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ECO-FRIENDLY AND HIGHLY EFFICIENT ONE-POT SYNTHESIS OF SYMMETRICAL AND UNSYMMETRICAL 1,4-DIHYDROPYRIDINE DERIVATIVES USING TRIETHYLAMINE AS CATALYST IN ETHANOL MEDIUM

Amar Djemoui [1,2,3]*; Mohammed Ridha Ouahrani [1]*;Abdelkader Naouri [1,2, 4] ;Lahcen Souli[2, 3]; Salah-Eddin Rahmani [2] andLahrech Mokhtar Boualem [3].

1. *Department of Chemistry, Faculty of Exact Sciences, Echahid Hamma Lakhdar University of El Oued, Algeria.*
2. *Department of Chemistry, Faculty of Exact Sciences and Informatics, ZIANE Achour University. Djelfa, Algeria*
3. *Laboratory of Organic Chemistry and Natural Substance, Faculty of Exact Sciences and informatics, ZIANE Achour University. Djelfa, Algeria.*
4. *Health Division, Centre of Scientific and Technical Analyses Physico-Chemical BP 384, Seat former Pasna Industrial Zone Bou-Ismail, Tipaza, Algeria.*

**Email:djamarchimie@yahoo.fr*
**Email: ouahrani_mr@hotmail.com*

ABSTRACT
A simple and efficient approach to the synthesis of 1,8-dioxo-decahydroacridines and hexahydroquinolines *via* one-pot multi-component condensation of an aromatic aldehyde, 1,3-diketones and ammonium acetate in ethanol with use of Triethylamine (TEA) as an efficient catalyst is described**.** The present method has several benefits such as excellent yields, relatively short reaction time (90-120 min), simple and easy work-up, green process, and use of a cheap solvent. All the synthesized 1,8-dioxodecahydro-acridines and hexahydroquinolines were characterized on the basis of their melting-points, elemental analysis and spectral data

INTRODUCTION
Multi-component reactions (MCRs) are a promising strategy in organic synthesis todeliver bioactive molecules because the synthesis of these molecules can be afford rapidly and efficiently without the isolation of intermediates and in just one reaction step.[i] The Hantzschsynthesis of 1,4-Dihydropyridines (1,4-DHPs) represents a typical sample of a multicomponent one-pot reaction between an aldehyde, 2 equivalents of α-methylene such as ethyl acetoacetate or 1,3-cyclo-hexanedione and a nitrogen donor such as ammonium acetate. The first successful example ofthis reaction was reported in 1881 by Arthur Rudolf Hantzsch.[ii]

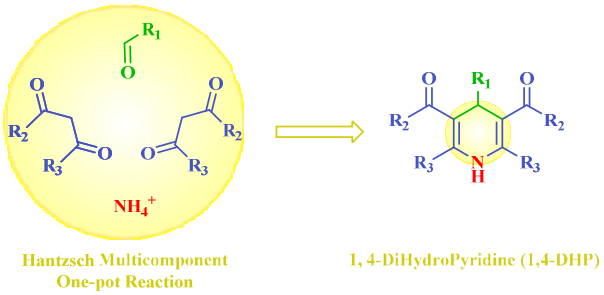


Fig 1. Hantzsch Reaction

Acridine derivatives are an importantclass of 1,4-Dihydropyridines, and they have occupied aunique position in medicinal chemistry due to their wide range of biological applications.[iii]Acridines are used in medicinal drugs as calcium channel blockers in the treatment of cardiovasculardiseases, such as hypertension[iv]. Recently, acridines were shown to inhibit multidrug resistance in tumour cell lines.[iv] They are also possessing antimalarial,[v] antiviral,[vi] antibacterial andantiallergic properties.[vii] Acridines act as effective drugs for anticancer activity both in vitro and in vivo against a range of murine and human cancers,[viii] and one of the most attractive features of thesemolecules is the ability to act as a fluorescent molecular probes for monitoring polymerization processes,[viv] and are used as n-type semiconductors and in the electroluminescent devices.[x]Recently florinated acridones are reported to possess anticancer activity,[xi] and anti-Alzheimer.[xii]

