CHAPTER-2

DESIGN AND SYNTHESIS OF N-SUBSTITUTED ACRIDONES AND C-5 SUBSTITUTED BARBITURIC ACIDS

INTRODUCTION

Drug resistance (Multiple Drug Resistance, MDR)\(^1,2\) which emanates due to the decrease in the intracellular drug concentration is a great hurdle in the successful practice of chemotherapy of various diseases like cancer, AIDS and even malaria. It is becoming a matter of great urgency to develop such chemical entities (MDR reversers) which could maintain the chemotherapeutic level of the drug inside the cell by blocking P-glycoprotein (P-gp, transporter protein of the ABC family of drug transporters)\(^3,4\) mediated efflux of the drug. Based upon the involvement of P-gp, ATP and Mg\(^{2+}\) \(^5,7\) in the working of efflux pump, it was planned to adopt a multi target approach for developing MDR modulators.

The planar, heterocyclic and considerably hydrophobic nature of acridone, making it to interact with several biomolecular targets, led to the investigations of a number of acridone derivatives for their anti-tumor\(^8,10\) antiprotozoan\(^11,13\) and anti-viral\(^14\) properties. Some of the acridone derivatives have also been studied for multi drug resistance (MDR) modulating\(^8,15,16\) properties amongst which GF 120918 was chosen for phase I clinical trials. Here, taking acridone as the heterocyclic moiety (present as the central core of a number of anti-tumor agents\(^8\) and introducing hydroxylamine fragment (active part of MDR modulators\(^17\)) at its N-10 position, molecules A, B, and C (chart 1) have been designed, synthesized and investigated for their interactions with P-gp, ATP and Mg\(^{2+}\).

Moreover, the barbiturates, having the pyrimidine nucleus as the basic skeleton, are biologically important molecules, used to treat anxiety, insomnia, seizure disorders, migraine and in surgery as general anesthetics. The acceptability of pyrimidine moiety in the biological systems and structural features of 5-fluorouracil (anti cancer agent) and MDR modulators prompted us to design and synthesize barbituric acid based MDR modulators D (chart 1) carrying a number of H-donor/acceptor sites. These molecules were also investigated for their interactions with P-gp, ATP and Mg\(^{2+}\) (MDR modulating properties).

A mixture 2-chlorobenzoic acid, aniline/antranillic acid/o-chloroaniline, powdered copper oxide (CuO), potassium carbonate (K₂CO₃) in isomyl alcohol was heated at 160 °C for 10 h. After cooling the mixture, alcohol was evaporated under vacuum and the residue was dissolved in hot water and acidified with conc. HCl. The precipitates formed were washed with hot water and dissolved in ethyl acetate and the solution was dried over sodium sulphate (Na₂SO₄) and then evaporated to get desired product (1-3) which further undergoes cyclization in the presence of conc. H₂SO₄ to give acridone 4 (88%, mp 350 °C; lit. mp 348-252 °C), 5 (85%, mp >300 °C), 6 (80%, mp >300 °C) (scheme 1).

The treatment of acridone 4 (1mmol) with sodium hydride (NaH) (1.2 mmol) in dimethyl sulphoxide (DMSO) was followed by stirring with epichlorohydrin (1.2 mmol) at 60-70 °C for 17-18 h. After usual work up of the reaction, the crude residue was purified by column chromatography using hexane-ethyl acetate as eluents to get compound 7 as brownish solid in a yield of 47%, mp 180-182 °C and FAB mass m/z 252 [M⁺+1]. ¹H NMR spectrum of compound 7 showed 1H doublet at δ 2.67-2.70 (H₃), 1H doublet at δ 2.92-2.95 (H₄), 1H multiplet at δ 3.48-3.52 (H₅),
two 1H double doublets at δ 4.37-4.44 and δ 4.83-4.89 (H₄ and H₅ respectively). Three 6H multiplets at δ 7.26-7.33, δ 7.55-7.60, δ 7.68-7.75 and a 2H double doublet at δ 8.51-8.54 correspond to aromatic protons. These signals showed that the oxiranyl methyl part of epichlorohydrin has been incorporated in the acridone moiety. Its ¹³C (normal/DEPT-135) NMR spectra showed two negative carbon signals at δ 44.98 and δ 47.55 due to OCH₂ and NCH₂ respectively, one positive carbon signal at 50.17 due to CH, four aromatic positive carbon signals at δ 115.06, δ 121.70, δ 127.73, δ 133.98 respectively, and one positive carbon signal at δ 178.15 which correspond to carbonyl of acridone moiety. All these spectral data corroborate structure 7 for this compound (scheme 2). The similar reactions of compounds 5 and 6 with epichlorohydrin gave compounds 8 (yellow solid, 65%, mp 105 °C, FAB mass m/z 296 [M⁺+1] ) and 9 (yellow solid, 68%, mp 130 °C, FAB mass m/z 285, 287 (3:1) [M⁺])(scheme 2).

![Scheme 2](image)

Further the mixture of compound 7 (1 mmol) and pyrrolidine (1 mmol) was irradiated in a microwave oven for 5-7 min and completion of the reaction was monitored by TLC. The reaction mixture was washed with diethyl ether to get pure compound 10 (86 %, mp 130 °C, FAB mass m/z 323[M⁺+1]). ¹H NMR spectrum of this compound showed 4H multiplet at δ 1.78-1.84 (C₁₂H₂/C₁₇H₂), 6H multiplet at δ 2.59-2.91(C₁₃H₂/C₁₄H₂, C₁₅H₂), 1H multiplet at δ 4.31-4.36 (C₁₃H), 1H double doublet at δ 4.40-4.46 (C₁₁H), 1H double doublet at δ 4.50-4.58 (C₁₁H), three 6H multiplets at δ 7.17-7.26, 7.63-7.72, 8.40-8.43 (ArH) and one 2H double doublet at δ 8.52-8.56 (ArH). Its ¹³C (normal/DEPT-135) NMR spectrum showed four negative carbon signals at δ 23.56 (C₁₂H₂/C₁₈H₂), 50.33 (C₁₅H₂/C₁₆H₂), 54.22 (C₁₃H₂), 59.80 (C₁₁H₂), one positive carbon signal at δ 67.81 (C₁₂H), four positive carbon signals at δ
115.46, δ 121.26, δ 127.52, δ 133.57 (ArH) and one quaternary carbon signals at δ 172.53 (C=O). This spectral data confirmed structure 10 for this compound (scheme 3). Similarly, compound 7 reacts with piperidine, morpholine, piperidino piperidine, diethylamine, disopropylamine to provide compound 11 (76%, mp 150 °C, FAB mass m/z 337[M+1]+), 12 (82%, mp 80 °C, FAB mass m/z 339[M+1]+), 13 (84%, mp 110 °C, FAB mass m/z 420[M+1]+), 14 (81%, mp120 °C, FAB mass m/z 325[M+1]+), 15 (74%, mp 135 °C, FAB mass m/z 353[M+1]+) respectively (scheme 3). Reaction of compound 8 and 9 with these amines gave compounds 16-21 and 22-27, respectively (scheme 3).

![Scheme 3](image_url)

In compounds 10-27, the ¹H NMR signal due to C₁₃H₂ appears upfield than the ¹H NMR signal of C₁₂H which otherwise could have been appear in the reverse positions if the isomeric product 27A was formed (through the reactions of amines at CH of...
epoxy ring, route b, scheme 4). Therefore, the reaction of amines at the epoxy ring regioselectively occurs through route ‘a’ (scheme 4) to provide a single product 10-27.

\[ \text{Scheme 4} \]

Reaction of compound 7 with benzylamine under microwave irradiations gave compound 28 (recrystallized from ethanol) in 68% yield mp 157-160 °C, FAB mass m/z 359[M+1]. 1H NMR spectrum of this compound showed 1H double doublet at δ 2.76 due to NHCH₂, double doublet at δ 2.89 due to second H of NHCH₂, one singlet at δ 3.77 due to benzyl CH₂, one double doublet at δ 4.24 due to 1H of NCH₂, one 1H multiplet at δ 4.33-4.37 due to CH, one 1H double doublet at δ 4.57 due to NCH₂. Its 13C (normal/DEPT-135) NMR spectrum shows three negative carbon signals at δ 50.2 (NHCH₂), 52.4 (benzyl CH₂), 53.9 (NCH₂), one positive carbon signal at δ 68.8 (CH), nine positive carbon signals at δ 115.4, 121.3, 121.6, 127.2, 128.1, 128.5, 133.6, 139.7, 142.3, (ArH) and one signal due to carbonyl carbon at δ 177.6. This spectral data confirms structure 28 for this compound (scheme 5). Similarly, compound 7 reacts with o-amo benzylamine and p-amo benzylamine upon irradiation in microwave oven to give compound 29 (67%, mp 170-172 °C, FAB mass m/z 374 [M+1]) and 30 (74%, mp 165-167 °C, FAB mass m/z 374 [M+1]) (scheme 5). Similar reactions of compound 9 with benzyl/o-amo benzyl/p-amo benzyl amine resulted in the formation of compounds 31-33.
Therefore, epoxy ring opening with amines under microwave irradiations provides a convenient approach for the synthesis of target compounds.

2.2. EXPERIMENTAL

Melting points were determined in capillaries and are uncorrected. \(^1\)H and \(^{13}\)C NMR spectra were recorded on JEOL 300 MHz and 75 MHz NMR spectrometer respectively using CDCl\(_3\) as solvent. Chemical shifts are given in ppm with TMS as an internal reference. \(J\) values are given in Hertz. IR and UV spectral data were recorded on FTIR 8400S Shimadzu and BioTek PowerWave XS instruments respectively. Fluorescence spectra were run on Varian (Cary Eclipse) spectrofluorophotometer using 5 nm as slit width (Excitation at 253 nm). The reactions corresponding to epoxy ring opening with amines were performed in domestic microwave oven (INALSA model 1MW17EG) with microwave power 700W and operating frequency 2450 MHz. Reactions were monitored by thin layer chromatography (TLC) on glass plates coated with silica gel GF-254. Column chromatography was performed with 100-200 mesh silica. In \(^{13}\)C NMR spectral data, +ve, -ve terms correspond to CH\(_3\), CH and CH\(_2\) signals respectively in DEPT-135 NMR spectra.

**General procedure for the synthesis of compounds 4-6 (Procedure A)**

2-Chlorobenzoic acid (1.56 g, 10 mmol), aniline/antranillic acid/o-cl aniline (10
mmol), powdered CuO (25 mg) and K₂CO₃ (1.5 g, ~11 mmol) were taken in isoamyl alcohol (50 ml) was heated at 160 °C for 10 h. After cooling, the alcohol was evaporated under vacuum and the residue was dissolved in hot water (120 ml) and acidified with 10N HCl. The precipitates were filtered and washed with hot water. The solid product was dissolved in ethyl acetate, the solution was dried over anhydrous Na₂SO₄ and evaporated to dryness. The crude product was purified by column chromatography over silica gel using a mixture of ethyl acetate and hexane as the eluent. This product was taken in conc. H₂SO₄ (just to dissolve the compound) and heated on water bath for 1.5 h. Reaction mixture was added to hot water and the resulting precipitates were filtered to get acridone 4/5/6.

**General procedure for the synthesis of compound 7-9 (Procedure B)**

Sodium hydride (3.0 mmol) was washed with dry hexane and taken in 15 ml of dimethyl sulfoxide. To this solution, acridone 4/5/6 (2.5 mmol) and epichlorohydrin (3.0 mmol) were added and the reaction mixture was stirred for 17-18 h at 70-80 °C (TLC monitoring). The reaction mixture was extracted with ethyl. The organic phase was dried over anhydrous Na₂SO₄. The solvent was distilled off and the residue was column chromatographed using ethyl acetate and hexane (6:1) in case of compound 4, 6 and (7:1) in case of compound 5 as eluents to isolate pure compounds 7-9.

