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One step cyclocondensation of (thio)barbituric acid with chalcones in glacial acetic acid and phosphorous pentoxide: Part-I

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Abstract

Some new 5, 7-diaryl-1,5-dihydro (or 1, 2, 3, 5-tetrahydro)- pyrano[2, 3-d] pyrimidin-2, 4-diones (or 2-thioxo-4-ones) (3a-h) have been synthesized in one-step by cyclocondensation of barbituric acid or thiobarbituric acid (1) with arylideneacetophenones (2a-d), in glacial acetic acid in the presence of phosphorous pentoxide. The structures of the compounds 3a-h have been determined by UV, IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses. The compounds 3a-h do not seem to be available in the literature.

Keywords: Arylideneacetophenone; Barbituric acid; Thiobarbituric acid; Cyclocondensation

Introduction

The synthesis of fused heterocycles has attracted considerable interest in heterocyclic chemistry as the fusion of biodynamic heterosystems has proved to be very attractive and constructive for the design of a new molecular framework of potential drugs with varying pharmacological activities. Pyran derivatives are ordinary structural subunits in a variety of important natural products, including carbohydrates, alkaloids, polyether antibiotics, pheromones, and iridoids (Tietze *et al.* 1997). Uracil and its fused derivatives, such as pyrano[2,3-d]pyrimidines, pyrido[2,3-d]pyrimidines or pyrimido[4,5-d]pyrimidines are well recognized by synthesis as well as biological chemists. These annelated uracils have received considerable attention over the past years due to their wide range of biological activity (Senda *et al.* 1968, Levitt 1982, O'Callaghan *et al*., 1983, Wrigglesworth *et al*.1984). Compounds with these ring systems have diverse pharmacological properties such as antiallergic (Kitamura *et al.,* 1984), antihypertensive (Furuya *et al.* 1994), cardiotonic (Heber *et al.,* 1993), bronchiodilator (Coates 1990), antitumour activity (Broom *et al.,* 1976). Pyrano[2,3-d]pyrimidine is unsaturated six membered heterocycle which is formed by fusion of pyran and pyrimidine rings together, consisting of one oxygen atom at position number 8 and two nitrogen atoms at position number 1 and 3 respectively. If pyrano[2,3-d]pyrimidine moieties are clubbed into one molecule, then resultant derivative enhances its pharmaceutical activity as abundant in biologically active compounds. The synthesis of pyrano[2,3-d]pyrimidines containing a pyran and an uracil ring poses significant synthetic challenges. Therefore, for the preparation of these complex molecules large efforts have been directed towards the synthetic manipulation of uracils. As a result, a number of methods for the synthesis of these compounds have been reported (Rao *et al.,* 1974, Junek *et al.*, 1973, Noboru *et al*., 1973, Bararjanian *et al.* 2009, Mohammadi Ziarani *et al.,* 2013), but the majority of them involve various steps, waste of organic solvents, long reaction time and the yields are relatively poor. This initiated to develop an efficient method for the synthesis of these compounds in better yields. Thus new routes for the synthesis of these molecules have attracted considerable attention in search for a rapid entry to these heterocycles. There is a report (Ahlwalia *et al.,* 1993) on the reactions of barbituric acids with α, β-unsaturated carbonyl systems.

With this background, in continuation to our works (Ahmed *et al.,* 2006, Ahmed *et al.,* 2011, Ullah *et al.,* 2012 and Rahman *et al.,* 2013) on the synthesis of barbituric acid and thio-barbituric acid derivatives, we report herein syntheses

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of 5, 7-diaryl-1,5-dihydro - pyrano[2, 3-*d*] pyrimidin-2, 4-diones (3a, 3c, 3e & 3g) and 5, 7-diaryl-2-thioxo - 1, 2, 3, 5-tetrahydro- pyrano[2, 3-d] pyrimidin -4-ones) (3b, 3d, 3f & 3h) by selecting a number of arylideneacetophenones (2a-*d*) as the α,β-unsaturated carbonyl system having different substituents on the aromatic rings for reaction with barbituric acid or thiobarbituric acid (1) as the active methylene component in presence of glacial acetic acid and phosphorus pentoxide (Scheme 1). The compounds 3a-h do not seem to be available in the literature.

Materials and methods

The UV spectra were run in methanol using SHIMADZU-UV-160A ultraviolet spectrophotometer with a scanning range of 800-200 nm using methanol as solvent. The IR spectra were recorded as KBr pellet using SHIMADZU FT-IR 8400S infra-red spectrophotometer in the range of 4000-400 cm^{-1}. The ^{1}H- and ^{13}C- NMR spectra were recorded on 600 MHz NMR spectrometer. The solvent used was d_6-DMSO and TMS is being used as a reference. All the compounds gave expected C, H and N analyses.

