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Research Article

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Synthesis of hydroacridines and 1,8-dioxooctahydroxanthenes using primary amino alcohols as reagent or catalysis via three-component condensation reactions

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ABSTRACT

Two major classes of compounds of hydroacridinones and hydroxanthenones have been synthesized in a satisfactory yield via three component condensation reaction of amino alcohols, dimedone and aromatic aldehydes. The applied amino alcohols acted as reactant in one reaction to afford 3,6,6-tetramethyl-,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-diones and acted as catalyst in the other reaction to afford 1,8-dioxooctahydroxanthenones. The structure of products has been characterized by X-ray crystal structural analyses, ^{13}C-NMR, ^{1}H-NMR, IR and Mass spectra.

Keywords: Three component reactions, amino alcohols, β-diketone, hydracridinones and hydroxanthenone.

INTRODUCTION

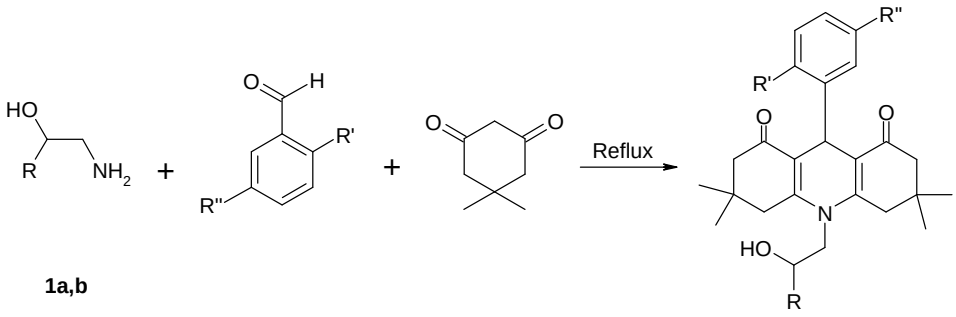
Undoubtedly, synthetic strategies involving multi-component reactions have manifested themselves as a powerful tool for the rapid introduction and expansion of molecular diversity [1-10]. Three-component reactions have emerged as useful methods because the combination of three components to generate new products in a single step is extremely economical among the multi-component reactions [11-15]. They provide an efficient and useful synthetic method of diverse and complex compounds, as well as small and drug-like heterocycles [16-19] in a higher product yield than classical chemistry [20-24]. The importance of these processes is underscored by the large number of publications [25].

Acridine derivatives have occupied a unique position in medicinal chemistry due to their wide range of biological applications. Acridinium cations substituted at the endocyclic N atom find numerous applications in immunological assays as well as in chemical, biochemical and environmental analyses [26]. Recently hydro derivatives showed numerous biological activities like antimicrobial activity and potassium channel blockers [27-29].

Recently, there have been many uses for xanthenes derivatives because of the broad spectrum of their biological and pharmaceutical properties such as, anticancer, antitumor blood, anti malarial, antibacterial, antiviral and anti-inflammatory activities specifically, antibacterial, anti-inflammatory, and antiviral activities. Xanthones have been reported to show antagonist activity [30-40], Photo toxicity, and cytotoxic potency [41-45].

Some xanthene derivatives have significant industry applications, such as florescent material for visualization of biomolecules [46], in laser technologies due to their useful spectroscopic properties [47-49] and as dyes [50]. Xanthenedione derivatives are valuable synthons because of the inherent reactivity of the inbuilt pyran ring [51]. They are also found as core units in several natural products. Xanthones are secondary metabolites found in higher plant families, fungi, and lichens [52].

As far as we know, most of the reported hydroacridines, particularly decahydroacridin-1,8-diones, have been synthesised by using aromatic amines as main substrate to get the acridino nitrogen atom but no one has tried to use the aliphatic amino alcohols in such one-pot reaction technique. The products 1,8-dioxooctahydroxanthene derivatives were obtained in satisfyactory yields during the reaction of aromatic aldehydes or aromatic di-aldehydes with dimedone under reflux in ethanol for 5 hours and catalysed by the amino alcohols. Further to our investigation of synthesis of heterocyclic compounds via the three-component condensation reactions and studying the relation of their functional activity with chemical structure [53-55], we are representing in this study a straightforward and efficient synthetic method for new decahydro acridine-1,8-dione derivatives **3a-c** and 1,8-dioxooctahydroxanthene derivative **3d-g** through three component condensation reactions The employed amino alcohols **1a,b** exhibit an excellent substrate for synthesis of acridinediones and a relevant Lewis base catalyst in synthesis of xanthenones under our reaction conditions.



