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NMR spectral and structural studies on some xanthenones and their thiosemicarbazone derivatives: Crystal and molecular structure of 12-(2-chlorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one

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ABSTRACT

A series of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones [**1a–9a**] were prepared employing a three component one-pot reaction of aryl aldehyde, 2-naphthol and 1,3-cyclohexanedione using $BF_3{\cdot}OEt_2$ as catalyst. Thiosemicarbazone derivatives [**1b–5b**] were also prepared in the presence of acid catalyst. All the synthesized compounds have been characterized by IR and NMR. The structure of **5b** was confirmed by HSQC spectral analysis. Single crystal X-ray structural analysis of 12-(2-chlorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one evidences the envelope and flattened-boat conformations of cyclohexenone and pyran rings respectively.

1. Introduction

Multi Component Reactions (MCRs) have been emerged as an extremely powerful tool in combinatorial chemistry and drug discovery, since it offers significant advantages over conventional linear step syntheses [1]. The challenge is to conduct an MCR in such a way that the network of pre-equilibrated reactions channel into the main product and do not yield side products. The result is clearly dependent on the reaction conditions: solvent, temperature, catalyst, concentration of the starting materials and functional groups.

Xanthones are secondary metabolites found in higher plant families, fungi and lichens [2]. This class of compounds exhibits interesting pharmaceutical properties; specifically, antibacterial, anti-inflammatory, anticancer and antiviral activities have been observed [3–6]. Xanthenes and benzoxanthenes constitute an important class of biologically active heterocycles and their synthesis has been received great attention in the field of medicinal and pharmaceutical chemistry owing to their broad spectrum of pharmacological activities such as antibacterial [7], anti-inflammatory [8] and antiviral [9]. Some of the xanthene based compounds have found applications as antagonists for paralyzing the action of zoxalamine and in photodynamic therapy [10]. In addition, their derivatives can be used as dyes, pH sensitive fluorescent materials for the visualization of biomolecular assemblies, agricultural bactericide activity and in laser technologies [11–15]. Because of their wide range of pharmacological, industrial and synthetic applications 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones are in lime light and recently many synthetic procedures are reported in the literature [16–29]. Most of the reported procedures for the synthesis of xanthenes derivatives accompanying with one or other kinds of the disadvantages, such as, expensive reagents, prolonged reaction time, tedious work-up procedures, high catalyst loading and strongly acidic conditions. Therefore, to avoid these limitations, a readily available catalyst with high catalytic activity, short reaction time and simple work-up for the preparation of xanthenes is highly desirable.

In this paper we report the synthesis of a series of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones and their thiosemicarbazone derivatives. The derived compounds were characterized by IR, NMR. The single crystal X-ray structural analysis of 12-(2-chlorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one (**2a**) is also reported.

2. Experimental

Chemicals obtained from commercially available analytical grade materials were used as supplied, without further purification. IR spectra were recorded on Avatar Nicholet FT-IR spectrophotometer (range 4000–400 cm^{-1}) as KBr pellets. ^1H NMR spectra were recorded on Bruker AMX-400 spectrometer operating at 400.23 MHz and Bruker AVIII 500 MHz spectrometer operating at 500.13 MHz using TMS as internal reference. ^{13}C NMR spectra

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were recorded on Bruker AMX-400 spectrometer operating at 100.63 MHz and Bruker AVIII 500 MHz spectrometer operating at 125.75 MHz.

2.1. General procedure for the preparation of compounds ***1a–9a***

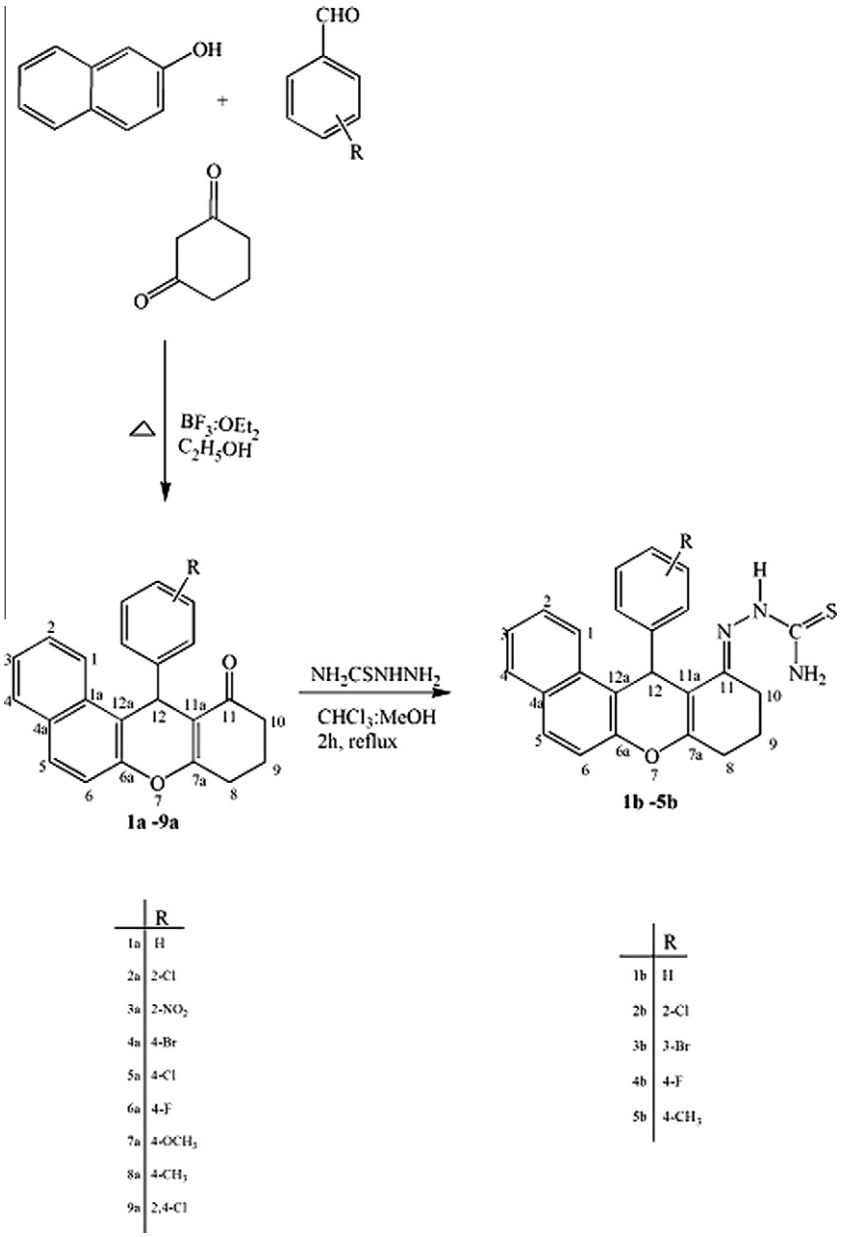
Compounds **1a–9a,** were prepared by the general procedure (Scheme 1) in which aldehyde (1.0 mmol), 2-naphthol (1.0 mmol) and 1,3-cyclohexanedione (1.0 mmol) were mixed thoroughly and placed in a 150 mL round-bottomed flask. The mixture was dissolved in 75 mL of distilled ethanol and BF_3:OEt_2 (0.04 mmol) was added to it. It was refluxed and the reaction was monitored by thin layer chromatography. After the completion of reaction (3 h), the reaction mixture was poured into cold water and the solid separated was filtered, washed with water and a small amount of ice cold ethanol. Then the obtained solid was purified by column chromatography (on neutral alumina gel and by using benzene and ethyl acetate (9.8:0.2) as eluent). The separated fractions were allowed to dry and the obtained solids were recrystallized using ethanol as solvent.

