



THE SYNTHESIS OF FUNCTIONALIZED ACRIDIONONES DERIVATIVES CATALYZED BY TBAB-CESIUM CARBONATE IN AQUEOUS PEG-600

Pavan R. Kale^{a, b} & Bhausaheb K. Magar^{b, *}

^a Department of Chemistry, Rajarshi Shahu Arts Commerce and Science College, Pathri, Tq. Phulambri, Dist. Chhatrapati Sambhajanagar, MS, India-431 111

^b Department of Chemistry, Shivaji Arts, Commerce and Science College, Kannad, Tq. Kannad, Dist. Chhatrapati Sambhajanagar, MS, India-431 103

Corresponding Author: magarb.2008@rediffmail.com

ABSTRACT:

The synthesis of a range of Functionalized Acridionones derivatives has been accomplished through a two-step reaction involving aromatic aldehydes, substituted aniline, and cyclic 1,3-dicarbonyl compounds. In the first step, synthesis of bis-hydroxy derivatives takes place, which are confirmed by using TLC as well as NMR and Mass spectroscopy. In second step, the synthesis of functionalized acridionones derivatives carried out using TBAB-Cesium carbonate in aqueous PEG-600 as a cost-effective and efficient catalyst. The reaction's progress was tracked using thin-layer chromatography (TLC), and the resulting products were examined using Fourier-transform infrared (FT-IR) spectroscopy, as well as ¹H and ¹³C nuclear magnetic resonance (NMR) and mass spectroscopy (MS).

KEYWORDS: Acridionones, TBAB, Cesium carbonate, PEG-600, cyclic 1,3-dicarbonyl compounds.

INTRODUCTION

Acridinediones are significant heterocyclic compounds known for their photochemical properties^{i,ii}, biological activities^{iii,iv}, and pharmacological effects^v. They are extensively utilized as anticancer agents^{vi,vii}, antibacterial substances^{viii}, DNA probes^{ix}, antitumor agents^x, among other applications. Consequently, numerous studies have focused on acridinedione derivatives^{xi-xiii}. Tetraketones serve as crucial precursors in the synthesis of various acridinediones. The first description of tetraketones was provided by Merling^{xiv} in 1894, during his groundbreaking work on synthesizing cyclohexane-1,3-dione from resorcinol. Since then, several reports have emerged aiming to achieve efficient synthesis of tetraketones^{xv-xviii}.

For first step, the synthesis of diketone was done by numerous researchers, using different solvent and different catalyst^{xix-xxiii}. But from diketone to formation of the acridionones has some limited work. Which was performed with the tetrabutylammonium bromide (TBAB) and Cs₂CO₃ in MeCN were used as a catalyst for the organic transformations^{xxiv}. Similar synthesis was done by various catalysts like 2-aminopyrazine^{xxv}, triethylbenzyl ammonium chloride in water^{xxvi}, γ -Fe₂O₃@Si-(CH₂)₃@mel@-(CH₂)₄SO₃H^{xxvii}, stannous chloride dehydrate^{xxviii}, TiO₂ NPs^{xxix}, NH₂SO₃H AND H₆P₂W₁₈O₆₂.18H₂O^{xxx}, Succinimide-N-sulfonic acid^{xxxi}, microwave

irradiation^{xxxii}, Iron(III) phosphate^{xxxiii}, [P₄VPH]C(NO₂)₃^{xxxiv}. However, a review of these reported method reveals persistent limitations, including extended reaction durations, undesirable side-product generation, the requirement for substantial quantities of catalysts (some of which are toxic or costly), and difficulties in catalyst recycling. This work, therefore, the TBAB-Cesium carbonate catalyst is environmentally friendly, easy separable, heterogeneous catalyst introduced for the synthesis of the Functionalized Acridionones. The continues our established efforts in applying heterogeneous solid catalysts to organic synthetic methodologies.

MATERIALS AND METHODS:

MATERIALS:

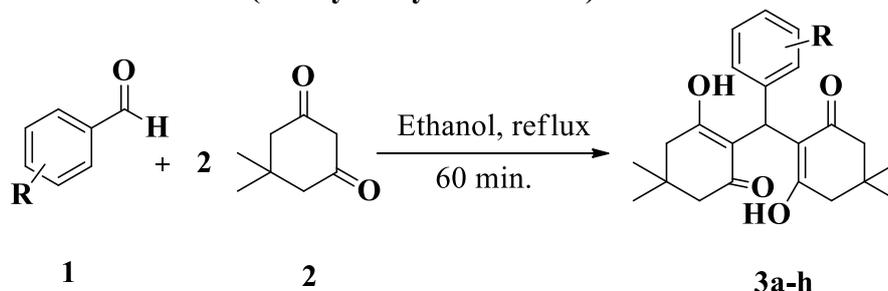
Aldehydes, amines, solvents, and required reagents were sourced from Merck Chemical Suppliers and SD-Fine. Thin-layer chromatography (TLC) was used to track the progress of all reactions, with UV light employed for detection and the yields mentioned pertain to the isolated products. Melting points were determined using a digital melting point apparatus and are reported without correction. Fourier transform infrared (FT-IR) spectra were obtained using a Shimadzu IR spectrophotometer. ¹H and ¹³C NMR spectra were recorded on a Bruker AVANCE III system at 400 MHz. The peak patterns were indicated as follows: s for singlet, d for doublet, t for triplet, m for multiplet, and q for quartet.

METHODS:

General chemical reaction for the preparation of Bis-hydroxy derivatives 3(a-h):

Before the synthesis of Functionalized Acridionones derivatives, we synthesized initially intermediate Michael adduct (Bis-hydroxy derivatives) 3(a-h).