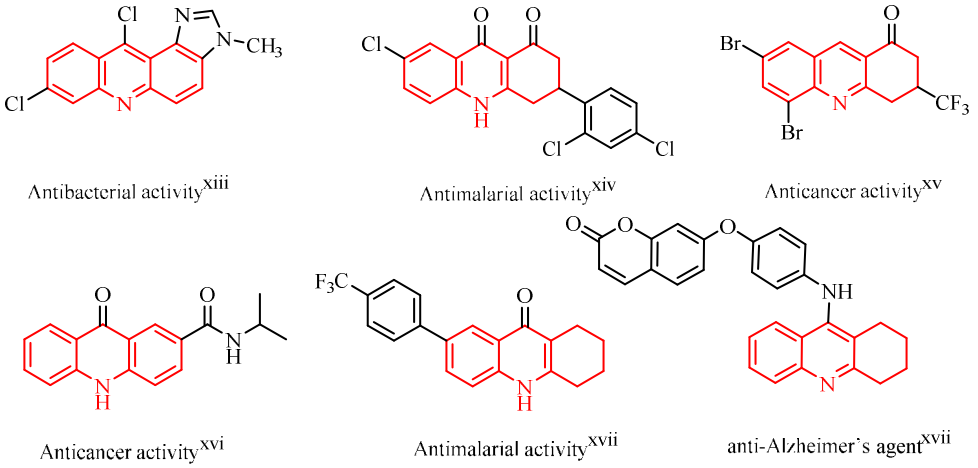
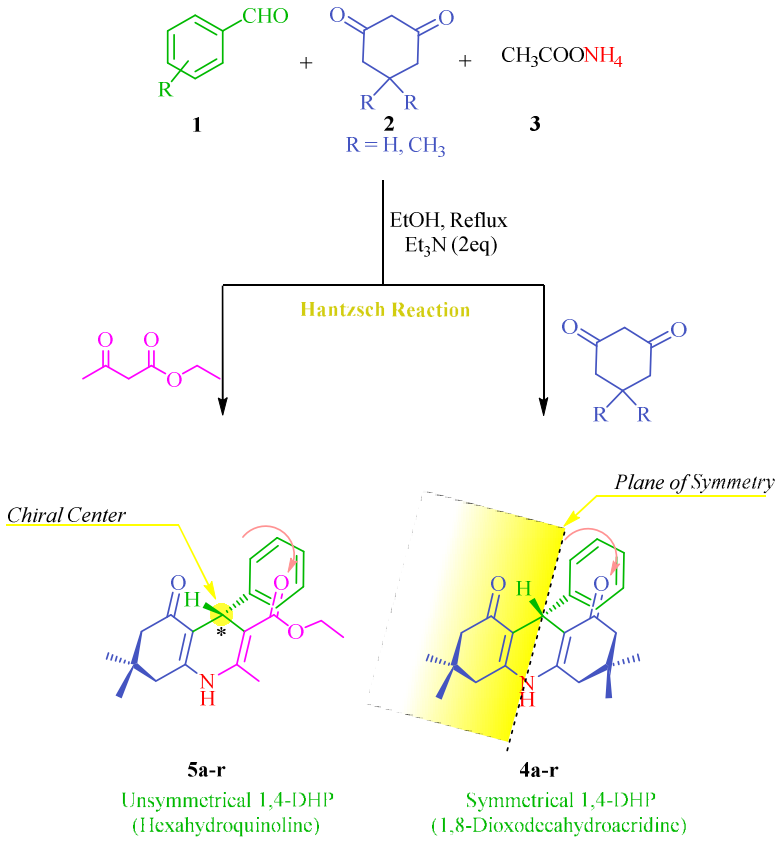


Fig 2. Examples of pharmacologically active synthetic 1,8-dioxodecahydroacridines.

A straightforward method for the synthesis of these compounds involves a condensation betweenaldehydes, 1,3-diketone and an amine that is catalysed by various compounds such as 2-Hydroxyethylammonium Acetate,[xix]L-proline,[xx] $[CMIM][HSO_4]$,[xxi]ZnOnano particles,[xxii] ρ-TsOH,[xxiii] CAN,[xxiv]Amberlsyt-15,[xxv] 4-toluenesulfonic acid,[xxvi] Sodium 1-DodecaneSulfonic (SDS),[xxvii] Alginic acid,[xxviii] $[H\text{-}NMP]^+[HSO_4]^-$,[xxix] $In(OTf)_3$ [30],[xxx] TPA NPs/PAA,[xxxi] Silica-supported sulfuric acid,[xxxii]Cu-doped ZnO,[xxxiii] Ultra sound,[xxxiv] ionic liquids,[xxxv] and microwave irradiation.[xxxvi]

Each of thesemethods has limitations such as poor yield, long reaction times, use of large quantities of volatileorganic solvents and cumbersome workup procedure. Therefore, the development of novel syntheticstrategies for acridines which have advantages with respect to using, less expensive and readilyavailable catalysts or reagents, cleaner reactions, and simple isolation of the product are ofinterest.[xxxvii]In continuation of our study on multi-component

reactions and polycyclic compounds synthesis,[xxxviii] we herein describe a green, facile and highly efficient method for the synthesis of 1,8-Dioxodecahydroacridines and hexahydroquinolines derivatives by the reaction of ammonium acetate with aldehydes and 1,3-dicarbonyls in the presence of triethylamine as cheap and efficient catalyst inethanol.



Scheme 1: One-pot reaction for the preparation of 1,8-dioxodecahydroacridines and hexahydroquinolines.

In order to develop an efficient and environmentally benign method forthe one-pot synthesis of 1,8-dioxodecahydroacridines, the reaction of 4-Hydroxybenzaldehyde (1mmole), 1,3-Cyclohexandione (2 mmole) and ammonium acetate (1.5 mmole) was studied (Table 1).
First, an uncatalyzed reaction was tested in ethanol at reflux but no significant yield was obtained*(Table 1, Entry 1),* the catalyst plays an important role in the formation of 1,8-dioxodecahydroacridines derivatives. Thus, we focused our attention on using base catalysts, which might helpto reduce the reaction time and improve the yields of the target compound.We resumed our studies by investigating the effect of different catalysts such as Piperidine, Pyridine,Et_3N, K_2CO_3, KOH and NaOH (Table 1).

Table 1: The synthesis of **4g** compound by using various catalysts

Entry	**Catalyst (2eq)**	**Solvent**	**Time (min)**	**Temp (°C)**	**Yield[a](%)**
1	-	Ethanol	420	Reflux	Trace
2	Piperidine	Ethanol	120	Reflux	82
3	Pyridine	Ethanol	105	Reflux	88
4	***Et_3N***	***Ethanol***	***90***	***Reflux***	***95***
5	K_2CO_3	Ethanol	120	Reflux	64

6	KOH	Ethanol	120	Reflux	72
7	NaOH	Ethanol	120	Reflux	75

a.Isolated yield.