2.1.1. 12-Phenyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one ***1a***

White crystals, yield: 75%. m.p. 188–191 °C; IR (KBr, cm^{-1}): 3056, 2957, 2927, 1647, 1592, 1373, 1187. ^1H NMR (**(**$CDCl_3$, 500 MHz, ppm) δ: 8.01–7.08 (m, 11H), 5.78 (s, 1H), 2.69–2.79 (m, 2H), 2.37–2.51 (m, 2H), 1.99–2.09 (m,2H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ: 197.0, 165.5, 147.8, 145.0, 131.5, 131.4, 128.8, 128.5, 128.3, 128.2, 127.0, 126.2, 124.9, 123.7, 117.7, 116.9, 115.6, 37.0, 34.6, 27.7, 20.3.

2.1.2. 12-(2-Chlorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one ***2a***

White crystals, yield: 80%. m.p. 228–230 °C; IR (KBr, cm^{-1}): 3057, 2958, 2924, 2849, 1653, 1593, 1371,1227, 1190, 746. ^1H NMR (**(**$CDCl_3$, 500 MHz, ppm) δ: 8.24–7.01 (m, 10H), 6.04 (s, 1H), 2.73–2.84 (m, 2H), 2.41–2.45 (m, 2H), 2.01–2.12 (m, 2H). ^{13}C



	R
1a	H
2a	2-Cl
3a	2-NO_2
4a	4-Br
5a	4-Cl
6a	4-F
7a	4-OCH_3
8a	4-CH_3
9a	2,4-Cl

	R
1b	H
2b	2-Cl
3b	3-Br
4b	4-F
5b	4-CH_3

Scheme 1.

Table 1
Crystal data and structure refinement details for **2a**.

Empirical formula	$C_{23}H_{17}ClO_2$
Formula weight	360.82
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P21/n
Unit cell dimensions	
a	9.1849(5) Å
b	9.9521(5) Å
c	19.5774(12) Å
α	90.0°
β	102.830(2)°
γ	90.0°
Volume	1744.87(17) Å^3
Z, calculated density	4, 1.374 mg/m^3
Absorption coefficient	0.233 mm^{-1}
F(000)	752
Crystal size	0.30 × 0.25 × 0.20 mm
Theta range for data collection	2.13–31.94°
Limiting indices	$-13 \leqslant h \leqslant 11$, $-11 \leqslant k \leqslant 14$, $-29 \leqslant l \leqslant 29$
Reflections collected/unique	24214/5997
Completeness to theta = 31.94	99.4%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9548 and 0.8833
Refinement method	Full-matrix least squares on F^2
Data/restraints/parameters	5997/3/237
Goodness-of-fit on F^2	1.043
Final *R*, R_W (obs., data)	0.0571, 0.1528

NMR ($CDCl_3$, 125 MHz, ppm) δ: 196.8, 165.9, 147.6, 142.4, 133.0, 131.8, 131.7, 131.4, 129.9, 129.1, 128.4, 127.6, 127.1, 126.9, 124.9, 123.9, 117.5, 117.0, 114.7, 37.1, 33.0, 27.8, 20.4.

2.1.3. 12-(2-Nitrophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one ***3a***

Pale yellow crystals, yield: 75%. m.p. 268–270 °C; IR (KBr, cm^{-1}): 3070, 2949, 2860, 1650, 1594, 1530, 1370, 1225. ^{1}H NMR ($CDCl_3$,300 MHz, ppm) δ: 8.55–7.02 (m, 10H), 6.56 (s, 1H), 2.61–2.70 (m, 2H), 2.34–2.61 (m, 2H), 1.85–2.06 (m, 2H). ^{13}C NMR ($CDCl_3$, 75.46 MHz, ppm) δ: 196.9, 165.4, 149.3, 148.2, 139.2, 132.7, 131.7, 131.5, 131.2, 129.7, 128.2, 127.5, 127.0, 125.2, 124.6, 124.4, 116.8, 116.2, 114.6, 36.7, 30.3, 27.7, 20.2.

2.1.4. 12-(3-Bromophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one ***4a***

Pale yellow crystals, yield: 75%. m.p. 192–194 °C; IR (KBr, cm^{-1}): 3053, 2950, 2885, 1650, 1592, 1565, 1371, 1184. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ: 7.94–7.06 (m, 10H), 5.75 (s, 1H), 2.74–2.79 (m, 1H), 2.63–2.69 (m, 1H), 2.46–2.52 (m, 1H), 2.36–2.43 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ: 196.9, 165.9, 147.8, 147.3, 131.6, 131.4, 131.3, 131.2, 129.8, 129.6, 129.2, 128.5, 127.4, 127.2, 125.1, 123.5, 122.6, 117.1, 116.8, 114.9, 36.9, 34.5, 27.8, 20.2.

2.1.5. 12-(4-Chlorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one ***5a***

White crystals, yield: 75%. m.p. 197–199 °C; IR (KBr, cm^{-1}): 3061, 2956, 2927, 2887, 1655, 1593, 1370, 1227, 1189, 751. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.88–7.11 (m, 10H), 5.71 (s, 1H), 2.66–2.75 (m, 2H), 2.33–2.47 (m, 2H), 1.96–2.08 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 196.9, 165.7, 147.7, 143.5, 131.9, 131.5, 131.2, 129.8, 129.0, 128.4, 128.5, 127.1, 125.0, 123.4, 117.0, 116.9, 115.1, 37.0, 34.1, 27.7, 20.2.

Table 2
Selected bond distances (Å) and angles for **2a**.