Synthesis of Michael Adduct (Bis-hydroxy derivatives):



Scheme 1: Synthesis of Bis-hydroxy derivative intermediate

A 50 mL round bottom flask was charged with substituted benzaldehyde (1 equiv), 5,5-dimethylcyclohexane-1,3-dione (2 equiv) and in ethanol (10 mL). The reaction mixture was subjected to reflux for 60 min. The progress of reaction was monitored by TLC. After completion, the reaction mixture was quenched by ice cold water and filtered under vacuum. Purification was carried out using a silica gel (100-200 mesh) column and mixture of 0.5–1 % MeOH + CHCl₃ as eluent to obtain The obtained product was dried under vacuum to deliver Michael adduct product (3a-h) was obtained. The product formation was confirmed by standard melting point and characterization done using the FT-IR, ¹H, ¹³C NMR and Mass spectroscopic techniques. Spectroscopic characterizations of some selected synthesized Michael Adducts 3(a-h) were confirmed by using ¹H, ¹³C NMR and Mass as given below:

2,2'-(phenylmethylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-enone) (3a):

IR $\nu_{\max}/\text{cm}^{-1}$: 2989 (CH), 1591 (C=O), 1482 (C=C), 1359 (HCH). **¹H-NMR (400 MHz, CDCl₃):** δ (ppm) 11.97 (s, 1H, OH), 7.29-7.11 (s, 5H, H-Ar), 5.57 (s, 1H, CH), 2.50 - 2.30 (m, 8H, 4CH₂), 1.24 (s, 6H, 2CH₃), 1.10 (s, 6H, 2CH₃). **¹³C-NMR (100 MHz, CDCl₃):** δ (ppm) 190.42, 189.43, 138.11, 125.82, 115.55, 47.07, 46.43, 32.75, 31.43, 29.62, 27.44. **MS, *m/z*:** 369.30 [M]⁺.

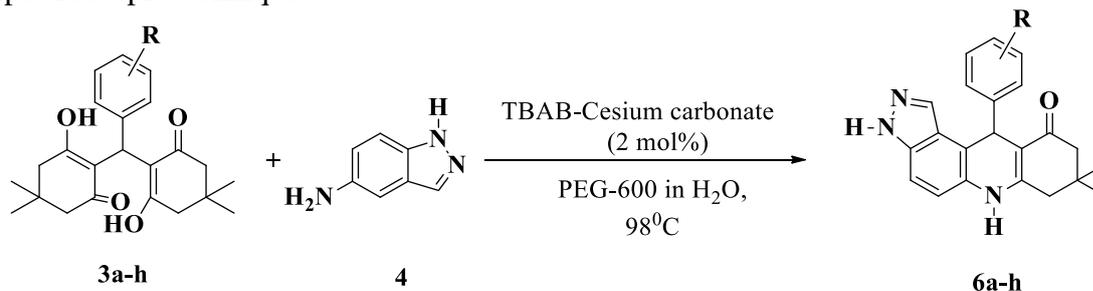
2,2'-((4-methoxyphenyl)methylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-enone) (3b):
 IR $\nu_{\max}/\text{cm}^{-1}$: 2978 (CH), 1583 (C=O), 1498 (C=C), 1370 (HCH). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ (ppm) 11.94 (s, 1H, OH), 7.00-6.79 (d, 4H, H-Ar), 5.49 (s, 1H, CH), 3.76 (s, 3H, OCH_3), 2.39 - 2.28 (m, 8H, 4 CH_2), 1.22 (s, 6H, 2 CH_3), 1.09 (s, 6H, 2 CH_3). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.35, 189.40, 157.58, 129.81, 127.77, 115.75, 113.63, 55.18, 46.41, 32.01, 31.38, 29.62, 27.38. MS, m/z : 421.30 $[\text{M}]^+$.

2,2'-((4-nitrophenyl)methylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-enone) (3c):
 IR $\nu_{\max}/\text{cm}^{-1}$: 2982 (CH), 1594 (C=O), 1485 (C=C), 1365 (HCH). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ (ppm) 11.78 (s, 1H, OH), 8.13-7.23 (d, 4H, H-Ar), 5.54 (s, 1H, CH), 2.46 - 2.30 (m, 8H, 4 CH_2), 1.23 (s, 6H, 2 CH_3), 1.11 (s, 6H, 2 CH_3). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.90, 189.55, 146.51, 146.09, 127.61, 123.48, 114.88, 46.97, 46.38, 33.24, 31.45, 29.49, 27.44. MS, m/z : 414.30 $[\text{M}]^+$.

After confirmation of the formation of the intermediate Michael Adducts **3(a-h)**; some selected intermediates were used further synthesis of derivatives of the functionalized Acridionones.

Procedure for the synthesis of Acridionones Derivatives using Bis-hydroxy derivatives 3(a-h) with 5-aminoindazole:

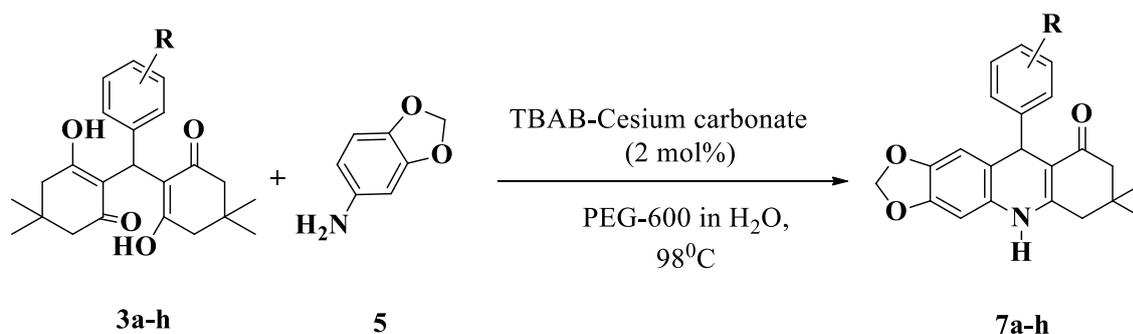
A 50 mL round bottom flask was charged with Bis-hydroxy derivatives **3(a-h)** (1 equiv), 5-aminoindazole (1 equiv) and TBAB-Cesium carbonate (2 mol%), in PEG (600) + H_2O mixture (2.7 mL/0.3 mL) and the mixture was stirred at 98°C for required time. The progress of reaction was monitored by TLC. After completion, the reaction mixture was concentrated at reduced pressure to afford crude product which was purified by column chromatography (EA/Hexanes:1/1) to obtain pure product. The product formation **6(a-h)** was confirmed by standard melting point and characterization done using the FT-IR, ^1H , ^{13}C NMR and Mass spectroscopic techniques.



