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Short Report

Synthesis of Quinolinediones by Catalyst-Free Formal Aza-[3+2+1] Cycloaddition of Enaminones, Aldehydes and Meldrum's Acid

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Este trabalho descreve um método simples de síntese de 4-aril-tetraidroquinoline-2,5-dionas através da reação tricomponente entre enaminonas *N*-aril-substituídas derivadas da dimedona, aldeídos aromáticos e o ácido de Meldrum. A síntese ocorre sem o uso de catálise e aquecimento, não sendo necessário o emprego de solventes especiais ou condições reacionais sofisticadas.

A simple green synthesis of 4-aryl-tetrahydroquinoline-2,5-diones was developed, improving the three-component reaction of *N*-aryl substituted dimedone-based enaminones, aromatic aldehydes and Meldrum's acid. The method does not employ catalyst, heating or any special solvent or reaction condition, and has facile work-up and purification. Variations of enaminones and aldehydes substituents were somewhat tolerated.

Keywords: enaminones; Meldrum's acid, quinolinediones, multicomponent reaction

Introduction

The occurrence of *N*-heterocycles in natural product and drug-like compounds has motivated the development of diverse approaches to their syntheses.[1] In the medicinal chemistry arena, a valorized characteristic of a preparative route is its simplicity, and the synthesis of biological active compounds by typical step-by-step reactions has been questioned, and many solutions have been envisioned.[2] In this context, multicomponent reactions have been intensively developed to efficiently access libraries of small molecules with the advantages of green chemistry philosophy.[3]

In the course of a project aimed at the synthesis of alkaloid-like compounds to biological evaluation based on formal cycloaddition of enaminones with Michael acceptors,[4] we identified the 4-aryl-tetrahydroquinoline-2,5-dione structural scaffold as synthetic target due to the potential biological activities of quinolone derivatives.[5]

We rationalized that quinolinediones can be conveniently accessed from dimedone-based enaminones as building block (Scheme 1).[6-10] However, to be effective, a practical synthetic route is desirable. A search in the literature revealed that two approaches are known to this target structural scaffold, a two-component one which involves the formal aza-[3+3] cycloaddition of dimedone-based enaminones, and two examples of multicomponent reactions. Among these, route A is the direct reaction of enaminone with arylidene derivatives of Meldrum's acid,[6] and appears to be more adequate because the alternative synthetic route B, which do not employ such derivatives, needs large amount of expensive base (Cs_2CO_3) and purification by column chromatography.[7]

The Meldum's acid route A suggested the possibility of *in situ* formation of arylidenes, and thus some multicomponent reactions were developed. Among the three-component approaches, route C is run in water under reflux and benzyltriethylammonium chloride catalysis, and is operationally very attractive, but it is limited to *ortho*-substituted aldehydes.[8] Complementarily, the use of ionic liquid is also known to this three-component synthesis, but still restricted to the same kind of aldehydes, and with somewhat laborious purifications.[9] The described four-component synthesis of route D has a broader aldehyde scope, but now it is more practical to aliphatic amines, and employs high boiling point solvent in the purification step.[10]

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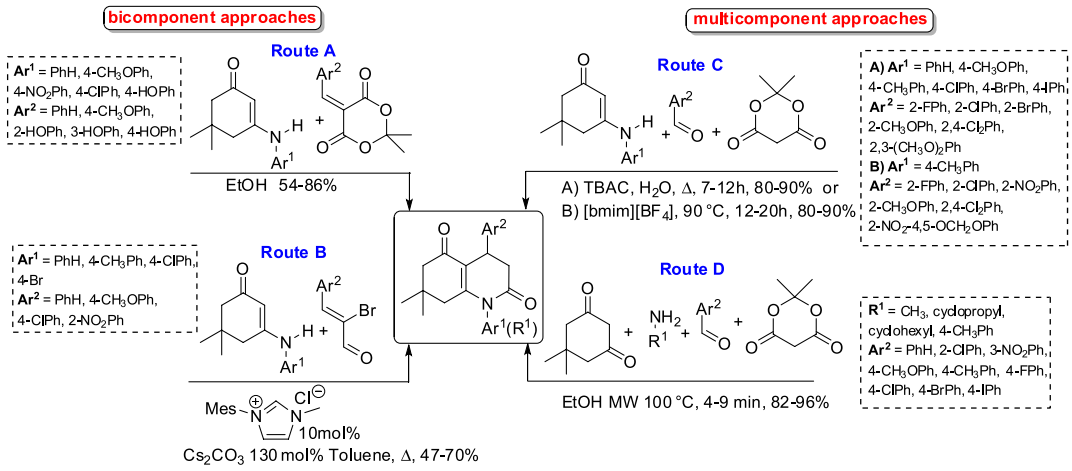


Scheme 1. Scope of known routes to 4-aryl-tetrahydroquinoline-2,5-diones via formal azacycloaddition of dimedone-based enaminones.

In spite the scenario depicted in Scheme 1 represents a significant contribution to the 4-aryl-tetrahydroquinoline-2,5-dione derivatives synthesis, the investigation of an approach which congregates the advantage of reported methods without their drawback would be desirable. Inspired by these results, we decided to develop a simple approach adequate to the purpose of synthesize a small set of mentioned quinolinedione derivatives. Moreover, it was our intention that such approach allowed variation of both position and nature of the aldehyde's substituent, and also in the *N*-aryl moiety of the dimedone-based enaminones.[11] Herein we developed a greener method of preparation of 4-aryl-tetrahydroquinoline-2,5-diones through catalyst-free multicomponent reaction, combining very simple reaction conditions, isolation and purification, and with the abovementioned structural variation.

Results and Discussion

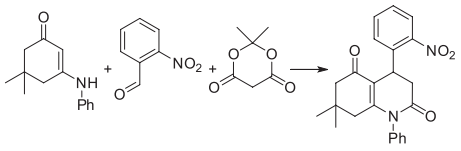
To develop a direct one-pot dimedone-based enaminones route towards 4-aryl-tetrahydroquinoline-2,5-dione derivatives involving simple work-up and purification, a careful analysis of strategies of Scheme 1 prompted us to test the three-component reaction which use Meldrum's acid and aldehydes. We rationalized that the combination of each green aspect of multicomponent routes C and D would be a reasonable initial start point. Thus, we first try a model reaction of equimolar amounts of enaminone (**1a**) with *ortho*-nitrobenzaldehyde (**2a**) and Meldrum's acid (**3a**) in water as solvent, under microwave heating without catalysis, Table 1 (entry 1). After a short reaction time, thin layer chromatography (TLC) analysis indicated disappearance of all reagents, but a complex mixture had formed. Alternatively, compound **4a** could be isolated when the reaction was performed at room temperature, albeit in low yield and with long reaction time (entry 2). The next green solvent tested was ethanol (entries 3-5). Despite the slow reaction, excellent yield was obtained when the reaction was realized at room temperature.

With satisfactory conditions to the three-component synthesis of 4-aryl-tetrahydroquinoline-2,5-dione in hand, the protocol was applied to cyclic enaminones (**1a**-**b**) and aromatic aldehydes (**2a**-**e**), in the presence of Meldrum's acid (**3**), Scheme 2. Modest to good yields were obtained and, moreover, variation in the nature and position of substituents in both enaminone and aldehydes were tolerated. Besides, the majority of the solid products precipitated during reaction, and simple filtration afforded pure quinolinediones. Only derivatives **4c** and **4e** did not precipitate, and were purified by column chromatography. With *para*-nitrobenzaldehyde reactions occurred only under reflux. In addition, complex mixtures were observed in the reactions of **1a** with 2-anisaldehyde, isatin, and aliphatic aldehydes valeraldehyde and isobutyraldehyde.

Contrary to the previous descriptions of three-component routes to 4-aryl-tetrahydroquinoline-2,5-diones,[8,9] the method herein developed is catalyst-free, and compatible with tested *ortho*, *meta* and *para* nitro-substituted aromatic aldehydes (**2a**-**c**), and with 6-nitropiperonal (**2d**) or heteroaromatic furfuraldehyde (**2e**). Indeed, dimedone-based enaminones from aniline and *para*-anisidine were effective also.

Full spectral data of obtained **4a**-**h** supported the structural determination of all quinolinediones here synthesized. In the majority of ^{1}H NMR spectra, the moiety corresponding to the endocyclic conformationally restricted NCOC$\underline{H}_2$C$\underline{H}$Ar spin system appears as an ABX system, as exemplified in Figure 1.[8-10] The multiplicities of CH_2 are two double doublets (2.99 ppm, *J* 16 and 8 Hz; 3.10 ppm, *J* 16 and 4 Hz) and the methynic hydrogen is a broad doublet

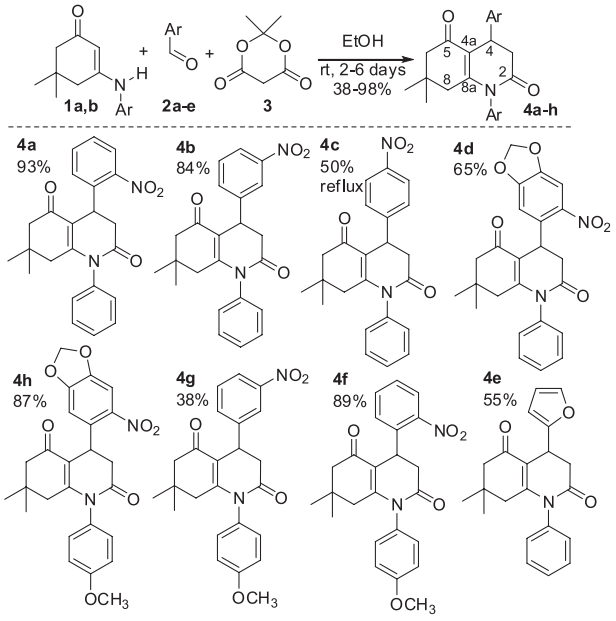
Table 1. Reaction conditions to the formal aza-[3+2+1] cycloaddition of enaminone (**1a**), aldehyde (**2a**) and Meldrum's acid to yield **4a**



entry	Solvent	Condition[a]	time	Yield / %
1	H_2O	MW 80°C 200W	10 min	cm[b]
2	H_2O	rt	3 days	10
3	EtOH	MW 80°C 200W	20 min	cm[b]
4	EtOH	reflux	1 day	53
5	EtOH	rt	2 days	93

[a]MW: microwave irradiation; [b]cm: complex mixture.

(3.78 ppm, 8 Hz). The measured values to the observed vicinal coupling constants (8 and 4 Hz) are large enough and expected to be easily assigned in this CH signal (of C-4) at the 7T field NMR spectrometer. However, as mentioned, the CH signal appears as a broad doublet due to the long range coupling ^5J with one of the hydrogen of the CH_2 at position 8, through the vinyl moiety of bridgehead carbons of the rigid bicycle 4-aryl-tetrahydroquinoline-2,5-dione nucleus.[12]



Scheme 2. Synthesis of 4-aryl-tetrahydroquinoline-2,5-diones.

From the mechanistic point of view, two convergent reactions pathways may be postulated to explain the formal aza-[3+2+1] cycloaddition products **4a**-**h** (Scheme 3). The first is the already invoked Knoevenagel reaction of Meldrum's acid and aromatic aldehydes, followed by sequential intermolecular Michael addition of the dimedone-based enaminones to the Knoevenagel adduct, and intramolecular carbonyl *N*-nucleophilic addition.[9,10,13] Alternatively, an intermolecular aza-ene type reaction between enaminones and Knoevenagel adducts cannot be ruled out, followed by intermolecular carbonyl addition and hydrogen migration, which in the sequence suffer acetone extrusion assisted by CO_2 elimination, which thus yield **4a**-**h** after 1,3H shift.

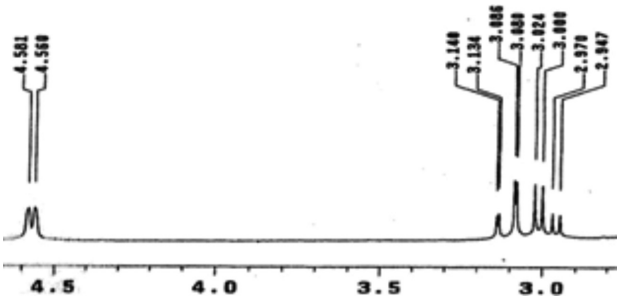


Figure 1. Partial ^{1}H NMR spectrum of **4e** with the typical ABX spin system NCOC$\underline{H}_2$C$\underline{H}$Ar.

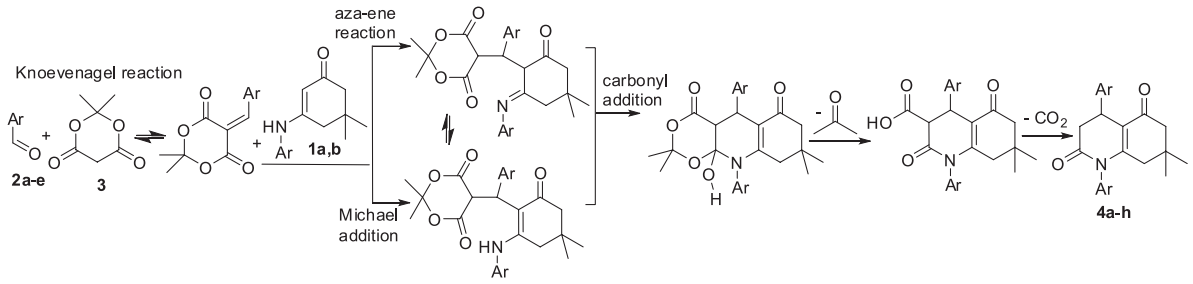
In conclusion, a very simple one-step green procedure was developed to the synthesis of 4-aryl-tetrahydroquinoline-2,5-diones, improving the scope of the domino three-component reaction of *N*-aryl substituted dimedone-based enaminones, aromatic aldehydes and Meldrum's acid. The method does not employ catalyst or any special solvent or reaction condition, and has facile work-up and purification. Moreover, variations of enaminones and aldehydes substituents were somewhat tolerated.

Experimental

Melting points were determined on a Microquímica MQAPF 301 hot plate apparatus and are uncorrected. Infrared spectra were recorded as KBr discs on a FT-IR BOMEM MB100 or SHIMADZU IR Affinity-1 instrument. Nuclear magnetic resonance (NMR) spectra were obtained for ^{1}H at 300 MHz and for ^{13}C at 75 MHz using a Varian Gemini 300 spectrometer, or 500 MHz for ^{1}H and for ^{13}C at 125 MHz using a Varian INOVA 500 spectrometer. Chemical shifts are reported in ppm units downfield from reference [internal tetramethylsilane (TMS) or residual undeuterated solvent]. Elemental analyses were performed on a Flash 2000 Thermo Scientific instrument at Instituto de Química/UFG. Enaminones **1a** e **1b** were prepared according known procedures.[14]

General synthetic procedure for syntheses of 4-aryl-7,7-dimethyl-1-aryl-3,4,7,8-tetrahydroquinoline-2,5(1H,6H)-diones **4a-4h**

A dry 25 mL flask was charged with aldehyde (0.5 mmol), Meldrum's acid (0.5 mmol), 3-arylamino-5,5-



Scheme 3. Possible convergent pathways to the formation of **4a**-**h**.

dimethylcyclohex-2-enone (0.5 mmol), and ethanol (5 mL). The reaction mixture was stirred at room temperature until consume of enaminone, observed by TLC. The generated solid was filtered in vacuum, washed with cold ethanol and dried a room temperature. **4b** reaction was performed under reflux. Products **4b** and **4e** were purified by silica gel column chromatography in hexane-ethyl acetate as eluent (80:20% to 50:50%).

7,7-dimethyl-4-(2-nitrophenyl)-1-phenyl-4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-dione (**4a**)

3 days; white solid; 93% yield; mp 242.7-243.9 °C; IR (KBr) ν/cm^{-1} 3066, 3040, 2959, 1701, 1658, 1627, 1530, 1494, 1452, 1415, 1377, 1340, 1494, 1452, 1415, 1377, 1340, 1261, 1213, 1195, 1157, 1140, 981, 855, 786, 739, 694; ^{1}H NMR (DMSO-D$_6$, 300 MHz) δ 0.92 (s, 3H), 0.90 (s, 3H), 2.02 (d, 1H, *J* 17.5), 2,13 (d, 1H, *J* 16.0), 2.25 (d, 1H, *J* 16.0), 2.28 (d, 1H, *J* 17.5), 2.67 (d, 1H, *J* 16.0), 3.43 (dd, 1H, *J* 16.0, 9.0), 4.67 (d, 1H, *J* 9.0), 7.31 (d, 1H, *J* 6.5), 7.38 (d, 1H, *J* 6.5), 7.45-7.55 (m, 5H), 7.74 (t, 1H, *J* 7.5), 7.96 (d, 1H, *J* 8.5); ^{13}C NMR (DMSO-D$_6$, 75 MHz) δ 27.0 (CH$_3$), 28.5 (CH$_3$), 29.3 (C), 32.7 (C), 38.0 (CH$_2$), 41.1 (CH$_2$), 48.1 (CH$_2$), 114.2 (C), 124.9 (CH), 127.9 (CH), 128.5 (CH), 128.7 (CH$_2$), 129.5 (CH), 133.9 (CH), 135.7 (C), 136.9 (C), 148.8 (C), 154.9 (C), 168.7 (C), 194.9 (C); anal. calcd. for $C_{23}H_{22}N_2O_4$: C, 70.75%; H, 5.68%; N, 7.17%; found: C, 70.54%; H, 5.42%; N, 6.88%.

7,7-dimethyl-4-(3-nitrophenyl)-1-phenyl-4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-dione (**4b**)

6 days; brown solid; 84% yield; mp 159.6-160.2 °C; IR (KBr) ν/cm^{-1} 3076, 2957, 1707, 1649, 1617, 1593, 1523, 1493, 1456, 1375, 1344, 1260, 1224, 1198, 1158, 1140, 981, 889, 798, 740, 703; ^{1}H NMR (DMSO-D$_6$, 300 MHz) δ 1.04 (s, 3H), 1.09 (s, 3H), 2.18 (dl, 2H, *J* 6.3), 2.35 (s, 2H), 3.01 (dd, 1H, *J* 16.5, 1.5), 3.20 (dd, 1H, *J* 16.2, 7.8), 4.61 (dl, 1H, *J* 7.2), 7.1-7.3 (m, 2H), 7.46-7.57 (m, 4H), 7.70 (dl, 1H, *J* 7.5), 8.12-8.15 (m, 1H), 8.20-8.21 (m, 1H); ^{13}C NMR (DMSO-D$_6$, 75 MHz) δ 28.1 (CH$_3$), 32.9 (C), 33.2 (CH), 38.5 (CH$_2$), 41.7 (CH$_2$), 49.9 (CH$_2$), 115.9 (C), 121.2 (CH), 122.2 (CH), 128.1 (CH), 129.0 (CH), 129.6 (CH), 129.9 (CH),133.6 (CH), 136.5 (C),143.4(C), 148.4 (C), 154.3 (C), 168.9 (C), 195.6 (C); anal. calcd. for $C_{23}H_{22}N_2O_4$: C, 70.75%; H, 5.68%; N, 7.17%; found: C, 70.88%; H, 5.76%; N, 7.03%.

7,7-dimethyl-4-(4-nitrophenyl)-1-phenyl-4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-dione (**4c**)

The reaction of the synthesis was performed under reflux, and product purified by silica gel column chromatography (hexane/ethyl acetate 20% to 50%), afforded pure compounds.

6 days; yellow oil; 50% yield; IR (KBr) ν/cm^{-1} 3042, 2949, 1707, 1647, 1617, 1595, 1522, 1493, 1453, 1372, 1348, 1298, 1279, 1226, 1177, 1160, 1074, 857, 741, 704, 693, 605, 573, 514; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.94 (s, 3H), 1.04 (s, 3H), 2.07 (s, 2H), 2.31 (s, 2H), 3.04 (dd, 1H, *J* 16.5, 2.1), 3.15 (dd, 1H, *J* 16.2, 7.5), 4.60 (dl, 1H, *J* 6.3), 6.92 (m, 1H), 7.22 (m, 1H), 7.48 (m, 2H), 7.49 (d, 2H, *J* 9.0), 8.16 (d, 2H, *J* 9.0), 8.17 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.1 (CH$_3$), 28.2 (CH$_3$), 32.9 (CH), 33.0 (C), 37.5 (CH$_2$), 41.7 (CH$_2$), 49.9 (CH$_2$), 116.3 (CH), 124.0 (CH), 127.6 (CH), 129.0 (CH), 136.5 (C), 146.8 (C), 149.5 (C), 153.8 (C), 169.4 (C), 195.8 (C); anal. calcd. for $C_{23}H_{22}N_2O_4$: C, 70.75%; H, 5.68%; N, 7.17%; found: C, 70.92%; H, 5.73%; N, 6.95%.

