Microwave-Assisted Synthesis and Evaluation of Substituted Aryl Propyl Acridone-4-Carboxamides as Potential Chemosensitizing Agents for Cancer

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Abstract: A novel class of compounds with structure Aryl propyl acridone-4-carboxamides were synthesized by conventional and microwave (MW) irradiation methods and evaluated for their inhibitory effects on the transport activity of P-glycoprotein (P-gp) by standard Hoechst 33342 assay method. The title compounds with phenoxy substitution exhibited better activity.

Keywords: Aryl propyl acridone-4-carboxamides, Microwave, Chemosensitizing agents.

INTRODUCTION

Every year, more than 6 million cancer deaths were reported in the world. Of the 10 million new cases each year, more than half occur in developing countries. WHO predictions show that, out of 15 million cases, 66% will occur in developing countries, by 2015.

Drug resistance is the major cause of death in cancer. 30 to 80% of cancers can become resistant to cytotoxic drugs, leaving patients and doctors with few options when treatment fails [1].

Multidrug Resistance (MDR) operated by extrusion pumps such as P-glycoprotein and multidrug-resistance-associated-proteins, is a major reason for poor responses and failures in cancer chemotherapy [2-4].

Many compounds have been investigated for their ability to inhibit the P-gp function, thus leading to development of several generations of MDR reversal agents.

The search for effective MDR reversal agents is now into the third generation. First generation candidates were drugs already approved for other non-cancerous indications, such as verapamil, cyclosporin A and progesterone [5,6]. Unfortunately, although successful *in vitro*, patients could not benefit from these MDR reversal agents, because their clinically relevant doses exceed safety limits resulting in unacceptable adverse effects, frequent poor solubility and toxicity [7-9]. Chemical modifications of first generation molecules and combinatorial chemistry lead to second and third generation MDR reversal agents, such as VX-710, PSC 833, XR9051, XR9576, MS-209, GF120918, LY335979 and ONT- 093, some of which are in clinical trials [10-14]. Several of the latter, whereas more potent and less toxic than first generation compounds, may still be prone to adverse effects, poor solubility and unfavorable changes in pharmacokinetics of the anticancer drugs [15, 16].

The continued development of these agents may establish the true therapeutic potential of P-gp-mediated MDR reversal. Moreover, given tumor diversity, it is rational to assume that more than one MDR reversal agent will be needed in clinic.

Microwave (MW) dielectric heating, as an emerging processing technology is attracting more and more attention. Due to the reduced reaction time significantly, increasing yield of products, high selectivity and safety as compared to conventional heating methods, it has been widely employed in the fields of organic synthesis, for example, drug intermediates and fine chemicals [17].

The use of MW irradiation has introduced several new concepts in chemistry, since the absorption and transmission of the energy is completely different from the conventional mode of heating. The MW technology has been applied to a number of useful research and development processes such as polymer technology, organic synthesis, and application to waste treatment; drug targeting; ceramic and alkane decomposition [18].

Very recently, we reported the MW irradiation method for the synthesis of substituted Acridone analogues [19].

In the present work, potent novel analogs of Aryl Propyl Acridone carboxamide were developed by Pharmacophore drug designing, MW-assisted technique and Standard Hoechst 33342 assay method.

A five point pharmacophore generation was developed by using fourteen active ligands belonging to acridone-4-carboxamide class [20]. All the ligands were first processed with the LigPrep software program to assign protonation states, generate stereoisomers and convert 2D to 3D structures. Conformer generation was carried out with the MacroModel ligand torsion search with OPLS_2005 force field.

Pharmacophore with five features common to all active ligands were identified then scored according to superposition of pharmacophore site, alignment of vector characteris-

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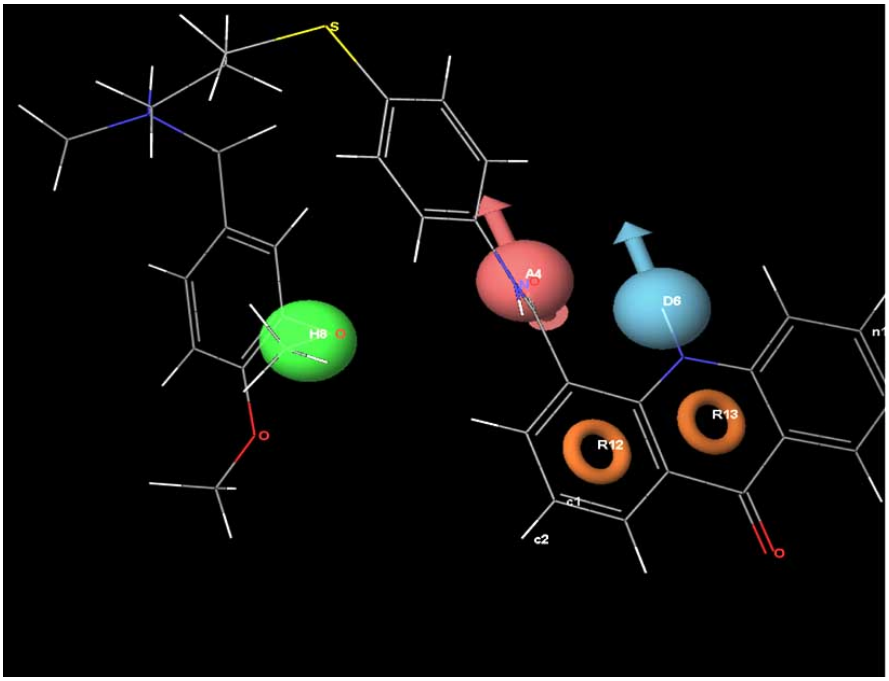


