DABCO prompted tandem and multicomponent synthetic protocol of pyrano[2,3-a]acridines

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An elegant synthesis of pyrano[2,3-a]acridines is presented, where 7-chloro-9-phenyl-3,4-dihydroacridin-1(2H)-one reacts with aryl aldehydes and malononitrile in a three-component system using 1,4-diazabicyclo[2.2.2]octane (DABCO) as catalyst in ethanol, giving excellent yields above those reached in a conventional step-wise approach. The structures of the synthesized compounds have been deduced by spectroscopic techniques, including X-ray diffraction.

Keywords: DABCO, multi-component reaction, tandem process, pyrano[2,3-a]acridines

The advantage of a multi-component methodology is in avoiding intermediates, leading to improved efficiency and reduced waste, thus, providing an eco-friendly protocol for building complex molecules from readily available starting materials. A strategy like this is considered most suitable in modern organic synthesis to generate compound libraries from core structures like acridine derivatives found in numerous pharmaceuticals and natural products for screening purposes, because of productivity, simplicity, convergence, atom economy, and facile execution\textsuperscript{1}. Acridine derivatives, known since the 19\textsuperscript{th} century, were first used as pigments and dyes\textsuperscript{2}. More recent reports demonstrate their biomedical potential, including antioxidant, anticancer, antimicrobial, antiparasitic, and antitumor activities\textsuperscript{3-5}. The acridine nucleus can be condensed with additional heterocyclic rings providing polycyclic molecules, also endowed with high cytotoxicity. Evidently, incorporation of six membered heterocyclic rings into the acridine chromophore highly favours passive cellular drug uptake, rendering the efflux by multi-drug resistant transmembrane proteins (MDR transporters) inefficient\textsuperscript{6}.

The heterocyclic pyran moiety is present in a large number of natural products, and synthetic methods to access the pyran ring system have been extensively studied\textsuperscript{7}. The natural pyranoacridone acronycine (I, Figure 1) was first isolated from \textit{Acronychiabaueri} Schott (Rutaceae)\textsuperscript{8} in 1948 exhibiting a broad-spectrum of biological activity\textsuperscript{9}.

Significant improvements in terms of solubility and potency were obtained by modifying the pyran ring. While preserving similar reactivity toward nucleophilic agents, the presence of the angularly fused dimethylpyran ring, for example, appears to be an indispensable structural requirement to maintain significant cytotoxic activity\textsuperscript{10}. 1,4-Diazabicyclo [2.2.2]octane (DABCO) has been used widely as a basic catalyst in organic reactions such as Baylis-Hillman reaction\textsuperscript{11} and the selective cleavage of esters\textsuperscript{12} as well as catalyst in multi-component reactions (MCRs) for synthesis of naphthopyran heterocyclic systems\textsuperscript{13}. In this work we would like to report DABCO as an efficient catalyst to promote the one-pot multi-component reaction and tandem synthesis of pyrano[2,3-a]acridine derivatives.

Results and Discussion

Herein we compare pyrano[2,3-a]acridine derivatives synthesis by a tandem processes with a multi-component approach. Recently, pyrano derivatives had been obtained by refluxing of reactive methylene compounds like malononitrile with aldehydes and ketone compounds using an organic base as a catalyst. Based on this, 2-amino-4-aryl-5,6-
dihydro-4H-pyrano[2,3-α]acridine-3-carbonitrile was synthesized via a multi-component as well as in a step-wise process in the presence of catalyst 1,4-diazabicyclo[2.2.2]octane (DABCO).

