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ARTICLE TYPE

First single step incorporation of carboxylic acid groups in the lower rim of calix[4]arenes: a new recyclable catalyst towards assembly of diverse five ring fused acridines

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This is the first report of an efficient protocol of incorporation of the –COOH moiety in a single step at the lower rim of calixarene to produce a new calix[4]arene grafted tricarboxylic acid, calix 4a. Generation of this catalyst was confirmed by NMR and HRMS analyses. The efficacy of this compound as an organocatalyst was successfully extended towards the synthesis of an assembly of new diversely substituted five ring fused acridine derivatives.

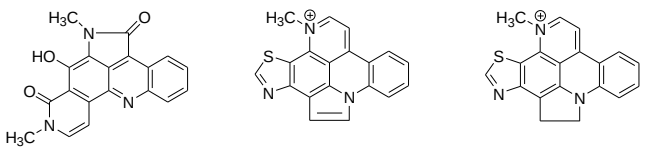
Introduction:

A catalyst lies at the heart of enormous organic reactions as it plays a crucial role to enforce the syntheses of many complex organic compounds.[1] In the recent decade, applicability of a catalyst has been judged from the point of recyclability along with its efficiency to reduce the environmental effect of catalytic chemical technology. If we try to focus on the greenness of an acid catalyst, avoiding usual organic (like acetic acid, butyric acid etc.) and inorganic (like H_2SO_4, HCl etc.) acids, solid supported or supramolecule supported acids get more impact.[2] Solid supported heterogeneous catalysts are of considerable interest in recent years, but in contrast to recyclable behaviour, low solubility is a drawback for many organic reactions. Thus, in recent times, the significance of macromolecular homogeneous organocatalysts has increased rapidly in synthetic organic chemistry.[3]

Calixarene grafted catalysts offer us the opportunity to improve the green aspect of many reactions.[4] Alignment of lipophilic and lipophobic groups establish them as highly efficient supramolecular organocatalysts in various organic protocols in gripping organic as well as aqueous mediums.[4] Their notable stability towards many organic and inorganic substances enable them to show reusable catalytic activities. In addition, their stability towards moisture and air keep them away from inconvenient air perceptive techniques. Considering these enormous perspectives, functionalized calixarenes have been widely used as organocatalysts for many organic syntheses since the last decade.[4] Strategic introduction of acid-functional substituents at upper and lower rim of calixarene core is very important, though the preparations of these are still a great challenge for their multi-step tedious synthetic procedure.

Previously reported upper rim substitution procedure contained at least three steps, (i) removal of tertiary-butyl group, (ii) protection of phenolic –OH group, and (iii) insertion of carbonyl or carboxyl group in order to incorporate acid functionality.[5] On the other hand, all the reported examples of acid group incorporation to the lower rim engaged protocols operating via protection-deprotection steps.[6] So, all those steps resulted in lowering of the reaction efficiency. Having secured a facile one step route to functionalize the lower rim with acid group, we tried to focus on the controlling factors of direct substitution of haloalkanes in the phenolic-OH group. It is our belief that an increased organization of those factors will assist in the rational extension of known methodology to allow incorporation of unprotected –COOH group in a single step. Interestingly, modification to temperature dependency and slow addition technology brought us success to gain 90% yield of acid substituted calixarene via a remarkably simple single step protocol using sodium hydride in DMF.

Now, utilizing the catalytic activity of the newly generated calixarene acid derivative, we thought to design a new method to synthesize a new biologically important polynuclear heterocyclic core. Polycyclic heteroaromatic alkaloids with 16-18 pi-electron containing cores are of great importance due to their various biological activities.[7] Multi-ring fused acridine systems are such type of alkaloids with high inhibition power to tumoral, fungal and bacterial activities.[8] Alpkinidines (**1**), cyclodercitine (**2**, **3**) etc. are marine sponge derived alkaloids having significant effect regarding DNA intercalation and Topoisomerase I and II inhibition.[8,9]



1 **2** **3**

Figure 1

For instance, as illustrated in Figure 1, several alkaloids having

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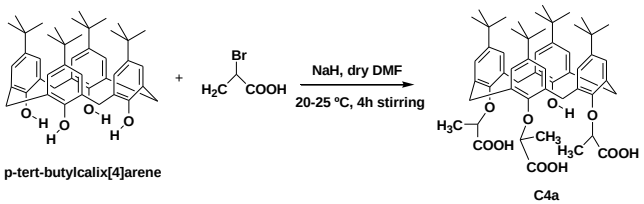
ring fused acridine skeletons were reported to exhibit different biological activities with therapeutic potential depending on the substitution patterns of the core structure. Only a single step towards this synthesis has been reported in literature.[10] Therefore, development of new strategy to install diverse functional groups at different positions of this core is still needed to extend versatility of this scaffold in various medicinal applications. In order to access a range of newly functionalized cores, we tried to push calixarene chemistry to the forefront of the synthesis of that core in a one pot atom economic multi-component fashion. In this context, our continuous effort enlightened an easy proficient protocol to produce a new series of five ring fused acridine derivatives with a variety of substitutions in excellent yields via reaction of equimolar (1 mmol of each) isatin, 5,5-dimethyl-1,3-cyclohexanedione, aromatic or aliphatic amines with a slight excess (1.2 mmol) of acetylene dicarboxylate ester in presence of catalytic amount (10 mol%) catalyst calixarene **C4a** in dimethylformamide solvent. The synthetic route is convergent and permits uncomplicated residency of substituent around the core.

Result and Discussion:

At the onset, we enlisted the bases that catalysed the o-alkylation of calixarene to synthesize calixarene **C4a**. We investigated with the usual weak bases K_2CO_3, Cs_2CO_3, etc. in high efficient solvents (pyridine, DMF etc.) that resulted in poor yield (upto 25%) at room temperature (25-30 ºC) rather than at 80-100 ºC. Also, the Arrhenius bases [NaOH, KOH, $Ba(OH)_2$, etc.] were ineffective to synthesize the desired acid substituted calixarene.



Scheme 1: Single step synthesis of **C4a**

This goal was achieved by stirring of p-tert-butylcalix[4]arene (0.3 mmol) with 2-bromopropionic acid (3.33 mmol) in presence of NaH (5 mmol) in 5 ml dry DMF (Scheme 1). The temperature dependency of this methodology was shown in Table 1. Any increase or decrease in reaction temperature from 20-25 ºC notably hampered the reaction. So, the ideal reaction was achieved at 20-25 ºC with a slow addition of the starting acid.

The crude product was taken for NMR after completion of 4 h of the reaction followed by quenching and washing with water. As the excess unreacted 2-bomopropionic acid washed out with water, we got only the three O-substituted acid **C4a** with a little bit of impurity as the crude product. This implies that, under this condition, the substitution selectivity was very high as no other mono, di or tetra O-alkylated product were formed with tri O-alkylated **C4a**. This was confirmed from comparison of crude NMR for formation of **C4a** with the pure product presented in Figure 2. The crude NMR also signifies nonexistence of any unreacted *p-tert*-butylcalix[4]arene after 4 h in reaction mixture as the peak of –OH of the starting *p-tert*-butylcalix[4]arene is totally absent in the crude NMR, i.e., 100% conversion occurred. One more vital evidence in support of 100% conversion was reflected from the HRMS data of the same crude product obtained from the reaction between *p-tert*-butylcalix[4]arene and 2-bromopropionic acid (Figure 4). No trace of peak around m/z=648.4179 convincingly proved the absence of the starting material *p-tert*-butylcalix[4]arene. Additionally generation of only the tri O-alkylated **C4a** can be confirmed from this spectrum. The single configuration of the calixarene **C4a** was further confirmed by taking ^{1}H-NMR of the pure **C4a** and secondly **C4a** with little amount of fixatives (NaI and CD_3CN) (Figure 3).[11] Interestingly addition of 0.005 mmol (0.75 mg) NaI and 0.04 ml CD_3CN to 0.5 ml 10 mM of **C4a** in $CDCl_3$ we got a simplified spectrum. For **C4a**, peak of tertiary butyl group (peak d, Figure 3) produces a multiplet signal which simplifies after addition of the fixatives. So, here fixation of only one i.e., cone conformer occurs in $CDCl_3$ solution confirming the presence of the only one single isomer of **C4a**. The structure of the **C4a** was established from ^{1}H-NMR, ^{13}C-NMR and HRMS.

Subsequently, to confirm the number of O-substitution, reactions of different ω-bromoalkylacids such as bromoacetic acid and 5-bromovaleric acid with *p-tert*-butylcalix[4]arene were performed (Scheme 2). In case of bromoacetic acid we got the tetra O-substituted product **C4b** as the only product. Any mono, di or tri

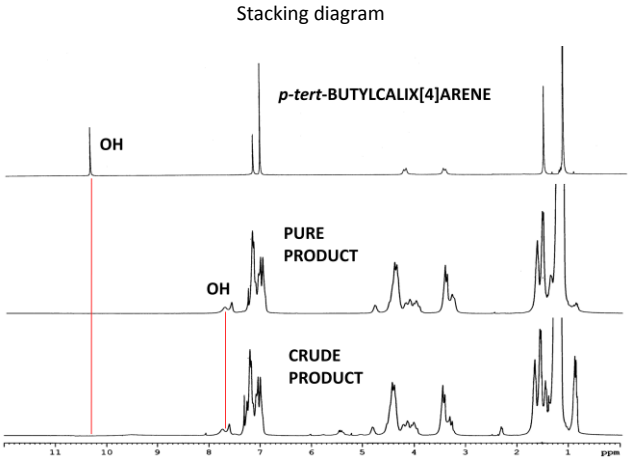


Figure 2: Study of conversion of *p-tert*-butylcalix[4]arene to **C4a**

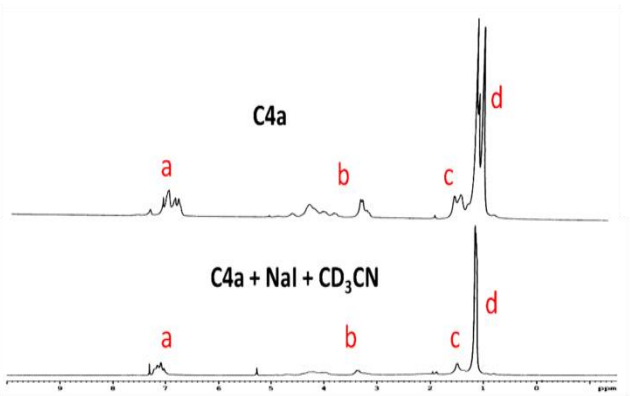


Figure 3: Study of conversion of calix[4]arene to **C4a**

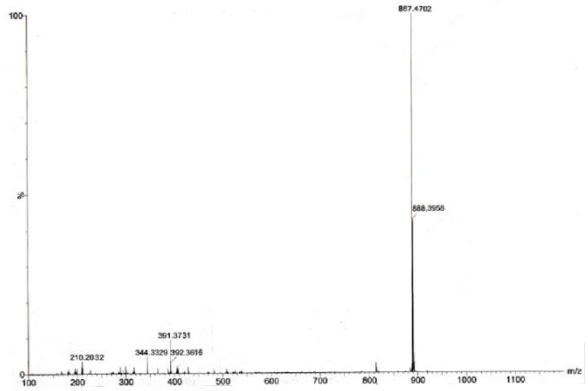
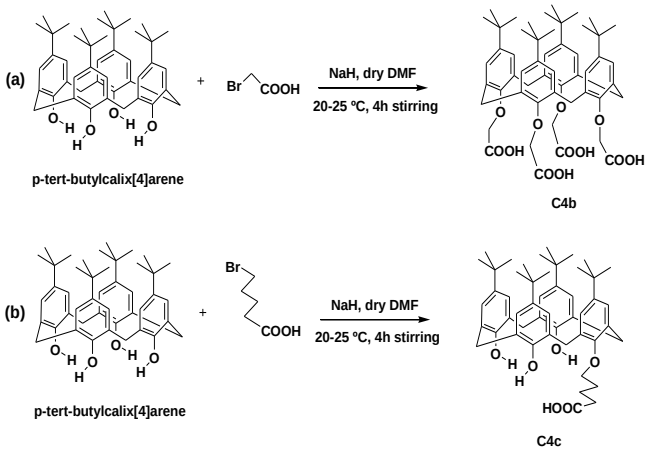