Bond length	
C(1)—C(6)	1.334(2)
C(1)—O(1)	1.360(2)
C(1)—C(2)	1.493(2)
C(2)—C(3′)	1.492(8)
C(2)—C(3)	1.5465(8)
C(3)—C(4)	1.431(3)
C(3′)—C(4)	1.447(8)
C(4)—C(5)	1.502(3)
C(5)—O(2)	1.209(2)
C(5)—C(6)	1.469(2)
C(6)—C(7)	1.515(2)
C(7)—C(8)	1.520(2)
C(7)—C(18)	1.529(2)
C(8)—C(17)	1.365(2)
C(17)—O(1)	1.384(2)
C(23)—Cl(1)	1.733(2)
Bond angle	
C(6)—C(1)—O(1)	123.22(15)
C(6)—C(1)—C(2)	126.14(15)
O(1)—C(1)—C(2)	110.64(14)
C(1)—C(2)—C(3′)	112.0(3)
C(1)—C(2)—C(3)	110.31(9)
C(3′)—C(2)—C(3)	36.8(4)
C(4)—C(3)—C(2)	113.54(12)
C(4)—C(3′)—C(2)	115.9(5)
C(3)—C(4)—C(3′)	39.0(4)
C(3)—C(4)—C(5)	115.5(2)
C(3′)—C(4)—C(5)	117.9(3)
O(2)—C(5)—C(6)	120.95(17)
O(2)—C(5)—C(4)	121.13(18)
C(6)—C(5)—C(4)	117.90(17)
C(1)—C(6)—C(5)	118.78(15)
C(1)—C(6)—C(7)	122.73(14)
C(5)—C(6)—C(7)	118.47(14)
C(6)—C(7)—C(8)	109.99(12)
C(6)—C(7)—C(18)	109.29(13)
C(8)—C(7)—C(18)	111.44(12)
C(17)—C(8)—C(9)	117.53(14)
C(17)—C(8)—C(7)	120.67(14)
C(9)—C(8)—C(7)	121.80(13)
C(8)—C(17)—O(1)	123.27(14)
O(1)—C(17)—C(16)	113.34(14)
C(18)—C(23)—Cl(1)	121.18(16)
C(22)—C(23)—Cl(1)	117.41(17)
C(1)—O(1)—C(17)	118.40(13)

2.1.6. 12-(4-Fluorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one ***6a***

White crystals, yield: 70%. m.p. 216–218 °C; IR (KBr, cm^{-1}): 3079, 2947,2924, 2854, 1653,1593, 1503, 1372, 1222. ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) δ: 8.35–6.82 (m, 10H), 5.75 (s, 1H), 2.49–2.72 (m, 2H), 2.31–2.48 (m, 2H), 2.03–2.07 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) δ: 196.9, 165.6, 165.5, 162.8, 159.6, 147.7, 140.8, 140.7, 131.5, 131.2, 129.9, 129.8, 128.4, 126.9, 124.9, 123.5, 117.4, 116.9, 115.4, 115.1, 114.8, 36.9, 33.9, 27.7, 20.2.

2.1.7. 12-(4-Methoxyphenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one ***7a***

White crystals, yield: 75%. m.p. 173–175 °C; IR (KBr, cm^{-1}): 3063, 2943, 2898, 2832, 1653, 1595, 1378, 1249, 1227. ^{1}H NMR (CDCl3, 500 MHz, ppm) δ: 8.00–6.73 (m, 10H), 5.72 (s, 1H), 3.71 (s, 3H), 2.64–2.74 (m, 2H) 2.37–2.51(m, 2H), 2.00–2.08 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ: 197.2, 165.4, 157.8, 147.7, 137.4, 131.5, 131.4, 129.4, 128.7, 128.3, 126.9, 124.8, 123.7, 117.9, 115.7, 113.6, 55.1, 37.0, 33.7, 27.7, 20.3.

2.1.8. 12-(4-Tolyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one ***8a***

White crystals, yield: 80%. m.p. 198–200 °C; IR (KBr, cm^{-1}): 3041, 3018, 2946, 2895, 2832, 1650, 1595, 1373, 1225, 1186,

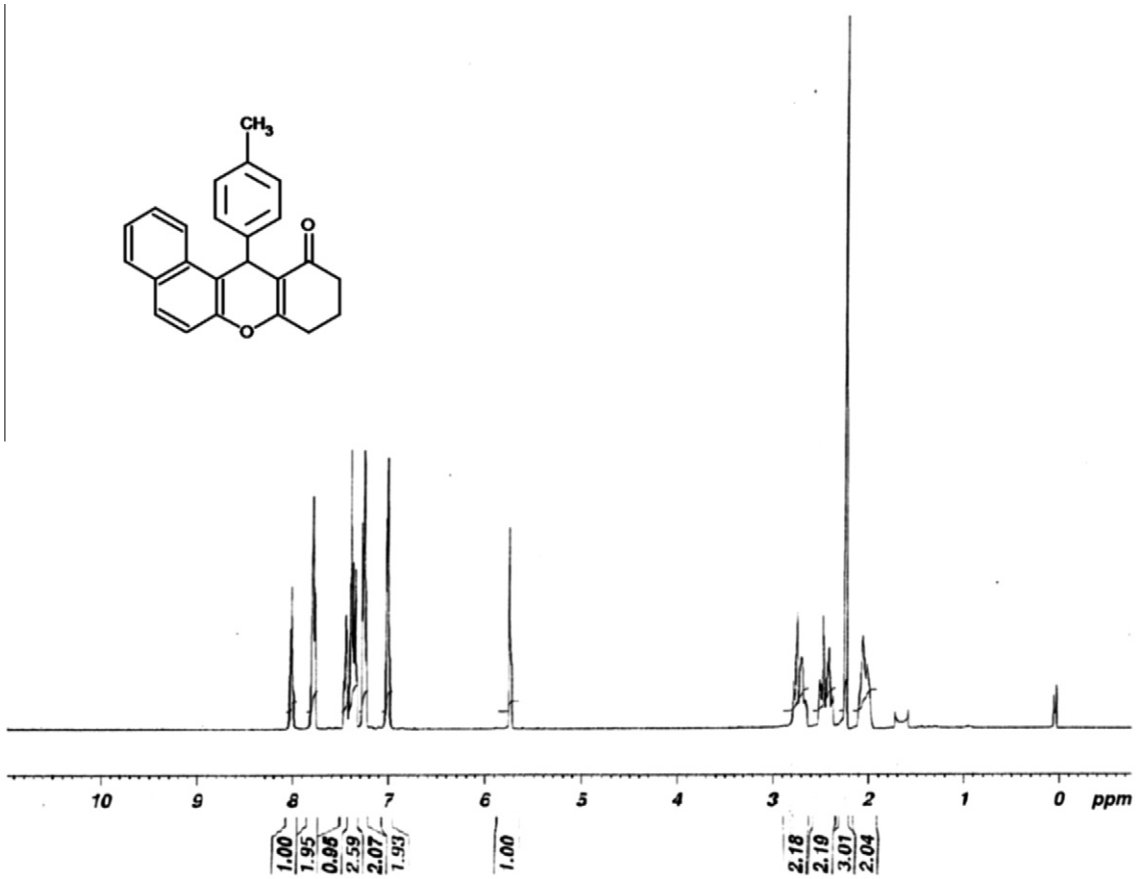


Fig. 1. ^{1}H NMR spectrum of compound **8a**.