**The two-step (tandem) synthesis method**

In an initial experiment we investigated the reaction of 7-chloro-9-phenyl-3,4-dihydroacridin-1(2H)-one 1 with thiophene-2-carboxaldehyde 2a in presence of alcoholic potassium hydroxide at RT for 4-5 h to form 3a (Scheme I). The IR spectrum (KBr, cm⁻¹) of 3a shows an absorption band at 1657 cm⁻¹ confirming the presence of C=O group and a sharp band at 1567 cm⁻¹ related to C=N group. The ¹H NMR spectrum of 3a shows a multiplet at δ 3.139-3.167 due to two aliphatic protons. The multiplet at δ 3.223-3.264 relates to the two aliphatic protons. The benzylidine proton is seen at δ 7.827 as a singlet. The total number of protons matched perfectly with the structure of 3a. Its ¹³C NMR spectrum shows the presence of 24 carbon signals. The structure of the derivatives 3a and 3d were confirmed via single crystal X-ray diffraction studies (Figure 2 and 3).

Further the condition to react 7-chloro-9-phenyl-2-(thiophen-2'-ylmethylene)-3,4-dihydroacridin-1(2H)-one (3a) and malononitrile was optimized in the presence of bases like triethylamine (TEA), K₂CO₃, KOH and DABCO in ethanol (Scheme II). Best conditions and yields for this reaction are shown in Table I. Best results were obtained for 15% DABCO as a catalyst in ethanol.

7-Chloro-9-phenyl-2-(thiophen-2'-ylidine)-3,4-dihydroacridin-1(2H)-one 3a was reacted with malononitrile in the presence of DABCO in ethanol at 70°C for 1-2 h to obtain crude product 4a. The product was purified by recrystallization from ethyl acetate. The infrared spectrum of 4a shows absorption peaks at 3457, 3360 and 2210 cm⁻¹, which attests to the presence of amino and cyano groups, respectively. The ¹H NMR spectrum of 4a exhibits a broad singlet at Δ 5.01, which is the characteristic representation of the amino group protons. The proton at the 4ᵗʰ-position of the pyrano[2,3-α]acridine appears at Δ 4.53. All the other 11 aromatic protons appeared in the corresponding region of Δ 6.98-8.01. The ¹³C NMR spectrum shows the presence of 27 carbon signals. The structure of derivative 4a was confirmed via single crystal X-ray diffraction studies (Figure 2 and 3).

![Figure 2](image2.png) — X-ray crystal structure of compound 3a, thermal ellipsoid representation at the 50% probability level. Disorder omitted for clarity

![Figure 3](image3.png) — X-ray crystal structure of compound 3d, thermal ellipsoid representation at the 50% probability level. Disorder omitted for clarity

![Scheme I](image1.png) — Synthesis of benzylidene derivatives of acridone 3a-f
further confirmed by single crystal X-ray diffraction studies (Figure 4).

The following mechanism is proposed for the reaction of arylidineacridinone 3 with malononitrile (Scheme III). Initially, a carbanion intermediate (I) was produced from malononitrile in presence of DABCO as a catalyst. Then the proposed mechanism involves classical Michael addition of carbanion of malononitrile intermediate (I) to arylidineacridinone 3 followed by subsequent heterocyclization and protonation to form the intermediate (IV). This tautomerizes i.e. imino-amination to form the final product 4.

The multi component methodology

We recently focused on the development of new methodologies for the synthesis and biological evaluation of various heteroannulated carbazoles and quinolines such as pyranocarbazoles and pyranoquinolines via multi-component methodologies. In the present MCR method, the base plays a crucial role in this reaction, which involves Knoevenagel condensation and Michael addition reactions. The importance of the base was verified in the step-wise procedure, but the expected 2-amino-10-chloro-9-phenyl-2-(thiophen-2'-ylidine)-3,4-dihydroacridin-1(2H)-one 3 and malononitrile were obtained in only moderate yield. To improve yields, we carried out multi-component reaction with 15% DABCO as a base under the same conditions as in the step-wise procedure, and the corresponding pyrano[2,3-a]acridine-3-carbonitriles 4a-f were obtained in better yields with no other by-products (Table II, Scheme IV). The final compounds by this method have been found to be identical to the compounds 4a-f obtained by the two step process, (m.m.p., co-TLC, superimposable IR spectra). Thus, we developed two methodologies to synthesize pyrano[2,3-a]acridines with the multi-component reaction which is a clear improvement over the two step synthesis. Thus, DABCO catalyst plays a crucial role for synthesizing pyrano [2,3-a]acridines 4.