7,7-dimethyl-4-(6-nitro-1,3-benzodioxol-5-yl)-1-phenyl-4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-dione (**4d**)

5 days; yellow solid; 65% yield; mp 226.5-227.4 °C; IR (KBr) ν/cm^{-1} 3067, 2957, 1717, 1650, 1623, 1515, 1486, 1418, 1381, 1368, 1349, 1324, 1292, 1265, 1220, 1171, 1150, 1115, 922, 880, 821,749, 701; ^{1}H NMR (DMSO-D$_6$, 300 MHz) δ 0.93 (s, 3H), 0.97 (s, 3H), 1.89 (d, 1H, *J* 17.1), 2.08 (d, 1H, *J* 16.0), 2.36 (d, 1H, *J* 16.2), 2.63 (d, 1H, *J* 14.7), 3.41 (dd, 1H, *J* 16.5, 8.7), 4.72 (d, 1H, *J* 8.4), 6.22 (m, 2H), 6.88 (s, 1H), 7.31-7.40 (m, 3H), 7.46-7.55 (m, 2H), 7.64 (s, 1H); ^{13}C NMR (DMSO-D$_6$, 75 MHz) δ 27.2 (CH$_3$), 29.9 (CH$_3$), 30.54 (CH), 33.60 (C), 38.9 (CH$_2$), 41.9 (CH$_2$), 49.8 (CH$_2$), 104.2 (CH$_2$), 106.7 (CH), 107.1 (CH), 115.1 (C), 129.1 (CH), 129.4 (CH), 130.1 (CH), 133.7 (C), 137.5 (C), 142.9 (C), 147.5 (C), 152.8 (C), 155.9 (C), 169.6

(C), 195.6 (C); anal. calcd for $C_{24}H_{22}N_2O_6$: C, 66.35%; H, 5.10%; N, 6.45%; found: C, 66.92%; H, 5.23%; N, 6.55%.

4-(2-furyl)-7,7-dimethyl-1-phenyl-4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-dione (**4e**)

Product purified by silica gel column chromatography (hexane/ethyl acetate 20% to 50%), afforded pure compounds.

2 days; brown oil; 55% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.98 (s, 3H), 1.05 (s, 3H), 2.05 (s, 2H), 2.34 (s, 2H), 2.96 (dd, 1H, *J* 16.2, 9.0), 3.11 (dd, 1H, *J* 16.2, 1.8), 4.60 (dl, 1H, *J* 6.3), 6.15 (d, 1H, *J* 3.3), 6.30 (dd, 1H, *J* 3.0, 1.8), 7.34-7.35 (m, 2H), 7.47-7.49 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.9 (CH_3), 27.6 (CH_3), 27.8 (C), 32.5 (C), 35.8 (CH), 41.2 (CH_2), 49.5 (CH_2),105.0 (CH), 109.7 (CH), 114.8 (C), 127.8 (CH), 128.3 (CH), 129.0 (CH), 136.6 (CH), 141.4 (C), 153.2 (C) 153.7 (C), 169.0 (C), 195.0 (C); anal. calcd. for $C_{21}H_{21}NO_3$: C, 75.20%; H, 6.31%; N, 4.18%; found: C, 74.92%; H, 6.47%; N, 3.96%.

1-(4-methoxyphenyl)-7,7-dimethyl-4-(2-nitrophenyl)-4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-dione (**4f**)

2 days; white solid; 89% yield; mp 191.5-192.0 °C; IR (KBr) ν/cm^{-1} 3036, 296, 1733, 1704, 1661, 1623, 1529, 1511, 1455, 1417, 1380, 1251, 1219, 1195, 1152, 1135, 985, 782, 751, 701; ^{1}H NMR (DMSO-D_6, 300 MHz) δ 0.93 (s, 3H), 0.98 (s, 3H), 2.04 (d, 1H, *J* 17.4), 2.12 (d, 1H, *J* 16.0), 2.25 (d, 1H, *J* 17.1), 2.31 (d, 1H, *J* 18.3), 2.66 (d, 1H, *J* 16.0), 3.41 (dd, 1H, *J* 16.2, 8.7), 3.82 (s, 3H), 4.65 (dl, 1H, *J* 8.4), 7.06 (d, 1H, *J* 9.0), 7.22 (d, 1H, *J* 7.8), 7.30 (d, 1H, *J* 7.8), 7.45 (d, 1H, *J* 7.5), 7.51 (t, 1H, *J* 7.8), 7.72 (t, 1H, *J* 7.5), 7.97 (d, 1H, *J* 9.0); ^{13}C NMR (DMSO-D_6, 75 MHz) δ 27.0 (CH_3), 28.7 (CH_3), 29.4 (C), 32.7 (CH), 38.1 (CH_2), 41.1 (CH_2), 49.1 (CH_2), 55.4 (OCH_3), 114.1 (C), 114.5 (CH), 124.9 (CH), 127.9 (CH), 128.4 (CH), 129.2 (CH), 129.6 (CH), 130.6 (CH), 133.9 (CH); 135.7 (C), 148.8 (C), 155.4 (C), 159.0 (C), 168.9 (C), 194.9 (C); anal. calcd. for $C_{24}H_{24}N_2O_5$: C, 75.20%; H, 6.31%; N, 4.18%; found: C, 75.59%; H, 6.18%; N, 3.87%.

1-(4-methoxyphenyl)-7,7-dimethyl-4-(3-nitrophenyl)-4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-dione (**4g**)

4 days; white solid; 38% yield; mp 150.0-150.8 °C; IR (KBr) ν/cm^{-1} 3073, 2961, 1704, 1695, 1662, 1628, 1527, 1512, 1422, 1417, 1381, 1344, 1294, 1253, 1215, 1196, 1153, 908, 884, 798, 744, 697; ^{1}H NMR (DMSO-D_6, 300 MHz) δ 0.93 (s, 3H), 0.99 (s, 3H), 2.08 (d, 1H, *J* 17.4), 2.20 (d, 1H, *J* 16.0), 2.25 (d, 1H, *J* 16.0), 2.3 (d, 1H, *J* 16.0), 2.76 (dl, 2H, *J* 16.0), 3.27 (dd, 1H, *J* 16.0, 8.0), 3.79 (s, 3H), 4.45 (dl, 1H, *J* 6.6), 7.04 (m, 2H), 7.21(d, 1H, *J* 7.8), 7.64 (d, 1H, *J* 8.1), 7.67 (d, 1H, *J* 8.4), 7.76 (d, 1H, *J* 8.1), 8.09-8.11 (m, 2H); ^{13}C NMR (DMSO-D_6, 75 MHz) δ 27.5 (CH_3), 28.2 (CH_3), 32.70 (C), 32.73 (CH), 40.3 (CH_2), 41.0 (CH_2), 49.3 (CH_2), 55.4 (OCH_3), 114.7 (C), 114.8 (CH), 121.2 (CH), 121.9 (CH), 129.2 (CH), 130.4 (CH), 130.6 (C),133.8 (CH), 144.1 (C), 148.0 (C), 154.9 (C), 158.9 (C),169.2 (C), 195.1 (C); anal. calcd. for $C_{24}H_{24}N_2O_5$: C, 75.20%; H, 6.31%; N, 4.18%; found: C, 75.26%; H, 6.22%; N, 4.31%.

1-(4-methoxyphenyl)-7,7-dimethyl-4-(6-nitro-1,3-benzodioxol-5-yl)-4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-dione (**4h**)

2 days; yellow solid; 87% yield; mp 218.7-219.7 °C; IR (KBr) ν/cm^{-1} 3002, 2955, 1727, 1708, 1654, 1606, 1595, 1527, 1507, 1484, 1372, 1296, 1252, 1215, 1206, 1165, 1152, 1031, 922, 859, 828,767, 648; ^{1}H NMR (DMSO-D_6, 300 MHz) δ 0.95 (s, 3H), 0.99 (s, 3H), 1.95 (d, 1H, *J* 17.4), 2.09 (d, 1H, *J* 15.9), 2.36 (d, 1H, *J* 16.2), 2.47 (d, 1H, *J* 18.0), 2.65 (d, 1H, *J* 15.3), 3.41 (dd, 1H, *J* 18.9, 9.0), 3,8 (s, 3H), 4.73 (dl, 1H, *J* 8,1), 6.23 (d, 2H, *J* 3.6), 6.88 (sl, 1H), 7.05-7.10 (m, 2H), 7.19-7.24 (m, 2H), 7.64 (s, 1H); ^{13}C NMR (DMSO-D_6, 75 MHz) δ 26.6 (CH_3), 29.2 (CH_3), 29.8 (CH), 32.8 (C), 38.3 (CH_2), 41.2 (CH_2), 49.1 (CH_2), 55.4 (OCH_3), 103.4 (CH_2), 105.9 (CH), 106.4 (CH), 114.5 (CH), 114.6 (C), 129.2 (CH), 129.9 (C), 130.6 (CH), 133.1 (C), 142.2 (C), 146.7 (C), 152.0 (C), 155.7 (C), 158.9 (C), 169.0 (C), 195.0 (C); anal. calcd. for $C_{25}H_{24}N_2O_7$: C, 64.65%; H, 5.21%; N, 6.03%; found: C, 64.30%; H, 5.55%; N, 5.87%.

Supplementary Information

Supplementary information (Figures S1-S54: IR, ^{1}H and ^{13}C NMR spectra for **4a**-**h**) is available free of charge at http://jbcs.sbq.org.br as PDF file.

Acknowledgments

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Supplementary Information

Synthesis of Quinolinediones by Catalyst-Free Formal Aza-[3+2+1] Cycloaddition of Enaminones, Aldehydes and Meldrum's Acid

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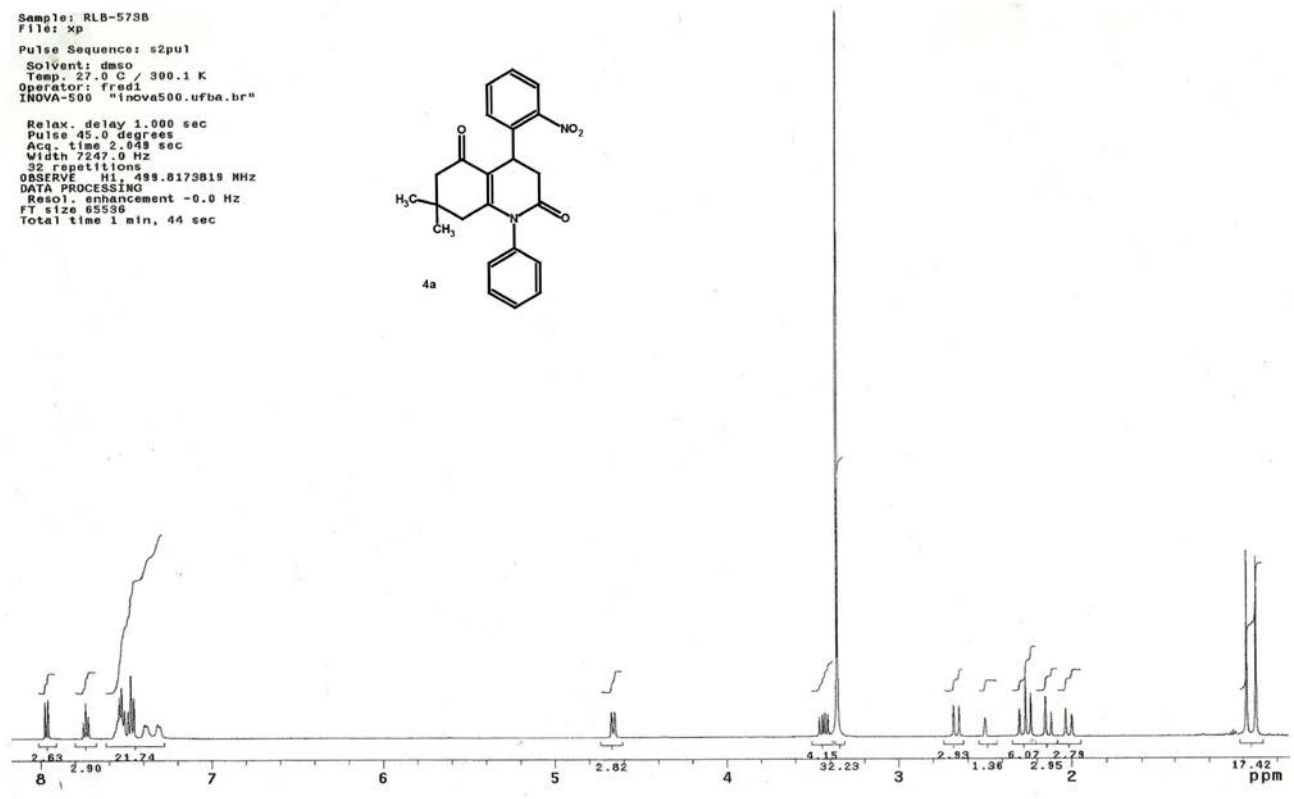

Figure S1. ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4a**.

*e-mail: silviodc@ufba.br

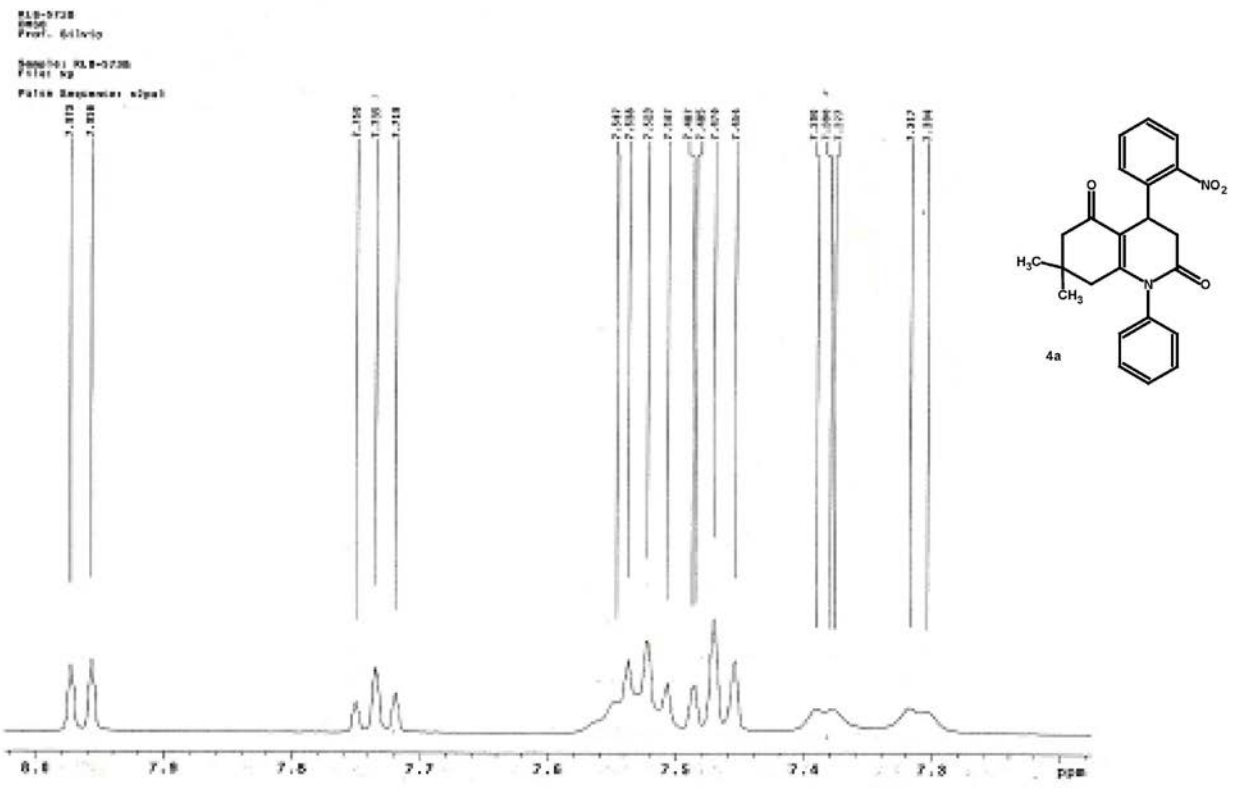

Figure S2. Expanded ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of compound **4a**.

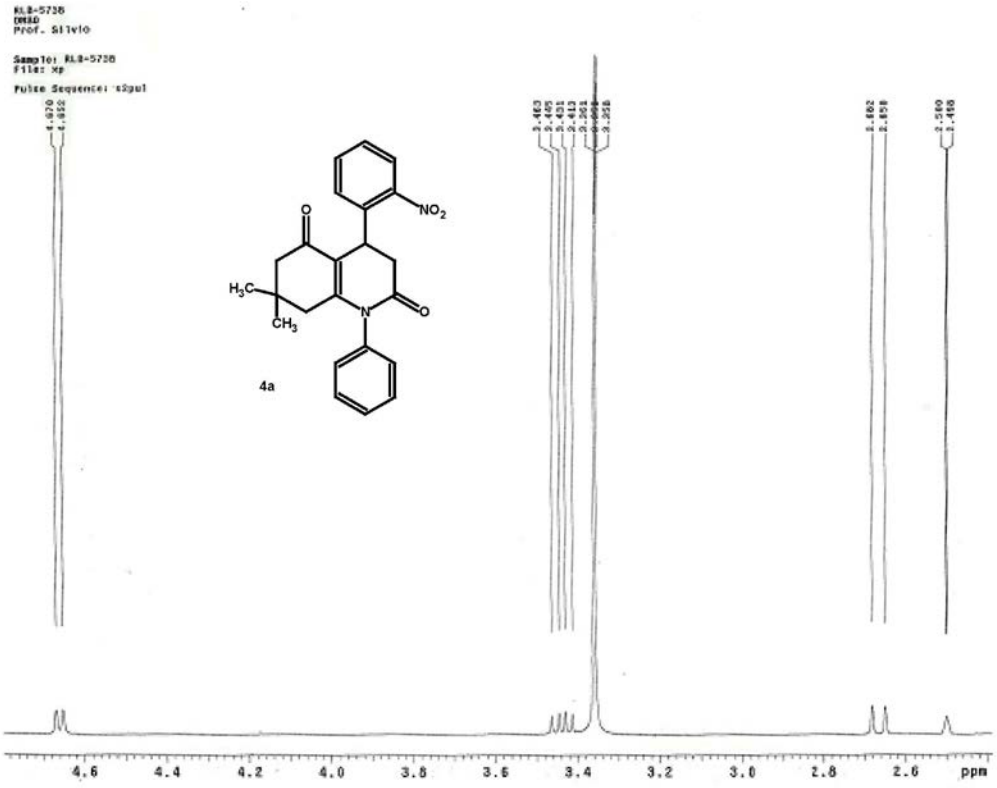

Figure S3. Expanded ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of compound **4a**.

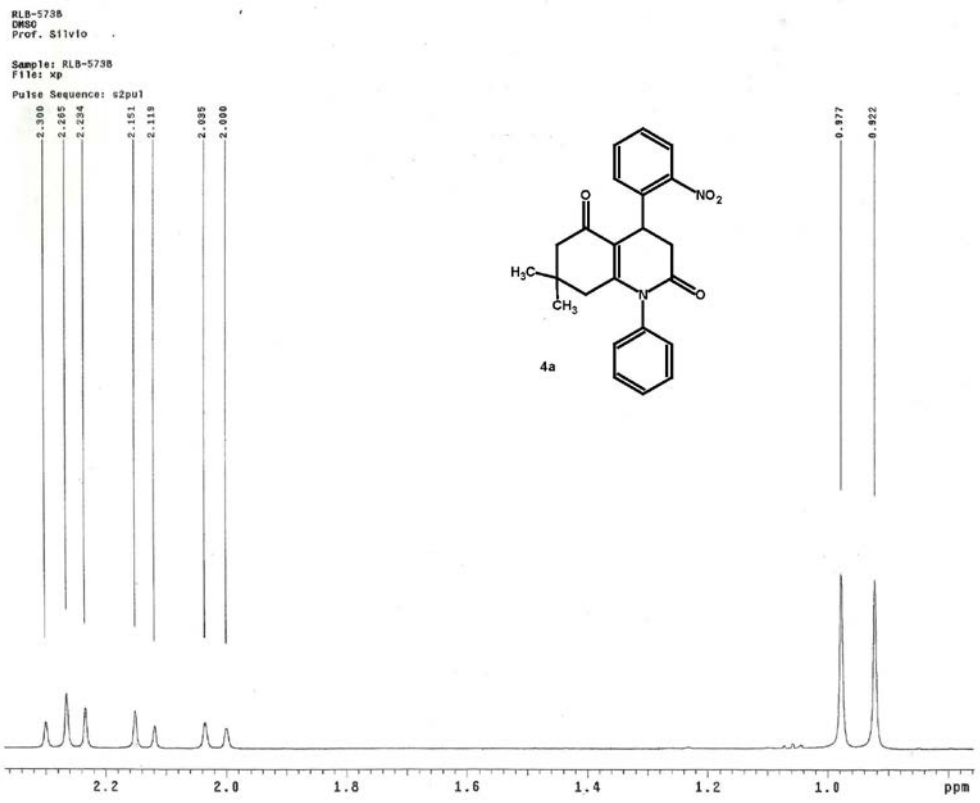

Figure S4. Expanded ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of compound **4a**.