Figure 4: High Resolution Mass Spectrum of the crude product of **C4a**

Table 1: Optimization for the synthesis of **C4a**

Entry	2-BPA addition (1 drop per 5 second)	Temperature (°C)	Yield (%)
1	acid	100	21
2	acid	75-80	32
3	acid	55-60	42
4	37.5% acid in DMF	30-35	72
5	37.5% acid in DMF	20-25	92
6	37.5% acid in DMF	15-20	76
7	37.5% acid in DMF	10-15	55



Scheme 2: Reaction of p-tert-butylcalix[4]arene with (a) bromoacetic acid (b) 5-bromovaleric acid

O-alkylated products were not found. On the other hand, when the number of carbon increases to five that is for 5-bromovaleric acid, mono O-substituted **C4c** was formed as the single product. So, the selectivity of O-substituted product of *p-tert*-butylcalix[4]arene depends on the bulk of the used acids exhibiting steric-controlled phenomenon. The structure of the **C4b** and **C4b** were established from ^{1}H-NMR, ^{13}C-NMR and HRMS.

The nature of substitution does not depend on the amount of the starting acid added. In all cases, as described in Table 2, only the trisubstituted **C4a** has been formed to different extent. This result also supports the steric-controlled single product formation phenomenon.

Our next target was to test the viability of our approach to synthesize five ring fused acridine derivatives using **C4a**. Initially, a screening was conducted to determine the optimal conditions considering a representative reaction between 5,5-dimethyl-1,3-cyclohexaedione (1 mmol), p-toluidine (1 mmol), isatin (1 mmol) and dimethylacetylenedicarboxylate (1.3 mmol) with variation of reaction parameters, such as catalyst, solvent, reaction temperature etc., and the results are summarized in Table 3. Screening of the reaction conditions established that the nature of the catalyst and the temperature of the reaction medium had a significant effect on the yield of the product.

Table 2: Optimization for the synthesis of **C4a** with respect to the amount of the starting acid[a]:

Entry	Amount of 2-BPA Added (eqiv.)	Amount[b] of unreacted p-tert-butylcalix[4]arene (%)	Yield[b] (%)
1	4	80	12
2	6	52	39
3	8	20	72
4	10	8	83
5	11.1	0	92
6	12	0	92

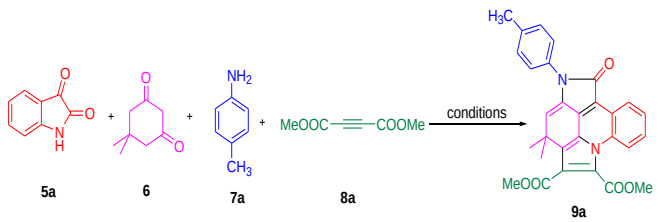
[a]Reaction conditions: p-tert-butylcalix[4]arene (0.3 mmol) with 2-bromopropionic acid (as mentioned) in presence of NaH (5 mmol) in 5 ml dry DMF was stirred at 20-25 °C for 4h. [b]Isolated.

With our focus on recyclability and easy work up procedure, we started searching the activity of well known organic acid catalysts, *p*-toluenesulphonic acid, benzoic acid etc., and found that their capability was much to low to produce the five ring fused acridine derivative (**9a**). Subsequently, we scrutinized the reaction with the aid of heterogeneous spherical mesoporous silica nanoparticle supported carboxylic acid (SMSNP-CA, Figure 5) and porous silica nanoparticle supported carboxylic acid (PSNP-CA, Figure 5) under the same reaction conditions. Although those acids performed a bit in water but the yields in water were not appreciable. After suffering a setback with heterogeneous catalyst, we turned our attention toward organocatalysis again. Capability of some dicarboxylic acids was screened but they furnished the expected product **9a** only in poor yields (entry 3-7). Further increment of one –COOH group was also unsuccessful to catalyze this multicomponent reaction efficiently (entry 8-10). To our delight one promising condition was identified using newly synthesized catalyst **C4a**. Thus the best yield, smooth reaction and easy work-up were achieved employing 1.0 equiv. of each of dimedone (1 mmol), isatin (1 mmol), and *p*-toluidine (1 mmol) with dimethylacetylenedicarboxylate (1.3 mmol) occupying 0.05 mol% of calixarene supported –COOH (**C4a**) as the exact picking of catalyst and was established to be the key to obtain good to excellent yields of the fused acridines (entry 16).

Further, to emphasize the importance of the present catalyst, we studied a comparison of citric and isocitric acid with the **C4a**. Although the former acids have the same functional groups, three –COOH (Figure 5), with the later **C4a** but they triggered poor

yields of the expected product **9a** in expense of longer reaction times (entry 8-10). Again when the monomer of the calixarene **C4a** (**MC4a**) (Figure 5) was used as catalyst no product was formed (entry 12). So, the obtained results proved the requirement of the cavity of the **C4a** to provide an affordable environment for this reaction. Probably the aromatic groups of the **C4a** provide stability towards the starting materials that reflects the increase in yield along with the reaction rate at the same time. We tried to find out the consequence of only the cavity with very mild acidity i.e., *p-tert*-butylcalix[4]arene, that resulted in failure to produce any product. But with increasing incorporation of acid substitution i.e., from mono (**C4c**) to triacidsubstituted calixarene (**C4a**), a continuous increase in yield was definitely found (entries 13-16). Decisively, both the cavity as well as the acidic substituents play simultaneous important role in this reaction. On the other hand, further enhancement of acid substitution i.e., use of the tetrasubstituted calixarene (**C4b**) did not show any mentionable increase in yield which established the **C4a** as the acceptable optimised catalyst. So, it can be concluded that a minimum of three COOH groups at the lower rim of this *p-tert*-butylcalix[4]arene are absolutely necessary, since four COOH groups also catalyse the reaction with equal efficiency.

Table 3: Effect of various reaction parameters[a]



Entry	Catalyst	Solvent	Temp. (°C)	Time (h)	Yield[b] (%)
1	SMSNP-CA	H_2O	100	72	18
2	PSNP-CA	H_2O	100	72	15
3	Oxalic acid	H_2O	100	72	35
4	Malonic acid	H_2O	100	72	27
5	Succinic acid	H_2O	100	72	25
6	Fumaric acid	H_2O	100	72	28
7	Maleic acid	H_2O	100	72	27
8	Propane-1,2,3-trycarboxylic acid	H_2O	100	72	36
9	Citric acid	H_2O	100	72	38
10	Isocitric acid	H_2O	100	72	38
11	Calix[4]arene	PEG+H_2O[c]	100	72	NF
12	**MC4a**	PEG+H_2O[c]	100	72	NF
13	**C4c**	PEG+H_2O[c]	100	72	12
14	**C4d**	PEG+H_2O[c]	100	72	33
15	**C4a**	PEG+H_2O[c]	80	72	NF
16	**C4a**	**PEG+H_2O[c]**	**100**	**12**	**76**
17	**C4a**	PEG+H_2O[c]	100	18	76
18	**C4a**	PEG+H_2O[c]	120	12	75
19	**C4a**	H_2O	100	72	30
20	**C4a**	toluene	100	72	NF
21	**C4a**	1,4-dioxane	100	72	NF
22	**C4a**	DMSO	100	72	22
23	**C4b**	PEG+H_2O[c]	100	72	75

[a]Reaction conditions: mixture of 1.0 equiv. of each of dimedone (1 mmol), isatin (1 mmol), and *p*-toluidine (1 mmol) with dimethylacetylenedicarboxylate (1.3 mmol) were heated with stirring in presence of different catalysts (10 mol% for heterogeneous catalysts and 5 mol% of calixarene catalysts) in 2 ml of solvent. [b]Isolated yield. [c](0.5 ml PEG-400 + 1.5 ml H_2O). NF= not found.

Several solvents like DMSO, toluene, 1,4-dioxane, water and PEG+H_2O (0.5 ml PEG-400 + 1.5 ml H_2O) were tested as reaction medium. In case of heterogeneous catalysts, little amount (15-18%) of product was generated due to some acidity in water. In comparison between organic catalysts in water, **C4a** showed comparatively better result. Actually we got the best result in 1:3

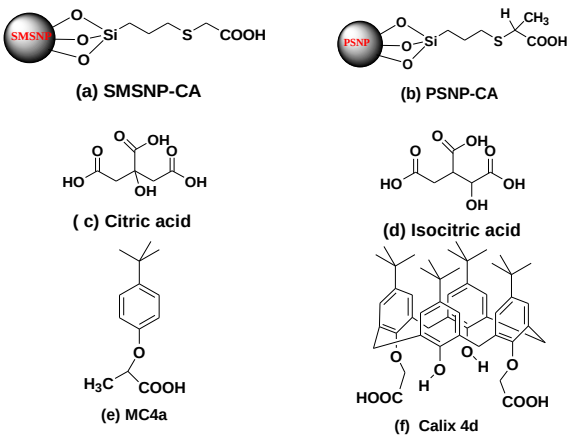


Figure 5: silica nanoparticle supported carboxylic acid (a) SMSNP-CA & (b) PSNP-CA, tricarboxylic acid (c) citric acid & (d) isocitric acid, monomer of **C4a** (e) MC4a and dicarboxylate calixarene (f) **C4d**[12]

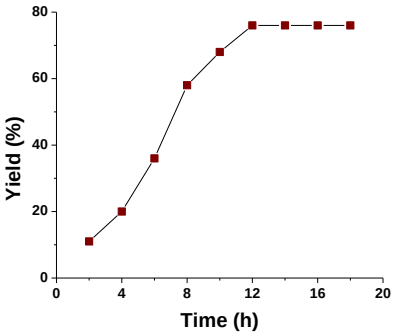


Figure 6: Selective productivity of compound **9a** vs. time plot using **C4a** as the catalyst

