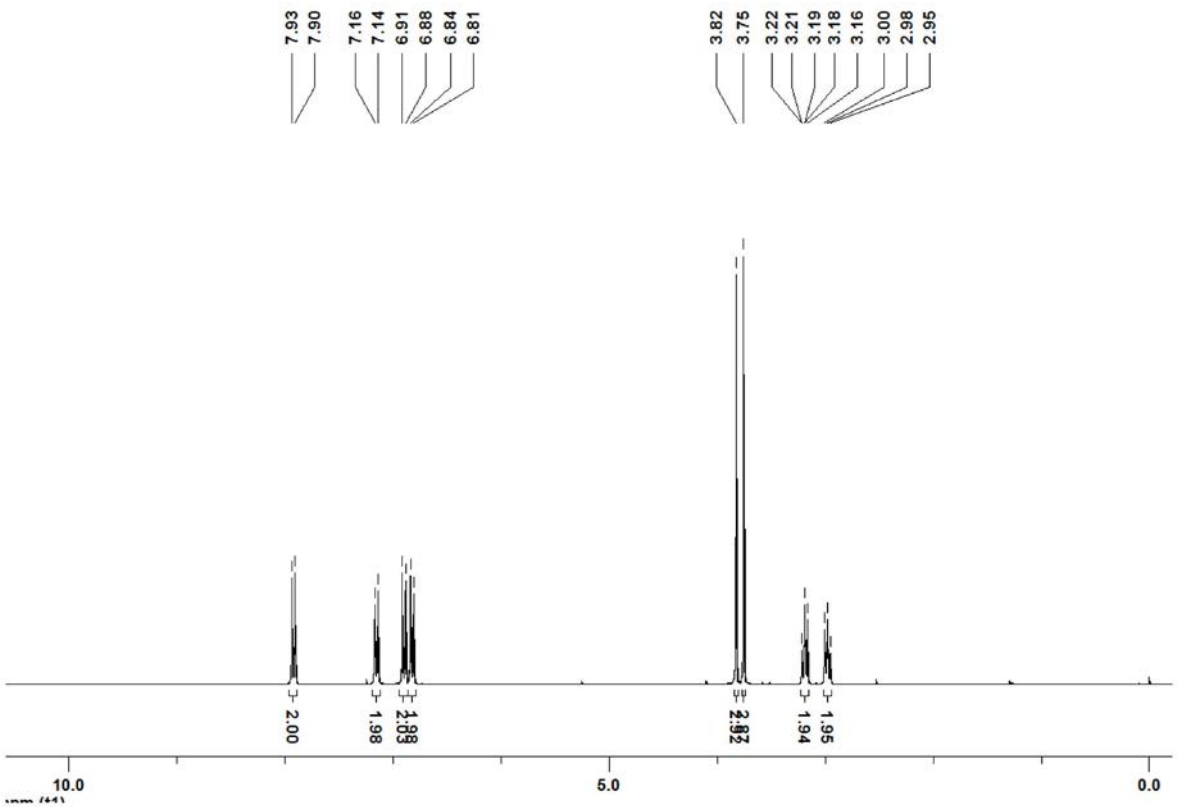

Figure S19. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of 1,3-bis(4-methoxyphenyl)propan-1-one (**4j**).