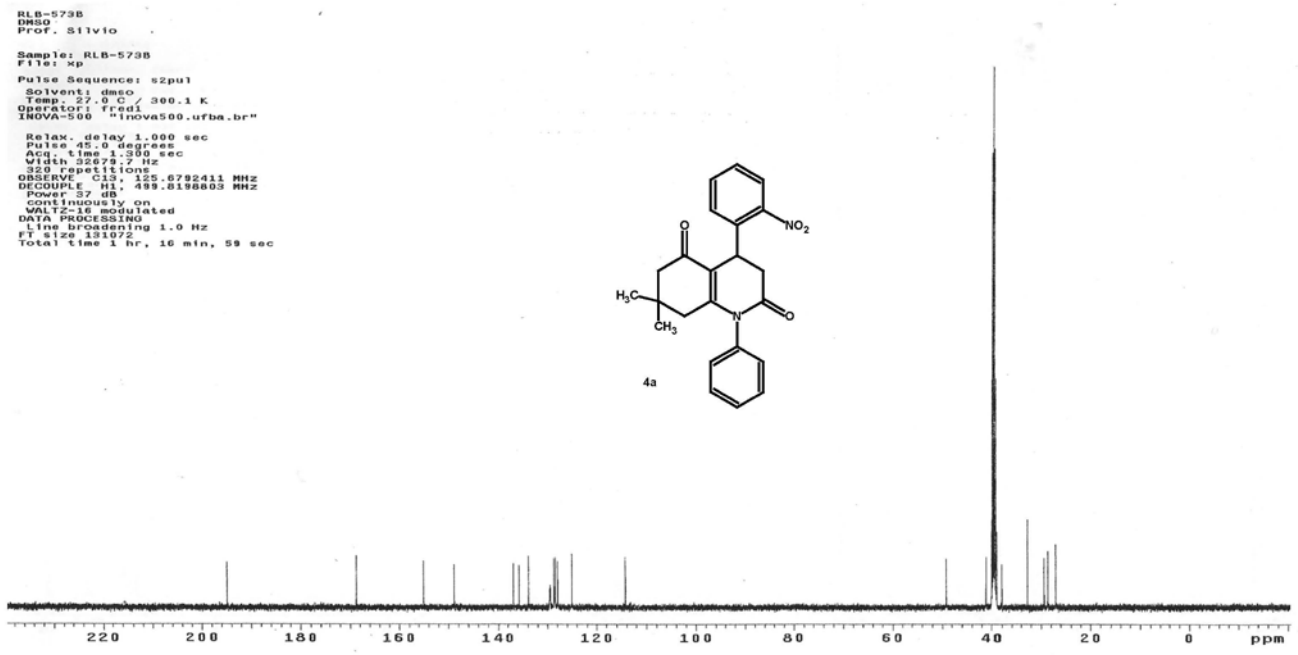

Figure S5. ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of compound **4a**.

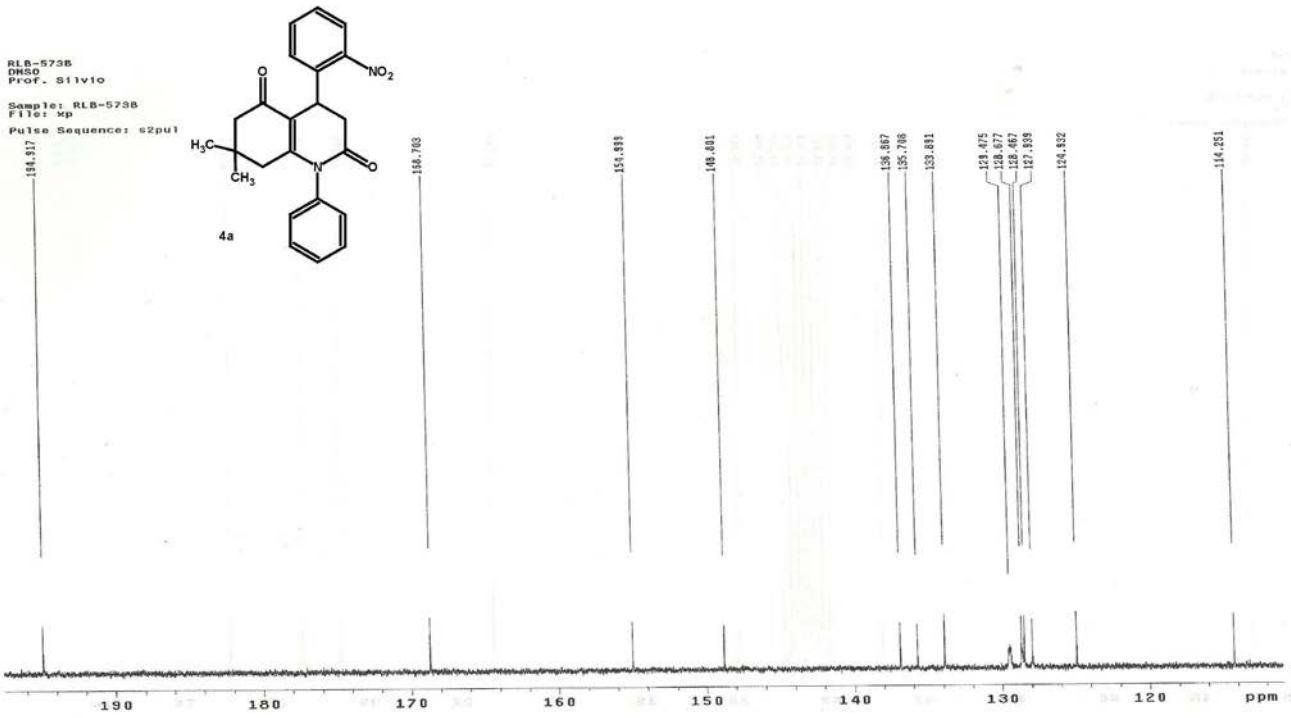

Figure S6. Expanded ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of compound **4a**.

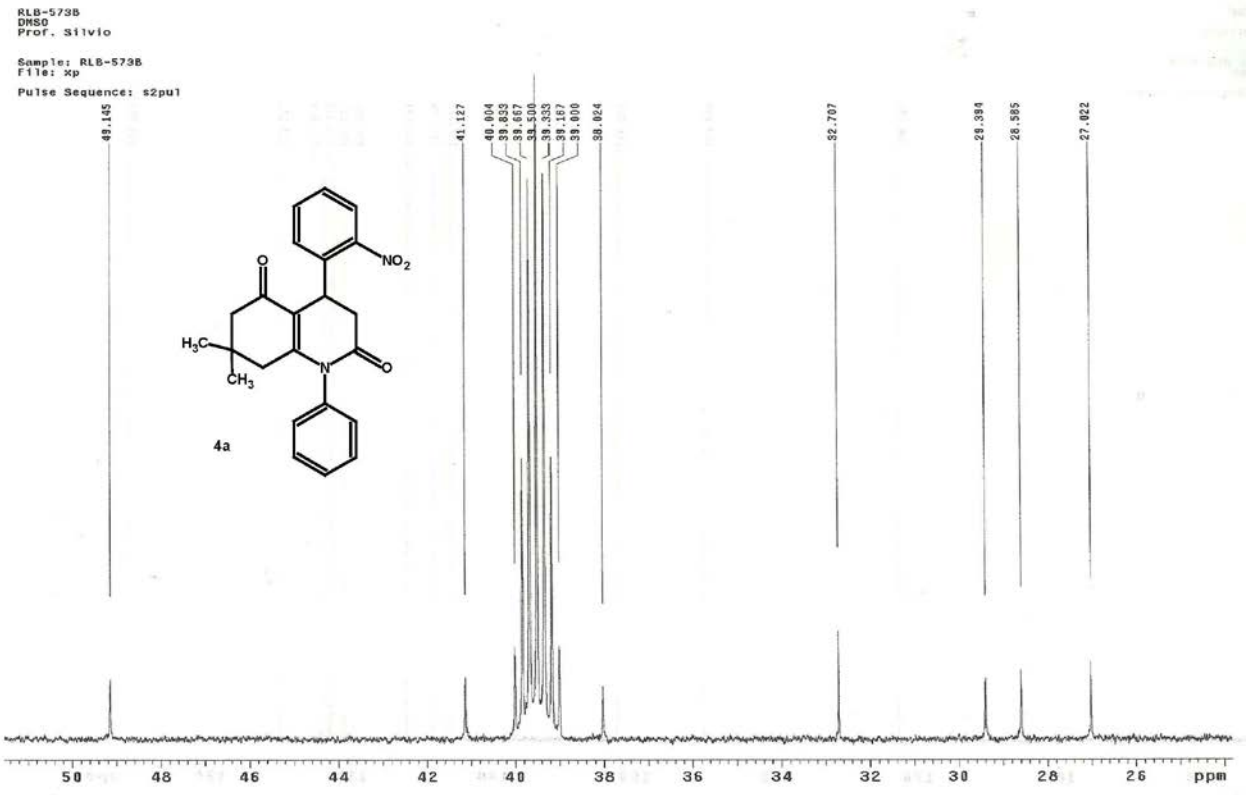

Figure S7. Expanded ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of compound **4a**.

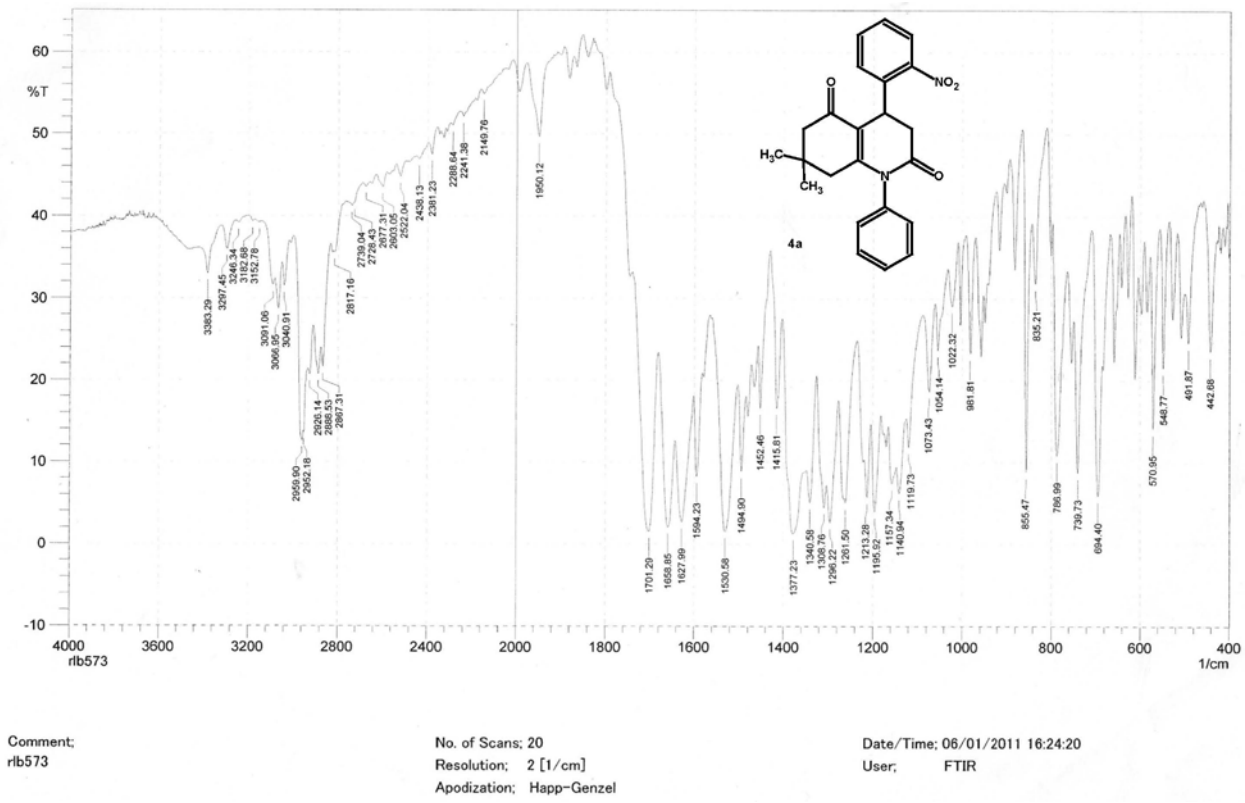

Figure S8. IR (KBr) spectrum of compound **4a**.

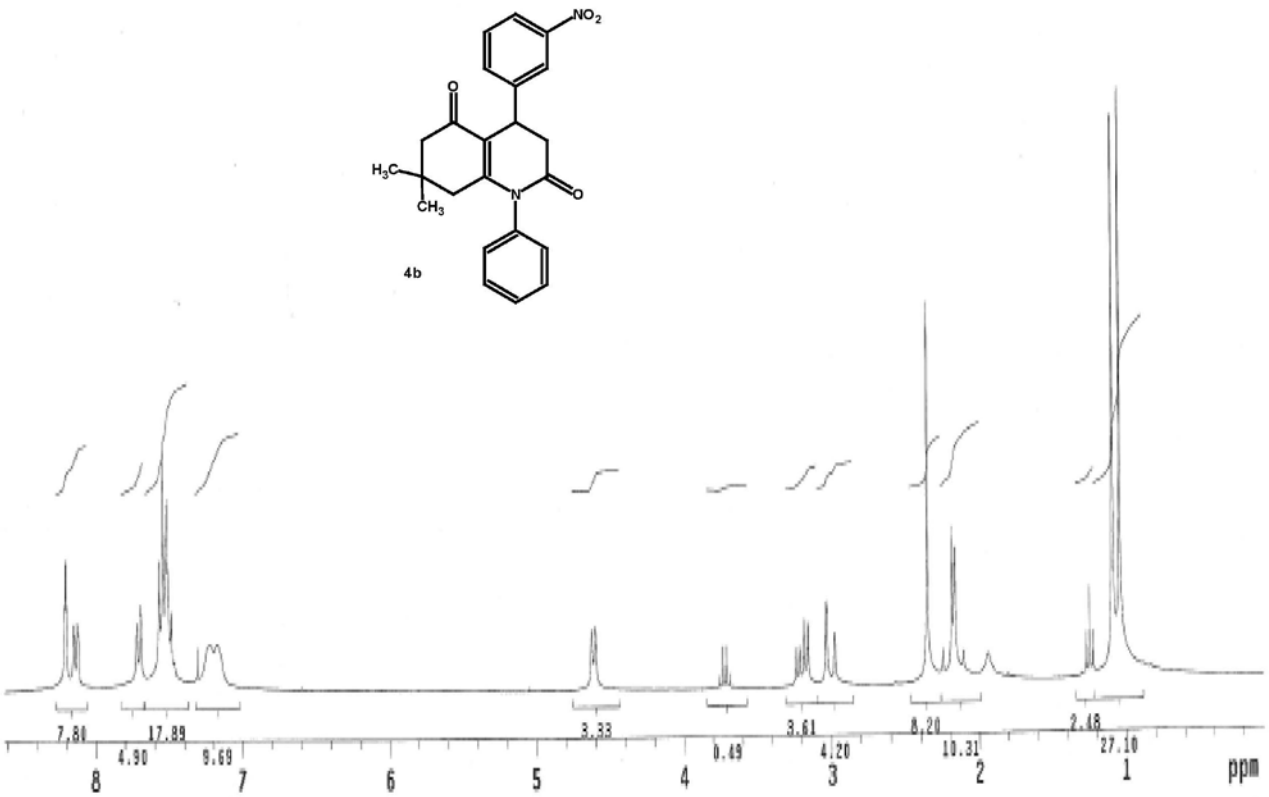

Figure S9. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of compound **4b**.

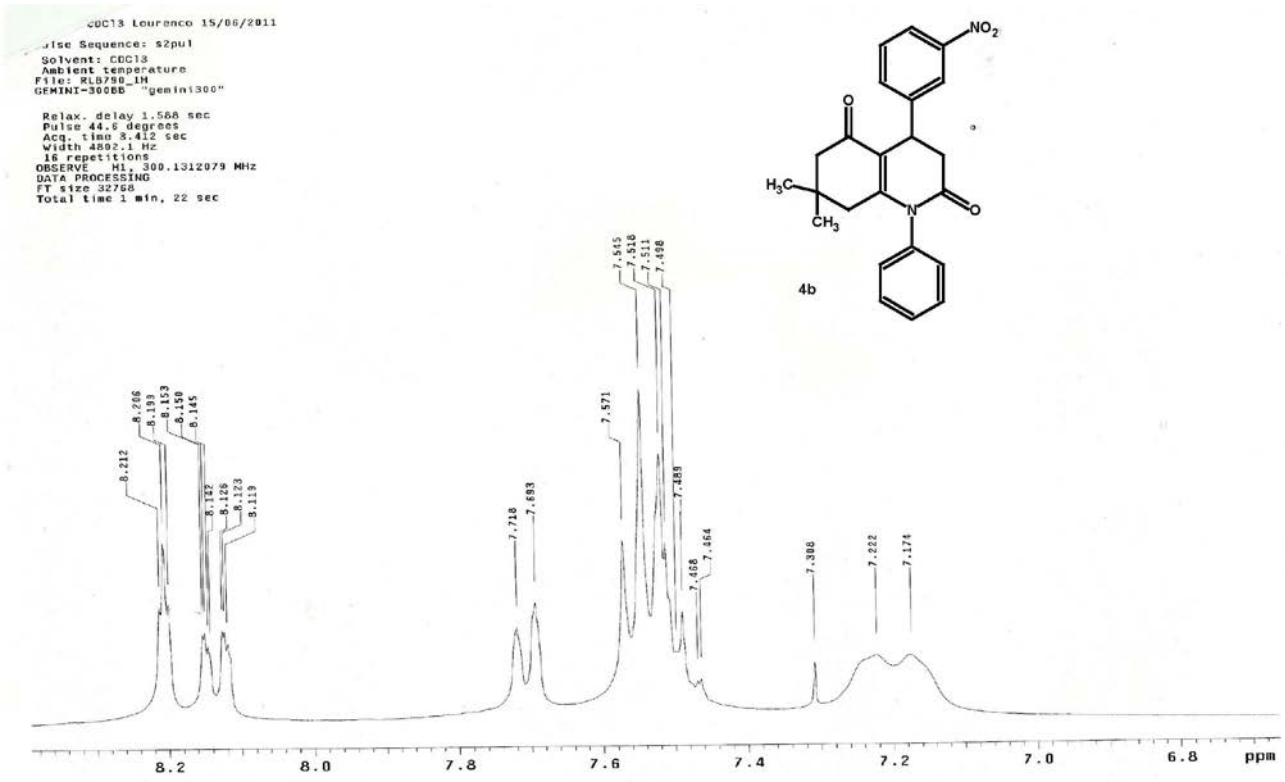

Figure S10. Expanded ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of compound **4b**.

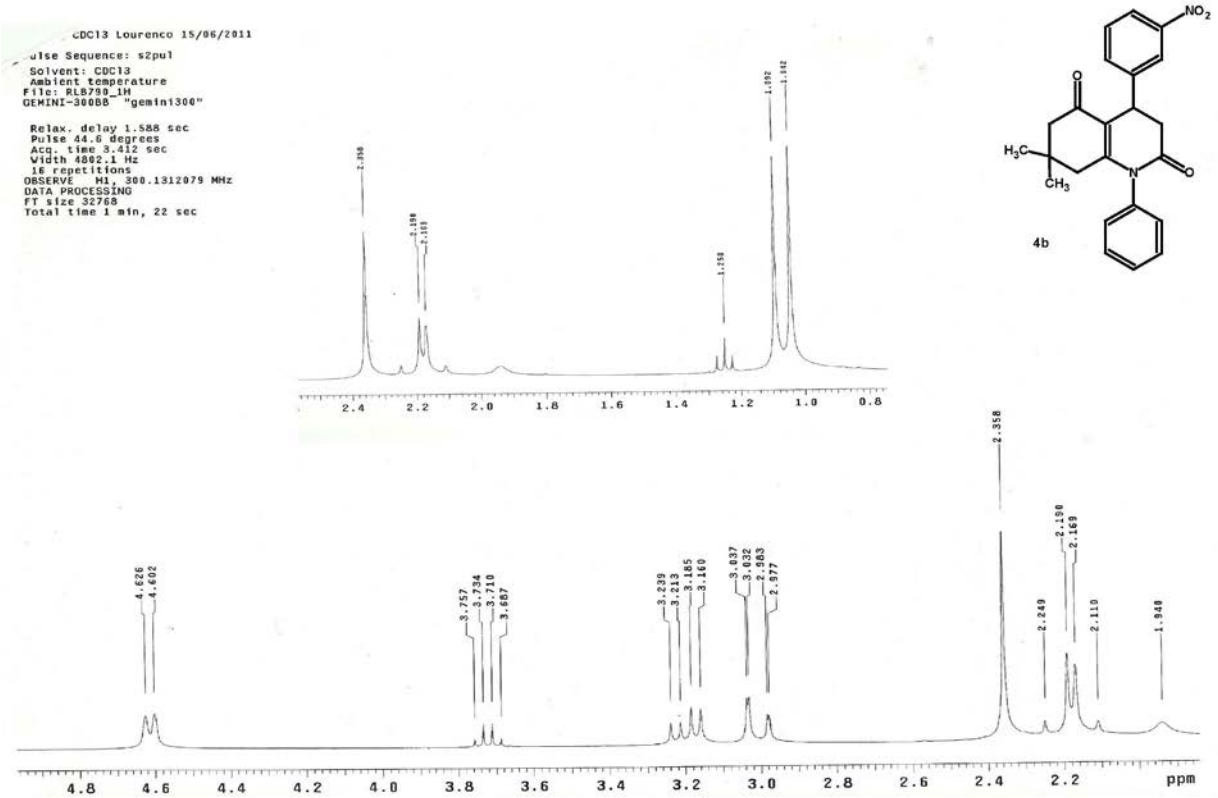

Figure S11. Expanded ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of compound **4b**.

