ejpmr, 2018,5(5), 59-65

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

SYNTHESIS AND ANTIPROLIFERATIVE ACTIVITY OF ACRIDINE-SULFONAMIDE CONJUGATES

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Article Received on 04/03/2018 **Article Revised on 24/03/2018** **Article Accepted on 15/04/2018**

ABSTRACT

The present study describes the synthesis and antiproliferative evaluation of several acridine analogues carrying sulfonamide and thiouredoside chain at C-9 position. The key intermediate aminoacridines5 were prepared by nucleophilic aromatic substitution (S_{NAr}) of 9-chloroacridine 4 with 4,4'-diaminodiphenylmethane or p-phenylenediamine. The 9-amino derivatives 5 were further reacted with phenylisothiocyanate or arylsulfonlychloridesto afford the corresponding thiourea-, or acridine sulfonamide analogues6 and 7 respectively. Some of the prepared derivatives showed a strong antiproliferative activity against the breast, colon and hepatocellular carcinoma cell lines. Among them, compounds 5b and 8bwere the most potentwith IC_{50} values 5.88, 8.30, 8.93 and 8.83, 14.51, 9.39 against breast, hepatocellular and coloncarcinoma cell lines respectively.

KEYWORDS: 9-Chloroacridin, Sulfonamide, Synthesis, Antiproliferative Activity.

INTRODUCTION

Acridine derivatives form an important class of heterocycles containing nitrogen compounds due to their broad range of pharmaceutical applications[1-5] Acridine derivatives are characterized by unique physical, chemical and biological activities, as well as industrial applications. It was reported that acridine derivatives have exhibited bioactivities such as anti-infammatory,[6,7] anticancer,[8] antimicrobial,[9] antitubercular,[10,11] antiparasitic,[12] antimalarial,[13-15] antiviral,[16-17] and fungicidal activities.[18] Acridine derivatives have been shown to be effective as inhibitors of acetylcholinesterase.[19] Furthermore, acridines are used as dyes, fluorescent materials for visualization of biomolecules, and in laser technologies.[20] These properties of acridines are attributed to their semi-planar heterocyclic structure, which appreciably interacts with different biomolecular targets. Acridine derivatives are found in natural plants and various marine organisms.[21,22] Notably, the anticancer activity of acridine derivatives has attracted increasing interest. To date, many derivatives of acridine have been synthesized and tested for anti-tumour activity. The unique planarring structure allows acridine derivatives to act as DNA intercalators[23,24] and to inhibit topoisomerase or telomerase enzymes.[25-28] Avariety of acridine derivatives have been synthesized; such as N-(2-(dimethylamino)ethyl)acridine-4-carboxamide(DACA) (1),[29-31] triazoloacridone(C-1305)(2)[32] and amsacrine(m-AMSA) (3)[33] (Fig.1) have entered clinical studies. Among them, m-AMSA (3) wasthe first synthetic drug exhibiting clinical efficacy as a topoisomerase inhibitor. Many m-AMSA derivatives (AHMA(4), D3CLP (5) (Fig.1) have been developed for stronger anti-cancer properties and removal of many harmful side effects.[31,34] Intermolecular interactions in acridine and acridinium derivatives determine their biological and physical properties including their chemiluminogenic abilities. Therefore, hydrogen bondingand □–□ interactions within the Hirshfeldsurface have been studied. Recently, Wera and co-workers reported the synthesis and structural investigations of some new acridine and acridinium derivatives.[35]