Fig. (1). The top scoring Pharmacophore hypothesis ADHRR (A4 is acceptor point, D6 is donor point, H8 is hydrophobic point, R12 and R13 are aromatic points).

tics, and penalization of matches to inactive training set molecules.

The basic nucleus, Aryl propyl acridone-4-carboxamides was build using the top scoring hypothesis ADHRR (Fig. **1**). The designing study was performed using phase drug designing software (SCHRODINGER,INC) on INTEL CORE 2 Duo 2 GHz computer.

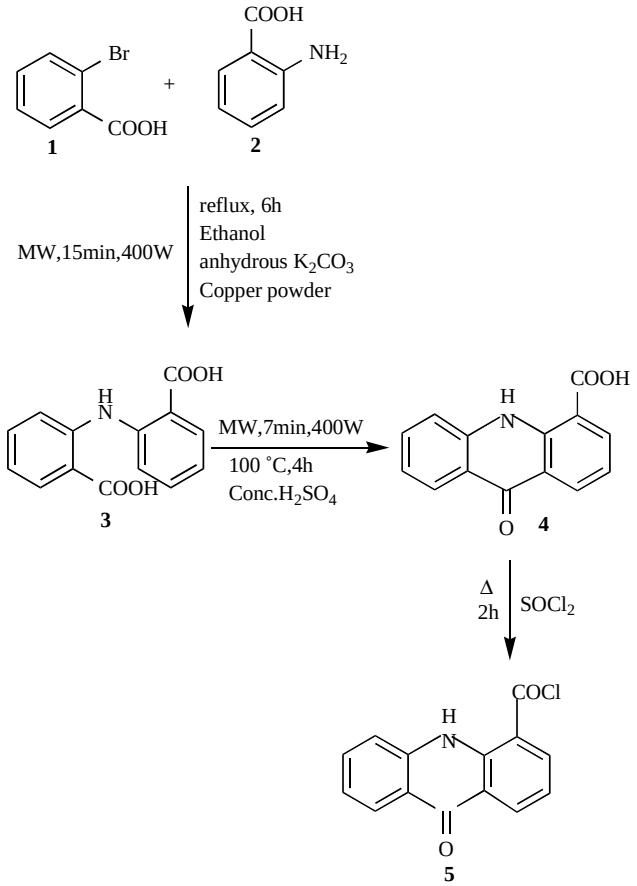
RESULTS AND DISCUSSION

Chemistry

Synthesis of substituted Aryl-propyl-acridone-4-carboxamide analogs involved N-arylation of o-bromobenzoic acid **1** with anthranilic acid **2** in presence of copper powder and anhydrous potassium carbonate in ethanol by MW heating at 400W MW intensity for 15min to get N-(2-carboxy phenyl) anthranilic acid **3** which on cyclization with concentrated sulfuric acid by MW irradiation at 400W MW intensity for 7min produced Acridone-4-carboxylic acid **4**. Acridone-4-carboxylic acid was converted to Acridone carbonyl chloride **5** using thionyl chloride (Scheme **1**).

Reduction of 3-chloro-propiophenone **6** using sodium borohydride in methanol gave 3-chloro-1-phenyl-1-propanol **7.** This was further reacted with sodium iodide in acetone by MW heating at 350W for 25min yielded 3-iodo-1-phenyl-1-propanol **8**.This iodo alcohol on reaction with methylamine in tetrahydrofuran gave N-methyl-3-phenyl-3-hydroxy propylamine **9** and on reaction with ammonia yielded 3-phenyl-3-hydroxy propylamine **10**.