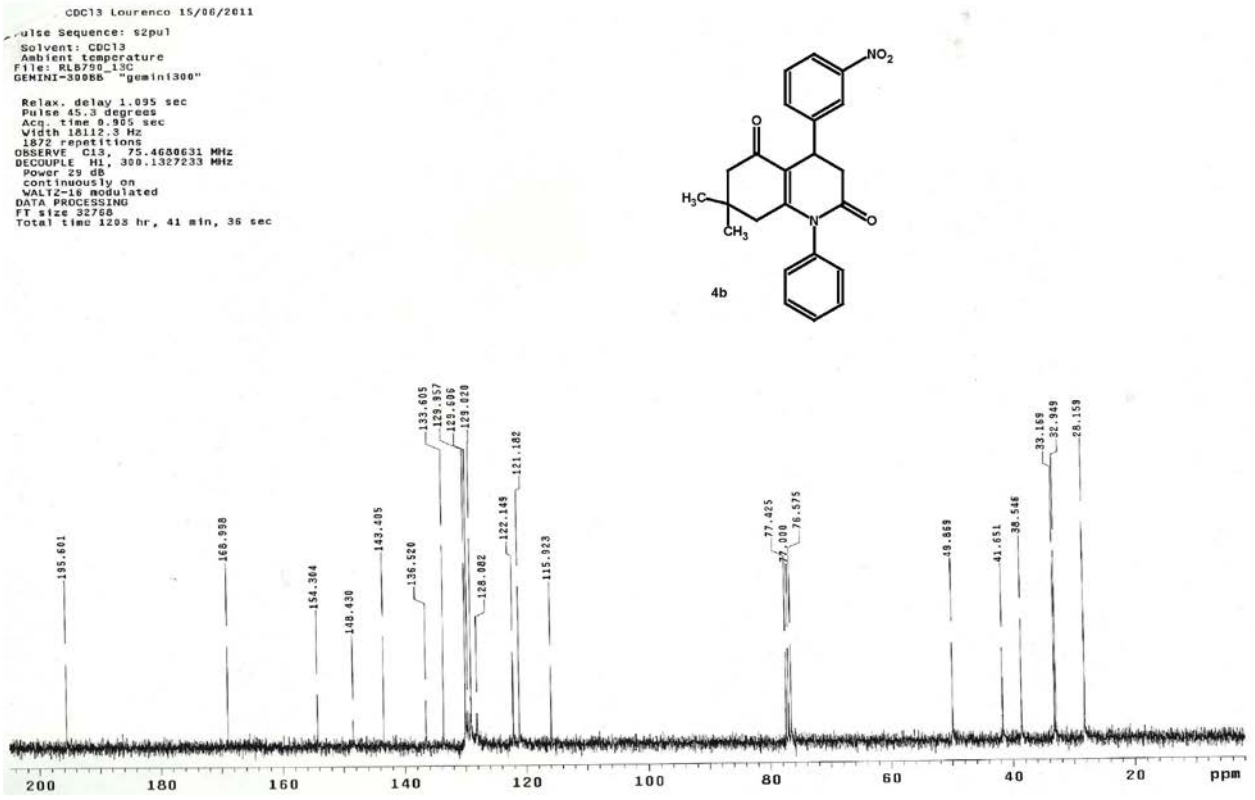

Figure S12. ^{13}C NMR ($CDCl_3$, 75 MHz) spectrum of compound **4b**.

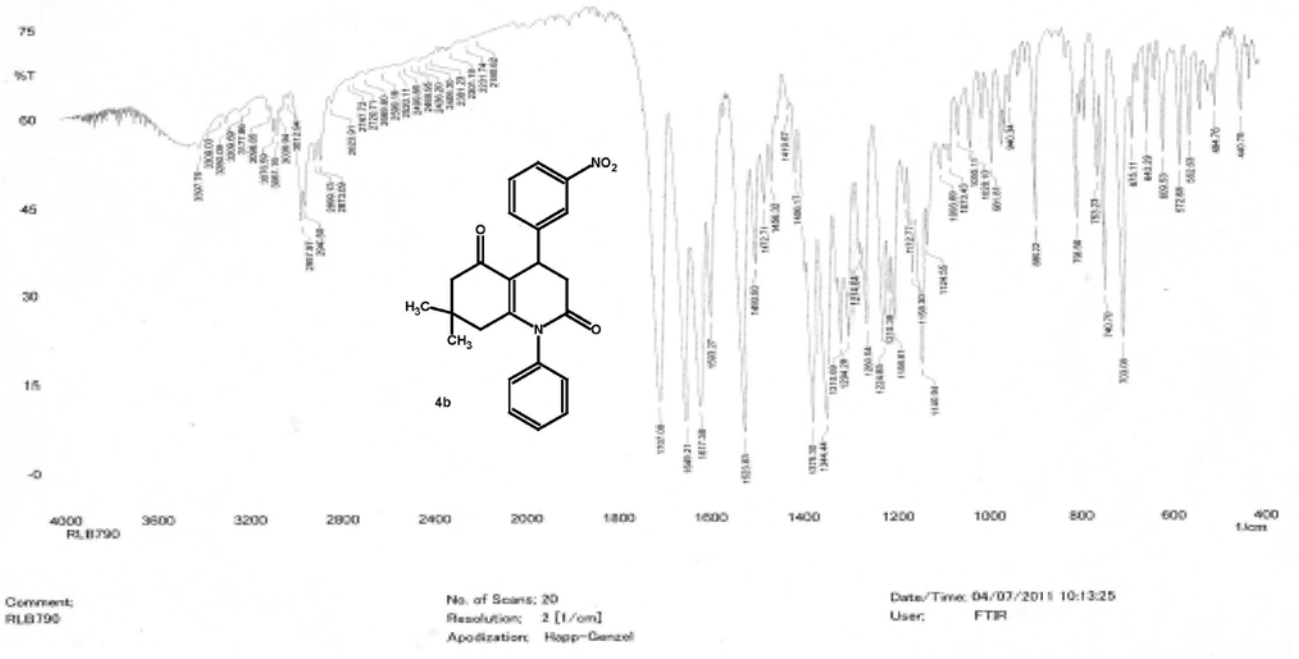

Figure S13. IR (KBr) spectrum of compound **4b**.

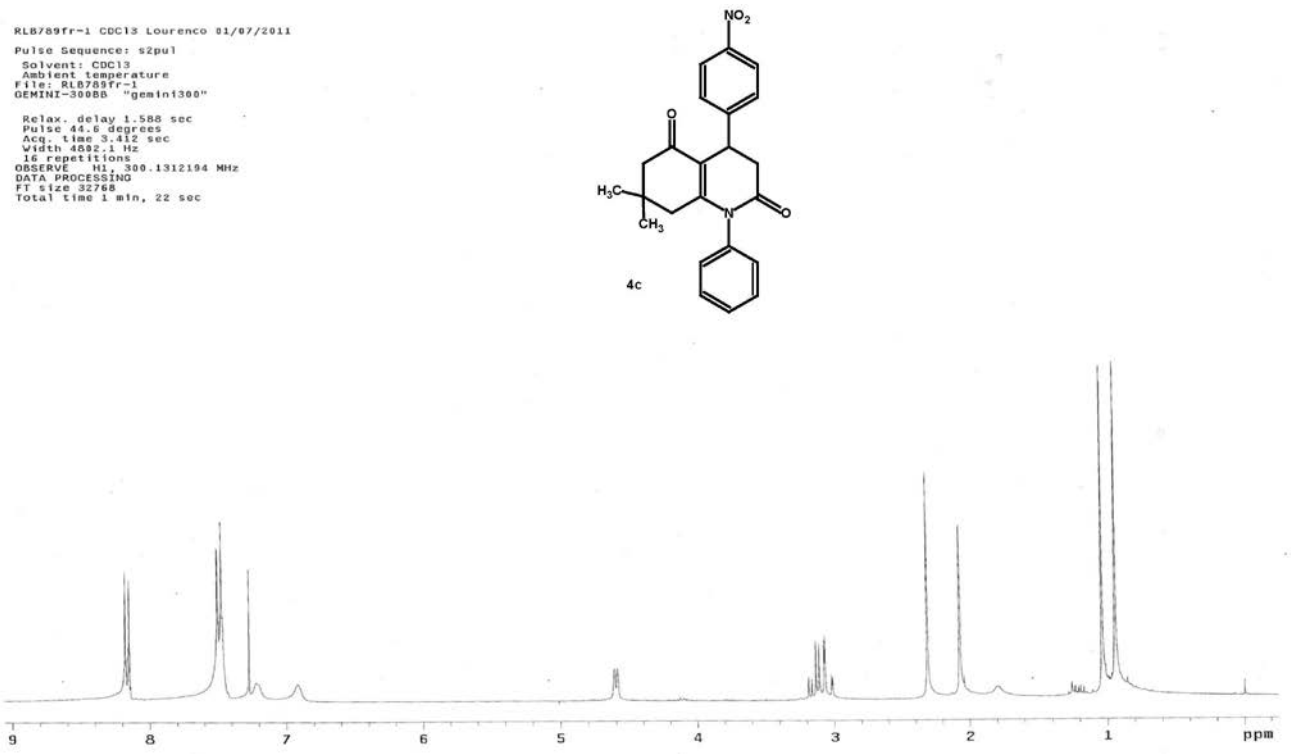

Figure S14. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of compound **4c**.

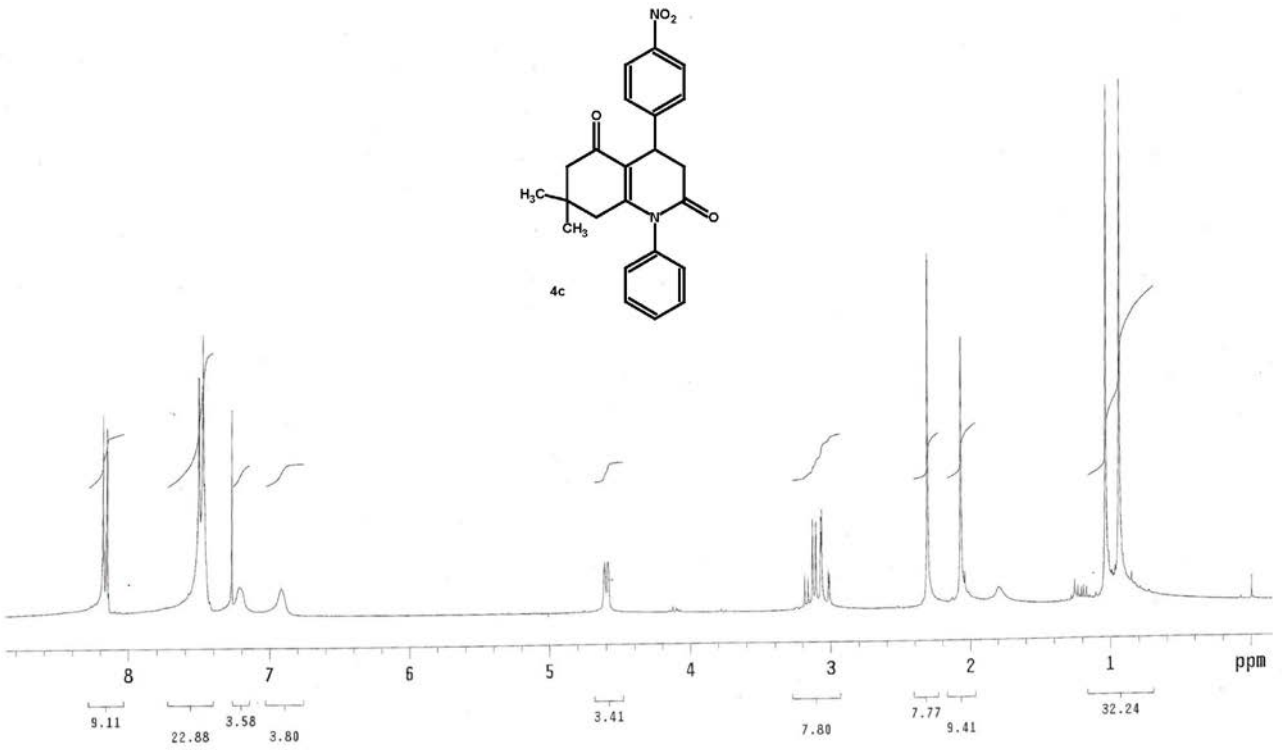

Figure S15. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of compound **4c**.

Figure S22. Expanded ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4d**.

Figure S23. Expanded ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4d**.

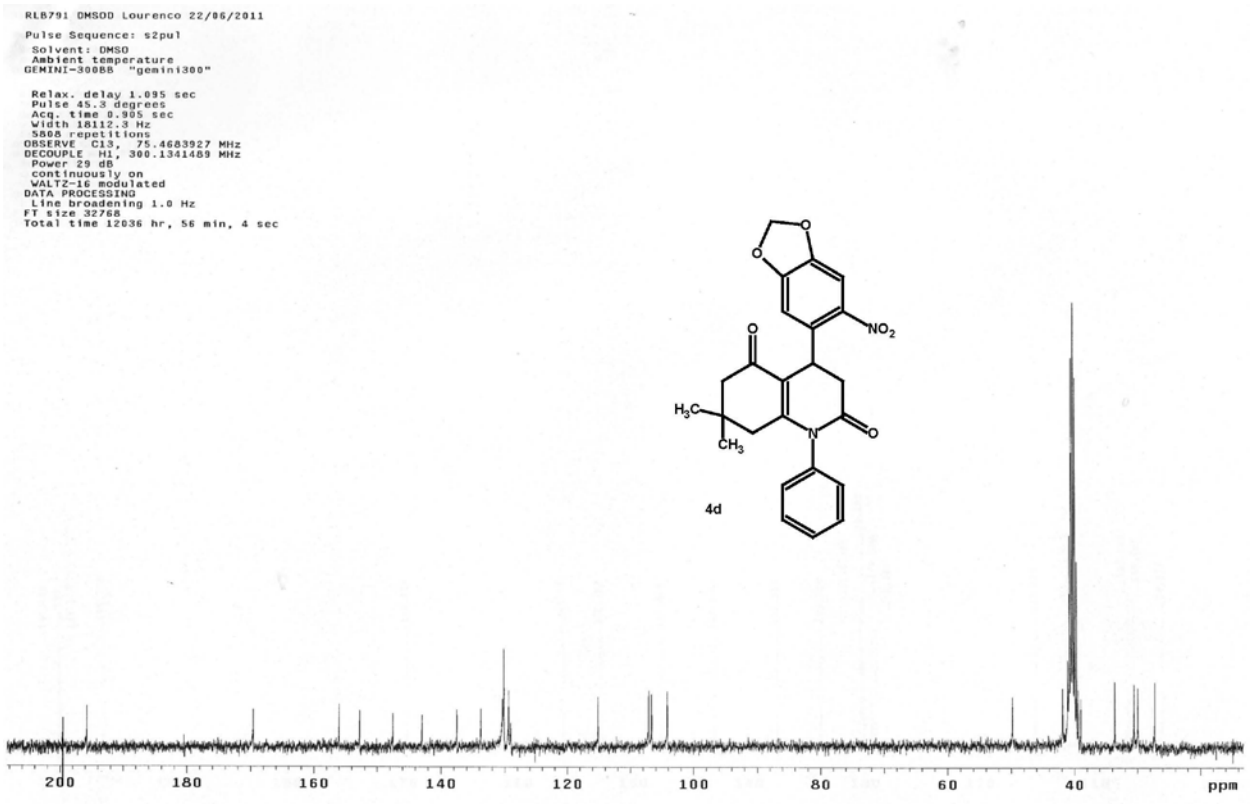

Figure S24. ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of compound **4d**.

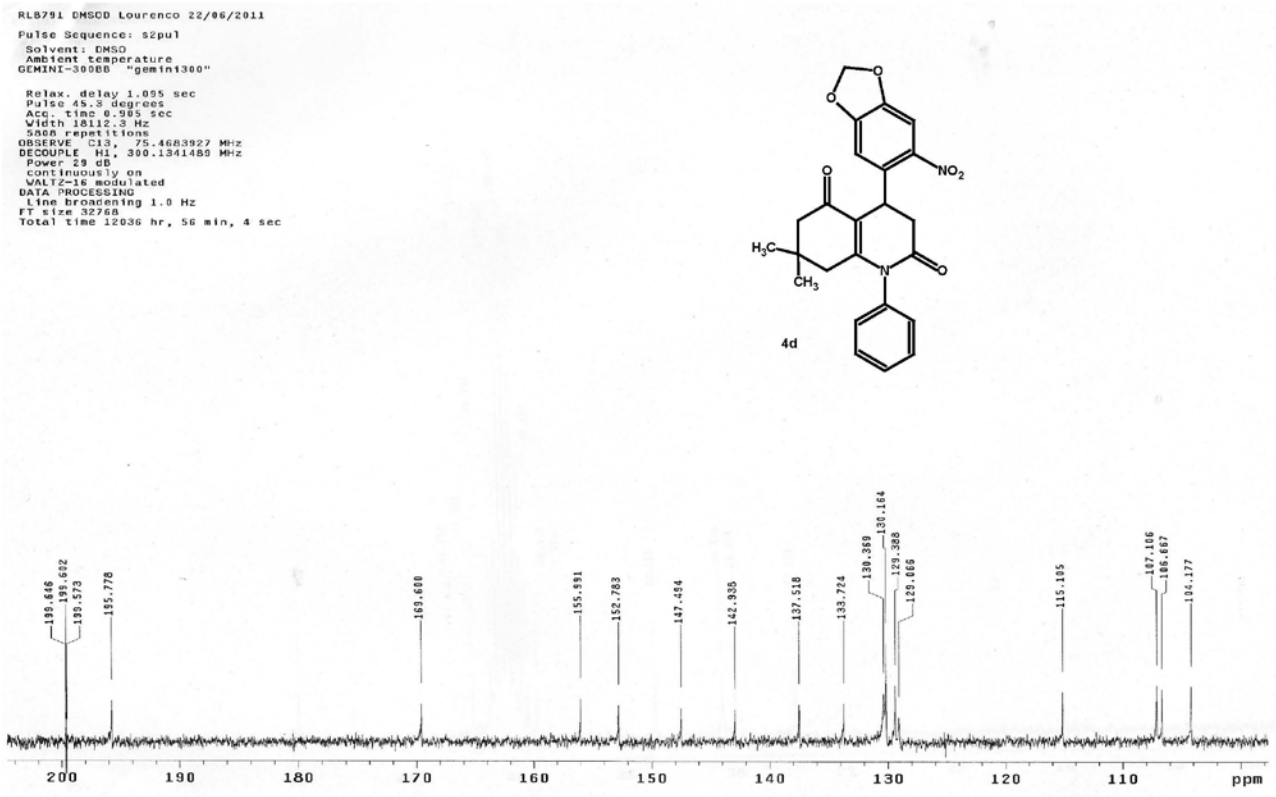

Figure S25. Expanded ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of compound **4d**.

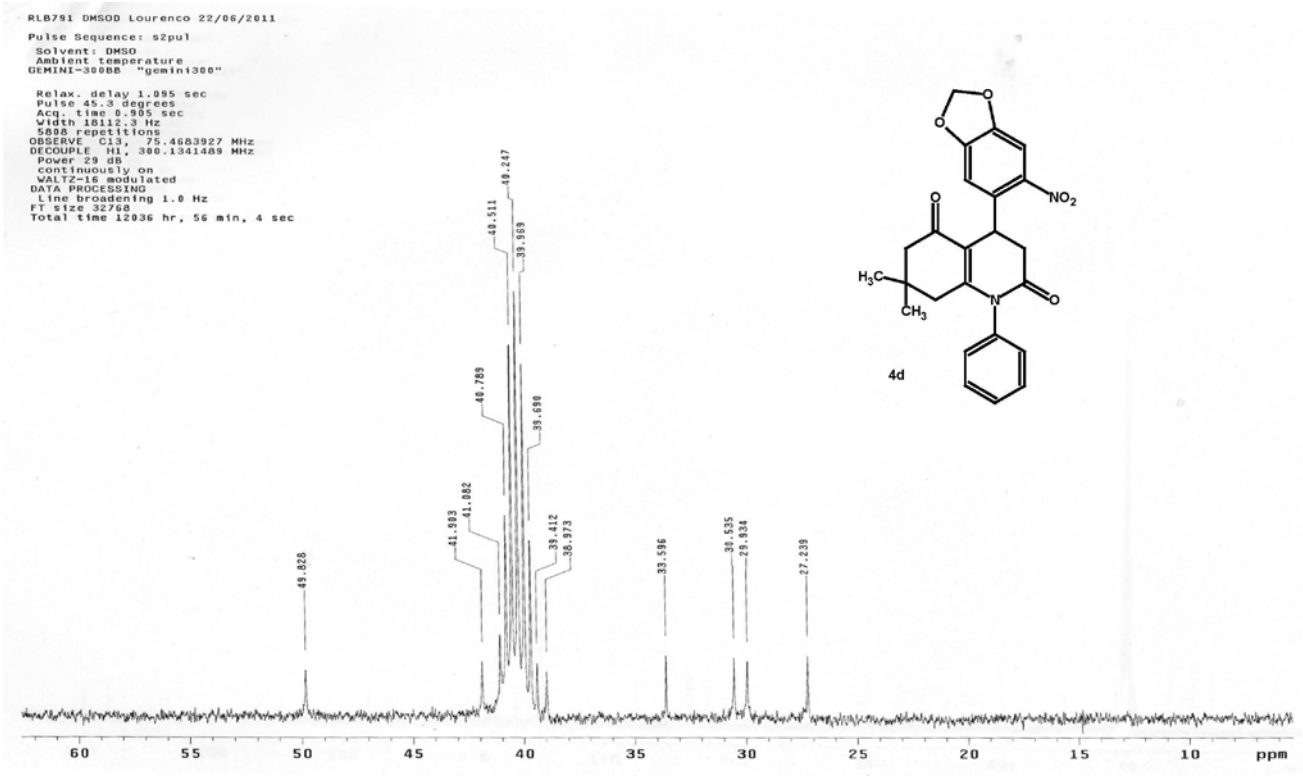

Figure S26. Expanded ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of compound **4d**.