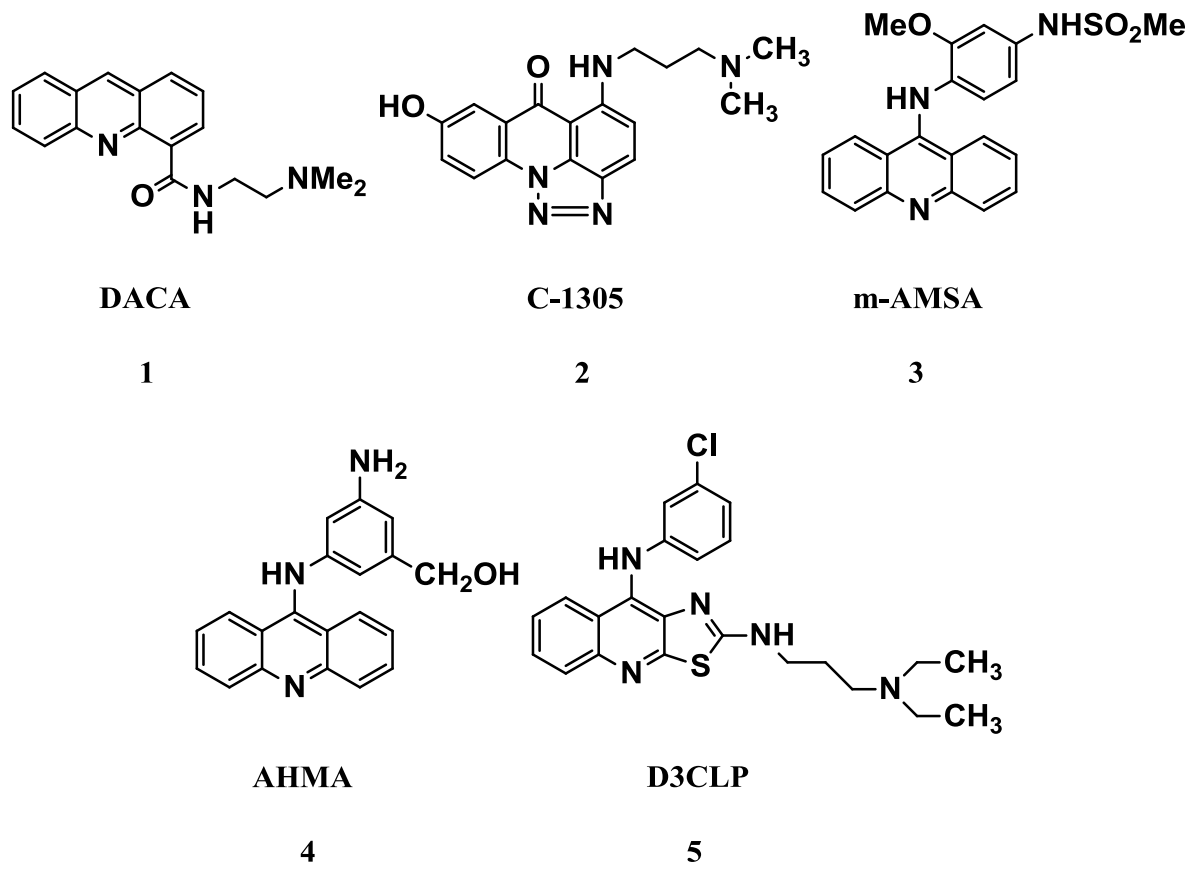


Fig. 1: Structuresof DACA (1), C-1305 (2), m-AMSA (3), AHMA(4), andD3CLP(5).[31–34]

In continuation of our efforts in synthesis and biological evaluation of N-heterocyclic containing compounds we became interested in synthesize of new acridinesulfonamide analogues and evaluate their anticancer activity against several cancer cell lines.

MATERIALS AND METHODS

^{1}HNMRexperiments (solvent $CDCl_3$ or DMSO-d_6) were carried out with a 300 MHz or 400 MHz at both Cairo University and the main chemical warfare laboratories , Ministry of Defence. Chemical shifts are reported in part per million (ppm) relative to respective solvent or tetramethylsilane (TMS) .massspectra was performed at Al-Azhar University, IR spectroscopy & Melting points (m.p) were performed at Cairo University. The anticancer activitywas performed at Al-Mansoura University, Faculty of pharmacy. All reactions were followed by thin layer chromatography (TLC).

