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Bangladesh J. Sci. Ind. Res. **52(2)**, 115-124, 2017

BANGLADESH JOURNAL OF SCIENTIFIC AND INDUSTRIAL RESEARCH

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One step cyclocondensation of (thio) barbituric acid with chalcones in glacial acetic acid and phosphorous pentoxide, Part-II.

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Abstract

A number of 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-g**) 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-g** have been determined by UV, IR, 1H NMR, 13C NMR, mass spectral data and elemental analyses. The compounds **3a-g** do not seem to be available in the literature.

Keywords: Arylideneacetophenone; Barbituric acid; Thiobarbituric acid; Cyclocondensation

Introduction

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 compound 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; 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; Rahman *et al.,* 2013; Akhter *et al.,* 2016) on the synthesis of barbituric acid and thio-barbituric acid derivatives, we report herein syntheses of 5, 7-diaryl-1,5-dihydro - pyrano [2, 3-*d*] pyrimidin-2, 4-diones (3b, 3d & 3e) and 5, 7-diaryl-2-thioxo - 1, 2, 3, 5-tetrahydro- pyrano [2, 3-*d*] pyrimidin -4-ones) (3a, 3c, 3f & 3g) by selecting a number of arylideneacetophenones (2a-d) as the α,β-unsaturated carbonyl system having different substituents on the aromatic

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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-g 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 was used as a reference. All the compounds gave expected C, H and N analyses. 3-(2-methoxyphenyl)-1-(4-methylphenyl)-propenone **2a**, 3-(2-methoxyphenyl)-1-(4-chlorophenyl)-propenone **2b**, 3-(4-methylphenyl)-1-phenyl-propenone **2c** and 3-(4-methylphenyl)-1-(4-nitrophenyl)-propenone **2d** were prepared from the reactions of corresponding substituted aldehydes and substituted acetophenones by following a literature method (Furniss *et al*., 1978) with modification 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 reflux condenser and a drying tube. The reaction mixture was refluxed at 130-140°C for 6-10 hours and the course of the reaction was followed by TLC on silica gel plates. 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-(2-Methoxyphenyl)-2-thioxo-7-*p*-tolyl-1,2,3,5-tetrahydro-pyrano[2,3-*d*]pyrimidin-4-one, 3a: Light brown solid; Yield 46%; mp. 230-232^{0}C; R_f 0.68 ($CHCl_3$:Pet-ether =1:4); UV: λ_{max} nm 301 ($\pi\rightarrow\pi^*$/$n\rightarrow\pi^*$ of C=O); IR: γ_{max} (cm^{-1}) 3451 (N-H), 1677 (C=O, non-conj.), 1636, 1562 (C=O arom, C-N) 1463, 1364, 1274, 1218, 1189, 1049, 1028, 949, 912, 860, 814 (C=C, arom. & bar. acid moieties), 1137 (C-O-C); ^{1}H NMR: δ 12.30 (s, 1H, N<u>H</u>, 3-H), 12.05 (s, 1H, N<u>H</u>, 1-H), 7.60 (d, $J_{8.0}$, 2H, H-2′,6′), 7.22 (d, $J_{8.0}$, 2H, H-3′, 5′), 6.84-7.18 (m, 4H, H-2″,3″,5″,6″), 5.93 (d, $J_{4.5}$,1H, 6-H), 4.40 (d, $J_{4.5}$,1H, 5-H), 3.70 (s, 3H, Ar-OC<u>H</u>$_3$), 2.39 (s, 3H, Ar-C<u>H</u>$_3$); ^{13}C NMR: δ 160.96 (4-C), 158.07 (9-C), 153.59 (7-C), 173.70 (2-C), 144.94, 138.79, 136.03, 129.15, 128.85, 128.49, 124.10, 113.80 (aromatic carbons), 103.26 (6-C), 92.92 (10-C), 33.91 (5-C), 55.07 (Ar-O<u>C</u>H$_3$), 20.79 (Ar-<u>C</u>H$_3$); MS: m/z 378.14 (M^+), 307.3, 289.07, 274.89, 154.1 (100%), 136.2, 89.3; Anal. Found: C, 66.55; H, 4.64; N, 7.44; Calcd. for $C_{21}H_{18}N_2O_3S$: C, 66.65; H, 4.79; N, 7.40%.