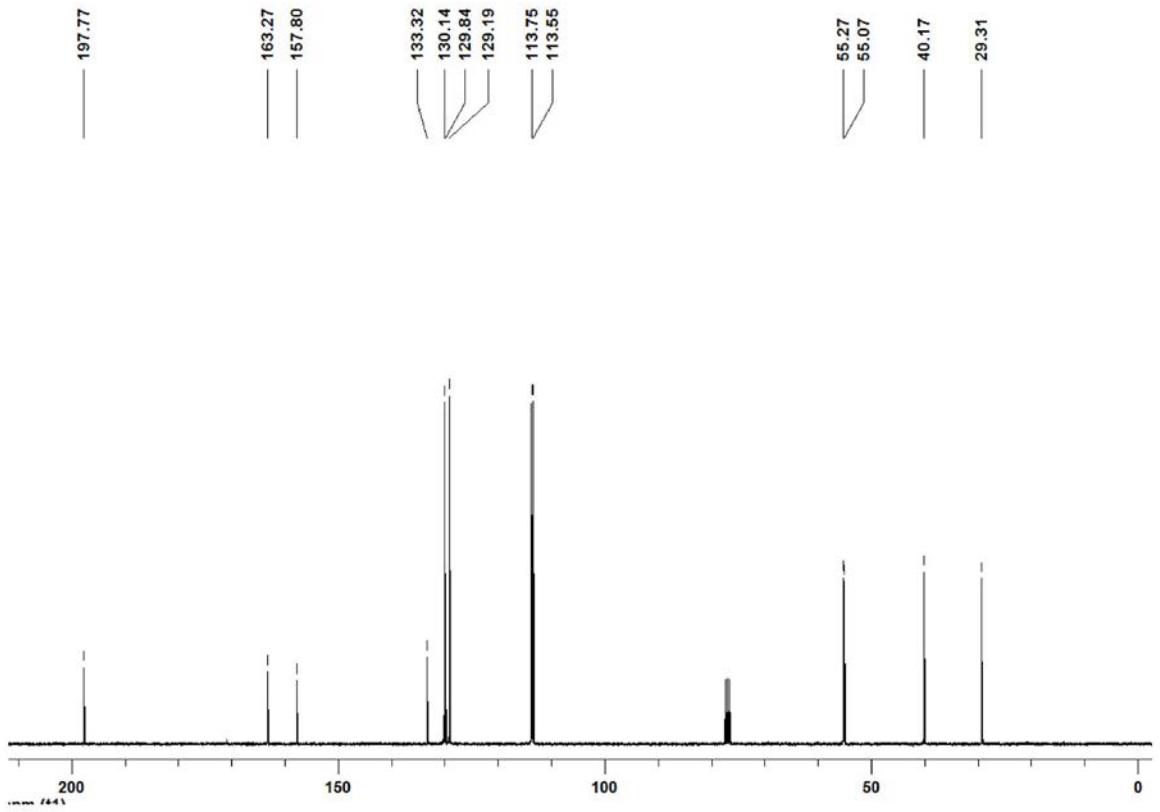

Figure S20. ^{13}C NMR ($CDCl_3$, 75 MHz) spectrum of 1,3-bis(4-methoxyphenyl)propan-1-one (**4j**).