2-amino-10-chloro-9-phenyl-2-(thiophen-2'-ylidine)-3,4-dihydroacridin-1(2H)-one (3a, 1mmol) and malononitrile (1mmol), 20 mL ethanol at reflux temperature of 70ºC.

Table I — Screening of various catalysts to form 4a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield (%)</th>
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<tbody>
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<td>-</td>
<td>EtOH</td>
<td>5</td>
<td>d</td>
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<tr>
<td>2.</td>
<td>TEA</td>
<td>EtOH</td>
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<tr>
<td>3.</td>
<td>K$_2$CO$_3$</td>
<td>EtOH</td>
<td>4</td>
<td>27</td>
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<tr>
<td>4.</td>
<td>KOH</td>
<td>EtOH</td>
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<td>5.</td>
<td>DABCO</td>
<td>EtOH</td>
<td>2</td>
<td>58</td>
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<td>6.</td>
<td>5%DABCO</td>
<td>EtOH</td>
<td>2</td>
<td>55</td>
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<td>7.</td>
<td>10%DABCO</td>
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<td>8.</td>
<td>15%DABCO</td>
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<td>9.</td>
<td>20%DABCO</td>
<td>EtOH</td>
<td>2</td>
<td>69</td>
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</tbody>
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Reaction conditions for 7-chloro-9-phenyl-2-(thiophen-2'-ylidine)-3,4-dihydroacridin-1(2H)-one (3a, 1mmol) and malononitrile (1mmol), 20 mL ethanol at reflux temperature of 70ºC.

Time duration of reaction in hours.

Isolated pure product.

d - Trace amounts.

Table II — Synthesis of pyrano[2,3-a]acridine derivatives 4a-f

<table>
<thead>
<tr>
<th>Step</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
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<tr>
<td>1.</td>
<td>DABCO</td>
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<td>58</td>
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<tr>
<td>2.</td>
<td>15%DABCO</td>
<td>EtOH</td>
<td>2</td>
<td>69</td>
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</table>

Figure 4 — X-ray crystal structure of compound 4a, thermal ellipsoid representation at the 50% probability level. Disorder omitted for clarity.
following reaction scheme (Scheme V) is a further indication that our proposed mechanism is correct.

In order to verify our proposed reaction mechanism (Scheme V) through the intermediate, 2-(4'-methoxybenzylidene) malononitrile\(^{19}\) 5d derived independently, it was reacted with 7-chloro-9-phenyl-3,4-dihydroacridin-1(2H)-one 1 under similar conditions using DABCO as a catalyst to give the final product 2-amino-10-chloro-4-(4'-methoxyphenyl)-12-phenyl-5,6-dihydro-4\(^H\)-pyrano[2,3-\(a\)]acridin-3-carbonitrile 4d (m.m.p., co-TLC, superimposable IR spectra) (Scheme VI).

The overall reaction scheme is summarized in Scheme VII.

### Experimental Section

Melting points (m.p.) were determined on a Mettler FP 51 apparatus (Mettler Instruments, Switzerland) and are uncorrected. They are expressed in degree centigrade (°C). A Nicolet Avatar Model FT-IR spectrophotometer was used to record the IR spectra (4000–400 cm\(^{-1}\)).\(^{1}\)H and \(^{13}\)C NMR spectra were recorded on Bruker AV 400 [500 MHz (\(^{1}\)H) and 100 MHz (\(^{13}\)C)] spectrometers using tetramethylsilane (TMS) as an internal reference. The chemical shifts are expressed in parts per million (ppm). Coupling constants (\(J\)) are reported in Hertz (Hz). The terms s, d, t, dd refer to singlet, doublet, triplet and doublet of

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Product</th>
<th>Yield(^a) (%)</th>
<th>(4^b)</th>
<th>(5^c)</th>
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<td><img src="product_image_4.png" alt="Product Image 4" /></td>
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<tr>
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<td>66%</td>
<td>87%</td>
<td></td>
</tr>
</tbody>
</table>

Reaction conditions: 7-chloro-9-phenyl-3,4-dihydroacridin-1(2H)-one (1) (1 mmol), malononitrile (1 mmol), thiophene-2-carbaldehyde (1 mmol) in 20 mL ethanol at reflux temperature.