**10-Oxiranmethyl-10H-acridin-9-one (7)**

Compound 7 was synthesized using compound 4 according to the synthetic procedure B as a brownish Solid, in a yield of 47%, mp 180 °C; ¹H NMR (300 MHz, CDCl₃): δ 2.68 (dd, 1H, J²= 4.5 Hz, J¹=2.7 Hz, H₉), 2.93 (dd, 1H, J²=4.5 Hz, J¹=4.5 Hz, H₈), 3.48-3.52 (m, 1H, (8 lines are visible), H₇), 4.40 (dd, 1H, J²= 13.2 Hz, J¹=4.8 Hz, H₆), 4.86 (dd, 1H, J²=17.2 Hz, J¹=2.1 Hz, H₅), 7.26-7.33 (m, 2H, ArH), 7.55-7.60 (m, 2H, ArH), 7.68-7.75 (m, 2H, ArH), 8.52 (dd, 2H, J²=8.4 Hz, J¹=1.8 Hz, ArH); ¹³C (Normal/DEPT-135): δ 44.98 (-ve, CH₂), 47.55 (-ve, CH₂), 50.17 (+ve, CH), 115.06 (+ve, ArCH), 121.70 (+ve, ArCH), 122.38 (absent, ArC), 127.73 (+ve, ArCH), 133.98 (+ve, ArCH), 142.53 (absent, ArC), 178.15 (C=O), MS (FAB) 252 (M⁺+1). Anal. for C₁₀H₁₃NO₂ Calcd%: C 76.48, H 5.21, N 5.57; Found%: C, 75.04; H, 5.60; N, 5.79. IR (KBr, cm⁻¹): 1604 (C=O).

**10-Oxiranmethyl-9-oxo-9,10-dihydro-acridine-4-carboxylic acid (8)**

Compound 8 was synthesized using compound 5 according to the synthetic procedure B as a yellow solid in a yield of 65%, mp 105 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.79
(dd, 1H, J\textsuperscript{A}=4.8 Hz, J\textsuperscript{B}=2.7 Hz, H\textsubscript{A}), 2.96 (dd, 1H, J\textsuperscript{A}=4.8 Hz, J\textsuperscript{B}=3.9 Hz, H\textsubscript{A}), 3.39-3.42 (m, 1H, H\textsubscript{A}), 4.28 (dd, 1H, J\textsuperscript{A}=12.3 Hz, J\textsuperscript{B}=6.3 Hz, H\textsubscript{A}), 4.74 (dd, 1H, J\textsuperscript{A}=12.3 Hz, J\textsuperscript{B}=3.0 Hz, H\textsubscript{A}), 7.23-7.39 (m, 3H, ArH), 7.65-7.70 (m, 1H, ArH), 8.41-8.71 (m, 2H, ArH), 8.74 (d, 1H, J=1.8 Hz, ArH), 11.59 (b, 1H, COOH); \textsuperscript{13}C (Normal/DEPT-135) \(\delta\) 42.61 (-ve, CH\textsubscript{2}), 44.64 (-ve, CH\textsubscript{2}), 49.26 (+ve, CH), 113.02 (absent, ArC), 117.48 (+ve, ArCH), 119.80 (+ve, ArCH), 121.34 (absent, ArC) 122.39 (+ve, ArCH), 126.95 (+ve, ArCH), 133.97 (+ve, ArCH), 134.21 (+ve, ArCH), 136.60 (+ve, ArCH), 139.21 (absent, ArC), 141.59 (absent, ArC), 167.37 (C=O), 177.71 (C=O); MS (FAB) 296 (M\textsuperscript{+}+1). Anal. for C\textsubscript{17}H\textsubscript{13}NO\textsubscript{4} Calcd\%: C 69.15, H 4.44, N 4.74. Found\%: C 69.18, H 4.48, N 4.79; IR (KBr, cm\textsuperscript{-1}): 1605 (C=O), 1680 (C=O), 3400 (OH).

**4-Chloro-10-((oxiran-2-yl)methyl)acridin-9(10H)-one (9)**

Compound 9 was synthesized using compound 6 according to the synthetic procedure B as a yellow solid in a yield of 68\%, mp 130°C; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 2.68 (dd, 1H, J\textsuperscript{A}=2.7 Hz, J\textsuperscript{B}=2.4 Hz, H\textsubscript{A}), 2.93 (dd, 1H, J\textsuperscript{A}=3.39 Hz, J\textsuperscript{B}=4.8 Hz, H\textsubscript{A}), 3.48-3.50 (m, 1H, H\textsubscript{A}), 4.39 (dd, 1H, J\textsuperscript{A}=16.9 Hz, J\textsuperscript{B}= 4.6 Hz, H\textsubscript{A}), 4.85 (dd, 1H, J\textsuperscript{A}=16.9 Hz, J\textsuperscript{B}=1.9 Hz, H\textsubscript{A}), 7.26-7.32 (m, 2H, ArH), 7.56-7.74 (m, 3H, ArH), 8.53 (dd, 2H, J\textsuperscript{A}=8.1 Hz, J\textsuperscript{B}=1.5 Hz, ArH); \textsuperscript{13}C (Normal/DEPT-135) \(\delta\) 45.03 (-ve, CH\textsubscript{2}), 47.55 (-ve, CH\textsubscript{2}), 50.23 (+ve, CH), 115.10 (+ve, ArCH), 120.13 (+ve, ArCH), 122.42 (+ve, ArCH), 122.69 (absent, ArC), 127.78 (absent, ArC), 133.95 (+ve, ArCH), 139.02 (absent, ArC), 142.51 (absent, ArC), 178.05 (C=O), MS (FAB) 285, 287 (3:1) (M\textsuperscript{+}). Anal. for C\textsubscript{17}H\textsubscript{13}NO\textsubscript{4} Calcd\%: C 67.26, H 4.23, N 4.90. Found\%: C 67.24, H 4.25, N 4.87; IR (KBr, cm\textsuperscript{-1}): 1635 (C=O).

**General procedure for the syntheses of compounds 10-33 (Procedure C).**

A mixture of acridone 7 (1 mmol) and appropriate amine (1 mmol) was irradiated in microwave oven for 5-7 minutes. On completion of the reaction (TLC), the reaction mixture was washed with diethyl ether to get pure compounds 10-33.

**10-(2-Hydroxy-3-pyrrolidin-1-yl-propyl)-10H-acridin-9-one (10)**

Compound 10 was synthesized using compound 7 according to the synthetic procedure C as a yellowish solid, in a yield of 86\%, mp 130°C; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta\) 1.78-1.84 (broadmultiplet, 4H, C\textsubscript{16}H\textsubscript{2}/C\textsubscript{17}H\textsubscript{2}), 2.59-2.91 (m, 6H, C\textsubscript{15}H\textsubscript{2}/C\textsubscript{12}H\textsubscript{2}, C\textsubscript{13}H\textsubscript{2}), 4.31-4.36 (m, 1H, C\textsubscript{12}H\textsubscript{2}), 4.43 (dd, 1H, J\textsuperscript{A}=15.75 Hz, J\textsuperscript{B}=3.45 Hz, C\textsubscript{11}H\textsubscript{2}), 4.54 (dd, 1H, J\textsuperscript{A}=16.05 Hz, J\textsuperscript{B}=7.35 Hz, C\textsubscript{11}H\textsubscript{2}), 7.17-7.26 (m, 2H, ArH), 7.63-7.72 (m, 2H, ArH), 8.40-8.43 (m, 2H, ArH), 8.54 (dd, 2H, J\textsuperscript{A}=8.4 Hz, J\textsuperscript{B}=1.8 Hz,
ArH); $^{13}$C NMR (normal/DEPT-135): $\delta$ 23.56 (-ve CH$_2$), 50.33 (-ve, CH$_2$), 54.22 (-ve, CH$_2$), 59.80 (-ve, CH$_2$), 67.81 (+ve, CH), 115.46 (+ve, ArCH), 121.26 (+ve, ArCH), 122.23 (absent, ArC) 127.52 (+ve, ArCH), 133.57 (+ve, ArCH), 142.53 (absent, ArC), 177.02 (C=O); MS (FAB) 323 (M$^+$+1); Anal. for C$_{20}$H$_{22}$N$_2$O$_2$ Calcd%: C 74.51, H 6.88, N 8.69. Found%: C 74.86, H 7.03, N 8.68; IR (KBr, cm$^{-1}$): 1593 (C=O), 3301 (OH).

**10-(2-Hydroxy-3-piperidin-1-yl-propyl)-10H-acridin-9-one (11)**

Compound 11 was synthesized using compound 7 according to the synthetic procedure C as a yellow crystalline solid in a yield of 76%, mp 150 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.25-1.60 (m, 6H, C$_{18}$H$_3$/C$_{17}$H$_2$/C$_{16}$H$_2$), 2.45-2.60 (m, 6H, C$_{18}$H$_3$/C$_{15}$H$_2$/C$_{14}$H$_2$), 4.30 (m, 1H, C$_{12}$H), 4.42 (dd, 1H, $J^\prime$=16.05 Hz, $J^\prime$=3.75 Hz, C$_{11}$H), 4.54 (dd, 1H, $J^\prime$=16.05 Hz, $J^\prime$=7.05 Hz, C$_{11}$H), 7.23-7.28 (m, 2H, ArH), 7.67-7.72 (m, 2H, ArH), 8.50 (d, 2H, J=8.1, ArH), 8.58 (dd, 2H, J$^\prime$=8.4 Hz, J$^\prime$=1.8 Hz, ArH); $^{13}$C NMR (normal/DEPT-135): $\delta$ 25.86 (-ve, CH$_2$), 50.24 (-ve, CH$_2$), 54.74 (-ve, CH$_2$), 62.36 (-ve, CH$_2$), 65.98 (+ve, CH), 115.41 (+ve, ArCH), 121.34 (+ve, ArCH), 122.35 (absent, ArC), 127.66 (+ve, ArCH), 133.66 (+ve, ArCH), 142.53 (absent, ArC) 172.63 (C=O); MS (FAB) 337 (M$^+$+1); Anal. for C$_{21}$H$_{24}$N$_2$O$_2$ Calcd%: C 74.97, H 7.19, N 8.33. Found%: C 74.66, H 7.27, N 8.47; IR (KBr, cm$^{-1}$): 1693 (C=O), 3334 (OH).

