Synthesis of polycyclic quinolines using SiO_2/H_2SO_4 *via* Friedländer synthetic method

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Graphical Abstract

Abstract

An attention to the novel synthetic route for the polycyclic quinolines (**3** & **5**) from cyclic-diketones, cyclohexan-1,2-dione (**2**) / cyclohexan-1,3-dione (**4**) with o-aminoarylketones (**1**) in the presence of SiO_2/H_2SO_4 yielded *via* Friedländer synthetic method. The catalytic efficiency of the SiO_2/H_2SO_4 was discussed through their utilization in the synthesis of biologically active substituted polycyclic quinoline derivatives (**3** & **5**) and the mechanism has been proposed. The SiO_2/H_2SO_4 was found as a effective catalyst for the Friedländer reaction and gave considerable isolated yield of the targeted products under the mild reaction condition. The synthesized polycyclic quinolines (**3** & **5**) were characterized through diverse analytical techniques like FT-IR, NMR spectroscopy and single crystal X-ray diffraction studies.

Key Words

Friedländer synthetic method

Polycyclic quinolines

2,3-Dihydroacridin-4-one

3,4-Dihydroacridin-1-one

SiO_2/H_2SO_4

Introduction

In the recent decades, diversity of rationale and remarkable attention of heterocyclic compounds are more featured their bio-activity and their utility as drug molecule, in particular, quinoline scaffolds are important in heterocyclic chemistry, because of broad range of biological properties and functions in the quinoline structured compounds and synthetic drugs.[1] By attempting a new methodologies and products of quinoline moieties are still desirable for researchers to syntheses.[2] A number of classical methods are used for achieving the quinoline core, including Skraup, Doebner-von Miller, Friedländer, Pfitzinger, Conrad-Limpach, Combes syntheses and Povarov reaction.[3] Friedländer synthesis is the most valuable methodology and evergreen tool for the synthesis of quinolines in the recent years. It is known from more than a century, Friedländer synthesis[4] was applied to prepare quinoline derivatives by condensation of easily accessible 2-aminoarylketones with carbonyl compounds possessing a reactive methylene group, followed by cyclodehydration.[5] Up to that time, polycyclic quinolines and annulated heterocycles synthesized from Friedländer method using various catalyst and methodology, such as protic acids, Bronsted acids, Lewis acids, greener methods, nano catalysts, ionic liquids and using various solvents.[6]

The most attractive method for the improvement of organic synthesis is continuously reporting new methodologies and catalytic reactions. The preparation of such a class of compounds, the most convenient method for the synthetic procedure of polycyclic quinolines described so far lead to poor yields, extended reaction times, and dependence on destructive and often expensive catalyst systems, constructing the growth of a simple, eco-friendly, low-cost attractive protocol. The synthesis of polycyclic quinolines is reported our group in the first time by using SiO_2/H_2SO_4 through Friedländer synthesis. This way, polycyclic quinoline derivatives have been prepared by condensation of 2-aminoarylketones with 1,2- / 1,3-carbonyl compounds. The 2,3-dihydroacridin-4-one **(3)** and 3,4-dihydroacridin-1-one **(5)** were synthesized from 2-aminoaryl ketones (**1**) and 1,2-cyclohexanedione (**2**) / 1,3-cyclohexanedione (**4**) in the presence of SiO_2/H_2SO_4 condition with good to excellent yields.

Methods

General

All the reagents and chemicals were purchased from Sigma Aldrich and AKSci. Unless otherwise specified, other reagents were obtained from commercial suppliers. When known compounds had to be prepared according to literature procedures, pertinent references are given. The purity of the products was tested by TLC silicagel 60 F254 25 folios de

aluminio 20 X 20 C (purchased from Merck) using petroleum ether and ethyl acetate in the ratio of 75:25 as developing solvents. The chemical shifts are expressed in parts per million (ppm). Coupling constants (J) are reported in hertz (Hz). The terms J_o and J_m refer to ortho coupling constant and metacoupling constant. The terms s, d, t, and dd refer to singlet, doublet, triplet, and doublet of doublet, respectively, and bs refers to a broad singlet.

Instrumentation

Melting points (M.p) were determined on a Kofler Thermogerate apparatus and were uncorrected. They are expressed in degree centigrade (°C). Fourier Transforms (FT-MIR) BRUKER brand, model VECTOR 22 was used to record the IR spectra (4000–400 cm^{-1}). ^{1}H NMR and ^{13}C NMR spectra were recorded on BRUKER AVANCE III HD-400 [400MHz (^{1}H) and 100MHz (^{13}C)] spectrometers using tetramethylsilane (TMS) as an internal reference. X-ray diffraction measurements were performed on a Bruker APEX-II CCD diffractometer at 100.04 K using monochromatic Mo K α radiation.

Synthesis

General procedure for the synthesis of 9-aryl-2,3-dihydro-1H-acridin-4-one (3) and 3,4-Dihydroacridin-1-one (5): An appropriate 2-amino-arylketone (**1,** 1 mmol) and 1,2-cyclohexanedione (**2,** 1.2 mmol) / 1,3-cyclohexanedione (**4,** 1.2 mmol) were dissolved in methanol (5mL) refluxed with SiO_2/H_2SO_4 (0.1 mmol) for 2 hrs. The completion of the reaction was monitored by TLC. The obtained product was isolated through recrystallization using ethyl acetate to yield the corresponding products (**3** & **5**).

9-Phenyl-2,3-dihydro-1*H*-acridin-4-one (3a)

Yellow solid; M.p. 213-215ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1701, 1598; ^{1}H NMR (400 MHz, $CDCl_3$) (**Figure S1**) (ppm) δ: 2.056-2.119 (m, 2H, C_4-CH_2), 2.796-2.872 (m, 4H, C_3-CH_2, C_5-CH_2), 7.207-7.234 (m, 2H, C_9-, C_{13}-H), 7.367-7.440 (m, 2H, C_{16}-, C_{17}- H,), 7.453-7.532 (m, 3H, C_{10}-, C_{11}-, C_{12}-H), 7.634-7.676 (m, 1H, C_{15}-H), 8.327 (d, 1H, C_{18}-H, *J*= 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (**Figure S2**) (ppm) δ: 22.60, 27.99, 40.22, 125.85, 128.37, 128.72, 128.84, 129.16, 129.51, 131.52, 133.46, 136.14, 147.14, 148.15, 148.41, 197.59; Anal. Calcd. for: $C_{19}H_{15}NO$: C, 83.49; H, 5.53; N, 5.12; found C, 83.40; H, 5.61; N, 5.06.

7-Chloro-9-phenyl-2,3-dihydro-1*H*-acridin-4-one (3b)

Yellow solid; M.p. 250-252ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1700, 1602; ^{1}H NMR (400 MHz, $CDCl_3$) (**Figure S3**) (ppm) δ: 2.093-2.125 (m, 2H, C_4-CH_2), 2.809-2.893 (m, 4H, C_3-CH_2, C_5-CH_2), 7.217-7.241 (m, 2H, C_9-, C_{13}-H), 7.369 (d, 1H, C_{15}-H, J_m = 2.40 Hz), 7.509-7.571 (m, 3H, C_{10}-, C_{11}-, C_{12}-H), 7.613 (dd, 1H, C_{17}-H, J_m= 2.40 Hz, J_o= 8.80 Hz), 8.285 (d, 1H, C_{18}-H, J= 8.80 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (**Figure S4**) (ppm) δ: 22.41, 28.03, 40.13, 124.61, 128.72, 129.07, 129.37, 130.72, 133.11, 134.44, 135.02, 135.40, 145.53, 147.43, 148.56, 197.22; Anal. Calcd. for: $C_{19}H_{14}ClNO$: C, 74.15; H, 4.59; N, 4.55; found C, 74.21; H, 4.63; N, 4.48.

7-Chloro-9-(2'-chlorophenyl)-2,3-dihydroacridin-4(*1H*)-one (3c)

Yellow solid; M.p. 185-187ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1700, 1599; ^{1}H NMR (400 MHz, $CDCl_3$) (**Figure S5**) (ppm) δ: 2.129-2.162 (m, 2H, C_4-CH_2), 2.690-2.820 (m, 2H, C_3-CH_2), 2.878-2.914 (m, 2H, C_5-CH_2), 7.177-7.230 (m, 2H, C_{11}-, C_{12}-H), 7.452-7.491 (m, 2H, C_{10}-, C_{13}-H),7.593-7.647 (m, 2H, C_{15}-, C_{17}-H), 8.310 (d, 1H, C_{18}-H, J= 8.80 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (**Figure S6**) (ppm) δ: 22.20, 27.38, 40.14, 123.94, 127.53, 128.91, 130.28, 130.46, 130.65, 130.93, 133.25, 133.31, 134.30, 135.06, 135.40, 144.51, 145.57, 148.63, 197.04; Anal. Calcd. for: $C_{19}H_{13}Cl_2NO$: C, 66.69; H, 3.83; N, 4.09; found C, 66.62; H, 3.88; N, 4.02.

7-Chloro-9-(2'-fluorophenyl)-2,3-dihydroacridin-4(*1H*)-one (3d)

Yellow solid; M.p. 199-201ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1705, 1597; ^{1}H NMR (400 MHz, $CDCl_3$) (**Figure S7**) (ppm) δ: 1.981-2.059 (m, 2H, C_4-CH_2), 2.643-2.806 (m, 4H, C_3-CH_2, C_5-CH_2), 7.076-7.119 (m, 1H, C_{12}-H), 7.138-7.186 (m, 1H, C_{10}-H), 7.208-7.249 (m, 2H, C_{11}-, C_{13}-H), 7.390-7.447 (m, 1H, C_{15}-H), 7.511 (dd, 1H, C_{17}-H, J_m= 2.40 Hz, J_o= 8.80 Hz), 8.182 (d, 1H, C_{18}-H, J= 8.80 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (**Figure S8**) (ppm) δ: 22.24, 27.57, 40.10, 116.36, 116.57, 122.76, 124.06, 124.83, 129.26, 130.87, 133.27, 135.43, 141.27, 145.52, 148.49, 158.26, 160.72, 196.97; Anal. Calcd. for: $C_{19}H_{13}ClFNO$: C, 70.05; H, 4.02; N, 4.30; found C, 70.15; H, 4.12; N, 4.19.

7-Bromo-9-(2'-fluorophenyl)-2,3-dihydroacridin-4(*1H*)-one (3e)

Yellow Sponges; M.p. 201-203ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1703, 1599; ^{1}H NMR (400 MHz, $CDCl_3$) (**Figure S9**) (ppm) δ: 2.094-2.187 (m, 2H, C_4-CH_2), 2.760-2.928 (m, 4H, C_3-CH_2, C_5-CH_2), 7.195-7.217 (m, 1H, C_{12}-H), 7.262-7.372 (m, 2H, C_{11}-, C_{13}-H), 7.514-7.571 (m, 2H,

C_{10}-, C_{15}-H), 7.769 (dd, 1H, C_{17}-H, J_m= 2.40 Hz, J_o= 8.80 Hz), 8.231 (d, 1H, C_{18}-H, J= 8.80 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (**Figure S10**) (ppm) δ: 22.24, 27.57, 40.11, 116.49, 122.57, 123.97, 124.84, 127.44, 129.66, 131.21, 133.30, 133.43, 135.48, 141.19, 145.71, 148.57, 158.27, 160.73, 196.97; Anal. Calcd. for: $C_{19}H_{13}BrFNO$: C, 61.64; H, 3.54; N, 3.78; found C, 61.58; H, 3.59; N, 3.68.

9-(4'-Bromophenyl)-2,3-dihydroacridin-4(*1H*)-one (3f)

Yellow solid; M.p. 244-246ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1701, 1598; ^{1}H NMR (400 MHz, $CDCl_3$) (**Figure S11**) (ppm) δ: 2.095-2.159 (m, 2H, C_4-CH_2), 2.813-2.843 (m, 2H, C_3-CH_2), 2.872-2.905 (m, 2H, C_5-CH_2), 7.144 (d, 2H, C_9-, C_{13}-H, J= 8.0 Hz), 7.382 (dd, 1H, C_{17}-H, J_m= 1.60 Hz, J_o= 8.80 Hz), 7.468-7.510 (m, 1H, C_{15}-H,), 7.674-7.722 (m, 3H, C_{10}-, C_{12}-, C_{16}-H), 8.362 (d, 1H, C_{18}-H, J= 8.80 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (**Figure S12**) (ppm) δ: 22.54, 27.99, 40.16, 122.76, 125.48, 128.43, 129.01, 129.68, 130.90, 131.68, 132.17, 133.34, 135.01, 146.78, 147.17, 148.41, 197.31; Anal. Calcd. for: $C_{19}H_{14}FNO$: C, 78.33; H, 4.84; N, 4.81; found C, 78.39; H, 4.76; N, 4.89.