Triethylamine (Et_3N) is the most efficient catalyst which causes the highest yield of **4g***(Table 1,Entry 4).*

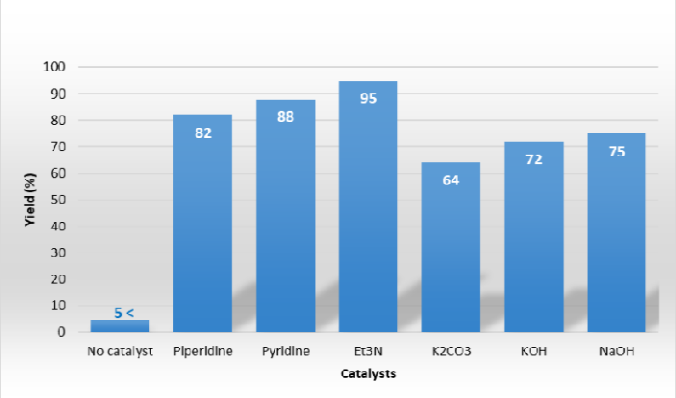


Fig 3: Effect of catalysts.

The reaction conditions were then optimized by conducting the reaction model at different solventssuch as methanol, water, ethanol, acetic acid, ethanol-water (1:1), ethanol-water (2:1) and also undersolvent-free condition (Table 2).

Table 2: The synthesis of **4g** compound by using different solvents.

Entry	**Catalyst (2eq)**	**Solvent**	**Time (min)**	**Temp (°C)**	**Yield[a] (%)**
1	Et_3N	Free Solvent	180	80	15
2	***Et_3N***	***Ethanol***	***90***	***Reflux***	***96***
3	Et_3N	Methanol	105	Reflux	90
4	Et_3N	Water	120	Reflux	85
5	Et_3N	Acetic acid	120	Reflux	88
6	Et_3N	Ethanol-water (1:1)	105	Reflux	86
7	Et_3N	Ethanol-water (2:1)	105	Reflux	90

a. Isolated yield.

As it is shown in table 2 the reaction model proceeded with the highest yield and shortest time by theassistance of ethanol compared to other used solvents (Table 2, Entry 2).

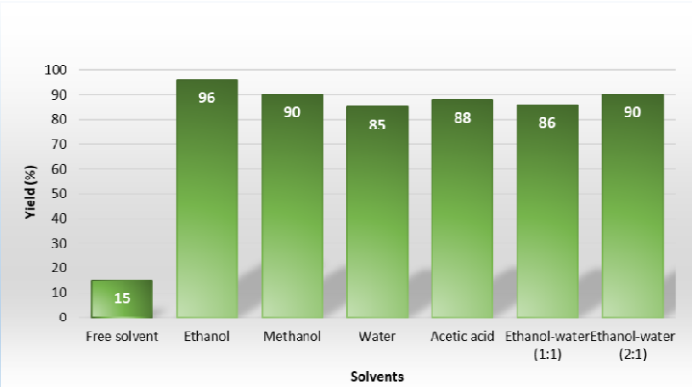
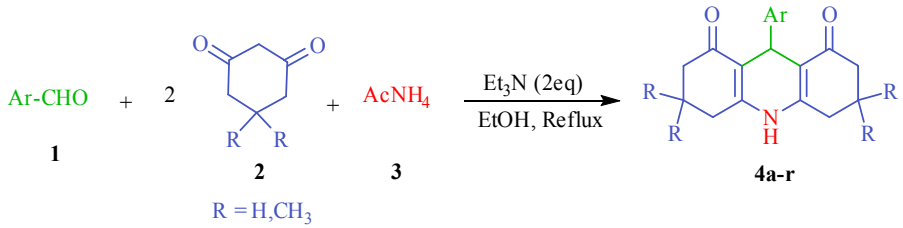


Fig 4: Effect of solvents.

The best result was obtained by carrying out the reaction of 4-Hydroxybenzaldehyde (1eq) and 1,3-cyclohexanedione (2eq) and ammonium acetate (1.5eq) in the presence of triethylamine (2eq) inethanol at reflux.The general process was examined by applying the reaction conditions to various substituted aromaticaldehydes bearing either, electron-withdrawing groups (such as nitro, halide), or electron donatinggroups (such as hydroxyl, methoxy). In all cases studied, the respective decahydroacridine-1,8-dioneswere obtained in good to excellent yields. The noteworthy feature of all the reactions was the easinessof product isolation, it can be effected by a simple filtration. The product obtained after sufficientwashings with water was found to be practically pure (Fig 5).



Scheme2: One-pot reaction for the preparation of 1,8-dioxodecahydroacridines derivatives

Table 3: Synthesis of products **4a-r**by the reactions of aromatic aldehydes with 1,3cyclohexanedione (or dimedone) and ammonium acetate.