\(^a\)Isolated pure product.

\(^b\)Stepwise synthesis yield.

\(^c\)Multi-component synthesis yield.
doublet, respectively. b s refers to a broad singlet. Microanalyses were performed on a Vario EL III model CHNS analyzer (Vario, Germany) at the Department of Chemistry, Bharathiar University. X-ray diffraction measurements were performed on a Bruker AXS SMART APEX CCD diffractometer at 100 K using monochromatic Mo Kα radiation with the omega scan technique. The homogeneity of the products was tested by TLC using plates coated with silica gel-G using petroleum ether and ethyl acetate in the ratio of 1:1 as developing solvents.

**General procedure for the synthesis of 7-chloro-9-phenyl-2-arylidine-3,4-dihydroacridin-1(2H)-one, 3**

A mixture of 7-chloro-9-phenyl-3,4-dihydroacridin-1(2H)-one (1, 0.001 mol) was reacted with arylaldehyde (2, 0.001 mol) in presence of 25 mL of a 5% alcoholic potassium hydroxide solution and stirred at RT for 4-5 h. The product precipitated out as a yellow crystalline mass. It was filtered off and washed with 50% ethanol. A further crop of condensation product was obtained on neutralization with 1:1 HCl and further dilution with water. The combined product was purified by recrystallisation from ethyl acetate to yield the respective 7-chloro-9-phenyl-2-(arylidine)-3,4-dihydroacridin-1(2H)-one 3.

**(E)-7-Chloro-9-phenyl-2-(thiophen-2'-ylidine)-3,4-dihydroacridin-1(2H)-one, 3a**

Yellow solid, m.p.204-206°C. Yield 93%. IR (KBr): 1657; 1567 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 3.139-3.167 (m, 2H, C₄-CH₂), 3.233-3.264 (m, 2H, C₃-CH₂), 7.035-7.089 (m, 1H, C₅'-H), 7.155-7.179
Scheme VI — Synthesis of pyrano[2,3-a]acridine 4d

Scheme VII — The overall reaction scheme for synthesis of pyrano[2,3-a]acridine derivatives

(E)-7-Chloro-2-(4’-fluorobenzylidine)-9-phenyl-3,4-dihydroacridin-1(2H)-one, 3b

Yellow solid. m.p.178-80°C. Yield 92%. IR (KBr): 1694; 1552 cm⁻¹; ¹H NMR (CDCl₃ 400 MHz): δ 3.139-3.167 (m, 2H, C₄'-CH₂), 3.233-3.264 (m, 2H, C₃'-CH₂), 7.22-7.27 (m, 3H, C₉-C₃'', C₄'', C₅''-H), 7.34-7.36 (m, 2H, C₉-C₃', C₄', C₆'', H), 7.50 (d, 1H, J = 2.40 Hz, C₈-H), 7.53-7.58 (m, 4H, C₂', C₃', C₄', C₆''-H), 7.72 (dd, 1H, Jₚ = 2.40 Hz, J₀ = 8.00 Hz, C₆-H), 7.75 (s, 1H, benzylidine proton), 8.06 (d, 1H, J = 8.00 Hz, C₅-H); ¹³C NMR (CDCl₃, 100 MHz): δ 21.37, 25.70, 33.32, 126.66, 126.76, 128.12, 128.39, 129.37, 130.24, 132.53, 132.57, 134.44, 136.67, 138.15, 139.53, 150.81, 161.40, 187.30. Anal. Calcd for C₂₅H₁₇ClFNO: C, 71.92; H, 4.58; N, 3.39. Found: C, 71.96; H, 4.50; N, 3.35%.