Synthesis

Synthesis of 9.chloroacridine (4): Acridone (0.5gm, 2.56 mmol) was dissolved in excess Phosphorus oxy chloride. The reaction mix was refluxed at 90 - 110°C for 3hr. After that the reaction mix was neutralized by poured it on ice gradually with stirring then added Sodium bicarbonate gradually with stirring until arrived to neutralization point which determined by pH paper , Then filterated it and left it to dry to obtained on light olive ppt, yield (0.4gm, 80%) as apale green solid, m.p. 90-92°C (lit. 116°C)[36.] IR (KBr) cm^{-1}: 3434 (NH), 3073 (CH-Ar), 1626(C=N), 1547 (C=CforAr), 1271 (C-N). ^{1}H NMR ($CDCl_3$, 300 MHz),δ(ppm): 7.66 – 7.71 (m, 2H, Ar-H), 7.84 – 7.89 (m, 2H, Ar-H), 8.31 – 8.34 (d,J=8.4 Hz, 2H, Ar-H), 8.46 – 8.49 (d, J=8.7Hz, 2H, Ar-H).

General procedure for synthesis of compounds(5a-b): **9-Chloroacridine** (0.2 gm, 0.53 mmol) and diamine (1:1eq) and 5 excess from Triethylamine (0.34 mL, 4.65 mmol) were dissolved in 2 – 3 mL ethanol. The reaction mix.was refluxed at 80°C until the starting materials were consumed as monitored by TLC (2.5-7h). The reaction mix.was poured into ice water and the precipitated solid was then filtered and dried.

N – (4-(4-Aminobenzyl)phenyl)acridin-9-amine(5a): Yield (0.65gm, 93%) as an orange solid, m.p. 202°C, IR (KBr) cm^{-1}: 3392(NH_2+NH) overlap, 3020(CH- Ar), 2923(CH- Alkane), 1619 (C=N), 1587(C=C – Ar), 1361(C-N, Aromatic amine), 1259(=C-N).^{1}H – NMR ($CDCl_3$, 300 MHz), δ(ppm):3.56 (br.s, 2H, NH_2), 3.84 (br.s, 2H, CH_2), 6.61–6.84 (m, 4H, Ar-H), 6.952–7.230 (m, 4H, Ar-H), 7.66 (br.s, 1H, NH-Ar), 8.01–8.04 (m, 8H, Ar-H). EIMS, m/z ($C_{26}H_{21}N_3$) calcd.,375.465 [M]+; found,375.11.

N^1-(Acridin-9-yl)bezene-1,4-diamine(5b): yield (0.267gm, 79%) as a deep orange solid, m.p. >250°C. IR (KBr) cm^{-1} : 3380(NH_2+NH) overlap, 3080(CH-Ar), 1622(C=N), 1561(C=C-Ar), 1364(C-N-Ar) , 1256(=C-N).^{1}H – NMR (DMSO-d_6, 400MHZ),δ(ppm): 4.78 (br.s,

2H, NH_2), 6.54 – 6.98 (m, 5H, 4Ar-H + NH-Ar), 7.47 – 7.54 (m, 8H, Ar-H). EIMS, m/z ($C_{19}H_{15}N_3$) calcd,285.34 $[M]^+$; found,285.07.

general procedure for synthesis of compounds (6a-b): Compound 5a (0.1 gm, 0.27 mmol)or5b (0.1 gm, 0.35 mmol) and phenylisothiocyanate(1:1eq) were dissolved in 3-4mL chloroform and left them on stirring at room temp until the starting materials were consumed as monitored by TLC (2-8 day).The solvent was removed and diethylether was added to the remaining residue to give pure ppt, which was filtered and dried.