1a,b

1a, R= H
1b; R= Me

2a; R'= OH, R''= H
2b; R'= OH, R''= Br

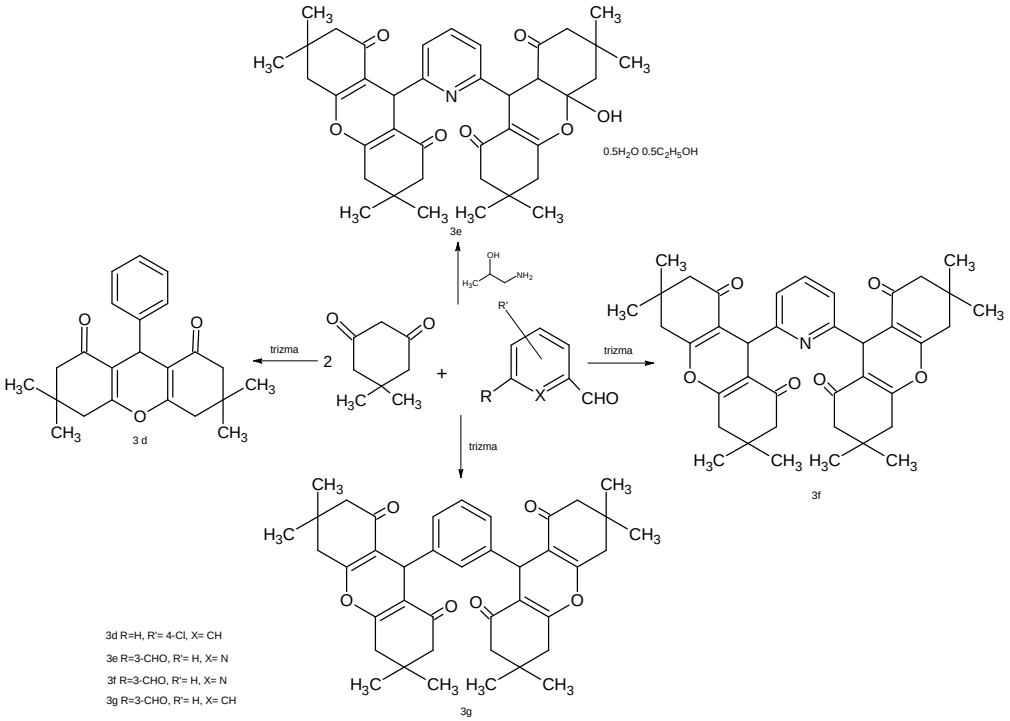
3a-c

3a; R= H, R'= OH, R''= H
3b; R= H, R'= OH, R''= Br
3c; R=Me, R'= OH, R''= Br

(Scheme 1)

Crystals of **3a-c** were grown in diluted ethanolic solutions, and their respective structures were determined by X-ray crystallography (Figures 1, 2 and 3). The structures confirmed the stereochemical assignment of the acridinedione derivatives **3a-c** and was identified as 10-(2-hydroxyethyl)-9-(2-hydroxyphenyl)-3,3,6,6-tetramethyl-,2,3,4,5,6,7,8,9,10- decahydroacridine-1,8-dione (**3a**), 9-(5-bromo-2-hydroxyphenyl)-10-(2-hydroxyethyl)-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione (**3b**) and 9-(5-bromo-2-hydroxyphenyl)-10-(2-hydroxypropyl)-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione (**3c**) respectively.

Crystals of **3d-e** were grown in diluted ethanolic solutions, and their respective structures were determined by X-ray crystallography (Figures 4, 5, 6, and 7). The structures confirmed the stereochemical assignment of the ,8-dioxooctahydroxanthene derivatives 4a-d and was identified as 3,4,6,7-Tetrahydro-3,3,6,6-tetramethyl-9-phenyl-2H-xanthene-1,8-(5H, 9H)-dione (**3d**), 4a-hydroxy-3, 3, 6, 6-tetramethyl-9-[6-(3, 3, 6, 6-tetramethyl -1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-9-xanthenyl)-2-pyridyl]-2,3,4,4a,5,6,7,8,9,9a-decahydro-1H-1,8-xanthenedione (**3e**), 3,3,6,6-tetramethyl-9-[6-(3,3,6,6-tetramethyl-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-9-xanthenyl)-2-pyridyl]-2,3,4, 5,6,7,8,9-octahydro-1H-1,8-xanthenedione (**3f**) and 3,3,6,6-tetramethyl-9-[3-(3,3,6,6-tetramethyl-1,8-dioxo-2, 3, 4, 5, 6, 7, 8, 9-octahydro-1H-9-xanthenyl) phenyl]-2, 3, 4,5,6,7,8,9-octahydro-1H-1,8-xanthenedione (**3g**) respectively.



(Scheme 2)

EXPERIMENTAL SECTION

Mp's were determined using open glass capillaries on a Gallenkamp digital melting point apparatus and are uncorrected. The IR spectra were recorded with Varian 3600 FT-IR instrument using potassium bromide pellets. The ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) spectra were measured in DMSO-d6 using a Firm Bruker AV300 system with TMS as an internal standard. Chemical shifts are expressed as d [ppm], s for singlet, m for multiplet and b for broad. Mass spectra have been obtained with Varian MAT CH-7 instrument in EPSRC National Centre Swansea, United kingdom, using electron impact ionization (70 eV). X-ray analyses have been determined by X-ray Bruker Smart Apex II in X ray analyses unit, Baku University, Baku State, Azerbaijan. All of the compounds in this study exhibited satisfactory, mass, ^{1}H-NMR and ^{13}C-NMR spectra.

Materials

Starting materials: Benzaldehyde, 2-hydroxybenzaldehyde, 4-bromo-2-hydroxybenzaldehyde, 5,5-dimethylcyclohexane-1,3-dione (dimedone), trizma, Isophthalaldehyde, 2,6-Pyridinedicarboxaldehyde and ethanolamine were used as received from chemical suppliers (Aldrich). 1-Amino propan-2-ol was prepared according to literature [58]. All employed solvents have been distilled and dried.

1-General procedure for the preparation of 3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione (3a-c):

A solution of 0.01 mole of aromatic aldehyde **2** was added to a solution of 0.01 mole of amino alcohols **1** in 50 ml of pyridine at room temperature with stirring. The reaction mixture was heated for 30 minutes. Then, a solution of 0.02 mole of dimedone (5,5-dimethyl-1,3-cyclohexanedione) was added with stirring. The reaction mixture was refluxed for another 5 hours and allowed to cool down to room temperature. A yellow precipitate of N-alcohol derivatives of 3,3,6,6-tetramethyl-9-aryl-1,2,3,4,5,6,7,8,9,10- decahydroacridine-1,8-diones **3a-c** was obtained in a good yield (average 62%). All products were crystallized from ethanol and showed one spot on TLC by using a mixture of isopropanol: heptane (3:1) as an eluent (Rf =0.95). The reaction has been repeated for **3a** by using ethanol as a solvent instead of pyridine, it afforded the same products but in a very good yield (80.7%). See table 1. Table 1: Yield of acridinedione derivatives in different employed solvents:

Compound	Mp (^{0}C).	solvent	Yield %
3a	189	ethanol	80.7
3b	199	pyridine	61.8
3c	235	pyridine	62.1

2- General procedure for synthesis of 1,8-dioxooctahydroxanthenone derivatives (3d-g):
A mixture of trizma or amino-iso-propanol (0.01mol), aromatic aldehyde or dialdehyde (0.01mol) and dimedone (0.04mol) in ethanol (50ml) was heated for 5 hours. The reaction was monitored by TLC; upon completion, the mixture was cooled to room temperature, filtered off and washed with water. The solid crude products were left to dry at room temperature and recrystallized from ethanol. The yield and melting points of products **3d-g** are listed in Table 2.