**10-(2-Hydroxy-3-morpholin-4-yl-propyl)-10H-acridin-9-one (12)**

Compound 12 was synthesized using compound 7 according to the synthetic procedure C as light yellow solid in a yield of 82%, mp 80 °C; $^1$H NMR (300 MHz CDCl$_3$): $\delta$ 2.59-2.71 (m, 6H, C$_{18}$H$_3$/C$_{15}$H$_2$/C$_{14}$H$_2$), 3.65-3.77 (m, 4H, C$_{16}$H$_2$/C$_{17}$H$_2$), 4.55 (m, 3H, C$_{12}$H$_2$/C$_{11}$H$_2$), 7.05-7.52 (m, 2H, ArH), 7.56-7.59 (m, 2H, ArH), 7.61-7.70 (m, 2H, ArH) 8.16-8.26 (dd, 2H, J$^\prime$=8.6 Hz, J$^\prime$=1.5 Hz, ArH); $^{13}$C NMR (normal/DEPT-135): $\delta$ 50.5 (-ve, CH$_2$), 53.98 (-ve, CH$_2$), 62.36 (-ve, CH$_2$), 66.41 (-ve, CH$_2$), 66.89 (+ve, CH), 115.44 (+ve, ArCH), 121.24 (+ve, ArCH), 121.78 (absent, ArC), 127.20 (+ve, ArCH), 133.56 (+ve, ArCH), 142.32 (absent, ArC), 177.70 (C=O); MS (FAB) 339 (M$^+$+1); Anal. for C$_{20}$H$_{22}$N$_2$O$_3$ Calcd%: C 70.09, H 6.55, N 8.28. Found%: C 70.12, H 6.10, N 8.64; IR (KBr, cm$^{-1}$): 1593 (C=O), 3323 (OH).
10-(3-[1,4′-Bipiperidinyl-1′-yl-2-hydroxy-propyl]-10H-acridin-9-one (13)

Compound 13 was synthesized using compound 7 according to the synthetic procedure C as yellowish solid in a yield of 84%, mp 110 °C; 1H NMR (300 MHz, CDCl3): δ 1.43-1.67 (m, 8H, C22H2/C23H2/C16H2/C18H2), 1.79-1.90 (m, 2H, C23H2), 2.22-2.34 (m, 2H, C21H2), 2.48-2.59 (broad multiplet, 6H, C23H2/C19H2/C13H2), 2.00-2.07 (m, 1H, C17H), 2.97-3.72 (m, 2H, C13H2), 4.27-4.30 (m, 1H, C12H), 4.43 (dd, 1H, J=15.9 Hz, J=3.3 Hz, C11H), 4.54 (dd, 1H, J=15.9 Hz, J=7.2 Hz, C11H), 7.21-7.26 (m, 2H, ArH), 7.66-7.70 (m, 4H, ArH), 8.47 (d, 2H, J=8.1 Hz, ArH); 13C NMR (normal/DEPT-135): δ 25.88 (-ve, CH2), 28.07 (-ve, CH2), 50.14 (-ve, CH2), 50.33 (-ve, CH2), 52.48 (-ve, CH2), 54.78 (-ve, CH2), 61.69 (+ve, CH), 66.42 (+ve, CH), 115.49 (+ve, ArCH), 121.29 (+ve, ArCH), 121.34 (absent, ArC), 127.56 (+ve, ArCH), 133.62 (+ve, ArCH), 142.48 (absent, ArC), 178.00 (C=O), MS (FAB) 420 (M⁺+1); Anal. for C26H12N3O2 Calcd%: C 74.43, H 7.93, N 10.82; Found%: C 74.03, H 8.01, N 10.52. IR (KBr, cm⁻¹): 1582 (C=O), 3344 (OH).

10-(3-(diethylamino)-2-hydroxypropyl)acridin-9(10H)-one (14)

Compound 14 was synthesized using compound 7 according to the synthetic procedure C as yellowish solid in a yield of 81%, mp 120 °C; 1H NMR (300 MHz, CDCl3): δ 1.04-1.27 (m, 6H, C18H3/C19H3), 2.53-2.74 (m, 6H, C13H2/C17H2/C13H2), 4.19-4.27 (m, 1H, C12H), 4.41 (dd, 1H, J=16.2 Hz, J=3.45 Hz, C11H), 4.53 (dd, 1H, J=16.05 Hz, J=7.35 Hz, C11H), 7.21-7.26 (m, 2H, ArH), 7.65-7.74 (m, 4H, ArH), 8.46-8.49 (d, 2H, J=7.5 Hz, ArH); 13C NMR (normal/DEPT-135): δ 11.94 (+ve, CH3), 47.27 (-ve, CH2), 50.44 (-ve, CH2), 57.31 (-ve, CH2), 66.74 (+ve, CH), 115.4 4 (+ve, ArCH), 121.30 (+ve, ArCH), 122.25 (absent, ArC), 127.57 (+ve, ArCH), 133.63 (+ve, ArCH), 142.52 (absent, ArC), 172.52 (C=O); MS (FAB) 325 (M⁺+1); Anal. for C20H24N2O2 Calcd%: C 74.04, H 7.46, N 8.64. Found%: C 74.14, H 7.89, N 8.93; IR (KBr, cm⁻¹): 1593 (C=O), 3342 (OH).

10-(3-(diisopropylamino)-2-hydroxypropyl)acridin-9(10H)-one (15)

Compound 15 was synthesized using compound 7 according to the synthetic procedure C as creamish solid, mp 135 °C, Yield 74%; 1H NMR (300 MHz, CDCl3): δ 1.04-1.10 (m, 12H, C18H3/C17H3/C19H3/C20H3), 2.67-2.69 (m, 1H, C13H), 2.80-2.93 (m, 1H, C13H), 2.95-3.10 (m, 1H, C12H), 3.46-3.50 (m, 1H, C12H), 4.37-4.89 (m, 3H, C12H/C11H2), 7.23-7.32 (m, 2H, ArH), 7.56-7.59 (m, 2H, ArH), 7.69-7.75 (m, 2H, ArH), 8.51-8.59 (m, 2H, ArH); 13C NMR (normal/DEPT-135): δ 19.88 (+ve CH3),
22.06 (+ve, CH₃), 45.05 (-ve, CH₂), 47.59 (-ve, CH₂), 50.23 (+ve, CH), 50.89 (+ve, CH), 66.61 (+ve, CH), 115.10 (+ve, ArCH), 115.49 (+ve, ArCH), 121.31 (+ve, ArCH), 121.71 (absent, ArC), 122.39 (+ve, ArCH), 142.61 (absent, ArC), 178.08 (C=O); MS (FAB) 353(M⁺+1); Anal. for C₂₂H₂₅N₂O₂ Calc’d: C 74.97, H 8.01, N 7.95; Found%: C 74.64, H 8.17, N 8.26. IR (KBr, cm⁻¹): 1543 (C=O), 3355 (OH).

10-(2-Hydroxy-3-pyrrolidin-1-yl-propyl)-9-oxo-9,10-dihydroacridine-4-carboxylic acid (16) Compound 16 was synthesized using compound 8 according to the synthetic procedure C as a yellow solid in a yield of 63%. mp 65 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.60-1.69 (m, 4H, 2xCH₂), 2.35-2.41 (m, 2H, NCH₂), 3.74-3.78 (m, 4H, 2xNCH₂), 4.15-4.23 (m, 1H, C₁₂H), 4.36-4.41 (dd, 1H, J=12.0 Hz, J=6.0 Hz, C₁₁H), 4.53(dd, 1H, J=12.0 Hz, J=3.0 Hz, C₁₁H), 7.21-7.39 (m, 3H, ArH), 7.65-7.70 (m, 1H, ArH), 8.42-8.45 (m, 2H, ArH), 8.69-8.73 (dd, 1H, J=7.8 Hz, J=1.8 Hz, ArH), 11.61 (b, 1H, COOH); ¹³C NMR (normal/DEPT-135) δ 25.32 (+ve, CH₂), 53.22 (+ve, CH₂), 64.76 (+ve, CH), 66.86 (-ve, CH₂), 67.13 (-ve, CH₂), 113.51 (absent, ArC), 117.49 (+ve, ArCH), 119.84 (+ve, ArCH), 121.38 (absent, ArC), 122.37 (+ve, ArCH), 126.93 (+ve, ArCH), 133.94 (+ve, ArCH), 133.99 (+ve, ArCH), 136.65 (+ve, ArCH), 139.46 (absent, ArC), 141.55 (absent, ArC), 167.15 (C=O), 177.15 (C=O); MS (FAB) 367 (M⁺+1); Anal. for C₂₁H₂₃N₂O₄ Calc’d: C 68.84, H 6.05, N 7.65. Found%: C 68.89, H 6.10, N 7.69; IR (KBr, cm⁻¹): 1620 (C=O), 1680 (C=O), 3210 (OH), 3320 (OH).

10-(2-Hydroxy-3-piperidin-1-yl-propyl)-9-oxo-9,10-dihydroacridine-4-carboxylic acid (17) Compound 17 was synthesized using compound 8 according to the synthetic procedure C as a yellow solid in a yield of 74%, mp 115 °C; ¹H NMR (300 MHz, CDCl₃): δ 1.25-1.50 (m, 2H, CH₂), 1.95-2.08 (m, 4H, 2xCH₂), 2.96 (m, 2H, CH₂), 3.32-3.58 (m, 2H CH₂), 3.83-3.98 (m, 2H, CH₂), 4.48-4.82 (m, 3H, C₁₁H₂/C₁₂H), 7.36-7.44 (m, 2H, ArH), 8.34-8.61 (m, 4H, ArH), 8.69-8.75 (m, 1H, ArH), 12.02 (b, 1H, COOH); ¹³C NMR (normal/DEPT-135) δ 23.14 (-ve, CH₂), 54.10 (-ve, CH₂), 59.96 (-ve, CH₂), 64.06 (-ve, CH₂), 66.50 (+ve, CH), 113.26 (absent, ArC), 117.68 (+ve, ArCH), 120.41 (+ve, ArCH), 121.29 (absent, ArC), 122.95 (+ve, ArCH), 126.46 (+ve, ArCH), 133.89 (+ve, ArCH), 134.76 (+ve, ArCH), 139.20 (absent, ArC), 143 21 (absent, ArC), 167.19 (C=O), 177.93 (C=O); MS (FAB) 381 (M⁺+1); Anal. for C₂₂H₂₅N₂O₄ Calc’d: C 69.46, H 6.36, N 7.36. Found%: C 69.49, H 6.40, N 7.38; IR (KBr, cm⁻¹): 1610 (C=O), 1680 (C=O), 3240 (OH), 3320 (OH).
10-(2-Hydroxy-3-morpholin-4-yl-propyl)-9-oxo-9,10-dihydroacridine-4-carboxylic acid (18) Compound 18 was synthesized using compound 8 according to the synthetic procedure C as a yellow solid in a yield of 88%. mp 110°C; ¹H NMR (300 MHz, CDCl₃) δ 2.48-2.57 (m, 4H, 2xCH₂), 2.68-2.75 (m, 2H, C₁₂H₂), 3.73-3.77 (m, 4H, 2xOCH₂), 4.19 (m, 1H, C₁₂H), 4.39 (dd, 1H, J₁₂=12.0 Hz, J₃=6.0 Hz, C₁₁H), 4.53 (dd, 1H, J₁₂=12.0 Hz, J₃=3.0 Hz, C₁₃H), 7.23-7.41 (m, 3H, ArH), 7.65-7.71 (m, 1H, ArH), 8.43-8.47 (m, 2H, ArH), 8.72 (dd, 1H, J₁₂=8.1 Hz, J₃=1.5 Hz, ArH), 11.63 (b, 1H, COOH); ¹³C NMR (Normal/DEPT-135) δ 53.62 (-ve, CH₂), 60.65 (-ve, CH₂), 64.77 (+ve, CH), 66.83 (-ve, CH₂), 67.15 (-ve, CH₂), 113.52 (absent, ArC), 117.49 (+ve, ArCH), 119.83 (+ve, ArCH), 121.35 (absent, ArC), 122.37 (+ve, ArCH), 126.92 (+ve, ArCH), 133.94 (+ve, ArCH), 136.65 (+ve, ArCH), 139.48 (absent, ArC), 141.51 (absent, ArC), 167.58 (C=O), 177.84 (C=O); MS (FAB) 383 (M⁺+1); Anal. for C₂₁H₂₂N₂O₅ Calcéd%: C 65.96, H 5.80, N 7.33. Found%: C 65.98, H 5.84, N 7.37; IR (KBr, cm⁻¹): 1610 (C=O), 1680 (C=O), 3200 (OH), 3280 (OH);