5-(2-Methoxyphenyl)-7-*p*-tolyl-1,5-dihydro-pyrano[2,3-*d*]pyrimidine-2,4-dione, 3b: Brown solid; Yield 43%; mp. 204-206^{0}C; R_f 0.68 ($CHCl_3$:Pet-ether =1:4); UV: λ_{max} nm 289 ($\pi\rightarrow\pi^*$/$n\rightarrow\pi^*$ of C=O); IR: γ_{max} (cm^{-1}) 3443 (N-H), 1690 (C=O, non-conj.), 1640, 1599, 1497 (C=O arom, C-N) 1462, 1353, 1186, 1028, 968, 819, 755 (C=C, arom. & bar. acid moieties), 1116 (C-O-C); ^{1}H NMR: δ 10.80 (s, 1H, N<u>H</u>, 3-H), 10.35 (s, 1H, N<u>H</u>, 1-H), 7.55 (d, $J_{8.0}$, 2H, H-2′, 6′), 7.20 (d, $J_{8.0}$, 2H, H-3, 5), 6.80-7.19 (m, 4H, H-2″, 3″, 5″, 6″), 5.99 (d, $J_{4.2'}$,1H, 6-H), 4.45 (d, $J_{4.2'}$,1H, 5-H), 3.71 (s, 3H, Ar-OC<u>H</u>$_3$), 2.40 (s, 3H, Ar-C<u>H</u>$_3$); ^{13}C NMR: δ 163.36 (4-C), 154.35 (9-C), 144.28 (7-C), 143.42 (2-C), 144.04, 138.90, 136.12, 129.35, 128.60, 128.21, 123.81, 113.15 (aromatic carbons), 104.26 (6-C), 92.82 (10-C), 34.01 (5-C), 55.71 (Ar-O<u>C</u>H$_3$), 20.80 (Ar-<u>C</u>H$_3$); MS: m/z 362.20 (M^+), 307.11, 289.3, 154.0 (100%), 136.2, 89.1; Anal. Found: C, 69.50; H, 5.00; N, 7.63; Calcd. for $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.01; N, 7.73%.

7-(4-Chlorophenyl)-5-(2-methoxyphenyl)-2-thioxo-1,2,3,5-tetrahydro-pyrano[2,3-*d*]pyrimidine-4-one, 3c: Light purple solid; Yield 41%; mp. 244-246^{o}C; R_f 0.73 ($CHCl_3$:Pet-ether =2:3); UV: λ_{max} nm 431, 300 ($\pi\rightarrow\pi^*$/$n\rightarrow$* of C=O); IR: γ_{max} (cm^{-1}) 3446 (N-H), 1680 (C=O, non-conj.), 1631, 1589, 1510 (C=O arom, C-N) 1461, 1251, 1178, 1012, 829 (C=C, arom. & bar. acid moieties), 1131, 1092 (C-O-C); ^{1}H NMR: δ 12.35 (s, 1H, N<u>H</u>, 3-H), 12.00 (s, 1H, N<u>H</u>, 1-H), 7.70 (d, $J_{8.0}$, 2H, H-2′,6′), 7.55 (d, $J_{8.0}$, 2H, H-3′, 5′), 6.98-7.20 (m, 4H, H-2″,3″,5″,6″), 5.88 (d, $J_{4.4'}$,1H, 6-H), 4.49 (d, $J_{4.4'}$,1H, 5-H), 3.69 (s, 3H, Ar-OC<u>H</u>$_3$); ^{13}C NMR: δ 161.96 (4-C), 155.43 (9-C), 145.01 (7-C), 173.70 (2-C), 145.92,

139.44, 132.90, 130.12, 129.77, 128.55, 128.22, 123.31, 114.10 (aromatic carbons), 103.72 (6-C), 88.45 (10-C), 32.85 (5-C), 56.10 (Ar-O<u>C</u>H_3); MS: m/z 398.06 (M^+), 307.6, 289.1, 154.1 (100%), 136.0, 89.2; Anal. Found: C, 60.30; H, 3.69; N, 7.09; Calcd. for $C_{20}H_{15}N_2O_3ClS$: C, 60.22; H, 3.79; N, 7.02%.