(E)-7-Chloro-2-(4’-methoxybenzylidine)-9-phenyl-3,4-dihydroacridin-1(2H)-one, 3d

Yellow solid. m.p.194-96°C. Yield 92%. IR (KBr): 1697; 1555 cm⁻¹; ¹H NMR (CDCl₃ 400 MHz): δ 3.139-3.167 (m, 2H, C₄'-CH₂), 3.233-3.264 (m, 2H, C₃'-CH₂), 7.017-7.060 (m, 2H, C₃', C₅'-H), 7.165-7.191 (m, 2H, C₂', C₆'-H), 7.22-7.27 (m, 3H, C₉-C₃'', C₄'', C₅''-H), 7.34-7.36 (m, 2H, C₉-C₃', C₄', C₆'', H), 7.50 (d, 1H, J = 2.40 Hz, C₈-H), 7.53-7.58 (m, 4H, C₂', C₃', C₄', C₆''-H), 7.72 (dd, 1H, Jₚ = 2.40 Hz, J₀ = 8.00 Hz, C₆-H), 7.75 (s, 1H, benzylidine proton), 8.06 (d, 1H, J = 8.00 Hz, C₅-H); ¹³C NMR (CDCl₃, 100 MHz): δ 21.37, 25.70, 33.32, 126.66, 126.76, 128.12, 128.39, 129.37, 130.24, 132.53, 132.57, 134.44, 136.67, 138.15, 139.53, 150.81, 161.40, 187.30. Anal. Calcd for C₂₅H₁₇ClFNO: C, 71.92; H, 4.58; N, 3.39. Found: C, 71.96; H, 4.50; N, 3.35%.
Anal. Calcd for C₂₂H₂₆ClNO: C, 74.45; H, 3.99; N, 8.76. Found: C, 74.39; H, 3.92; N, 8.72%.

(E)-7-Chloro-2-(3',4'-diethoxybenzylidene)-9-phenyl-3,4-dihydroacridin-1(2H)-one, 3f

Yellow solid. m.p. 190-200°C. Yield 89%. IR (KBr): 3448, 3246, 2190 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.21-2.48 (m, 2H, C₄-H₂), 3.50 (s, 2H, C₄-H₂), 3.56-3.77 (m, 4H, C₂-H₂, C₄-H₂, C₅-H₂), 7.46-7.51 (m, 3H, C₅-H₂, C₆-H₂). Found: C, 72.50; H, 3.88; N, 8.89%.

2-Amino-10-chloro-12-phenyl-4-((thiophen-2'-yl)-5,6-dihydro-4H-pyrrano[2,3-a]acridin-3-carbonitrile, 4a

Yellow solid. m.p. 208-10°C. Yield 69%. IR (KBr): 3457, 3360, 2210 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.21-2.48 (m, 2H, C₄-H₂), 3.50 (s, 2H, C₄-H₂), 3.56-3.77 (m, 4H, C₂-H₂, C₄-H₂, C₅-H₂), 7.46-7.51 (m, 3H, C₅-H₂, C₆-H₂). Found: C, 72.50; H, 3.88; N, 8.89%.

2-Amino-10-chloro-12-phenyl-4-(4'fluorophenyl)-12-phenyl-5,6-dihydro-4H-pyrrano[2,3-a]acridin-3-carbonitrile, 4b

Yellow solid. m.p. 212-14°C. Yield 67%. IR (KBr): 3448, 3246, 2190 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.21-2.48 (m, 2H, C₄-H₂), 3.50 (s, 2H, C₄-H₂), 3.56-3.77 (m, 4H, C₂-H₂, C₄-H₂, C₅-H₂), 7.46-7.51 (m, 3H, C₅-H₂, C₆-H₂). Found: C, 72.50; H, 3.88; N, 8.89%.