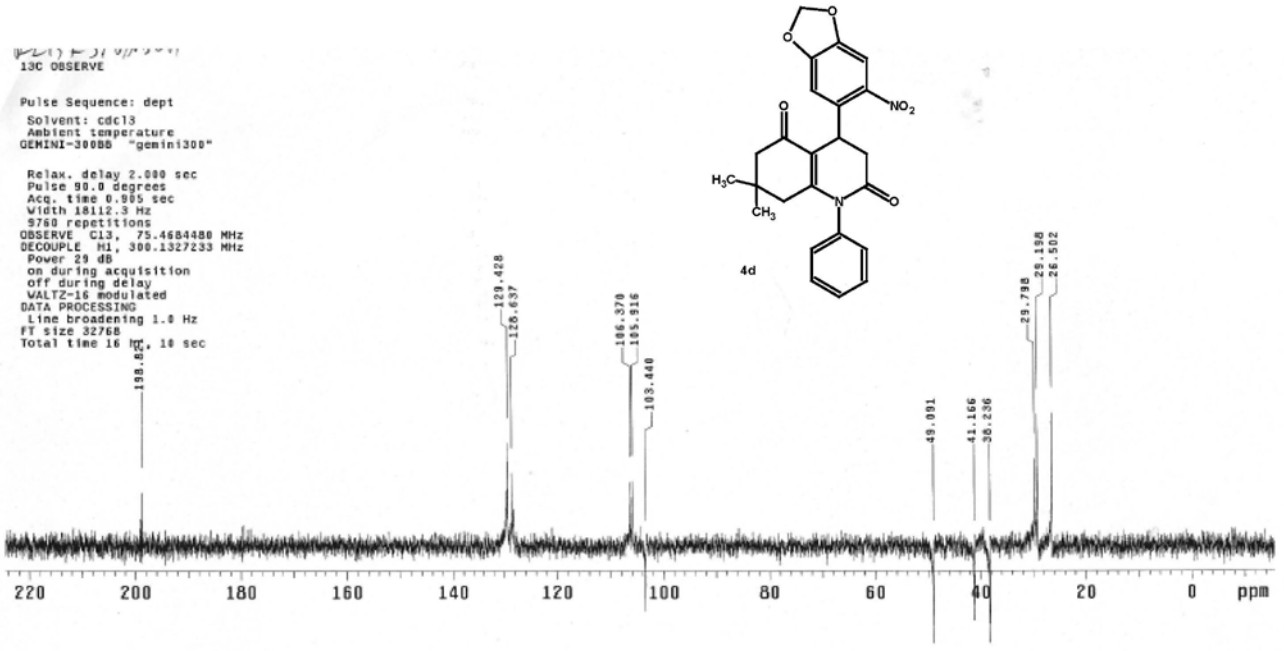

Figure S27. DEPT-135 NMR (DMSO-D_6, 75 MHz) spectrum of compound **4d**.

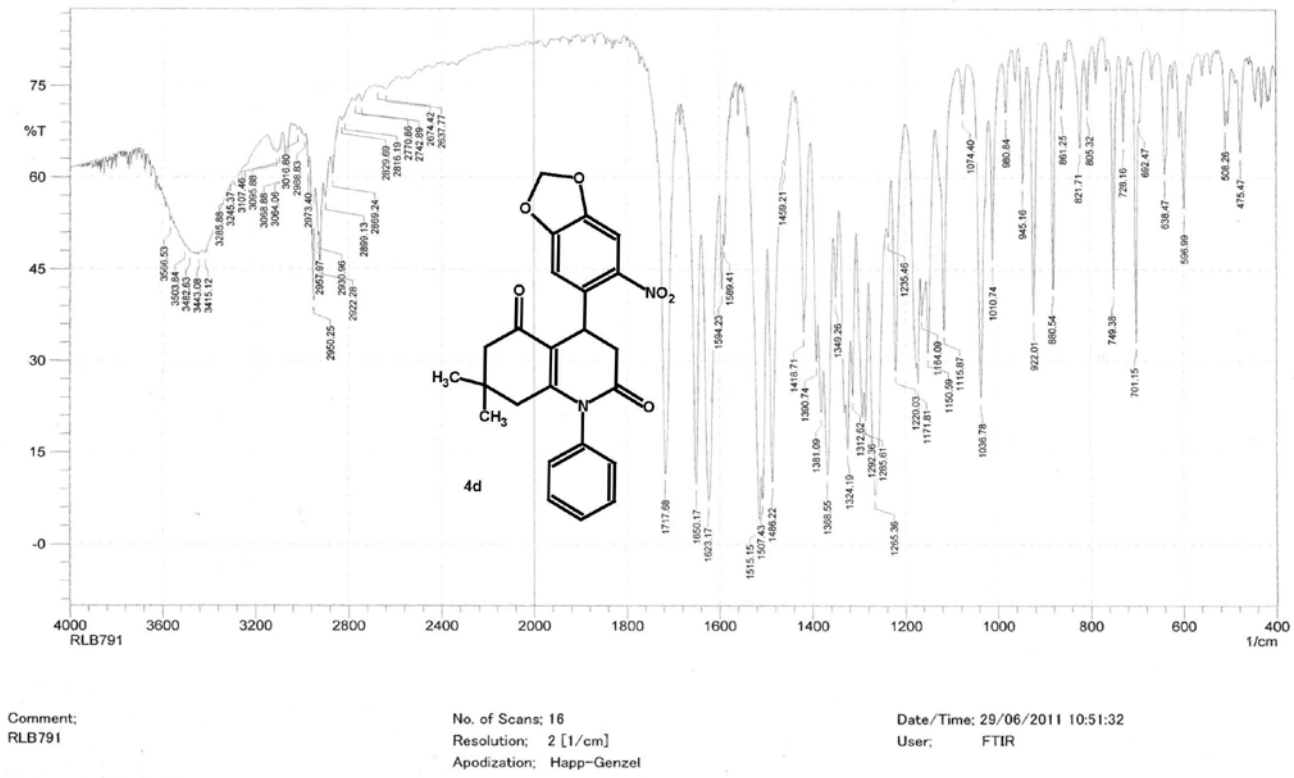

Figure S28. IR (KBr) spectrum of compound **4d**.

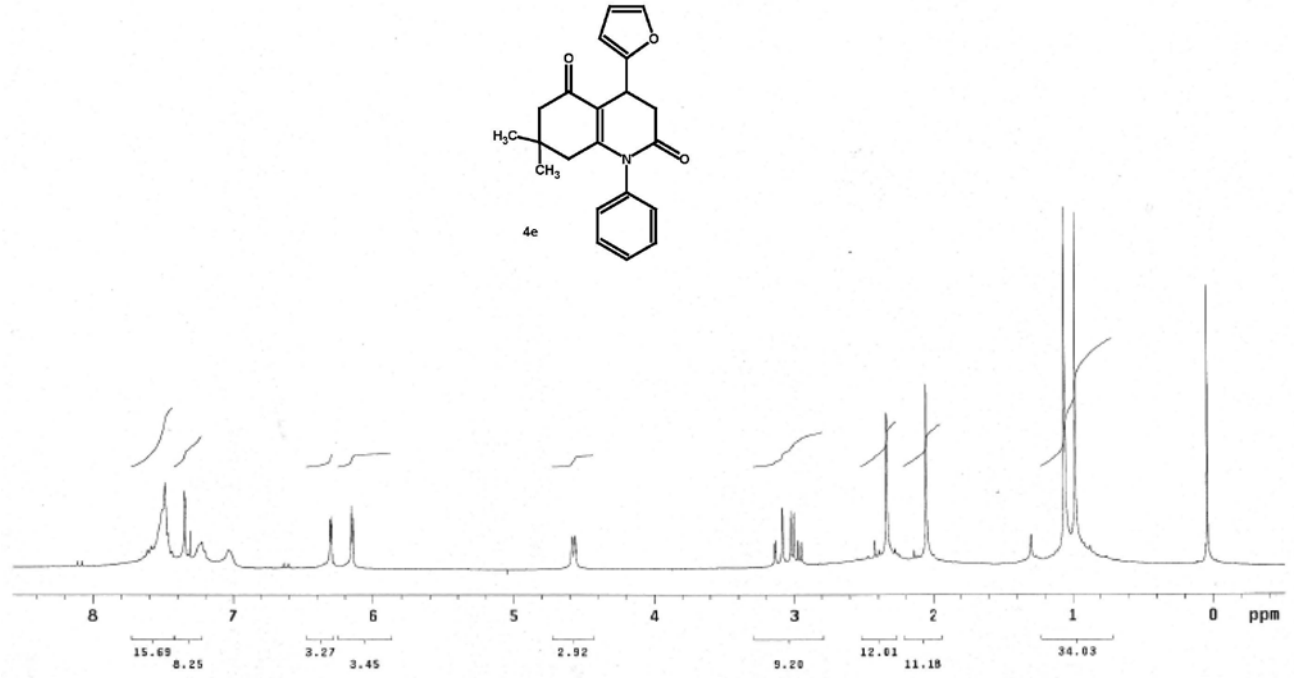

Figure S29. ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of **4e**.

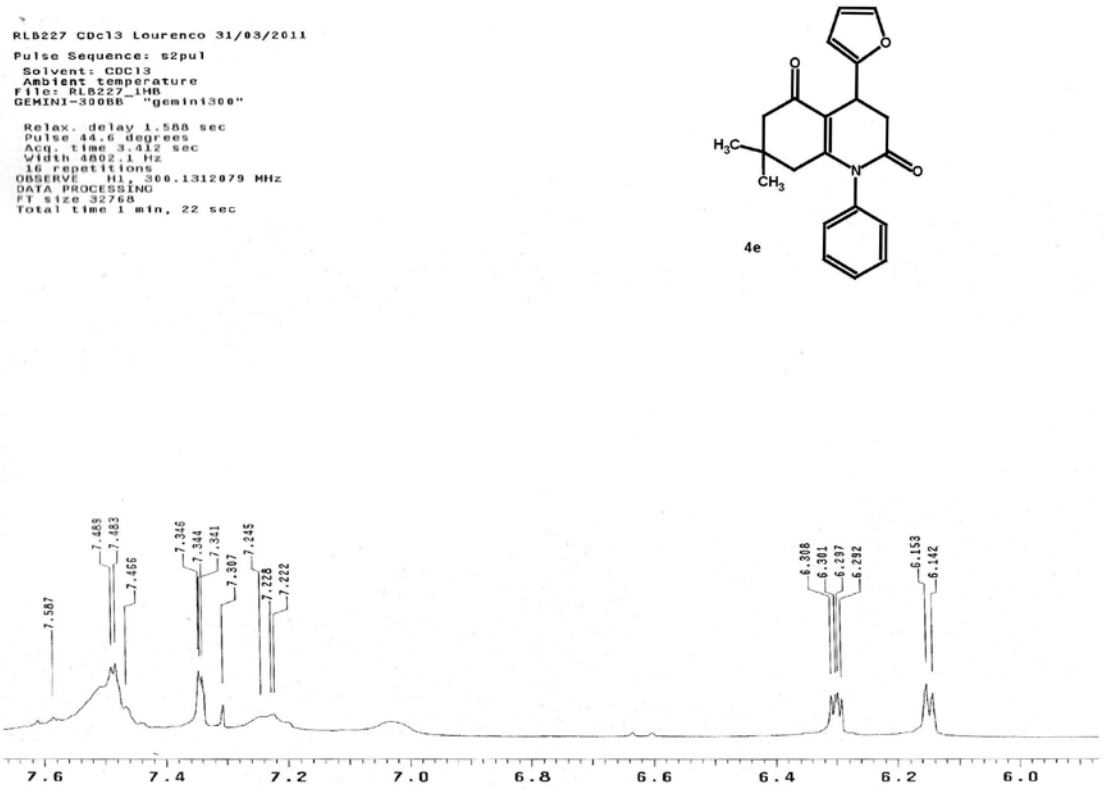

Figure S30. Expanded ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of **4e**.

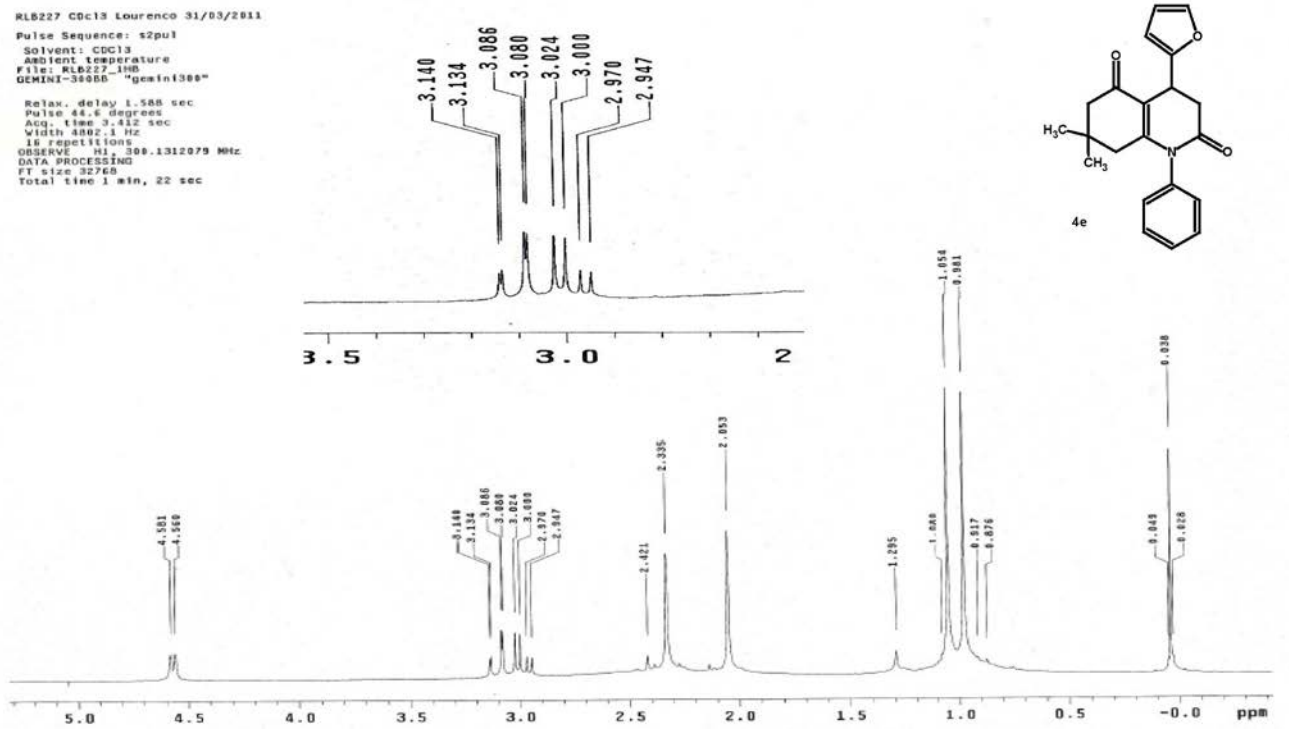

Figure S31. Expanded ^{1}H NMR ($CDCl_3$, 300 MHz) spectrum of **4e**.

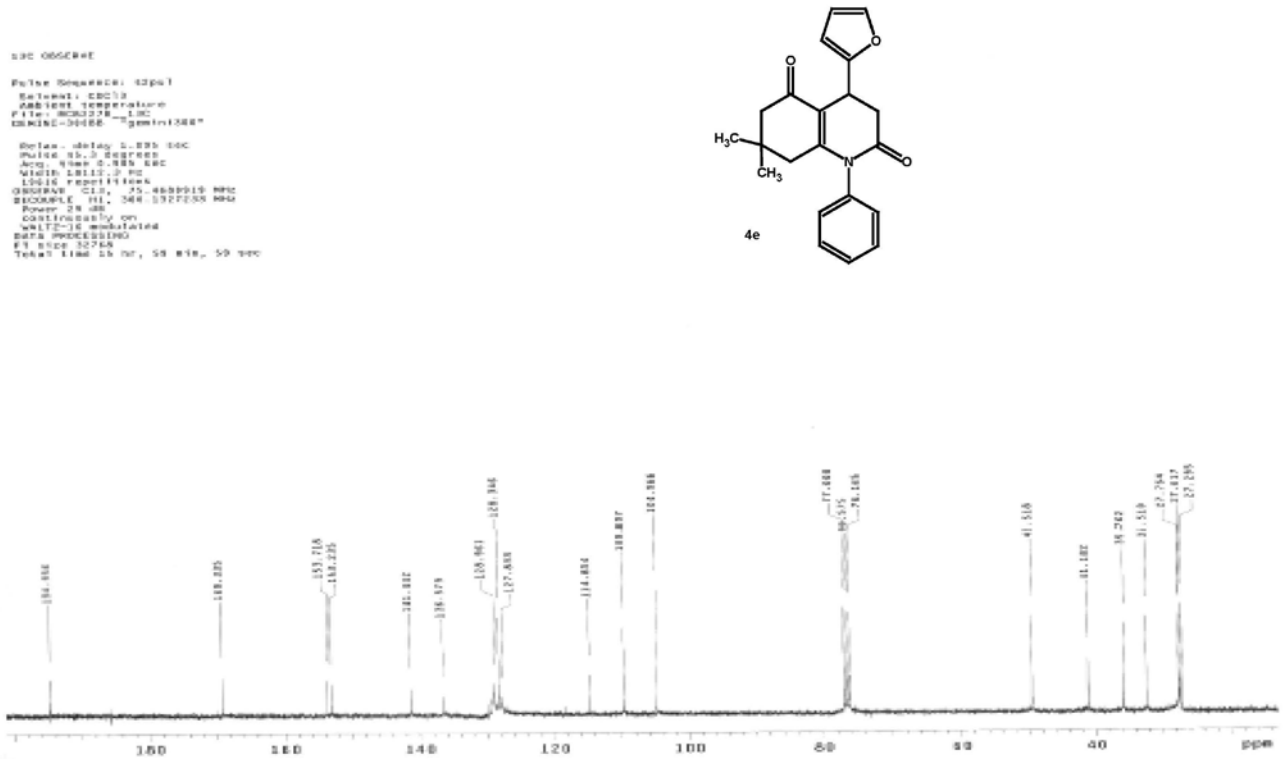

Figure S32. ^{13}C NMR($CDCl_3$, 75 MHz) spectrum of **4e**.

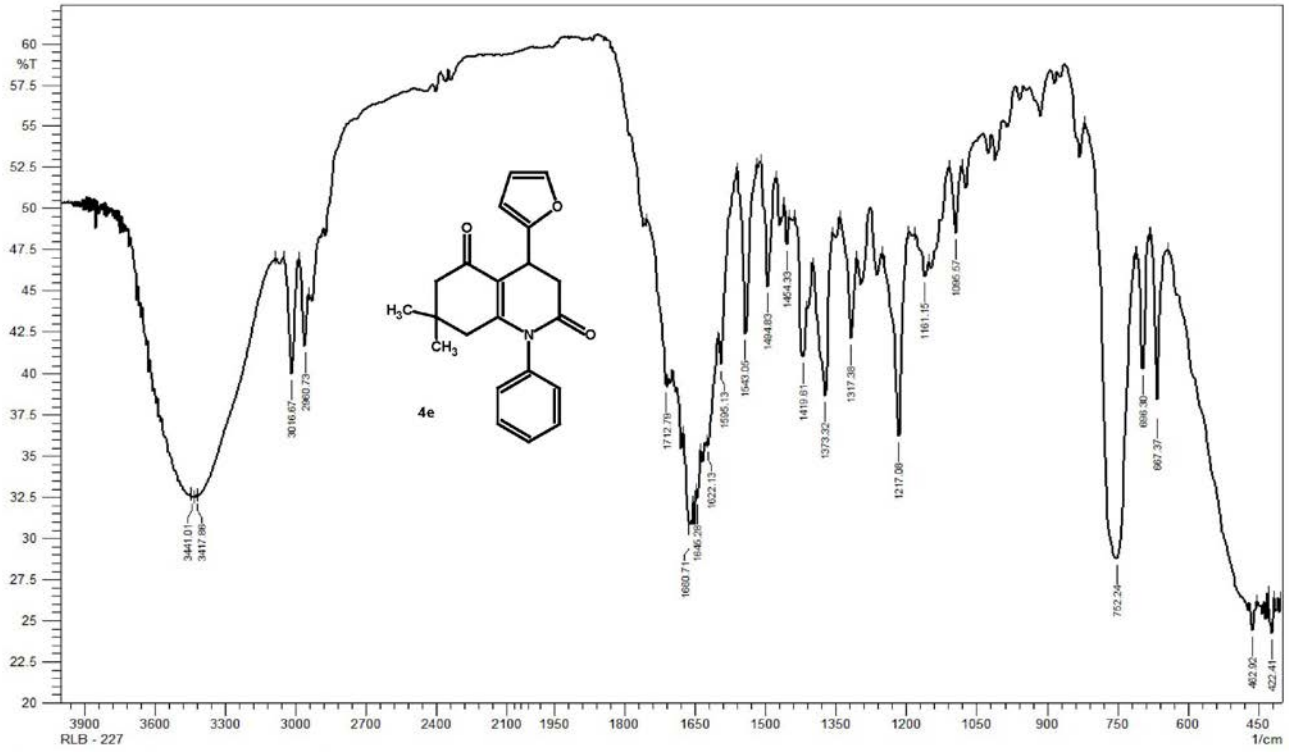

Figure S33. IR (film) spectrum of **4e**.