3-(4-chlorophenyl)-1-(4-chlorophenyl)-propenone 2a, 3-(4-chlorophenyl)-1-(4-aminophenyl)-propenone 2b, 3-(2-chlorophenyl)-1-(4-chlorophenyl)-propenone 2c and 3-(2-chlorophenyl)-1-(4-methoxyphenyl)-propenone 2d were prepared from the reactions of corresponding substituted aldehydes and substituted acetophenones by following primarily literature method (Furniss *et al.* 1978) with modification of the reaction conditions wherever necessary. The reactions described in the present paper were carried out following a general procedure (Ahlwalia *et al.,* 1993).

General procedure

A mixture of arylideneacetophenone (0.005 mol) and barbituric acid or thiobarbituric acid (0.005 mol) were dissolved in acetic acid (15 mL) and P_2O_5 (1.5 g) in a round-bottomed flask equipped with a magnetic stirrer, a refluxing condenser and a drying tube. The reaction mixture was refluxed at 135-140^{o}C for 6-8 hours and the course of the reaction was followed by TLC on silica gel plates (eluting solvent; CH_3OH: $CHCl_3$ =1:9). The mixture was allowed to cool and treated with crushed ice. The solid, thus obtained, was filtered off, washed with cold water, dried and purified by recrystallization from rectified spirit.

5,7-bis-(4-chlorophenyl-1,5-dihydro-pyrano[2,3-d]pyrimidine-2,4-dione, 3a

White solid; Yield 58%; mp. 267-269^{o}C; R_f 0.78; UV: λ_{max} nm 288, 474 ($\pi\rightarrow\pi^*$/n $\rightarrow\pi^*$ of C=O); IR: γ_{max} (cm^{-1}) 3460 (N-H), 1724, 1682 (C=O, non-conj.), 1610, 1541 (C=O arom, C-N) 1437, 1276, 1244, 1176, 1039, 1016, 970, 819 (C=C, arom. & bar. acid moieties), 1120, 1087 (C-O-C); ^{1}H NMR: δ 11.91 (s, 1H, NH, 3-H), 10.99 (s, 1H, NH, 1-H), 7.69 (d, $J_{8.4}$, 2H, H-2',6'), 7.50 (d, $J_{7.8}$, 2H, H-3', 5'), 7.29-7.34 (m, 4H, H-2",3",5",6"), 6.07 (d, $J_{3.6}$,1H, 6-H), 4.34 (d, $J_{4.5}$,1H, 5-H); ^{13}C NMR: δ 163.21 (4-C), 154.35 (9-C), 144.18 (7-C), 143.22 (2-C), 133.77, 131.10, 130.22, 129.64, 128.68, 128.26, 125.92 (aromatic carbons), 104.64 (6-C), 87.01 (10-C), 34.36 (5-C); MS: m/z 386.99 (M^+), 307.1, 289.05, 274.99, 154.0 (100%), 136.0, 89.2; Anal. Found: C, 58.67; H, 3.14; N, 7.04; Calcd. for $C_{19}H_{12}N_2$ O3Cl_2: C, 58.93; H, 3.12; N, 7.23%.

5,7-bis-(4-chlorophenyl)-2-thioxo-1,2,3,5-tetrahydro-pyrano[2,3-d]pyrimidin-4-one, 3b

Gray solid; Yield 33%; mp. 279-281^{o}C; R_f 0.75; UV: λ_{max} nm 295, 497 ($\pi\rightarrow\pi^*$/n $\rightarrow\pi^*$ of C=O); IR: γ_{max} (cm^{-1}) 3480 (N-H), 1676 (C=O, non-conj.), 1570 (C=O arom, C-N) 1410, 1273, 1238, 1220, 1055, 1012, 955, 914, 829 (C=C, arom. & bar. acid moieties), 1136, 1093 (C-O-C); 1H NMR: δ12.38 (s, 1H, NH, 3-H), 10.98 (s, 1H, NH, 1-H), 7.74 (d, $J_{8.4}$, 2H, H-2',6'), 7.50 (d, $J_{8.4}$, 2H, H-3', 5'), 7.31-7.35 (m, 4H, H-2",3",5",6"), 6.09 (d, $J_{4.2}$,1H, 6-H), 4.49 (d, $J_{4.8}$,1H, 5-H); ^{13}C NMR: 160.89 (4-C), 153.68 (9-C), 144.08 (7-C), 173.78 (2-C), 142.58, 133.85, 131.28, 129.97, 129.78, 128.65, 128.28, 125.99 (aromatic carbons), 104.18 (6-C), 92.03 (10-C), 34.29 (5-C); MS: m/z 403.02 (M^+), 371.3, 307.1, 289.1, 154.0 (100%), 136.0, 89.3; Anal. Found: C, 55.98; H, 3.78; N, 6.25; Calcd. for $C_{19}H_{12}Cl_2N_2O_2S$: C, 56.59; H, 3.00; N, 6.95%.