2-Amino-10-chloro-12-phenyl-4-(4'methylphenyl)-5,6-dihydro-4H-pyrrano[2,3-a]acridin-3-carbonitrile, 4c

Yellow solid. m.p. 206-208°C. Yield 69%. IR (KBr): 3451, 3322, 2190 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 3.168-3.199 (m, 2H, C₄-H₂), 3.230-3.259 (m, 2H, C₄-H₂), 3.779 (s, 3H, C₁'-OCH₃), 6.861-6.882 (m, 2H, C₁', C₂'-H), 7.166-7.190 (m, 2H, C₂', C₃'-H), 7.341-7.363 (m, 2H, C₂'-C₁', C₃'-C₂', C₄'-H), 7.417 (d, 1H, J = 2.00 Hz, C₅-H), 7.448-7.480 (m, 3H, C₂'-C₁', C₄', C₃'-H), 7.627 (dd, 1H, J₉ = 2.00 Hz, J₈ = 9.20 Hz, C₆-H), 7.654 (s, 1H, benzylidine proton). The yield was 8.84%.

2-Amino-10-chloro-12-phenyl-4-(4'-fluorophenyl)-12-phenyl-5,6-dihydro-4H-pyrrano[2,3-a]acridin-3-carbonitrile, 4b

Yellow solid. m.p. 212-14°C. Yield 67%. IR (KBr): 3448, 3246, 2190 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.21-2.48 (m, 2H, C₄-H₂), 3.50 (s, 2H, C₄-H₂), 3.56-3.77 (m, 4H, C₂-H₂, C₄-H₂, C₅-H₂), 7.46-7.51 (m, 3H, C₅-H₂, C₆-H₂). Found: C, 72.50; H, 3.88; N, 8.89%.

2-Amino-10-chloro-12-phenyl-4-(4'methylphenyl)-5,6-dihydro-4H-pyrrano[2,3-a]acridin-3-carbonitrile, 4c

Yellow solid. m.p. 206-208°C. Yield 69%. IR (KBr): 3451, 3322, 2190 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 3.168-3.199 (m, 2H, C₄-H₂), 3.230-3.259 (m, 2H, C₄-H₂), 3.779 (s, 3H, C₁'-OCH₃), 6.861-6.882 (m, 2H, C₁', C₂'-H), 7.166-7.190 (m, 2H, C₂', C₃'-H), 7.341-7.363 (m, 2H, C₂'-C₁', C₃'-C₂', C₄'-H), 7.417 (d, 1H, J = 2.00 Hz, C₅-H), 7.448-7.480 (m, 3H, C₂'-C₁', C₄', C₃'-H), 7.627 (dd, 1H, J₉ = 2.00 Hz, J₈ = 9.20 Hz, C₆-H), 7.654 (s, 1H, benzylidine proton). The yield was 8.84%.
2-Amino-10-chloro-4,12-diphenyl-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4d

Yellow solid. m.p.216-18°C. Yield 68%. IR (KBr): 3477, 3369, 2215 cm-1, 1H NMR (CDCl3 400 MHz): δ 2.861-2.939 (m, 2H, C4-CH2), 3.042-3.099 (m, 2H, C6-CH2), 3.731 (s, 3H, C4-CH3), 4.069 (s, 1H, C2-H), 4.856 (s, 2H, C5-NH2), 6.909 (d, 2H, J = 8.40 Hz, C2-C2', C3-C3'), 7.140 (d, 2H, J = 8.80 Hz, C4-C4', C5-C5'), 7.208 (d, 1H, J = 2.00 Hz, C11-H), 7.328-7.389 (m, 2H, C12-C12', C9-C9'), 7.559-7.595 (m, 3H, C12-C3', C3-C3', C10-C10'), 7.701 (dd, 1H, J = 2.00 Hz, C2 = 8.80 Hz, C9), 7.960 (d, 1H, J = 8.80 Hz, C6-C6'), 13C NMR (CDCl3, 100 MHz): δ 23.51, 32.07, 35.87, 75.72, 114.12, 118.45, 119.64, 120.61, 124.49, 127.66, 127.91, 128.08, 128.17, 128.64, 128.81, 129.76, 130.54, 130.90, 135.23, 137.56, 139.59, 139.77, 144.28, 158.84. Anal. Calcd for C20H14ClN2O: C, 73.24; H, 4.51; N, 8.54. Found: C, 73.30; H, 4.42; N, 8.69%.