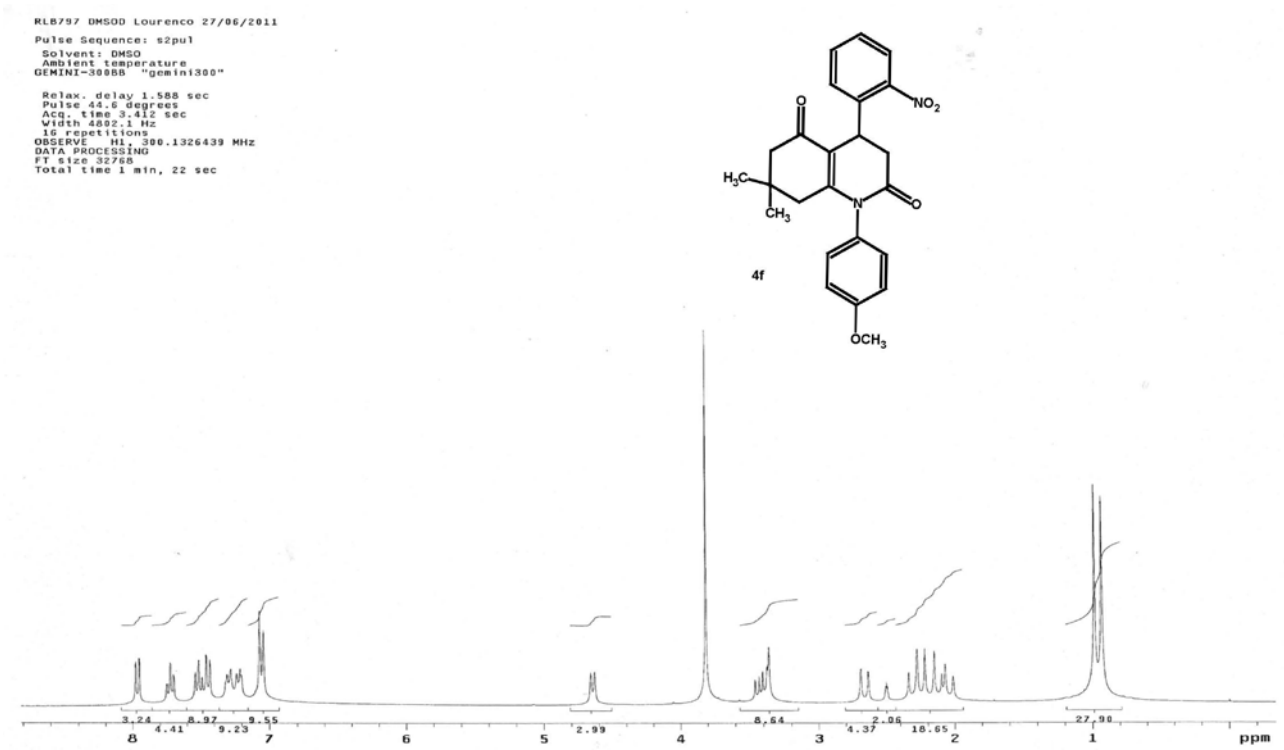

Figure S34. ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4f**.

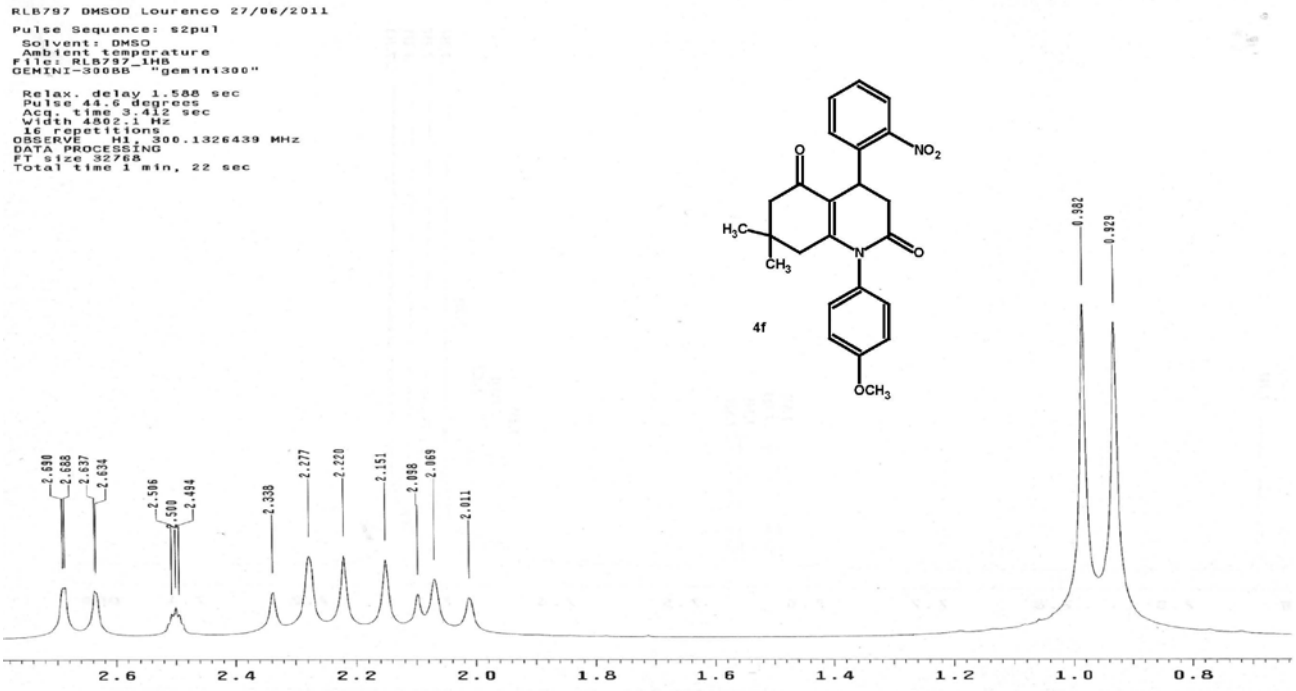

Figure S35. Expanded ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4f**.

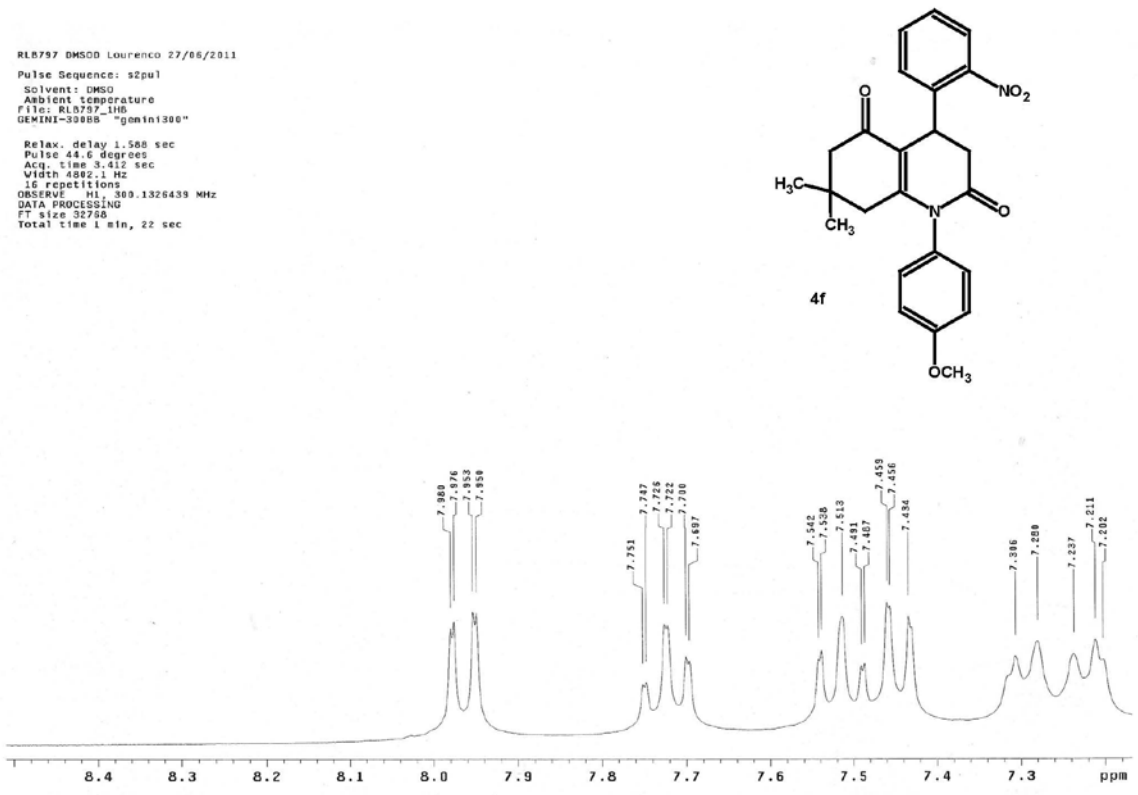

Figure S36. Expanded ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4f**.

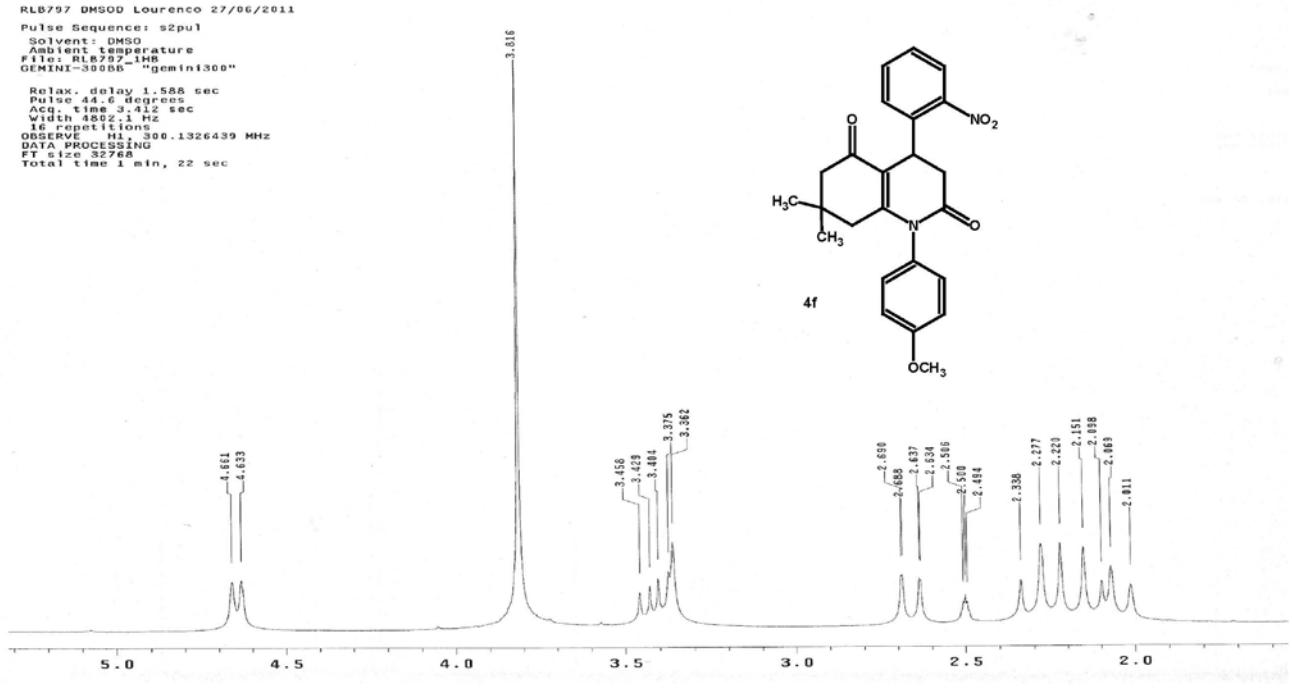

Figure S37. Expanded ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4f**.

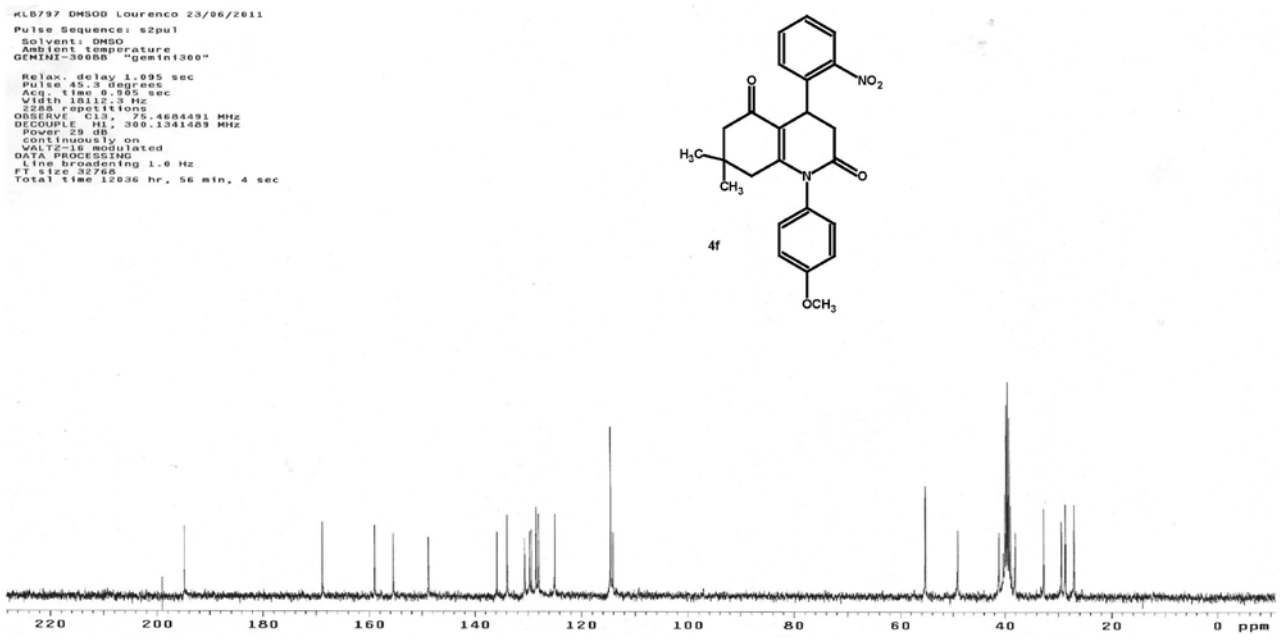

Figure S38. ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of **4f**.

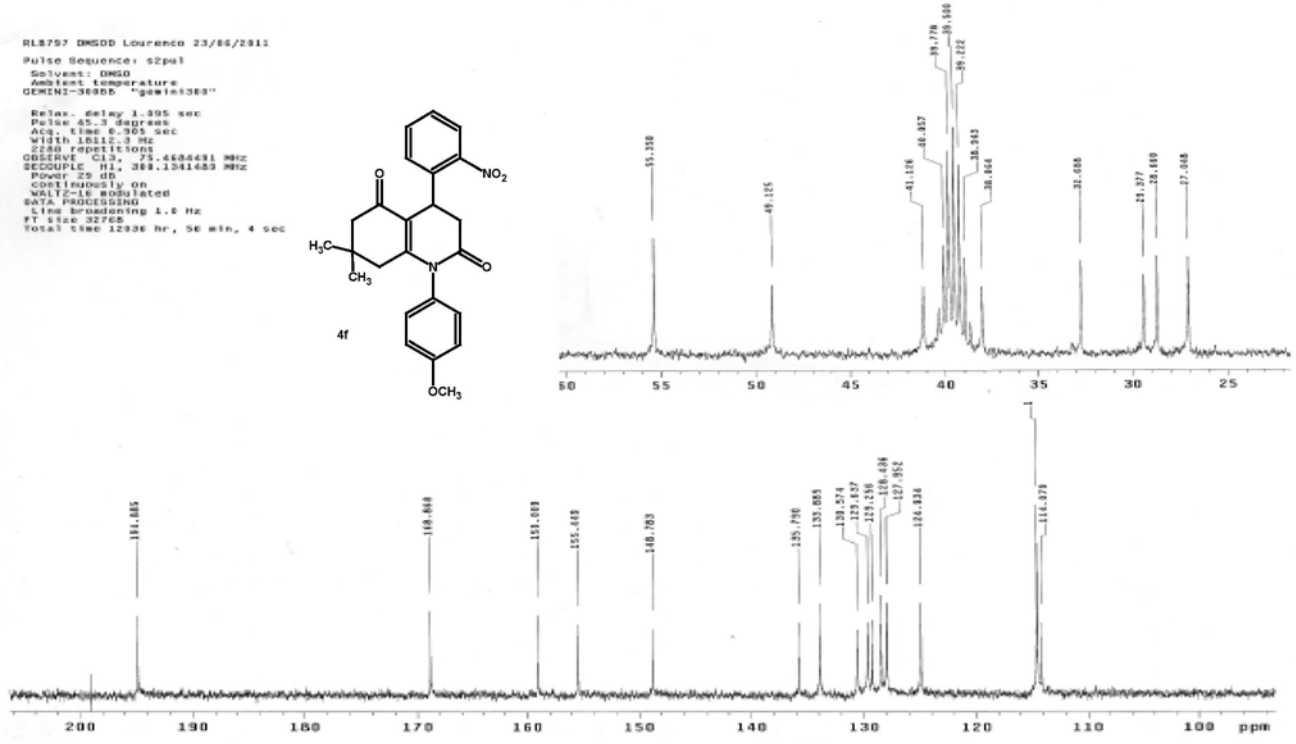

Figure S39. Expanded ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of **4f**.

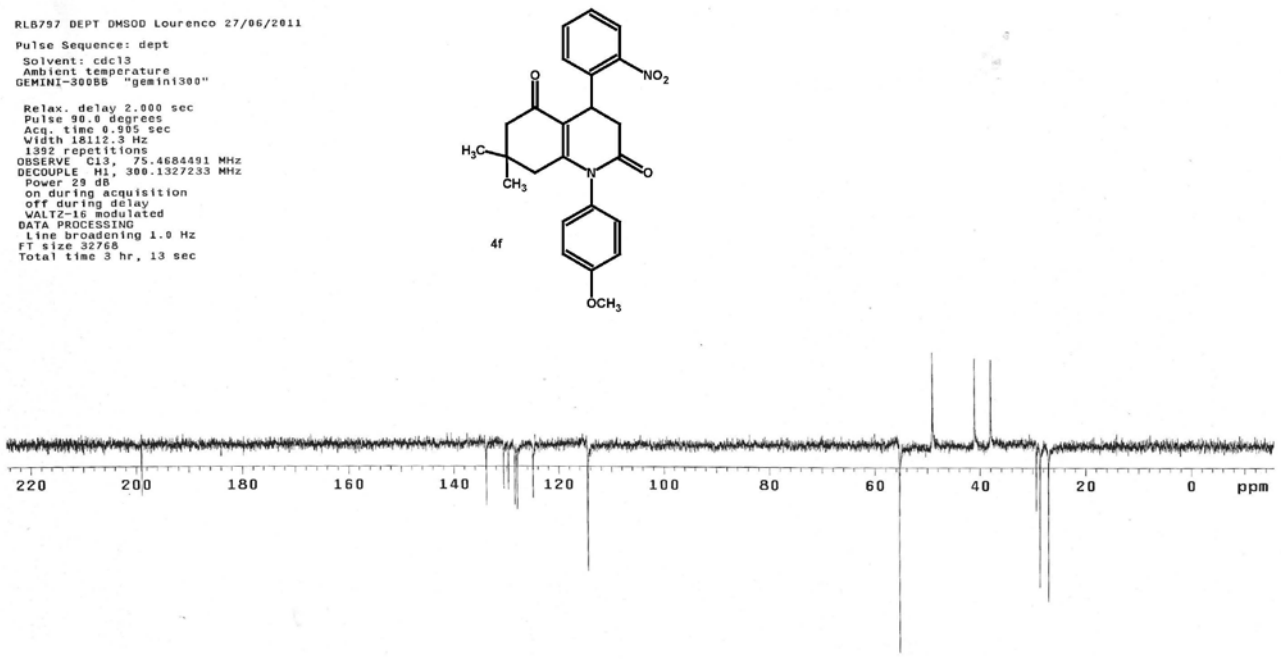

Figure S40. DEPT 135 NMR (DMSO-D_6, 75 MHz) spectrum of **4f**.