9-Phenyl-3,4-dihydroacridin-1(*2H*)-one (5a)

Yellow solid; M.p. 152-154ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1693, 1558; ^{1}H NMR (400 MHz, $CDCl_3$) (**Figure S13**) (ppm) δ: 2.193-2.258 (m, 2H, C_3-CH_2), 2.662-2.695 (m, 2H, C_4-CH_2), 3.337-3.368 (m, 2H, C_2-CH_2), 7.139-7.163 (m, 2H, C_9-, C_{13}-H), 7.351-7.392 (m, 1H, C_{17}- H,), 7.424-7.488 (m, 4H, C_{10}-, C_{11}-, C_{12}-, C_{16}- H), 7.713-7.755 (m, 1H, C_{15}-H), 8.040 (d, 1H, C_{18}-H, J= 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (**Figure S14**) (ppm) δ: 21.40, 34.62, 40.66, 123.90, 126.45, 127.57, 128.05, 128.13, 128.26, 128.50, 131.76, 137.67, 148.69, 151.50, 162.27, 197.98; Anal. Calcd. for: $C_{19}H_{15}NO$: C, 83.49; H, 5.53; N, 5.12; found C, 83.41; H, 5.61; N, 5.04.

7-Chloro-9-phenyl-3,4-dihydroacridin-1(*2H*)-one (5b)

Yellow solid; M.p. 185-187ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1686, 1556; ^{1}H NMR (400 MHz, $CDCl_3$) (**Figure S15**) (ppm) δ: 2.189-2.254 (m, 2H, C_3-CH_2), 2.661-2.694 (m, 2H, C_4-CH_2), 3.313-3.344 (m, 2H, C_2-CH_2), 7.117-7.142 (m, 2H, C_9-, C_{13}-H), 7.387 (d, 1H, C_{15}-H, J_m = 2.40 Hz), 7.463-7.514 (m, 3H, C_{10}-, C_{11}-, C_{12}-H), 7.659 (dd, 1H, C_{17}-H, J_m= 2.40 Hz, J_o= 8.80 Hz), 7.970 (d, 1H, C_{18}-H, J= 8.80 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (**Figure S16**) (ppm) δ: 21.28, 34.55, 40.60, 124.48, 126.75, 127.92, 128.01, 128.31, 128.34, 130.22,

132.44, 132.59, 136.87, 147.09, 150.53, 162.55, 197.70; Anal. Calcd. for: $C_{19}H_{14}ClNO$: C, 74.15; H, 4.59; N, 4.55; found C, 74.08; H, 4.51; N, 4.62.

7-Chloro-9-(2'-chlorophenyl)-3,4-dihydroacridin-1(2*H*)-one (5c)

Pale yellow solid; M.p. 194-196ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1692; 1556; ^1H NMR ($CDCl_3$ 400 MHz) (**Figure S17**) (ppm) δ: 2.197-2.267 (m, 2H, C_3-CH_2), 2.620-2.773 (m, 2H, C_4-CH_2), 3.333-3.370 (m, 2H, C_2-CH_2), 7.078 (dd, 1H, J_m= 2.00 Hz, J_o= 7.20 Hz, C_{11}-H), 7.273 (d, 1H, J = 2.40 Hz, C_{15}-H), 7.371-7.452 (m, 2H, C_{10}, C_{13}-H), 7.525 (dd, 1H, J_m= 2.00 Hz, J_o= 7.20 Hz, C_{12}-H), 7.682 (dd, 1H, J_m= 2.40 Hz, J_o= 8.80 Hz, C_{17}-H), 8.002 (d, 1H, J = 8.80 Hz, C_{18}-H); ^{13}C NMR ($CDCl_3$, 100 MHz) (**Figure S18**) (ppm) δ: 21.26, 34.41, 40.13, 124.55, 125.92, 126.91, 127.47, 129.37, 129.46, 129.62, 130.40, 132.12, 132.86, 135.97, 147.09, 162.51, 197.36; Anal. Calcd. for: $C_{19}H_{13}Cl_2NO$: C, 66.68; H, 3.83; N, 4.09. Found: C, 66.63; H, 3.89; N, 4.15%.

7-Nitro-9-phenyl-3,4-dihydroacridin-1(2*H*)-one (5d)

Yellow solid; M.p. 188-190ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1694; 1552; ^1H NMR ($CDCl_3$ 400 MHz) (**Figure S19**) (ppm) δ: 2.227-2.292 (m, 2H, C_3-CH_2), 2.704-2.737 (m, 2H, C_4-CH_2), 3.374-3.406 (m, 2H, C_2-CH_2), 7.147- 7.174 (m, 2H, C_{10}, C_{12}-H), 7.509-7.535 (m, 3H, C_9, C_{11}, C_{13}-H), 8.151 (d, 1H, J = 9.20 Hz, C_{18}-H), 8.390 (d, 1H, J = 2.40 Hz, C_{15}-H), 8.475 (dd, 1H, J_m= 2.40 Hz, J_o= 9.20 Hz, C_{17}-H); ^{13}C NMR ($CDCl_3$, 100 MHz) (**Figure S20**) (ppm) δ: 21.03, 34.85, 40.47, 124.91, 125.05, 125.33, 126.81, 128.05, 128.57, 130.59, 135.81, 145.58, 150.48, 153.25, 166.14, 197.10; Anal. Calcd. for: $C_{19}H_{14}N_2O_3$: C, 71.69; H, 4.43; N, 8.80. Found: C, 71.66; H, 4.47; N, 8.84%.

9-(4'-Bromophenyl)-3,4-dihydroacridin-1(*2H*)-one (5e)

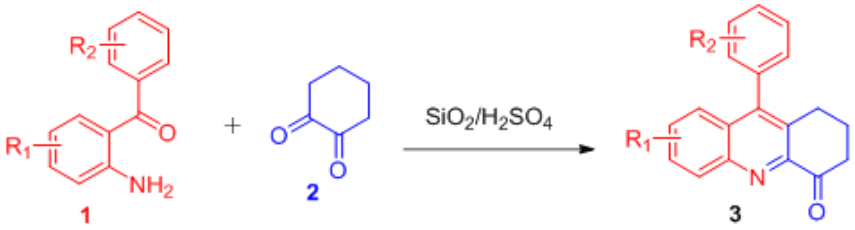
Yellow solid; M.p. 224-226ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1682, 1560; ^1H NMR (400 MHz, $CDCl_3$) (**Figure S21**) (ppm) δ: 2.386-2.451 (m, 2H, C_3-CH_2), 2.861-2.894 (m, 2H, C_4-CH_2), 3.565-3.597 (m, 2H, C_2-CH_2), 7.220 (d, 2H, C_{10}-, C_{12}-H, J= 8.40 Hz), 7.600 (d, 2H, C_{16}-, C_{17}-H, J= 4.00 Hz), 7.793 (d, 2H, C_9-, C_{13}-H, J= 8.40 Hz), 7.934-7.976 (m, 1H, C_{15}-H), 8.315 (d, 1H, C_{18}-H, J= 8.80 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (**Figure S22**) (ppm) δ: 21.03, 33.69, 40.49, 121.89, 123.88, 126.92, 127.29, 127.83, 129.72, 131.40, 132.29, 136.38, 148.01, 150.78, 162.33, 197.84; Anal. Calcd. for: $C_{19}H_{14}BrNO$: C, 64.79; H, 4.01; N, 3.98; found C, 64.71; H, 4.09; N, 3.88.

9-(4'-Fluorophenyl)-3,4-dihydroacridin-1(*2H*)-one (5f)

Yellow solid; M.p. 166-168ºC, FT-IR (KBr, cm^{-1}) ν_{max}: 1680, 1563; ^1H NMR (400 MHz, $CDCl_3$) (**Figure S23**) (ppm) δ: 2.253-2.318 (m, 2H, C_3-CH_2), 2.727-2.760 (m, 2H, C_4-CH_2), 3.430-3.462 (m, 2H, C_2-CH_2), 7.164-7.252 (m, 4H, C_9-, C_{10}-, C_{12}-, C_{13}-H), 7.446-7.516 (m, 2H, C_{16}-, C_{17}-H), 7.792-7.837 (m, 1H, C_{15}-H), 8.180 (d, 1H, C_{18}-H, *J*= 8.40 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (**Figure S24**) (ppm) δ: 21.09, 33.85, 40.56, 115.28, 124.14, 126.79, 127.94, 127.97, 129.78, 129.86, 132.12, 148.11, 150.93, 161.16, 162.33, 163.61, 197.88; Anal. Calcd. for: $C_{19}H_{14}FNO$: C, 78.33; H, 4.84; N, 4.81; found C, 78.41; H, 4.78; N, 4.89.

Results and discussion

Synthesis



Scheme. 1 Synthesis of 2,3-dihydroacridin-4-ones (**3**)

The 2-aminobenzophenone (**1a**) was treated with 1,2-diketone, 1,2-cyclohexanedione (**2**) in the presence of SiO_2/H_2SO_4 in methanol medium to yield 92% of 9-phenyl-2,3-dihydroacridin-4(1*H*)-one (**3a**) (**Scheme 1**). To develop the methodology of this reaction, 2-aminobenzophenone (**1a**) was treated with 1,2-cyclohexanedione (**2**) in the presence of SiO_2/H_2SO_4, yielded yellow coloured (**3a**) solid (**Scheme 1**). The reaction environment was optimized through various reaction condition, catalysts and solvents (**Table 1**) to get better yield. So the finest reaction condition preferred for Friedlander synthesis is 0.1 mmol SiO_2/H_2SO_4. The synthesis of 9-phenyl-2,3-dihydroacridin-4(1*H*)-one (**3a**) is our first assignment technique for the synthesis of 2,3-dihydroacridin-4-one derivatives. So, we tried to get better yield in this reaction, in viewing a set of solvents, we observed using SiO_2/H_2SO_4 to obtain moderate to high yield. To the best approach of our awareness, SiO_2/H_2SO_4 catalytic method have been no reports on the preparation of 2,3-dihydroacridin-4-one derivatives *via* Friedländer synthesis. After optimizing the reaction condition, 2-aminobenzophenone (**1a**) was reacted with 1,2-cyclohexanedione (**2**) in the presence of SiO_2/H_2SO_4 (0.10mmol) condition, the completeness of the reaction was checked by thin-

layer chromatography. After 2 h, the obtained crude product (**3a**) was recrystallised using ethylacetate to get yellow color product (**3a**). Compound **3a** was furthermore confirmed by elemental analysis, FT-IR, NMR spectra, and single-crystal X-ray diffraction studies (**Figure 1**).

Table 1 Optimization of reaction condition to synthesize compound **3a**

Entry	Catalyst	Solvent	Temperature	Time[a]	Yield[b]
1.	-	CH_3OH	Reflux	5	42%
2.	SiO_2	CH_3OH	Reflux	5	52%
3.	H_2SO_4	CH_3OH	Reflux	8	65%
4.	SiO_2/H_2SO_4	CH_3OH	RT	12	60%
5.	**SiO_2/H_2SO_4**	**CH_3OH**	**Reflux**	**2**	**92%**
6.	SiO_2/H_2SO_4	CH_3CN	Reflux	6	70%
7.	SiO_2/H_2SO_4	H_2O	Reflux	2	66%
8.	SiO_2/H_2SO_4	CH_3COOH	Reflux	6	80%
9.	SiO_2/H_2SO_4	C_2H_5OH	Reflux	4	85%

[a] Time duration of reaction in hours.
[b] Isolated pure products.

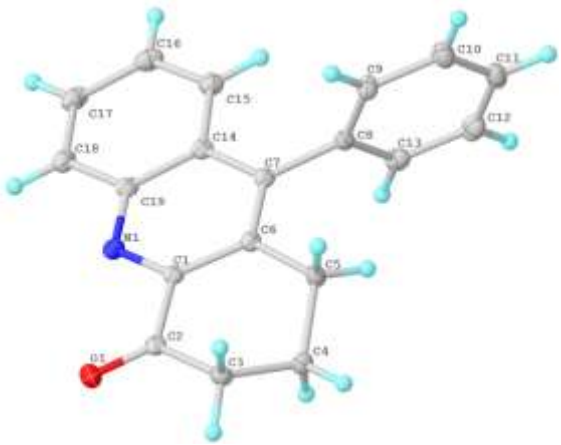
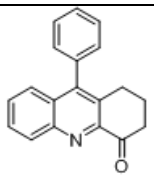
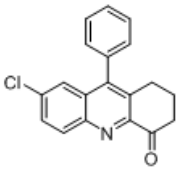
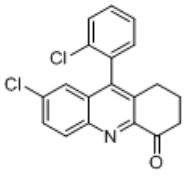
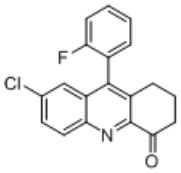
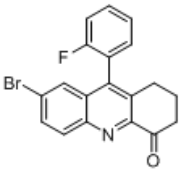
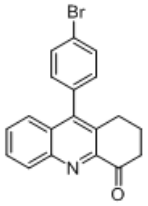


Fig.1 ORTEP crystal structure of compound **3a**

In signifying the efficacy of SiO_2/H_2SO_4 for the synthesis of polycyclic quinolines, 1,2-cyclohexanedione easily condensed with *o*-aminoarylketones to yield the relevant polycyclic quinolines (**Scheme 1**). In most cases, the products were isolated by simple filtration and the crude products were purified by recrystallization from ethylacetate. All the compounds (**Table 2**) were isolated by recrystallization only and no chromatographic workup was required to obtain pure products. The crystal data collection details of compound **3a** has been summarised in **Table 3**.