Entry	Ar	R	Product	Time (h)	Yield[b] (%)	M.P (°C) Found	Reported[Ref]
1	C_6H_5	H	**4a**	1.5	93	278-280	278–279[xxxiv]
2	2-$OCH_3C_6H_5$	H	**4b**	1.5	94	300-302	301–302[xxxiv]
3	2-ClC_6H_5	H	**4c**	2	96	302-304	302-304[xxxiv]
4	4-$OCH_3C_6H_5$	H	**4d**	1.5	97	303-305	302–304[xl]
5	4-$NO_2C_6H_5$	H	**4e**	1.5	88	294-297	301-302[xl]
6	4-ClC_6H_5	H	**4f**	2	92	301-303	295–297[xl]
7	4-OHC_6H_5	H	**4g**	1.5	96	304-306	303–305[xl]
8	4-OH,3-$OCH_3C_6H_5$	H	**4h**	1.5	92	288-290	390-393[xl]
9	4-BrC_6H_5	H	**4i**	1.5	94	309-311	311–312[xl]
10	C_6H_5	CH_3	**4j**	2	93	272-274	277–278[xl]
11	2-$OCH_3C_6H_5$	CH_3	**4k**	1.5	89	291-293	293–295[xl]

12	2-ClC_6H_5	CH_3	**4l**	2	91	226-227	222–224[xl]
13	4-$OCH_3C_6H_5$	CH_3	**4m**	2	96	274-275	275–277[xl]
14	4-$NO_2C_6H_5$	CH_3	**4n**	1.5	94	285-286	287–289[xl]
15	4-ClC_6H_5	CH_3	**4o**	1.5	88	296-298	295–297[xl]
16	4-OHC_6H_5	CH_3	**4p**	2	96	301-304	302–304[xl]
17	4-OH,3-$OCH_3C_6H_5$	CH_3	**4q**	1.5	94	293-296	295–298[xli]
18	4-BrC_6H_5	CH_3	**4r**	1.5	94	308-311	310–312[xl]

a. Reaction conditions: Arylaldehydes (1 mmol), 1,3-Cyclohexanedione / Dimedone (2 mmol), Ammonium acetate (3 mmol) in the presence of TEA (2mmol), at Reflux in Ethanol.
b. Isolated yield.

The reaction profile for **4g** is very clean and no side products are formed. All the synthesized 1,8-dioxodecahydroacridines derivatives were assigned based on their spectral analyses as well as bymatching their melting points with reported analogues. The IR spectrum of **4g**showedcharacteristic absorptions at 3746 cm^{-1} for the NH group, the carbonyl groups were observed at 1631cm^{-1}. ^1H NMR spectrum of **4g** (Fig 5) remarked a singlet at 5.44 ppm for aliphatic CH while NHgroup was observed at chemical shifts of 9.65 ppm. Aromatic signals were observed at 7.18 and 7.57ppm. Signals at 2.39, 2.79 and 3.12 ppm were assigned for CH_2protons and the hydroxyl group wasobserved at 9.99 ppm. ^{13}C NMR of this compound showed two characteristic peaks at 194.27 ppmfor carbonyl groups, signals around 150.34 and 113.91 ppm were assigned to the quaternary carbonatoms and the resonating peak CH was observed at 30.45 ppm.

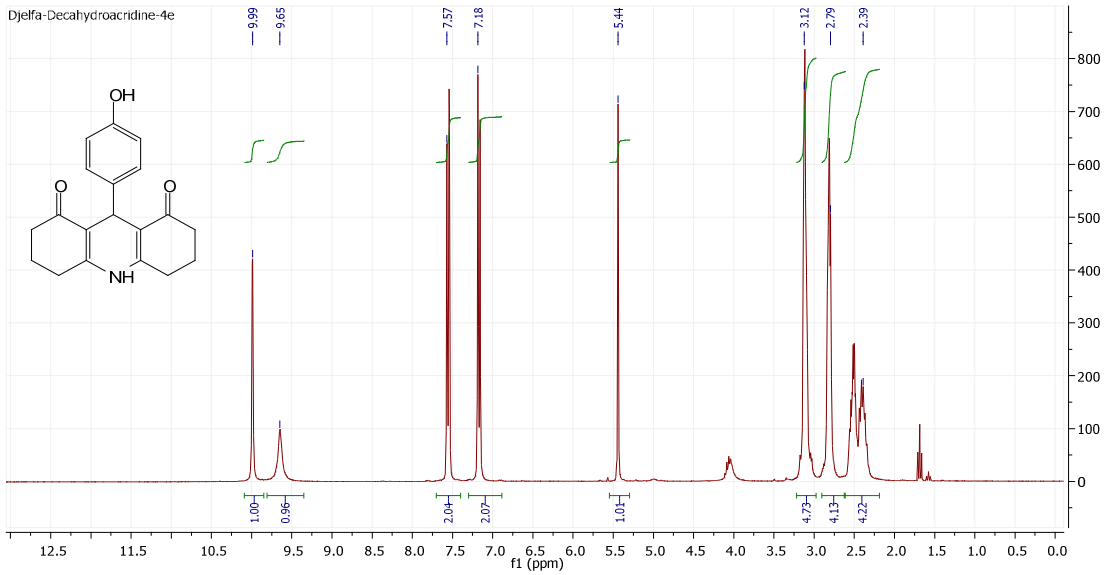
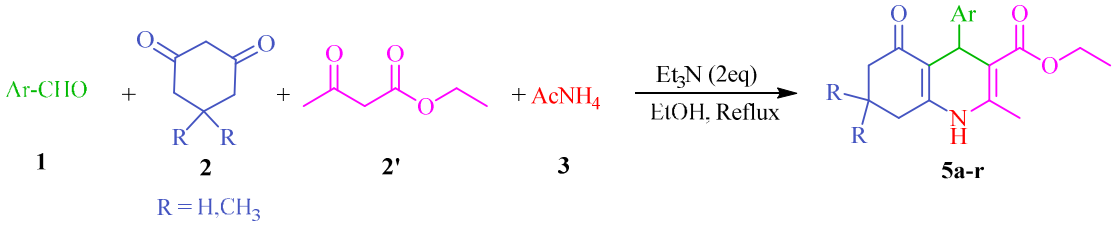


Fig 5. The ^1H NMR spectrum of compound **4g** in DMSO-d^6 solvent.