10-(3-[1,4|Bipiperidinyl-1'-yl-2-hydroxypropyl]-9-oxo-9,10-dihydroacridine-4-carboxylic acid (19)

Compound 19 was synthesized using compound 8 according to the synthetic procedure C as a light yellow solid in a yield of 78%. mp 100°C; ¹H NMR (300 MHz, CDCl₃) δ 1.43-1.45 (m, 2H, CH₂), 1.53-1.65 (m, 6H, 3xCH₂), 1.83-1.87 (m, 2H, CH₂), 1.98-2.06 (m, 1H, CH), 2.23-2.38 (m, 2H, CH₂), 2.45-2.52 (m, 6H, 3xCH₂), 2.89 (m, 1H, C₁₂H), 3.07 (m, 1H, C₁₃H), 4.11-4.13 (m, 1H, C₁₂H), 4.35 (dd, 1H, J₁₂=11.4 Hz, J₃=6.0 Hz, C₁₁H), 4.50 (dd, 1H, J₁₂=9.0 Hz, J₃=3.0 Hz, C₁₁H), 7.22-7.40 (m, 3H, ArH), 7.65-7.70 (m, 1H, ArH), 8.43 (m, 2H, ArH), 8.71(d, 1H, J=8.1 Hz, ArH), 11.63 (b, 1H, COOH); ¹³C NMR (normal/DEPT-135) δ 24.50 (-ve, CH₂), 25.86 (-ve, CH₂), 27.82 (-ve, CH₂), 50.28 (-ve, CH₂), 51.84 (-ve, CH₂), 55.36 (-ve, CH₂), 59.75 (-ve, CH₂), 62.39 (+ve, CH), 65.03 (+ve, CH), 113.40 (absent, ArC), 117.47 (+ve, ArCH), 119.91 (+ve, ArCH), 121.35 (absent, ArC), 122.36 (+ve, ArCH), 126.84 (+ve, ArCH), 133.88 (+ve, ArCH), 136.81 (+ve, ArCH), 139.19 (absent, ArC), 143.11 (absent, ArC), 167.00 (C=O), 178.00 (C=O); MS (FAB) 464 (M⁺+1); Anal. for C₂₁H₂₁N₂O₅ Calcéd%: C 69.95, H 7.18, N 9.06. Found%: C 69.98, H 7.20, N 9.10; IR (KBr, cm⁻¹): 1604 (C=O), 1670 (C=O), 3240 (OH), 3355 (OH);

10-(3-Diethylamino-2-hydroxy-propyl)-9-oxo-9,10-dihydro-acridine-4-carboxylic
**Acid (20)** Compound 20 was synthesized using compound 8 according to the synthetic procedure C as a yellow solid in a yield of 67%, mp 115 °C; 1H NMR (300 MHz, CDCl3) δ 1.25-1.40 (m, 6H, 2xCH3), 3.20-3.53 (m, 6H, 13-H + 2xNCH2), 4.67-4.92 (m, 3H, 12-H + 11-H), 7.26-7.40 (m, 2H, ArH), 7.42-7.46 (m, 3H, ArH), 8.35-8.64 (m, 2H, ArH), 12.09 (b, 1H, COOH); 13C NMR (normal/DEPT-135) δ 12.02 (+ve, CH3), 47.75 (-ve, CH2), 50.20 (-ve, CH2), 57.64 (-ve, CH2), 66.36 (+ve, C-12), 115.80 (absent, ArC), 120.20 (+ve, ArCH) 121.48 (absent, ArC), 122.55 (+ve, ArCH), 127.64 (+ve, ArCH), 128.42 (+ve, ArCH), 133.90 (+ve, ArCH), 139.21 (absent, ArC), 143.15 (absent, ArC), 167.12 (C=O), 178.52 (C=O), MS (FAB) 369 (M+1); Anal. for C21H24N2O4 Caled%: C 68.46, H 6.57, N 7.60. Found%: C 68.48, H 6.55, N 7.65; IR (KBr, cm⁻¹): 1610 (C=O), 1680 (C=O), 3250 (OH), 3360 (OH).

**10-(3-Diisopropylamino-2-hydroxy-propyl)-9-oxo-9,10-dihydro-acridine-4-carboxylic acid (21)**

Compound 21 was synthesized using compound 8 according to the synthetic procedure C as a light yellow solid in a yield of 62%, mp 120°C; 1H NMR (300 MHz, CDCl3) δ 1.56 (d, J=6.6 Hz, 12H, 4xCH3), 3.13-3.18 (m, 1H, NCH), 3.71-3.73 (m, 3H, 13-H + NCH), 4.46-4.55 (m, 3H, 11-H + 12-H), 7.21-7.36 (m, 3H, ArH), 7.68-7.69 (m, 2H, ArH), 8.35-8.73 (m, 2H, ArH), 11.51 (b, 1H, COOH); 13C NMR (normal/DEPT-135) δ 19.35 (+ve, CH3), 21.44 (+ve, CH3), 45.05 (-ve, CH2), 47.59 (-ve, CH2), 49.41 (+ve, CH), 50.42 (+ve, CH), 66.26 (+ve, C-12), 115.36 (absent, ArC), 121.32 (+ve, ArCH), 121.74 (absent, ArC), 122.43 (+ve, ArCH), 127.85 (+ve, ArCH), 133.78 (+ve, ArCH), 134.00 (+ve, ArCH), 139.10 (absent, ArC), 142.33 (absent, ArC), 167.35 (C=O), 178.08 (C=O); MS (FAB) 397 (M+1); Anal. for C23H28N2O4 Caled%: C 69.67, H 7.12, N 7.07. Found%: C 69.65, H 7.16, N 7.09. IR (KBr, cm⁻¹): 1605 (C=O), 1685 (C=O), 3220 (OH), 3380 (OH).

**4-Chloro-10-(2-hydroxy-3-(pyrrolidin-1-yl)propyl)acridin-9(10H)-one (22)**

Compound 22 was synthesized using compound 9 according to the synthetic procedure C as a yellow solid in a yield of 68%, mp 105°C; 1H NMR (300 MHz, CDCl3) δ 1.79-1.84 (m, 4H, 2xCH2pyrrol), 2.58-2.66 (m, 3H, 1H of 13-H + 2H of NCH2), 2.75 (dd, 2H, J=6.7 Hz, J2=2.2 Hz, NCH2), 2.78 (dd, 1H, J=11.8 Hz, J2=9.7 Hz, 1H of 13-H), 4.29-4.32 (m, 1H, 12-H), 4.45 (dd, 1H, J=16.2 Hz, J2=4.2 Hz, 11-H), 4.57 (dd, 1H, J=16.0 Hz, J2=7.60 Hz, 11-H), 7.29 (dd, 2H, J=8.1 Hz, J=4.2 Hz, ArH), 7.71 (dd, 3H, J=4.2 Hz, J=0.9 Hz, ArH), 8.53 (t, 1H, J=1.2 Hz, ArH), 8.56 (t,
1H, J=1.2 Hz, ArH); 13C NMR (normal/DEPT-135) δ 23.82 (-ve, CH3), 50.09 (-ve, CH3), 54.00 (-ve, CH3), 59.76 (-ve, CH3), 67.77 (+ve, C-12), 115.33 (+ve, ArCH), 121.38 (+ve, ArCH), 122.37 (+ve, ArCH), 122.75 (absent, ArC), 126.12 (absent, ArC), 127.73 (+ve, ArCH), 133.69 (+ve, ArCH), 139.22 (absent, ArC), 143.12 (absent, ArC), 177.88 (C=O); MS (FAB) 356, 358 (3:1) (M+); Anal. for C20H21ClN2O2 Calcd%: C 67.32, H 5.93, N 7.85. Found%: C 67.34, H 5.99, N 7.88; IR (KBr, cm⁻¹): 1595 (C=O), 3355 (OH).

4-Chloro-10-(2-hydroxy-3-(piperidin-1-yl)propyl)acridin-9(10H)-one (23)

Compound 23 was synthesized using compound 9 according to the synthetic procedure C as a yellow solid in a yield of 63 %, mp 110 °C; 1H NMR (300 MHz, CDCl3) δ 1.63 (br s, 6H, 3xCH2), 2.51-2.62 (m, 6H, 3xNCH2), 4.30-4.40 (m, 1H, 12-H), 4.44 (dd, 1H, J=16.2 Hz, J=3.6 Hz, 11-H), 4.55 (dd, 1H, J=16.0 Hz, J=7.0 Hz, 11-H), 7.23-7.29 (m, 2H, ArH), 7.70-7.73 (m, 3H, ArH), 8.49 (t, 1H, J=1.2 Hz, ArH), 8.52 (t, 1H, J= 1.0 Hz, ArH); 13C NMR (normal/DEPT-135) δ 25.86 (-ve, CH2), 50.24 (-ve, CH2), 54.74 (-ve, CH2), 62.36 (-ve, CH2), 65.98 (+ve, C-12), 115.41 (+ve, ArCH), 117.30 (+ve, ArCH), 119.52 (+ve, ArCH), 121.34 (absent, ArC), 127.66 (absent, ArC), 133.66 (+ve, ArCH), 139.08 (absent, ArC), 142.22 (absent, ArC), 178.53 (C=O), MS (FAB) 370, 372 (3:1) (M+); Anal. for C21H23ClN2O2 Calcd%: C 68.01, H 6.25, N 7.55. Found%: C 68.06, H 6.28, N 7.57; IR (KBr, cm⁻¹): 1585 (C=O), 3354 (OH).

4-Chloro-10-(2-hydroxy-3-morpholinopropyl)acridin-9(10H)-one (24)

Compound 24 was synthesized using compound 9 according to the synthetic procedure C as a yellow solid in a yield of 63%, mp 120 °C; 1H NMR (300 MHz, CDCl3) δ 2.53-2.64 (m, 2H, 13-H), 2.66-2.71 (m, 4H, 2xNCH2), 3.75 (t, 4H, J= 4.5 Hz, 2xOCH2), 4.33-4.42 (m, 1H, 12-H), 4.48 (dd, 1H, J=16.2 Hz, J=3.6 Hz, 11-H), 4.58 (dd, 1H, J=16.0 Hz, J=7.2 Hz, 11-H), 7.19-7.26 (m, 2H, ArH), 7.65-7.70 (m, 3H, ArH), 8.42 (t, 1H, J= 0.9 Hz, ArH), 8.45 (t, 1H, J= 1.2 Hz, ArH); 13C NMR (normal/DEPT-135) δ 50.16 (-ve, CH3), 53.85 (-ve, CH3), 62.33 (-ve, CH3), 66.10 (-ve, CH3), 66.92 (+ve, C-12), 115.37 (+ve, ArCH), 119.21 (+ve, ArCH), 120.23 (+ve, ArCH), 121.43 (absent, ArC), 127.70 (absent, ArC), 133.71 (+ve, ArCH), 139.40 (absent, ArC), 142.23 (absent, ArC), 177.65 (C=O), MS (FAB) 372, 374 (3:1) (M+);
Anal. for C_{20}H_{25}ClN_{3}O_{2} Calcd\%: C 64.43, H 5.68, N 7.51. Found\%: C 64.45, H 5.71, N 7.55; IR (KBr, cm^{-1}): 1592 (C=O), 3343 (OH).