1–(4-(4-(Acridin-9-ylamino)benzyl)phenyl)-3-phenylthiourea(6a): yield (0.107gm, 78.5%), as a red solid, m.p. 198°C, IR (KBr) cm^{-1}: 3427 (NH), 3024 (CH-Ar), 2918 (CH-Alkane), 1633 (C=N), 1585(C=C –Ar) , 1311(C-N , Aromatic amine), 1245(=C-N), 1110 (C=S).¹H – NMR ($CDCl_3$, 300MHZ),δ(ppm): 3.53 (br.s, 2H, CH_2), 7.08– 7.20 (m, 8H, Ar-H), 7.31– 7.44 (m, 5H, 5Ar-H), 7.76 – 7.85 (br.s, 1H, NH-Ar), 8.01– 8.04 (m, 8H, Ar-H), 10.76- 10.84 (br.s, 1H, -CS-HN-C_6H_5), 12.05 - 12.25 (br.s, 1H, -C_6H_4-HN-CS-). EIMS, m/z ($C_{33}H_{26}N_4S$) calcd,510.65 [M]+; found,510.43.

1 –(4-(Acridin-9-ylamino)phenyl)-3-phenylthiourea(6b): yield (0.093gm, 63.33%), as abrownish red solid, m.p. >250°C. IR (KBr)cm^{-1}: 3427 (NH), 3030 (CH-Ar), 1630 (C=N), 1588(C=C-Ar),1315(C-N, Aramine), 1243(=C-N), 1161(C=S).¹H – NMR (DMSO-d_6, 400MHZ),δ(ppm): 6.53 – 7.17 (m, 4H, Ar-H), 7.21 – 7.68 (m, 5H, Ar-H), 7.87 – 8.30 (m, 8H, Ar-H), 9.257 (br.s, 1H, NH-Ar), 10.06 (s, 1H, -CS-NH-C_6H_5), 10.10 (s, 1H, -C_6H_4-NH-CS-). EIMS, m/z ($C_{26}H_{20}N_4S$) calcd,420.53 $[M]^+$; found, 419.14.

general procedure for synthesis (7a-e) and (8a-d): Compound 5a (0.1 gm, 0.27 mmol) or 5b (0.1 gm, 0.35 mmol), arylsulfonyl chloride (1:1.2 eq) for 7 (a,b,c), 8(a,b,d), and (1:2.4 eq) for 7(d, e), 8(c) and 3 excess from triethylamine were dissolved in DMF.7aWas left on stirring at room temp for 5 day.7b – 5e were refluxed until the starting materials were consumed as monitored by TLC (13-26h).

8a[at room temp., 8d], 8b [at room temp., 3d], 8c[reflux, 3d], 8d[at room temp, 20d]

After the completion of the reaction,the mix.was poured into ice to afford a solid product which was filtered and dried.

N-(4-(4-(Acridin-9-ylamino)benzyl)phenyl)-2-nitrobenzenesulfonamide (7a): Yield (0.072gm, 48%) as a light orange solid, m.p. 172°C, IR (KBr) cm^{-1}: 3431 (NH), 3038 (CH – Ar), 2924 (CH – Alkane), 1623 (C=N), 1511(C=C –Ar), 1258 (C-N Aromatic amine), 1160 (=C-N), 1509, 1346(N-O, asym, sym). ¹H – NMR ($CDCl_3$, 300MHZ),δ(ppm): 2.90 (s, 2H, CH_2), 6.75 – 7.11 (m, 9H, 8Ar-H+NH-Ar), 7.56 – 8.03 (m, 12H, Ar-H), 8.20 – 8.38 (m, 1H, HN-SO2). EIMS, m/z ($C_{32}H_{24}N_4SO_4$) calcd,560.62[M]+; found,560.07.

N-(4-(4-(Acridin-9-ylamino)benzyl)phenyl)-4-methylbenzenesulfonamide(7b): Yield (0.08gm, 57%) as a yellow solid, m.p. >250°C. IR (KBr) cm^{-1}: 3426 (NH), 3028 (CH-Ar), 2923 (CH-Alkane), 1620 (C=N), 1592 (C=C-Ar), 1418 (C-N-Ar amine), 1334, 1092(S=O,asym,sym),1157(=C-N).¹H – NMR ($CDCl_3$, 300MHZ), δ(ppm): 2.39 (br.s, 3H, CH_3), 2.89 (br.s, 2H, CH_2), 6.26 – 6 .40 (br.s, 1H, NH-Ar), 6.96 – 7.24 (m, 8H, Ar-H), 7.62 – 7.64 (m, 12H, Ar-H), 7.98 – 8.05 (br.s, H, HN-SO_2). EIMS , m/z ($C_{33}H_{27}N_3SO_2$) calcd,529.65 [M]+; found,529.34.