814. ^{1}H NMR (CDCl$_3$, 500 MHz, ppm) δ: 8.03–7.01 (m, 10H), 5.74 (s, 1H), 2.68–2.78 (m, 2H), 2.40–2.50 (m, 2H), 2.24 (s, 3H), 2.01–2.06 (m, 2H). ^{13}C NMR (CDCl$_3$, 125 MHz, ppm) δ: 197.0, 165.5, 147.7, 142.2, 135.7, 131.5, 131.4, 129.0, 128.7, 128.3, 126.9, 124.8, 123.7, 117.9, 116.9, 115.7, 37.0, 34.2, 27.7, 21.0, 20.3.

2.1.9. 12-(2,4-Dichlorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one ***9a***

White crystals, yield: 70%. m.p. 194–196 °C; IR (KBr, cm^{-1}):3061, 2922, 2849, 1647, 1593, 818. ^{1}H NMR (CDCl$_3$, 300 MHz, ppm) δ: 7.85–7.13 (m, 9H), 5.70 (s, 1H), 2.73–2.75 (m, 2H), 2.39–2.47 (m, 2H), 2.04–2.07 (m, 2H). ^{13}C NMR (CDCl$_3$, 75 MHz, ppm) δ: 196.8, 165.9, 147.8, 145.1, 132.3, 131.5, 131.1, 130.3, 130.1, 129.4, 128.5, 128.0, 127.2, 125.1, 123.3, 116.9, 116.3, 114.6, 36.9, 34.0, 27.7, 20.2.

2.2. General procedure for the preparation of compounds ***1b–5b***

To a boiling solution of **1a, 2a, 4a, 6a** and **8a** (1.0 mmol) in methanol-chloroform (1:1, 40 mL), thiosemicarbazide (1.5 mmol) and few drops of acetic acid were added and refluxed for 24 h on a water bath. After cooling, the separated solid was filtered off and purified by column chromatography using benzene and ethyl acetate (9.5:0.5) as eluent. The separated fractions were allowed to dry and the obtained solids were recrystallized using ethanol as solvent.

2.2.1. 12-(Phenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one thiosemicarbazone ***1b***

Pale yellow crystals, yield: 68%. m.p. 188–191 °C; IR (KBr, cm^{-1}): 3227, 3073, 3013, 2958, 2887, 1660, 1585, 1231, 1012. ^{1}H NMR (CDCl$_3$, 500 MHz, ppm) δ: 8.70–6.43 (m, 14H), 5.71 (s, 1H), 2.68–2.74 (m, 1H), 2.58–2.65 (m, 2H), 2.26–2.33 (m, 1H), 2.09–2.30 (m, 1H), 1.87–1.94 (m, 1H). ^{13}C NMR (CDCl$_3$, 125 MHz, ppm) δ: 178.5, 156.4, 149.3, 145.4, 131.3, 131.2, 128.7, 128.6, 128.3, 128.2, 126.7, 126.5, 124.6, 123.1, 117.3, 117.1, 111.3, 36.1, 26.9, 23.9, 19.9.

2.2.2. 12-(2-Chorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one thiosemicarbazone ***2b***

Pale yellow crystals, yield: 65%. m.p. 235–237 °C; IR (KBr, cm^{-1}): 3408, 3347, 3277, 3163, 3046, 2923, 2853, 1650, 1600, 1494, 1233. ^{1}H NMR (CDCl$_3$, 500 MHz, ppm) δ: 8.62–6.39 (m, 3H), 6.11 (s, 1H), 2.73–2.78 (m, 1H), 2.60–2.67 (m, 2H), 2.29–2.36 (m, 1H), 2.04–2.10 (m, 1H), 1.85–1.90 (m, 1H). ^{13}C NMR (CDCl$_3$, 125 MHz, ppm) δ: 178.2, 157.2, 149.2, 147.8, 143.3, 131.4, 131.3, 131.2, 130.8, 129.6, 128.9, 128.5, 128.0, 127.8, 126.9, 124.7, 123.6, 117.8, 117.4, 111.6, 32.5, 29.7, 27.2, 24.3, 19.7.

2.2.3. 12-(3-Bromophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one thiosemicarbazone ***3b***

Pale yellow crystals, yield: 73%. m.p. 218–220 °C; IR (KBr, cm^{-1}): 3418, 3363, 3225, 3133, 3035, 2943, 1654, 1588, 1501, 1475, 1232. ^{1}H NMR (DMSO, 500 MHz, ppm) δ: 9.86–7.08 (m, 13H), 6.03 (s, 1H), 2.61–2.71 (m, 2H), 2.54–2.56 (m, 1H) 2.32–2.38 (m, 1H), 1.84–1.89 (m, 1H), 1.66–1.71 (m, 1H). ^{13}C NMR (CDCl$_3$, 125 MHz, ppm) δ: 178.6, 155.8, 149.3, 149.0, 147.7, 131.6, 131.2, 131.2, 130.5, 129.4, 129.3, 128.8, 127.8, 127.2, 125.1, 124.5, 121.7, 117.7, 117.4, 111.6, 34.6, 26.9, 24.7, 20.3.

2.2.4. 12-(4-Fluorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one thiosemicarbazone ***4b***

Pale yellow crystals, yield: 65%. m.p. 238–240 °C; IR (KBr, cm^{-1}): 3426, 3352, 3232, 3148, 3041, 2937, 2865, 1656, 1596,