4.4.6. 4-Chloro-10-(2-hydroxy-3-(4-(piperidin-1-yl)piperidin-1-yl)propyl)acridin-9(10H)-one (25)

Compound 25 was synthesized using compound 9 according to the synthetic procedure C as a yellow solid in a yield of 65 \%, mp 115^\circ C; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \delta 1.45-1.60 (m, 2H, CH\textsubscript{2}), 1.74-1.75 (m, 8H, 4xCH\textsubscript{2}), 1.98-2.25 (m, 1H, CH), 2.28-2.48 (m, 2H, NCH\textsubscript{2}), 2.50-2.58 (m, 6H, 3xNCH\textsubscript{2}), 2.95-2.98 (m, 2H, 13-H), 4.27-4.32 (m, 1H, 12-H), 4.42 (dd, 1H, \textit{J}^\text{H}=16.2 Hz, \textit{J}^\text{H}=3.3 Hz, 11-H), 4.55 (dd, 1H, \textit{J}^\text{H}=15.9 Hz, \textit{J}^\text{H}=7.2 Hz, 11-H), 7.24-7.29 (m, 1H, ArH), 7.69-7.71 (m, 4H, ArH), 8.50 (t, 1H, \textit{J}=1.0 Hz, ArH), 8.53 (t, 1H, \textit{J}=0.9 Hz, ArH); \textsuperscript{13}C NMR (normal/DEPT-135) \delta 24.83 (-ve, CH\textsubscript{2}), 26.42 (-ve, CH\textsubscript{2}), 50.28 (-ve, CH\textsubscript{2}), 52.66 (-ve, CH\textsubscript{2}), 55.30 (-ve, CH\textsubscript{2}), 61.49 (-ve, CH\textsubscript{3}), 62.15 (+ve, CH), 66.50 (+ve, C-12), 115.56 (+ve, ArCH), 119.25 (+ve, ArCH), 121.11 (+ve, ArCH), 121.23 (absent, ArC), 127.69 (absent, ArC), 133.62 (+ve, ArCH), 139.22 (absent, ArC), 142.24 (absent, ArC), 177.00 (C=O); MS (FAB) 453, 455 (3:1) (M\textsuperscript{+}); Anal. for C\textsubscript{20}H\textsubscript{25}ClN\textsubscript{3}O\textsubscript{2} Calcd\%: C 68.78, H 7.10, N 9.26. Found\%: C 68.81, H 7.16, N 9.29; IR (KBr, cm\textsuperscript{-1}): 1590 (C=O), 3345 (OH);

4-Chloro-10-(3-(diethylamino)-2-hydroxypropyl)acridin-9(10H)-one (26)

Compound 26 was synthesized using compound 9 according to the synthetic procedure C as a yellow solid in a yield of 64 \%, mp 120^\circ C; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \delta 1.06 (t, 6H, \textit{J}=7.3 Hz, 2xCH\textsubscript{3}), 2.54-2.74 (m, 6H, 13-H + 2xNCH\textsubscript{2}), 4.20-4.28 (m, 1H, 12-H), 4.42 (dd, 1H, \textit{J}^\text{H}=15.9 Hz, \textit{J}^\text{H}=3.3 Hz, 11-H), 4.54 (dd, 1H, \textit{J}^\text{H}=16.05 Hz, \textit{J}^\text{H}=7.35 Hz, 11-H), 7.25-7.27 (m, 2H, ArH), 7.70-7.72 (m, 3H, ArH), 8.48 (t, 1H, \textit{J}=1.0 Hz, ArH), 8.51 (t, 1H, \textit{J}=0.3 Hz, ArH); \textsuperscript{13}C NMR (normal/DEPT-135) \delta 11.82 (+ve, CH\textsubscript{3}), 47.56 (-ve, CH\textsubscript{3}), 50.20 (-ve, CH\textsubscript{2}), 57.35 (-ve, CH\textsubscript{2}), 66.45 (+ve, C-12), 115.70 (+ve, ArCH), 121.48 (+ve, ArCH), 122.36 (absent, ArC), 122.75 (absent, ArC), 127.54 (+ve, ArCH), 128.04 (+ve, ArCH), 133.90 (+ve, ArCH), 139.69 (absent, ArC), 142.23 (absent, ArC), 178.52 (C=O), MS (FAB) 358, 360 (3:1) (M\textsuperscript{+}); Anal. for C\textsubscript{20}H\textsubscript{23}ClN\textsubscript{3}O\textsubscript{2} Calcd\%: C 66.94, H 6.46, N 7.81. Found\%: C 66.98, H 6.47, N 7.86; IR (KBr, cm\textsuperscript{-1}): 1595 (C=O), 3345 (OH);

4-Chloro-10-(3-(diisopropylamino)-2-hydroxypropyl)acridin-9(10H)-one (27)
Compound 27 was synthesized using compound 9 according to the synthetic procedure C as a yellow solid in a yield of 67%, mp 100°C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.07 (d, $J=6.8$ Hz, 6H, 2xCH$_3$), 1.10 (d, $J=6.6$ Hz, 6H, 2xCH$_3$), 2.63 (dd, 1H, $J^1=13.6$ Hz, $J^2=9.4$ Hz, 13-H), 2.79 (dd, 1H, $J^1=13.8$ Hz, $J^2=4.0$ Hz, 13-H), 3.07-3.16 (m, 2H, NCH$_2$), 4.19-4.26 (m, 1H, 12-H), 4.42 (dd, 1H, $J^2=16.0$ Hz, $J^1=3.4$ Hz, 11-H), 4.54 (dd, 1H, $J^1=16.0$ Hz, $J^2=7.3$ Hz, 11-H), 7.22-7.33 (m, 2H, ArH), 7.69-7.75 (m, 3H, ArH), 8.52 (t, 1H, $J=1.0$ Hz, ArH), 8.59 (t, 1H, $J=0.9$ Hz, ArH); $^{13}$C NMR (normal/DEPT-135): $\delta$ 19.89 (+ve CH$_3$), 23.06 (+ve, CH$_3$), 45.06 (-ve, CH$_2$), 47.58 (-ve, CH$_2$), 50.33 (+ve, CH), 50.79 (+ve, CH), 66.63 (+ve, C-12), 115.12 (+ve, ArCH), 115.48 (+ve, ArCH), 118.18 (+ve, ArCH), 120.32 (absent, ArC), 121.33 (absent, ArC), 122.39 (+ve, ArCH), 139.22 (absent, ArC), 142.24 (absent, ArC), 178.09 (C=O); MS (FAB) 386, 388 (3:1) (M$^+$); Anal. for C$_{22}$H$_{27}$ClN$_2$O$_2$: C 68.29, H 7.03, N 7.24. Found%: C 68.27, H 7.06, N 7.28; IR (KBr, cm$^{-1}$): 1592 (C=O), 3342 (OH).

2.5 10-(3-Benzylamino-2-hydroxy-propyl)-10H-acridin-9-one (28)

Compound 28 was synthesized using compound 7 according to the synthetic procedure C as yellow solid in a yield of 68%, mp 157-160°C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.76 (dd, 1H, $J^1=11.8$ Hz, $J^2=7.5$ Hz, NHCH$_2$), 2.89 (dd, 1H, $J^1=12.0$ Hz, $J^2=3.9$ Hz, NHCH$_2$), 3.77 (s, 2H, Benzyl CH$_2$), 4.24 (dd, 1H, $J^1=15.1$ Hz, $J^2=3.1$ Hz, NCH$_2$), 4.33-4.37 (m, 1H, CH), 4.57 (dd, 1H, $J^1=15.1$ Hz, $J^2=8.2$ Hz, NCH$_2$), 6.89-6.94 (m, 2H, ArH), 7.19-7.25 (m, 5H, ArH), 7.43-7.53 (m, 4H, ArH), 8.0-8.03 (m, 2H, ArH); $^{13}$C NMR (normal/DEPT-135): $\delta$ 50.2 (-ve, CH$_2$), 52.4 (+ve, CH$_3$), 53.9 (-ve, CH$_2$), 68.8 (+ve, CH), 115.4 (+ve, ArCH), 121.3 (+ve, ArCH), 121.6 (+ve, ArCH), 127.2 (+ve, ArCH), 128.1 (+ve, ArCH), 128.5 (absent, ArC), 133.6 (+ve, ArCH), 139.7 (absent, ArC), 142.3 (absent, ArC), 177.6 (C=O); MS (FAB) 359 (M$^+$+1); Anal. for C$_{22}$H$_{22}$N$_2$O$_2$: C 77.07, H 6.19, N 7.82. Found%: C 77.09, H 6.16, N 7.84; IR (KBr, cm$^{-1}$): 1580 (C=O), 3345 (NH), 3420 (OH).

10-[3-(2-Amino-benzylamino)-2-hydroxy-propyl]-10H-acridin-9-one (29)

Compound 29 was synthesized using compound 7 according to the synthetic procedure C as yellow solid in a yield of 67%, mp 170-172°C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.81 (dd, 1H, $J^1=11.8$ Hz, $J^2=6.7$ Hz, NHCH$_2$), 2.90 (dd, 1H, $J^1=14.8$ Hz, $J^2=6.7$ Hz, NHCH$_2$), 3.83 (s, 2H, Benzyl CH$_2$), 4.12 (dd, 1H, $J^1=15.9$ Hz, $J^2=2.1$ Hz, NCH$_2$), 4.40-4.52 (m, 2H, CH/1H of NCH$_2$), 6.57-6.64 (m, 2H, ArH), 6.82-6.87 (m,
2H, ArH), 6.98-7.04 (m, 2H, ArH), 7.43-7.45 (m, 4H, ArH), 7.85-7.88 (m, 2H, ArH); 
\(^{13}\)C NMR (normal/DEPT-135): 50.3 (-ve, CH2), 52.5 (-ve, CH2), 52.6 (-ve, CH2), 68.9
(+ve, CH), 115.8 (+ve, ArCH), 118.1 (+ve, ArCH), 121.3 (+ve, ArCH), 121.6 (+ve,
ArCH), 123.5 (+ve, ArCH), 127.2 (+ve, ArCH), 128.7 (absent, ArC), 130.2 (+ve,
ArCH), 133.7 (absent, ArC), 142.3 (absent, ArC), 146.4 (absent, ArC), 177.6 (C=O);
MS (FAB) 374 (M\(^+\)+1); Anal. for C\(_{23}\)H\(_{23}\)N\(_3\)O\(_2\) Calcd\%: C 73.97, H 6.21, N 11.25;
Found\%: C 73.93, H 6.19, N 11.20. IR (KBr, cm\(^{-1}\)): 1575 (C=O), 3395 (NH), 3410
(OH).

10-[3-(4-Amino-benzylamino)-2-hydroxy-propyl]-10H-acridin-9-one (30)

Compound 30 was synthesized using compound 7 according to the synthetic
procedure C as yellow solid in a yield of 74\%, mp 165-166°C; \(^1\)H NMR (300 MHz,
CDCl\(_3\)): \(\delta 2.53 \) (dd, 1H, \(J^2=11.7 \) Hz, \(J^3=4.5 \) Hz, NHCH\(_2\)), 2.65 (dd, 1H, \(J^2=12.4 \)
Hz, \(J^3=4.3 \) Hz, NHCH\(_2\)), 3.45 (s, 2H, Benzyl CH\(_2\)), 4.03-4.06 (m, 1H, CH), 4.31-4.33 (m, 
2H, NCH\(_3\)), 6.39-6.40 (m, 2H, ArH), 6.42-6.88 (m, 2H, ArH), 6.99-7.04 (m, 2H,
ArH), 7.43-7.47 (m, 2H, ArH), 7.62-7.64 (m, 2H, ArH), 8.22-8.24 (m, 2H, ArH); \(^{13}\)C
NMR (normal/DEPT-135): \(\delta 50.1 \) 3 (-ve, CH\(_2\)), 52.4 3 (-ve, CH\(_2\)), 52.5 3 (-ve, CH\(_2\)),
68.7 (+ve, CH), 115.2 (+ve, ArCH), 118.3 (+ve, ArCH), 121.5 (+ve, ArCH), 121.7
(+ve, ArCH), 123.3 (+ve, ArCH), 127.5 (+ve, ArCH), 128.8 (absent, ArC), 130.1
(+ve, ArCH), 133.5 (absent, ArC), 142.2 (absent, ArC), 146.5 (absent, ArC), 177.3
(C=O); MS (FAB) 374 (M\(^+\)+1); Anal. Caled. for C\(_{23}\)H\(_{23}\)N\(_3\)O\(_2\): C 73.97; H, 6.21; N,
11.25. Found: C, 73.98; H, 6.23; N, 11.22; IR (KBr, cm\(^{-1}\)): 1585 (C=O), 3390 (NH), 3415
(OH).