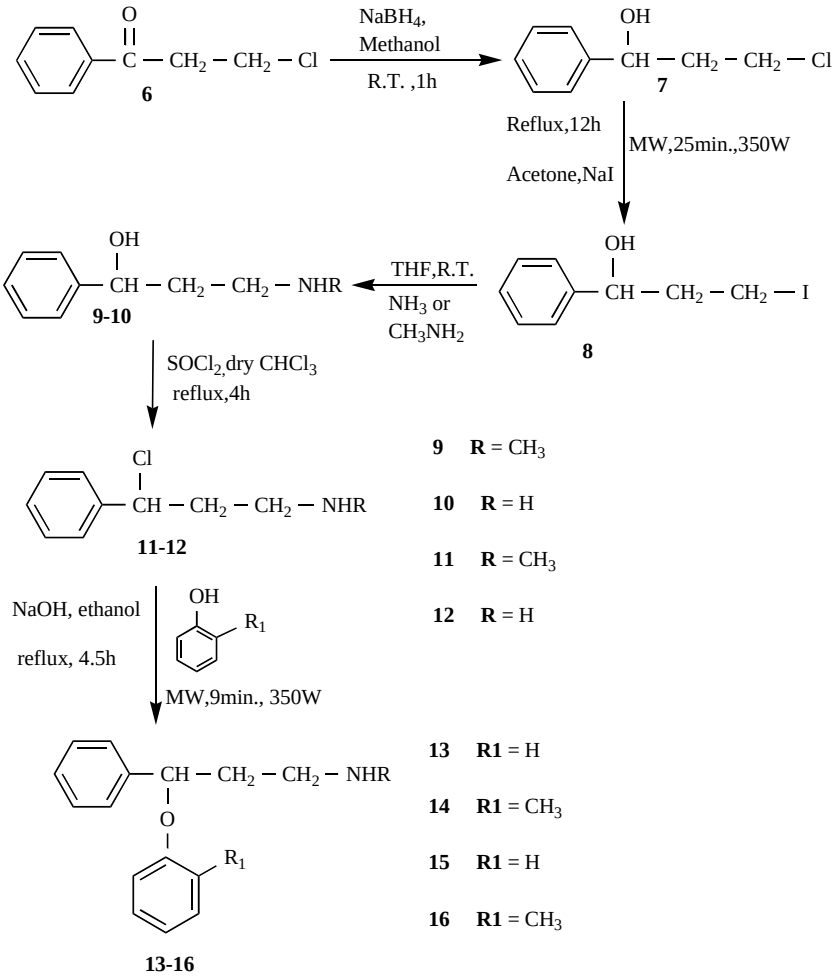
Compounds **9** and **10** were respectively treated by thionyl chloride to afford the corresponding derivatives **11** and **12**. Both the chloro propylamines (compounds **11** and **12**) were individually treated with substituted phenol by MW heating for 9min at 350W to get compounds **13-16** (Scheme **2**). Compound **6** was reacted with sodium iodide in acetone by



Scheme 1. Synthesis of compounds **4-5**.

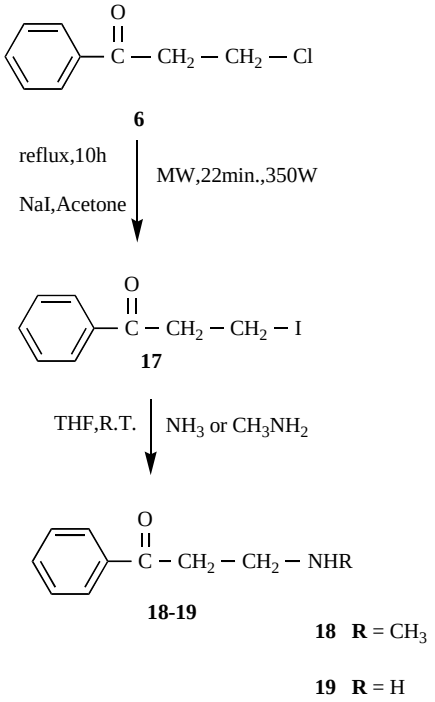
Table 1. Comparative Reaction Time and Percentage Yield of Intermediates and Title Compounds by Conventional and MW Method

Compound No.	Reaction Time		Yield	
	Conventional (h)	MW (min)	Conventional (%)	MW (%)
3	6	15	64	79
4	4	7	55	71
5	2	-----	63	-----
7	1	-----	83	-----
8	12	25	75	86
11	4	-----	46	-----
12	4.5	-----	48	-----
13	4.5	9	48	58
14	4.5	9	53	62
15	4.5	9	53	60
16	4.5	9	54	67
17	10	22	63	75
22	6	15	46	64
23	6.5	16	45	62
24	5	12	42	58
25	5.5	14	40	54
26	5.5	14	40	52