After successfully synthesizing a series of 1,8-dioxodecahydroacridine derivatives in excellentyields using 1,3-cyclohexanedione and dimedone as 1,3-diketones, We turned our attention togeneralizing our methodology towards other 1,3-dicarbonyl compounds. The reactions of 1,3-cyclohexanedione (or dimedone), ethyl acetoacetate and NH_4OAc with different aldehydes for thesynthesis of hexahydroquinoline derivatives in ethanol catalysed

by Et_3N (2eq) was carried out usingalready established reaction conditions, the results summarized in table 4 showed the high efficiencyfor the one-pot multicomponent reaction.



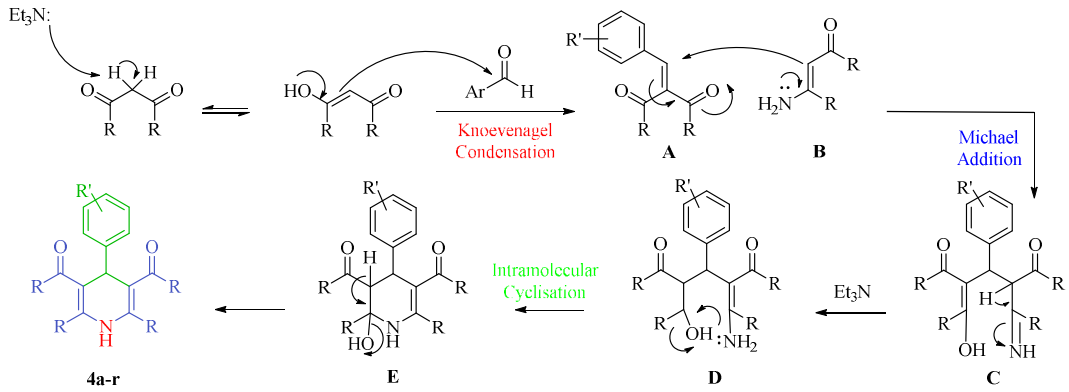
Scheme 3: One-pot reaction for the preparation of hexahydroquinoline derivatives

Table 4: Synthesis of products 5a-t by the reactions of aromatic aldehydes with dimedone, ethyl acetoacetate andammonium acetate.

Entry	Ar	R	Product	Time(h)	Yield[b] (%)	M.P (°C) Found	Reported[Ref]
1	C_6H_5	H	**5a**	2	90	239-241	240-241[xlii]
2	2-$OCH_3C_6H_5$	H	**5b**	1.5	96	246-248	247-249[xlii]
3	2-ClC_6H_5	H	**5c**	2	92	235-236	236-238[xlii]
4	4-$OCH_3C_6H_5$	H	**5d**	1.5	94	194-197	198-200[xlii]
5	4-$NO_2C_6H_5$	H	**5e**	1.5	87	201-203	204-206[xlii]
6	4-ClC_6H_5	H	**5f**	2	96	235-237	235-236[xlii]
7	4-OHC_6H_5	H	**5g**	2	96	220-222	221-223[xlii]
8	4-OH,3-$OCH_3C_6H_5$	H	**5h**	1.5	89	235-237	236-237[xlii]
9	4-BrC_6H_5	H	**5i**	1.5	90	253-255	254-255[xlii]
10	C_6H_5	CH_3	**5j**	2	89	201-203	203-205[xlii]
11	2-$OCH_3C_6H_5$	CH_3	**5k**	2	94	251-253	255–256[xlii]
12	2-ClC_6H_5	CH_3	**5l**	1.5	92	208-209	207-209[xlii]
13	4-$OCH_3C_6H_5$	CH_3	**5m**	2	96	259-262	258-259[xlii]
14	4-$NO_2C_6H_5$	CH_3	**5n**	1.5	94	243-244	241-243[xlii]
15	4-ClC_6H_5	CH_3	**5o**	2	87	237-239	235-236[xlii]
16	4-OHC_6H_5	CH_3	**5p**	2	94	233-235	234–235[xliii]
17	4-OH,3-$OCH_3C_6H_5$	CH_3	**5q**	2	94	215-217	212-214[xliv]
18	4-BrC_6H_5	CH_3	**5r**	1.5	90	251-253	252-254[xliv]