7-(4-Chlorophenyl)-5-(2-methoxyphenyl)-1,5-dihydro-pyrano[2,3-*d*]pyrimidine-2,4-dione, 3d: Brown solid; Yield 38%; mp. 216-218^{0}C; R_f 0.67 ($CHCl_3$:Pet-ether =2:3); UV:

λ_{max} nm 293 ($\pi\rightarrow\pi^*/n\rightarrow\pi^*$ of C=O); IR: γ_{max} (cm^{-1}) 3463 (N-H), 1691 (C=O, non-conj.), 1630, 1589, 1491 (C=O arom, C-N) 1250, 1181, 1012, 971, 829, 760 (C=C, arom. & bar. acid moieties), 1092 (C-O-C); ^{1}H NMR: δ 10.95 (s, 1H, N<u>H</u>, 3-H), 10.35 (s, 1H, N<u>H</u>, 1-H), 7.69 (d, $J_{8.0}$, 2H, H-2′,6′), 7.52 (d, $J_{8.0}$, 2H, H-3′, 5’), 6.95-7.22 (m, 4H, H-2″,3″,5″,6″), 5.91 (d, $J_{4.1}$,1H, 6-H), 4.45 (d, $J_{4.1}$,1H, 5-H), 3.70 (s, 3H, Ar-OC<u>H</u>$_3$); ^{13}C NMR: δ 163.10 (4-C), 155.41 (9-C), 145.91 (7-C), 143.70 (2-C), 144.44, 132.71, 130.11, 129.67, 128.53, 128.12, 123.21, 114.00 (aromatic carbons), 103.90 (6-C), 89.35 (10-C), 32.82 (5-C), 56.15 (Ar-O<u>C</u>H_3); MS: m/z 382.19 (M^+), 307.2, 289.0, 154.0 (100%), 136.1, 89.2; Anal. Found: C, 62.70; H, 3.89; N, 7.22; Calcd. for $C_{20}H_{15}N_2O_4Cl$: C, 62.75; H, 3.95; N, 7.32%.

7-Phenyl-5-*p*-tolyl--1,5-dihydro-pyrano[2,3-*d*]pyrimidine-2,4-dione, 3e: Brown solid; Yield 51%; mp. 246-248^{0}C; R_f 0.68 (Neat $CHCl_3$); UV: λ_{max} nm 315 ($\pi\rightarrow\pi^*/n\rightarrow\pi^*$ of C=O); IR: γ_{max} (cm^{-1}) 3434 (N-H), 1699 (C=O, non-conj.), 1631, 1530 (C=O arom, C-N) 1446, 1279, 1251, 1038, 917, 818, 765 (C=C, arom. & bar. acid moieties), 1118 (C-O-C); ^{1}H NMR: δ 10.93 (s, 1H, N<u>H</u>, 3-H), 10.42 (s, 1H, N<u>H</u>, 1-H), 7.68 (d, $J_{8.2}$, 2H, H-2′,6′), 7.39 (d, $J_{8.2}$, 2H, H-3′, 5′), 7.09-7.14 (m, 5H, H-2″,3″,4″,5″,6″) 5.98 (bs,1H, 6-H), 4.41 (bs,1H, 5-H), 2.24 (s, 3H, Ar-C<u>H</u>$_3$); ^{13}C NMR: δ 163.02 (4-C), 155.08 (9-C), 149.63 (7-C), 144.59 (2-C), 139.79, 135.83, 131.88, 130.11, 129.71, 128.27, 127.68, 125.97 (aromatic carbons), 102.67 (6-C), 85.94 (10-C), 32.44 (5-C), 21.13 (Ar-<u>C</u>H_3); MS: m/z 332.25 (M^+), 289.12, 238.11, 154.0 (100%), 136.0, 89.3, 57.2; Anal. Found: C, 72.33; H, 4.70; N, 8.40; Calcd. for $C_{20}H_{16}N_2O_3$: C, 72.28; H, 4.85; N, 8.43%.