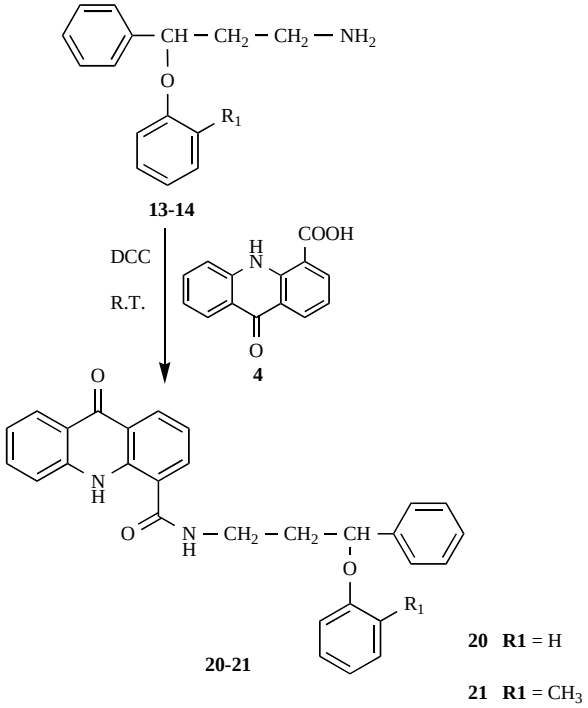


Scheme 2. Synthesis of compounds **13-16**.

MW irradiation for 22min at 350W MW intensity produced 3-iodopropiophenone **17** which on reaction with methylamine in tetrahydrofuran yielded 3-(N-methylamino) propiophenone **18** and on reaction with ammonia gave 3-amino propiophenone **19** (Scheme **3**).

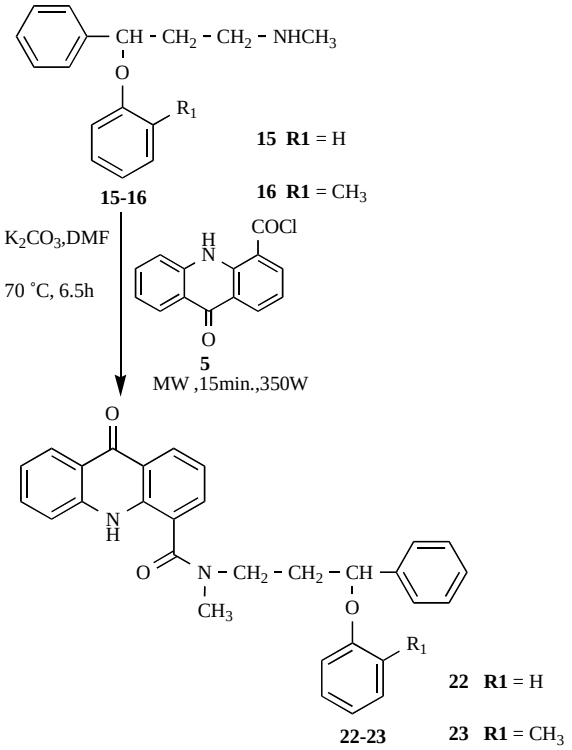


Scheme 3. Synthesis of compounds **18-19**.

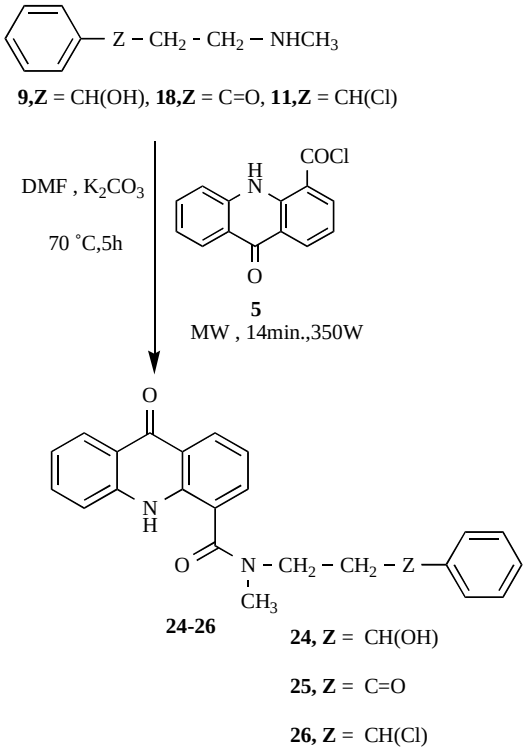


Scheme 4. Synthesis of compounds **20-21**.