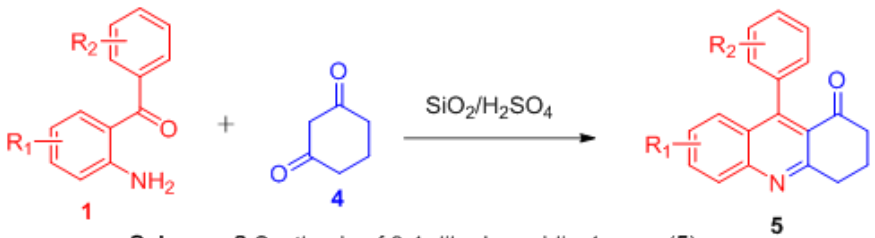
Table 2 Synthesis of 2,3-dihydroacridin-4(1*H*)-one derivatives (**3a-f**)

Entry	R_1	R_2	Product	Yield[a]	M.p °C
3a	H	H		92%	213-215
3b[5]	Cl	H		93%	250-252
3c[5]	Cl	Cl		93%	185-187
3d[5]	Cl	F		90%	199-201
3e	Br	F		91%	201-203
3f	H	Br		93%	244-246

Reaction conditions: 2-aminobenzophenone **1a** (1 mmol) and 1,2-cyclohexanedione **2** (1.2 mmol, 1.2 equiv.) in the presence of SiO_2/H_2SO_4 as a catalyst.
[a]Recrystallised pure products.

Table 3 Crystal data and structure refinement for 3a.	
CCDC number	1962353
Empirical formula	$C_{19}H_{15}NO$
Formula weight	273.32
Temperature/K	100.04
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	11.0175(3)

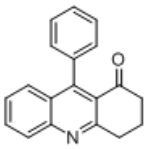
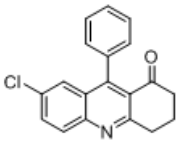
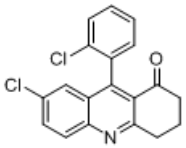
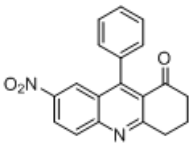
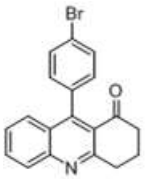
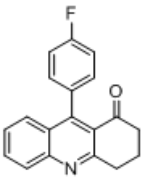
b/Å	9.2363(3)
c/Å	13.5893(5)
α/°	90
β/°	95.9170(10)
γ/°	90
Volume/Å^3	1375.49(8)
Z	4
ρ_{calc}g/cm^3	1.320
μ/mm^{-1}	0.081
F(000)	576.0
Crystal size/mm^3	0.185 × 0.178 × 0.168
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.684 to 56.646
Index ranges	-14 ≤ h ≤ 14, -12 ≤ k ≤ 12, -18 ≤ l ≤ 18
Reflections collected	34520
Independent reflections	3421 [R_{int} = 0.0428, R_{sigma} = 0.0206]
Data/restraints/parameters	3421/0/190
Goodness-of-fit on F^2	1.024
Final R indexes [I>=2σ (I)]	R_1 = 0.0398, wR_2 = 0.1026
Final R indexes [all data]	R_1 = 0.0510, wR_2 = 0.1109
Largest diff. peak/hole / e Å^{-3}	0.40/-0.22



Scheme. 2 Synthesis of 3,4-dihydroacridin-1-ones (**5**)

To authenticate the Friedländer synthesis, 1,3-diketone, 1,3-cyclohexanedione was used instead of 1,2-diketone, 1,2-cyclohexanedione with *o*-aminoarylketones to yield 3,4-dihydroacridin-1-ones. To improved the better performance of catalytic system, the efficiency of the Friedländer synthesis of 1,3-diketone, 1,3-cyclohexanedione (**4**) has been extended to different *o*-aminoarylketones (**1**) in the presence of SiO_2/H_2SO_4 (0.10 mmol) to afford (**5**) in 90-95% yield (**Scheme 2**). The uniqueness of all of the compounds (**Table 4**) was confirmed by FT-IR and NMR spectroscopic methods.

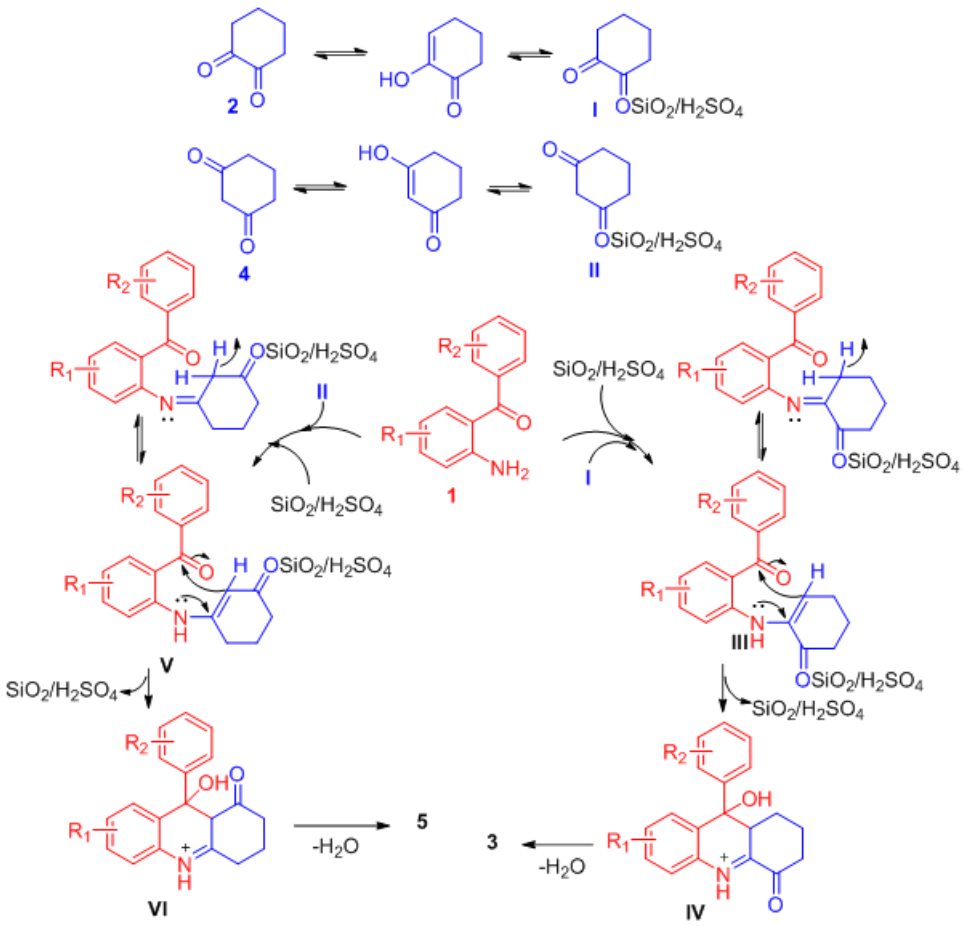
Table 4 Synthesis of 3,4-dihydroacridin-1(2*H*)-one derivatives (**5a-f**)

Entry	R_1	R_2	Product	Yield[a]	M.p °C
5a	H	H		95%	152-154
5b[5]	Cl	H		92%	185-187
5c[5]	Cl	Cl		93%	194-196
5d[5]	NO_2	H		90%	188-190
5e	H	Br		92%	224-226
5f[5]	H	F		93%	166-168

Reaction conditions: 2-aminobenzophenone **1a** (1 mmol) and 1,3-cyclohexanedione **4** (1.2 mmol, 1.2 equiv.) in the presence of SiO_2/H_2SO_4 as a catalyst.
[a]Recrystallised pure products.

The plausible mechanism for the formation of products **3** & **5** as described below (**Scheme 3**). 1,2-cyclohexanedione / 1,3-cyclohexanedione underwent tautomerization cum complex formation with SiO_2/H_2SO_4 to give intermediates **I** & **II**. The condensation of o-aminoaryl ketone (**1**) with intermediates **I** & **II** in the presence of SiO_2/H_2SO_4 to give the stable enamine intermediates (**III** / **V**), which is formed through imine intermediates while on tautomerisation. Then the enamine intermediates (**III** / **V**), cyclized through nucleophilic attack of carbonyl carbon results the intermediates (**IV** / **V**) *via* SiO_2/H_2SO_4, which is

subsequently loses of water molecules followed by aromatisation to give the products (**3** & **5**).



Scheme. 3 The plausible mechanism for the formation of products **3 & 5**

Conclusion

The novel synthetic route for the polycyclic quinolines (**3** & **5**) from cyclic-diketones, cyclohexan-1,2-dione (**2**) / cyclohexan-1,3-dione (**4**) with o-aminoarylketones (**1**) in the presence of SiO_2/H_2SO_4 yielded *via* Friedländer synthetic method. The efficiency catalyst SiO_2/H_2SO_4 was discussed during their utilization in the synthesis of biologically active substituted polycyclic quinoline derivatives (**3** & **5**) and the plausible mechanism has been proposed. The SiO_2/H_2SO_4 was found as an effective catalyst for the Friedländer reaction and gave considerable isolated yield of the polycyclic quinolines, which is doesn't required high temperature and harsh conditions. The salient features of this reaction are the mild reaction conditions, the executive easiness, good to high yields, and the use of a low-cost and easily accessible reagent.

Supplementary data

CIF files for compounds **3a** have been deposited with the Cambridge Crystallographic Data Centre as CCDC number 1962353. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK. [Fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk.

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Supporting Information

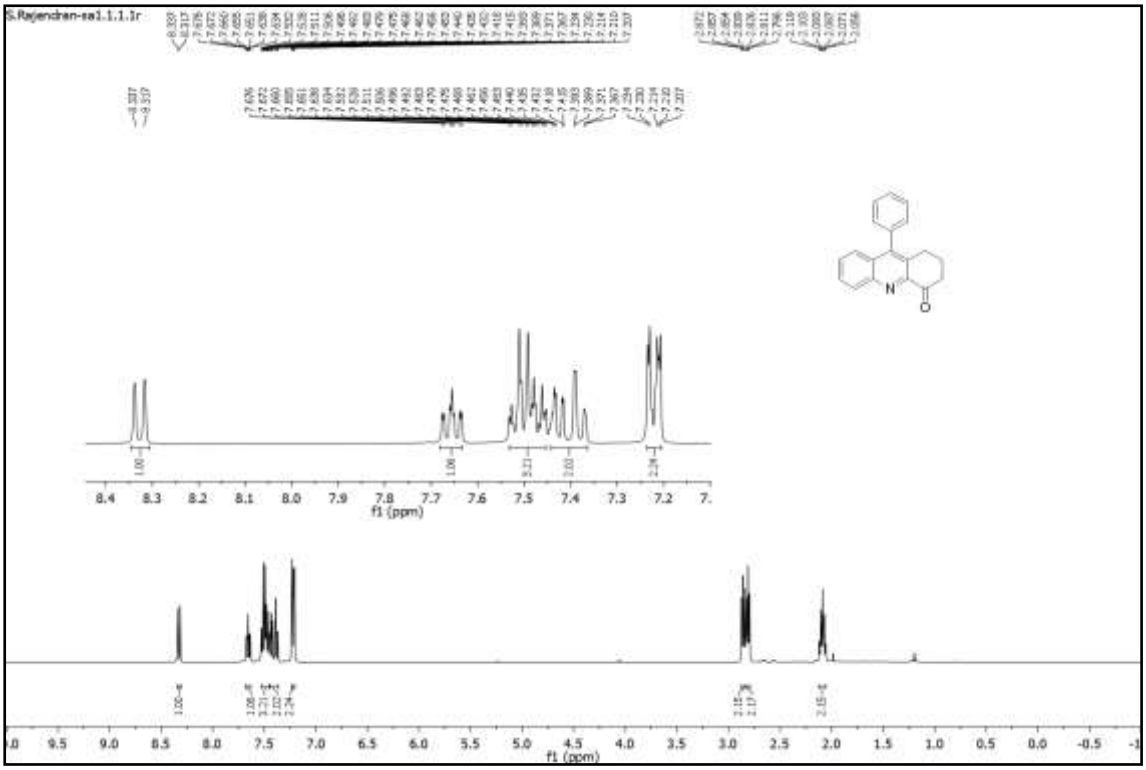

Fig. S1 ^{1}H NMR spectrum of the compound (**3a**)