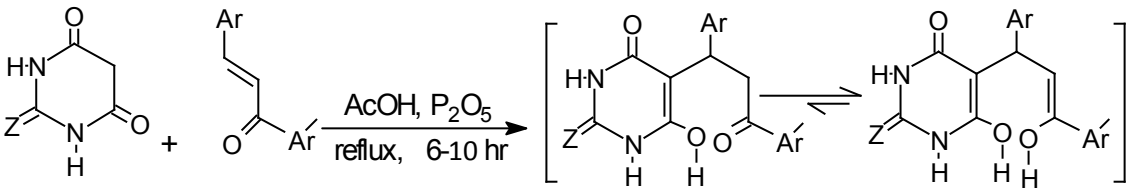
7-Phenyl-2-thioxo-5-*p*-tolyl-1,2,3,5-tetrahydro-pyrano[2,3-*d*]pyrimidin-4-one, 3f: Brown solid; Yield 55%; mp. 267-269^{0}C; R_f 0.74 (Neat $CHCl_3$); UV: λ_{max} nm 318, 209 ($\pi\pi^*/n\rightarrow\pi^*$ of C=O); IR: γ_{max} (cm^{-1}) 3400 (N-H), 1700, 1650 (C=O, non-conj.), 1590, 1555 (C=O arom, C-N) 1430, 1320, 1215, 1180, 1030, 1005, 810 (C=C, arom. & bar. acid moieties), 1131, 1078 (C-O-C); ^{1}H NMR: δ 12.66 (s, 1H, N<u>H</u>, 3-H), 12.05 (s, 1H, N<u>H</u>, 1-H), 7.70 (d, $J_{8.1}$, 2H, H-2′,6′), 7.42 (d, $J_{8.1}$, 2H, H-3′, 5′), 7.02-7.19 (m, 5H, H-2″,3″,4″,5″,6″), 5.95 (bs,1H, 6-H), 4.60 (bs,1H, 5-H), 2.26 (s, 3H, Ar-C<u>H</u>$_3$); ^{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, 128.75, 127.70, 125.51 (aromatic carbons), 102.62 (6-C), 86.15 (10-C), 32.40 (5-C), 20.97 (Ar-<u>C</u>H_3); MS: m/z 348.12 (M^+), 289.33, 154.0 (100%), 136.2, 89.0; Anal. Found: C, 68.78; H, 4.90; N, 8.03; Calcd. for $C_{20}H_{16}N_2O_2S$: C, 68.94; H, 4.63; N, 8.04%.

7-(4-Nitrophenyl)-2-thioxo-5-*p*-tolyl-1,2,3,5-tetrahydro-pyrano[2,3-*d*]pyrimidin-4-one, 3g: Reddish brown solid; Yield 58%; mp. 232-234^{0}C; R_f 0.66 ($CHCl_3$:Pet-ether =4:1); UV: λ_{max} nm 335, 213 ($\pi\rightarrow\pi^*/n\rightarrow\pi^*$ of C=O); IR: γ_{max} (cm^{-1}) 3446 (N-H), 1665 (C=O, non-conj.), 1598, 1518 (C=O arom, C-N) 1345, 1206, 1032, 853, 812, 751 (C=C, arom. & bar. acid moieties), 1151 (C-O-C); ^{1}H NMR: δ 12.39 (s, 1H, N<u>H</u>, 3-H), 12.15 (s, 1H, N<u>H</u>, 1-H), 8.30 (d, $J_{7.9}$, 2H, H-2′,6′), 7.85 (d, $J_{7.9}$, 2H, H-3′, 5′), 6.98-7.29 (m, 4H, H-2″,3″,5″,6″), 5.99 (d, $J_{3.9}$,1H, 6-H), 4.50 (d, $J_{3.9}$,1H, 5-H), 2.35 (s, 3H, Ar-C<u>H</u>$_3$); ^{13}C NMR: δ 165.40 (4-C), 154.50 (9-C), 148.60 (7-C), 175.59 (2-C), 149.53, 142.80, 134.50, 130.87, 129.70, 128.75, 127.28, 123.77 (aromatic carbons), 105.65 (6-C), 89.65 (10-C), 34.44 (5-C), 21.70 (Ar-<u>C</u>H_3); MS: m/z 393.22 (M^+), 383.0 (100%), 271.0, 256.0, 135.0, 88.4; Anal. Found: C, 61.14; H, 3.98; N, 10.64; Calcd. for $C_{20}H_{15}N_3O_4S$: C, 61.06; H, 3.84; N, 10.68%.