N-(4-(N-(4-(4-(Acridin-9-ylamino)benzyl)phenyl)sulfamoyl)phenyl)acetamide(7c): yield (0.043gm, 28.67%) as a dark yellow solid, m.p. >250°C. IR (KBr) cm^{-1}:3434 (NH), 3037 (CH-Ar), 2922 (CH-Alkane), 1623 (C=N), 1511 (C=O), 1473(C=C-Ar), 1420, 1157(S=O asym, sym), 1260 (C-N, Ar amine), 1157(=C-N).¹H NMR ($CDCl_3$, 300MHZ),δ(ppm): 2.89 (m, 2H, CH_2), 3.60 (br.s, H, NH), 3.84 (s, 3H, CH_3), 6.61 – 6.65 (m, 4H, Ar-H) , 6.81 – 6.85 (m, 4H, Ar-H), 6.95 – 7.11 (m, 4H, 4Ar-H), 7.63– 7.68 (m, 8H, Ar-H), 8.00 – 8.03 (m, 2H, HN-SO_2 +HN-CO). EIMS, m/z ($C_{34}H_{28}N_4SO_3$) calcd,572.68[M]+;found,572.39.

N-(4-(4-(Acridine-9-ylamino)benzyl)phenyl)-4-(phenyldiazenyl)benzenesulfonamide(7d): yield (0.125gm, 75%), as an orange solid, m.p.>250°C. IR (KBr) cm^{-1}: 3433 (NH), 3040 (CH-Ar), 2925 (CH-Alk), 1631 (C=N), 1590 (C=C-Ar), 1512 (N=N), 1439, 1119 (S=O, asym, sym), 1342 (C-N, Ar amine), 1165 (=C-N).¹H – NMR ($CDCl_3$, 300MHZ),δ(ppm):2.89(s, 2H, CH_2), 6.58 – 6.65 (br.s, 1H, NH-Ar), 7.00 – 7.07 (m, 8H, Ar-H), 7.27 – 7.55 (m, 4H, Ar-H), 7.74 – 8.05 (m, 8H, Ar-H), 8.25 – 8.49(m, 5H, Ar-H), 10.80 – 10.90 (brs, 1H, HN-SO_2) . EIMS, m/z ($C_{38}H_{29}N_5SO_2$) calcd,619.73[M]+; found,619.34.

N-(4-(4-(Acridine-9-ylamino)benzyl)phenyl)-2,4,6-triisopropylbenzenesulfonamide(7e): yield (0.07gm, 78.5%), as an olive solid, m.p. 168°C. IR (KBr) cm^{-1}: 3418 (NH), 3033 (CH-Ar), 2958 (CH-Alkane), 1672 (C=N), 1628 (C=C), 1472, 1158 (S=O, asym, sym), 1339 (C-N,Ar amine), 1262 (=C-N).¹H – NMR ($CDCl_3$, 300MHZ),δ(ppm): 1.25 – 1.35(br.s, 18H, $6CH_3$), 2.89 (m, 2H, CH_2), 3.86-3.92 (m, 3H, CH), 6.65 – 7.23 (m, 11H, 10Ar-H + NH-Ar), 7.35 – 8.42 (m, 8H, Ar-H), 9.70 – 9.80 (br.s, 1H, HN-SO_2). EIMS, m/z ($C_{41}H_{43}N_3SO_2$) calcd,641.86$[M]^+$; found,641.71.