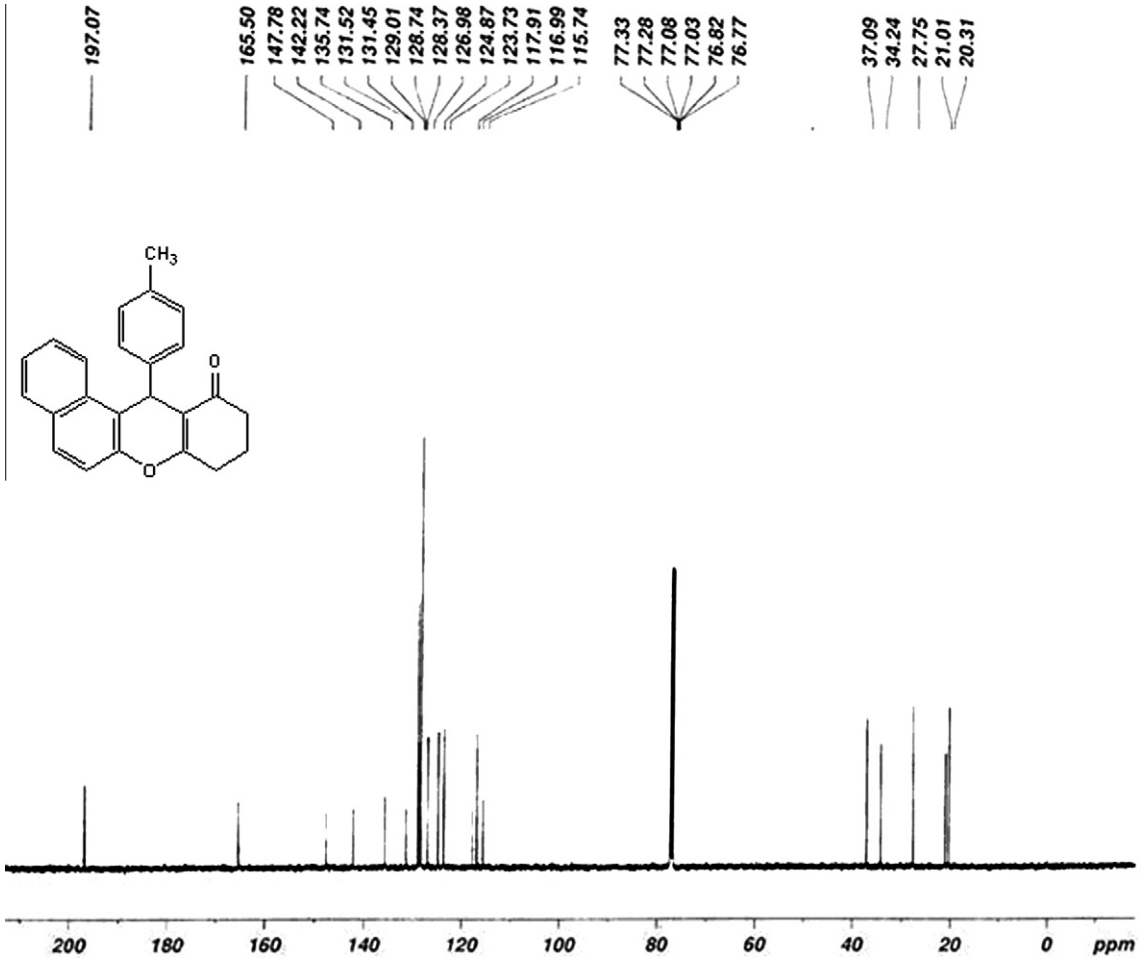


Fig. 2. ^{13}C NMR spectrum of compound **8a**.

1226, 837. ^{1}H NMR (DMSO, 500 MHz, ppm) δ: 9.90–6.95 (m, 13H), 6.04 (s, 1H), 2.67–2.72 (m, 1H), 2.59–2.65 (m, 1H), 2.54–2.56 (m, 1H), 2.32–2.38 (m, 1H), 1.85–1.89 (m, 1H) 1.67–1.70 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ: 178.6, 161.7, 159.8, 155.6, 149.3, 147.7, 142.9, 142.8, 132.2, 130.6, 130.5, 129.1, 128.8, 127.1, 125.0, 124.7, 117.9, 117.7, 115.1, 114.9, 111.9, 34.1, 26.9, 24.7, 20.3.

*2.2.5. 12-(4-Tolyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one thiosemicarbazone **5b***

Pale yellow crystals, yield: 70%. m.p. 194–196 °C; IR (KBr, cm^{-1}): 3418, 3358, 3257, 3144, 3035, 3051, 2928, 2865, 1654, 1586, 1501, 1233, 1086. ^{1}H NMR (DMSO, 500 MHz, ppm) δ: 8.61–6.33 (m, 13H), 5.67 (s, 1H), 2.68–2.72 (m, 1H) 2.57–2.65 (m, 2H), 2.26–2.31 (m, 1H), 2.22 (s, 3H), 1.92–2.08 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ: 178.7, 156.3, 149.2, 147.4, 142.4, 136.0, 131.3, 131.2, 129.0, 128.6, 128.5, 128.3, 128.1, 126.7, 124.5, 123.1, 117.2, 111.4, 35.7, 26.8, 23.8, 20.9, 19.9.

2.3. X-ray crystallography

Crystal was grown by slow evaporation technique using ethanol as solvent. Diffraction data were collected on a Bruker, 2004 APEX 2 diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) at 293 K with crystal size of 0.30 × 0.25 × 0.20 mm. Crystal data and structure refinement details are given in Table 1. Selected bond distances and angles are given in Table 2. The structure was solved by direct methods and successive Fourier difference syntheses (SHELXS-97) [30] and refined by full matrix least square procedure on F^2 with anisotropic thermal parameters. All non-hydrogen atoms were refined (SHELXL-97) [31] and placed at chemically acceptable positions. A total of 237 parameters were refined with 5997 unique reflections which covered the residuals to R_1 = 0.0571. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 809606 for **2a**. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223 336 033: or e-mail: deposit@ccdc.cam.ac.uk.

3. Results and discussion

In the present study a series of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones [**1a–9a**] were prepared using $BF_3{\cdot}OEt_2$ as catalyst. In this synthetic procedure the difficulty in separation of catalyst from the reaction mixture was completely avoided and also both the electron rich and electron deficient aryl aldehydes undergo the reaction conveniently. Thiosemicarbazone derivatives [**1b–5b**] were also prepared in the presence of acid catalyst.

*3.1. IR spectral analysis of compounds **1a–9a***

For **1a–9a** the observed maxima in the region of 1647–1655 cm^{-1} are characteristic for carbonyl (C=O) stretching