Further, compound **4** was condensed with compounds **13** and **14** respectively using N,N'-dicyclohexylcarbodiimide (DCC) to get compounds **20** and **21** (Scheme **4**). Compound



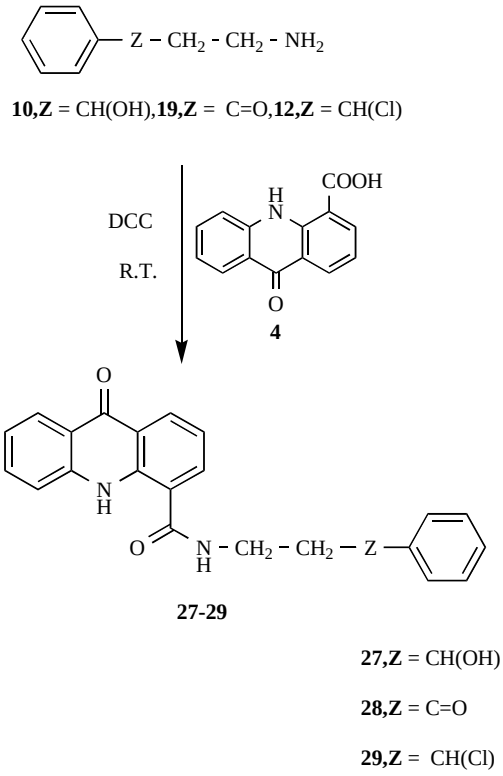
Scheme 5. Synthesis of compounds **22-23**.



Scheme 6. Synthesis of compounds **24-26**.

5 was condensed with compounds **15** and **16** in presence of anhydrous potassium carbonate in dimethylformamide by MW irradiation for 17min at 350W and 6.5h by conventional

method offered compounds **22** and **23**, respectively (Scheme **5**). Condensation of compound **5** with compounds **9, 18** and **11** individually using potassium carbonate in dimethylformamide by MW technique for 14min at 350W and conventional method for 5h gave compound **24**, **25** and **26** (Scheme **6**). Compound **4** was condensed with compounds **10, 19** and **12** respectively using DCC gave compounds **27**, **28** and **29** respectively (Scheme **7**).



Scheme 7. Synthesis of compounds **27-29**.

A new MW-assisted method for the rapid and efficient synthesis of substituted Aryl propyl acridone-4-carboxamides has been developed. The MW irradiation effectively reduced reaction time with considerable increase in the yields as compared to the conventional method.

Pharmacological Evaluation

The title compounds **20-29** were screened to evaluate their inhibitory effects on the transport activity of P-glycoprotein (P-gp) by standard Hoechst 33342 assay method [21].

Human ovarian carcinoma cell lines A2780 were cultivated in RPMI-1640 medium supplemented with 10% fetal bovine serum, 50 μg/mL streptomycin, 50U/mL penicillin G, and 365 μg/mL L-glutamine. Cells were grown to 80–90% confluence and treated with trypsin–EDTA before subculturing. Every 5th passage doxorubicin (0.1 μM final concentration) was added to the cell culture medium of A2780adr cells to maintain a resistance pressure and to conserve P-gp overexpression.

Human ovarian carcinoma cell lines A2780 and the corresponding adriamycin-resistant A2780adr cell line were grown in T75 or T175-flasks. At a confluence of approximately 80% cells were harvested by trypsination. Pelleted cells were resuspended in fresh culture medium and counted with a Casy I Modell TT cell counter. After three washing steps with Krebs–Hepes buffer, cells were seeded into black 96 well plates at a density of approximately 30,000 cells in a volume of 90 μl per well. Then, 10 μl of various title compounds in different concentrations were added, resulting in a final volume of 100 μl per well. The prepared 96-well plates were kept under 5% CO_2 at 37^0C for 30 min After this preincubation period, 20 μl of a 30 μM Hoechst 33342 solution were added to each well. Subsequently, fluorescence was measured immediately at constant time intervals (120 s) up to 46 min at an excitation wavelength of 365 nm and an emission wavelength of 450 nm using a 37^0C tempered BMG POLARstar microplate reader.

The fluorescence-data points were measured in 46 min. The slopes were calculated by linear regression and used as dependent parameters.

From these data concentration–response curves were generated by nonlinear regression using the 4-parameter logistic equation with variable Hill slope. The inhibitory effects are reported as logarithm of the reciprocal IC_{50} values ($_pIC_{50}$).

The inhibitory effect of P-gp is expressed in terms of $_pIC_{50}$ value (Table **2**). It was observed that the test compounds **20, 21 and 22** exhibited better activity as compared to the standard Verapamil.