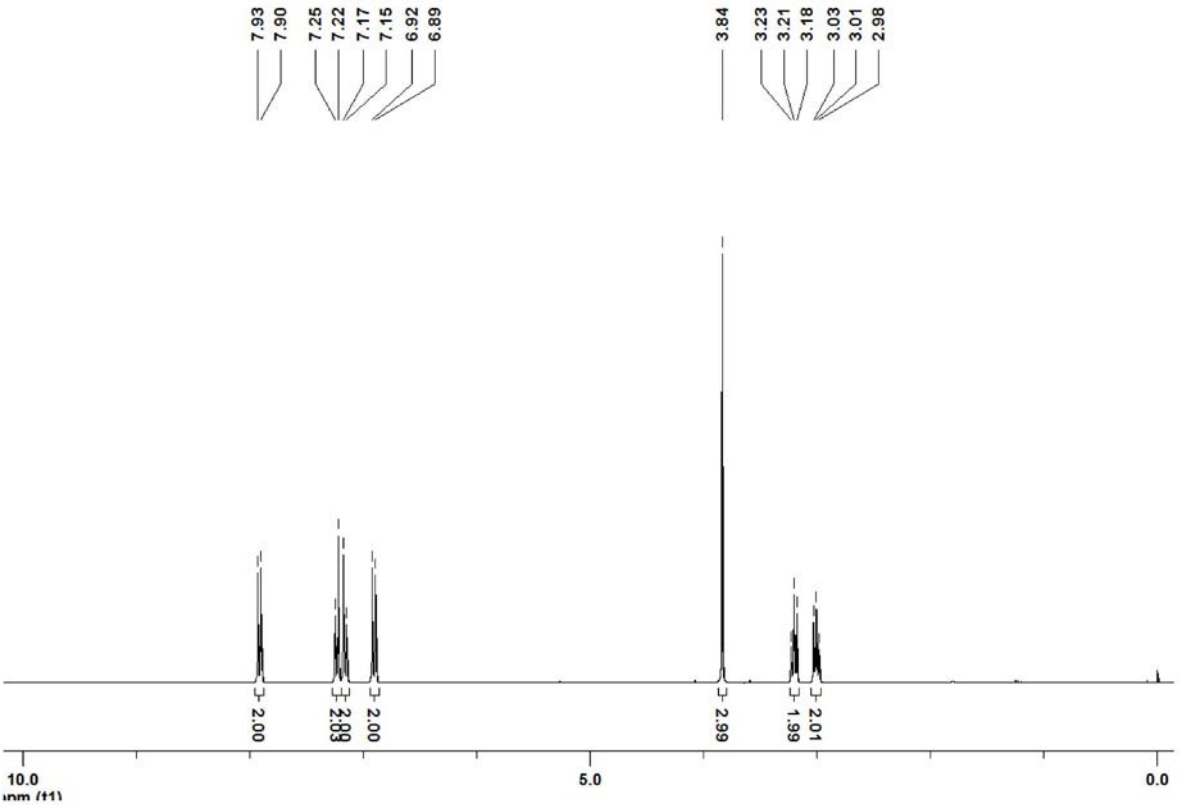

Figure S21. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of 3-(4-chlorophenyl)-1-(4-methoxyphenyl)propan-1-one (**4k**).