7-(4-aminophenyl)-5-(4-chlorophenyl)- 1,5-dihydro-pyrano[2,3-d]pyrimidine-2,4-dione, 3c

Red solid; Yield 30%; mp. 264-266^{o}C; R_f 0.72; UV: λ_{max} nm 320 ($\pi\rightarrow\pi^*$/n $\rightarrow\pi^*$ of C=O); IR: γ_{max} (cm^{-1}) 3400, 3306 (N-H, NH_2), 1685 (C=O, non-conj.), 1595, 1534 (C=O arom, C-

N) 1400, 1263, 1012, 831, 762 (C=C, arom. & bar. acid moieties), 1140, 1091 (C-O-C); ^{1}H NMR: δ 11.88 (s, 1H, NH, 3-H), 10.98 (s, 1H, NH, 1-H), 7.72 (d, 2H, H-2',6'), 7.60 (d, 2H, H-3', 5'), 7.20-7.40 (m, 4H, H-2",3",5",6"), 5.87 (d, $J_{3.5}$,1H, 6-H), 4.44 (d, $J_{4.0}$,1H, 5-H), 3.37 (s, 2H, Ar-NH_2); ^{13}C NMR: δ161.96 (4-C), 153.23 (9-C), 145.91 (7-C), 143.77 (2-C), 145.78, 135.80, 130.81, 130.55, 128.78, 127.85, 124.90, 115.75 (aromatic carbons), 103.76 (6-C), 87.45 (10-C), 31.85 (5-C); MS: m/z 367.22 (M^+), 307.1, 289.1, 154.0 (100%), 136.0, 89.2; Anal. Found: C, 60.30; H, 4.33; N, 7.79; Calcd. for $C_{19}H_{14}ClN_3O_3$: C, 62.05; H, 3.84; N, 11.43%.

7-(4-aminophenyl)-5-(4-chlorophenyl)-2-thioxo-1,2,3,5-tetrahydro-pyrano[2,3-d] pyrimidine-4-one, 3d:

Red solid; Yield 35%; mp. 248-250°C; R_f 0.65; UV: λ_{max} nm 301 (π→π*/n →π* of C=O); IR: γ_{max} (cm^{-1}) 3395, 3300 (N-H, NH_2), 1687 (C=O, non-conj.), 1592, 1524 (C=O arom, C-N) 1407, 1310, 1222, 1182, 1013, 827 (C=C, arom. & bar. acid moieties), 1133, 1091 (C-O-C); ^{1}H NMR: δ 12.48 (s, 1H, NH, 3-H), 10.85 (s, 1H, NH, 1-H), 7.75 (d, 2H, H-2', 6'), 7.68 (d, 2H, H-3', 5'), 7.20-7.40 (m, 4H, H-2",3",5",6"), 5.88 (bs, 1H, 6-H), 4.49 (d, $J_{4.0}$,1H, 5-H), 3.44 (s, 2H, Ar-NH_2); ^{13}C NMR: δ 161.99 (4-C), 155.47 (9-C), 145.00 (7-C), 173.01 (2-C), 145.90, 135.85, 130.80, 130.60, 128.80, 127.85, 125.00, 113.99 (aromatic carbons), 103.75 (6-C), 88.13 (10-C), 32.28 (5-C); MS: m/z 383.05 (M^+), 307.1, 289.1, 154.0 (100%), 136.0, 89.2; Anal. Found: C, 55.51; H, 3.83; N, 9.08; Calcd. for $C_{19}H_{14}ClN_3O_2S$: C, 59.45; H, 3.68; N, 10.95%.