Scheme 2: The synthesis of Acridionones Derivatives using Bis-hydroxy derivatives **3(a-h)** with 5-aminoindazole

Procedure for the synthesis of Acridionones Derivatives using Bis-hydroxy derivatives 3(a-h) with 3,4-(Methylenedioxy) aniline:

A 50 mL round bottom flask was charged with Bis-hydroxy derivatives **3(a-h)** (0.3 g, 1 equiv), 3,4-(methylenedioxy)aniline (0.18 g, 2 equiv) and TBAB-Cesium carbonate (2 mol%), in PEG-600 in H_2O mixture (2.7 mL/0.3 mL) and the mixture was stirred at 98°C for 15 hr. The progress of reaction was monitored by TLC. After completion, the reaction mixture was concentrated at reduced pressure to afford crude product which was purified by column chromatography (EA/Hexanes:1/1) to obtain pure product.



Scheme 3: The synthesis of Acridionones Derivatives using Bis-hydroxy derivatives 3(a-h) with 3,4-(methylenedioxy)aniline

Spectroscopic characterizations of some selected synthesized Acridionones Derivatives were confirmed by using ^1H , ^{13}C NMR and Mass as given below:

8,8-dimethyl-11-phenyl-3,6,7,8,9,11-hexahydro-10H-pyrazolo[4,3-a]acridin-10-one (6a):

IR $\nu_{\text{max}}/\text{cm}^{-1}$: = 3255.43, 3080.50, 2953.64, 2868.51, 1685.38, 1599.31, 1380.33, 1229.57, 800.30, 695.80 cm^{-1} , **$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ (ppm)** 9.45 (s, 1H, NH), 8.21 (s, 1H, NH), 7.31–7.06 (m, 8H, Ar-H), 5.46 (s, 1H, CH), 2.08–1.96 (dd, 4H, CH_2), 1.05–0.91 (s, 6H, CH_3), **$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ (ppm)** 192.3, 151.7, 148.1, 137.4, 128.9, 127.4, 122.1, 116.2, 109.3, 105.1, 50.3, 32.4, 29.1, 27.1 ppm. **MS, m/z :** 344.2 $[\text{M}]^+$.

11-(4-methoxyphenyl)-8,8-dimethyl-3,6,7,8,9,11-hexahydro-10H-pyrazolo[4,3-a]acridin-10-one (6b):

IR $\nu_{\text{max}}/\text{cm}^{-1}$: = 3240.48, 3128.05, 2954.08, 2922.09, 1688.78, 1581.06, 1383.96, 1243.73, 1031.23, 830.91, 700.05 cm^{-1} , **$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ (ppm)** 9.42 (s, 1H, NH), 7.98 (s, 1H, NH), 7.19–6.66 (m, 7H, Ar-H), 5.38 (s, 1H, CH), 3.60 (s, 3H, OCH_3), 2.40–1.94 (dd, 4H, CH_2), 1.07–0.92 (s, 6H, CH_3), **$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ (ppm)** 193.4, 157.9, 151.1, 137.3, 128.2, 127.4, 122.9, 117.4, 115.7, 113.9, 109.9, 106.1, 55.8, 50.6, 37.1, 32.3, 29.2, 27.5 ppm. **MS, m/z :** 374.3 $[\text{M}]^+$.

11-(4-Nitrophenyl)-8,8-dimethyl-3,6,7,8,9,11-hexahydro-10H-pyrazolo[4,3-a]acridin-10-one (6c):

IR $\nu_{\text{max}}/\text{cm}^{-1}$: = 3212.86, 3033.7, 2913.96, 2850.92, 1648.00, 1582.52, 1330.10, 1228.00, 914.82, 724.91 cm^{-1} , **$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ (ppm)** 9.44 (s, 1H, NH), 8.72 (s, 1H, NH), 8.24–7.27 (m, 7H, Ar-H), 5.93 (s, 1H, CH), 2.61–2.13 (dd, 4H, CH_2), 1.45–1.02 (s, 6H, CH_3), **$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ (ppm)** 192.4, 156.3, 152.0, 149.7, 137.5, 129.6, 125.6, 122.0, 117.3, 113.5, 109.9, 104.7, 50.6, 32.6, 29.7, 27.3 ppm. **MS, m/z :** 389.1 $[\text{M}]^+$.

10-(4-phenyl)-7,7-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-b]acridin-9(6H)-one (7a):

IR $\nu_{\text{max}}/\text{cm}^{-1}$: = 3279.82, 3070.53, 2934.43, 2885.39, 1720.75, 1643.17, 1601.17, 1257.06, 1034.74, 914.99, 699.13 cm^{-1} , **$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ (ppm)** 9.28 (s, 1H, NH), 7.02–6.49 (m, 7H, Ar-H), 5.79–5.85 (s, 2H, CH_2), 4.93 (s, 1H, CH), 2.49–1.92 (dd, 4H, CH_2), 0.99–0.90 (s, 6H, CH_3), **$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ (ppm)** 193.74, 152.41, 149.17, 143.49, 130.54, 128.38, 126.00, 118.76, 109.12, 105.74, 101.20, 96.99, 50.45, 32.34, 29.35, 26.85 ppm. **MS, m/z :** 348.3 $[\text{M}]^+$.