Table 2. pIC_{50} Values of Title Compounds by Standard Hoechst 33342 Assay Method

Compound No.	pIC_{50} ± SD
20	5.70 ± 0.16
21	5.48 ± 0.14
22	5.28 ± 0.16
23	5.12 ± 0.09
24	4.22 ± 0.18
25	4.34 ± 0.16
26	4.32 ± 0.07
27	4.28 ± 0.06
28	4.66 ± 0.18
29	4.35 ± 0.23
Verapamil	5.18 ± 0.25

EXPERIMENTAL

All the chemicals and solvents were obtained from commercial source and purified by the established methods. Melting points of the synthesized molecules were determined by open capillary tube and were uncorrected. The purity of the compounds was ascertained by thin layer chromatography (TLC) on pre-coated silica gel G plate.

All intermediates were characterized by recording their physical constant and I.R. spectroscopy. The title compounds

were characterized by I.R., ^{1}H NMR, mass spectroscopy and Elemental analysis.

I.R. spectra were recorded on Jasco FT/IR-5300 spectrometer using KBr pellet method. Nuclear magnetic resonance spectra were recorded using Joel FT/NMR 300 MHz spectrometer using TMS as internal standard. Mass spectroscopy was carried out on Q-Tof micro (YA-105), Micromass (Water's) Mass spectrometer. Elemental analysis was performed using EA-112, Thermoquest CHN analyzer. MW heating was done in a QPro-M, Questron Tech. MW oven.

Synthesis of Acridone-4-Carboxylic Acid (4)

Conventional Synthesis

A mixture of N-(2-carboxy phenyl) anthranilic acid, 15 g (0.066 mole) and conc. sulfuric acid,48 ml was heated at 100^{0}C for 4 h, cooled at room temperature and then poured into ice water. The precipitate formed was collected and washed with water. The crude product was purified by recrystallization using ethanol.

MW-Assisted Synthesis

A mixture of N-(2-carboxy phenyl) anthranilic acid, 15 g (0.066 mole) and conc. sulfuric acid, 48 ml was irradiated with MW at 400W MW intensity for 7 min, cooled at room temperature and then poured into ice water. The precipitate formed was collected and washed with water. The crude product was purified by recrystallization using ethanol.

(4): Yield 71%. mp 325^{0}C ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 7.41-7.89 (m,7H,Ar), 7.54 (s,1H,NH), 10.80 (s,1H,COOH). IR (KBr) cm^{-1}: 3331 (NH), 2964 (CH), 2883(OH), 1666 (C=O),1618(C=O),1579(NH). ESMS m/z = 240.1171 [MH$^+$].Anal Calcd for $C_{29}H_{24}N_2O_3$: C, 70.29; H, 3.79; N, 5.85; Found: C, 70.18; H, 3.58; N, 5.64.

General Procedure for Synthesis of 4-[3-phenyl-3-(substituted phenoxy) propyl]acridone carboxamide (20-21)

Acridone carboxylic acid **4** (0.035 mole) was dissolved in 35 ml DMF in RBF with guard tube attached at the neck and stirred at 200 r.p.m. for 30 min at 0-4^{0}C. DCC (0.035 mole) was dissolved separately in 35ml DMF in a beaker and was then added drop-wise to a solution of acridone carboxylic acid and stirred at 200 r.p.m. for 2 h at 0-4^{0}C. Appropriate 3-phenyl-3-(substituted phenoxy) propylamine **13-14** (0.035 mole) was dissolved in 50 ml DMF in a beaker and stirred at 200 r.p.m. for 1 h at 0-4^{0}C. This solution was then added to above mixture and stirred at 200 r.p.m. for 4 h at 0-4^{0}C and then overnight at room temp. The reaction mixture was filtered; the filtrate was then concentrated under vacuum at 80^{0}C and extracted with dichloromethane. The organic layer was washed with water and evaporated to give a residue that was finally purified by column chromatography.

(20): Yield 40%. mp 168^{0}C. ^{1}H-NMR (300 MHz, CDCl3) δ: 2.34 (q, 2H, CH_2), 3.38 (t, J=6.2 Hz, 2H, CH_2), 4.68 (t, J=8.0 Hz, 1H, CH), 7.40 (s,1H,NH), 6.24-8.40 (m,17H,Ar). IR (KBr) cm^{-1}: 3334 (NH), 2998 (CH), 1688 (C=O), 1596 (C=O), 1448 (NH), 1268, 1106(C-O). ESMSm/z=448.1521[M]$^+$.Anal Calcd for $C_{29}H_{24}N_2O_3$: C, 77.66; H, 5.39; N, 6.25; Found: C, 77.52; H, 5.35; N, 6.20.