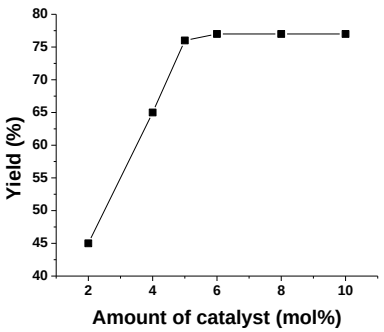
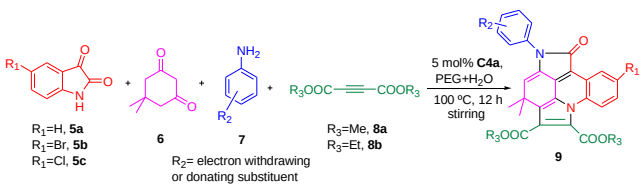
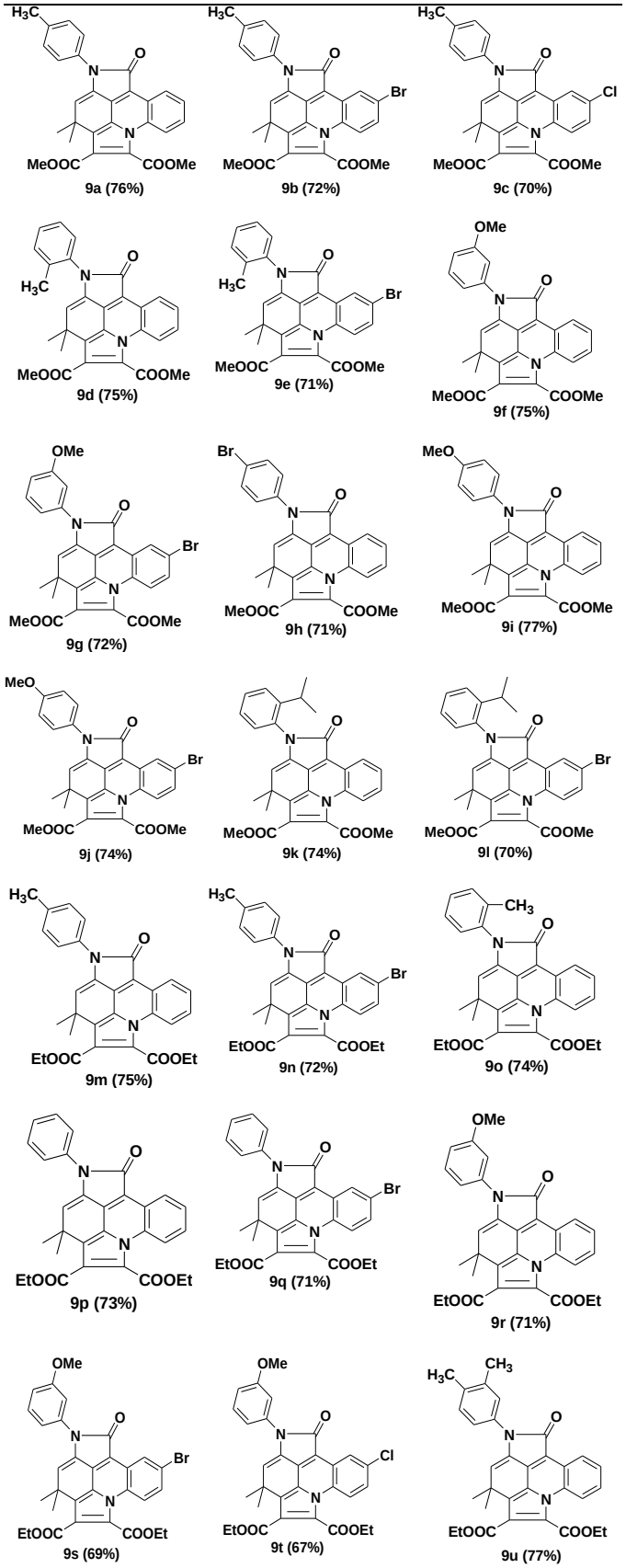


Figure 7: yields at different catalyst loading





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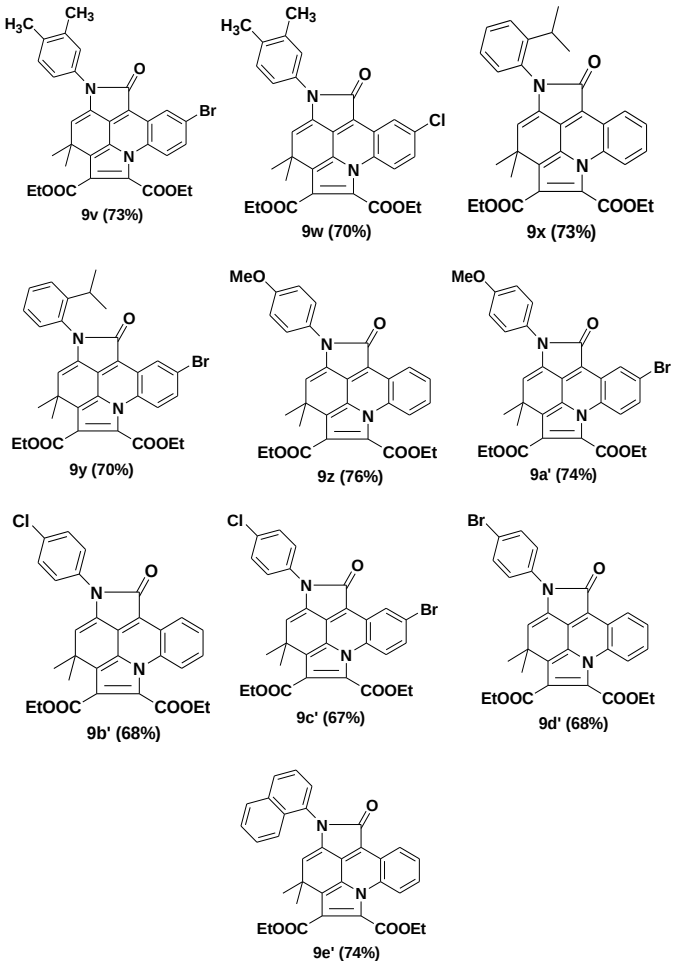


Scheme 3: C4a catalyzed synthesis of some acridine derivatives with aromatic substitution

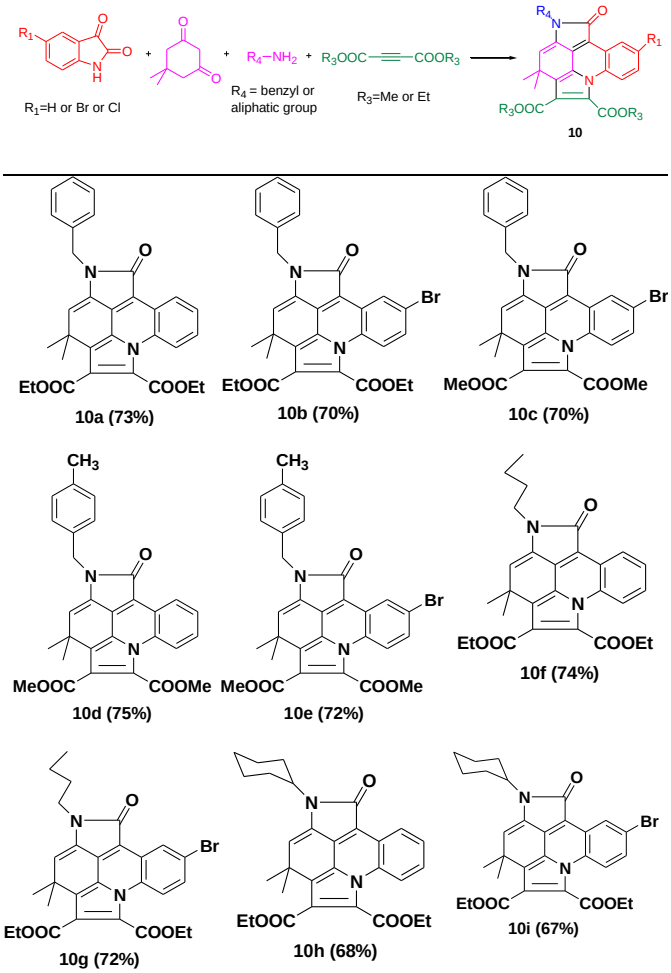
PEG-400 and H_2O mixture as the PEG, being a phase-transfer-catalyst, increases the missibility of the catalyst in water. Where as in DMSO the four ring containing pyrrolo fused acridine intermediate (**D**) was obtained.

Temperature also played a crucial role to the fruitfulness of five ring fusion which was reflected from the reaction occurring at 80ºC employing **C4a** in PEG+H_2O producing only the same intermediate (**D**). 100ºC was the critical temperature for this reaction. The kinetics of the reaction i.e., the dependence of the reaction on time was also studied (Figure 6), which revealed the reaction completion time was just 12 h and further increase in time up to 18 h did not hamper the amount of the product **9a** formation.

To determine the appropriate amount of the catalyst, the synthesis of the product (**9a**) was carried out in the presence of various amounts of catalyst in (PEG+H_2O) at 100 ºC. Figure 7 shows a striking increase in productivity consistent with the increase in the quantity of the catalyst up to 5 mol%. No significant increase in the yield was observed with a further higher amount of catalyst. With the intention of using the minimum amount of the catalyst, we have been restricted to 5 mol% for continuation purpose.

After our successful efforts, we shifted our attention to generalize this approach with various substituted isatins, amines and dialkylacetylenedicarboxylates and all were successful towards the library synthesis of an assembly of compounds and the results are shown in Scheme 3.

We examined the reactivity of electron deficient 5-chloro or 5-bromo isatin which resulted in moderate yields (67-72%) of the product. The behaviour of electronic variation to the amine part was also observed. So, the starting materials that are selected in Scheme 3, contained a wide range of functionalities with the purpose to maximize diversity to a reasonable extent. As expected, using the standard set of the reaction conditions, benzyl amines also incorporated assortment in acridine derivative (**10**, Scheme 4) with a good yield of 72-75% range. Aliphatic substitutions on pyrrole counterpart were also carefully investigated employing aliphatic amines (Scheme 4).



Scheme 4: C4a catalyzed synthesis of some acridine derivatives with aliphatic substitution

The structure of newly generated five ring fused acridine derivative was confirmed by single crystal X-ray analysis of compound **9a** (crystallized from EtOAc) (Figure 8).