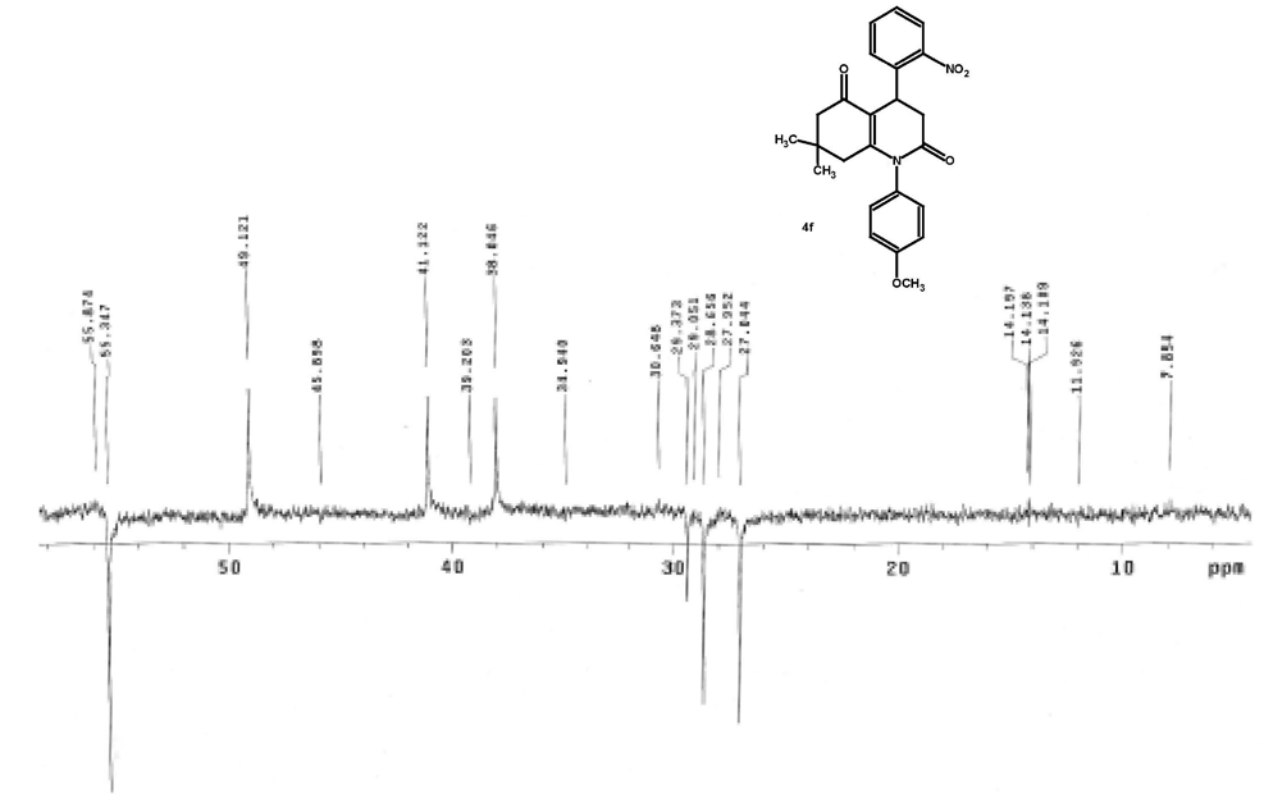

Figure S41. Expanded DEPT 135 NMR (DMSO-D_6, 75 MHz) spectrum of **4f**.

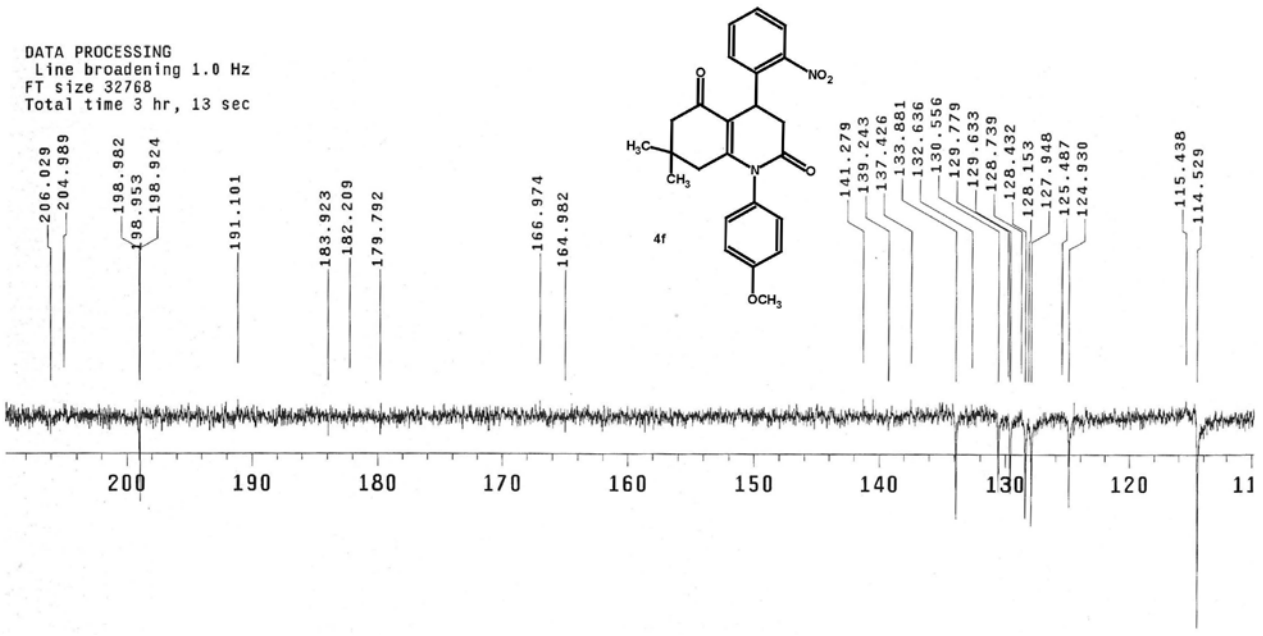

Figure S42. Expanded DEPT 135 NMR (DMSO-D_6, 75 MHz) spectrum of **4f**.

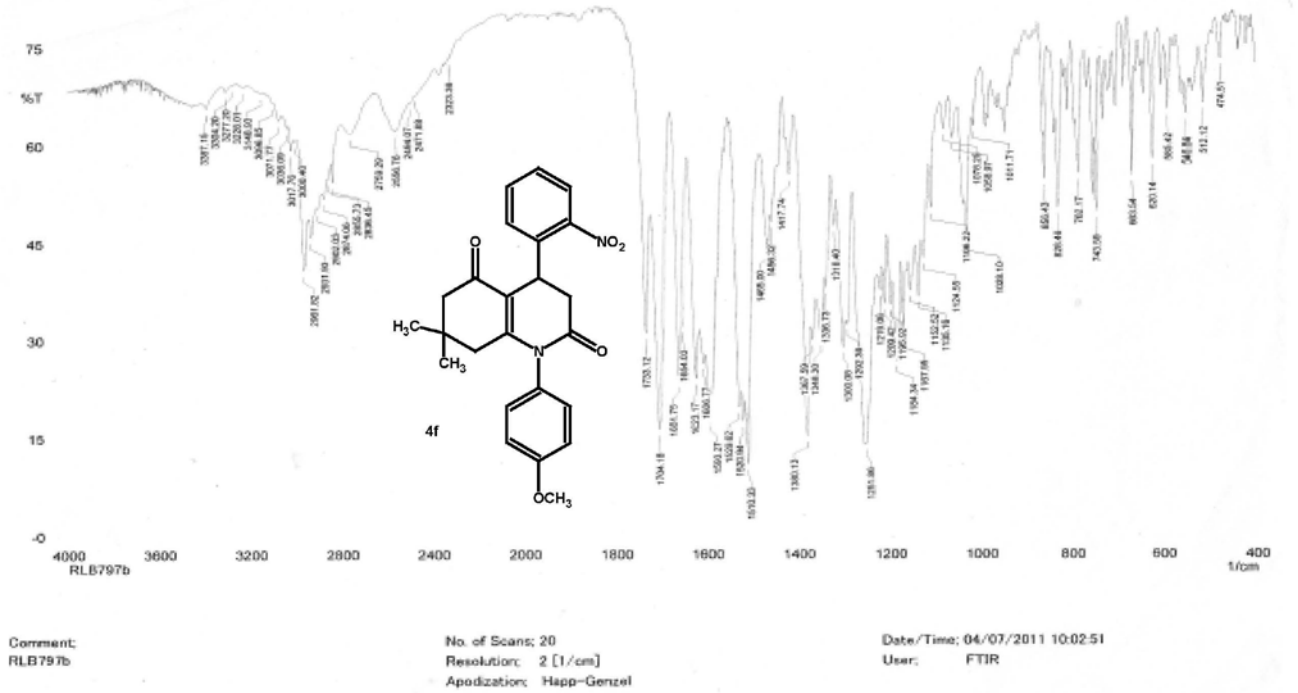

Figure S43. IR (KBr) spectrum of compound **4f**.

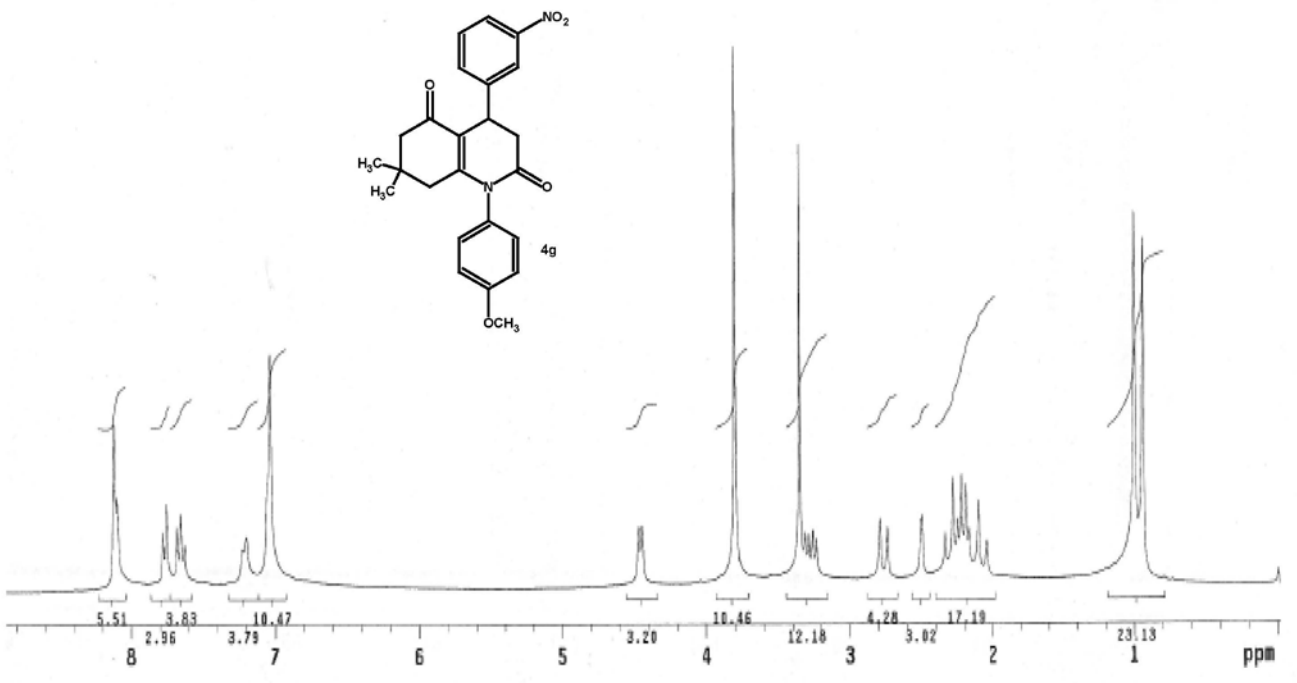

Figure S44. ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4g**.

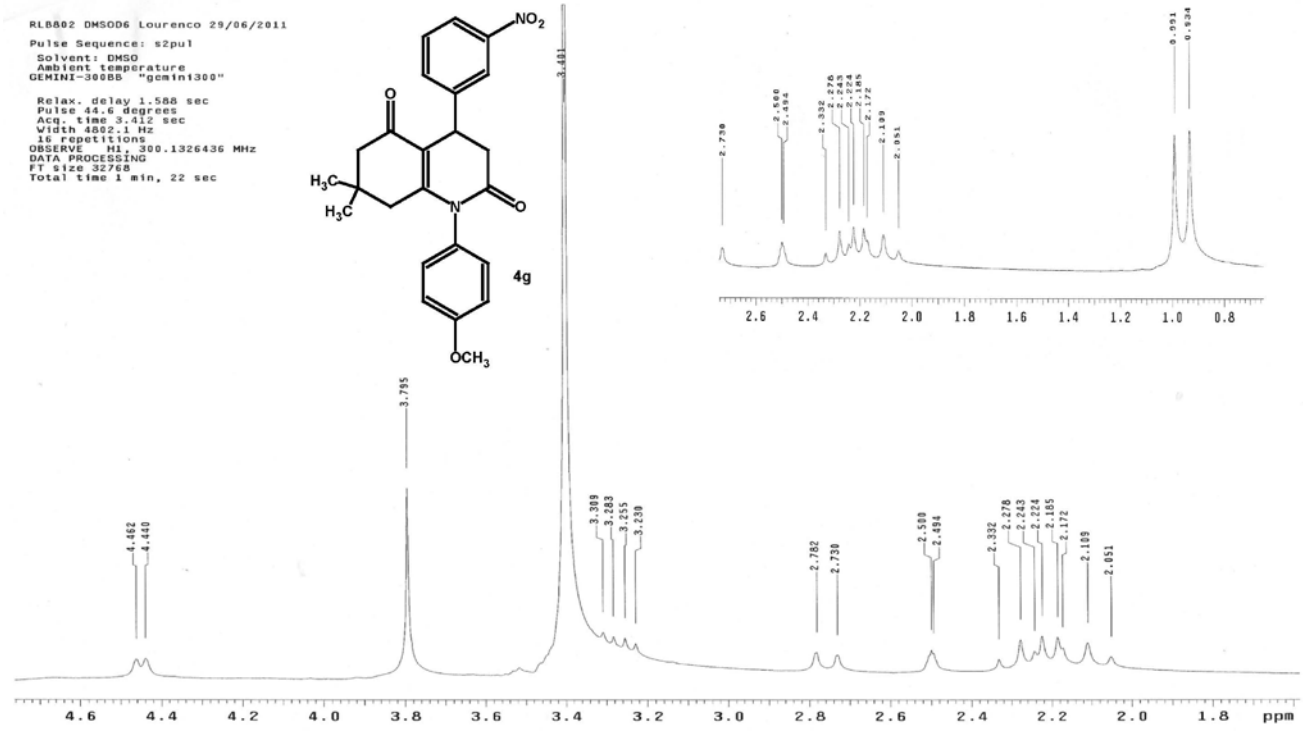

Figure S45. Expanded^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4g**.

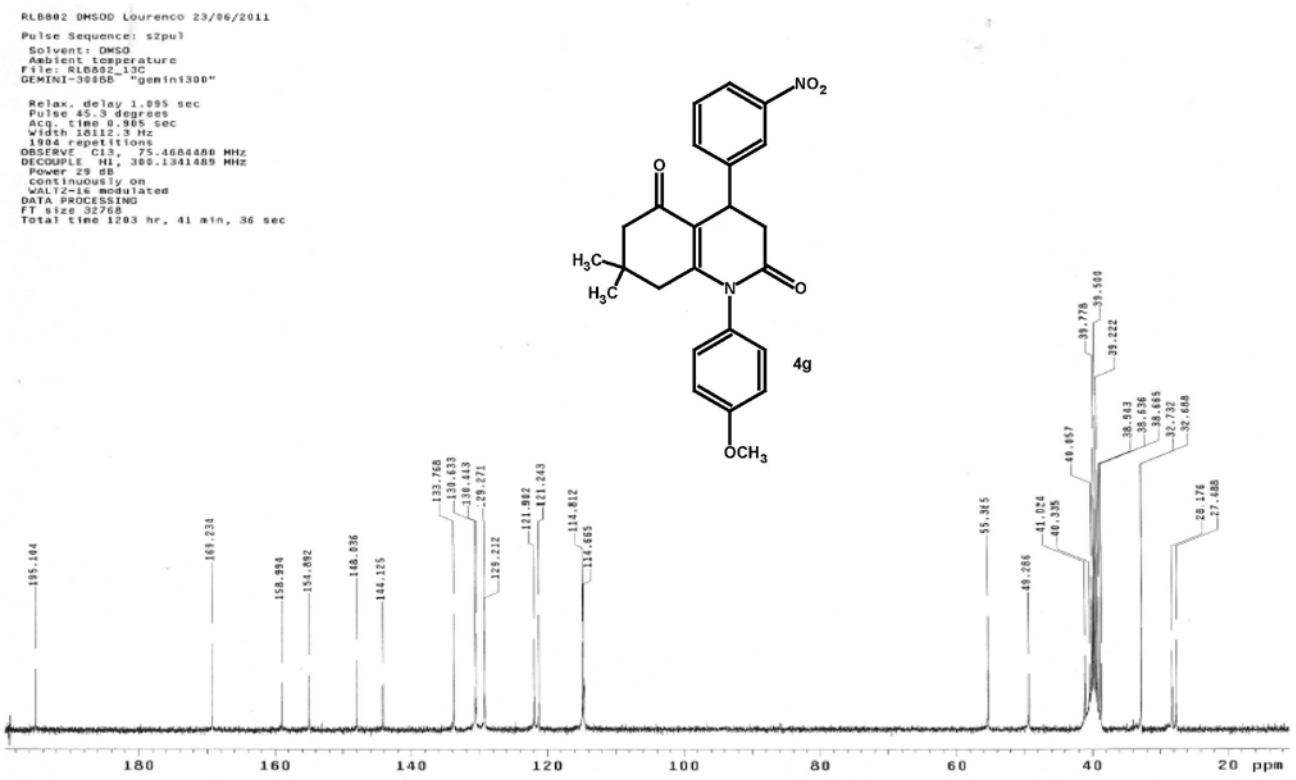

Figure S46. ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of **4g**.

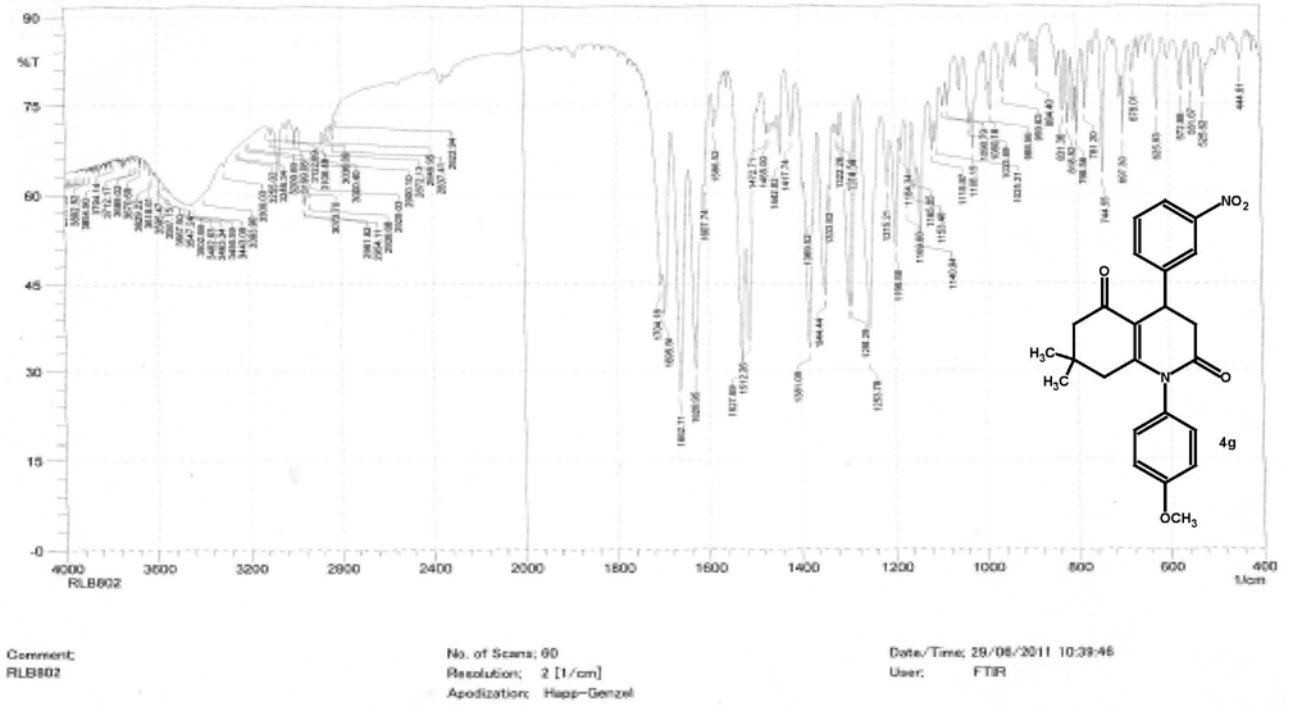

Figure S47. IR (KBr) spectrum of compound **4g**.