Table 2: Yield and melting points of 1,8-dioxooctahydroxanthene derivatives 3d-g:

Compound	Mp (^{0}C).	Yield %
3d	230	63.3
3e	200	61.2
3f	175	60.4
3g	234	90.1

1-10-(2-hydroxyethyl)-9-(2-hydroxyphenyl)-3,3,6,6-tetramethyl-,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione (3a): This compound was obtained as colorless needles (Ethyl alcohol), mp 189 °C; ir: OH phenolic and acoholic 3441, Ar 3031, CH-aliphatic 2857& 2886, CO 1716, C=C 1622 cm^{-1}; ^{1}H NMR: δ 10.0 (s, 1H, OH phenolic), 7.2-7.6 (br t, 4H, Ar), 5.7 (d, 1H, C9), 5.2 (s, 1H, OH alcoholic), 4.5 (m, 2H, C2), 4.3 (m, 2H, C7), 3.4 (m, 2H, C4), 3.0 (m, 2H, C5), 2.5 (m. 4H, ethyl group), 1.3-1.6 (m, 12H, 4 methyl groups); ^{13}CNMR: δ_c 198 (C=O at C-1, C-8), 155 (C=C Ar), 128,129 (C=C, in acredine fused rings), 115, 62(C-O alcoholic), 50, 48 ($2CH_{2\ a}$ at C2 and C7), 40 (quaternary carbon at C3 and C6), 35 (CH_2-$CH_2$of ethanol) and 18-20 (C of 4 Me groups). *Anal*.Calc. for $C_{25}H_{31}NO_4$ (409.51): C, 73.32; H, 7.63; N, 3.42. Found: C, 73.14; H, 8.06; N, 3.66.

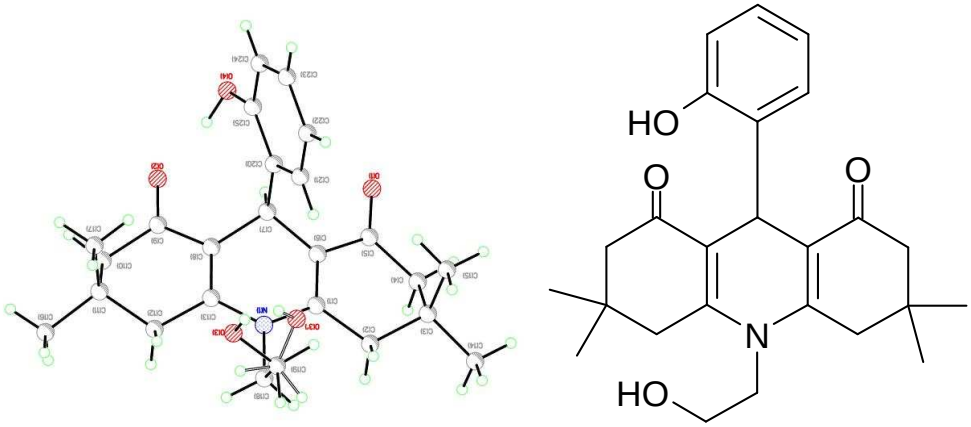
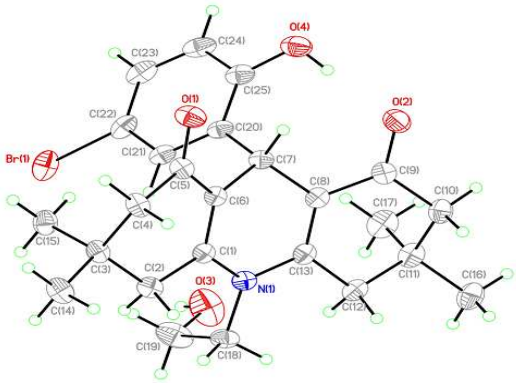


Fig.1: X-ray image of compound 3a

Crystal data and structure refinement of compound (3a): Empirical formula $C_{25}H_{31}NO_4$; Formula weight 409.51; Independent reflections 5369 [R(int) = 0.0406]; Temperature 296(2) K; Completeness to theta = 28.00° and 99.6 % ; Wavelength 0.71073 Å; Max. and min. transmission 0.976 and 0.976; Space group P2(1)/n; Density (calculated) 1.219 Mg/m^3; Absorption coefficient 0.082 mm^{-1}; Crystal size 0.30 x 0.30 x 0.30 mm^3

Selected bond length [Å] and angels [°] in (3a): O(1)-C(5) 1.230(2), O(2)-C(9) 1.243(2), C(8)-C(9) 1.448(2), C(5)-C(6) 1.464(2), C(8)-C(13) 1.361(2), C(1)-C(6) 1.355(2), N(1)-C(13) 1.397(2), N(1)-C(1) 1.402(2), O(4)-C(25) 1.365(3). O(2)-C(9)-C(8) 121.57(16), O(1)-C(5)-C(6) 120.90(16), C(13)-C(8)-C(9) 121.00(15), C(1)-C(6)-C(5) 121.01(15), C(8)-C(13)-N(1) 120.61(14), C(6)-C(1)-N(1) 120.32(15), C(13)-N(1)-C(1) 119.00(13), C(5)-C(6)-C(7) 117.03(14).