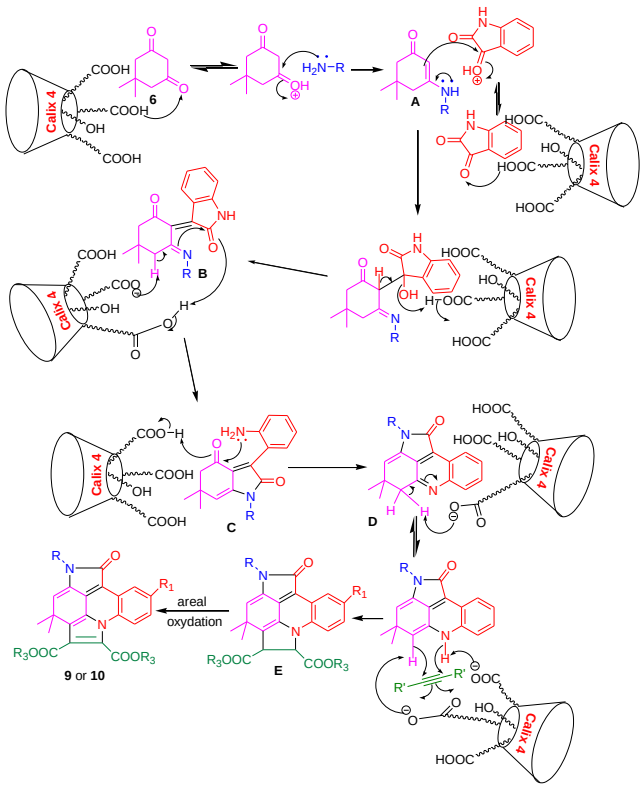
Reprocessing of catalyst recovered from column was investigated and it had been seen that the catalytic activity did not hamper the

yield notably up to five cycles that was reflected in Table 3. Thus the catalyst had the potential of reworking at least five times. The ^{1}H NMR data of the catalyst after each 2 cycles was taken to prove that it still remains the same and the NMR data is given in the supplementary section which reveals that after recycling, the catalysts remains unchanged.

Table 3: Recyclability of the **C4a** for the synthesis of **9a**

No of cycles [a]	yield [b] (%)
1	76
2	75
3	75
4	74
5	73
6	70

[a] Reaction was carried out with recovered catalyst. [b] Isolated yield.



Scheme 5: Suggested mechanism for the **C4a** catalyzed synthesis of acridine derivative [the probable weak interactions of starting materials and the aromatic groups of the **C4a** have not been shown in mechanism due to shake of simplicity and also all amines are represented as R-NH$_2$ for the same simplicity reason]

The mechanism of this multicomponent reaction (Scheme 5) expectedly passes through a series of condensations followed by the ring closure cascade reactions. Intermediate B may be formed via condensation of initially formed enaminoketone A with isatin. Then the catalyst promoted intramolecular ring opening in concurrence with ring closing involving B to produce C which upon further condensation produce intermediate D. The structure of D is confirmed from the NMR spectrum of the major product (D, see SI), isolated by quenching the reaction after 1 h. The third ring closer of D with acetylenedicarboxylate forms intermediate E that undergoes aerial oxidation to produce the desired product. We also got the same final product starting from the intermediate D.

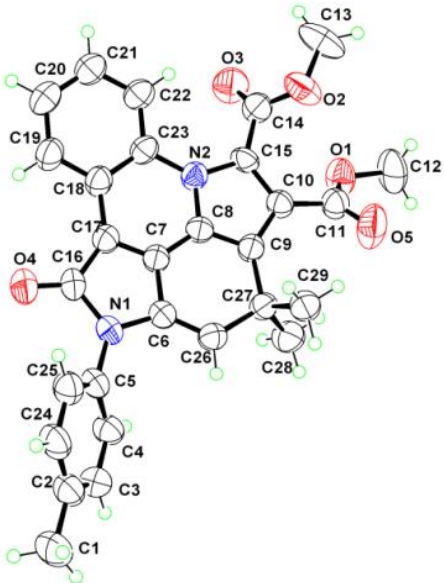


Figure 8: X-ray single crystal structure of **9a**. (CCDC 1014291)

Conclusions

In summary, we have developed the first, efficient and novel one step strategy of incorporation of carboxylic acid group at the lower rim of simple p-tert-butylcalix[4]arene with high throughput yield upon 100% conversion. The most important application of this newly synthesized calixarene grafted acid was investigated towards multiring conjunction as recyclable organocatalyst in organic synthesis. A fruitful result evident from this investigation is the generation of a new series of five ring fused acridine derivatives. So, in this paper, we report a new and competent methodology for the synthesis of that core in high yields in a multicomponent fashion from simple commercially available reagents. The use of the recyclable catalyst makes this organic protocol more environmentally benign from the point of catalytic chemistry. This new entry to the calixrene member is hoped to stride towards sensing and hosting of many inorganic and organic compounds along with organocatalysis. Also our new series of diverse acridine derivatives may bright a part of medicinal chemistry.

Experimental section

Synthesis of *p-tert*-butylcalix[4]arene:

p-tert-Butylcalix[4]arene was synthesized from the mixture of *p-tert*-butylphenol (2 g, 13.32 mmol), 37% formaldehyde solution (1.24 mL, 16.6 mmol of HCHO), and NaOH (240 mg, 0.6 mmol) according to our reported procedure.[4a]

Synthesis of 25-hydroxy-26, 27, 28-tris(1-carboxy-1-methylmethoxy)-*p-tert*-butylcalix[4]arene (C4a):

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p-tert-Butylcalix[4]arene (200mg, 0.3 mmol) was mixed with NaH (120 mg, 5 mmol) in a 25 ml round bottom flask, 10 ml of dry DMF was added to it. The mixture was allowed to stir for 30 mins at room temperature (25-30 ºC). 2-Bromopropionic acid (3 ml, 3.3 mmol) was diluted with dry DMF (5 ml) up to 37.5%. Then it was added drop wise (1 drop per 5 sec) maintaining the temperature at 20-25 ºC. After the complete addition the reaction mixture was stirred for 4 h. As the reaction progressed, the suspended particles changed into a form of viscous mass. The disappearance of starting *p-tert*-Butylcalix[4]arene was checked by TLC. After complete conversion the reaction mixture was placed in an ice bath and was quenched via acidification using 5% HCl solution. Then 20 ml of chilled water was added to it and we got the crude product by filtration. 245 mg (92%) pure product, color less solid was gained via column chromatography at 25% ethyl acetate in petroleum ether as eluent. mp. 298 ºC; IR (KBr, υ cm^{-1}): 3384, 2962, 2874, 2365, 1686, 1479, 1362, 1194, 1106, 1043. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74-7.61 (m, 1H, -OH), 7.20-7.14 (m, 4H, Ar-H), 7.08-7.00 (m, 4H, Ar-H), 4.80 (br s, 1H, -CH), 4.43-4.39 (m, 4H, $-CH_2$), 4.20-3.95 (m, 2H, -CH), 3.45-3.31 (m, 4H, $-CH_2$),1.66 (br s, 3H, $-CH_3$),1.55 (d, J = 8.4 Hz, 4H, $-CH_3$), 1.66 (br s, 2H, $-CH_3$), 1.27-1.15 (m, 36H, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.0, 177.7, 177.3, 176.9, 148.9, 148.8, 148.3, 147.3, 142.8, 135.2, 134.9, 134.4, 134.1, 132.0, 126.9, 126.2, 125.4, 125.2, 125.0, 83.8, 82.7, 82.0, 78.7, 34.1, 34.1, 33.9, 32.3, 32.0, 31.6, 31.4, 31.2, 30.3, 17.9, 17.3, 16.7, 16.4; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $[C_{53}H_{68}O_{10}Na]$: 887.4705. Found 887. 4702. Anal. calcd. for $C_{53}H_{68}O_{10}$; C: 73.58; H: 7.92. Found: C: 73.52; H: 7.95.

Synthesis of 25, 26, 27, 28-tetrakis(1-carboxy-1-methoxy)-*p-tert*-butylcalix[4]arene (C4b):

C4b was synthesized from *p-tert*-Butylcalix[4]arene at the same procedure like **C4a**. 211 mg (80%) pure product, white solid was gained via column chromatography at 80% ethyl acetate in petroleum ether as eluent. mp. Above 300 ºC; IR (KBr, υ cm^{-1}): 3392, 2961, 2868, 1603, 1736, 1482, 1393, 1193, 1056. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26-7.23 (m, 3H, Ar-H), 7.18-7.02 (m, 3H, Ar-H), 6.79-6.74 (m, 2H, Ar-H), 4.81-4.21 (m, 14H, $-CH_2$), 3.32 (bs, 2H, $-CH_2$), 1.25-0.94 (m, 36H, $-CH_3$); HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $[C_{52}H_{64}O_{12}Na]$: 903.4290. Found 903.4294. Anal. calcd. for $C_{52}H_{64}O_{12}$; C: 70.89; H: 7.32. Found: C: 70.85; H: 7.35.

Synthesis of 25, 26, 27-trihydroxy-28-(4-carboxy-1-butoxy)-*p-tert*-butylcalix[4]arene (C4c):

C4c was synthesized from *p-tert*-Butylcalix[4]arene at the same procedure like **C4a**. 197 mg (85%) pure product, color less gummy solid was gained via column chromatography at 15% ethyl acetate in petroleum ether as eluent. IR (KBr, υ cm^{-1}): 3350, 2960, 2870, 1710, 1485, 1362, 1202, 1123.. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.09 (bs, 1H, -OH), 9.49 (bs, 2H, -OH), 7.01-6.91 (m, 8H, Ar-H), 4.27-4.18 (m, 4H, $-CH_2$), 4.08-4.06 (m, 2H, $-CH_2$), 3.38-3.34 (m, 4H, $-CH_2$), 2.53(t, J = 6.75 Hz, 2H, $-CH_2$), 2.14-1.99 (m, 4H, $-CH_2$), 1.14-1.12 (m, 36H, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.84, 149.2, 148.4, 148.2, 147.7, 143.6, 143.2, 133.4, 128.3, 128.0, 127.6, 126.5, 125.9, 125.8, 125.7, 125.6, 114.7, 76.6, 53.4, 34.0, 33.9, 33.5, 33.0, 32.2, 31.9, 31.5, 31.2, 29.7, 29.2, 22.7, 21.2; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $[C_{49}H_{64}O_6Na]$: 771.4595. Found 771.4495. Anal. calcd. for $C_{49}H_{64}O_6$; C: 78.57; H: 8.61. Found: C: 78.54; H: 8.63.

General procedure for the synthesis of five ring fused acridine derivatives (all entries of Scheme 3 & 4):

First 43 mg (5 mol%) of **C4a** was dissolved in 2ml of PEG+H_2O (1:3) (v/v) by slight heating and stirring. Then 5,5-dimethyl-1,3-cyclohexaedione (140 mg, 1 mmol), aromatic or aliphatic amine (1 mmol), isatin (147 mg, 1 mmol) and dialkylacetylenedicarboxylate (1.3 mmol) were added to the solution. This reaction mixture was heated to 100 ºC and stirred for 12 h at that temperature. The progress of the reaction was measured by TLC and the time of completion was monitored by disappearance of spot for isatin. After that the reaction mixture was poured into crushed ice and filtered. The residue was submitted to column chromatography with using 60-120 mesh silica gel and petroleum ether-ethyl acetate mixture as eluent. We got the pure products at 5-6% ethyl acetate at petroleum ether and the pure catalyst at 22% ethyl acetate at petroleum ether.