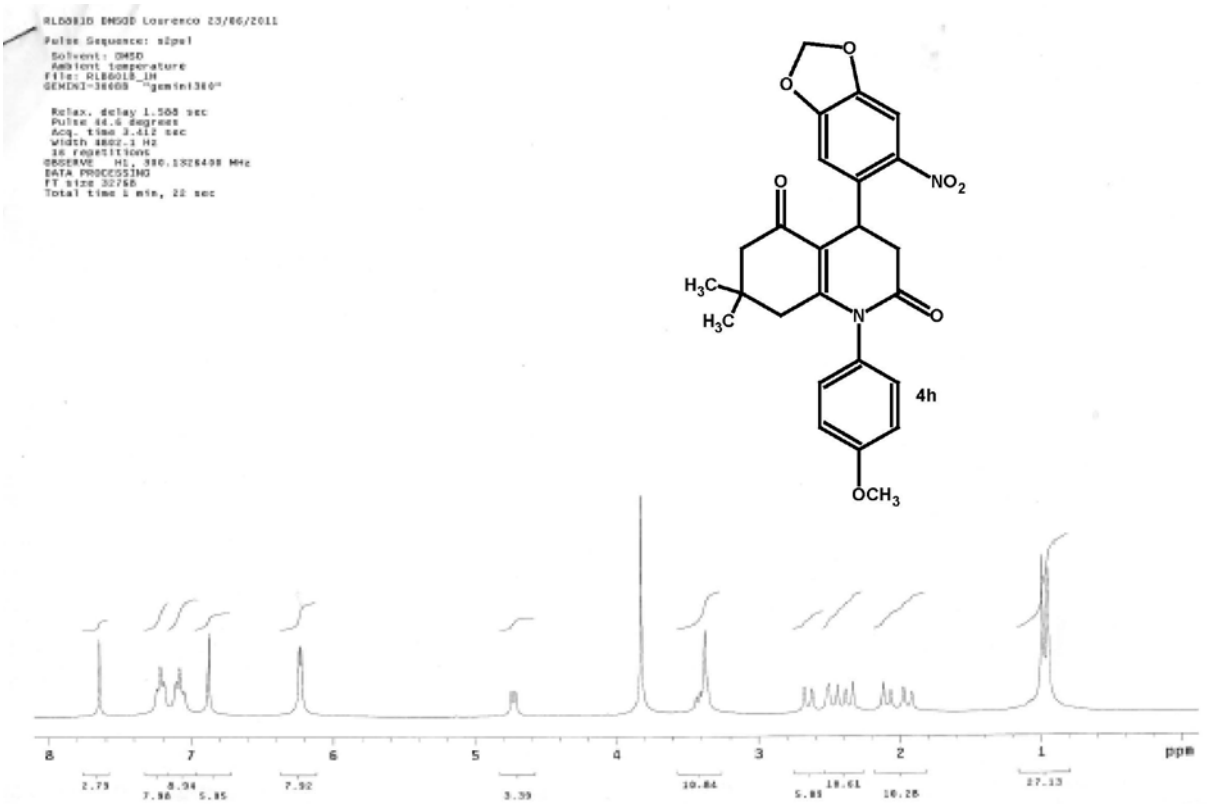

Figure S48. ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4h**.

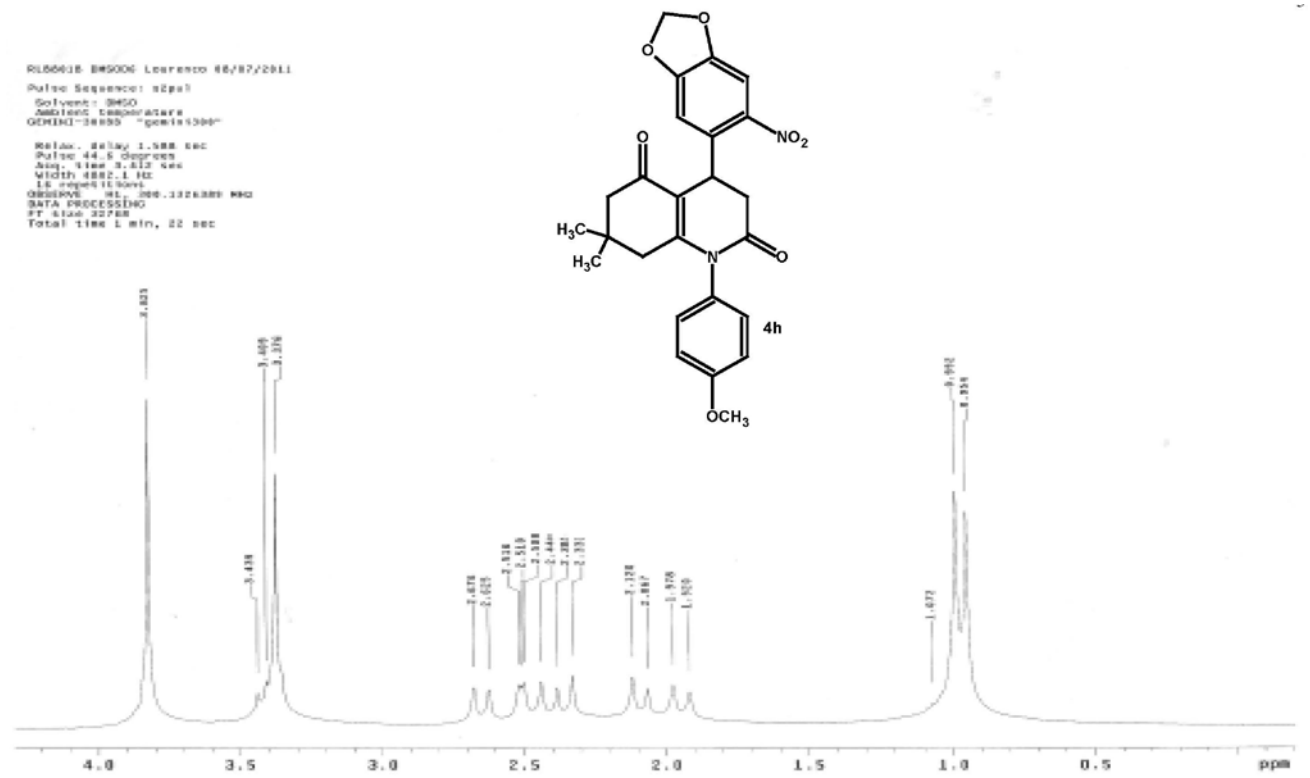

Figure S49. Expanded ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4h**.

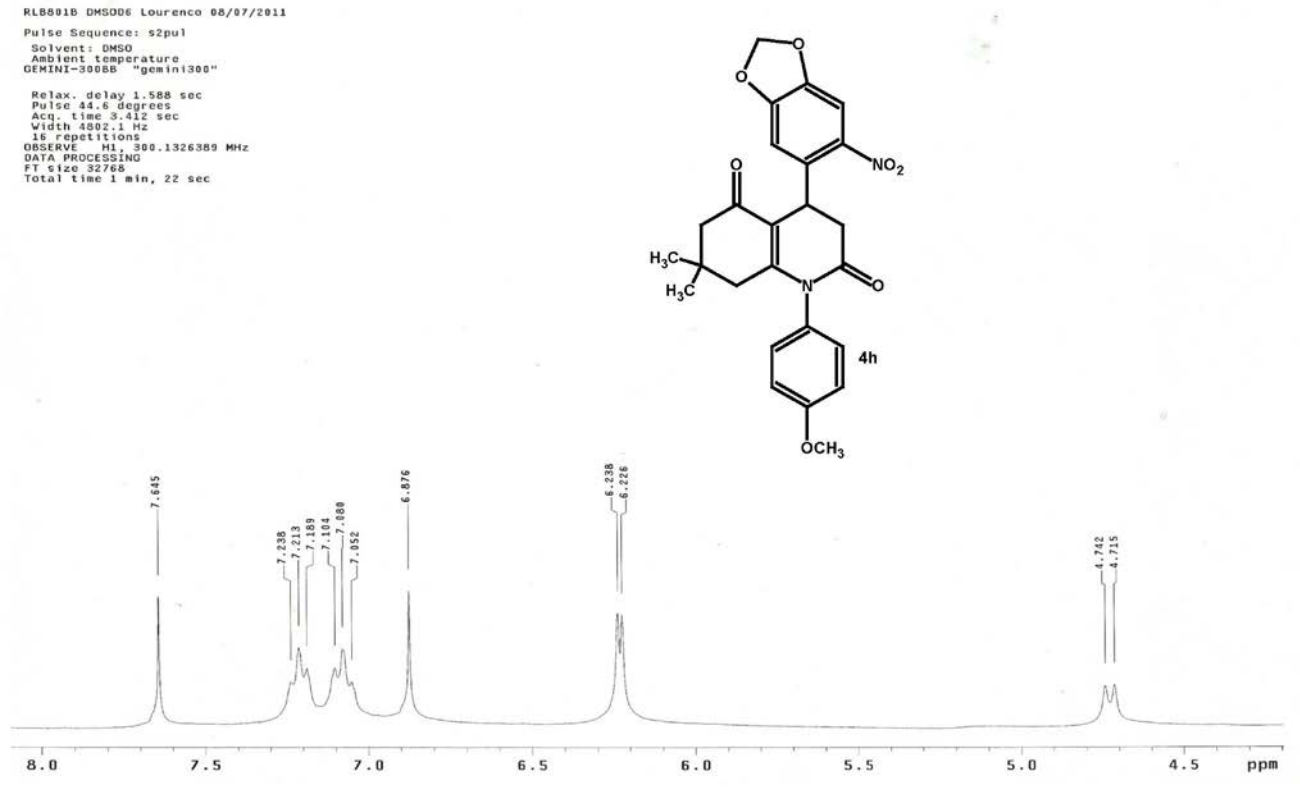

Figure S50. Expanded ^{1}H NMR (DMSO-D_6, 300 MHz) spectrum of **4h**.

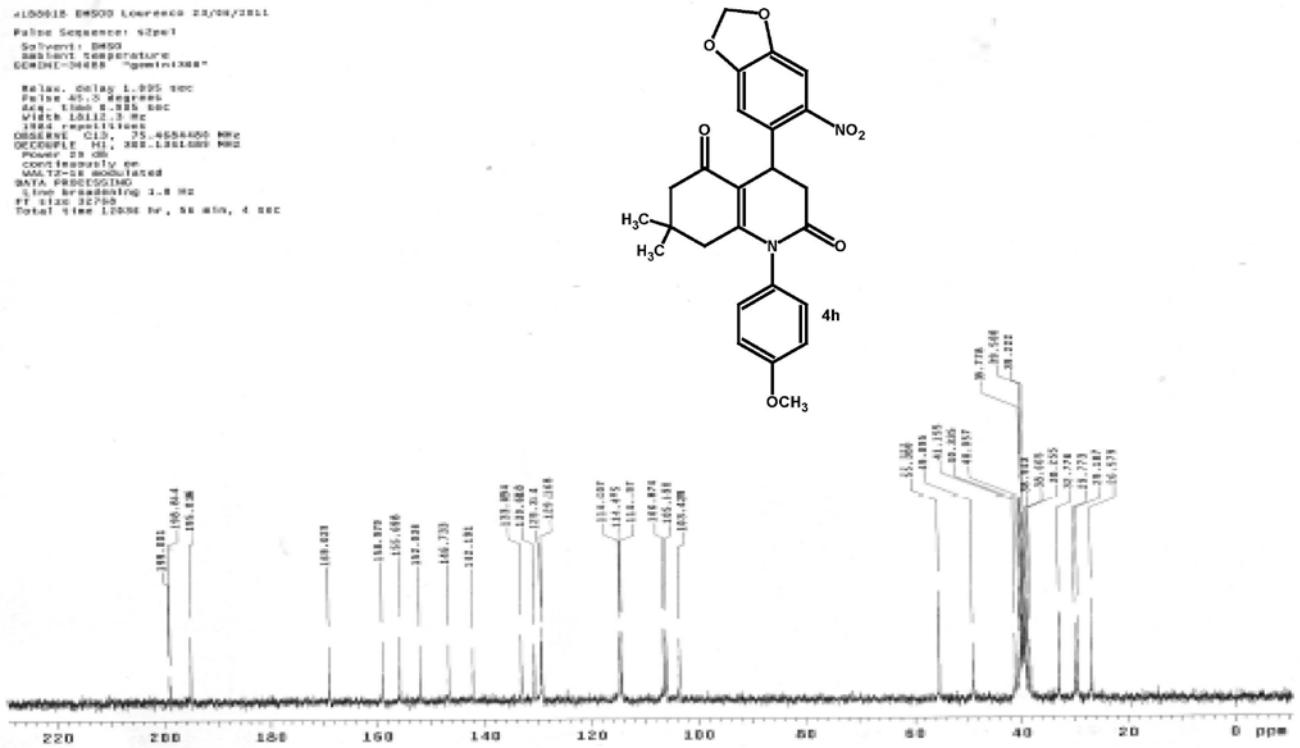

Figure S51. ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of **4h**.

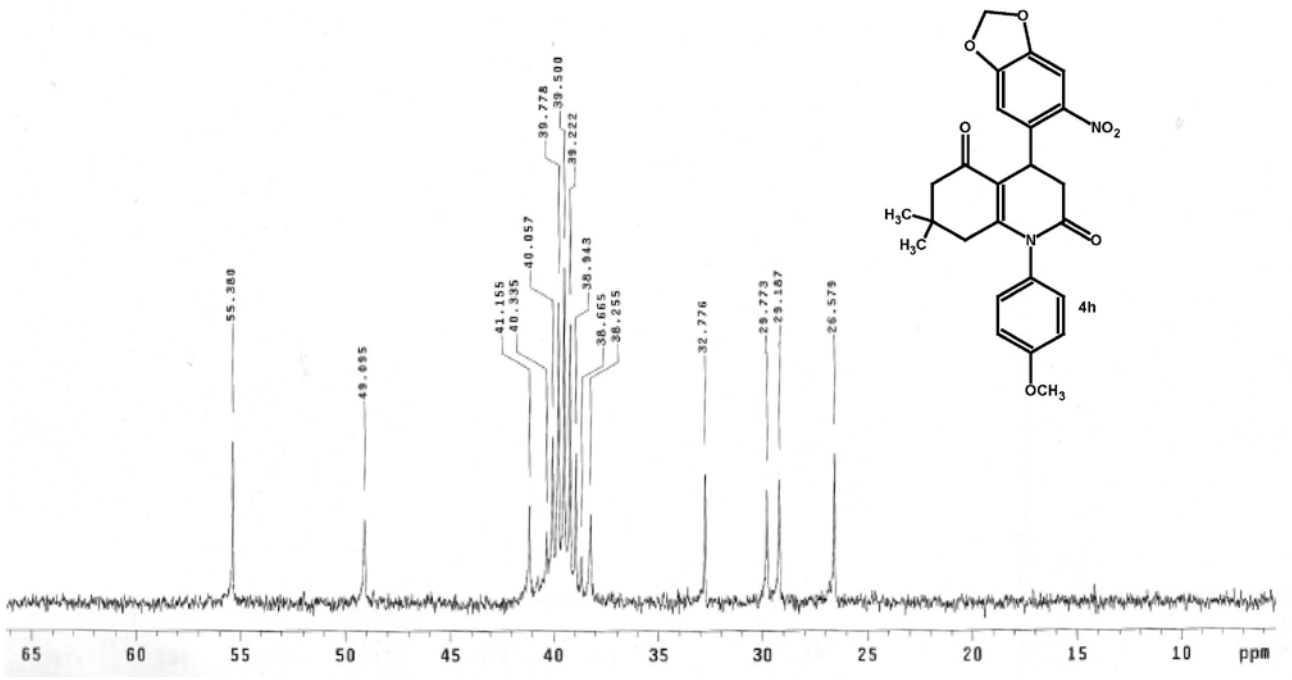

Figure S52. Expanded ^{13}C NMR (DMSO-D_6, 75 MHz) spectrum of **4h**.

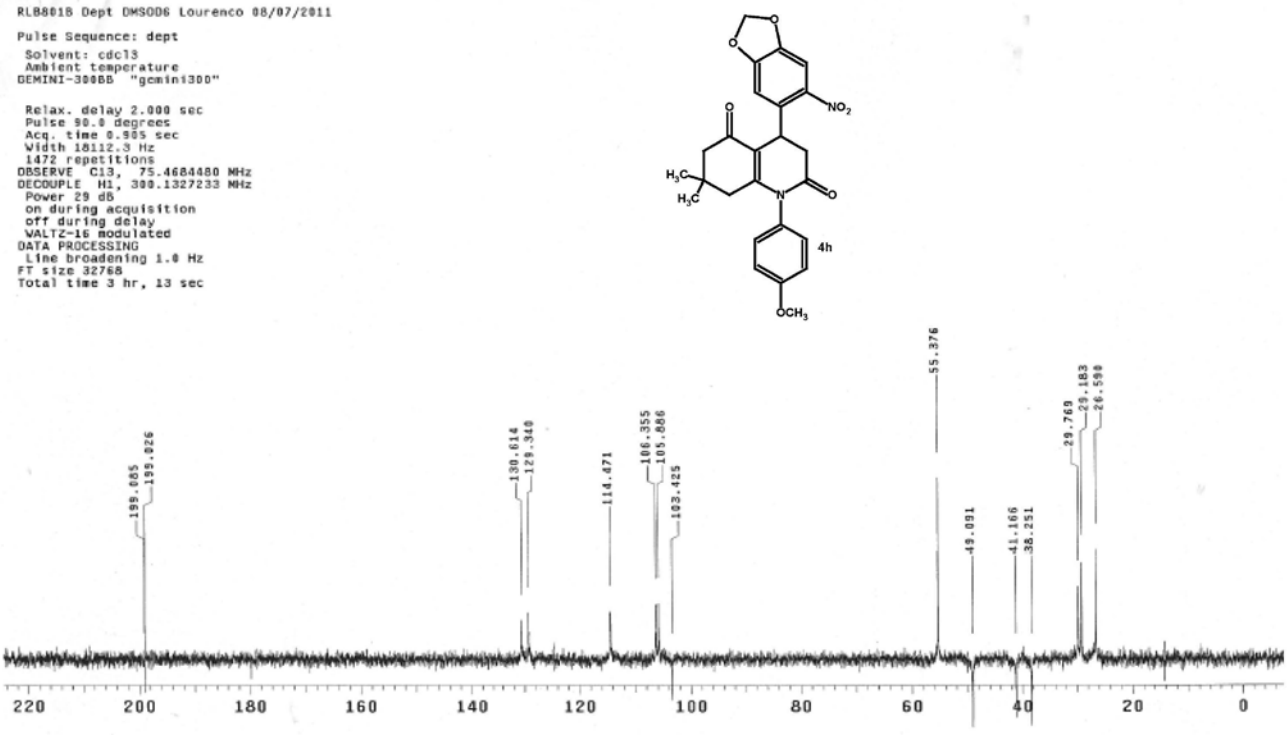

Figure S53. DEPT 135 NMR (DMSO-D_6, 75 MHz) spectrum of **4h**.

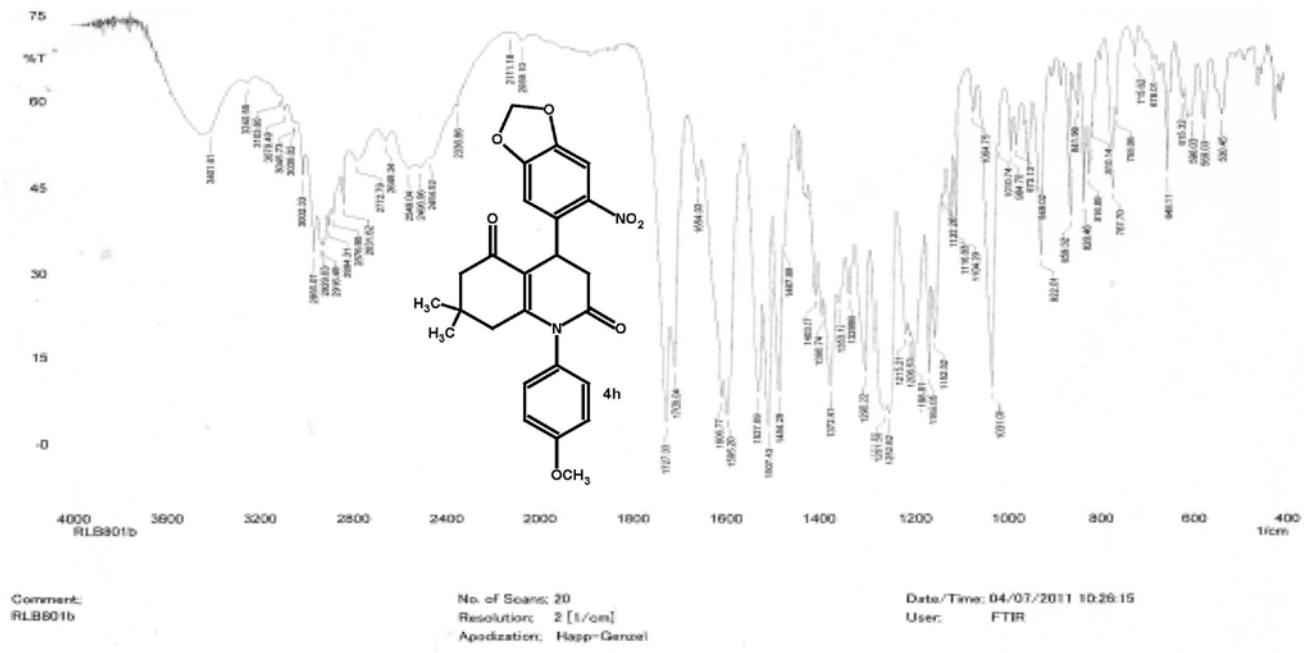

Figure S54. IR (KBr) spectrum of compound **4h**.