7-(4-chlorophenyl)-5-(2-chlorophenyl)-1,5-dihydro-pyrano[2,3-d]pyrimidine-2,4-dione, 3e:

Light orange solid; Yield 53%; mp. 306-308°C; R_f 0.76; UV: λ_{max} nm 284, 348 (π→π*/n →π* of C=O); IR: γ_{max} (cm^{-1}) 3393 (N-H), 1730 (C=O, non-conj.), 1611, 1543 (C=O arom, C-N) 1405, 1255, 1023, 836, 761 (C=C, arom. & bar. acid moieties), 1123, 1077 (C-O-C); ^{1}H NMR: δ 11.96 (s, 1H, NH, 3-H), 11.02 (s, 1H, NH, 1-H), 7.68 (d, $J_{8.4}$, 2H, H-2',6'), 7.47 (d, J8.4, 2H, H-3', 5'), 7.21-7.42 (m, 4H, H-2",3",5",6") 5.98 (d, $J_{3.5}$,1H, 6-H), 4.85 (d, $J_{4.2}$,1H, 5-H); ^{13}C NMR: δ 163.02 (4-C), 155.08 (9-C), 149.63 (7-C), 144.59 (2-C), 140.79, 133.83, 131.88, 130.11, 129.71, 129.37, 128.64, 128.27, 127.68, 125.97 (aromatic carbons), 102.67 (6-C), 85.94 (10-C), 32.44 (5-C); MS: m/z 387.01 (M^+), 289.1, 238.1, 154.0 (100%), 136.0, 89.2, 57.4; Anal. Found: C, 58.33; H, 3.20; N, 7.22; Calcd. for $C_{19}H_{12}Cl_2N_2O_3$: C, 58.33; H, 3.12; N, 7.23%.

7-(4-chlorophenyl)-5-(2-chlorophenyl)-2-thioxo-1,2,3,5-tetrahydro-pyrano[2,3-d]pyrimidine-4-one, 3f:

White solid; Yield 57%; mp. 313-315°C; R_f 0.68; UV: λ_{max} nm 290, 359 (π→π*/n →π* of C=O); IR: γ_{max} (cm^{-1}) 3369 (N-H), 1681 (C=O, non-conj.), 1615, 1568 (C=O arom, C-N) 1411, 1274, 1221, 835, 757 (C=C, arom. & bar. acid moieties), 1134, 1088 (C-O-C); ^{1}H NMR: δ 12.56 (s, 1H, NH, 3-H), 11.71 (s, 1H, NH, 1-H), 7.69 (d, $J_{8.4}$, 2H, H-2',6'), 7.46 (d, $J_{8.4}$, 2H, H-3', 5'), 7.20-7.43 (m, 4H, H-2",3",5",6"), 5.95 (d, $J_{3.5}$,1H, 6-H), 4.75 (d, $J_{4.2}$,1H, 5-H); ^{13}C NMR: δ 163.20 (4-C), 155.80 (9-C), 148.61 (7-C), 174.59 (2-C), 139.80, 133.73, 131.78, 130.10, 129.70, 129.27, 128.75, 128.20, 127.70, 125.51 (aromatic carbons), 102.62 (6-C), 86.15 (10-C), 32.40 (5-C); MS: m/z 403.00 (M^+), 371.3, 289.1, 154.0 (100%), 136.0, 89.2; Anal. Found: C, 56.28; H, 2.90; N, 6.73; Calcd. for $C_{19}H_{12}Cl_2N_2O_2S$: C, 56.59; H, 3.00; N, 6.95%.

5-(2-chlorophenyl)-7-(4-methoxyphenyl)-1,5-dihydro-pyrano[2,3-d]pyrimidine-2,4-dione, 3g:

Brown solid; Yield 60%; mp. 283-285°C; R_f 0.70; UV: λ_{max} nm 285, 350 (π→π*/n →π* of C=O); IR: γ_{max} (cm^{-1}) 3402 (N-H), 1725, 1683 (C=O, non-conj.), 1606 (C=O arom, C-N) 1441, 1307, 1252, 1035, 968, 756 (C=C, arom. & bar. acid moieties), 1145, 1070 (C-O-C); 1H NMR: δ 11.06 (s, 1H, NH, 3-H), 10.02 (s, 1H, NH, 1-H), 7.65 (d, J8.1, 2H, H-2',6'), 7.50 (d, $J_{7.9}$, 2H, H-3', 5'), 7.30-7.41 (m, 4H, H-2",3",5",6"), 5.70 (d, $J_{3.7}$,1H, 6-H), 4.55 (d, $J_{4.4}$,1H, 5-H), 3.49 (s, 3H, Ar-OCH_3); ^{13}C NMR: δ 166.40 (4-C), 153.50 (9-C), 149.60 (7-C), 145.59 (2-C), 160.53, 139.80, 134.50, 130.87, 129.70, 128.75, 127.28, 126.95, 125.99, 113.77 (aromatic carbons), 107.65 (6-C), 86.65 (10-C), 35.44 (5-C), 55.70 (Ar-OCH_3); MS: m/z 382.04 (M^+), 383.0 (100%), 271.0, 255.0, 135.0, 88.3; Anal. Found: C, 62.14; H, 4.00; N, 7.24; Calcd. for $C_{20}H_{15}ClN_2O_4$: C, 62.75; H, 3.95; N, 7.32%.