2-Amino-10-chloro-4-(3',4'-diethoxyphenyl)-12-phenyl-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4e

Yellow solid. m.p.216-18°C. Yield 60%. IR (KBr): 3457, 3360, 2210 cm-1, 1H NMR (CDCl3 400 MHz): δ 1.32-1.49 (m, 6H, C4-C4', C5-OCH2CH3), 3.50 (s, 2H, C5-CH2), 3.51 (2H, C6-CH2), 3.94 (s, 1H, C2-H), 4.10-4.22 (m, 4H, C4-C4', C5-OCH2CH3), 5.02 (s, 2H, C2-NH2), 6.69-6.92 (m, 1H, C4-C4'-H), 6.29 (s, 1H, C5-C5'-H), 7.08 (d, 1H, J = 8.00 Hz, C6-C6'-H), 7.24-7.27 (m, 2H, C12-C12', C10-C10'), 7.53-7.59 (m, 4H, C12-C12', C10-C10', C10'-C10', C9-C9'), 7.72 (s, 1H, C11-H), 7.80 (d, 1H, J = 8.00 Hz, C10-H), 13C NMR (CDCl3, 100 MHz): δ 14.61, 25.42, 57.47, 64.44, 64.71, 114.12, 118.45, 119.64, 120.61, 124.49, 127.66, 127.91, 128.26, 128.35, 128.84, 129.77, 136.54, 139.95, 140.08, 144.52, 148.32, 158.39, 159.01. Anal. Calcd for C23H23ClN2O: C, 72.06; H, 5.13; N, 7.64. Found: C, 72.16; H, 5.05; N, 7.76%.

2-Amino-10-chloro-4,12-diphenyl-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4f

Yellow solid. m.p.206-208°C. Yield 66%. IR (KBr): 3471, 3361, 2219 cm-1, 1H NMR (CDCl3 400 MHz): δ 2.00-2.43 (m, 2H, C3-CH2), 2.91-3.13 (m, 2H, C5-CH2), 4.20 (s, 1H, C4-H), 4.94 (s, 2H, C2-NH2), 7.17-7.23 (m, 3H, C4-C4', C5-C5'-H), 7.27-7.30 (m, 2H, C2-C2', C3-C3'), 7.35-7.63 (m, 3H, C12-C12', C9-C9', C10-C10'), 7.54-7.63 (m, 3H, C12-C12', C9-C9', C10-C10'), 7.75 (dd, 1H, J = 2.40 Hz, J = 8.80 Hz, C7), 8.00 (d, 1H, J = 8.80 Hz, C8-H), 13C NMR (CDCl3, 100 MHz): δ 23.51, 32.07, 57.08, 115.57, 115.78, 118.07, 119.65, 120.68, 124.66, 127.84, 128.26, 128.35, 128.84, 129.77, 129.86, 130.72, 131.08, 137.65, 139.86, 140.22, 144.50, 158.32, 159.04, 160.32, 162.75. Anal. Calcd for C20H14ClN2O: C, 73.50; H, 4.36; N, 9.10. Found: C, 75.49; H, 4.29; N, 9.11%.

General procedure for the synthesis of 2-amino-10-chloro-4-aryl-12-phenyl-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4a-f

A mixture of 7-chloro-9-phenyl-3,4-dihydroacridin-1(2H)-one (1H, 0.001 mol), aromatic/ hetero aromatic aldehyde (2, 0.001 mol), malononitrile (0.001 mol), and 15 mol% DABCO (0.0015 mol) in dry ethanol (15 mL) was heated under reflux for 2 h. After completion of the reaction, the excess solvent was evaporated. The residue was poured in ice water and extracted with ethyl acetate. The combined organic layers were dried over anhydrous magnesium sulphate. It was then purified over a silica-gel chromatographic column (elucent: petroleum ether/ethyl acetate, 95:5). The pure product was purified by recrystallisation from ethyl acetate. These compounds are found to be identical with the compounds 4a-f obtained by two step process (m.m.p., co-TLC, super-imposable IR spectra).