Spectral and Analytical Data of the products:

Dimethyl-4,4-dimethyl-1-oxo-2-p-tolyl-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9a): Yellow solid (76%), mp. 216 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2949, 2342, 1718, 1689, 1448, 1326, 1232, 760 ; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.51-8.48 (m, 1H, Ar-H), 8.02-7.99 (m, 1H, Ar-H), 7.52-7.49 (m, 2H, Ar-H), 7.42 (d, J = 8.4 Hz, 2H, Ar-H), 7.34 (d, J = 8.4 Hz, 2H, Ar-H), 5.78 (s, 1H, vinylic-H), 4.13 (s, 3H, $-OCH_3$), 3.96 (s, 3H, $-OCH_3$), 2.44 (s, 3H, $-CH_3$), 1.68 (s, 6H, $-CH_3$) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.2, 164.4, 164.3, 136.6, 134.0, 133.1, 131.4, 131.0, 129.9, 127.5, 126.4, 125.6, 125.5, 124.7, 123.3, 122.8, 122.1, 119.6, 117.6, 108.3, 53.3, 52.0, 42.5, 28.1, 21.1 ; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $[C_{29}H_{24}N_2O_5Na]$: 503.1577. Found 503.1554. Anal. calcd. for $C_{29}H_{24}N_2O_5$; C: 72.49; H: 5.03; N: 5.83. Found: C: 72.41; H: 5.01; N: 5.80.

Dimethyl-9-bromo-4,4-dimethyl-1-oxo-2-p-tolyl-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9b): Reddish yellow solid (72%), mp. 252 ºC (EtOAc) ; IR (KBr, υ cm^{-1}): 2950, 2366, 1715, 1677, 1478, 1345, 1281, 992; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.49 (s, 1H, Ar-H), 8.12 (s, 1H, Ar-H), 7.34-7.27 (m, 5H, Ar-H), 5.74 (s, 1H, vinylic-H), 3.92 (s, 3H, $-OCH_3$), 3.87 (s, 3H, $-OCH_3$), 2.38 (s, 3H, $-CH_3$), 1.63 (s, 6H, $-CH_3$) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.4, 162.5, 162.4, 135.5, 135.0, 133.1, 132.3, 130.1, 129.9, 128.6, 126.2, 125.3, 125.2, 121.2, 119.1, 117.1, 55.6, 53.3, 52.1, 42.6, 27.8, 21.2; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $[C_{29}H_{23}BrN_2O_5Na]$: 581.0683. Found 581.0674. Anal. calcd. for $C_{29}H_{23}BrN_2O_5$; C: 62.26; H: 4.14; N: 5.01. Found: C: 62.20; H: 4.11; N: 5.04.

Dimethyl-9-chloro-4,4-dimethyl-1-oxo-2-p-tolyl-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9c): Yellow solid (70%), mp. 244 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2945, 2401, 1721, 1447, 1326, 1294, 1056; ^{1}H NMR (300 MHz,

$CDCl_3$): δ 8.42 (d, *J* = 4.2 Hz, 1H, Ar-H), 7.79 (d, *J* = 9.3 Hz, 1H, Ar-H), 7.50 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H, Ar-H), 7.34-7.24 (m, 4H, Ar-H), 5.72 (s, 1H, vinylic-H), 4.52 (s, 3H, -OCH_3), 4.37 (s, 3H, -OCH_3), 2.36 (s, 3H, -CH_3), 1.59 (s, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 164.5, 164.2, 136.4, 135.2, 134.6, 134.2, 134.0, 133.6, 131.2, 130.7, 129.4, 127.9, 127.8, 125.3, 122.8, 121.6, 115.2, 113.2, 112.6, 53.4, 52.6, 43.3, 29.3, 21.0; Anal. calcd. for $C_{29}H_{23}ClN_2O_5$; C: 67. 64; H: 4.50; N: 5.44. Found: C: 67.59; H: 4.51; N: 5.42.

Dimethyl-4,4-dimethyl-1-oxo-2-o-tolyl-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9d): Yellow solid (75%), mp. 228 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2951, 2355, 1705, 1621, 1436, 1293, 1151, 762; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43-8.40 (m, 1H, Ar-H), 7.95-7.92 (m, 1H, Ar-H), 7.47-7.42 (m, 2H, Ar-H), 7.31-7.26 (m, 4H, Ar-H), 5.35 (s, 1H, vinylic-H), 4.04 (s, 3H, -OCH_3), 3.87 (s, 3H, -OCH_3), 2.18 (s, 3H, -CH_3), 1.57(s, 3H, -CH_3), 1.56 (s, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.4, 164.5, 164.3, 136.9, 134.1, 131.8, 131.4, 128.8, 128.6, 127.6, 126.9, 126.6, 126.4, 125.6, 124.8, 123.3, 123.0, 121.8, 119.7, 117.6, 108.5, 53.4, 52.0, 42.5, 28.1, 28.0, 18.1; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $[C_{29}H_{24}N_2O_5Na]$: 503.1577. Found 503.1561. Anal. calcd. for $C_{29}H_{24}N_2O_5$; C: 72.49; H: 5.03; N: 5.83. Found: C: 72.43; H: 5.07; N: 5.86.

Dimethyl-9-bromo-4,4-dimethyl-1-oxo-2-o-tolyl-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9e): Yellow solid (71%), mp. 260-262 ºC (EtOAc); IR (KBr, υ cm^{-1}): 3011, 2301, 1719, 1655, 1391, 1293, 1175, 769; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.58 (s, 1H, Ar-H), 8.08-8.07 (m, 1H, Ar-H), 7.79-7.78 (m, 2H, Ar-H), 7.66-7.65 (m, 2H, Ar-H), 7.50-7.49 (m, 1H, Ar-H), 5.68 (s, 1H, vinylic-H), 3.92 (s, 3H, -OCH_3), 3.86 (s, 3H, -OCH_3), 2.11 (s, 3H, -CH_3), 1.56 (s, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 165.0, 164.8, 138.1, 136.6, 134.4, 133.3, 132.0, 131.9, 130.6, 129.9, 127.0, 126.8, 126.3, 124.3, 123.4, 123.2, 122.3, 119.9, 115.2, 108.6, 53.9, 52.9, 43.7, 27.9, 21.1; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $[C_{29}H_{23}BrN_2O_5Na]$: 581.0683. Found 581.0704. Anal. calcd. for $C_{29}H_{23}BrN_2O_5$; C: 62.26; H: 4.14; N: 5.01. Found: C: 62.28; H: 4.15; N: 4.99.

Dimethyl-2-(3-methoxyphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9f): Yellow solid (75%), mp. 232 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2973, 2347, 1702, 1500, 1425, 1228, 731; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.52-8.48 (m, 1H, Ar-H), 8.00-7.96 (m, 1H, Ar-H), 7.52-7.49 (m, 2H, Ar-H), 7.43 (t, *J* = 8.4 Hz, 1H, Ar-H), 7.12-7.10 (m, 2H, Ar-H), 6.93-6.89 (m, 1H, Ar-H), 5.84 (s, 1H, vinylic-H), 4.12 (s, 3H, -OCH_3), 3.95 (s, 3H, -OCH_3), 3.88 (s, 3H, -OCH_3), 1.67 (s, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.1, 164.4, 164.4, 160.3, 136.9, 134.0, 131.6, 130.8, 129.9, 129.6, 127.6, 126.5, 125.7, 124.6, 123.4, 122.8, 122.7, 119.6, 117.7, 117.6, 112.5, 111.4, 108.2, 55.5, 53.4, 52.1, 42.6, 28.1; Anal. calcd. for $C_{29}H_{24}N_2O_6$; C: 70.15; H: 4.87; N: 5.64. Found: C: 70.18; H: 4.85; N: 5.69.

Dimethyl-9-bromo-2-(3-methoxyphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9g): Yellow solid (72%), mp. 266 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2927, 2342, 1708, 1621, 1319, 1209, 851; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43 (s, 1H, Ar-H), 7.88 (d, *J* = 9.3 Hz, 1H, Ar-H), 7.41-7.33 (m, 4H, Ar-H), 7.12-7.05 (m, 1H, Ar-H), 5.41 (s, 1H, vinylic-H), 3.92 (s, 3H, -OCH_3), 3.88 (s, 3H, -OCH_3), 3.80 (s, 3H, -OCH_3), 1.60 (s, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.0, 164.0, 163.8, 160.7, 137.0, 134.2, 131.5, 130.9, 129.8, 127.5, 126.4, 126.1, 124.5, 123.3, 122.9, 122.7, 119.7, 117.7, 112.4, 111.4, 107.4, 55.5, 54.4, 53.7, 42.6, 28.1; Anal. calcd. for $C_{29}H_{23}BrN_2O_6$; C: 60.53; H: 4.03; N: 4.87. Found: C: 60.50; H: 4.05; N: 4.89.

Dimethyl-2-(4-bromophenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9h): Reddish yellow solid (71%), mp. 258 ºC (EtOAc): IR (KBr, υ cm^{-1}): 2969, 2352, 1711, 1591, 1425, 1149, 887; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.47-8.44 (m, 1H, Ar-H), 7.98-7.95 (m, 1H, Ar-H), 7.69-7.61 (m, 2H, Ar-H), 7.52-7.38 (m, 4H, Ar-H), 5.79 (s, 1H, vinylic-H), 4.12 (s, 3H, -OCH_3), 3.95 (s, 3H, -OCH_3), 1.68 (s, 6H, -CH_3); Anal. calcd. for $C_{28}H_{21}BrN_2O_5$; C: 61.66; H: 3.88; N: 5.14. Found: C: 61.63; H: 3.87; N: 5.11.

Dimethyl-2-(4-methoxyphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9i): Reddish yellow solid (77%), mp. 236 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2960, 2297, 1715, 1604, 1502, 1166, 955; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59-8.58 (m, 1H, Ar-H), 8.09-8.06 (m, 1H, Ar-H), 7.97-7.94 (m, 2H, Ar-H), 7.44-7.41 (m, 2H, Ar-H),6.98 (d, *J* = 9 Hz, 1H, Ar-H), 5.71 (s, 1H, vinylic-H), 3.97 (s, 3H, -OCH_3), 3.87 (s, 3H, -OCH_3), 3.85 (s, 3H, -OCH_3), 1.67 (s, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.6, 169.0, 167.9, 167.2, 138.6, 137.2, 133.8, 133.5, 131.2, 130.7, 129.3, 127.9, 127.8, 127.5, 122.8, 121.6, 115.2, 113.1, 110.8, 53.4, 52.7, 52.4, 43.1, 28.5; Anal. calcd. for $C_{29}H_{24}N_2O_6$; C: 70.15; H: 4.87; N: 5.64. Found: C: 70.12; H: 4.85; N: 5.66.