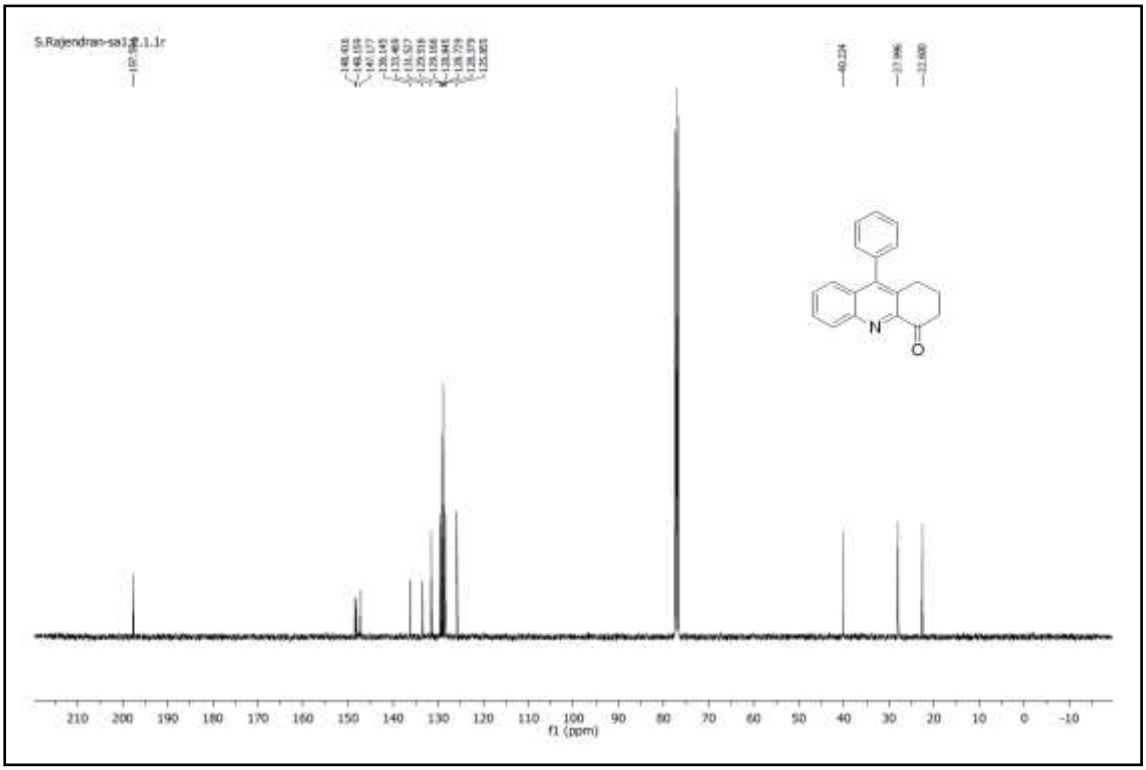

Fig. S2 ^{13}C NMR spectrum of the compound (**3a**)

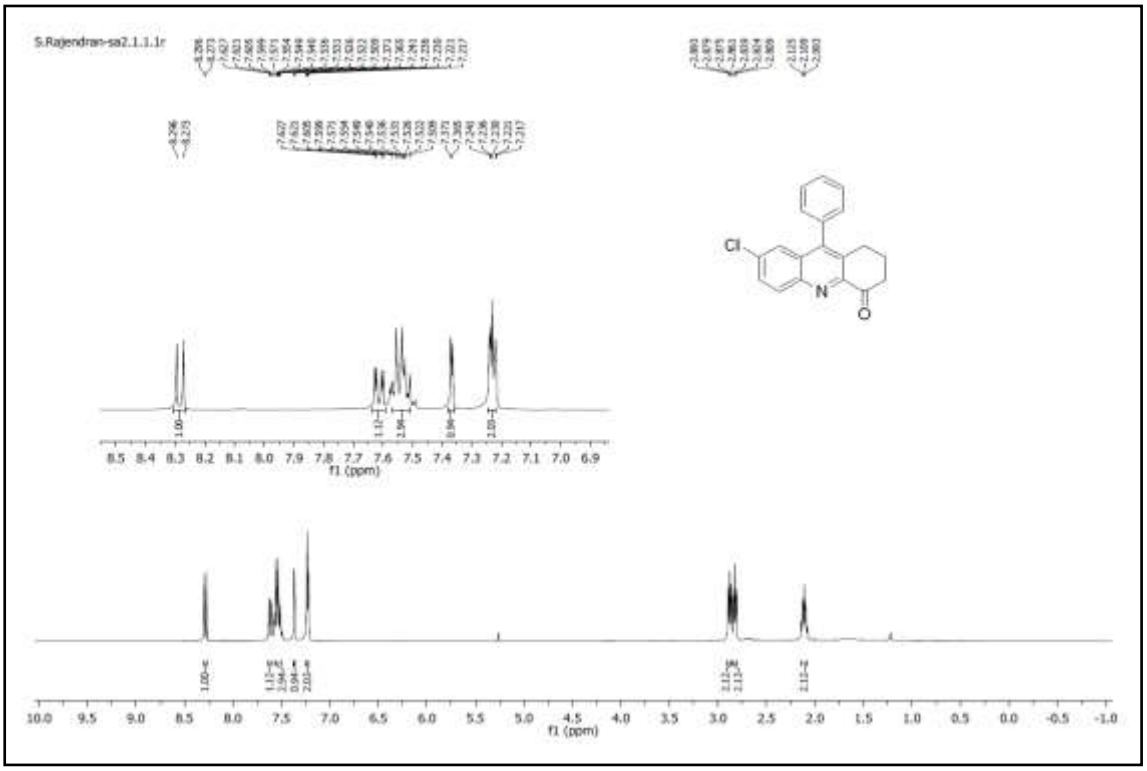

Fig. S3 ^{1}H NMR spectrum of the compound (**3b**)

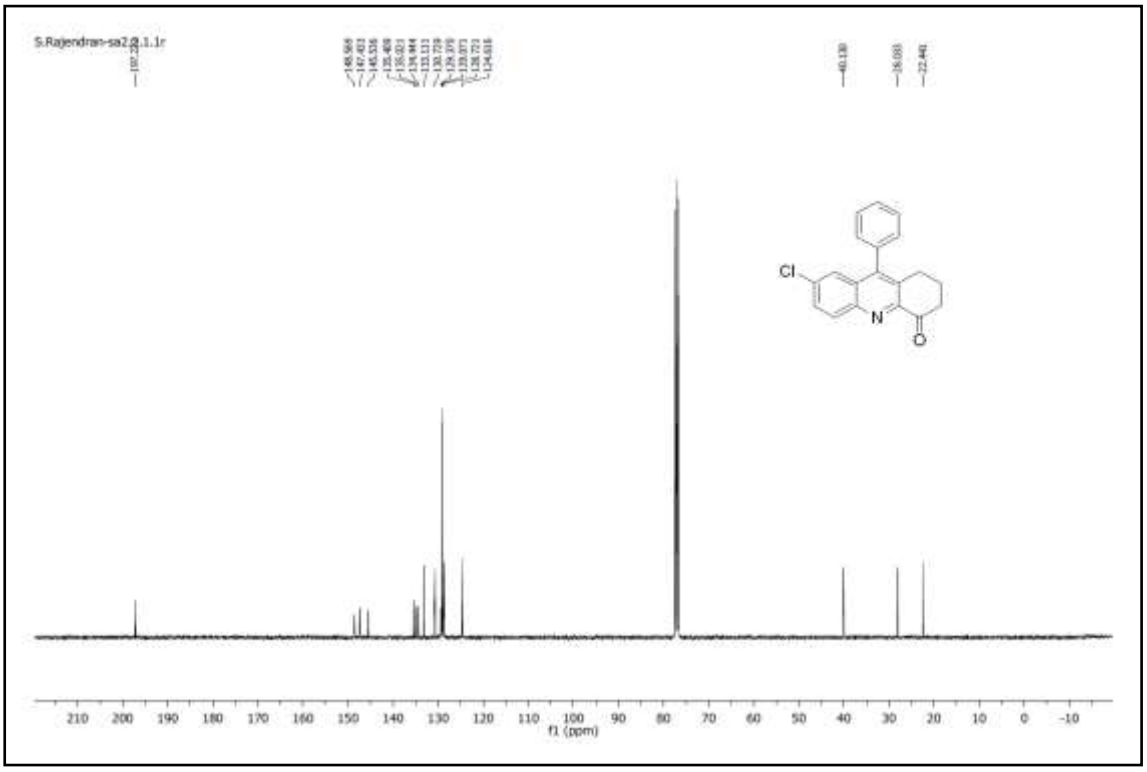

Fig. S4 ^{13}C NMR spectrum of the compound (**3b**)

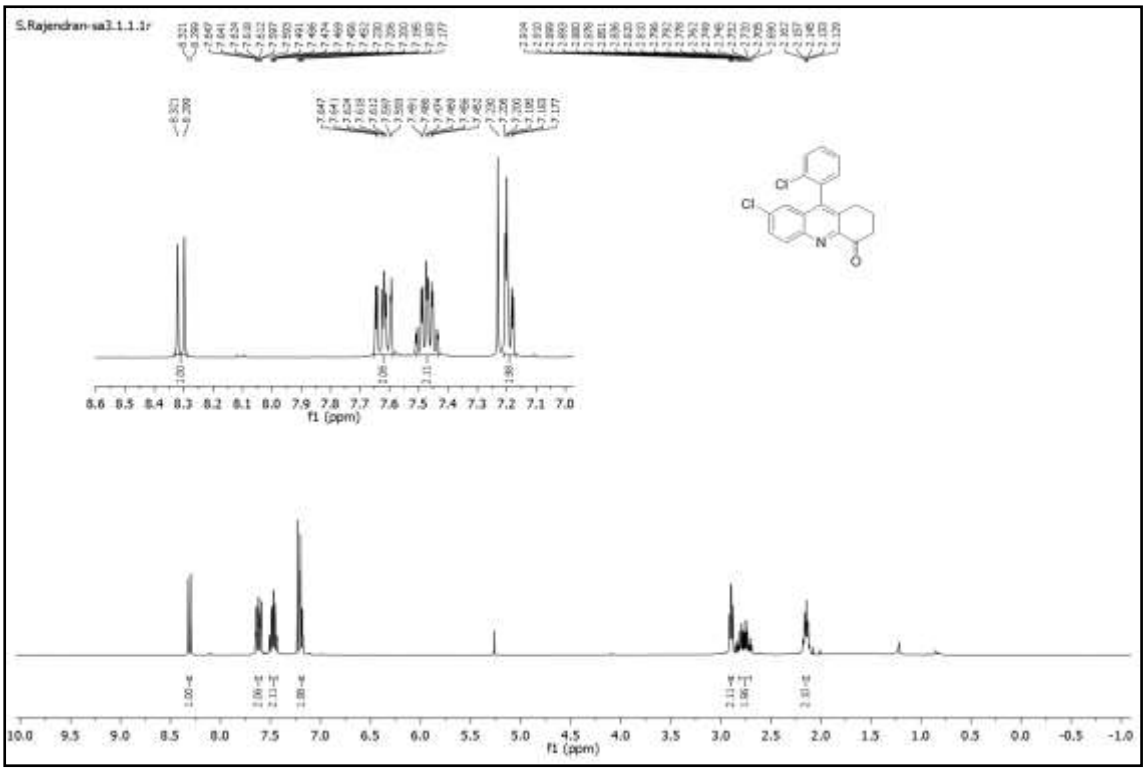

Fig. S5 ^{1}H NMR spectrum of the compound (**3c**)

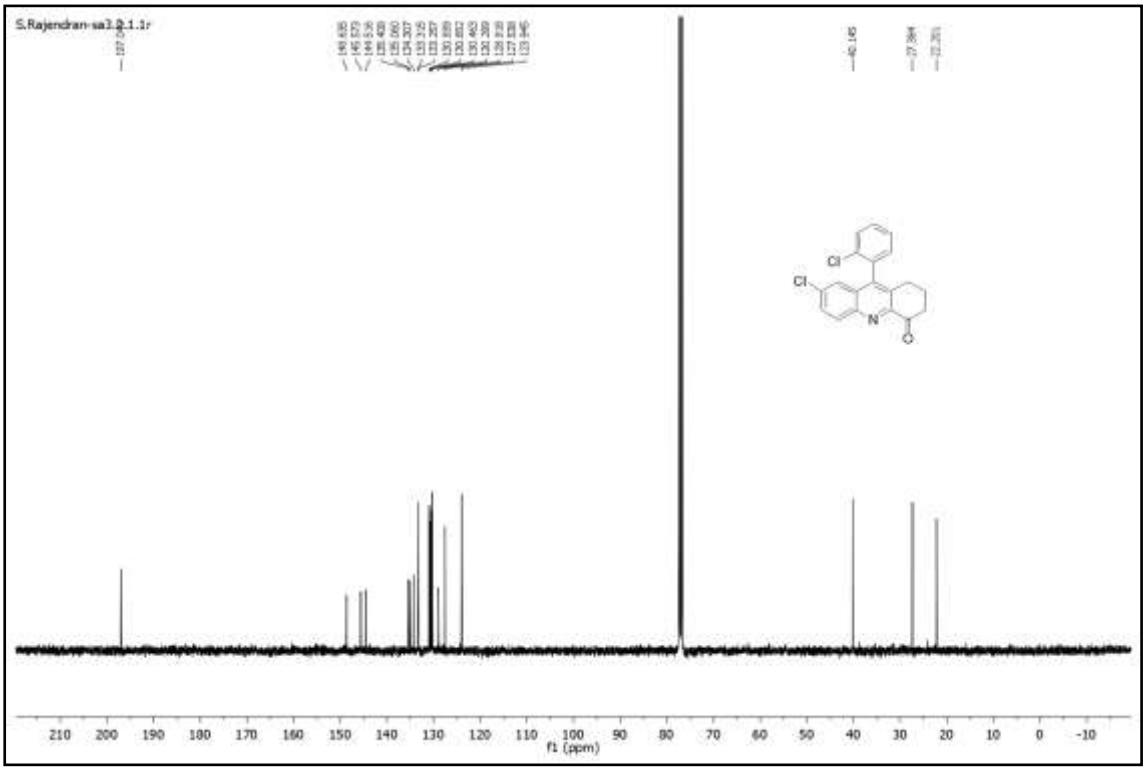

Fig. S6 ^{13}C NMR spectrum of the compound (**3c**)