5-(2-chlorophenyl)-7-(4-methoxyphenyl)-2-thioxo-1,2,3,5-tetrahydro-pyrano[2,3-d]pyrimidin-4-one, 3h:

Light brown solid; Yield 58%; mp. 268-270°C; R_f 0.71; UV:

λ_{max} nm 288, 358 ($\pi\rightarrow\pi^*$/n $\rightarrow\pi^*$ of C=O); IR: γ_{max} (cm^{-1}) 3384 (N-H), 1690 (C=O, non-conj.), 1610, 1556 (C=O arom, C-N) 1420, 1257, 1038, 914, 835, 756 (C=C, arom. & bar. acid moieties), 1132, 1071 (C-O-C); ^{1}H NMR: δ 12.96 (s, 1H, NH, 3-H), 11.92 (s, 1H, NH, 1-H), 7.63 (d, $J_{8.1}$, 2H, H-2',6'), 7.49 (d, $J_{7.8}$, 2H, H-3', 5'), 7.22-7.40 (m, 4H, H-2",3",5",6"), 5.69 (d, J3.7,1H, 6-H), 4.65 (d, J4.4,1H, 5-H); ^{13}C NMR: δ 165.30 (4-C), 156.28 (9-C), 149.65 (7-C), 182.59 (2-C), 160.63, 139.82, 134.60, 131.07, 129.65, 128.77, 127.29, 126.93, 126.10, 113.87 (aromatic carbons), 107.63 (6-C), 87.85 (10-C), 34.44 (5-C), 55.70 (Ar-OCH_3); MS: m/z 398.05 (M^+), 399.05, 307.1, 154 (100%), 136.0, 89.2, 57.4; Anal. Found: C, 60.11; H, 3.76; N, 6.98; Calcd. for $C_{20}H_{15}ClN_2O_3S$: C, 60.22; H, 3.79; N, 7.02%.

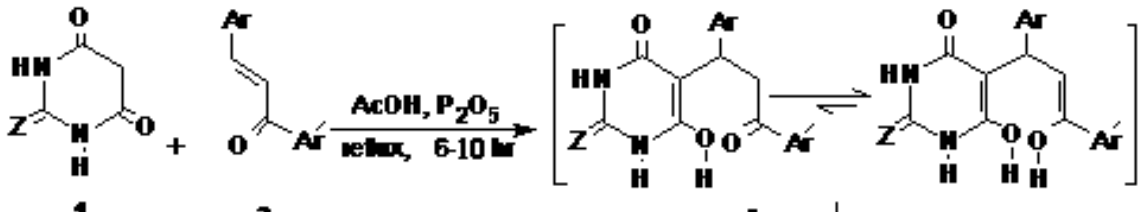
Results and discussion

The Compounds 3a-h have been synthesized from 1 and the corresponding 2a-d in presence of glacial acetic acid and P_2O_5 under refluxing conditions in an analogous manner reported previously (Ahlwalia *et al.,* 1993). The Compounds 3a-h have been characterized on the basis of their UV/Vis, IR, ^{1}H NMR, ^{13}C NMR, mass and elemental analyses. The formation of compounds 3a-h may be explained by the initial formation of a 1:1 adduct (A) followed by cyclocondensation (Scheme 1). The formation of such an adduct has been reported (Kharchenko *et al*., 1976) in the literature.

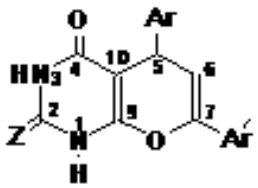
In their UV spectra of compounds 3a-h the observed λ_{max} values agree well to the expected values. The absorption bands in the range 312-286 nm may be assigned to the $\pi\rightarrow\pi^*$ of C=O in these compounds. The weak $n\rightarrow\pi^*$ absorption bands in the cases of these compounds due to C=O were probably masked within the $\pi\rightarrow\pi^*$ absorption range of 312-286 nm.

The IR data of the compounds 3a-h (Table II) showed sharp as well as broad bands in the range (ν_{max}) 3480-3300 cm^{-1} indicating the presence of N-H group. The absorption bands at 1730-1676 cm^{-1} indicate the presence of non-conjugated C=O stretching present in the barbituric acid moieties (Bojarski *et al.*1985). The bands at 1615-1524 cm^{-1} were assigned to C=C of aromatic rings and C=N of the conjugated form of barbituric acid part. Additional bands were observed at 1441-756 cm^{-1} due to these structural units (Bojarski *et al*.,1985).