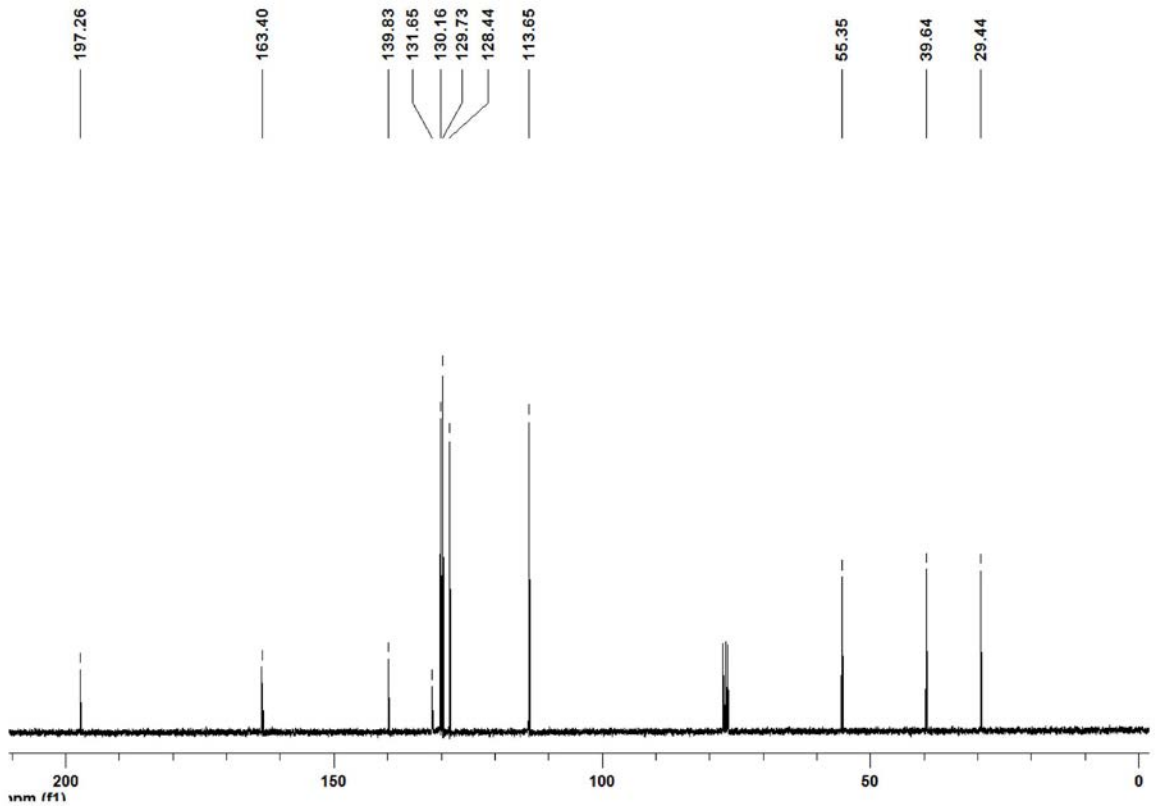

Figure S22. ^{13}C NMR ($CDCl_3$, 75 MHz) spectrum of 3-(4-chlorophenyl)-1-(4-methoxyphenyl)propan-1-one (**4k**).