2-Amino-10-chloro-12-phenyl-4-(thiophen-2'-yl)-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4a

Yellow solid. Yield 89%.

2-Amino-10-chloro-4-(4'-fluorophenyl)-12-phenyl-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4b

Yellow solid. Yield 85%.

2-Amino-10-chloro-12-phenyl-4-(4'-methylphenyl)-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4c

Yellow solid. Yield 86%.

2-Amino-10-chloro-4-(4'-methoxyphenyl)-12-phenyl-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4d

Yellow solid. Yield 87%.

2-Amino-10-chloro-4-(3',4'-diethoxyphenyl)-12-phenyl-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4e

Yellow solid. Yield 82%.
2-Amino-10-chloro-4,12-diphenyl-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4f

Yellow solid. Yield 87%.

**General procedure for the synthesis of 2-amino-10-chloro-4-(4'-methoxyphenyl)-12-phenyl-5,6-dihydro-4H-pyrano[2,3-a]acridin-3-carbonitrile, 4d**

A mixture of 7-chloro-9-phenyl-3,4-dihydroacridin-1(2H)-one (1, 0.001 mol), 2-(4'-methoxybenzylidene)malononitrile (5d, 0.001 mol), and 15 mol% DABCO (0.0015 mol) in dry ethanol (15 mL) was heated under reflux for 2 h. After completion of the reaction, the excess solvent was evaporated. The residue was poured in ice water and extracted with ethyl acetate. Combined organic layers were dried over anhydrous magnesium sulphate. It was then purified over a silica-gel chromatographic column (eluent: petroleum ether/ethyl acetate, 95:5). The pure product was purified by recrystallisation from ethyl acetate. This compound was found to be identical with the compound 4d obtained by two step process and MCR method.

**X-ray experimental details for 3f, 4b and 5b**

X-ray diffraction experiments on 3a, 3d and 4a were carried out on a Bruker AXS SMART APEX CCD diffractometer at 100 K using monochromatic Mo Kα radiation with the omega scan technique. The data was integrated and scaled using SAINT.
SADABS within the APEX2 software package by Bruker\textsuperscript{23}. Solution by direct methods [SHELXS, SIR97 (Ref 24)] produced a complete heavy atom phasing model consistent with the proposed structure. The structure was completed by difference Fourier synthesis with SHELXL97 (Ref 25). Scattering factors were from Waasmair and Kirfel\textsuperscript{26}, and all of the structures were refined against $F^2$ in SHELXL using ORTEP\textsuperscript{27}. Crystal structure and refinement data are given in Table III.

**Conclusion**

In conclusion, a systematic study on the synthesis and structural elucidation of 2-amino-10-chloro-4-aryl-5,6-dihydro-4H-pyran\textsubscript{2,3-a}acridine-3-carbonitrile has been presented. A mild and efficient method has been developed for the synthesis of pyrano\textsubscript{2,3-a}acridines via three-component reaction and two-step process of 7-chloro-9-phenyl-3,4-dihydroacridin-1(2H)-one with aromatic aldehydes and malononitrile using DABCO as a catalyst to afford 2-amino-10-chloro-4-aryl-5,6-dihydro-4H-pyran\textsubscript{2,3-a}acridine-3-carbonitrile. The features of this procedure are mild reaction conditions, good to high yield, and operational simplicity. Unlike the earlier reported methods, the multi-component reaction gave higher yields compared to the step wise synthesis. The present protocol does not require high temperature or drastic conditions.

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**Supplementary data**

Complete cif files for compounds 3\textsubscript{a}, 3\textsubscript{d} and 4\textsubscript{a} have been deposited with the Cambridge Crystallographic Data Centre as CCDC number 1009621, 984317 and 1019264 respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK. Fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk.

**References**