Results and discussion

The Compounds **3a-g** 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-g** 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-g** 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.

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



Products	Ar	Ar´	Z
3a	2-$CH_3OC_6H_5$	4-$CH_3C_6H_5$	S
3b	2-$CH_3OC_6H_5$	4-$CH_3C_6H_4$	O
3c	2-$CH_3OC_6H_5$	4-ClC_6H_4	S
3d	2-$CH_3OC_6H_5$	4-ClC_6H_4	O
3e	4-$CH_3C_6H_5$	4-C_6H_5	O
3f	4-$CH_3C_6H_5$	4-C_6H_5	S
3g	4-$CH_3C_6H_5$	4-$O_2NC_6H_4$	S

(1:1 molarratio)

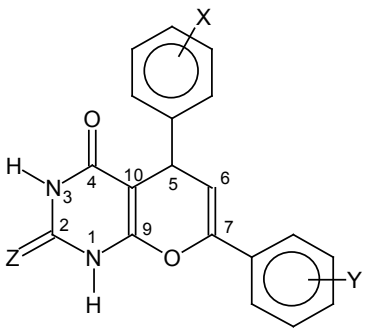
Table I. Reaction conditions and analytical data of the compounds 3a-g

Compound	Reflux time (hr)	Reaction temp.(^oC)	% C Found (Calcd)	% H Found (Calcd)	%N Found (Calcd)	Mol. formula	MS (m/z)
3a	7	130	66.55 (66.65)	4.64 (4.79)	7.44 (7.40)	$C_{21}H_{18}N_2O_3S$	378.14
3b	8	140	69.50 (69.60)	5.00 (5.01)	7.63 (7.73)	$C_{21}H_{18}N_2O_4$	362.20
3c	7.5	139	60.30 (60.22)	3.69 (3.79)	7.09 (7.02)	$C_{20}H_{15}N_2O_3ClS$	398.06
3d	6.5	136	62.70 (62.75)	3.89 (3.95)	7.22 (7.32)	$C_{20}H_{15}N_2O_4Cl$	382.19
3e	6.5	140	72.33 (72.28)	4.70 (4.85)	8.40 (8.43)	$C_{20}H_{16}N_2O_3$	332.25
3f	10	130	68.78 (68.94)	4.90 (4.63)	8.03 (8.04)	$C_{20}H_{16}N_2O_2S$	348.12
3g	6	135	61.14 (61.06)	3.98 (3.84)	10.64 (10.68)	$C_{20}H_{15}N_3O_4S$	393.22

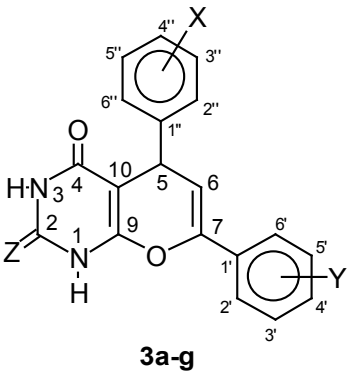
In their UV spectra of compounds **3a-g** the observed λ_{max} values agree well to the expected values. The absorption bands in the range 431-209 nm may be assigned to the $\pi\rightarrow\pi^*$ of C=O in these compounds. The weak $n\rightarrow\pi^*$ absorption bands in the cases of these compounds due to C=O were probably masked within the $\pi\rightarrow\pi^*$ absorption range.