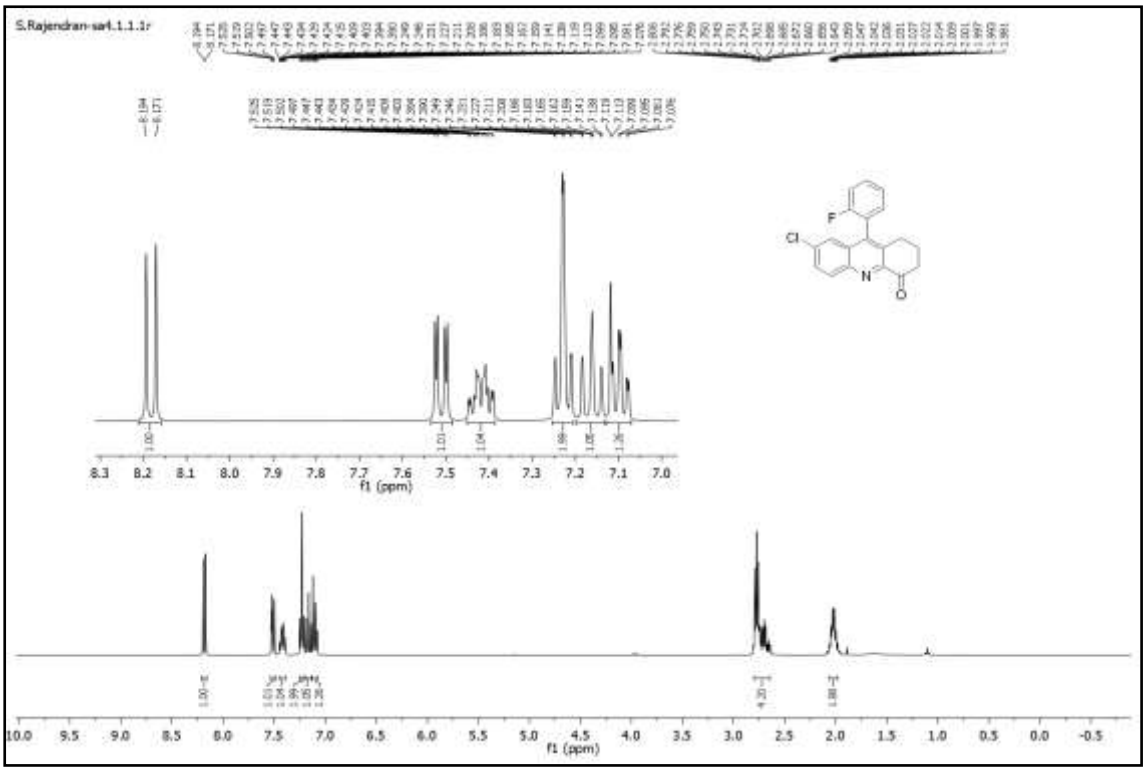

Fig. S7 ^{1}H NMR spectrum of the compound (**3d**)

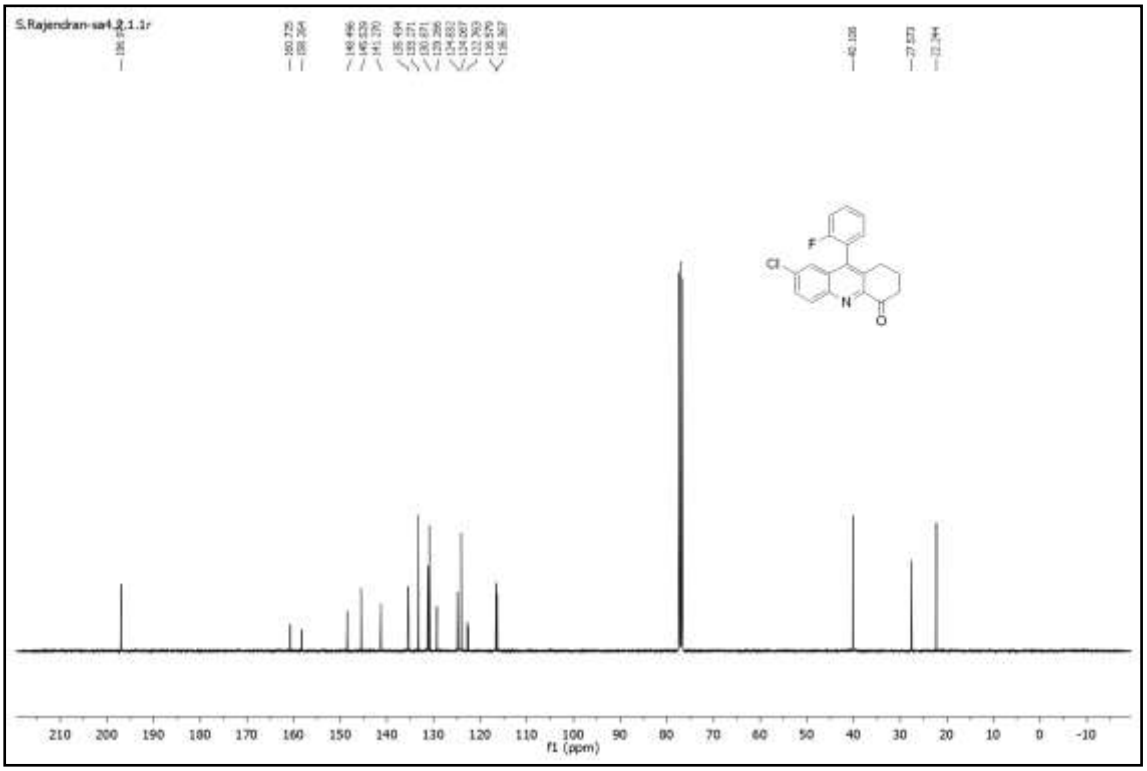

Fig. S8 ^{13}C NMR spectrum of the compound (**3d**)

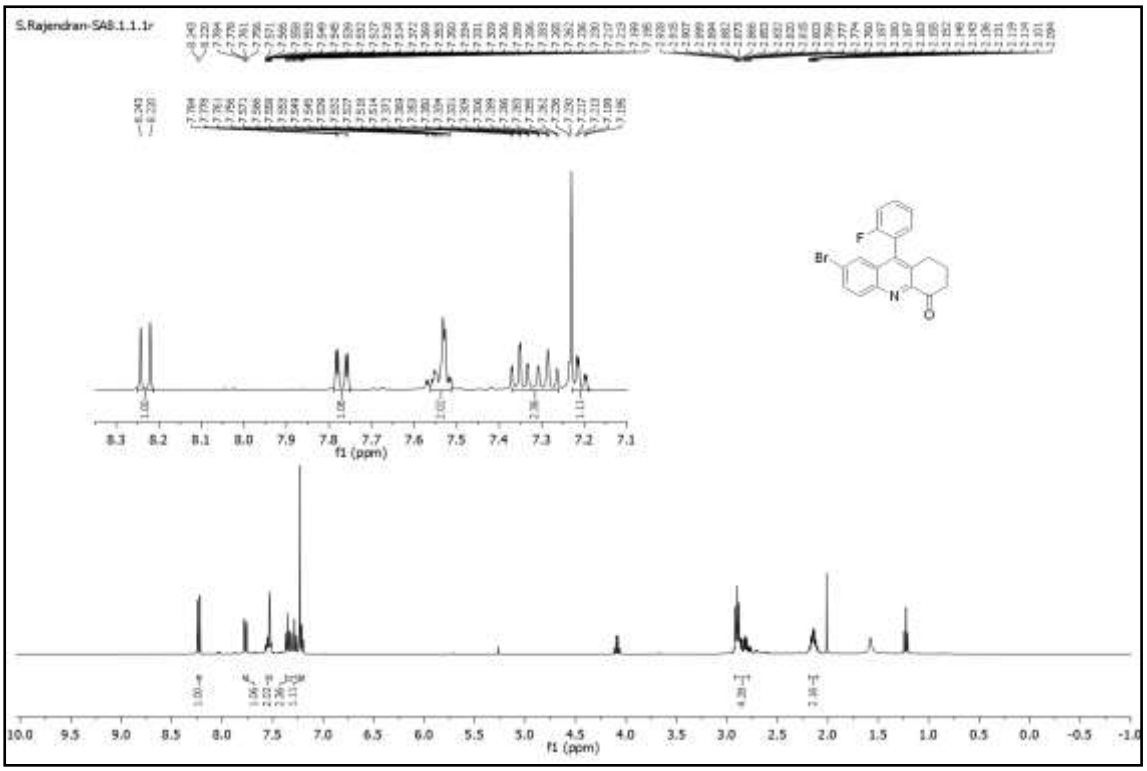

Fig. S9 ^{1}H NMR spectrum of the compound (**3e**)

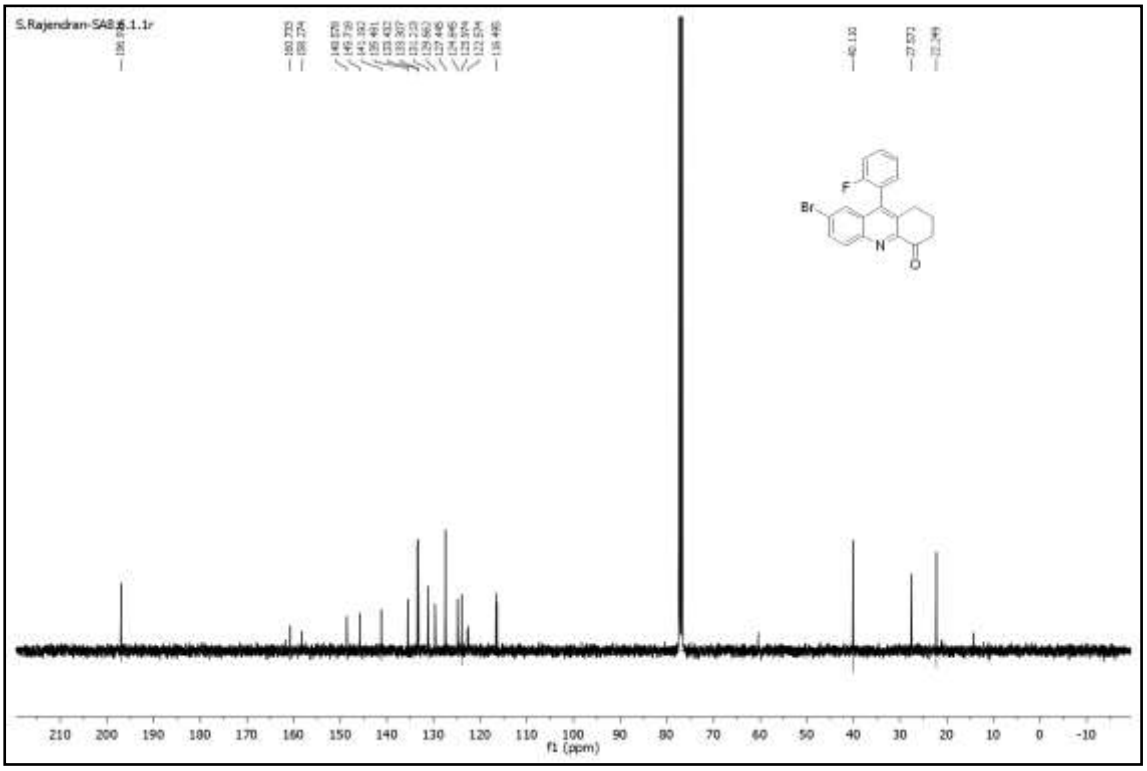

Fig. S10 ^{13}C NMR spectrum of the compound (**3e**)