2-9-(5-bromo-2-hydroxyphenyl)-10-(2-hydroxyethyl)-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione (3b): This compound was obtained as colorless needles (Ethyl alcohol), mp 199 °C; IR: OH phenolic 3410, OH acoholic 3339, Ar 2957, CH-aliphatic 2886, CO 1704, C=C 1595, C-Br 625 cm^{-1}; ^{1}H NMR: δ 9.8 (s, 1H, OH phenolic), 7.2 (s, 1H, Ar), 7.1 (d, 2H, Ar), 6.6 (d, 1H, C9), 5.1(s, 1H, OH alcoholic), 4.15(t, 2H, C2), 3.85(t, 2H, C7), 3.0 (d, 2H, C4), 2.7(d, 2H, C5), 2.3(m, 4H, ethyl group), 1-1.1(m, 12H, 4 methyl groups); ^{13}C nmr: ^{13}C nmr: d 197,198 (C=O, C-1, C-8), 155, 135 and 131 (C=C Ar), 111, 112 (C=C, in acridine fused rings), 120 (C-N), 64(C-Br), 50 (C-OH), 20, 28, 30 and 32 (C-C of CH_3CH_2 and $5CH_3$); ms: m/z 488 (100), 489 (30), 490 (100), 491 (30), 443 (56), 363 (39), 271 (42), 172 (29), 92 (74). Anal. , 6.19; Br, 16.36; N, 2.87. Found: C, 61.16; H, 5.96; Br, 15.99; N, 3.06



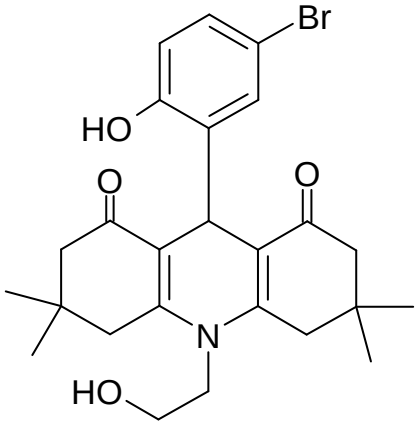
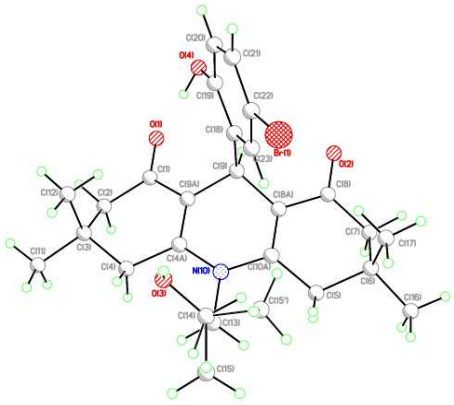


Fig. 2: X-ray image of compound 3b

Crystal data and structure refinement of compound (3b): Empirical formula $C_{25}H_{30}Br\ N\ O_4$; Formula weight 488.41; Independent reflections 5137 [R(int) = 0.0714]; Temperature 296(2) K; Completeness to theta = 27.00° and 99.7 % ; Wavelength 0.71073 Å; Max. and min. transmission 0.8427 and 0.6185; Space group P2(1)/n; Density (calculated) 1.374 Mg/m^3; Absorption coefficient 1.772 mm^{-1}; Crystal size 0.30 x 0.20 x 0.10 mm^3.

Selected bond length [Å] and angels [°] in (3b): O(1)-C(5) 1.220(3), O(2)-C(9) 1.244(4), C(5)-C(6) 1.453(4), C(8)-C(9) 1.423(5), C(1)-C(6) 1.355(4) 1.355(4), C(8)-C(13) 1.345(4), N(1)-C(1) 1.398(3), N(1)-C(13) 1.393(4), O(4)-H(4C) 0.8200, 1.895(4); O(1)-C(5)-C(6) 120.6(3), O(2)-C(9)-C(8) 122.1(3), C(1)-C(6)-C(5) 120.7(3), C(13)-C(8)-C(9) 120.8(3), C(6)-C(1)-N(1) 119.2(3), C(8)-C(13)-N(1) 120.2(3), C(13)-N(1)-C(1) 119.8(2), C(9)-C(8)-C(7) 118.7(2), C(5)-C(6)-C(7) 117.7(2), C(6)-C(7)-C(8) 108.4(2).



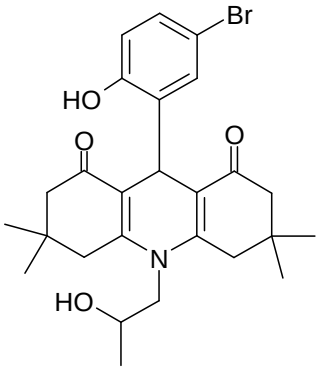


Fig. 3: X-ray image of compound 3c

3-9-(5-bromo-2-hydroxyphenyl)-10-(2-hydroxypropyl)-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione (3c): This compound was obtained as pale yellow crystal (ethanol), mp 235ºC; IR: OH phenolic 3401, OH alcoholic 3369, Ar 2957, C-H aliphatic 2871& 2666, C=O 1626, C=C 1594, C-Br 667 cm^{-1}; ^{1}HNMR: δ 9.9 (s,1H, OH phenolic), 7.3(s, 1H, Ar), 7.2(d, 2H, Ar), 5.1(s, 1H, alcoholic), 4.8(s, 1H, C9), 3.9(s, 4H, $2CH_2$ of C2, C7), 3.2 (s, 4H, $2CH_2$ at C4, C5) 2.8-2.9(d, 2H, CH_2 of propyl group), 2.5-2.7(m, 1H, CH of propyl group), 0.9-1.2(m, 15H, $5CH_3$); ^{13}C nmr; 198 (C=O), 153 and 130 (C=C 62(C-Br), 49 (C-OH), 40,22 and 18 (C-C of CH,$3CH_2$ and $5CH_3$); ms: m/z 502(100), 503(30), 504(100), 505(30), 484 (29), 443 (53), 422 (41), 330 (62), 271 (49), 172 (27); Anal.Calc. For $C_{26}H_{32}Br\ N\ O_4$ (502.44): C, 62.15; H, 6.42; Br, 15.90; N, 2.79. Found: C, 61.96; H, 6.15; Br, 16.08; N, 3.01.