10-(4-methoxyphenyl)-7,7-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-b]acridin-9(6H)-one (7b):

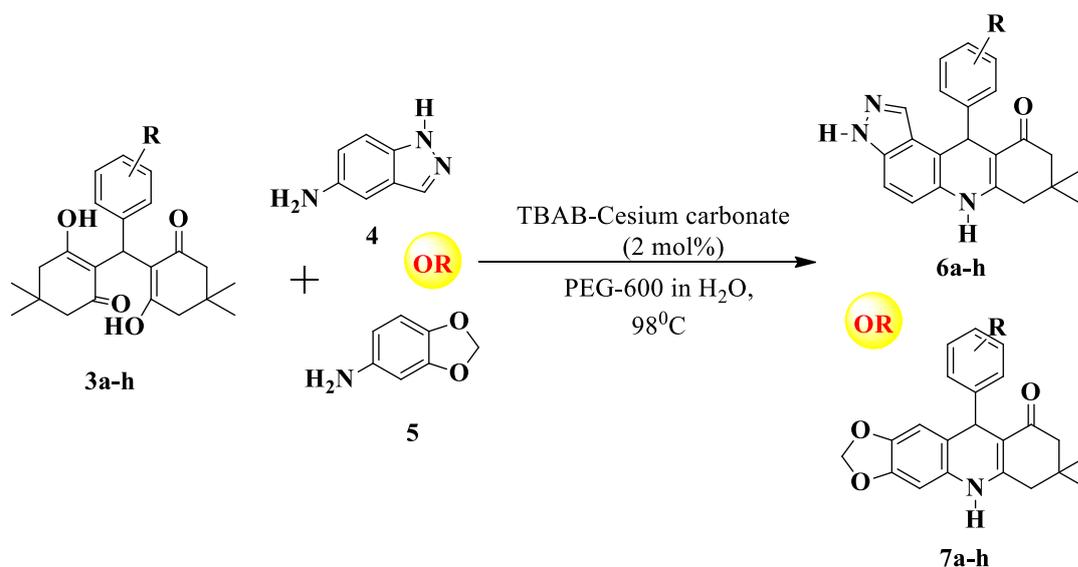
IR $\nu_{\text{max}}/\text{cm}^{-1}$: = 3241.29, 2998.92, 2947.48, 2883.44, 1722.19, 1642.55, 1591.98, 1237.06, 1035.75, 930.80, 834.98 cm^{-1} , **$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ (ppm)** 8.67 (s, 1H, NH), 7.33–

6.75 (m, 6H, Ar-H), 6.07 (s, 2H, CH₂), 3.89 (s, 1H, CH), 3.18 (s, 3H, OCH₃), 2.51–1.21 (dd, 4H, CH₂), 1.13-0.85 (s, 6H, CH₃), ¹³C-NMR (100 MHz, CDCl₃): δ (ppm) 193.98, 163.48, 157.33, 141.01, 133.14, 125.73, 111.20, 106.26, 99.87, 55.25, 50.71, 37.51, 32.50, 29.69, 27.03 ppm. MS, m/z: 376.2 [M]⁺.

10-(4-nitrophenyl)-7,7-dimethyl-6,7,8,10-tetrahydro-[1,3]dioxolo[4,5-b]acridin-9(5H)-one (7a):

IR ν_{max}/cm⁻¹: = 3270.02, 3099.26, 2958.21, 2887.33, 1718.54, 1605.80, 1476.08, 1238.56, 1038.35, 935.70, 743.88 cm⁻¹, ¹H-NMR (400 MHz, CDCl₃): δ (ppm) 9.47 (s, 1H, NH), 8.07–6.52 (m, 6H, Ar-H), 5.91-5.82 (s, 2H, CH₂), 5.13 (s, 1H, CH), 2.45–1.87 (dd, 4H, CH₂), 1.06-0.85 (s, 6H, CH₃), ¹³C-NMR (100 MHz, CDCl₃): δ (ppm) 193.6, 158.5, 152.6, 147.0, 130.3, 128.7, 123.1, 117.2, 109.4, 104.4, 101.4, 97.36, 50.51, 32.51, 31.13, 29.52, 27.17 ppm. MS, m/z: 393.3 [M]⁺.

RESULTS AND DISCUSSION:



Scheme 4: Synthesis of the functionalized Acridionones using (4) 5-aminoindazole and (5) 3,4-(Methylenedioxy)aniline

Initially, in the first step of the synthesis of the Bis-hydroxy derivatives, various substituted benzaldehyde reacts with the two moles of dimedone molecule. In this reaction, electron withdrawing as well as electron donating substituted benzaldehydes were utilized in this reaction. Reaction performed in aqueous ethanol for reflux condition at various time intervals (Scheme 4). From the given results we found that, electron donation substituted bis-hydroxy derivatives yields excellent product (3a, 3b, 3d, and 3f) whereas electron withdrawing substituted bis-hydroxy derivatives got much better product yield (3c, 3e, and 3g) (Figure 1).