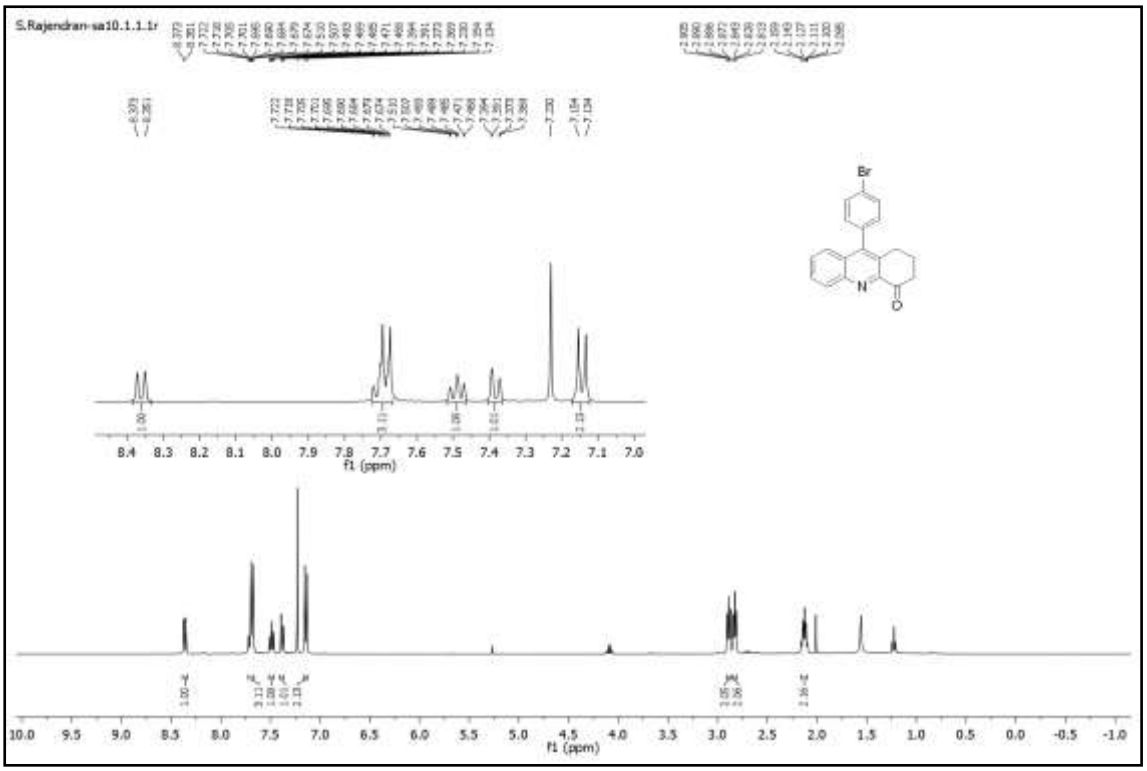

Fig. S11 ^{1}H NMR spectrum of the compound (**3f**)

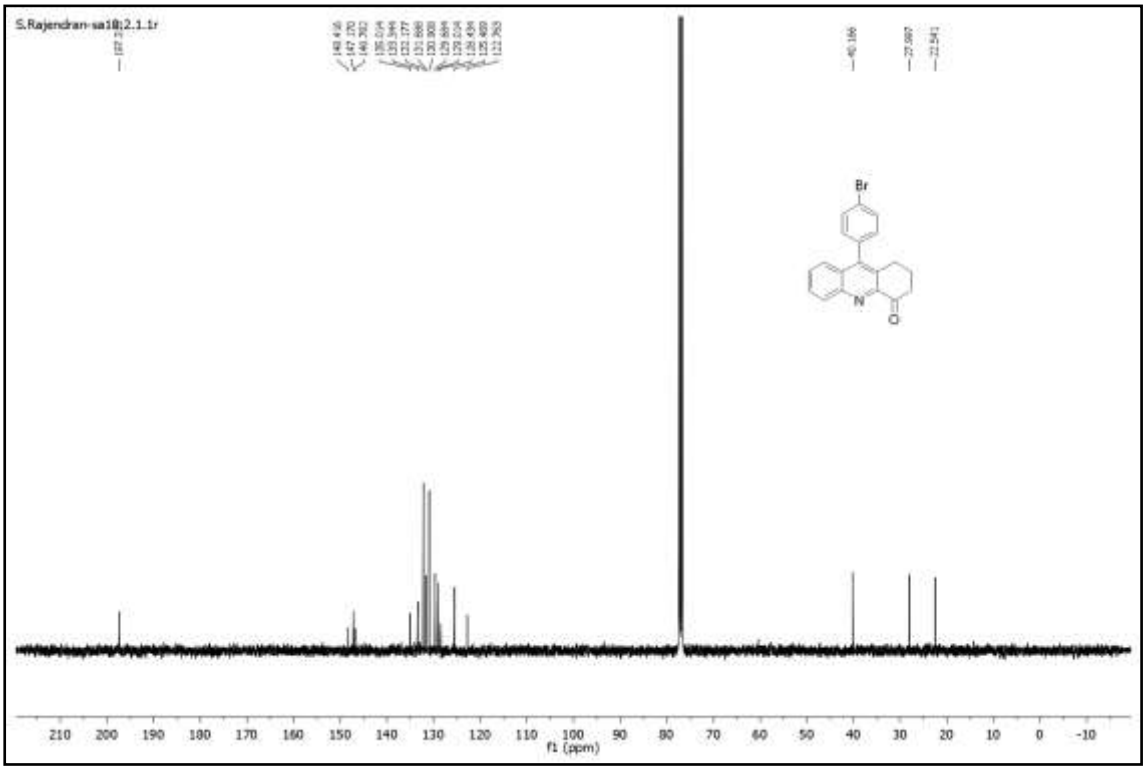

Fig. S12 ^{13}C NMR spectrum of the compound (**3f**)

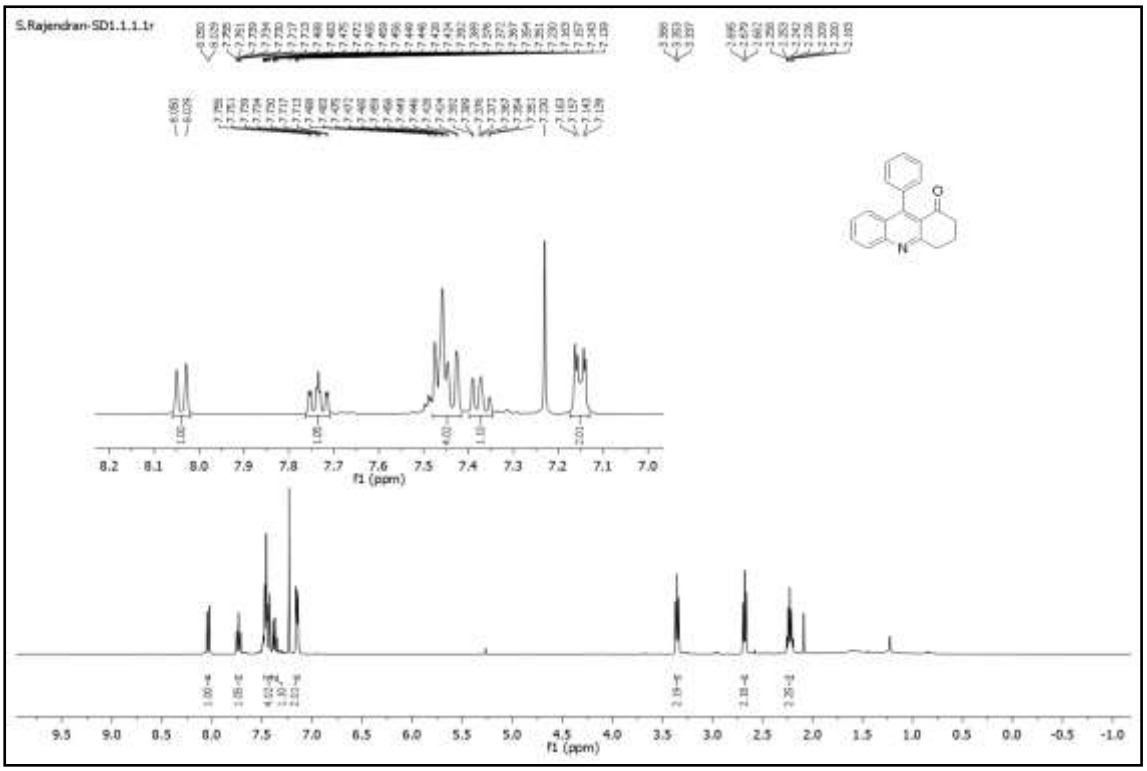

Fig. S13 ^{1}H NMR spectrum of the compound (**5a**)

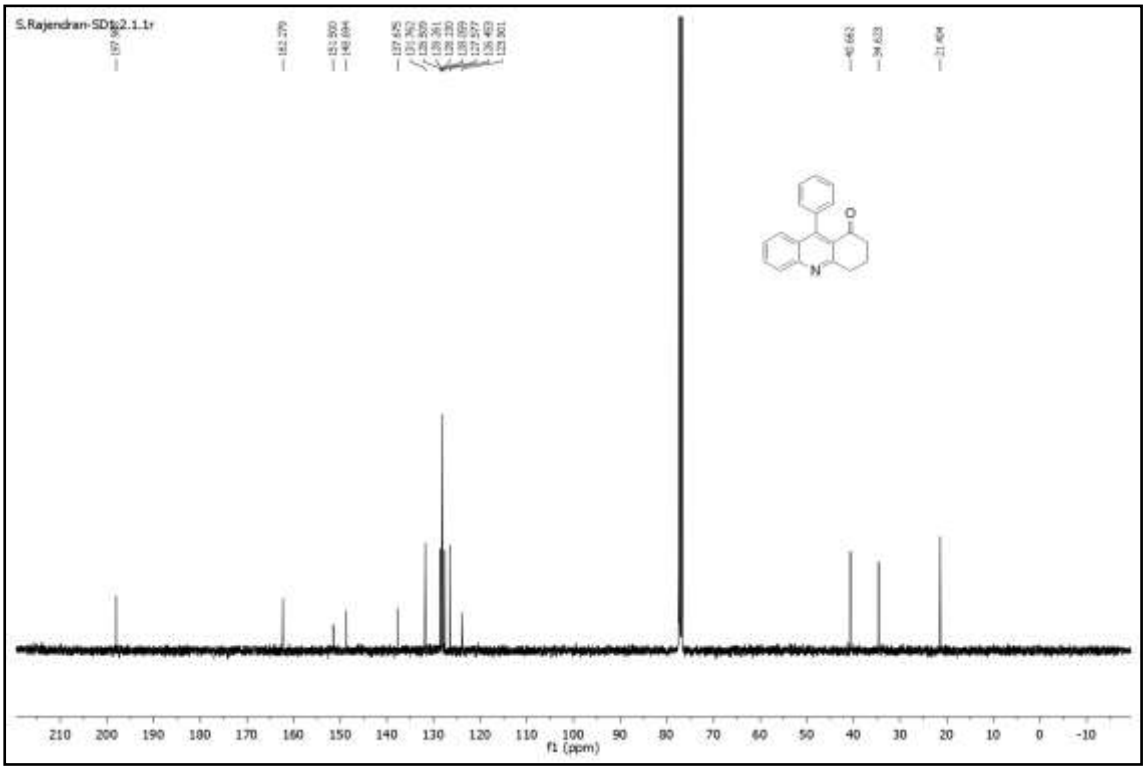

Fig. S14 ^{13}C NMR spectrum of the compound (**5a**)

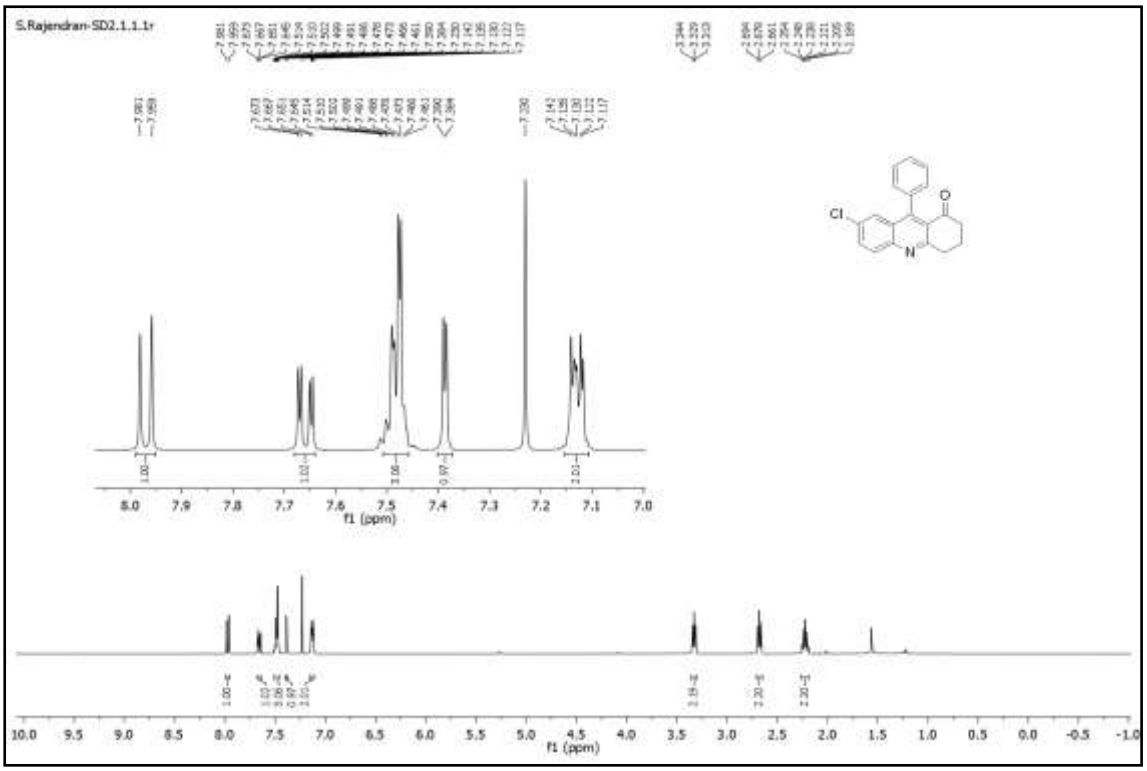

Fig. S15 ^{1}H NMR spectrum of the compound (**5b**)