Crystal data and structure refinement of (3c): Empirical formula $C_{26}H_{32}Br\ N\ O_4$, formula weight 502.44, Independent reflections 6209 [R(int) = 0.0663], Temperature 296(2) K, Completeness to theta = 28.50° and 98.3 % , Wavelength 0.71073 Å, Max. and min. transmission 0.729 and 0.632, Space group P 21/n, Density (calculated) 1.342 Mg/m^3, Absorption coefficient 1.684 mm^{-1}, Crystal size 0.30 x 0.20 x 0.20 mm^3.

Selected bond length [Å] and angels [°] in (3c): O(1)-C(1) 1.237(5), O(2)-C(8) 1.223(4), C(1)-C(9A) 1.443(5), C(8)-C(8A) 1.467(4), C(4A)-C(9A) 1.361(5), C(8A)-C(10A) 1.345(4), C(4A)-N(10) 1.386(4), N(10)-C(10A) 1.398(4), O(4)-C(19) 1.351(5), Br(1)-C(22) 1.890(4); O(1)-C(1)-C(9A) 121.5(3), O(2)-C(8)-C(8A) 120.8(3), C(4A)-C(9A)-C(1) 120.4(3), C(10A)-C(8A)-C(8) 121.0(3), C(9A)-C(4A)-N(10) 119.9(3), C(8A)-C(10A)-N(10) 119.6(3), C(4A)-N(10)-C(10A) 119.9(3), C(8)-C(8A)-C(9) 117.2(3), C(1)-C(9A)-C(9) 119.3(3), C(8A)-C(9)-C(9A) 108.0(3).

4-3,4,6,7-Tetrahydro-3,3,6,6-tetramethyl-9-phenyl-2H-xanthene-1,8-(5H,9H)-dione (3d) [59,60]:
Crystal data and structure refinement of (3d): Empirical formula $C_{23}H_{26}O_3$, formula weight 350.44, Independent reflections 4638 [R (int) = 0.0226], Temperature 296(2) K, Completeness to theta = 28.00° 99.7 %, Wavelength 0.71073 Å, Max. and min. transmission 0.9845 and 0.9845, Space group P 21/c, Density (calculated) 1.205 Mg/m^3, Absorption coefficient 0.078 mm^{-1}, Crystal size 0.20 x 0.20 x 0.20 mm^3.

Selected bond length [Å] and angels [°] in (3d): O(1)-C(7) 1.3729(14), O(1)-C(13) 1.3762(14), O(2)-C(5) 1.2150(17), O(3)-C(15) 1.2163(17), C(1)-C(3) 1.530(2), C(2)-C(3) 1.528(3), C(3)-C(4) 1.525(2), C(3)-C(8) 1.5283(19), C(4)-C(5) 1.507(2), C(5)-C(6) 1.4709(17), C(6)-C(7) 1.3337(17), C(6)-C(17) 1.5105(16),C(7)-C(8) 1.4919(17), C(9)-C(11) 1.527(2), C(10)-C(11) 1.527(2), C(11)-C(16) 1.527(2), C(11)-C(12) 1.5316(18), C(12)-C(13) 1.4867(16), C(13)-C(14) 1.3332(17), C(14)-C(15) 1.4677(17), C(14)-C(17) 1.5081(16), C(15)-C(16) 1.5071(19), C(17)-C(18) 1.5267(17), C(18)-C(19) 1.3839(18), C(18)-C(23) 1.3839(17), C(19)-C(20) 1.386(2), C(20)-C(21) 1.379(2), C(21)-C(22) 1.371(2), C(22)-C(23) 1.386(2).

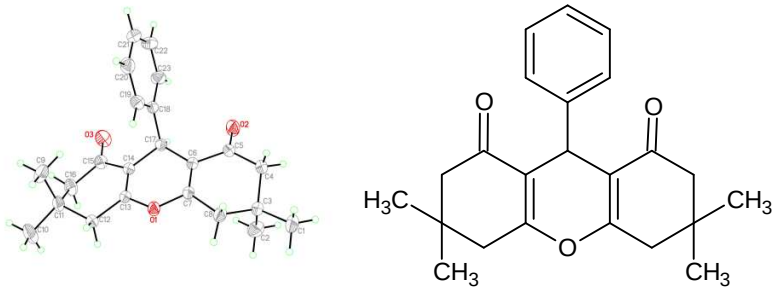


Fig. 4: X-ray image of compound 3d

5-4a-hydroxy-3,3,6,6-tetramethyl-9-[6-(3,3,6,6-tetramethyl-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-9-xanthenyl)-2-pyridyl]-2,3,4,4a,5,6,7,8,9,9a-decahydro-1H-1,8-xanthenedione (3e) [61]:
Crystal data and structure refinement of compound (3e): Empirical formula $C_{39}H_{47}NO_7.0.5C_2H_5OH.0.5H_2O$; Formula weight 673.82; Independent reflections 8332 [R(int) = 0.035]; Temperature 100(2) K; Completeness to theta = 28.00° and 99.6 % ; Wavelength 0.71073 Å; Max. and min. transmission 0.983 and 0.992; Space group P2(1)/n; Density (calculated) 1.215 Mg/m^3; Absorption coefficient 0.08 mm^{-1}; Crystal size 0.20 x 0.15 x 0.10 mm^3.