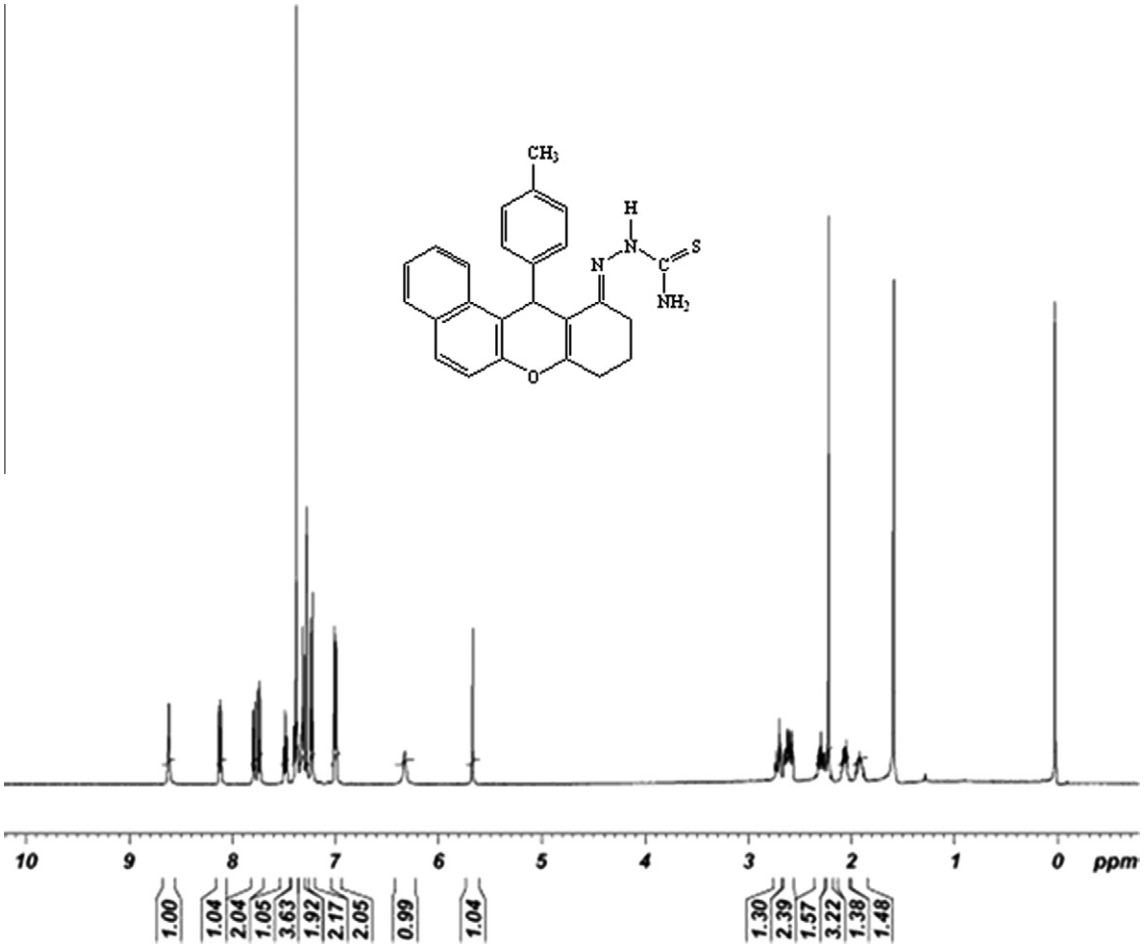


Fig. 3. ^{1}H NMR spectrum of compound **5b**.

frequencies of α,β-unsaturated ketones. Similarly, the C=C stretching frequencies associated with the α,β-unsaturated ketones are observed in the region of 1592–1595 cm^{-1} as reported earlier [9]. The C—H stretching vibration bands are observed in the region of 2832–3063 cm^{-1}. In all the cases the weak aromatic C—H bands are obtained in the region of 3018–3063 cm^{-1}.

3.2. IR spectral analysis of compounds *1b–5b*

Earlier studies [32] indicated that the characteristic vibrational bands observed around 1645 cm^{-1} is due to C=N stretching frequency of thiosemicarbazone moiety. Similarly, thiosemicarbazone derivatives of xanthones (**1b–5b**) also show the C=N stretching frequency in the region of 1650–1654 cm^{-1}. The strong absorption band observed about 3300 cm^{-1} in the IR spectrum is normally assigned to N—H stretching mode of amines. In **1b–5b**, the characteristic IR bands in the region 3257 and 3277 cm^{-1} are due to N—H stretching frequency of the thiosemicarbazone moiety. Generally, the absorption arising from the aromatic and aliphatic C—H stretching frequencies occur in the general region 3075–2775 cm^{-1}. In **1b–5b** also the similar absorption bands are noted in the region 3051–2928 and 3046–2853 cm^{-1}, respectively. Hence, these stretching frequencies can be ascribed to aromatic and aliphatic C—H stretching frequencies. Wiles et al. [33] reported that the C=S stretching vibrations of several thiosemicarbazones exhibit a band at 1135 cm^{-1} and for **1b–5b** also, an intense absorption band is observed in the region of 1193 cm^{-1}, respectively due to C=S stretching.

3.3. NMR spectra

3.3.1. ^{1}H NMR spectral analysis of compound *8a*

^{1}H NMR spectrum of compound **8a** (Fig. 1) exhibit three multiplets in the region of 2.01–2.78 ppm (2.04, 2.44 and 2.72 ppm). A signal appeared at 2.72 ppm is assigned to H_a and H_b protons at C-8 carbon. The remaining two multiplets at 2.44 and 2.04 ppm are assigned to protons (H_a and H_b) at C-10 and C-9 carbons, respectively. The benzylic proton at C-12 resonated at 5.74 ppm as a singlet with one proton integral value. The aromatic protons appeared in the region of 7.01–8.03 ppm. A sharp singlet appeared at 2.24 ppm is assigned to the methyl substituent at *para*-position of phenyl group.

3.3.2. ^{13}C NMR spectral analysis of compound *8a*

^{13}C NMR spectrum of compound **8a** is shown in Fig. 2. In general, the aromatic carbons could be readily distinguished from the other carbons due to their characteristic absorption in the region of 120–140 ppm. For **8a**, the aromatic carbon signals appeared in the range of 115.7–147.7 ppm. Two less intense signals in the higher frequency region (197.0 and 165.50 ppm) are assigned to carbonyl sp^2 carbon and C-7a carbon, respectively. ^{13}C NMR spectrum of compound **8a** showed four signals in the aliphatic region. The signals at 27.7, 34.2 and 20.3 ppm are due to C-10, C-8 and C-9 carbons, respectively. The deshielded signal (34.2 ppm) is assigned to methylene carbon at C-8. The other two signals at 27.7 and 20.3 ppm are assigned to C-10 and C-9 carbons, respectively. The shielding chemical shift differences between C-8 and C-10 carbons