(21): Yield 45%. mp 142^{0}C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.31 (s, 3H, CH_3), 2.26 (q, 2H, CH_2), 3.36 (t, J=5.8 Hz,2H, CH_2), 4.48 (t, J=8.2 Hz,1H, CH), 7.30 (s,1H,NH),6.32-8.39 (m, 16H, Ar). IR (KBr) cm^{-1}: 3474 (NH), 3394 (CH), 1626 (C=O), 1554 (C =O), 1462 (NH), 1310, 1202 (C-O). ESMS m/z = 461.9865[M]$^+$.Anal Calcd for $C_{30}H_{26}N_2O_3$: C, 77.90; H, 5.67; N, 6.06; Found: C, 77.86; H, 5.54; N, 6.01.

General Procedure for Synthesis of 4-[N-methyl-3-phenyl-3-(substituted phenoxy) propyl]acridone carboxamide (22-23)

Conventional Synthesis

A mixture of acridone carbonyl chloride **5** (0.038 mole), (0.038 mole) suitable N-methyl-3-phenyl-3-(substituted phenoxy) propylamine **15-16**, 2.8g of anhydrous potassium carbonate in 100 ml of DMF was heated at 70^{0}C with stirring for 6.5 h To the mixture, 100 ml ice cold water was added and extracted with dichloromethane. The organic layer was washed with water and evaporated to give a residue that was purified by column chromatography.

MW-Assisted Synthesis

A mixture of acridone carbonyl chloride **5** (0.038 mole), (0.038 mole) suitable N-methyl-3-phenyl-3-(substituted phenoxy) propylamine **15-16**, 2.8g of anhydrous potassium carbonate in 100 ml of DMF was irradiated with MW at 350W MW intensity for 15min After completion of reaction, the work-up was done in a manner similar to the conventional method.

(22): Yield 64%. mp 172^{0}C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.32 (q, 2H, CH_2), 2.67 (s, 3H, CH_3), 3.28 (t, J=6.0 Hz,2H, CH_2), 4.74 (t, J=8.4 Hz, 1H, CH), 7.38 (s,1H,NH), 6.70-8.38 (m, 17H, Ar). IR (KBr) cm^{-1}: 3382 (C-H), 1638 (C=O), 1594 (C=O), 1532 (NH), 1204,1016 (C-O), 1016 (C-N). ESMS m/z = 461.7684 [M]$^+$. Anal Calcd for $C_{30}H_{26}N_2O_3$: C, 77.90; H, 5.67; N, 6.06. Found: C, 77.82; H, 5.63; N, 6.02.

(23): Yield 62%. mp 158^{0}C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.22 (q, 2H, CH_2), 2.44 (s, 3H, CH_3), 2.85 (s, 3H, CH_3), 3.21 (t, J=5.4 Hz,2H, CH_2), 5.08 (t, J=7.8 Hz,1H, CH), 7.36 (s,1H,NH), 6.67-8.42 (m, 16H, Ar). IR (KBr) cm^{-1} : 3292 (C-H), 1652 (C=O),1594 (C=O), 1504 (NH), 1088, 1208 (C-O), 1088 (C-N). ESMS m/z = 475.9981[M]$^+$.Anal Calcd for $C_{31}H_{28}N_2O_3$: C, 78.13; H, 5.92; N, 5.88; Found: C, 78.08; H, 5.88; N, 5.78.

General Procedure for Synthesis of 4-(N-methyl-3-phenyl-3-substituted propyl)acridone-carboxamide (24-26)

Conventional Synthesis

A mixture of acridone carbonyl chloride **5** (0.030 mole), (0.030 mole) appropriate N-methyl–3-phenyl–3-substituted propylamine **9**, **18**, **11** and 1.4g of anhydrous potassium carbonate in 50 ml of DMF was heated at 70^{0}C with stirring for 5h. To the mixture, 50 ml ice-cold water was added and extracted with ethylacetate. The organic layer was washed and

evaporated to give a residue that was purified by column chromatography.

MW-Assisted Synthesis

A mixture of acridone carbonyl chloride **5** (0.030 mole), (0.030 mole) appropriate N-methyl–3-phenyl–3-substituted propylamine **9, 18, 11** and 1.4g of anhydrous potassium carbonate in 50 ml of DMF was irradiated with MW at 350W MW intensity for 14 min. After completion of reaction, the work-up was done in a manner similar to the conventional method.

(24): Yield 58%. mp 176^{0}C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.01 (q, 3H, CH_2 and OH), 2.84 (s, 3H, CH_3), 3.41 (t, J=6.4 Hz, 2H, CH_2), 3.82 (q, 1H, CH), 7.21 (s,1H,NH), 6.64–8.22(m, 12H, Ar); IR (KBr) cm^{-1}: 3406 (OH), 2906 (C-H), 1684 (NH), 1685 (C=O),1618 (C=O), 1094 (C-N). ESMS m/z = 386.1143 $[M]^+$.Anal Calcd for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25; Found: C, 74.48; H, 5.68; N, 7.18.