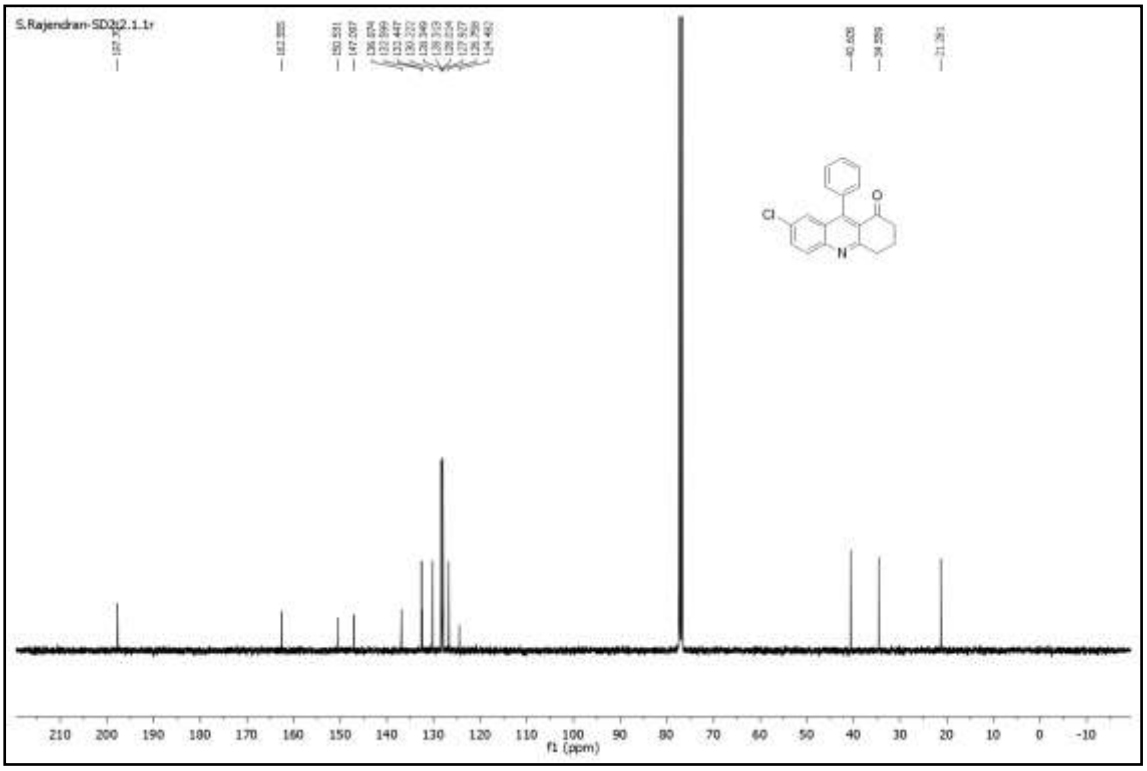

Fig. S16 ^{13}C NMR spectrum of the compound (**5b**)

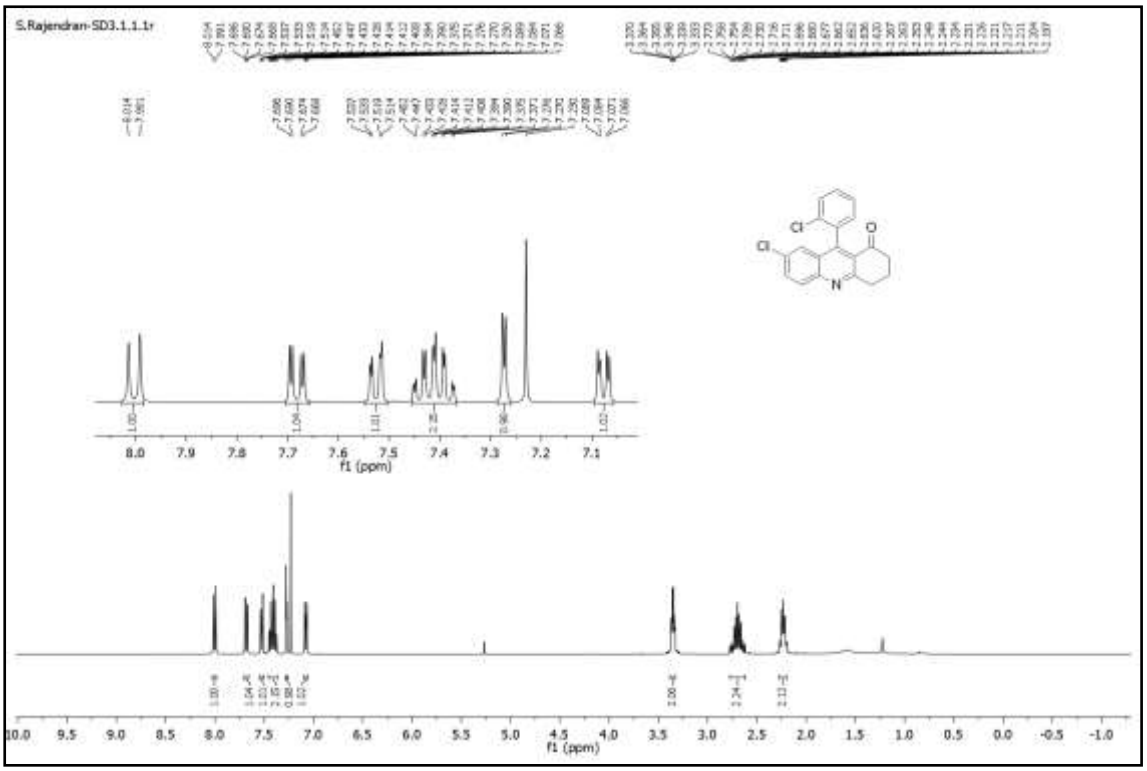

Fig. S17 ^{1}H NMR spectrum of the compound (**5c**)

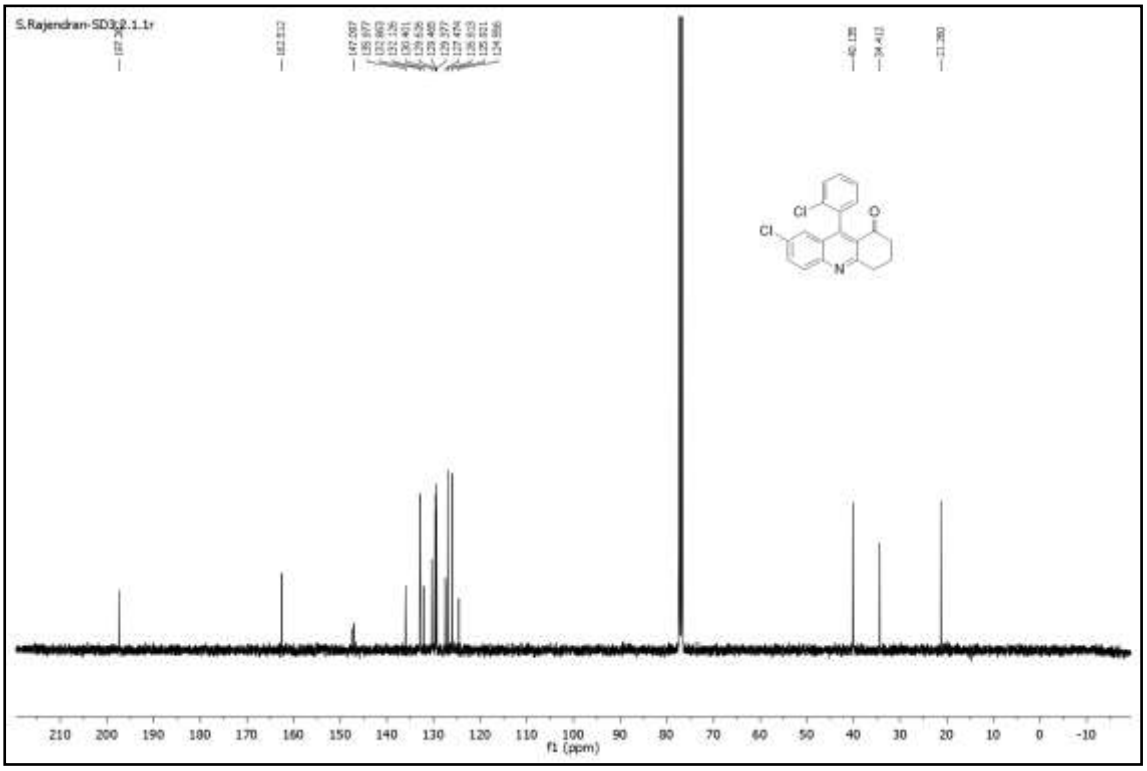

Fig. S18 ^{13}C NMR spectrum of the compound (**5c**)

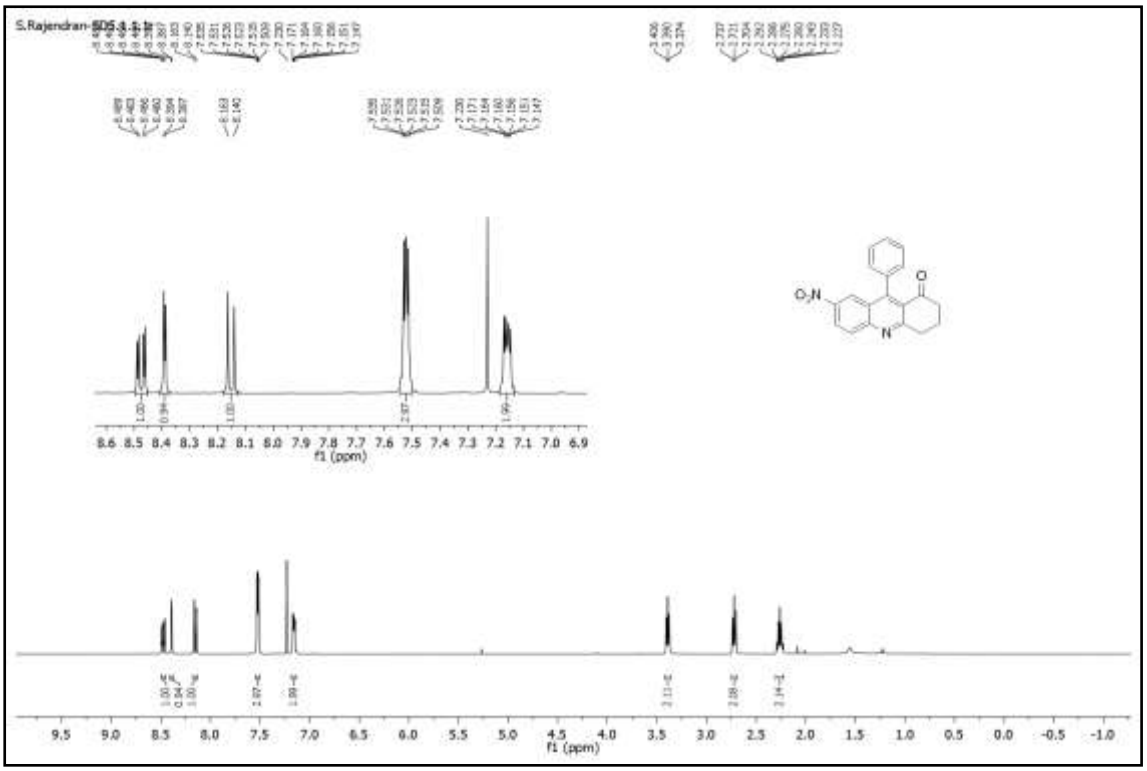

Fig. S19 ^{1}H NMR spectrum of the compound (**5d**)