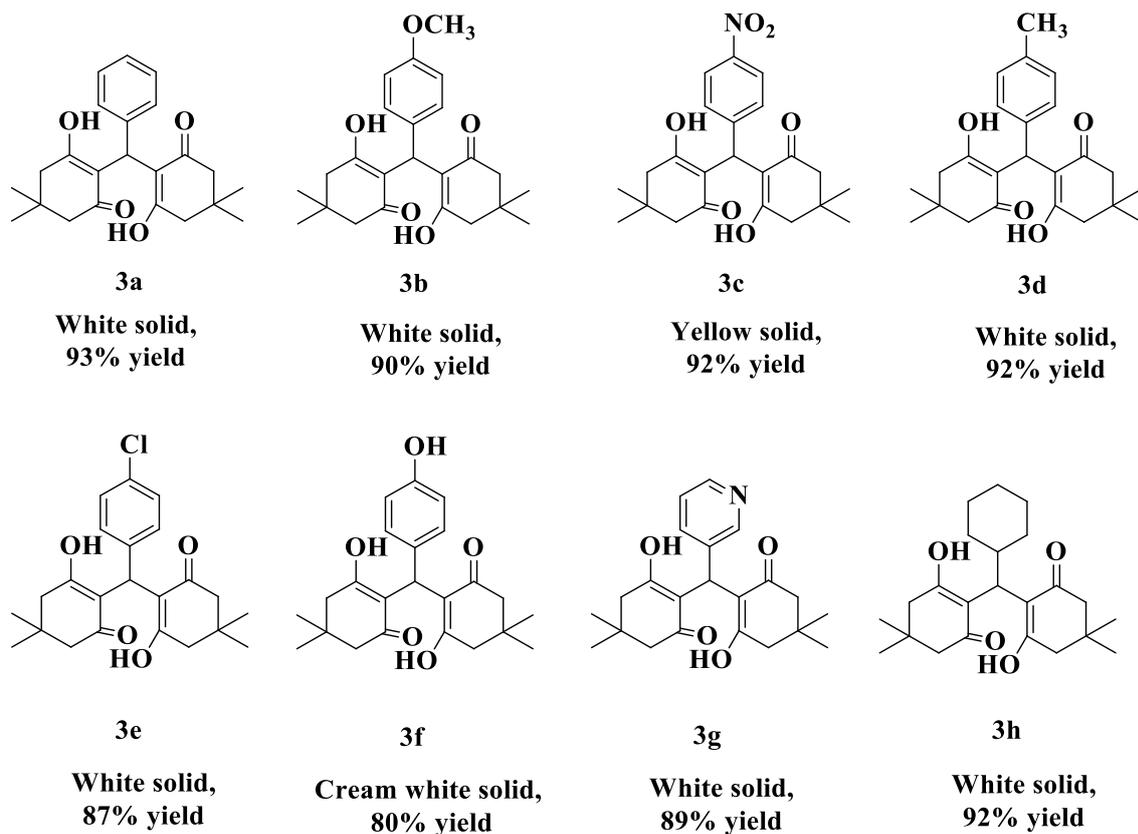
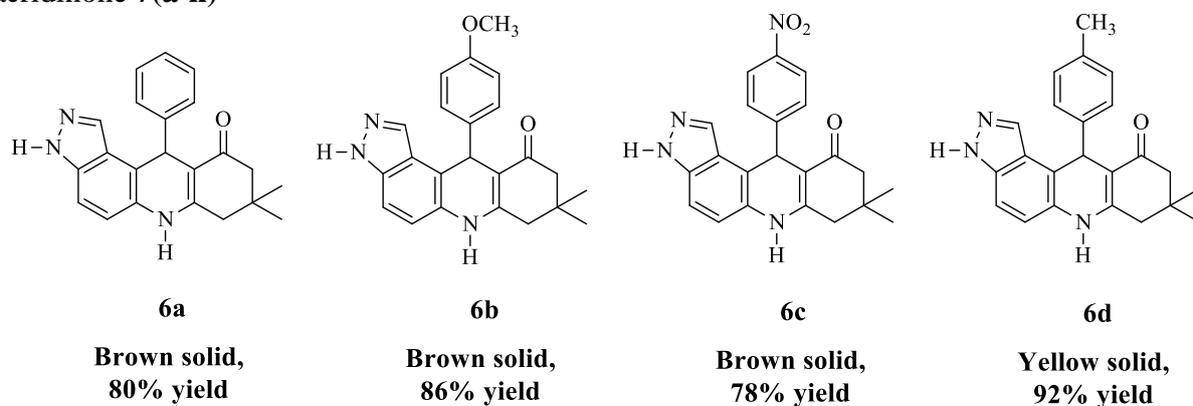


Figure 1: Derivatives of intermediate Michael adduct (bis-hydroxy derivatives)

After the completion of the formation of bis-hydroxy derivatives, from these derivatives were used for further synthesis of functionalized acridinone derivatives. In the synthesis of acridinones derivatives, bis-hydroxy derivatives **3(a-h)** reacts with 5-aminoindazole **4** and then 3,4-(methylenedioxy)aniline **5** at 98°C temperature and environmentally friendly catalyst TBAB-Cesium carbonate (2 mol%), in PEG-600 + H₂O mixture (2.7 mL/0.3 mL) and stirred this mixture for specific time intervals and finally found the given results below. In **figure 2** shows the products of functionalized acridinone **6(a-h)** and **figure 3** shows, derivatives of acridinone **7(a-h)**