Selected bond length [Å] and angels [°] in (3e): O1-C8 1.226(4), O2-C19 1.228(4), O3-C15 1.369(3), O3-C12 1.369(3), O4-C25 1.230(4), O5-C29 1.346(4), O5-C32 1.464(3), O6-C32 1.383(3), O7-C36 1.210(4), N1-C5 1.338(3), N1-C1 1.347(4), C1-C2 1.385(4), C1-C23 1.514(4), C2-C3 1.391(4), C3-C4 1.380(4), C4-C5 1.390(4), C5-C6 1.525(4), C6-C20 1.511(4), C6-C7 1.511(4) C7-C12 1.337(4) C7-C8 1.468(4), C8-C9 1.502(5), C9-C10 1.531(4), C10-C11 1.521(4), C10-C14 1.526(5) C10-C13 1.538(4) C11-C12 1.486(4), C15-C20 1.332(4), C15-C16 1.495(4), C16-C17 1.539 (4), C17-C18 1.525(4), C17-C21 1.531(5), C17-C22 1.536(5), C18-C19 1.516(5), C19-C20 1.475(4), C23-C24 1.514(4), C23-C37 1.533(4), C24-C29 1.356(4), C24-C25 1.460(4), C25-C26 1.516(4), C26-C27 1.535(5), C27-C31 1.527(5), C27-C28 1.527(4), C27-C30 1.533(5), C28-C29 1.484(4), C32-C33 1.511(4), C32-C37 1.540(4), C33-C34 1.545(4), C34-C39 1.524(4), C34-C38 1.529(4), C34-C35 1.543(4), C35-C36 1.492(4), C36-C37 1.538(4), O8-C40 1.437(5), C40-C41 1.482 (5).

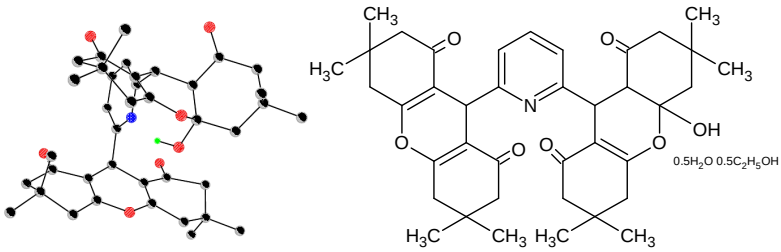


Fig. 5: X-ray image of compound 3e

6-3,3,6,6-tetramethyl-9-[6-(3,3,6,6-tetramethyl-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-9-xanthenyl)-2-pyridyl]-2,3,4,5,6,7,8,9-octahydro-1H-1,8-xanthenedione (**3f**) [62]:
Crystal data and structure refinement of compound (3f): Empirical formula $C_{39}H_{45}NO_6$; Formula weight 623.67; Independent reflections 8347 [R (int) = 0.0357]; Temperature 100(2) K; Completeness to theta = 28.34° and 99.3 %; Wavelength 0.71073 Å; Max. and min. transmission 0.9758 and 0.9758; Space group P21/c; Density (calculated) 1.231 Mg/m^3; Absorption coefficient 0.082 mm^{-1}; Crystal size 0.30 x 0.30 x 0.30 mm^3.

Selected bond length [Å] and angels [°] in (3f): O1-C12 1.3757(14), O1-C20 1.3800(14), O2-C16 1.2242(16), O3-C8 1.2242(15), O4-C29 1.3732(15), O4-C37 1.3761(15), O5-C25 1.2220(15), O6-C33 1.2200(16), N1-C1 1.3438(16), N1-C5 1.3443(15), C1-C2 1.3829(17), C1-C6 1.5264(16), C2-C3 1.3853 (18), C3-C4 1.3771(18), C4-C5 1.3865(16), C5-C23 1.5270(17), C6-C15 1.5051(17), C6-C7 1.5133(16), C7-C12 1.3393(17), C7-C8 1.4696(17), C8-C9 1.5103(17), C9-C10 1.5338(18), C10-C14 1.5321(19), C10-C13 1.5336(18), C10-C11 1.5387(17), C11-C12 1.4958 (17), C15-C20 1.3368(17), C15-C16 1.4719(17), C16-C17 1.5111(18), C17-C18 1.5328(18), C18-C21 1.5269(17), C18-C22 1.5332(18), C18-C19 1.5403(17), C19-C20 1.4926 (17), C23-C32 1.5060 (17), C23-C24 1.5082(17), C24-C29 1.3393(17), C24-C25 1.4688(17), C25-C26 1.5157(18), C26-C27 1.5335(17), C27-C30 1.5261(18), C27-C31 1.5296(19), C27-C28 1.5325(17), C28-C29 1.4884(17), C32-C37 1.3363(17), C32-C33 1.4687(17), C33-C34 1.5129(18), C34-C35 1.5301(18), C35-C38 1.5293(18), C35-C39 1.5292(18), C35-C36 1.5341(18), C36-C37 1.4903(17).

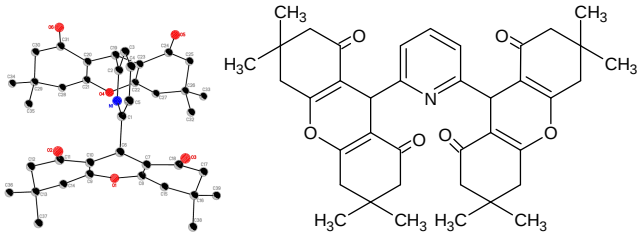


Fig. 6: X-ray image of compound 3f

7-3,3,6,6-tetramethyl-9-[3-(3,3,6,6-tetramethyl-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-9-xanthenyl)phenyl]-2,3,4,5,6,7,8,9-octahydro-1H-1,8-xanthenedione (3g) [59]:
Crystal data and structure refinement of compound (3g): Empirical formula $C_{40}H_{36}O_6$; Formula weight 622.77; Independent reflections 8347 [R(int)= 0.0357]; Temperature 296(2) K; Completeness to theta = 28.37° and 99.5 % ;

Wavelength 0.71073 Å; Max. and min. transmission 0.9844 and 0.9844; Space group P21/c; Density (calculated) 1.190 Mg/m^3; Absorption coefficient 0.079 mm^{-1}; Crystal size 0.20 x 0.20 x 0.20 mm^3.