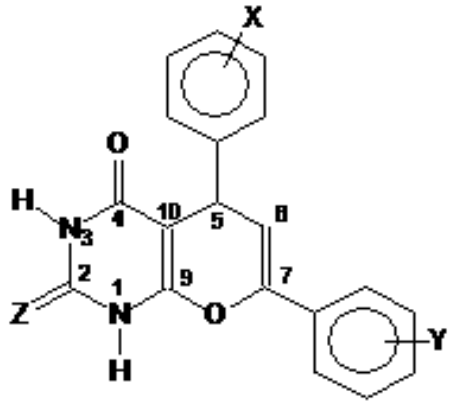
Scheme 1: Synthesis of Pyrano[2,3-d]pyrimidines



Products	Z	Ar	Ar´
3a	O	4-ClC_6H_5	4-ClC_6H_5
3b	S	4-ClC_6H_5	4-ClC_6H_4
3c	O	4-ClC_6H_5	4-$NH_2C_6H_4$
3d	S	4-ClC_6H_5	4-$NH_2C_6H_4$
3e	O	2-ClC_6H_5	4-ClC_6H_4
3f	S	2-ClC_6H_5	4-ClC_6H_4
3g	O	2-ClC_6H_5	4-$CH_3OC_6H_4$
3h	S	2-ClC_6H_5	4-$CH_3OC_6H_4$



3a-h
(1:1 molar ratio)



3a-h

Substituent	3a	3b	3c	3d	3e	3f	3g	3h
X	4-Cl	4-Cl	4-Cl	4-Cl	2-Cl	2-Cl	2-Cl	2-Cl
Y	4-Cl	4-Cl	4-NH_2	4-NH_2	4-Cl	4-Cl	4-OCH_3	4-OCH_3
Z	O	S	O	S	O	S	O	S

Table I. Reaction conditions and analytical data of the compounds 3a-h

Compound	Reflux time (hr)	Reaction temp.(°C)	% C Found (Calcd)	% H Found (Calcd)	%N Found (Calcd)	Mol. formula	MS (m/z)
3a	8	135	58.67 (58.93)	3.14 (3.12)	7.04 (7.23)	$C_{19}H_{12}N_2$ O3Cl_2	386.99
3b	8	140	55.98 (56.59)	3.78 (3.00)	6.25 (6.95)	$C_{19}H_{12}N_2$ O_2Cl_2S	403.02
3c	7	137	60.30 (62.05)	4.33 (3.84)	7.79 (11.43)	$C_{19}H_{14}N_3$ O_3Cl	367.22
3d	6.5	138	55.51 (59.45)	3.83 (3.68)	9.08 (10.95)	$C_{19}H_{14}N_3$ O_2ClS	383.05
3e	6	140	58.33 (58.33)	3.20 (3.12)	7.22 (7.23)	$C_{19}H_{12}N_2$ O_3Cl_2	387.01
3f	6	140	56.28 (56.59)	2.90 (3.00)	6.73 (6.95)	$C_{19}H_{12}N_2$ O_2Cl_2S	403.00
3g	7.5	135	62.14 (62.75)	4.00 (3.95)	7.24 (7.32)	$C_{20}H_{15}N_2$ O_4Cl	382.04
3h	7	136	60.11 (60.22)	3.76 (3.79)	6.98 (7.02)	$C_{20}H_{15}N_2$ O_3 Cl S	398.05

Table II. Physical constants, IR and UV of compounds 3a-h

Compound	m.p. (°C)	Yield (%)	R_f value (CH_3OH: $CHCl_3$, 1:9)	IR, ν_{max} in cm^{-1}					UV, λ_{max} (nm)
				N-H/ NH_2	C=O non-conj.	C=O arom, C-N	C=C (arom. & bar. acid moieties)	C-O-C	$\pi\rightarrow*$, $n\rightarrow\pi*$
3a	267-269	58	0.78	3460	1724, 1682	1610, 1541	1437, 1276, 1244, 1176, 1039, 1016, 970, 819	1120, 1087	288, 474
3b	279-281	33	0.75	3480	1676	1570	1410, 1273, 1238, 1220, 1055, 1012, 955, 914, 829	1136, 1093	295, 497
3c	264-266	30	0.72	3400, 3306	1685	1595, 1534	1400, 1263, 1012, 831, 762	1140, 1091	320
3d	248-250	35	0.65	3395, 3300	1687	1592, 1524	1407, 1310, 1222, 1182, 1013, 827	1133, 1091	301
3e	306-308	53	0.76	3393	1730	1611, 1543	1405, 1255, 1023, 836,761	1123, 1077	284, 348
3f	313-315	57	0.68	3369	1681	1615, 1568	1411, 1274, 1221, 835, 757	1134, 1088	290, 359
3g	283-285	60	0.70	3402	1725, 1683	1606	1441, 1307, 1252, 1035, 968, 756	1145, 1070	285, 350
3h	268-270	58	0.71	3384	1690	1610, 1556	1420, 1257, 1038, 914, 835, 756	1132, 1071	288, 358