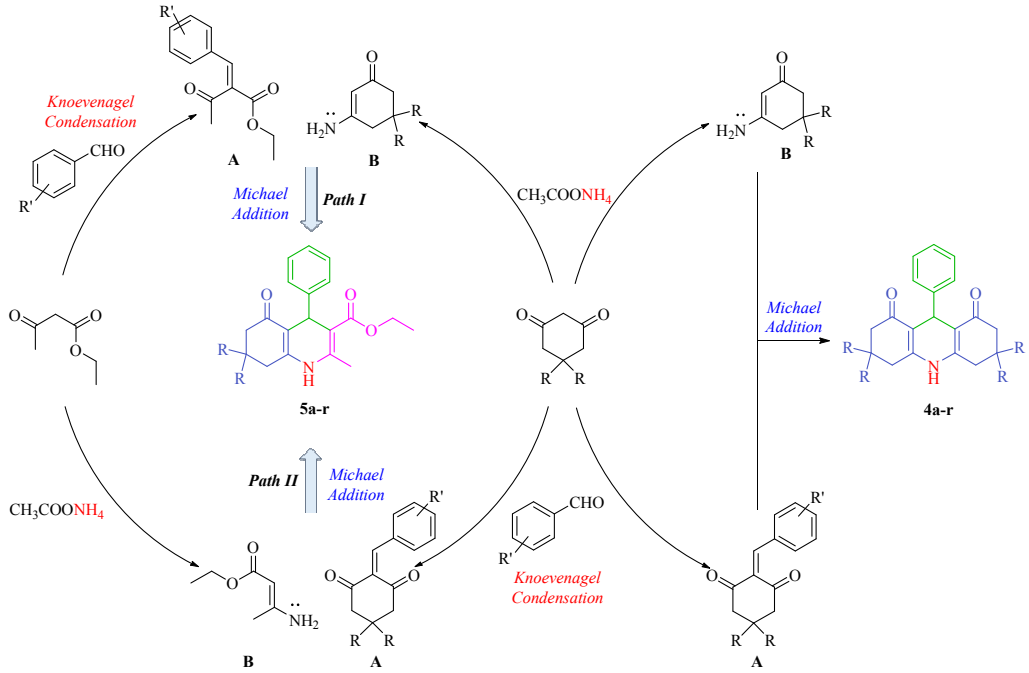
a. Reaction conditions: Arylaldehydes (1 mmole), 1,3-Cyclohexanedione / Dimedone (1 mmole), ethyl acetoacetate(1mmole), Ammonium acetate (3 mmole) in the presence of TEA (2mmole), at Reflux in Ethanol.
b. Isolated yield.

The formation of **4a–rand 5a-r**in the presence of TEA can be explained by the general mechanism shown in Scheme4. Aldehyde attacked by 1,3-diketone to produce the intermediate **A** through Knoevenagelcondensation. Michael addition of **B** to **A** gives another intermediate **C**, which undergoesdeprotonation to yield **D**. Cyclodehydration of **D** under TEA provides the desired cycloadduct **4a-r**.



Scheme 4:A possible mechanism for the synthesis of 1,4-DiHydroPyridine in the presence of TEA in ethanol.

In Scheme 5, the possible paths for the synthesis of 1,8-dioxooctahydroxanthenes **(4a-r)** and Hexahydroquinolines **(5a-r)** are presented.



Scheme 5: Possible paths for the synthesis of 1,8-dioxooctahydroxanthene**(4a-r)**and Hexahydroquinoline **(5a-r)** derivatives.

In order to prove the efficiency of the present protocol for the synthesis of 1,8-dioxodecahydroacridines we have compared our results obtained using triethylamine (TEA) with those obtained using other catalysts that have been recently reported in the literature. As shown in table 5 there are some disadvantages of these methods like long reaction times neededto produce the target compounds in reasonable yields *(Table 4, entries 4-9),* toxic and nonenvironmentally safe solvents *(Table 4, entries 11-14)*, high temperatures *(Table 4, entries 1-4)*, pooryields *(Table 4, entries 8-9)* and the use of catalysts requires complex purification procedures *(Table4, entries 8-11)*. Therefore, the use of TEA as acatalyst has several advantages such as excellentyields, relatively short reaction time (90-120 min) simple and easy work-up, green process, and theuse of a cheap solvent. As one can see, our results show a very good comparability with previouslyreported methods in this regard.

Table 5: Comparison of this method with other methods for synthesis of 1,8-dioxodecahydroacridines and hexahydroquinolines derivatives.

Entry	Catalyst	Solvent	Temp (°C)	Time (min)	Yield (%)[Ref]
1	DBH or DCH	Solvent free	130	20-45	82-93 [xlv]
2	nano-Fe_3O_4	Solvent free	120	10-50	70-95 [xlvi]
3	SiO_2-Pr-SO_3H	Solvent free	120	120	82-95 [xlvii]
4	KH_2PO_4	EtOH:H_2O 3:1	120	300	24-97 [xlvii]
5	[Hbet][Lac]	Ethanol	80	60-480	75-96 [xlvii]
6	L-Proline	Ethanol	65	300-360	73-88 [xlviii]
7	Cellulose sulfuric acid.	Solvent free	100	120-300	78-92[xlix]
8	SDS	H_2O	90	360-1200	56-72 [xxvii]
9	FSG-Hf(NPf2)$_4$	EtOH:H_2O 1:1	100	180-490	Trace-83 [l]
10	CeO_2–Eu_2O_3	Water	80	120-150	69-91 [li]
11	In(OTf)$_3$	DMF	100	120-180	60-90 [xxx]
12	CAN	PEG 400	25	10-25	90-98 [lii]
13	Pt NPs@GO	DMF	75	50-120	93-96 [liii]
14	$CeCl_3.7H_2O$	[bmim][BF_4]	55	180	82-95 [liv]
15	***Et_3N***	***EtOH***	***80***	***90-120***	***87-97*** **This Work**

In conclusion, a new and facile method for the synthesis of biologically interestingsymmetrical and unsymmetricalacridinediones by triethylamine catalyzed multi-component reaction was developed starting from aldehydes, 1,3-diketones, and ammonium acetate in ethanol. The promising points for the presentedprotocols are efficiency, high yields, short reaction times, cleaner reaction profile, simplicity, lowcost, and compliance with the green chemistry protocols.