Selected bond length [Å] and angels [°] in (3g): O(1)-C(10) 1.374(2),O(1)-C(9) 1.377(2), O(2)-C(12) 1.217(2), O(3)-C(19) 1.214(2), O(4)-C(22) 1.3782(19), O(4)-C(23) 1.3810(19), O(5)-C(25) 1.222(2), O(6)-C(32) 1.221(2), C(1)-C(6) 1.382(2), C(1)-C(2) 1.390(2), C(1)-C(7) 1.526(2), C(2)-C(3) 1.383(2), C(3)-C(4) 1.381(2), C(3)-C(20) 1.529(2), C(4)-C(5) 1.381(2), C(5)-C(6) 1.366(2), C(7)-C(11) 1.502(2), C(7)-C(8) 1.506(2), C(8)-C(9) 1.336(2), C(8)-C(19) 1.460(3), C(9)-C(16) 1.484(2), C(10)-C(11) 1.334(2), C(10)-C(15) 1.484(2), C(11)-C(12) 1.466(2), C(12)-C(13) 1.501(3), C(13)-C(14) 1.523(2), C(14)-C(38) 1.521(3), C(14)-C(15) 1.522(3), C(14)-C(37) 1.528(3), C(16)-C(17) 1.524(3), C(17)-C(40) 1.521(3), C(17)-C(18) 1.523(3), C(17)-C(39) 1.526(3), C(18)-C(19) 1.498(3), C(20)-C(24) 1.505(2), C(20)-C(21) 1.510(2), C(21)-C(22) 1.333(2), C(21)-C(32) 1.468(2), C(22)-C(29) 1.490(2) C(23)-C(24) 1.336(2), C(23)-C(28) 1.487(2), C(24)-C(25) 1.466(2), C(25)-C(26) 1.502(3), C(26)-C(27) 1.531(3), C(27)-C(34) 1.524(3), C(27)-C(33) 1.526(3), C(27)-C(28) 1.532(3), C(29)-C(30) 1.529(2), C(30)-C(31) 1.530(3), C(30)-C(35) 1.531(3), C(30)-C(36) 1.531(3), C(31)-C(32) 1.497(3).

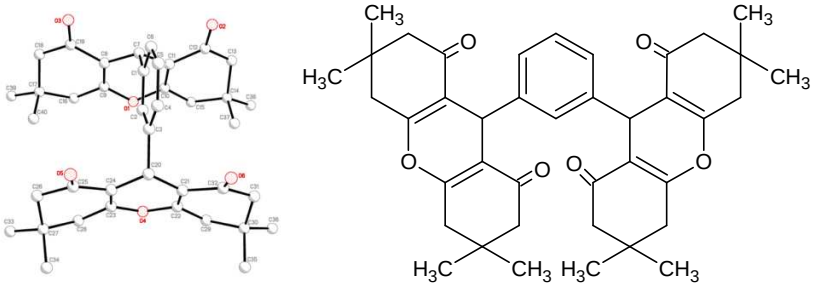


Fig. 7: X-ray image of compound 3g

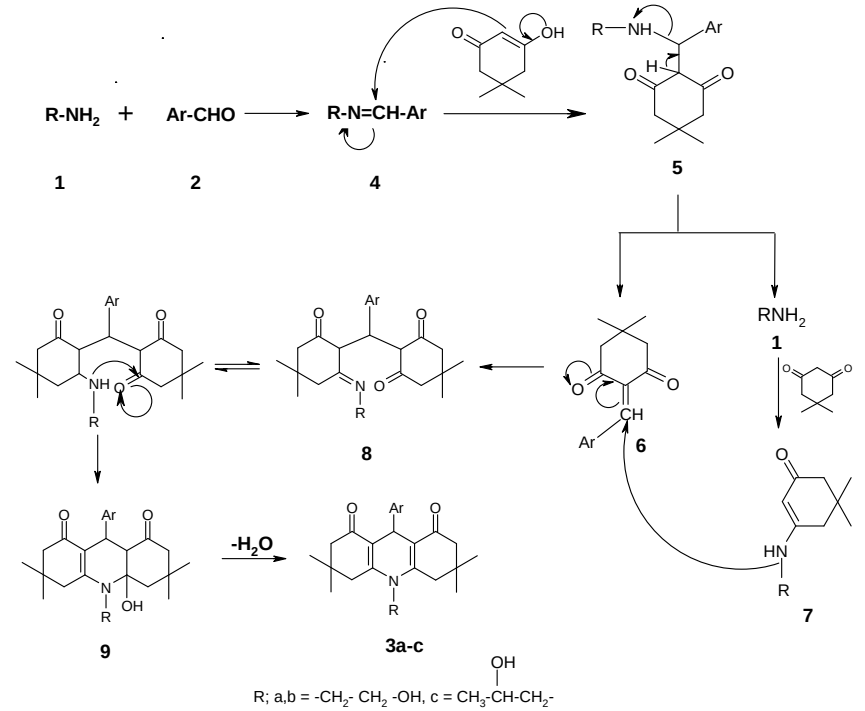
RESULTS AND DISCUSSION

On refluxing an ethanolic solution of dimedone, appropriate aromatic aldehydes and amino alcohols (Scheme 1) in a stiochiometrical ratio 2:1:1 for 5-6 hours followed by evaporation of the solvent under vacuum it afforded the formation of the solid fused three membered ring of acridinedione derivatives **3a-c** in a satisfactory yield (62-80%) (see Scheme 1).