The N-H protons at positions 1 and 3 in the compounds 3a-h were strongly deshielded (δ 12.56-10.02) and appeared as singlet in their ^{1}H NMR spectra (Table III). The N-H protons at position 3 in these compounds were found comparatively more deshielded than protons at position 1. In some compounds (3b, 3d, 3f & 3h) more deshielding of the N-H protons were observed due to presence of thiocarbonyl group. This may be attributed to the greater polarizability of sulfur in comparison to oxygen.

The proton at position 6 in 3a-h appeared as a doublet (or broad singlet) due to the vicinal coupling with the proton at position 5. The chemical shifts were observed at δ 6.09-5.69. The 6-H in these compounds gave signals at δ 4.85-4.44 as doublet due to the coupling received from the proton at position 5.

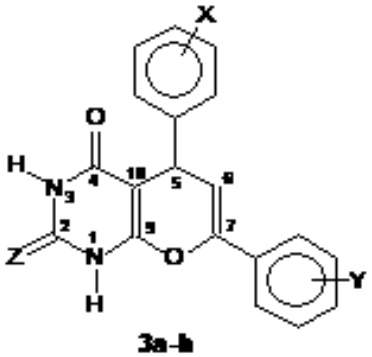
The chemical shifts for the aromatic protons in 3a-h were found in good agreement with the literature values (Silverstein *et al.,* 1991 and Kemp 1991).

The structures of the compounds 3a-h were further confirmed by their ^{13}C NMR spectra (Table IV). The chemical shifts of carbonyl carbon at 4-C were found to be deshielded in the range of δ 166.40-160.89. The chemical shifts of 9-C were also deshielded (δ 156.28-153.23). This value is comparable with the ^{13}C NMR chemical shifts of cyclohexyl methyl ketone (Marr *et al.,* 1965).

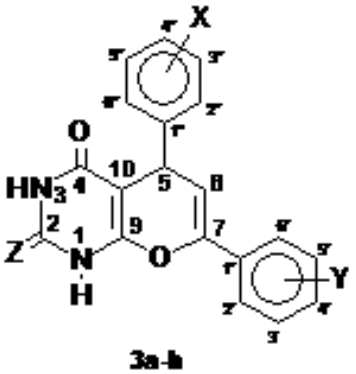
In the compounds 3a, 3c, 3e and 3g, the chemical shifts of carbonyl carbons at 2-C were found to be at δ 145.59-143.22 and are relatively less deshielded due to the resonance of amide functional group. In the compounds 3b, 3d, 3f and 3h,

Table III. ^{1}H NMR spectral data of the compounds 3a-h. [(δ) in ppm]