EXPERIMENTAL SECTION

All reactions were followed by TLC (E. Merck Kieselgel 60 F-254), using Ethylacetate: Hexane (5:5) as eluent with detection by UV light at 254 nm. IR spectra were recorded onALPHA's Platinum ATR single reflection diamond ATR spectrophotometer.^{1}H and ^{13}C NMR spectrawere recorded on a Bruker AC 300 MHZ FTNMR spectrometer, in DMSO-d^6 Chemical shifts (δ)were reported in parts per million (ppm) relative to tetramethylsilane (0 ppm) as an internal referenceand the following multiplicity abbreviations were used: s, singlet; d, doublet; t, triplet; q, quadruplet;m, multiplet. All chemicalswere obtained from Biochem and sigma Aldrich and were used withoutfurther purification.

General procedure for synthesis of 1,8-dioxodecahydroacridines derivatives (4a-r):A mixture of aldehyde **1** (1 mmole), 1,3-cyclohexanedione / dimedone **2** (2 mmole), ammonium acetate**3** (3 mmole), triethylamine (2 mmole) and ethanol (10 mL) was placed in a 50 mL flask, reflexed andstirred for the appropriate time as monitored by thin-layer chromatography TLC (Hexane : EthylAcetate); (5:5/v:v). After completion of the reaction, the mixture was poured into coled water andcrushed ice with stirring, the resulting product was filtered, washed with waterand dried to providethe pure product without further purification. All the products were fully characterized on the basisof their melting-points and spectral data (IR, ^{1}H NMR and ^{13}C NMR).

General procedure for synthesis of hexahydroquinolines derivatives (5a-r): A mixture of aldehyde **1** (1 mmol), 1,3-cyclohexanedione / dimedone **2** (1 mmol), ethyl acetoacetate(1 mmol), ammonium acetate **3**(3 mmol), triethylamine (2 mmol) and ethanol (10 mL) was placedin a 50 mL flask, reflexed and stirred for the appropriate time as monitored by thin-layerchromatography TLC (Hexane : Ethyl Acetate); (5:5/v:v). After completion of the reaction, themixture was poured into coled water and crushed ice with stirring, the resulting product was filtered, washed with waterand dried to provide the pure product without further purification. All the productswere fully characterized on the basis of their melting-points and spectral data (IR, ^{1} H NMR and ^{13}CNMR). Spectroscopic and physical data of some representative compounds are given below:

9-(4-hydroxyphenyl)-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione(4g): Pale-yellow solid;yield 96% M. P: 304-306°C; IR (Cm^{-1}) ν max: 1225 (CN stretching), 1488, 1589 (C=C stretching ofaromatic ring), 1631 (C=O– of 1,3-diketone), 3061 (–CH stretching of aromatic ring), 3746 (–NHstretching). ^{1}H NMR (300 MHz, DMSO-d^6) δ 9.39 (s, 1H, NH), 9.05 (s, 1H), 6.95 (d, J = 8.5 Hz,2H), 6.57 (d, J = 8.5 Hz, 2H), 4.84 (s, 1H), 2.69 – 2.34 (m, 4H), 2.30 – 2.06 (m, 4H), 2.04 – 1.49 (m,4H). ^{13}C NMR (75 MHz, DMSO-d^6) δ: 194.27, 154.56, 150.34, 137.49, 127.76, 113.91, 112.36,36.29, 30.45, 25.78, 20.28.

9-(4-methoxyphenyl)-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione(4d): yellow solid; yield97% M. P: 303-305°C; IR (Cm^{-1}) ν max: 1222 (CN stretching), 1492, 1582 (C=C stretching ofaromatic ring), 1645 (C=O– of 1,3-diketone), 3023 (–CH stretching of aromatic ring), 3745 (–NHstretching). ^{1}H NMR (300 MHz, DMSO-d^6) δ : 9.22 (s, 1H, NH), 7.32 – 7.10 (m, 2H), 6.74 – 6.52(m, 2H), 4.71 (s, 1H), 3.82 (s, 3H), 2.74 –2.46 (m, 4H), 2.41 – 2.17 (m, 4H), 2.11 – 1.79 (m, 4H).^{13}CNMR (75 MHz, DMSO-d^6) δ: 194.60, 153.7, 151.0, 138.30, 127.05, 113.55, 111.66, 37.07, 30.85,26.11, 20.35.

9-(4-bromophenyl)-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione(4i): Pale-yellow solid; yield94% M. P: 309-311°C; IR (Cm^{-1}) ν max: 1280 (CN stretching), 1520 (C=C stretching of aromaticring), 1662 (C=O– of 1,3-diketone), 2933 (–CH stretching of aromatic ring), 3698 (–NH stretching).^{1}H NMR (300 MHz, DMSO-d^6) δ: 9.42 (s, 1H), 7.12 (d, J = 8.5 Hz, 2H), 6.71 (d, J = 8.5 Hz, 2H),5.02 (s, 1H), 2.71 – 2.36 (m, 4H, NH), 2.32 – 2.06 (m, 4H), 2.05 – 1.53 (m, 4H). ^{13}C NMR (75 MHz,DMSO-d^6) δ: 192.16, 155.49, 151.17, 135.52, 128.45, 112.16, 110.14, 35.23, 29.44, 25.77, 19.94.