N-(4-(Acridin-9-ylamino)phenyl)-2-nitrobenzenesulfonamide(8a): yield (0.078gm, 47%), as abrownishsolid, m.p.>250°C. IR (KBr) cm^{-1}: 3423 (NH), 3112 (CH-Ar), 1628 (C=N), 1584 (C=C-Ar), 1505 , 1288 (N-O asym, sym), 1366, 1104 (S=O, asym, sym), 1254 (C-N).¹H – NMR (DMSO-d6, 400MHZ), δ(ppm): 6.54 – 6.72 (m, 4H, Ar-H), 7.01 – 7.43 (m, 8H, Ar-H), 7.81 – 7.96 (m, 4H, Ar-H), 10.22 (br.s, 1H, NH-Ar),

10.84 (br.s, 1H, NH-SO_2). EIMS, m/z ($C_{25}H_{18}N_4SO_4$) calcd,470.50[M]+; found, 470.05.

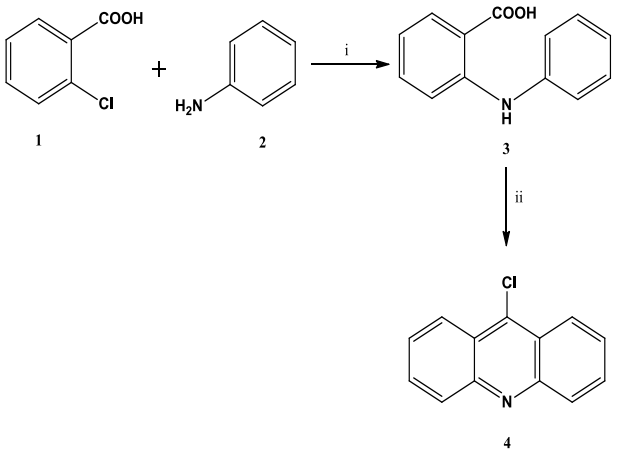
N-(4-(Acridin-9-ylamino)phenyl)-4-methylbenzenesulfonamide(8b): yield (0.096gm, 62%), as alight brown solid, m.p. >250°C. IR (KBr)cm^{-1}: 3324(NH), 3089 (CH-Ar), 1619 (C=N), 1589 (C=C-Ar), 1328, 1154 (S=O, asym, sym), 1258 (C-N).¹H – NMR (DMSO-d6, 400MHZ),δ(ppm): 2.35 (s, 3H, CH_3), 6.57 – 6.99 (m, 8H, Ar-H), 7.25 – 7.60 (m, 8H, Ar-H), 8.03(br.s, 1H, NH-Ar), 9.80 (br.s, 1H, NH-SO_2). EIMS, m/z ($C_{26}H_{21}N_3SO_2$) calcd,439.53 [M]+; found,439.19.

N-(4-(Acridin-9-ylamino)phenyl)-4-(phenyldiazenyl)benzenesulfonmide(8c): yield (0.158gm, 84.98%), as abrown solid, m.p. >250°C. IR (KBr)cm^{-1}: 3420(NH), 3250 (CH-Ar), 1626 (C=N), 1510(C=C-Ar), 1470 (N=N), 1335, 1035 (S=O, asym, sym), 1158(C-N). ¹H – NMR (DMSO-d6, 400MHZ),δ(ppm): 6.37 – 6.94 (m, 4H, Ar-H), 7.00 – 8.22 (m, 17H, Ar-H), 10.16 (br.s, H, NH-Ar), 10.41(br.s, H, NH-SO_2). EIMS, m/z ($C_{31}H_{23}N_5SO_2$) calcd,529.61[M]+; found,529.21.

N-(4-(Acridin-9-ylamino)phenyl)-2,4,6-triisopropylbenzenesulfonamide(8d): yield (0.078gm, 40%), as alight brown solid, m.p. >250°C. IR (KBr)cm^{-1}: 3425 (NH), 3250 (CH-Ar),2958(CH-Alkane), 1619 (C=N), 1563(C=C), 1369, 1152 (S=O, asym, sym), 1259 (C-N). ¹H – NMR (DMSO-d6, 400MHZ),δ(ppm): 2.43 (s, 18H, 6CH_3), 2.87 – 2.91 (m, 3H, 3CH), 6.59 – 6.98 (m, 4H, Ar-H), 7.20 – 7.26 (m, 2H, Ar-H), 7.41 – 8.01 (m, 8H,Ar-H), 8.30(br.s, 1H, NH-Ar), 9.82 (br.s, 1H, NH-SO_2) . EIMS, m/z (C43H37N3SO2) calcd,551.74$[M]^+$; found,551.42.