Dimethyl-9-bromo-2-(4-methoxyphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9j): Yellow solid (74%), mp. 266 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2939, 2331, 1712, 1598, 1365, 1203, 1012; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.52 (d, *J* = 2.1 Hz, 1H, Ar-H), 7.86 (d, *J* = 9.3 Hz, 1H, Ar-H), 7.52-7.48 (m, 1H, Ar-H), 7.33 (d, *J* = 9 Hz, 2H, Ar-H), 6.97 (d, *J* = 9 Hz, 2H, Ar-H), 5.67 (s, 1H, vinylic-H), 4.02 (s, 3H, -OCH_3), 3.87 (s, 3H, -OCH_3), 3.80 (s, 3H, -OCH_3), 1.58 (s, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.9, 164.4, 163.9, 158.4, 132.9, 132.0, 131.1, 130.3, 128.7, 128.2, 127.7, 127.0, 126.9, 125.5, 124.7, 124.4, 123.7, 122.6, 121.7, 120.5, 120.1, 119.2, 114.6, 114.1, 107.4, 55.5, 53.4, 52.1, 42.6, 28.1; Anal. calcd. for $C_{29}H_{23}BrN_2O_6$; C: 60.53; H: 4.03; N: 4.87. Found: C: 60.57; H: 4.01; N: 4.90.

Dimethyl-2-(2-isopropylphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9k): Yellow solid (74%), mp. 240 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2921, 2402, 1699, 1614, 1298, 1087, 934; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39 (dd, *J* = 6.2 Hz, *J* = 3.3 Hz, 1H, Ar-H), 7.92 (dd, *J* = 6.3 Hz, *J* = 3.3 Hz, 1H, Ar-H), 7.43-7.34 (m, 3H, Ar-H), 7.27-7.17 (m, 3H, Ar-H), 5.29 (s, 1H, vinylic-H), 4.02 (s, 3H, -OCH_3), 3.85 (s, 3H, -OCH_3), 2.88-2.83 (m, 1H, -

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CH), 1.55 (s, 3H, -CH_3), 1.52 (s, 3H, -CH_3), 1.14 (d, *J* = 6.9 Hz, 3H, -CH_3), 1.06 (d, *J* = 6.6 Hz, 3H, -CH_3);^{13}C NMR (75 MHz, $CDCl_3$): δ 167.9, 164.4, 164.2, 147.8, 134.8, 134.0, 132.5, 131.6, 129.5, 129.4, 129.3, 129.2, 127.6, 127.5, 126.7, 126.5, 126.3, 125.5, 125.1, 124.7, 124.3, 123.2, 123.0, 122.7, 121.5, 119.6, 117.6, 108.3, 53.3, 52.0, 42.4, 28.0, 27.9, 23.9, 23.6; Anal. calcd. for $C_{31}H_{28}N_2O_5$; C: 73.21; H: 5.55; N: 5.51. Found: C: 73.15; H: 5.51; N: 5.56.

Dimethyl-9-bromo-2-(2-isopropylphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9l): Yellow solid (70%), mp. 280 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2960, 1697, 1627, 1428, 1225, 1036, 725; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.42 (d, *J* = 2.4 Hz, 1H, Ar-H), 7.86 (d, *J* = 10.2 Hz, 1H, Ar-H), 7.52 (d, *J* = 4.5 Hz, 1H, Ar-H), 7.41-7.38 (m, 2H, Ar-H), 7.28-7.20 (m, 2H, Ar-H), 5.32 (s, 1H, vinylic-H), 4.04 (s, 3H, -OCH_3), 3.89 (s, 3H, -OCH_3), 2.85-2.81 (m, 1H, -CH), 1.56 (s, 6H, -CH_3), 1.17 (d, *J* = 8.4 Hz, 3H, -CH_3), 1.07 (d, *J* = 5.7 Hz, 3H, -CH_3); HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for [$C_{31}H_{27}BrN_2O_5Na$]: 531.1890. Found 531.1856. Anal. calcd. for $C_{31}H_{27}BrN_2O_5$; C: 63.38; H: 4.63; N: 4.77. Found: C: 63.35; H: 4.67; N: 4.72.

Diethyl-4,4-dimethyl-1-oxo-2-p-tolyl-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9m): Yellow solid (75%), mp. 188 ºC (EtOAc)**;** IR (KBr, υ cm^{-1}): 2932, 1700, 1514, 1249, 1096, 791; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.53-8.51 (m, 1H, Ar-H), 8.04-8.02 (m, 1H, Ar-H), 7.52-7.50 (m, 2H, Ar-H), 7.42 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.34 (d, *J* = 8.1 Hz, 2H, Ar-H), 5.77 (s, 1H, vinylic-H), 4.60 (q, *J* = 7 Hz, 2H, -OCH_2), 4.43 (q, *J* = 7 Hz, 2H, -OCH_2), 2.44 (s, 3H, -CH_3), 1.69 (s, 6H, -CH_3), 1.50 (t, *J* = 7.2 Hz, 3H, -CH_3), 1.44 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.4, 164.0, 163.9, 148.6, 136.6, 134.1, 131.6, 129.9, 127.4, 126.5, 126.4, 125.5, 123.2, 122.9, 122.2, 117.6, 117.1, 62.7, 61.2, 42.6, 22.6, 14.2, 14.1; Anal. calcd. for $C_{31}H_{28}N_2O_5$; C: 73.21; H: 5.55; N: 5.51. Found: C: 73.25; H: 5.58; N: 5.49.

Diethyl-9-bromo-4,4-dimethyl-1-oxo-2-p-tolyl-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9n): Reddish yellow solid (72%), mp. 225 ºC (EtOAc); IR (KBr, υ cm^{-1}): 3001, 1708, 1540, 1122, 1096, 791; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.54 (d, *J* = 2.1 Hz, 1H, Ar-H), 7.88 (d, *J* = 9 Hz, 1H, Ar-H), 7.50 (dd, *J* = 9.2 Hz, *J* = 2.6 Hz, 1H, Ar-H), 7.33-7.24 (m, 4H, Ar-H), 5.72 (s, 1H, vinylic-H), 4.49 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.34 (q, *J* = 7.2 Hz, 2H, -OCH_2), 2.36 (s, 3H, -CH_3), 1.59 (s, 6H, -CH_3), 1.43-1.33 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.8, 164.0, 163.5, 136.7, 133.0, 132.2, 130.9, 130.2, 129.9, 128.8, 125.4, 124.5, 123.6, 122.8, 120.6, 120.1, 119.2, 107.3, 62.8, 61.3, 42.6, 28.1, 21.1, 14.2, 14.0; Anal. calcd. for $C_{31}H_{27}BrN_2O_5$; C: 63.38; H: 4.63; N: 4.77. Found: C: 63.35; H: 4.60; N: 4.79.

Diethyl-4,4-dimethyl-1-oxo-2-o-tolyl-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9o): Reddish yellow solid (74%), mp. 185 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2940, 1710, 1634, 1321, 1156, 1032, 828; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43-8.40 (m, 1H, Ar-H), 7.97-7.94 (m, 1H, Ar-H), 7.46-7.41 (m, 2H, Ar-H), 7.31-7.26 (m, 4H, Ar-H), 5.34 (s, 1H, vinylic-H), 4.52 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.34 (q, *J* = 7.2 Hz, 2H, -OCH_2), 2.18 (s, 3H, -CH_3), 1.58 (s, 6H, -CH_3), 1.42 (t, *J* = 7.2 Hz, 3H, -CH_3), 1.36 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.5, 164.1, 163.9, 136.9, 134.2, 131.4, 131.3, 128.8, 128.6, 127.4, 126.9, 126.5, 126.3, 126.0, 124.6, 123.2, 123.0, 121.9, 119.8, 117.7, 108.3, 62.7, 61.1, 42.5, 28.0, 18.1, 14.2, 14.0; Anal. calcd. for $C_{31}H_{28}N_2O_5$; C: 73.21; H: 5.55; N: 5.51. Found: C: 73.26; H: 5.53; N: 5.48.

Diethyl-4,4-dimethyl-1-oxo-2-phenyl-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9p): Yellow solid (73%), mp. 234 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2965, 1708, 1642, 1464, 1192, 1015, 991; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.50-8.46 (m, 1H, Ar-H), 8.09-8.06 (m, 1H, Ar-H), 7.51-7.46 (m, 2H, Ar-H), 7.36-7.32 (m, 5H, Ar-H), 5.71 (s, 1H, vinylic-H), 4.59 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.44 (q, *J* = 7.2 Hz, 2H, -OCH_2), 1.67 (s, 6H, -CH_3), 1.49 (t, *J* = 7.2 Hz, 3H, -CH_3), 1.43 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.6, 163.1, 162.0, 136.7, 135.8, 133.2, 132.6, 132.3, 130.9, 129.8, 126.8, 126.6, 124.4, 122.6, 120.4, 119.2, 118.2, 117.5, 113.9, 112.6, 112.0, 62.6, 61.3, 41.2, 29.7, 14.2, 14.0; Anal. calcd. for $C_{30}H_{26}N_2O_5$; C: 72.86; H: 5.30; N: 5.66. Found: C: 72.80; H: 5.31; N: 5.68.

Diethyl-9-bromo-4,4-dimethyl-1-oxo-2-phenyl-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9q): Yellow solid (71%), mp. 254 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2956, 1702, 1631, 1501, 1203, 864; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.61 (d, *J* = 2.1 Hz, 1H, Ar-H), 8.00 (d, *J* = 9.3 Hz, 1H, Ar-H), 7.48 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.32-7.22 (m, 5H, Ar-H), 5.66 (s, 1H, vinylic-H), 4.54 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.39 (q, *J* = 7.2 Hz, 2H, -OCH_2), 1.62 (s, 6H, -CH_3), 1.44 (t, *J* = 7.2 Hz, 3H, -CH_3), 1.38 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.4, 164.2, 164.1, 141.2, 133.9, 131.2, 127.2, 126.4, 126.3, 124.7, 123.1, 122.6, 120.7, 117.7, 108.8, 62.7, 61.2, 42.3, 28.1, 20.2, 14.2, 14.0; Anal. calcd. for $C_{30}H_{25}BrN_2O_5$; C: 62.84; H: 4.39; N: 4.89. Found: C: 62.80; H: 4.35; N: 4.93.