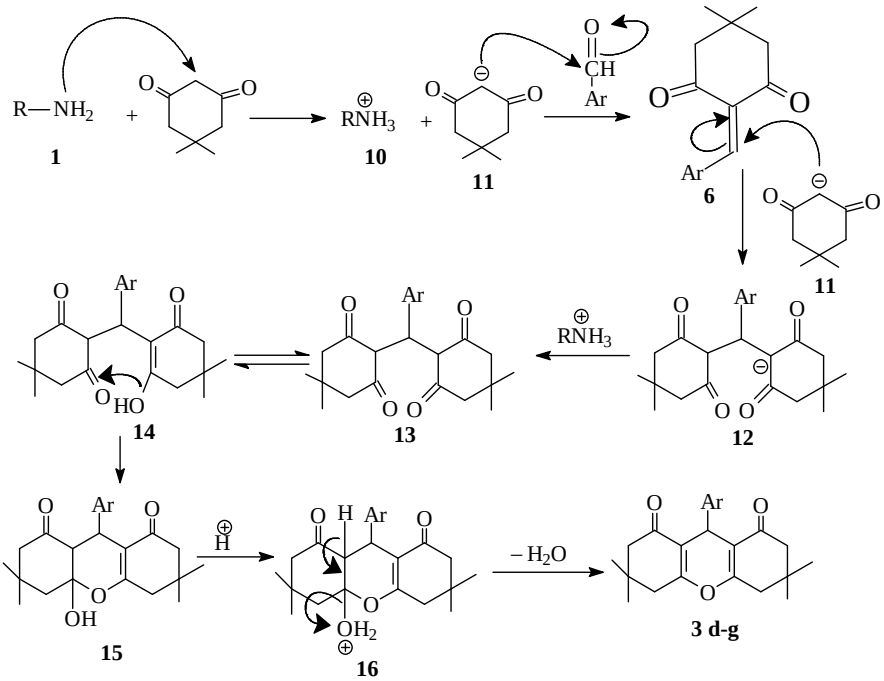
The X-ray crystal structure analysis of **3a-c** was carried out (see figures 1,2 and 3 in experimental section). It clearly demonstrated the three fused hydro acredinedione structures along with the aromatic and alcoholic chain substituent. The x-ray studies of the single crystals of **3a-c** showed that the three fused rings of acridinedione moiety are not planar and are stabilized by by intra- and intermolecular O-H…O, C-H…O [56] and C-H…Br hydrogen bonds for **3c** [57]. Some crystal data and some selected bond length have been recorded (see experimental section).

The IR spectra showed characteristic absorptions between 3401-3410cm^{-1} and at 3339-3369cm^{-1} for the phenolic and alcoholic hydroxyl groups respectively. Absorptions between 2957– 3010cm^{-1} were assigned for the aromatic substituent while absorptions between 2886- 2666cm^{-1} were attributed to asymmetric and symmetric aliphatic stretch. The cyclic carbonyl group was remarked at a strong stretch absorption between 1704 and 1716cm^{-1}. The mass specta of **3a-c**, exhibited the correct molecular ion peaks at 488 (100%) and 490 (100%) for the bromo isomers of **3b** and 502 (100%) and 505 (100%) for isomers of **3c**. ^{1}H-NMR spectra of **3a-c** remarked a chemical shift betweens δ = 10 and 9.8ppm for phenolic OH group while alcoholic OH group was observed at chemical shift between 5.4 and 5.1ppm. Aromatic signals were observed at 6.8- 7.6ppm. Signal at δ= 3.8- 4.5 were assigned for proton at C2 and C7 respectively while peaks at 2.8 -3.5 for protons at C4 and C5 were observed. Ethyl protons were assigned at chemical shifts between 2.6 and 3.0ppm for **3a** & **3b** and between 2.6 and 2.5-2.9ppm for **3c**. Multiple peaks were observed at 1 -1.5ppm in **3a-c** and were attributed to the methyl groups of dimedone and that of the isopropanol. ^{13}C-NMR of **3a-c** showed a characteristic peak at δ_c 198ppm for carbonyl group and 155-157ppm for aromatic substituent. The chemical shift of C=C in pyridyl ring appeared clearly as two peaks at 129 and 130ppm. C alcoholic appeared between 68 and 62 ppm. Two peaks at 49 and 51ppm were attributed to two carbon atoms at C2 and C7 while a single peak at 40ppm was assigned to two carbon atoms of C3 and C6. Multiple peaks

of the four methyl carbons of dimedone were observed at 20 ppm for **3a-c** while one single peak appeared at 10ppm and was attributed to the methyl carbon atom of isopropanol chain in **3c**.



(Scheme 3)



(Scheme 4)

Formation of the hydro acridinediones **3a-c** may be rationalized by an initial formation of the imine **4** from the condensation of the aromatic aldehydes **2** with the appropriate amino alcohol **1** (see Scheme 2). The attacking of

enol form of dimedone on the imine **4** could have afforded the formation of adduct **5** which in turn could have undergone an internal arrangement to release the aminoalcohols **1** and arylidenes **6**. The released aminoalcohols **1** could have reacted with another molecule of dimedone to give the amino enone **7** which in turn could have attacked through its nucleophilic amino group into the electrophilic carbon atom of the former arylidenes **6** to give the imine **8**. The unstable imine **8** could have been rearranged into the relatively stable structure of the hydroxy hydroacredindiones **9** which ultimately could have stabilized easily into the title structure of hydro acridindiones **3a-c** by elimination of a molecule of water (Scheme 3).

Formation of the 1,8-dioxooctahydroxanthene derivative **3 d-g** might have been initiated by Aldol condensation between dimedone and aromatic aldehyde in the presence of amino compounds **1** as Lewis base catalyst to form the corresponding arylidines **6** (see Scheme 4). Micheal addition of the nucleophile **11** onto **6** could have afforded the tetracarbonyl compound **13** via intermedium **12**. An interamolecular arrangment of the enol form **13** could have resulted in formation of the hydroxy hydroxanthenone **14** which could have undergone an elemination of water molecule to reveal the final stable form of the corresponding hydroxanthenone derivatives **3d-g** via the intermedium **16**.

CONCLUSION

In this approach we have developed a one pot efficient synthesis of new potentially biologically active derivatives of hydroacridinones **3a-c** and hydroxanthenones **3d-g** from simple common chemicals by using the economical technique of three-component condensation reactions.

Supporting Information:
X-ray data of compounds **3a-g** are available when required.

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