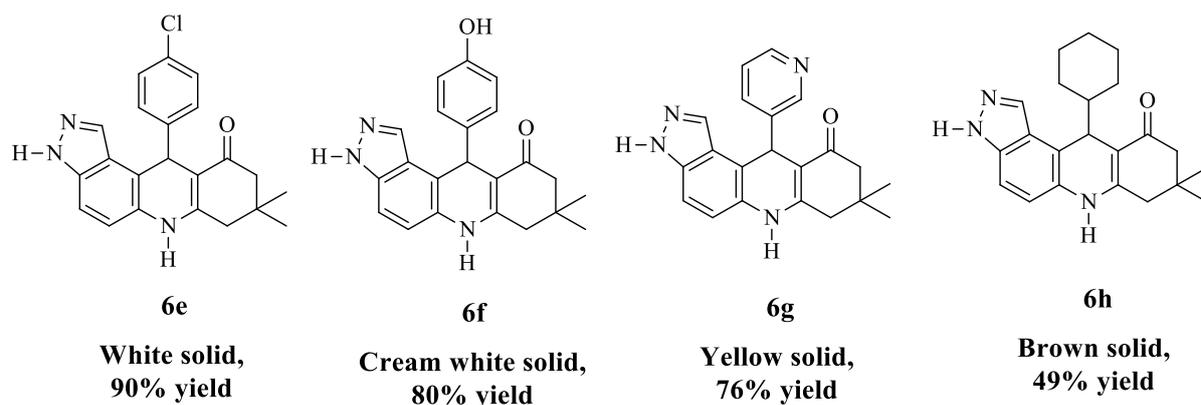


Figure 2: The Acridionones Derivatives using Bis-hydroxy derivatives with 5-aminoindazole

When Bis-hydroxy derivatives of cyclohexanone reacts with the 5-aminoindazole in presence of the TBAB-Cesium carbonate (2 mol%), in aqueous PEG-600, this results the lower yield as compare to other substituted derivatives **6h**, whereas other got excellent results (**Figure 2**).

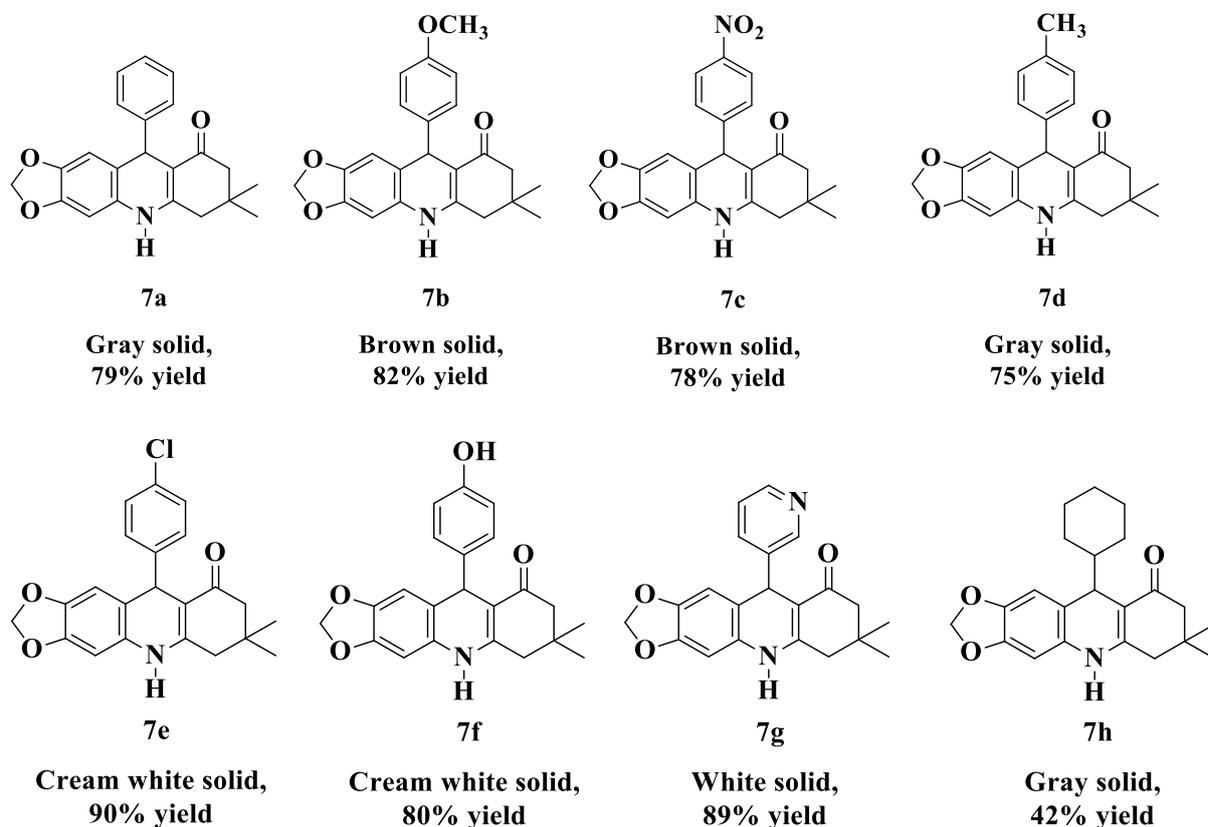


Figure 3: The Acridionones Derivatives using Bis-hydroxy derivatives with 3,4-(methylenedioxy)aniline

Similarly, When Bis-hydroxy derivatives of cyclohexanone reacts with the 3,4-(methylenedioxy) aniline in presence of the TBAB-Cesium carbonate (2 mol%), in aqueous PEG-600, this results the much lower yield 42% as compared to other substituted derivatives **7h**, whereas other got excellent results (**Figure 3**). From the overall results found that all the electron withdrawing as well as electron donating substituents of the bis-hydroxy derivatives

gives excellent yield of product except product **6h** and **7h**. From this we can say that the TBAB-Cesium carbonate (2 mol%), in aqueous PEG-600 catalyst gives excellent product of yield at 98°C for given time. This catalyst is a cheap, easily removable, environmentally friendly catalyst for this reaction.