Compound	3-H	1-H	Aromatic	6-H	5-H	X	Y
3a	11.91 (s,1H,NH)	10.99 (s,1H,NH)	7.69 (d, $J_{8.4}$, 2H, H-2',6') 7.50 (d, $J_{7.8}$, 2H, H-3', 5') 7.29-7.34 (m, 4H, H-2",3",5",6")	6.07 (d,$J_{3.6}$,1H)	4.47 (d,$J_{3.6}$,1H)	.....	.....
3b	12.38 (s,1H, NH)	10.98 (s,1H,NH)	7.74 (d, $J_{8.4}$, 2H, H-2',6') 7.50 (d, $J_{8.4}$, 2H, H-3', 5') 7.31-7.35 (m, 4H, H-2",3",5",6")	6.09 (d,$J_{4.2}$,1H)	4.49 (d,$J_{4.2}$,1H)	.....	.....
3c	11.88 (s,1H, NH)	10.98 (s,1H,NH)	7.72 (d, J_{8}, 2H, H-3", 5") 7.60 (d, $J_{7.2}$, 2H, H-2', 6') 7.30-7.35 (m, 4H, H-2", 3', 5', 6")	5.87 (d,$J_{4.0}$,1H)	4.44 (d,$J_{4.0}$,1H)	.....	3.37 (Ar-NH_2)
3d	12.48 (s,1H, NH)	10.85 (s,1H,NH)	7.70 (d, $J_{8.2}$,2H, H-3", 5") 7.60 (d, $J_{7.4}$, 2H, H-2', 6') 7.30-7.35 (m, 4H, H-2", 3', 5', 6")	5.88 (bs,1H)	4.49 (d,$J_{4.0}$,1H)	.....	3.44 (Ar-NH_2)
3e	11.96 (s,1H, NH)	11.02 (s,1H,NH)	7.68 (d, $J_{8.4}$, 2H, H-2',6') 7.47 (d, $J_{8.4}$, 2H, H-3', 5') 7.21-7.42 (m, 4H, H-2",3",5",6")	5.98 (d,$J_{4.2}$,1H)	4.85 (d,$J_{4.2}$,1H)	.....	.....
3f	12.56 (s,1H, NH)	11.71 (s,1H,NH)	7.69 (d, $J_{8.4}$, 2H, H-2',6') 7.46 (d, $J_{8.4}$, 2H, H-3', 5') 7.20-7.43 (m, 4H, H-2",3",5",6")	5.95 (d,$J_{4.1}$,1H)	4.75 (d,$J_{4.1}$,1H)	.....	.....
3g	11.06 (s,1H, NH)	10.02 (s,1H,NH)	7.65 (d, $J_{8.1}$, 2H, H-2',6') 7.50 (d, $J_{7.9}$, 2H, H-3', 5') 7.30-7.41 (m, 4H, H-2",3",5",6")	5.70 (d,$J_{4.0}$,1H)	4.55 (d,$J_{4.0}$,1H)	.....	3.49 (Ar-OCH_3)
3h	12.96 (s,1H, NH)	11.92 (s,1H,NH)	7.63 (d, $J_{8.1}$, 2H, H-2',6') 7.49 (d, $J_{7.8}$, 2H, H-3', 5') 7.22-7.40 (m, 4H, H-2",3",5",6")	5.69 (d,$J_{4.1}$,1H)	4.65 (d,$J_{4.1}$,1H)	.....	3.50 (Ar-OCH_3)



3a-h



3a-h

Table IV. ^{13}C NMR spectral data of the compounds 3a-h. [(δ) in ppm]

Compound	3-C	9-C	7-C	2-C	Aromatic carbons	6-C	10-C	5-C	X	Y
3a	163.21	154.35	144.18	143.22	133.77-125.92	104.64	87.01	34.36	…	…
3b	160.89	153.68	144.08	173.78	142.58- 125.99	104.18	92.03	34.29	…	…
3c	161.96	153.23	145.91	143.77	145.78-115.75	103.76	87.45	31.85	…	…
3d	161.99	155.47	145.00	173.01	145.90-113.99	103.75	88.13	32.28	…	…
3e	163.02	155.08	149.63	144.59	140.79-125.97	102.67	85.94	32.44	…	…
3f	163.20	155.80	148.61	174.59	139.80-125.51	102.62	86.15	32.40	…	…
3g	166.40	153.50	149.60	145.59	160.53-113.77	107.65	86.65	35.44	…	55.70 (Ar-OCH_3)
3h	165.30	156.28	149.65	182.59	160.63-113.87	107.63	87.85	34.44	…	55.70 (Ar-OCH_3)

the chemical shifts of thioxo carbon at 2-C were found to be at δ 182.59-173.01. This explains that the replacement of a carbonyl group by a thiocarbonyl group results in a down-field shift (Otto *et al*., 1976, Ahmed *et al.,* 2005).

The chemical shift values for 7-C and 6-C in these compounds were observed at δ 149.65-144.08 and δ 107.65-103.75 respectively. The 10-C of the compounds showed chemical shift values at δ 92.03-86.15 which were comparable to the earlier report (Bojarski *et al.*1985) of the ^{13}C NMR spectral data of the monosubstituted barbiturates at 10-C. The chemical shift values for 5-C in these compounds were observed at δ 35.44-31.85.

The ^{13}C NMR chemical shifts for the carbons of aromatic rings were assigned on the basis of a correlation chart available in the literature (Levy *et al*., 1972).

The compounds 3a-h showed peaks for their respective molecular ions (M^+) in their high resolution mass spectra at m/z 386.99 (67%), 403.02 (20.7%), 367.22 (5%), 383.05 (10.0%), 387.01 (47.4%), 403.00 (13.7%), 382.04 (20.0%) and 398.05 (7.0%) respectively. The isotopic pattern for Cl atom ($^{35}Cl/^{37}Cl$, 3:1) was observed in the molecular mass of the compounds 3a-h.

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