Table II. Physical Constants, IR and UV of compounds 3a-g

Compou nd	m.p. (^{o}C)	Yield (%)	R_f value	IR, ν_{max} in cm^{-1}					UV, λ_{max} (nm)
				N-H	C=O non-conj.	C=O arom, C-N	C=C (arom. & bar. acid moieties)	C-O-C	$\pi\rightarrow\pi^*$, $n\rightarrow\pi^*$
3a	230-232	46	0.68 ($CHCl_3$: Pet-ether = 1:4)	3451	1677	1636, 1562	1463, 1364, 1274, 1218, 1189, 1049, 1028, 949, 912, 860, 814	1137	301
3b	204-206	43	0.68 ($CHCl_3$: Pet-ether = 1:4)	3443	1690	1640, 1599	1462, 1353, 1186, 1028, 968, 819, 755	1116	289
3c	244-246	41	0.73 ($CHCl_3$: Pet-ether = 2:3)	3446	1680	1631, 1589	1461, 1251, 1178, 1012, 829	1131, 1092	431, 300
3d	216-218	38	0.67 ($CHCl_3$: Pet-ether = 2:3)	3463	1691	1630, 1589	1250, 1181, 1012, 971, 829, 760	1092	293
3e	246-248	51	0.68 (Neat $CHCl_3$)	3434	1699	1631, 1530	1446, 1279, 1251, 1038, 917, 818, 765	1118	315
3f	267-269	55	0.74 (Neat $CHCl_3$)	3400	1700, 1650	1590, 1555	1430, 1320, 1215, 1180, 1030, 1005, 810	1131, 1078	318, 209
3g	232-234	58	0.66 ($CHCl_3$: Pet-ether = 4:1)	3446	1665	1598, 1518	1345, 1206, 1032, 853, 812, 751	1151	335, 213



3a-g



3a-g

The IR data of the compounds **3a-g** (Table 2) showed sharp as well as broad bands in the range (ν_{max}) 3463-3400 cm^{-1} indicating the presence of N-H group. The absorption bands at 1700-1650 cm^{-1} indicate the presence of non-conjugated C=O stretching including the barbituric acid moieties (Bojarski *et al*., 1985). The bands at

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

Compound	3-H	1-H	Aromatic	6-H	5-H	X	Y
3a	12.30 (s,1H,NH)	12.05 (s,1H,NH)	7.60 (d, $J_{8.0}$, 2H, H-2',6') 7.22 (d, $J_{8.0}$, 2H, H-3', 5') 6.84-7.18 (m, 4H, H-2",3",5",6")	5.93 (d,$J_{4.5}$,1H)	4.40 (d,$J_{4.5}$,1H)	3.70 (Ar-OCH_3)	2.39 (Ar-CH_3)
3b	10.80 (s,1H, NH)	10.35 (s,1H,NH)	7.55 (d, $J_{8.0}$, 2H, H-2',6') 7.20 (d, $J_{8.0}$, 2H, H-3', 5') 6.80-7.19 (m, 4H, H-2",3",5",6")	5.99 (d,$J_{4.2}$,1H)	4.45 (d,$J_{4.2}$,1H)	3.71 (Ar-OCH_3)	2.40 (Ar-CH_3)
3c	12.35 (s,1H, NH)	12.00 (s,1H,NH)	7.70 (d, $J_{8.0}$, 2H, H-3", 5") 7.55 (d, $J_{8.0}$, 2H, H-2', 6') 6.98-7.20 (m, 4H, H-2", 3', 5', 6")	5.88 (d,$J_{4.4}$,1H)	4.49 (d,$J_{4.4}$,1H)	3.69 (Ar-OCH_3)	…
3d	10.95 (s,1H, NH)	10.35 (s,1H,NH)	7.69 (d, $J_{8.0}$,2H, H-3", 5") 7.52 (d, $J_{8.0}$, 2H, H-2', 6') 6.95-7.22 (m, 4H, H-2", 3', 5', 6")	5.91 (d,$J_{4.1}$,1H)	4.45 (d,$J_{4.1}$,1H)	3.70 (Ar-OCH_3)	…
3e	10.93 (s,1H, NH)	10.42 (s,1H,NH)	7.68 (d, $J_{8.2}$, 2H, H-2',6') 7.39 (d, $J_{8.2}$, 2H, H-3', 5') 7.09-7.14 (m, 5H, H-2",3", 4",5",6")	5.98 (bs,1H)	4.41 (bs,1H)	2.24 (Ar-CH_3)	…
3f	12.66 (s,1H, NH)	12.05 (s,1H,NH)	7.70 (d, $J_{8.3}$, 2H, H-2',6') 7.42 (d, $J_{8.3}$, 2H, H-3', 5') 7.02-7.19 (m, 5H, H-2",3", 4",5",6")	5.95 (bs,1H)	4.60 (bs,1H)	2.26 (Ar-CH_3)	…
3g	12.39 (s,1H, NH)	12.15 (s,1H,NH)	8.30 (d, $J_{7.9}$, 2H, H-2',6') 7.85 (d, $J_{7.9}$, 2H, H-3', 5') 6.98-7.29 (m, 4H, H-2",3",5",6")	5.99 (d,$J_{3.9}$,1H)	4.55 (d,$J_{3.9}$,1H)	2.35 (Ar-CH_3)	…

1640-1491 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 1463-751 cm^{-1} due to these structural units (Bojarski *et al*., 1985) including bands for C-O-C at 1151-1078 cm^{-1}.