Diethyl-2-(3-methoxyphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9r): Yellow solid (71%), mp. 236 ºC (EtOAc); IR (KBr, υ cm^{-1}): 3001, 1711, 1589, 1364, 1115, 992, 735; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43-8.41 (m, 1H, Ar-H), 7.96-7.92 (m, 1H, Ar-H), 7.44-7.41 (m, 2H, Ar-H), 7.39-7.33 (m, 1H, Ar-H), 7.05-7.03 (m, 2H, Ar-H), 6.85-6.82 (m, 1H, Ar-H), 5.76 (s, 1H, vinylic-H), 4.52 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.34 (q, *J* = 7.2 Hz, 2H, -OCH_2), 3.81 (s, 3H, -OCH_3), 1.61 (s, 6H, -CH_3), 1.44-1.34 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.0, 164.0, 163.9, 160.3, 137.0, 134.1, 131.7, 130.8, 129.9, 127.5, 126.4, 126.2, 124.4, 123.3, 122.8, 122.7, 119.7, 117.7, 112.5, 111.4, 62.7, 61.2, 55.5, 42.6, 28.1, 14.2, 14.0; Anal. calcd. for $C_{31}H_{28}N_2O_6$; C: 70.98; H: 5.38; N: 5.34. Found: C: 71.01; H: 5.33; N: 5.38.

Diethyl-9-bromo-2-(3-methoxyphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9s): Yellow solid (69%), mp. 248 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2977, 1703, 1605, 1399, 1011, 903, 814; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.52 (s, 1H, Ar-H), 7.94-7.85 (m, 1H, Ar-H), 7.52-7.49 (m, 1H, Ar-H), 7.37-7.31 (m, 1H, Ar-H), 7.09-7.00

(m, 2H, Ar-H), 6.90-6.82 (m, 1H, Ar-H), 5.79 (s, 1H, vinylic-H), 4.49 (q, J = 7.2 Hz, 2H, -OCH_2), 4.34 (q, J = 7.2 Hz, 2H, -OCH_2), 3.79 (s, 3H, -OCH_3), 1.60 (s, 6H, -CH_3), 1.43-1.33 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.6, 163.9, 163.5, 160.3, 136.7, 133.0, 132.2, 130.3, 130.1, 129.9, 128.7, 126.5, 126.1, 124.4, 123.7, 123.4, 120.6, 120.1, 119.2, 117.6, 112.6, 111.3, 107.1, 62.8, 61.3, 55.5, 42.7, 28.0, 14.1, 14.0; Anal. calcd. for $C_{31}H_{27}BrN_2O_6$; C: 61.70; H: 4.51; N: 4.64. Found: C: 61.76; H: 4.47; N: 4.60.

Diethyl-9-chloro-2-(3-methoxyphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9t): Yellow solid (67%), mp. 242 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2966, 1706, 1595, 1245, 1156, 863; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.38 (d, J = 2.4 Hz, 1H, Ar-H), 7.94 (d, J = 9.3 Hz, 1H, Ar-H), 7.38-7.32 (m, 2H, Ar-H), 7.03-7.01 (m, 2H, Ar-H), 6.86-6.82 (m, 1H, Ar-H), 5.80 (s, 1H, vinylic-H), 4.50 (q, J = 7.2 Hz, 2H, -OCH_2), 4.34 (q, J = 7.2 Hz, 2H, -OCH_2), 3.80 (s, 3H, -OCH_3), 1.60 (s, 6H, -CH_3), 1.47-1.33 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 164.0, 163.5, 160.4, 136.7, 132.6, 132.3, 130.6, 130.0, 127.4, 125.8, 124.5, 124.2, 123.7, 123.3, 119.0, 117.6, 112.6, 111.4, 62.8, 61.3, 55.5, 42.7, 28.1, 14.2, 14.0; Anal. calcd. for $C_{31}H_{27}ClN_2O_6$; C: 66.61; H: 4.87; N: 5.01. Found: C: 66.67; H: 4.85; N: 5.04.

Diethyl-2-(3,4-dimethylphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9u): Reddish yellow solid (77%), mp. 228 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2973, 1713, 1605, 1273, 1159, 747; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43-8.40 (m, 1H, Ar-H), 7.95-7.92 (m, 1H, Ar-H), 7.42-7.40 (m, 2H, Ar-H), 7.24-7.15 (m, 3H, Ar-H), 5.67 (s, 1H, vinylic-H), 4.51 (q, J = 7.2 Hz, 2H, -OCH_2), 4.34 (q, J = 7.2 Hz, 2H, -OCH_2), 2.27 (s, 3H, -CH_3), 2.25 (s, 3H, -CH_3), 1.59 (s, 6H, -CH_3), 1.44-1.33 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.4, 164.0, 163.9, 137.7, 135.4, 134.1, 133.3, 131.5, 131.1, 130.3, 127.4, 126.9, 126.4, 126.3, 126.0, 124.6, 123.2, 123.0, 122.9, 122.2, 119.8, 117.6, 108.1, 62.6, 61.1, 42.5, 28.1, 19.9, 19.4, 14.2, 14.0; Anal. calcd. for $C_{32}H_{30}N_2O_5$; C: 73.55; H: 5.79; N: 5.36. Found: C: 73.50; H: 5.84; N: 5.34.

Diethyl-9-bromo-2-(3,4-dimethylphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9v): Orange solid (73%), mp. 250 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2961, 1702, 1610, 1277, 1049, 962, 754; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.56-8.54 (m, 1H, Ar-H), 7.90-7.87 (m, 1H, Ar-H), 7.52-7.48 (m, 1H, Ar-H), 7.22-7.12 (m, 3H, Ar-H), 5.72 (s, 1H, vinylic-H), 4.49 (q, J = 7.2 Hz, 2H, -OCH_2), 4.34 (q, J = 7.2 Hz, 2H, -OCH_2), 2.27 (s, 3H, -CH_3), 2.26 (s, 3H, -CH_3), 1.59 (s, 6H, -CH_3), 1.43-1.33 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.4, 162.9, 161.3, 137.9, 137.2, 135.1, 133.1, 130.9, 130.4, 130.2, 129.2, 128.2, 126.9, 125.8, 124.5, 123.8, 122.9, 122.8, 120.1, 119.9, 119.2, 62.7, 61.3, 42.6, 28.1, 19.9, 19.4, 14.2, 14.0; Anal. calcd. for $C_{32}H_{29}BrN_2O_5$; C: 63.90; H: 4.86; N: 4.66. Found: C: 63.87; H: 4.87; N: 4.60.

Diethyl-9-chloro-2-(3,4-dimethylphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9w): Orange solid (70%), mp. 238 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2987, 1707, 1565, 1197, 1045, 857; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43 (d, J = 2.7 Hz, 1H, Ar-H), 8.01 (d, J = 9.3 Hz, 1H, Ar-H), 7.42 (dd, J = 9.2 Hz, J = 2.6 Hz, 1H, Ar-H), 7.29-7.25 (m, 2H, Ar-H), 7.21-7.18 (m, 1H, Ar-H), 5.78 (s, 1H, vinylic-H), 4.57 (q, J = 7.2 Hz, 2H, -OCH_2), 4.42 (q, J = 7.2 Hz, 2H, -OCH_2), 2.33 (s, 3H, -CH_3), 2.32 (s, 3H, -CH_3),1.67 (s, 6H, -CH_3), 1.48 (t, J = 7.2 Hz, 3H, -CH_3), 1.43 (t, J = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.9, 164.0, 163.5, 137.8, 135.5, 133.1, 132.5, 132.2, 131.0, 130.3, 127.3, 126.8, 125.9, 125.7, 124.6, 124.2, 123.6, 122.9, 122.9, 120.6, 119.0, 107.4, 62.7, 61.3, 42.6, 28.1, 19.9, 19.4, 14.2, 14.0; Anal. calcd. for $C_{32}H_{29}ClN_2O_5$; C: 69.00; H: 5.25; N: 5.03. Found: C: 69.07; H: 5.22; N: 4.99.

Diethyl-2-(2-isopropylphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9x): Greenish yellow solid (73%), mp. 224 ºC (EtOAc); IR (KBr, υ cm^{-1}): 3004, 1710, 1538, 1206, 998, 811; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.50-8.47 (m, 1H, Ar-H), 8.06-8.02 (m, 1H, Ar-H), 7.51-7.45 (m, 4H, Ar-H), 7.36-7.26 (m, 2H, Ar-H), 5.38(s, 1H, vinylic-H), 4.59 (q, J = 7.2 Hz, 2H, -OCH_2), 4.41 (q, J = 7.2 Hz, 2H, -OCH_2), 2.97-2.92 (m, 1H, -CH), 1.65 (s, 3H, -CH_3), 1.62 (s, 3H, -CH_3), 1.49 (t, J = 7.2 Hz, 3H, -CH_3), 1.42 (t, J = 7.2 Hz, 3H, -CH_3), 1.23 (d, J = 6.9 Hz, 3H, -CH_3), 1.15 (d, J = 6.9 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.9, 164.0, 163.8, 147.8, 134.1, 132.6, 132.5, 131.7, 129.4, 129.3, 129.2, 127.3, 126.7, 126.6, 126.6, 126.5, 126.2, 126.0, 124.5, 123.1, 123.0, 121.6, 119.8, 117.6, 108.1, 62.6, 61.0, 42.4, 28.2, 28.0, 27.9, 23.8, 23.6, 14.1, 14.0; Anal. calcd. for $C_{33}H_{32}N_2O_5$; C: 73.86; H: 6.01; N: 5.22. Found: C: 73.90; H: 5.98; N: 5.18.

Diethyl-9-bromo-2-(2-isopropylphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9y): Greenish yellow solid (70%), mp. 252 ºC (EtOAc); IR (KBr, υ cm^{-1}): 3005, 1709, 1622, 1315, 1032, 943; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.53 (s, 1H, Ar-H), 7.90 (d, J = 9 Hz, 1H, Ar-H), 7.50 (dd, J = 9.2 Hz, J = 2 Hz, 1H, Ar-H), 7.41-7.38 (m, 2H, Ar-H), 7.28-7.18 (m, 2H, Ar-H), 5.33 (s, 1H, vinylic-H), 4.48 (q, J = 6.9 Hz, 2H, -OCH_2), 4.33 (q, J = 6.9 Hz, 2H, -OCH_2), 2.85-2.82 (m, 1H, -CH), 1.56 (s, 3H, -CH_3), 1.53 (s, 3H, -CH_3), 1.42-1.32 (m, 6H, -CH_3), 1.23-1.14 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.4, 164.0, 163.4, 147.8, 133.0, 132.4, 130.1, 129.4, 129.3, 128.8, 127.0, 126.8, 126.6, 125.9, 124.6, 124.6, 123.6, 122.2, 120.7, 120.0, 119.2, 107.3, 62.7, 61.2, 42.5, 28.0, 27.9, 23.9, 23.6, 14.2, 13.9; Anal. calcd. for $C_{33}H_{31}BrN_2O_5$; C: 64.39; H: 5.08; N: 4.55. Found: C: 64.31; H: 5.04; N: 4.61.