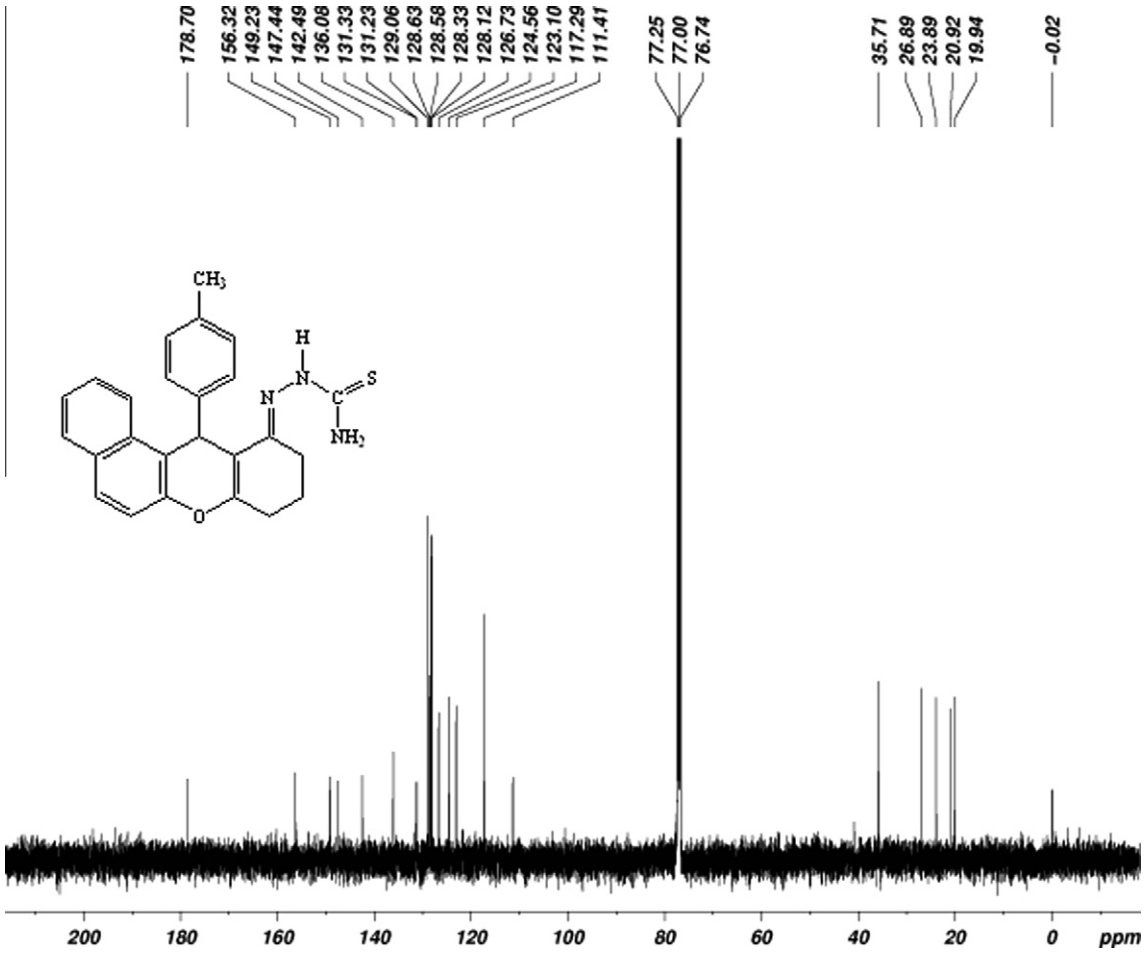


Fig. 4. ^{13}C NMR spectrum of compound **5b**.

are about 6.5 ppm. The methine carbon (C-12) is slightly deshielded and obtained at 37.0 ppm.

3.3.3. ^{1}H NMR spectral analysis of compound **5b**

^{1}H NMR spectrum of compound **5b** (Fig. 3) showed a multiplet in the range 6.99–8.12 ppm which corresponds to 10 protons and is attributed to aromatic protons. The three multiplets appeared at 1.99, 2.43 and 2.66 ppm are assigned to H_a and H_b protons attached to C-9, C-10 and C-8 carbons, respectively. Moreover, the observed two sharp singlets at 2.22 and 5.67 ppm are assigned to methyl substituent at *para*-position of phenyl ring and benzylic proton at C-12, respectively. A broad singlet at 6.33 ppm with one proton integration is due to NH proton of thiosemicarbazone moiety. Similarly, a sharp singlet observed at 8.61 ppm is conveniently assigned to one of the —NH_2 protons. The signal due to another proton in —NH_2 group might be merged with the aromatic proton signals. This is also supported by the observation of higher integral values for the aromatic protons.

3.3.4. ^{13}C NMR spectral analysis of compound **5b**

^{13}C NMR spectrum of compound **5b** is shown in Fig. 4. The ^{13}C NMR spectral assignment has been made based on characteristic signal positions of the functional groups and comparison with those of parent compound. In ^{13}C NMR spectrum of compound **5b**, the signals appeared in the range 111.4–147.4 ppm are due to aromatic carbons. The less intense signals resonated in the deshielded region of 178.7 and 156.3 ppm are assigned to C=S and C=N carbons, respectively. The three signals appeared at 19.9, 23.8 and 26.8 ppm are assigned to methylene carbons at C-9, C-10 and C-8 positions. The methine carbon (C-12) signal is observed at 35.7 ppm. The signal observed at 20.9 ppm is due to methyl carbon at *para*-position of phenyl group. The disappearance of carbonyl carbon signal (around 195 ppm) and the appearance of two new signals at 178.7 (C=S) and 156.3 ppm (C=N) corroborates the formation of compound 5b.

3.3.5. HSQC spectral analysis of compound **5b**

From the ^{1}H–^{13}C COSY spectrum of **5b** (Fig. 5), the following important assignments can be made in the aliphatic region: The two multiplets at 1.92 and 2.06 ppm show cross peak with the signal at 19.9 ppm. This suggests that the carbon signal is due to C-9 carbon. Likewise, the other two multiplets at 2.28 and 2.58 ppm show cross peak with the carbon signal at 23.8 ppm and it suggests that the carbon signal is due to C-10 carbon whereas, the remaining multiplets at 2.70 and 2.63 ppm show cross peak with the signal at 26.8 ppm denotes that the signal is due to C-8 carbon. Similarly, two singlets at 5.57 and 2.22 ppm show cross peaks with the carbon signals at 35.7 and 20.9 ppm, respectively. It infers that the carbon signals are due to benzylic carbon (C-12) and CH_3 carbon present in the phenyl group. The assignment of —NH— proton signal (at 6.33 ppm) and one of the —NH_2 protons signal (at 8.61 ppm) from ^{1}H NMR spectrum is confirmed unambiguously by HSQC spectral analysis as there are no correlations for the above mentioned signals. In the higher frequency region of the ^{13}C spectrum, apart from the C=S signal at 178.7 ppm there are eight signals without correlations respectively at 156.3, 149.2, 147.4,

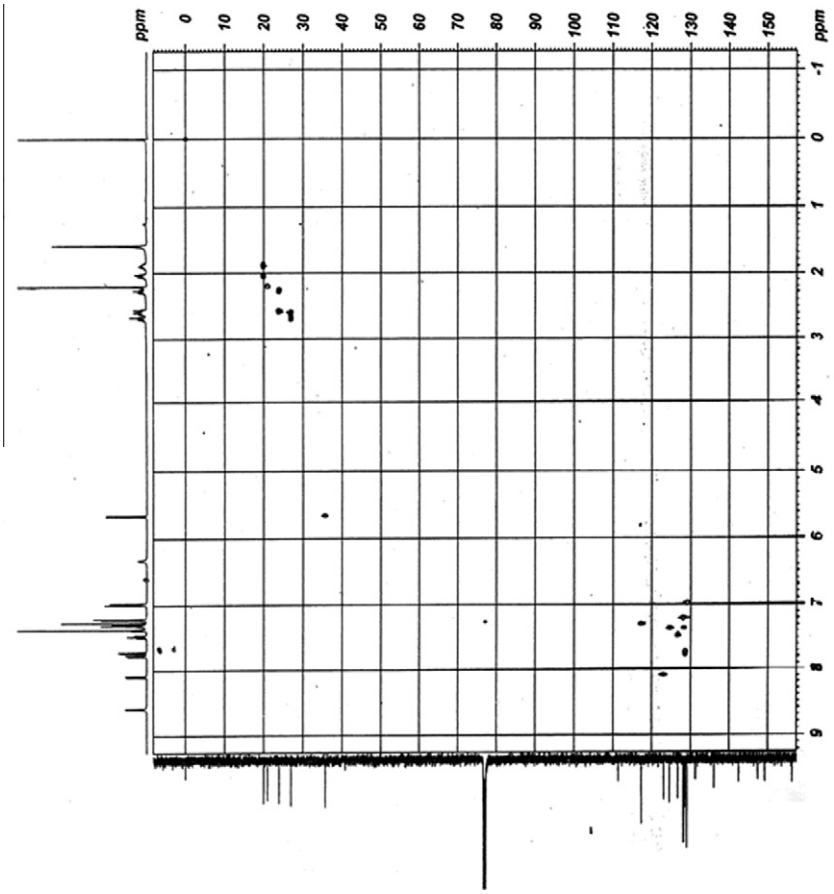


Fig. 5. HSQC spectrum of compound **5b**.