RESULTS AND DISCUSSION

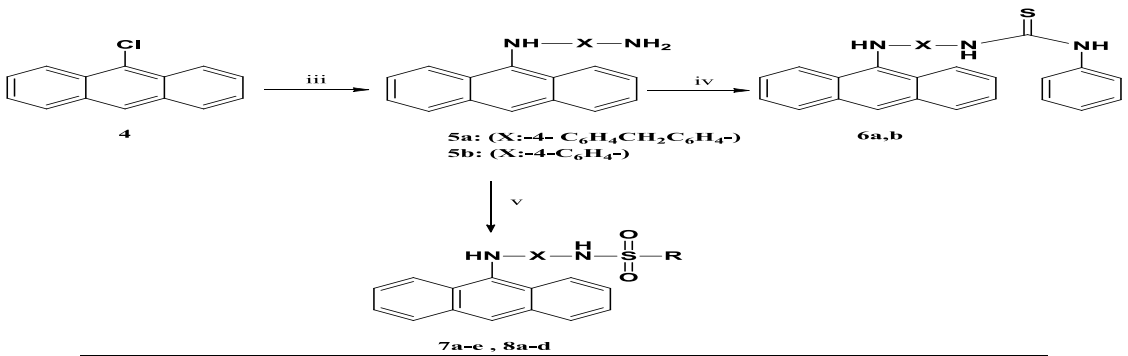
The synthesis of 9-chloroacridine was synthesized according to the literature procedure following scheme 1.[36] The synthesis included the reaction of o-chlorobenzoic acid **1** with aniline **2** in DMF in presence of potassium carbonate anhydrous and copper metal as catalyst. After workup and crystallization in chloroform afforded the intermediate 3 with good yields as a pale yellow color. Compound **3** was then cyclized and dehydroxy chlorinated by phosphorus oxychloride under heating condition to give the key intermediate 9-chloroacridine **4** as a pale green powder in good yield.



Scheme. (1): Synthesis of 9-chloroacridine.

(i).K_2CO_3, Cu, and DMF, 130°C, 4-8h. (ii).$POCl_3$,90-110°C, (reflux), 2-3h.

The key intermediate 9-chloroacridine was further diversitised by nucleophilic aromatic substitution ($S_{NA}r$) reaction. Therefore, compound **4** was reacted with diamines such as p-phenylenediamine and bis (4-aminophenyl) methane in ethanol with presence of triethylamine as a base catalyst to afford the diaminosubstituted acridine derivatives in excellent yields as shown in Scheme 2.



Compound No.	R	Compound No.	R
7a	2-NO_2-C_6H_4-	7e	2,4.6-[$(CH_3)_2CH]_3C_6H_3$-
7b	4-CH_3-C_6H_4-	8a	2-NO_2-C_6H_4-
7c	4-(CH_3CO-NH)-C_6H_4-	8b	4-CH_3-C_6H_4-
7d	-C_6H_4-N=N-C_6H_5	8c	-C_6H_4-N=N-C_6H_5

Scheme. 2: (iii). H_2N-R-NH_2,EtOH,Et_3N,Reflux(80°C),2.5-7h. (iv). Chloroform, Ph-N=C=S,stirring at room temp. (2-8 day). (v).DMF, Et_3N, RSO_2Cl (rt. or reflux).

The synthesis of 9-chloroacridine was shown in scheme 1, the reaction of o-Chloro benzoic acid with the anilines in DMF produced compound **3** which was refluxed in $POCl_3$ to give 9- Chloroacridine in Reaction of Chloroacridine and diamine in excess from Triethylamine which were refluxed in ethanol to give compounds **6a,b** as shown in Scheme 2.