10-(3-Benzylamino-2-hydroxy-propyl)-4-chloro-10H-acridin-9-one (31)

Compound 31 was synthesized using compound 9 according to the synthetic
procedure C as yellow solid in a yield of 73\%, mp 160-163°C; \(^1\)H NMR (300 MHz,
CDCl\(_3\)): \(\delta 2.87 \) (dd, 1H, \(J^2=11.7 \) Hz, \(J^3=7.5 \) Hz, NHCH\(_2\)), 3.00 (dd, 1H, \(J^2=11.8 \)
Hz, \(J^3=4.0 \) Hz, NHCH\(_2\)), 3.88 (s, 2H, Benzyl CH\(_2\)), 4.34 (dd, 1H, \(J^2=15.3 \) Hz, \(J^3=2.7 \)
Hz, NCH\(_2\)), 4.41-4.49 (m, 1H, CH), 4.57 (dd, 1H, \(J^2=15.1 \) Hz, \(J^3=8.4 \) Hz, NCH\(_2\)),
6.99-7.04 (m, 2H, ArH), 7.28-7.35 (m, 4H, ArH), 7.54-7.63 (m, 4H, ArH), 8.10-8.13 (2H,
ArH); \(^{13}\)C NMR (normal/DEPT-135): \(\delta 49.93 \) (-ve, CH\(_2\)), 52.09 (-ve, CH\(_2\)), 52.31
(-ve, CH\(_2\)), 68.47 (+ve, CH), 115.05 (+ve, ArCH), 115.47 (+ve, ArCH), 117.62 (+ve,
ArCH), 120.92 (+ve, ArCH), 121.24 (+ve, ArCH), 123.17 (absent, ArC), 126.74 (+ve,
ArCH), 128.23 (+ve, ArCH), 129.73 (absent, ArC), 133.24 (+ve, ArCH), 141.91
(absent, ArC), 146.02 (absent, ArC), 177.6 (C=O); MS (FAB) 407, 409 (3:1) (M⁺);
Anal. for C₂₃H₂₃ClN₂O₂ Calcd%: C 70.31, H 5.39, N 7.13. Found%: C 70.28, H 5.33,
N 7.10; IR (KBr, cm⁻¹): 1570 (C=O), 3245 (NH), 3410 (OH).

10-[3-(2-Amino-benzylamino)-2-hydroxy-propyl]-4-chloro-10H-acridin-9-one (32)
Compound 32 was synthesized using compound 9 according to the synthetic
procedure C as yellow solid in a yield of 63%, mp 175-177°C; ¹H NMR (300 MHz,
CDCl₃): δ 2.92 (dd, 1H, J²=12.7 Hz, J¹=7.3 Hz, NHCH₂), 3.01 (dd, 1H, J²=11.8 Hz,
J¹=4.3 Hz, NHCH₂), 3.93 (s, 2H, Benzyl CH₂), 4.25 (dd, 1H, J²=15.7 Hz, J¹=1.9 Hz,
NCH₂), 4.50-4.63 (m, 2H, CH/1H of NCH₂), 6.67-6.74 (m, 2H, ArH), 6.97-7.01 (m,
2H, ArH), 7.08-7.12 (m, 2H, ArH), 7.55-7.58 (m, 3H, ArH), 8.03-8.05 (m, 2H, ArH);
¹³C NMR (normal/DEPT-135): 50.3 (-ve, CH₂), 52.5 (-ve, CH₂), 52.6 (-ve, CH₂), 68.9
(+ve, CH), 115.4 (+ve, ArCH), 115.9 (+ve, ArCH), 118.1 (+ve, ArCH), 121.3 (+ve,
ArCH), 121.8 (+ve, ArCH), 123.4 (+ve, ArCH), 127.3 (+ve, ArCH), 128.7 (absent,
ArC), 130.2 (+ve, ArCH), 133.7 (absent, ArC), 142.3 (absent, ArC), 146.3 (absent,
ArC), 177.7 (C=O); MS (FAB) 407, 409 (3:1) (M⁺); Anal. for C₂₃H₂₂N₂O₂ Calcd%: C
67.73, H 5.44, N 10.30. Found%: C 67.75, H 5.40, N 10.27; IR (KBr, cm⁻¹): 1572
(C=O), 3390 (NH), 3430 (OH).

10-[3-(4-Amino-benzylamino)-2-hydroxy-propyl]-4-chloro-10H-acridin-9-one (33)
Compound 33 was synthesized using compound 9 according to the synthetic
procedure C as yellow solid in a yield of 67%, mp 172-174°C; ¹H NMR (300 MHz,
CDCl₃): δ 2.52 (dd, 1H, J²=11.7 Hz, J¹=6.0 Hz, NHCH₂), 2.65 (dd, 1H, J²=12.1Hz,
J¹=4.0 Hz, NHCH₂), 3.45 (s, 2H, Benzyl CH₂), 4.03-4.06 (m, 1H, CH), 4.30-4.33 (m,
2H, NCH₂), 6.38-6.42 (m, 2H, ArH), 6.83-6.88 (m, 2H, ArH), 6.99-7.04 (m, 2H,
ArH), 7.43-7.47 (m, 2H, ArH), 7.62-7.64 (m, 1H, ArH), 8.22-8.24 (m, 2H, ArH); ¹³C
NMR (normal/DEPT-135): δ 49.3 (-ve, CH₂), 51.9 (-ve, CH₂), 52.9 (-ve, CH₂), 67.8
(+ve, CH), 114.4 (+ve, ArCH), 115.6 (+ve, ArCH), 118.1 (+ve, ArCH), 120.6 (+ve,
ArCH), 121.6 (+ve, ArCH), 126.7 (absent, ArC), 128.7 (+ve, ArCH), 128.9 (absent,
ArC), 133.1 (absent, ArC), 142.2 (absent, ArC), 145.4 (absent, ArC), 177.3 (C=O);
MS (FAB) 407, 409 (M⁺); Anal. for C₂₃H₂₃N₂O₂ Calcd%: C 67.73, H 5.44, N 10.30.
Found%: C 67.78, H 5.42, N 10.25; IR (KBr, cm⁻¹): 1577 (C=O), 3382 (NH), 3420
(OH).
2.3. SYNTHESIS OF BARBITURIC ACID DERIVATIVES ‘D’

6-Hydroxy-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-carbaldehyde (34) was prepared by the formylation of 1,3-dimethylpyrimidin-2,4,6-trione with CHCl₃/KOH in ethanol/H₂O. Compounds 35 and 36 were prepared by the microwave assisted cinnamoylation and benzylation of 1,3-dimethylpyrimidin-2,4,6-trione. A solution of 34 and o-phenylene diamine, stirred in methanol at 35 °C, after usual work up provided compound 37 as yellow solid (77%, mp 252 °C, FAB mass m/z 274 [M⁺+1]) which could exist in tautomeric forms ‘a’ and ‘b’. Presence of two 1H doublets at δ 8.63 (due to =CH, converted to singlet after adding D₂O) and 12.35 (due to NH, exchangeable with D₂O), besides the signals due to two CH₃ groups at δ 3.36, four ArHs’ in the region δ 6.84-7.24 and another D₂O exchangeable signal at δ 12.30 (due to NH₂) in the ¹H NMR spectrum of 37 implies its existence in tautomeric form ‘a’. Its ¹³C NMR spectrum showed two positive signals at δ 27.28 and 28.05 due to two CH₃, one positive signal at δ 161.74 due to CH, four aromatic carbon signals at δ 118.17, 119.05, 120.54 and 127.8, two aromatic quaternary carbon signals at δ 126.66, 137.84 and four quaternary carbon signals at δ 93.07 (barbituric acid, C₃), 151.89 (barbituric acid, C₂), 162.64 (barbituric acid, C₃/C₄), 165.15 (barbituric acid, C₃/C₄). This spectral data corroborate structure 37 for this compound (scheme 5). Under the same reaction conditions as for the synthesis of compound 37, stirring of a solution of 1,3-dimethyl-5-formyl/ benzoyl/ cinnamoyl barbituric acid and o-phenylene diamine/o-anisidine/ anthranilic acid/ o-nitroaniline/ o-hydroxyaniline/ 2-aminocterephthalic acid in methanol at 35 °C provided the desirable compounds 38-44 (scheme 6).
In order to increase the spacing and H-donor/acceptor sites between the two pyrimidines, the reactions of 34-36 with ethylene diamine, hydrazines and aminomethyl pyridines were carried out. The reaction of compound 34 with ethylene diamine in methanol at 35 °C resulted in the formation of compound 45 as white solid (73%, mp 218°C, FAB Mass m/z 393 [M+1]). 1H NMR spectrum of this compound showed 6H singlet at δ 3.32 due to two CH₃, another 6H singlet at δ 3.35 due to other two CH₃, 4H multiplet at δ 3.95 due to two CH₂, 2H doublet at δ 8.52 due to two CH and 2H broad doublet at δ 10.55 due to two NH (exchanges with D₂O). Its DEPT-135 13C NMR spectrum showed two positive signals at δ 27.66 and 28.48 due to two CH₃, one negative signal at δ 50.29 due to CH₂, one positive signal at δ 161.74 due to CH and four quaternary carbon signals at δ 91.34 (barbituric acid, C₃), 151.76 (barbituric acid, C₂), 164.37 (barbituric acid, C₆/C₄), 164.95 (barbituric acid, C₆/C₄). This spectral data clearly represent structure 45 for this compound. Under similar reaction conditions, the reaction of compound 35 with ethylene diamine resulted in the formation of compound 46 (scheme 7). But surprisingly, in the reaction of compound 36 with ethylene diamine, only monomer product 47 was formed (scheme 7).

![Scheme 7](image)

Likewise, the reactions of 35 and 36 with hydrazine in methanol provided the compounds 48 and 49 respectively (scheme 7) and the reactions of 1,3-dimethyl-5-formyl barbituric acid (34) with phenyl hydrazine and 2,4-dinitrophenyl hydrazine gave compounds 50 and 51 respectively (scheme 8).
Under similar conditions as mentioned above, the reaction of compound 34 with 2,6-diaminopyridine and 2-aminomethyl pyridine provided compounds 52 and 53 respectively (scheme 9).

Interestingly, the reactions of hydrazine and ethylene diamine with 1,3-dimethyl-5-formyl/benzoyl/cinnamoyl barbituric acids gave dimer type of products 45, 46, 48, 49 but similar reactions of these barbituric acids with o-phenylene diamine and 2,6-diamino pyridine gave mono-substituted products 37-39 and 52. Probably, this is due to the low reactivity of aromatic amines which further get decreased when one amino group gets attached to the barbituric acid moiety. The structures of all the compounds were elucidated with $^1$H, $^{13}$C NMR spectra, mass spectra and CHN analysis. Characteristically, all these compounds exist in enamine form ($^1$H NMR spectra).