(25): Yield 54%. mp 186^{0}C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.61 (t, J=6.8 Hz,2H, CH_2), 2.88 (s, 3H, CH_3), 3.51 (t, J=6.4 Hz, 2H, CH_2), 7.49 (s,1H,NH) 7.16-8.31 (m,12H,Ar). IR (KBr) cm^{-1}: 2934 (CH), 1696 (C=O), 1682 (NH), 1588 (C=O), 1526 (C=O), 1056 (C-N).ESMS m/z =385.0602 $[MH^+]$.Anal Calcd for $C_{24}H_{20}N_2O_3$: C, 74.98; H, 5.24; N, 7.29; Found: C, 74.72; H, 5.22; N, 7.21.

(26): Yield 52%. mp 158^{0}C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.14 (q, 2H, CH_2), 2.91 (s, 3H, CH_3), 3.52 (t, J=5.4 Hz,2H, CH_2), 3.84 (t, J=6.4 Hz, 1H, CH), 7.33 (s,1H,NH), 6.62 – 8.42 (m, 12 H, Ar). IR (KBr) cm^{-1}: 2962(CH), 1672 (C=O), 1656 (C=O), 1518 (NH), 1032 (C –N), 704 (C-Cl).ESMS m/z = 403.0422$[M]^+$. Anal Calcd for $C_{24}H_{21}Cl\ N_2O_2$: C, 71.19; H, 5.23; N, 6.92; Found: C, 71.11; H, 5.19; N, 6.84.

General Procedure for Synthesis of 4-(3-phenyl-3-substituted propyl) acridone carboxamide (27-29)

Acridone-4-carboxylic acid **4** (0.035 mole) was dissolved in 35 ml DMF in RBF with guard tube attached at the neck and stirred at 200 r.p.m. for 30 min at 0-4^{0}C. DCC (0.035 mole) was dissolved separately in 35 ml, DMF in a beaker and was then added dropwise to a solution of acridone carboxylic acid & stirred at 200 r.p.m. for 2h at 0-4^{0}C. 3-phenyl 3-substituted propylamine **10, 19, 12** (0.005 mole) was dissolved in 50 ml DMF in a beaker and stirred at 200 r.p.m. for 1 h at 0-4^{0}C. This solution was then added to the above mixture and stirred continuously at 200 r.p.m. for 4 h at 0-4^{0}C and overnight at room temp. The reaction mixture was further filtered; the filtrate was then concentrated under vacuum at 80^{0}Cand extracted with ethylacetate. The organic layer was washed with water and evaporated to give a residue that was finally purified by column chromatography.

(27): Yield 40%. mp 182^{0}C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.01 (q, 3H, CH_2 and OH), 3.36 (t, J=6.0 Hz,2H, CH_2), 3.78 (q, 1H, CH), 5.25 (s, 1H, NH), 7.52 (s,1H,NH), 7.16 – 8.42 (m, 12H, Ar). IR (KBr) cm^{-1}: 3494 (NH)**,** 3396 (CH), 3002 (OH), 1688 (C=O), 1622 (C=O), 1582(NH). ESMSm/z=372.1498$[M]^+$. Anal Calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52. Found: C, 74.12; H, 5.23; N,7.42.

(28): Yield 41%. mp 138^{0}C.^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.75 (t, J=6.8 Hz,2H, CH_2), 3.83 (t, J=6.0 Hz, 2H, CH_2), 5.49 (s, 1H, NH), 7.52 (s,1H,NH), 6.51-8.15 (m,12H,Ar). IR (KBr) cm^{-1}: 3356 (NH), 2921 (CH), 1694 (C=O), 1682 (C=O), 1628 (NH). ESMS m/z = 370.1648$[M]^+$.Anal Calcd for $C_{23}H_{18}N_2O_3$: C, 74.58; H, 4.90; N, 7.56; Found: C, 74.52; H, 4.78; N, 7.53.

(29): Yield 40%. mp 146^{0}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.11 (q, 2H, -CH_2), 3.42 (t, J=5.4 Hz, 2H, -CH_2), 3.67 (t, J=7.4 Hz, 1H, -CH), 5.12 (s, 1H, NH), 7.35 (s, 1H, NH), 6.69-8.03 (m, 12H, Ar). IR (KBr) cm^{-1}: 3412 (NH), 3324 (CH), 1686 (C=O), 1672 (C=O), 1624 (NH), 754 (C-Cl). ESMS m/z = 390.2144$[M]^+$. Anal Calcd for $C_{23}H_{19}\ ClN_2O_2$: C, 70.68; H, 4.90; N, 7.17; Found: C, 70.67; H, 4.78; N, 7.14.

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