CONCLUSION

We synthesized functionalized acridinone derivatives in two step reaction. This reaction was performed in presence of TBAB-Cesium carbonate (2 mol%), in aqueous PEG-600 environmentally friendly catalyst at 98°C temperature condition. This gives excellent product yield of acridinone derivatives. from this novelty of this reaction was maintained by this new catalyst. Some of the derivatives of acridinone was confirmed by their standard melting points, FT-IR, ¹H and ¹³C nuclear magnetic resonance (NMR) and mass spectroscopy (MS) characterization techniques.

ACKNOWLEDGEMENT:

Author is thankful to the Principal and the Department of Chemistry of Shivaji Arts, Commerce and Science college, Kannad for providing infrastructure facility.

CONFLICTS OF INTEREST

Authors has no any conflicts of interest about this research work.

REFERENCES:

- [i]. Ashokkumar, P.; Ramakrishnan, V. T.; Ramamurthy, P. Specific Ca²⁺ Fluorescent Sensor: Signaling by Conformationally Induced PET Suppression in a Bichromophoric Acridinedione. *Eur. J. Org. Chem.* **2009**, 2009, 5941–5947.
- [ii]. Velu, R.; Malar, E. J. P.; Ramakrishnan, V. T.; Ramamurthy, P. Acridinedione-Functionalized Gold Nanoparticles and Model for the Binding of 1,3-Dithiol-Linked Acridinedione on Gold Clusters. *Tetrahedron Lett.* **2010**, 51, 5680–5685.
- [iii]. Cuenca, F.; Moore, M. J. B.; Johnson, K.; Guyenne, S.; De Cian, A.; Neidle, S. Design, Synthesis, and Evaluation of 4,5-Disubstituted Acridone Ligands with High G-Quadruplex Affinity and Selectivity Together with Low Toxicity to Normal Cells. *Bioorg. Med. Chem. Lett.* **2009**, 19, 5109–5113.
- [iv]. Opegard, L. M.; Ougolkov, A. V.; Luchini, D. N.; Schoon, R. A.; Goodell, J. R.; Kaur, H.; Billadeau, D. D.; Ferguson, D. M.; Hiasa, H. Novel Acridine-Based Compounds That Exhibit Anti-Pancreatic Cancer Activity Are Catalytic Inhibitors of Human Topoisomerase II. *Eur. J. Pharmacol.* **2009**, 602, 223–229.
- [v]. Putic, A.; Stecher, L.; Prinz, H.; Müller, K. Structure–Activity Relationship Studies of Acridones as Potential Antipsoriatic Agents. 1. Synthesis and Antiproliferative Activity of Simple N-Unsubstituted 10H-Acridin-9-ones against Human Keratinocyte Growth. *Eur. J. Med. Chem.* **2010**, 45, 3299–3310.
- [vi]. Gopinath, V. S.; Thimmaiah, P.; Thimmaiah, K. N. Acridones Circumvent P-Glycoprotein-Associated Multidrug Resistance (MDR) in Cancer Cells. *Bioorg. Med. Chem.* **2008**, 16, 474–487.
- [vii]. Boumendjel, A.; Macalou, S.; Ahmed-Belkacem, A.; Blanc, M.; Di Pietro, A. Acridone Derivatives: Design, Synthesis, and Inhibition of Breast Cancer Resistance Protein ABCG2. *Bioorg. Med. Chem.* **2007**, 15, 2892–2897.
- [viii]. Singh, P.; Kaur, J.; Yadav, B.; Komath, S. S. Design, Synthesis, and Evaluation of Acridone Derivatives Using *Candida albicans*: Identification of an Anti-Candidiasis Agent. *Bioorg. Med. Chem.* **2009**, 17, 3973–3979.
- [ix]. Qiu, B.; Guo, L.; Chen, Z.; Chi, Y.; Zhang, L.; Chen, G. Synthesis of N-(4-Butylamino)acridone and Its Use as a Fluorescent Probe for ctDNA. *Biosens. Bioelectron.* **2009**, 24, 1281–1285.