Therefore, following a simple synthetic procedure, a series of small organic molecules having a number of polar interacting sites were prepared.

2.4. EXPERIMENTAL

General procedure for the syntheses of compounds 37-53

The solution of 5-substituted-6-hydroxy-1,3-dimethylpyrimidin-2,4-dione and the appropriate amine (phenylene diamine/ ethylene diamine/ hydrazine /phenyl
hydrazine/ 2,4-dinitrophenylhydrazine/ anthranilic acid/ o-anisidine/ 2,6-diaminopyridine/ 2-aminomethylpyridine/ 2-nitroaniline/ 2-aminophenol/ 2-aminoterephthalic acid) (1.2 equiv. for compounds 37-44, 50-53 and 0.5 equiv. for compounds 45-49) in methanol was stirred at 35 °C for 3-5 h. The solid suspension on filtration and washing with diethyl ether provided the pure compounds 37-53.

5-[(2-Amino-phenylimino)-methylene]-1,3-dimethyl-pyrimidine-
2,4,6(1H,3H,5H)-trione (37)

Compound 37 was synthesized using compound 34 according to the synthetic procedure mentioned above as yellow solid in a yield of 77%, mp 252°C; ¹H NMR (300 MHz, CDCl₃): δ 3.36 (s, 6H, CH₃), 6.84-7.41 (m, 4H, ArH), 8.63 (d, 1H, J = 10.5 Hz, =CH), 12.30 (broad doublet, 2H, J = 11.7 Hz, NH₂, exchangeable with D₂O), 12.35 (broad doublet, 1H, J = 11.7 Hz, NH, exchangeable with D₂O); ¹³C NMR (normal/DEPT-135): δ 27.28 (+ve, CH₃), 28.05 (+ve, CH₃), 93.07 (absent, C₂), 118.17 (+ve, ArCH), 119.05 (+ve, ArCH), 120.54 (+ve, ArCH), 126.66 (ArC), 127.8 (+ve, ArCH), 137.84 (absent, ArC), 151.89 (absent, C₂), 153.65 (+ve, CH), 162.64 (absent, C₆/C₄), 165.15 (absent, C₆/C₄); MS (FAB) 274 (M⁺+1); Anal. for C₁₂H₁₄N₄O₃
Calcd%: C 56.93, H 5.14, N 20.43. Found%: C 56.73, H 5.44, N 20.23; IR (KBr, cm⁻¹): 1630 (C=O), 1670 (C=O), 3420 (NH), 3480 (NH).

5-[(1-(2-Amino-phenylamino)-3-phenyl-allylidene]-1,3-dimethyl-pyrimidine-
2,4,6(1H, 3H,5H) -trione (38)

Compound 38 was synthesized using compound 35 according to the synthetic procedure mentioned above as yellow solid in a yield of 73%, mp 165°C; ¹H NMR (300 MHz, CDCl₃): δ 3.32 (s, 3H, CH₃), 3.48 (s, 3H, CH₃), 4.49 (d, 1H, J = 8.7 Hz, CH), 5.27 (d, 1H, J = 8.7 Hz, CH), 6.89-7.42 (m, 9H, ArH); ¹³C NMR (normal/DEPT-135): δ 27.83 (+ve, CH₃), 28.02 (+ve, CH₃), 94.56 (C₃), 115.87 (+ve, ArCH), 118.18 (+ve, ArCH), 123.06 (absent, ArC), 126.6 (+ve, ArCH), 127.5 (+ve, ArCH), 128.09 (+ve, ArCH), 133.68 (+ve, CH), 136.97 (absent, ArC), 141.77 (absent, C₂), 151.55 (absent, C-N), 174.01 (absent, C₆/C₄); MS (FAB) 376 (M⁺+1); Anal. for C₁₃H₁₈N₄O₃
Calcd%: C 67.01, H 5.36, N 14.88. Found%: C 67.34, H 5.25, N 14.95; IR (KBr, cm⁻¹): 1630 (C=O), 1690 (C=O), 3600 (NH), 3670 (NH).

5-[(2-Amino-phenylamino)-phenyl-methylene]-1,3-dimethyl-pyrimidin-
2,4,6(1H,3H,5H)-trione (39)

Compound 39 was synthesized using compound 36 according to the synthetic
procedure mentioned above as yellow solid in a yield of 79%, mp 182°C; 1H NMR (300 MHz, CDCl3): δ 3.20 (s, 3H, CH3), 3.42 (s, 3H, CH3), 6.40 (t, 1H, J = 7.5 Hz, ArH), 6.45 (d, 1H, J = 7.5 Hz, ArH), 6.64 (d, 1H, J = 7.8 Hz, ArH), 6.90 (t, 1H, J = 7.5 Hz, ArH), 7.14-7.30 (m, 5H, ArH); 13C NMR (normal/DEPT-135): δ 27.83 (+ve, CH3), 28.02 (+ve, CH3), 93.0 (absent, C3), 115.87 (+ve, ArCH), 118.18 (+ve, ArCH), 123.06 (absent, ArC), 126.6 (+ve, ArCH), 127.5 (+ve, ArCH), 128.09 (+ve, ArCH), 133.68 (absent, ArC), 141.77 (absent, C2), 151.55 (absent, C-N), 174.01 (absent, C6/C5); MS (FAB) 350 (M+1); Anal. for C10H18N4O5 Calcd%: C 68.66, H 4.85, N 16.86. Found%: C 68.91, H 5.15, N 16.63; IR (KBr, cm⁻¹): 1658 (C=O), 1697 (C=O), 3400 (NH).

2-((Tetrahydro-1,3-dimethyl-2,4,6-trioxopyrimidin-5(6H)-ylidene)methylamino)benzoic acid (40)

Compound 40 was synthesized using compound 34 according to the synthetic procedure mentioned above as creamish white solid in a yield of 78%, mp 210°C; 1H NMR (300 MHz, CDCl3+ TFA): δ 3.39 (s, 6H, CH3), 7.42 (t, 1H, J = 7.5 Hz, ArH), 7.69 (d, 1H, J = 8.1 Hz, ArH), 7.78 (t, 1H, J = 7.8 Hz, ArH), 8.23 (dd, 1H, J = 8.1 Hz, J' = 1.5 Hz, ArH), 8.93 (d, 1H, J = 13.8 Hz, =CH), 13.69 (broad doublet, 1H, J =13.2 Hz, NH); 13C NMR (normal/DEPT-135): δ 27.90 (+ve, CH3), 28.72 (+ve, CH3), 108.07 (C3), 112.48 (+ve, ArCH), 116.25 (+ve, ArCH), 117.12 (+ve, ArCH), 120.03 (absent, ArC), 126.77 (+ve, ArCH), 136.29 (absent, ArC), 150.90 (absent, C2), 152.64 (+ve, CH), 160.14 (absent, C6/C5), 160.71 (absent, C6/C5); MS (FAB) 304 (M+1); Anal. for C14H13N3O5 Calcd%: C 55.45, H 4.32, N 13.86. Found%: C 55.50, H 4.39, N 13.91; IR (KBr, cm⁻¹): 1632 (C=O), 1675 (C=O), 3425 (NH), 3480 (COOH).

5-((4-Methoxyphenylamino)methylene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)--trione (41)

Compound 41 was synthesized using compound 34 according to the synthetic procedure mentioned above as creamish white solid in a yield of 81%, mp 190°C; 1H NMR (300 MHz, CDCl3+ TFA): δ 3.36 (s, 6H, CH3), 3.85 (s, 3H, OCH3), 6.96 (d, 2H, J = 8.7 Hz, ArH), 7.19-7.28(m, 2H, ArH), 8.61 (d, 1H, J = 14.1 Hz, =CH), 12.08 (broad doublet, 1H, J =13.2 Hz, NH); 13C NMR (normal/DEPT-135): δ 27.24 (+ve, CH3), 27.96 (+ve, CH3), 55.60 (+ve, OCH3), 92.30 (absent, C3), 115.21 (+ve, ArCH), 119.48 (+ve, ArCH), 131.35 (absent, ArC), 152.09 (+ve, CH), 158.35 (absent, ArC), 162.77 (absent, C2), 165.04 (absent C6/C5); MS (FAB) 290 (M+1); Anal. for
C_{14}H_{13}N_{2}O_{5} Calcd\%: C 58.13, H 5.23, N 14.53. Found\%: C 58.15, H 5.22, N 14.48; IR (KBr, cm\(^{-1}\)): 1630 (C=O), 1650 (C=O), 3220 (NH).
5-((2-Nitrophenylamino)methylene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (42)

Compound 42 was synthesized using compound 34 according to the synthetic procedure mentioned above as greenish solid in a yield of 73%, mp 235°C; \(^1\)H NMR (300 MHz, CDCl\(_3\) + TFA): \(\delta\) 3.30 (s, 6H, CH\(_3\)), 6.83-6.96 (m, 2H, ArH), 7.19-7.28 (m, 2H, ArH), 8.61 (d, 1H, \(J = 13.9\) Hz, =CH), 12.06 (broad doublet, 1H, \(J =13.2\) Hz, NH); MS (FAB) 305 (M\(^+\)+1); Anal. for C_{14}H_{13}N_{2}O_{5} Calcd\%: C 51.32, H 3.98, N 18.41. Found\%: 51.35, H 3.96, N 18.43. IR (KBr, cm\(^{-1}\)): 1635 (C=O), 1680 (C=O), 3250 (NH).

5-((2-hydroxyphenylamino)methylene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (43)

Compound 43 was synthesized using compound 34 according to the synthetic procedure mentioned above as dark brown solid in a yield of 70%, mp 250°C; \(^1\)H NMR (300 MHz, CDCl\(_3\) + TFA): \(\delta\) 3.35 (s, 6H, CH\(_3\)), 6.89-6.98 (m, 2H, ArH), 7.25-7.37 (m, 2H, ArH), 8.67 (d, 1H, \(J = 13.9\) Hz, =CH), 12.46 (broad doublet, 1H, \(J =13.2\) Hz, NH); MS (FAB) 276 (M\(^+\)+1); Anal. for C_{14}H_{13}N_{2}O_{5} Calcd\%: C 56.72, H 4.76, N 15.27. Found\%: C 56.78, H 4.78, N 15.29. IR (KBr, cm\(^{-1}\)): 1642 (C=O), 1665 (C=O), 3211 (OH), 3225 (NH).

2-((Tetrahydro-1,3-dimethyl-2,4,6-trioxopyrimidin-5(6H)ylidene)methylamino) benzene-1,4-dioic acid (44)

Compound 44 was synthesized using compound 34 according to the synthetic procedure mentioned above as creamish white solid in a yield of 75%, mp 255°C; \(^1\)H NMR (300 MHz, CDCl\(_3\) + TFA): \(\delta\) 3.32 (s, 6H, CH\(_3\)), 6.90-6.97 (m, 2H, ArH), 7.75-7.80 (m, 1H, ArH), 8.67 (d, 1H, \(J = 14.4\) Hz, =CH), 13.21 (broad doublet, 1H, \(J =13.7\) Hz, NH); MS (FAB) 348 (M\(^+\)+1); Anal. for C_{14}H_{13}N_{2}O_{5} Calcd\%: C 51.88, H 3.77, N 12.10. Found\%: C 51.82, H 3.79, N 12.12; IR (KBr, cm\(^{-1}\)): 1624(C=O), 1655(C=O), 3220 (NH), 3450 (COOH).