The N-H protons at positions 1 and 3 in the compounds **3a-g** were strongly deshielded (δ 12.66-10.35) and appeared as singlet in their ^{1}H NMR spectra (Table 3). The N-H protons at position 3 in these compounds were found comparatively more deshielded than protons at position 1. In some compounds (**3a**, **3c, 3f** & **3g**) 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-g** 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 5.99-5.88. The 5-H in these compounds gave signals at δ 4.60-4.40 as doublet due to the coupling received from the proton at position 6. The chemical shifts for the aromatic protons in **3a-g** were found in good agreement with the literature values (Silverstein *et al*., 1991; Kemp 1991).

The structures of the compounds **3a-g** were further confirmed by their ^{13}C NMR spectra (Table IV). The chemical shifts of carbonyl carbons at 4-C were found to be deshielded in the range of δ 165.40-160.96. The chemical shifts of 9-C were also deshielded (δ 158.07-154.35). This value is comparable with the ^{13}C NMR chemical shifts of cyclohexyl methyl ketone (Marr *et al*., 1965).

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

Compound	4-C	9-C	7-C	2-C	Aromatic carbons	6-C	10-C	5-C	X	Y
3a	160.96	158.07	153.59	173.70	144.94-113.80	103.26	92.92	33.91	55.07 (Ar-O<u>C</u>H₃)	20.79 (Ar-<u>C</u>H₃)
3b	163.36	154.35	144.18	143.42	144.04-113.15	104.26	92.82	34.01	55.71 (Ar-O<u>C</u>H₃)	20.80 (Ar-<u>C</u>H₃)
3c	161.96	155.43	145.01	173.70	145.92-114.10	103.72	88.45	32.85	56.10 (Ar-O<u>C</u>H₃)	…
3d	163.10	155.41	145.91	143.70	144.44-114.00	103.90	89.35	32.82	56.15 (Ar-O<u>C</u>H₃)	…
3e	163.02	155.08	149.63	144.59	139.79-125.97	102.67	85.94	32.44	21.13 (Ar-<u>C</u>H₃)	…
3f	163.20	155.80	148.61	174.59	139.80-125.51	102.62	86.15	32.40	20.97 (Ar-<u>C</u>H₃)	…
3g	165.40	154.50	148.60	175.59	149.53-123.77	105.65	89.65	34.44	21.70 (Ar-<u>C</u>H₃)	…

The chemical shifts of carbonyl carbons at 2-C in the compounds **3b**, **3d** and **3e** were found to be at δ 144.59-143.42 and are relatively less deshielded due to the resonance of amide functional group. The chemical shifts of thioxo carbon at 2-C in the compounds **3a**, **3c**, **3f** and **3g** were found to be at δ 175.59-173.70. This explains that the replacement of a carbonyl group by a thiocarbonyl group results in a downfield 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 153.59-144.18 and δ 105.65-102.62 respectively. The 10-C of the compounds showed chemical shift values at δ 92.92-85.94 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 34.44-32.40.

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-g** showed peaks for their respective molecular ions (M^+) in their high resolution mass spectra at m/z 378.14 (47%), 362.20 (10.7%), 398.06 (15%), 382.19 (13.0%), 332.25 (40.5%), 348.12 (10.3%) and 393.22 (9.0%) respectively. The isotopic pattern for Cl atom ($^{35}Cl/^{37}Cl$, 3:1) was observed in the molecular mass of the compounds **3c** and **3d**.

Acknowledgement

Authors gratefully acknowledge the help of Prof. Teruo Shinmyozu, Department of Molecular Chemistry, Kyushu University, Fukuoka, Japan for recording proton and carbon-13 nmr spectra, mass spectra and determining elemental analyses of the compounds.

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Received: 28 May 2016; Revised: 5 June 2016 ; Accepted: 28 December 2016.