Moreover, the compounds **5a,b** were reacted with phenyl isothiocyanate in chloroform at room temperature to give the thiourea derivatives **6a**, and **6b** in good yields. Furthermore, the reaction of aminoacridines **5** with arysulfonyl chlorides in DMF in presence of excess triethylamine either on stirring at room temp. or under refluxed afforded the sulfonamide **7a-e** , and **8a-d** in good yields.

Structures characterization: The structure elucidation for all end products and their intermediates were performed using IR, ^{1}HNMR and mass spectroscopy. The IR showed a characteristic peaks at 3438, 3380 and 3392 , 3240 cm^{-1}which are characteristic for NH_2 and NH absorption in compounds **5a** and **5b** respectively.On the other hand, compounds **6a, 6b** showed in characteristic peaks corresponds to NH absorption respectively. Compounds **7a-7e** show acharacteristic peak for NH absorption ranging from 3418 for **7e** and 3434 for **7c** respectively.Compounds **8a-8d** show acharacteristic peak for NH absorption ranging from 3324 for **8b** and 3425 for **8d** respectively.

Antiproliferative Activity: In this investigation all compounds were examined in vitro for their anticancer activity against human hepatic (HepG2), colon (HCT-8) and breast (MF-7)carcinomacell lines. Screening for in vitro anticancer activity included measurement of inhibitory concentration $IC_{50}$by using MTT colorimetric assay at 100 µM concentration.[37] The results shown in Table (1) indicated that compounds **5b, 8b, 6b** and **8a** exhibited significant anticancer activity against all three cancer cell lines. It is worth to note that **5b** and **8b** are the most active against HepG2. HCT-116, MCF-7 with IC_{50} 8.30, 8.93, 5.88 and 14.51, 9.39, 8.83µM respectively when compared with reference drug DOX used in the same assay.The obtained results also indicated that the incorporation of basic side-chains with para-phenylenediamine into acridines caffold at C-9 position significantly increased the anticancer activity in vitro against human HepG2, colon (HCT-8) and breast (MCF-7) carcinoma.

Table. 1: Antiproliferativeactivityinduced by acridine analogues in humanhepatic ((HepG$_2$)), colon (HCT-8), and breast (MCF-7) carcinoma cell lines after 72 hs.

Compounds	In vitro Cytotoxicity IC50 (µM)•		
	HePG2	HCT-116	MCF-7
DOX	4.50±0.2	5.23±0.3	4.17±0.2
5a	45.34±3.6	51.44±4.1	64.43±4.5
5b	8.30±0.7	8.93±0.8	5.88±0.4
6a	36.71±3.5	47.21±3.9	40.93±3.8
6b	17.98±1.7	13.07±1.2	16.47±1.5
7a	62.32±4.4	72.16±4.7	88.36±5.1
7b	93.60±5.3	88.53±4.8	73.81±4.5
7c	31.07±3.1	40.61±3.7	29.08±2.7
7d	45.49±3.9	57.96±4.3	33.65±3.3
7e	55.35±4.2	66.67±4.5	50.76±4.0
8a	20.63±1.8	15.18±1.6	10.54±1.0
8b	14.51±1.4	9.39±0.9	8.83±0.9
8c	22.38±2.0	35.69±3.4	25.47±2.4
8d	23.13±2.2	29.85±2.8	19.69±1.7

•IC50 (µM): 1 – 10 (very strong). 11 – 20 (strong). 21 – 50 (moderate). 51 – 100 (weak) and above 100 (non-cytotoxic), • DOX: Doxorubicin.

CONCLUSION

In conclusion, a series of novel acridine bearing sulfonyl and thiouredo moieties have been synthesized. The *in vitro* anticancer activity was evaluated in vitro in three cancer cell lines. The obtained data revealed that, among the tested compounds, four of them showed a strong activity.

ACKNOWLEDGMENT

We would like to acknowledge the financial support of Menoufia University throughout the project number Ib-C2013.

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