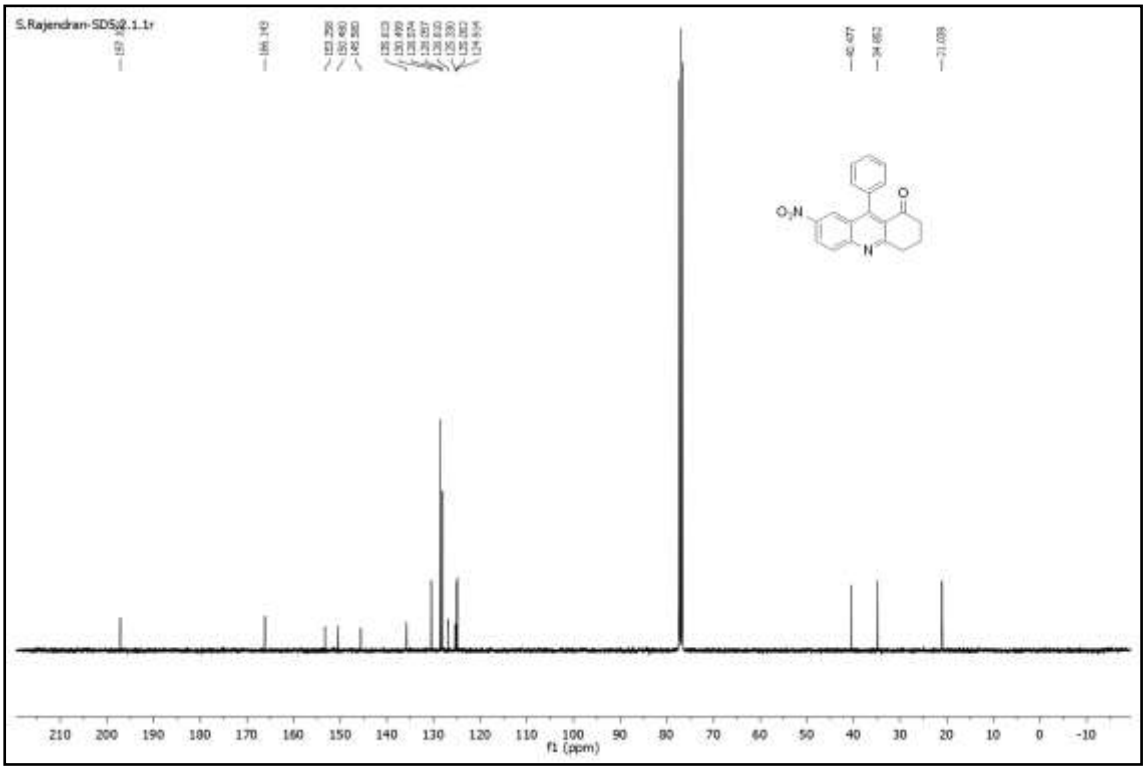

Fig. S20 ^{13}C NMR spectrum of the compound (**5d**)

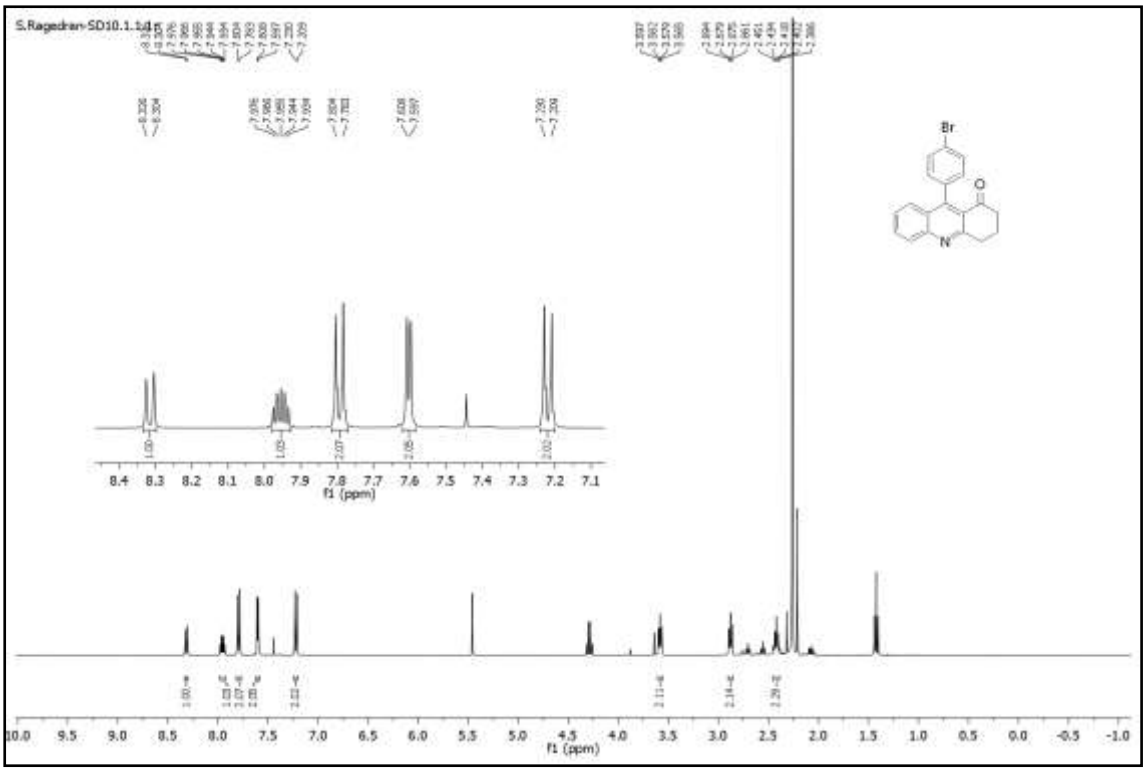

Fig. S21 ^{1}H NMR spectrum of the compound (**5e**)

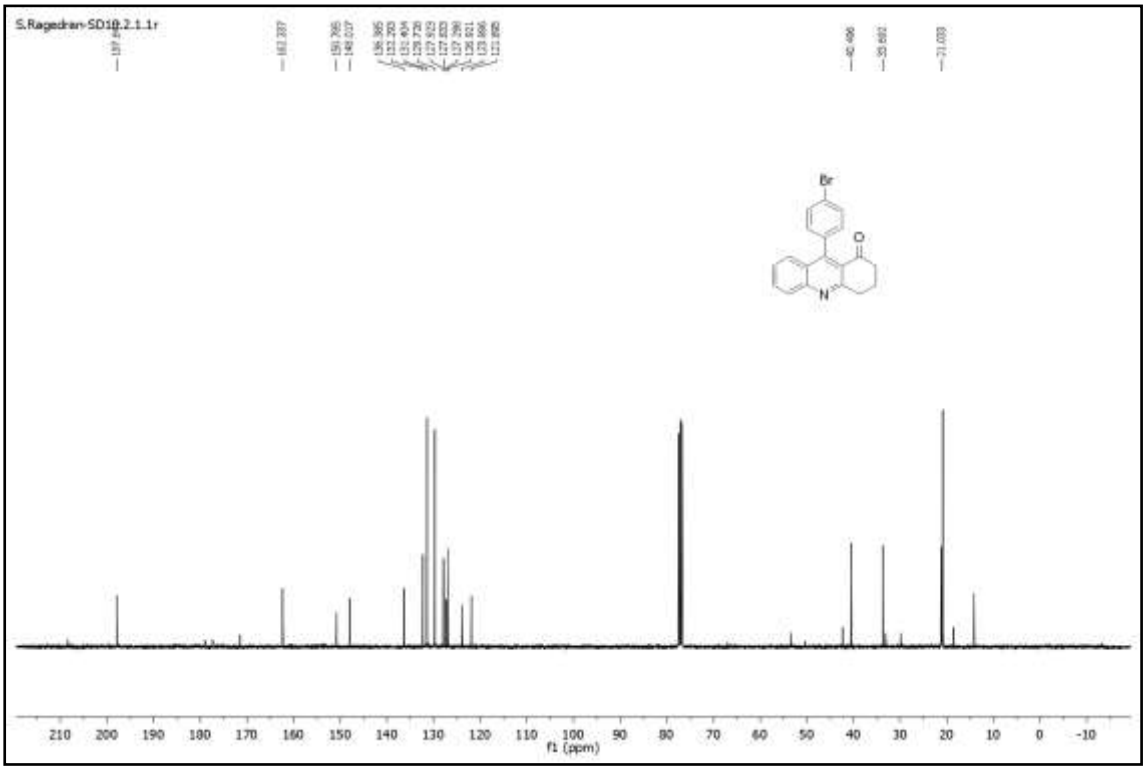

Fig. S22 ^{13}C NMR spectrum of the compound (**5e**)

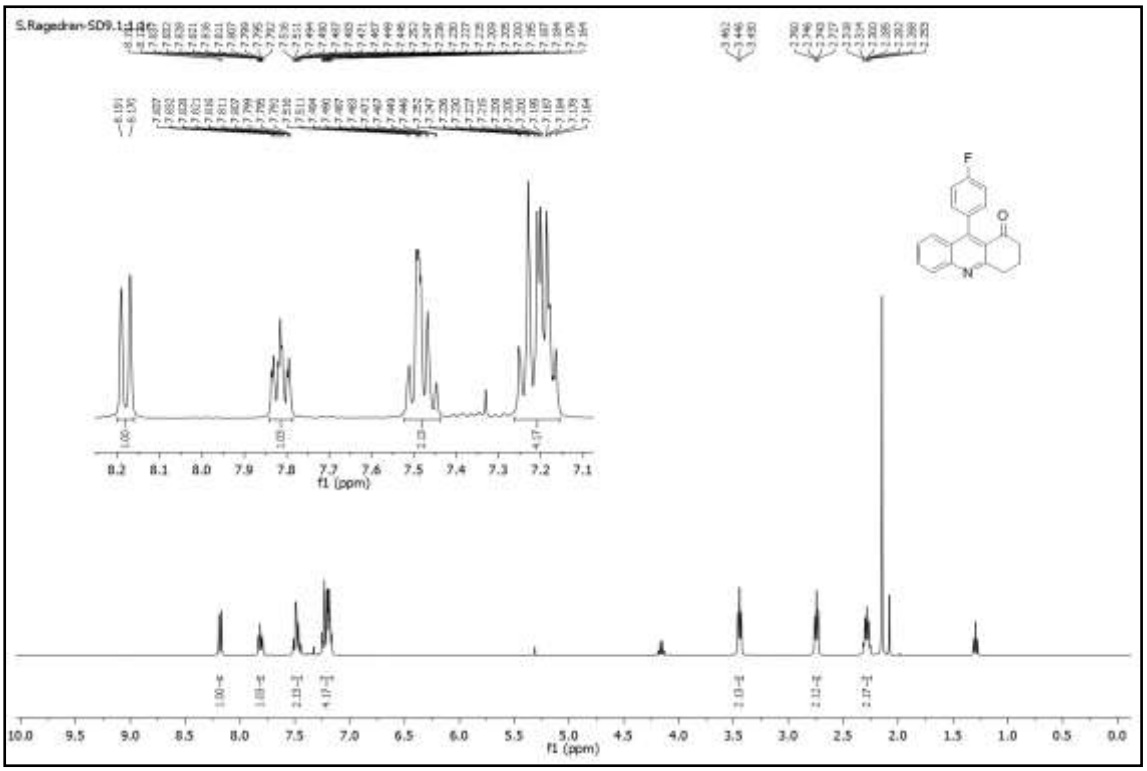

Fig. S23 ^{1}H NMR spectrum of the compound (**5f**)

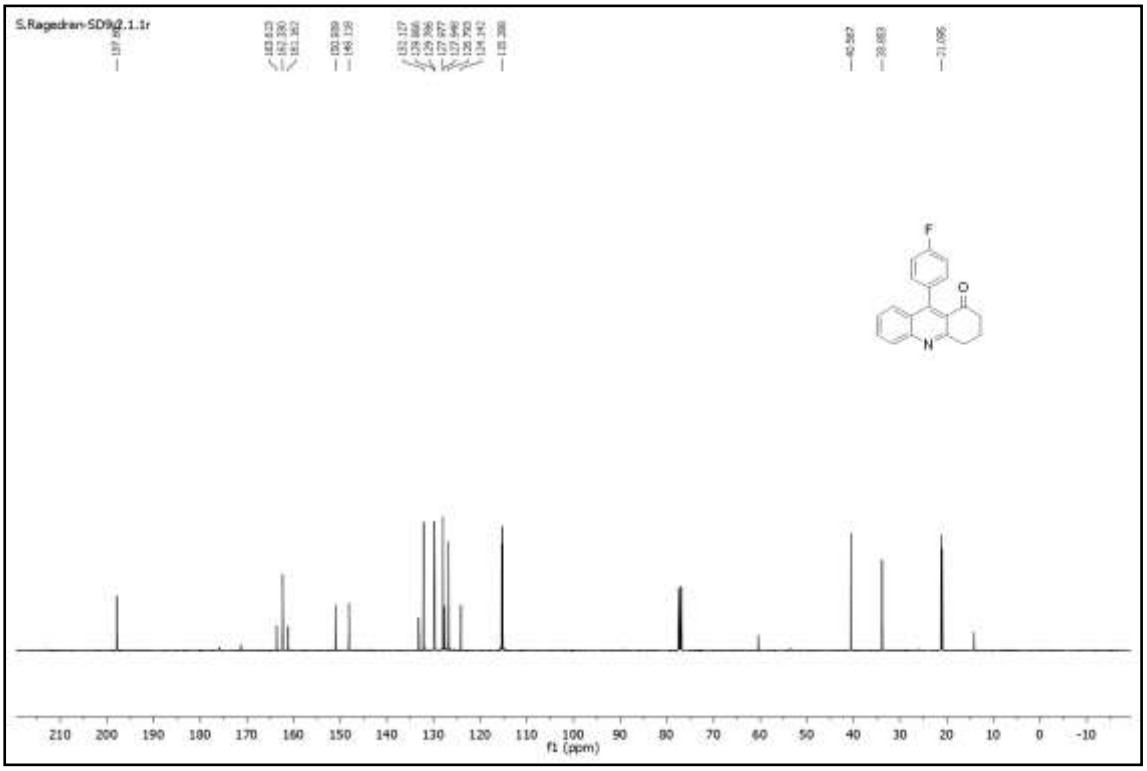

Fig. S24 ^{13}C NMR spectrum of the compound (**5f**)