- [x]. Belmont, P.; Bosson, J.; Godet, T.; Tiano, M. Acridine and Acridone Derivatives: Anticancer Properties and Synthetic Methods—Where Are We Now? *Anti-Cancer Agents Med. Chem.* **2007**, *7*, 139–169.
- [xi]. Zang, H.; Zhang, Y.; Zang, Y.; Cheng, B.-W. An Efficient Ultrasound-Promoted Method for the One-Pot Synthesis of Tetrahydrobenzo[*c*]acridin-8(9H)-one Derivatives. *Ultrason. Sonochem.* **2010**, *17*, 495–499.
- [xii]. Xia, J.-J.; Zhang, K.-H. Synthesis of N-Substituted Acridinediones and Polyhydroquinoline Derivatives in Refluxing Water. *Molecules* **2012**, *17*, 5339–5345.
- [xiii]. Crawford, L. A.; McNab, H.; Mount, A. R.; Verhille, J.; Wharton, S. I. Synthesis of Azapyrrolo[3,2,1-*jk*]carbazoles, Azaindolo[3,2,1-*jk*]carbazoles, and Carbazole-1-carbonitriles by Gas-Phase Cyclization of Aryl Radicals. *Synthesis* **2010**, *2010*, 923–928.
- [xiv]. Wang, F.; Zhou, L.; Li, J.; Bao, D.; Chen, L. Synthesis, Structure, and Biological Activities of 10-Substituted Tetramethyl Hexahydroacridinedione Derivatives. *J. Heterocycl. Chem.* **2017**, *54*, 3120–3125.
- [xv]. Murugan, P.; Hwang, K. C.; Thirumalai, D.; Ramakrishnan, V. T. Facile and Simple Route to the Synthesis of Condensed Acridine Systems. *Synth. Commun.* **2005**, *35*, 1781–1788.
- [xvi]. Kozlov, N. G.; Gusak, K. N. Condensation of Fluorosubstituted Benzaldehydes with Amines and Cyclic 1,3-Diketones. *Russ. J. Org. Chem.* **2006**, *42*, 1668–1674.
- [xvii]. Kozlov, N. G.; Gusak, K. N.; Tkachev, A. V. Three-Component Condensation of 6-Quinolylamine with Aromatic Aldehydes and Cyclohexyl 1,3-Diketones. *Chem. Heterocycl. Compd.* **2007**, *43*, 740–747.
- [xviii]. Karimian, R.; Piri, F.; Karimi, B.; Moghimi, A. Silica Chloride Nanoparticle-Catalyzed Synthesis of Arylmethylene Bis(5,5-dimethylcyclohexane-1,3-dione) Derivatives. *Croat. Chem. Acta* **2011**, *84*, 111–115.
- [xix]. Li, J.-T.; Li, Y.-W.; Song, Y.-L.; Chen, G.-F. Improved Synthesis of Arylmethylene Bis(3-hydroxy-5,5-dimethylcyclohex-2-en-1-one) Derivatives Catalyzed by Urea under Ultrasound. *Ultrason. Sonochem.* **2012**, *19*, 1–4.
- [xx]. Banerjee, B.; Brahmachari, G. Ammonium Chloride-Catalyzed One-Pot Multicomponent Synthesis of Xanthenes and Acridines under Solvent-Free Conditions. *J. Chem. Res.* **2014**, *38*, 745–750.
- [xxi]. Navarro, C. A.; Sierra, C. A.; Ochoa-Puentes, C. Evaluation of Sodium Acetate Trihydrate–Urea DES as a Benign Reaction Medium for the Biginelli Reaction. *RSC Adv.* **2016**, *6*, 65355–65365.
- [xxii]. Ashtarian, J.; Heydari, R.; Maghsoodlou, M. T.; Yazdani-Elah-Abadi, A. Brønsted Acidic Ionic Liquid-Catalyzed Synthesis of Xanthene and Bis-enone Derivatives under Eco-Friendly Conditions. *Iran. J. Sci. Technol., Trans. A* **2020**, *44*, 51–64.
- [xxiii]. Niasar, F. N.; Moradian, M. Synthesis of Xanthene and Acridine Derivatives Using Metal Ion-Exchanged NaY Zeolite as a Heterogeneous Catalyst. *RSC Adv.* **2024**, *14*, 10322–10330.
- [xxiv]. Khalafi-Nezhad, A.; Zare, A.; Parhami, A.; Soltani Rad, M. N. Practical Synthesis of Novel Unsymmetrical 1,3-Dialkylpyrimidine Derivatives at Room Temperature. *Arkivoc* **2006**, *2006*, 161–172.

- [xxv]. Thakur, D.; Kaur, M.; Malhi, D. S.; Garg, S.; Sharma, A.; Sohal, H. S. Atom-Economical Synthesis and Antioxidant Activity of Arylmethylene Bis-enone Crystals. *Monatsh. Chem.* **2021**, *152*, 537–543.
- [xxvi]. Road, T. B.; Area, I. Synthesis of Benzo[c]acridine Derivatives via N-Arylidene-naphthalen-1-amine Reactions. *Asian J. Chem.* **2008**, *20*, 4678–4684.
- [xxvii]. Karimirad, F.; Behbahani, F. K. Magnetically Retrievable Nanocatalyst for Green Synthesis of Benzo[c]acridin-8(9H)-ones and 2-Amino-4H-chromenes. *Inorg. Nano-Met. Chem.* **2020**, *51*, 656–666.
- [xxviii]. Zang, H.; Zhang, Y.; Mo, Y.; Cheng, B. Ultrasound-Promoted One-Pot Synthesis of Tetrahydrobenzo[c]acridin-8(9H)-one Derivatives. *Synth. Commun.* **2011**, *41*, 3207–3214.
- [xxix]. Abdolmohammadi, S.; Mohammadnejad, M. TiO₂ Nanoparticles as an Efficient Catalyst for the One-Pot Preparation of Tetrahydrobenzo[c]acridines in Aqueous Media. *Z. Naturforsch., B* **2013**, *68*, 362–366.
- [xxx]. Heravi, M. M.; Alinejhad, H.; Derikvand, F.; Oskooie, H. A.; Baghernejad, B.; Bamoharram, F. F. Sulfamic Acid and Heteropolyacid-Catalyzed One-Pot Synthesis of Benzo[c]acridine Derivatives. *Synth. Commun.* **2012**, *42*, 2033–2039.
- [xxxii]. Ghashang, M.; Mansoor, S. S.; Aswin, K. Succinimide-N-sulfonic Acid as an Efficient and Recyclable Catalyst for the Synthesis of Tetrahydrobenzo[c]acridinones. *J. Saudi Chem. Soc.* **2017**, *21*, S44–S51.
- [xxxiii]. Tu, S.; Jia, R.; Jiang, B.; Zhang, Y.; Zhang, J. Efficient Microwave-Assisted One-Pot Synthesis of Polyhydrobenzoacridine-1-one Derivatives without Catalyst. *J. Heterocycl. Chem.* **2006**, *43*, 1621–1627.
- [xxxiiii]. Behbahani, F. K.; Farahani, M. Iron(III) Phosphate-Catalyzed Synthesis of Tetrahydrobenzo[c]acridin-8(9H)-ones. *Synth. Commun.* **2015**, *45*, 151–153.
- [xxxv]. Nasirmahale, L. N.; Shirini, F. Synthesis of Benzo[c]acridine Derivatives Using Poly(4-vinylpyridinium) Trinitromethanide as an Efficient Catalyst. *Chem. Pap.* **2024**, *78*, 6617–6625.

Received on August 5, 2025.