Compound 45

Compound 45 was synthesized using compound 34 according to the synthetic procedure mentioned above as white solid in a yield of 73%, mp 218°C; \(^1\)H NMR (300 MHz, CDCl\(_3\) + TFA): \(\delta\) 3.32 (s, 6H, CH\(_3\)), 3.35 (s, 6H, CH\(_3\)), 3.95 (m, 4H,
2X(CH₃), 8.52 (d, 2H, J = 14.7 Hz, CH), 10.55 (broad doublet, 1H, NH, exchanges with D₂O); ¹³C NMR (normal/DEPT-135): δ 27.66 (+ve, CH₃), 28.48 (+ve, CH₃), 50.29 (-ve, CH₂), 91.34 (absent, C₆), 151.76 (absent, C₂), 161.74 (+ve, CH), 164.37 (absent, C₆/C₄), 164.95 (absent, C₆/C₄). Anal. for C₁₆H₂₀N₆O₆: Calcd%: C 48.98, H 5.14, N 21.42. Found%: C 49.12, H 5.05, N 21.58; MS (FAB) 393 (M⁺+1). IR (KBr, cm⁻¹): 1510 (C=O), 1650 (C=O), 3610 (NH).

Compound 46

Compound 46 was synthesized using compound 35 according to the synthetic procedure mentioned above as white solid in a yield of 70%, mp 158⁰C; ¹H NMR (300 MHz, CDCl₃+ TFA): δ 2.81 (dd, 1H, J₁ = 10.8 Hz, J₂ = 5.6 Hz, 1H of CH₂), 2.95 (dd, 1H, J₁ = 10.8 Hz, J₂ = 5.8 Hz, 1H of CH₂), 3.24 (s, 6H, CH₃), 3.27 (m, 1H, 1H of CH₂), 3.33 (s, 6H, CH₃), 3.68 (m, 1H, 1H of CH₂), 4.10 (d, 2H, J = 8.7 Hz, CH), 5.01 (d, 2H, J = 8.7 Hz, CH), 7.25-7.40 (m, 10H, ArH); ¹³C NMR (normal/DEPT-135): δ 28.25 (+ve, CH₃), 28.55 (+ve, CH₂), 37.07 (-ve, CH₂), 68.76 (-ve, CH₂), 91.19 (absent, C₆), 116.8 (+ve, CH), 122.10 (+ve, ArCH), 122.34 (+ve, ArCH), 124.96 (+ve, ArCH), 126.26 (+ve, ArCH), 127.53 (+ve, ArCH), 128.58 (+ve, ArCH), 128.8 (+ve, ArCH), 129.4 (absent, ArC), 140.72 (absent, ArC), 145.32 (+ve, CH), 155.32 (absent, C-N), 163.37 (absent, C₂), 166.7 (absent, C₆/C₄), 171.5 (absent, C₆/C₄); MS (FAB) 596 (M⁺+1); Anal. for C₁₂H₃₂N₆O₆: Calcd%: C 64.42, H 5.41, N 14.09. Found%: C 64.60 H 5.81, N 14.35; IR (KBr, cm⁻¹): 1520 (C=O), 1600 (C=O), 3600 (NH).

Compound 47

Compound 47 was synthesized using compound 36 according to the synthetic procedure mentioned above as white solid in a yield of 72%, mp 156⁰C; ¹H NMR (300 MHz, CDCl₃): δ 2.84 (t, 2H, J = 5.4 Hz, CH₂), 3.08 (t, 2H, J = 5.4 Hz, CH₂), 3.18 (s, 3H, CH₃), 3.38 (s, 3H, CH₃), 6.23 (broad, 2H, NH₂, exchangeable with D₂O), 7.0-7.49 (m, 5H, ArH), 12.58 (broad doublet, 1H, NH, exchangeable with D₂O); ¹³C NMR (normal/DEPT-135): δ 27.64 (+ve CH₃), 27.83 (+ve CH₃), 41.11 (-ve CH₂), 44.14 (+ve, CH₂), 90.39 (absent, C₆), 125.55 (+ve, ArCH), 128.76 (+ve, ArCH), 129.02 (+ve, ArCH), 130.12 (absent, ArC), 134.61 (+ve, ArCH), 151.68 (absent, C-N), 155.16 (absent, C₂), 160.38 (absent, C₆/C₄); MS (FAB) 303 (M⁺+1). Anal. for C₁₅H₁₈N₄O₃: Calcd%: C 59.59, H 6.0, N 18.53. Found%: C 59.42, H 6.28, N 18.75; IR (KBr, cm⁻¹): 1650 (C=O), 1700 (C=O), 3620 (NH).
**Compound 48**

Compound 48 was synthesized using compound 35 according to the synthetic procedure mentioned above as white solid in a yield of 64%, mp 170°C; $^1$H NMR (300 MHz, CDCl$_3$): δ 3.24 (s, 12H, CH$_3$), 4.17 (d, 2H, J = 9 Hz, CH), 4.42 (d, 2H, J = 9 Hz, CH), 7.38-7.49 (m, 10H, ArH); $^{13}$C NMR (normal/DEPT-135): δ 25.85 (+ve, CH$_3$), 83.74 (absent, C$_5$), 114.78 (+ve, CH), 124.76 (+ve, ArCH), 126.22 (absent, ArC), 127.08 (+ve, ArCH), 126.20 (+ve, ArCH), 127.38 (+ve, ArCH), 138.92 (absent, C$_2$), 146.90 (+ve, CH), 150.27 (absent, C-N), 161.54 (absent, C$_6$/C$_4$); MS (FAB) 568, (M$^+$+1). Anal. for C$_{30}$H$_{29}$N$_6$O$_6$ Calcd%: C 63.37, H 4.96, N 14.78. Found%: C 63.58, H 5.23; N 14.58; IR (KBr, cm$^{-1}$): 1610 (C=O), 1660 (C=O), 3300-3350 (NH).

**Compound 49**

Compound 49 was synthesized using compound 36 according to the synthetic procedure mentioned above as white solid in a yield of 65%, mp 204°C; $^1$H NMR (300 MHz, CDCl$_3$): δ 3.24 (s,12H, CH$_3$), 7.24-7.60 (m, 10H, ArH); $^{13}$C NMR (normal/DEPT-135): δ 27.21 (+ve, CH$_3$), 87.17 (absent, C$_5$), 125.98 (+ve, ArCH), 127.9 (+ve, ArCH), 128.55 (+ve, ArCH), 131.78 (absent, ArC), 140.7 (absent, C$_2$), 152.32 (absent, C-N), 166.29 (absent, C$_6$/C$_4$); MS (FAB) 517 (M$^+$+1); Anal. for C$_{29}$H$_{29}$N$_6$O$_6$ Calcd%: C 60.46, H 4.68, N 16.27. Found%: C 60.01, H 5.01, N, 16.51; IR (KBr, cm$^{-1}$): 1645 (C=O), 1705 (C=O), 3340 (NH).

**Compound 50**

Compound 50 was synthesized using compound 34 according to the synthetic procedure mentioned above as white solid in a yield of 80%, mp 210°C; $^1$H NMR (300 MHz, CDCl$_3$+TFA): δ 3.27 (s, 6H, CH$_3$), 7.28 (d, 1H, J = 6.5 Hz, ArH), 8.30 (d, 1H, J = 7.6 Hz, ArH), 8.37 (d, 1H, J = 5.5 Hz, ArH), 8.51-8.56 (m, 2H, ArH), 8.68 (d, 1H, J = 10.7 Hz, =CH), 9.25 (broad singlet, 1H, NH), 10.16 (broad singlet, 1H, NH); MS (FAB) 275 (M$^+$+1); Anal. for C$_{14}$H$_{13}$N$_3$O$_5$ Calcd%: C 56.93, H 5.14, N 20.43. Found%: C 56.95, H 5.17, N 20.46; IR (KBr, cm$^{-1}$): 1635 (C=O), 1680 (C=O), 3385 (NH).

5-(N’-(2,4-Dinitrophenyl)-hydrazinomethylene)-1,3-dimethylpyrimidine-2,4,6(1H,3H, 5H)-trione (51)

Compound 51 was synthesized using compound 34 according to the synthetic procedure mentioned above as brownish solid in a yield of 75%, mp 225°C; $^1$H NMR (300 MHz, CDCl$_3$+TFA): δ 3.25 (s, 6H, CH$_3$), 7.37 (d, 1H, J = 6.6 Hz, ArH), 8.41 (d, 1H, J = 7.5 Hz, ArH), 8.51(d, 1H, J =5.7 Hz, ArH), 8.63 (d, 1H, J = 10.8 Hz, =CH),
9.18 (broad singlet, 1H, NH), 10.23 (broad singlet, 1H, NH); \(^{13}\text{C}\) NMR (normal/DEPT-135): \(\delta\) 28.25 (+ve, CH\(_3\)), 28.98 (+ve, CH\(_3\)), 108.74 (absent, C\(_3\)), 112.51 (+ve, ArCH), 114.90 (+ve, ArCH), 116.27 (+ve, ArCH), 123.88 (absent, ArC), 131.07 (absent, ArC), 140.21 (absent, ArC), 146.44 (absent, C\(_2\)), 161.61 (+ve, CH), 162.76 (absent, C\(_6\)/C\(_4\)), 163.04 (absent, C\(_6\)/C\(_4\)). MS (FAB) 365 (M\(^+\)+1); Anal. for C\(_{14}\)H\(_{13}\)N\(_3\)O\(_5\) Calcd\%: C 42.86, H 3.32, N 23.07. Found\%: C 42.89, H 3.38, N 23.10; IR (KBr, cm\(^{-1}\)): 1635 (C=O), 1655 (C=O), 3390 (NH).

5-((6-Aminopyridine-2-yl)methylamino)methylene)-1,3-dimethylpyrimidine-2,4,6(1H, 3H,5H)-trione (52)

Compound 52 was synthesized using compound 34 according to the synthetic procedure mentioned above as brownish solid in a yield of 72\%, mp 240\(^\circ\)C; \(^1\)H NMR (300 MHz, CDCl\(_3\)+TFA): \(\delta\) 3.38 (s, 6H, CH\(_3\)), 4.00 (s, 2H, NH\(_2\)), 6.10-6.19 (m, 2H, ArH), 7.28-7.35 (m, 1H, ArH), 7.67 (d, 1H, \(J = 13.9\) Hz, =CH), 12.27 (broad doublet, 1H, \(J = 13.2\) Hz, NH); MS (FAB) 276 (M\(^+\)); Anal. for C\(_{14}\)H\(_{13}\)N\(_3\)O\(_5\) Calcd\%: C 52.36, H 4.76, N 25.44. Found\%: C 52.32, H 4.75, N 25.48; IR (KBr, cm\(^{-1}\)): 1632 (C=O), 1675 (C=O), 3258 (NH).

5-((Pyridine-2-yl)methylamino)methylene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (53)

Compound 53 was synthesized using compound 34 according to the synthetic procedure mentioned above as brownish solid in a yield of 70\%, mp 170\(^\circ\)C; \(^1\)H NMR (300 MHz, CDCl\(_3\)+TFA): \(\delta\) 3.38 (s, 6H, CH\(_3\)), 4.12 (s, 2H, CH\(_2\)), 6.90-6.98 (m, 2H, ArH), 7.85-7.95 (m, 2H, ArH), 8.68 (d, 1H, \(J = 13.9\) Hz, =CH), 12.37 (broad, 1H, NH); MS (FAB) 275 (M\(^+\)+1); Anal. for C\(_{14}\)H\(_{13}\)N\(_3\)O\(_5\) Calcd\%: C 56.93, H 5.14, N 20.43. Found\%: C 56.92, H 5.17, N 20.45; IR (KBr, cm\(^{-1}\)): 1645 (C=O), 1687 (C=O), 3236 (NH).

REFERENCES