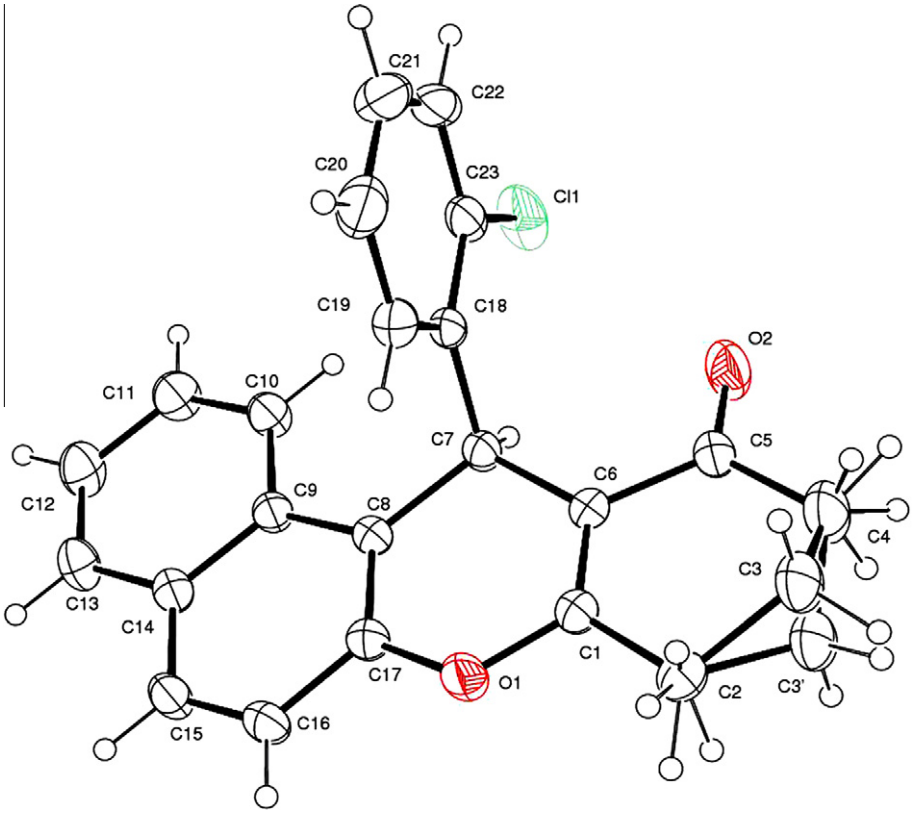


Fig. 6. ORTEP diagram of **2a**.

142.4, 136.0, 131.3, 131.2 and 111.4 ppm. Among the eight signals the deshielded signals at 149.2 and 147.4 ppm are conveniently assigned to C-7a and C-6a carbons respectively as they are α to electronegative oxygen. Similarly, the signal which is comparatively shielded (111.4 ppm) is due to olefinic carbon at C-11a. The signals at 142.4 and 136.0 ppm might be due to the *ipso* carbons of 4-methylphenyl ring. The remaining signals at 131.3 and 131.2 ppm are assigned to C-4a and C-1a carbons, respectively.

*3.4. Single crystal X-ray structural analysis of 12-(2-chlorophenyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one (**2a**)*

ORTEP of **2a** is given in Fig. 6. Compound **2a** crystallizes in the monoclinic space group P21/n with four discrete molecules in the unit cell. In the pyran ring C(8)—C(17) and C(1)—C(6) bonds are double bonded in character [C(8)—C(17) = 1.365(2) and C(1)—C(6) = 1.334(2) Å] as evidenced by the bond distances. C(8)—C(7)—C(18) [111.44(12)°] and C(6)—C(7)—C(8) [109.99(12)°] angles are observed with very little difference. The conformation of the pyran ring can be described as ''flattened boat'' which is evidenced from the small puckering parameters coupled with the O(1) and C(7) atoms present at 1st and 4th positions respectively of the pyran ring. The atoms O(1) and C(7) are displaced by 0.085 and 0.151 Å respectively from the plane defined by C(1), C(6), C(8) and C(17) [34]. In the cyclohexenone ring the observed carbonyl [C(5)—O(2) = 1.209(2) Å] bond distance is normal. Interestingly, positional disorder was observed for C-3 methylene carbon and the protons attached to it. The protons attached to C-2 and C-4 were also positionally disordered over two positions. Cyclohexenone ring exhibit envelope conformation, with slightly more pronounced puckering of the C(3) atom by 0.546 Å from the C(2)/C(1)/C(6)/C(5)/C(4) plane [similarly, C(3′) is also deviates from the C(2)/C(1)/C(6)/C(5)/C(4) plane to the extent of 0.412 Å]. In this conformation C (3) [or C (3′)] can be better described as a ''flap'' atom being away from the plane of the ring. The 2-chlorophenyl group is almost perpendicular to the pyran ring with the angle of 89.90°. Other structural parameters associated with the 2-chlorophenyl and naphthyl rings are normal.

4. Conclusions

A series of tetrahydrobenzo[a]xanthen-11-ones (**1a–9a**) have been synthesized by the MCR of 2-naphthol, aryl aldehyde and 1,3-cyclohexanedione using BF_3:OEt_2 as a catalyst. Thiosemicarbazone derivatives (**1b–5b**) were also derived and the synthesized compounds were characterized by IR, 1D and 2D-NMR spectra. From the single crystal XRD analysis of **2a** the conformation of the pyran ring can be described as ''flattened boat''. Positional disorder was observed for C-3 and the protons attached to it. The protons attached to C-2 and C-4 were also positionally disordered over two positions. Cyclohexenone ring exhibit envelope conformation, with slightly more pronounced puckering of the C(3) atom by 0.546 Å from the C(2)/C(1)/C(6)/C(5)/C(4) plane [similarly, C(3′) is also deviates from the C (2)/C(1)/C(6)/C(5)/C(4) plane to the extent of 0.412 Å].

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