9-(phenyl)-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione(4j): yellow solid; yield 93% M. P: 272-274°C; IR (Cm^{-1}) ν max: 1284 (CN stretching), 1543 (C=C stretching of aromatic ring), 1617 (C=O– of 1,3-diketone), 2912 (–CH stretching of aromatic ring), 3713 (–NH stretching). ^{1}H NMR(300 MHz, DMSO-d^6) δ: 9.35 (s, 1H, NH), 7.41 – 7.23 (m, 2H), 7.21 – 7.13 (m, 2H), 7.07 (ddd, J = 7.4, 3.8, 1.3 Hz, 1H), 4.78 (s, 1H), 2.76 – 2.45 (m, 4H), 2.11 – 1.82 (m, 4H), 1.11 (s, 6H), 1.02 (s, 6H). ^{13}C NMR (75 MHz, DMSO-d^6) δ: 193.54, 153.77, 150.01, 126.15, 125.88, 123.11, 109.70, 50.24, 36.88, 27.17, 24.21, 20.40.

9-(4-chlorophenyl)-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione(4o): yellow solid; yield 88% M. P: 296-298°C; IR (Cm^{-1}) ν max: 1210 (CN stretching), 1510 (C=C stretching of aromatic ring), 1628 (C=O– of 1,3-diketone), 3105 (–CH stretching of aromatic ring), 3715 (–NH stretching).^{1}H NMR (300 MHz, DMSO-d^6) δ : 9.42 (s, 1H), 7.29-7.26 (d, J= 8.2 Hz, 2H), 7.21-7.19 (d, J= 8.2 Hz, 2H), 4.50 (s, 1H), 2.60-2.51 (dd, J= 14.65, 4H), 2.29-2.25 (d, J= 16, 2H), 2.13-2.08 (d, J= 16, 2H), 1.08 (s, 6H), 0.92 (s, 6H),^{13}C NMR (75 MHz, DMSO-d^6) δ: 194.46, 149.60, 149.30, 147.17, 127.87, 127.80, 126.07, 111.94, 50.73, 32.20, 31.22, 29.26, 27.29.

ethyl 2-methyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5a): Pale-yellow solid; yield 90% M. P: 239-241°C; IR (Cm^{-1}) ν max: 1284 (CO stretching), 1485 (CN stretching), 1612 (C=C stretching of aromatic ring), 1697 (C=O– of 1,3-diketone), 2962.5 (–

CH stretching of aromatic ring), 3286.5 (–NH stretching). ^{1}H-NMR (300 MHz, DMSO-d^{6}) d 8.75 (s, 1H, NH), 7.27- 7.21 (m, 2H), 7.20 – 7.17 (m, 2H), 7.15 – 7.11 (ddd, J = 7.4, 3.8, 1.3 Hz, 1H), 4.85 (s, 1H), 4.05 (q, J = 7.0 Hz, 2H), 2.51–2.45 (m, 2H), 2.30–2.21 (m, 5H), 2.01–1.79 (m, 2H), 1.15 (t, J = 7.0 Hz, 3H).^{13}CNMR (75 MHz, DMSO-d^{6}) δ: 194.6, 166.5, 149.3, 147.2, 144.4, 127.6, 127.0, 125.1, 110.9; 104.2, 58.8, 50.1, 35.5, 31.6, 28.8, 26.4, 18.5, 13.4.

ethyl 4-(4-methoxyphenyl)-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5d):yellow solid; yield 94% M. P: 194-197°C; IR (Cm^{-1}) ν max: 1232 (CO stretching), 1482 (CN stretching), 1610 (C=C stretching of aromatic ring), 1692 (C=O– of 1,3-diketone), 2946 (–CH stretching of aromatic ring), 3284 (–NH stretching). ^{1}H-NMR (300 MHz, DMSO-d^{6}) δ: 7.29 – 7.22 (m, 2H), 6.76 – 6.74 (m, 2H), 6.72 (s, 1H, NH), 5.01 (s, 1H), 4.11- 4.06 (m, J = 7.0 Hz, 2H), 3.74 (s,3H), 2.36 (s, 3H), 2.27–2.24 (m, 2H), 2.21–2.17 (m, 2H), 1.28 (s, 3H) 1.19 (m, 2H). ^{13}C NMR (75MHz, DMSO-d^{6}) δ: 195.9, 167.2, 157.4, 149.2, 143.4, 140.1, 128.1, 113.2, 113.5, 106.4, 60.2, 55.4, 37.5, 35.4, 27.5, 21.2, 19.8, 14.4.

ethyl 4-(4-methoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate(5m) : yellow solid; yield 96% M. P: 259-262°C; IR (Cm^{-1}) ν max: 1237 (CO stretching), 1475 (CN stretching), 1614 (C=C stretching of aromatic ring), 1709 (C=O– of 1,3-diketone), 3020 (–CH stretching of aromatic ring), 3321 (–NH stretching). ^{1}H-NMR (300 MHz, DMSO-d^{6}) δ: 9.05 (s, 1H, NH), 6.62- 7.18 (m, 4H), 4.81 (s, 1H), 4.00 (q, 2H), 3.65 (s, 3H), 1.94-2.43 (m, 7H), 1.13 (t, 3H), 0.99 (s, 3H), 0.85 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d^{6}) δ: 195.60, 167.55, 159.28, 150.65, 149.49, 145.37, 129.40, 120.23, 114.06, 111.10, 110.15, 104.16, 59.42, 55.17, 50.58, 26.19, 29.59, 26.78, 18.57, 14.61.

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