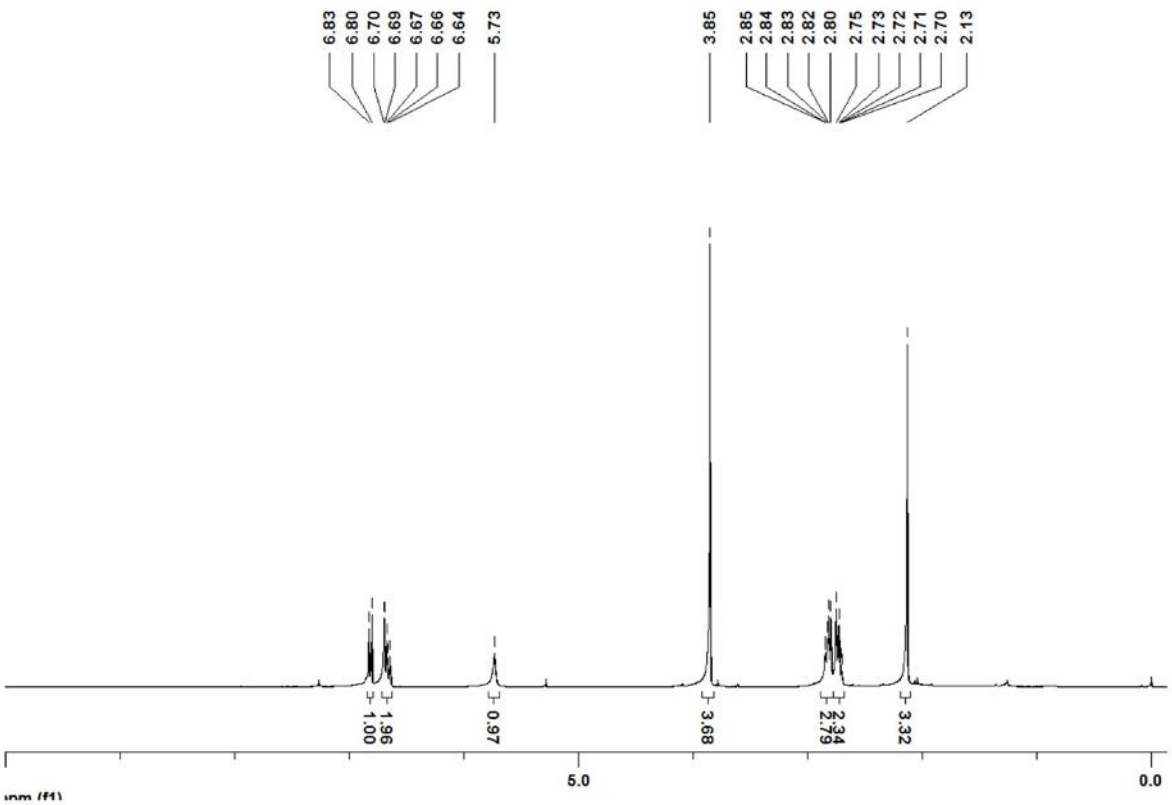

Figure S23. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of 4-(4-hydroxy-3-methoxyphenyl)-2-butanone (**4l**).

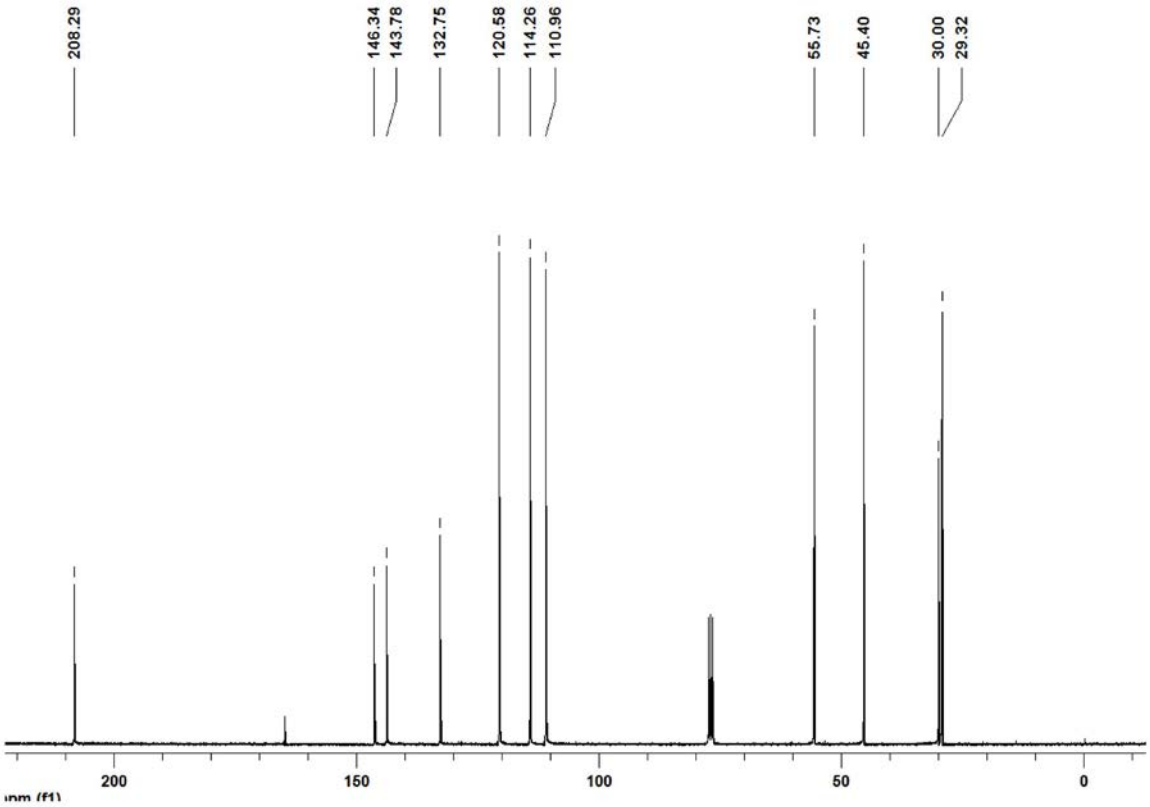

Figure S24. ^{13}C NMR ($CDCl_3$, 75 MHz) spectrum of 4-(4-hydroxy-3-methoxyphenyl)-2-butanone (**4l**).