Diethyl-2-(4-methoxyphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9z): Reddish yellow solid (76%), mp. 202 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2971, 1712, 1589, 1321, 1054, 868; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.50-8.47 (m, 1H, Ar-H), 8.08-8.03 (m, 1H, Ar-H), 7.51-7.46 (m, 2H, Ar-H), 7.33 (d, J = 8.4 Hz, 2H, Ar-H), 6.97 (d, J = 9 Hz, 2H, Ar-H), 5.67 (s, 1H, vinylic-H), 4.50 (q, J = 6.9 Hz, 2H, -OCH_2), 4.33 (q, J = 6.9 Hz, 2H, -OCH_2), 3.80 (s, 3H, -OCH_3), 1.62 (s, 6H, -CH_3), 1.40 (t, J = 7.2 Hz, 3H, -CH_3), 1.34 (t, J = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.5, 163.1, 162.8, 160.3, 136.0, 134.1, 133.3, 132.6, 132.3, 130.9, 129.9, 128.5, 126.6, 125.8, 124.2, 123.3, 121.5, 119.1, 119.0,

118.3, 117.6, 113.8, 108.0, 62.8, 61.6, 55.5, 41.1, 31.0, 14.1, 13.9; Anal. calcd. for $C_{31}H_{28}N_2O_6$; C: 70.98; H: 5.38; N: 5.34. Found: C: 71.00; H: 5.41; N: 5.30.

Diethyl-9-bromo-2-(4-methoxyphenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9a'): Reddish yellow solid (74%), mp. 218 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2984, 1709, 1535, 1405, 1143, 980, 764; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.47 (d, *J* = 2.4 Hz, 1H, Ar-H), 7.86 (d, *J* = 9 Hz, 1H, Ar-H), 7.48 (d, *J* = 6.9 Hz, 1H, Ar-H), 7.32 (d, *J* = 8.7 Hz, 2H, Ar-H), 6.94 (m, 2H, Ar-H), 5.66 (s, 1H, vinylic-H), 4.48 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.33 (q, *J* = 7.2 Hz, 2H, -OCH_2), 3.78(s, 3H, -OCH_3), 1.59 (s, 6H, -CH_3), 1.42-1.32 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.9, 163.9, 163.4, 158.4, 132.9, 132.0, 131.1, 130.1, 128.6, 128.2, 127.7, 127.6, 127.0, 125.9, 124.5, 124.4, 123.6, 122.6, 120.6, 119.9, 119.2, 114.6, 114.6, 107.2, 62.7, 61.2, 55.5, 42.6, 30.8, 28.0; Anal. calcd. for $C_{31}H_{27}BrN_2O_6$; C: 61.70; H: 4.51; N: 4.64. Found: C: 61.66; H: 4.47; N: 4.69.

Diethyl-2-(4-chlorophenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9b'): Yellow solid (68%), mp. 222 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2970, 1710, 1544, 1413, 1201, 894, 755; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.48-8.46 (m, 1H, Ar-H), 8.01-7.99 (m, 1H, Ar-H), 7.51-7.49 (m, 6H, Ar-H), 5.79 (s, 1H, vinylic-H), 4.59 (q, *J* = 6.9 Hz, 2H, -OCH_2), 4.42 (q, *J* = 6.9 Hz, 2H, -OCH_2), 1.69 (s, 6H, -CH_3), 1.52-1.41 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.1, 163.9, 134.4, 134.1, 132.2, 131.8, 130.6, 129.5, 127.6, 126.7, 126.4, 123.4, 122.7, 122.5, 119.7, 117.6, 107.8, 62.8, 61.2, 42.7, 28.1, 14.2, 14.0; Anal. calcd. for $C_{30}H_{25}ClN_2O_5$; C: 68.12; H: 4.76; N: 5.30. Found: C: 68.05; H: 4.80; N: 5.27.

Diethyl-9-bromo-2-(4-chlorophenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9c'): Yellow solid (67%), mp. 218 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2983, 1703, 1604, 1364, 1214, 897; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.58 (d, *J* = 2.1 Hz, 1H, Ar-H), 7.94 (d, *J* = 9 Hz, 1H, Ar-H), 7.59 (d, *J* = 9.3 Hz, 1H, Ar-H), 7.48-7.41 (m, 4H, Ar-H), 5.81 (s, 1H, vinylic-H), 4.57 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.42 (q, *J* = 7.2 Hz, 2H, -OCH_2), 1.68 (s, 6H, -CH_3), 1.51-1.41 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.5, 163.8, 163.5, 134.2, 133.0, 132.4, 130.4, 129.5, 128.8, 126.6, 124.3, 123.8, 123.1, 120.5, 120.2, 119.2, 107.0, 62.8, 61.3, 42.8, 28.1, 14.2, 14.0; Anal. calcd. for $C_{30}H_{24}BrClN_2O_5$; C: 59.28; H: 3.98; N: 4.61. Found: C: 59.33; H: 3.95; N: 4.62.

Diethyl-2-(4-bromophenyl)-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9d'): Yellow solid (68%), mp. 231 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2962, 1702, 1591, 1352, 1144, 1021, 902; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12-8.08 (m, 1H, Ar-H), 7.71-7.68 (m, 1H, Ar-H), 7.36-7.33 (m, 2H, Ar-H), 7.22-7.13 (m, 4H, Ar-H), 5.54 (s, 1H, vinylic-H), 4.30 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.13 (q, *J* = 7.2 Hz, 2H, -OCH_2), 1.41 (s, 6H, -CH_3), 1.21(t, *J* = 7.2 Hz, 3H, -CH_3), 1.15 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.3, 163.3, 163.1, 134.4, 133.4, 131.8, 131.2, 129.8, 127.1, 126.5, 125.8, 123.7, 122.9, 122.1, 122.0, 119.4, 119.2, 117.1, 107.1, 62.2, 60.6, 42.1, 27.5, 13.7, 13.4; Anal. calcd. for $C_{30}H_{25}BrN_2O_5$; C: 62.84; H: 4.39; N: 4.89. Found: C: 62.82; H: 4.36; N: 4.93.

Diethyl-4,4-dimethyl-2-naphthalen-1-yl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (9e'): Reddish yellow solid (74%), mp. 282 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2969, 1705, 1577, 1385, 1051, 927; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.51 (dd, *J* = 6 Hz, *J* = 3.3 Hz, 1H, Ar-H), 8.06 (dd, *J* = 6.3 Hz, *J* = 3.3 Hz, 1H, Ar-H), 7.96 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.76 (d, *J* = 8.1 Hz, 1H, Ar-H), 7.64-7.46 (m, 6H, Ar-H), 5.37 (s, 1H, vinylic-H), 4.60 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.41 (q, *J* = 7.2 Hz, 2H, -OCH_2), 1.62 (s, 3H, -CH_3), 1.60 (s, 3H, -CH_3), 1.52(t, *J* = 7.2 Hz, 3H, -CH_3), 1.42 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.0, 164.0, 163.8, 134.7, 134.2, 132.2, 132.0, 131.9, 130.6, 128.9, 128.4, 127.4, 126.7, 126.7, 126.5, 126.4, 126.4, 126.1, 125.7, 125.6, 124.5, 123.3, 123.0, 122.4, 119.9, 117.7, 108.1, 62.6, 61.1, 42.6, 28.0, 27.9, 14.2, 14.0; Anal. calcd. for $C_{34}H_{28}N_2O_5$; C: 74.98; H: 5.18; N: 5.14. Found: C: 75.03; H: 5.16; N: 5.12.

Diethyl-2-benzyl-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (10a): Reddish yellow solid (73%), mp. 182 ºC (EtOAc); IR (KBr, υ cm^{-1}): 3003, 1712, 1610, 1489, 1154, 988, 745; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43-8.41 (m, 1H, Ar-H), 8.02-7.98 (m, 1H, Ar-H), 7.46-7.43 (m, 2H, Ar-H), 7.32-7.31 (m, 4H, Ar-H), 7.28-7.22 (m, 1H, Ar-H), 5.50 (s, 1H, vinylic-H), 4.97 (s, 2H, -CH_2), 4.57 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.40 (q, *J* = 7.2 Hz, 2H, -OCH_2), 1.61 (s, 6H, -CH_3), 1.47 (t, *J* = 7.2 Hz, 3H, -CH_3), 1.41 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.2, 164.1, 163.8, 137.3, 134.0, 131.5, 130.7, 128.6, 128.6, 127.4, 127.2, 126.2, 125.7, 124.6, 122.9, 121.8, 119.9, 117.7, 108.3, 62.6, 61.1, 44.2, 42.4, 28.0, 14.2, 14.0; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $[C_{31}H_{28}N_2O_5Na]$: 531.1890. Found 531.1799. Anal. calcd. for $C_{31}H_{28}N_2O_5$; C: 73.21; H: 5.55; N: 5.51. Found: C: 73.27; H: 5.54; N: 5.49.

Diethyl-2-benzyl-9-bromo-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (10b): Reddish yellow solid (70%), mp. 210-212 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2979, 1709, 1541, 1488, 1161, 931, 832; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32-8.28 (m, 1H, Ar-H), 7.90-7.87 (m, 1H, Ar-H), 7.38-7.29 (m, 3H, Ar-H), 6.95-6.90 (m, 3H, Ar-H), 5.62 (s, 1H, vinylic-H), 4.48 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.31 (q, *J* = 7.2 Hz, 2H, -OCH_2), 3.74 (s, 2H, -CH_2), 1.58 (s, 6H, -CH_3), 1.39 (t, *J* = 7.2 Hz, 3H, -CH_3), 1.32 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.9, 164.0, 163.8, 158.3, 134.0, 131.4, 131.3, 129.4, 128.5, 127.6, 127.4, 127.1, 126.2, 126.0, 124.5, 124.2, 123.2, 122.8, 122.6, 121.6, 119.8, 117.6, 114.5, 108.0, 62.7, 61.1, 55.5, 42.5, 28.1, 14.2, 14.0; Anal. calcd. for $C_{31}H_{27}BrN_2O_5$; C: 63.38; H: 4.63; N: 4.77. Found: C: 63.40; H: 4.61; N: 4.72.

Dimethyl-2-benzyl-9-bromo-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (10c): Reddish yellow solid (70%), mp. 221 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2968, 1708, 1495, 1397, 1213, 935; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.38 (d, *J* = 2.1 Hz, 1H, Ar-H), 8.19 (d, *J* = 9.6 Hz, 1H, Ar-H), 7.57 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.43 (dd, *J* = 8.7

Hz, *J* = 2.1 Hz, 1H, Ar-H), 7.24-7.18 (m, 4H, Ar-H), 5.44 (s, 1H, vinylic-H), 4.86 (s, 2H, -CH_2), 3.83 (s, 3H, -OCH_3), 3.79 (s, 3H, -OCH_3), 1.54 (s, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.1, 164.4, 137.2, 133.1, 132.0, 130.5, 129.8, 128.7, 128.6, 127.5, 127.5, 124.5, 124.0, 123.9, 122.9, 120.5, 119.4, 118.5, 117.0, 115.6, 51.5, 44.2, 43.0, 27.6; Anal. calcd. for $C_{29}H_{23}BrN_2O_5$; C: 62.26; H: 4.14; N: 5.01. Found: C: 62.30; H: 4.15; N: 4.98.

Dimethyl-4,4-dimethyl-2-(4-methylbenzyl)-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (10d): Reddish yellow solid (75%), mp. 205-206 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2955, 1711, 1588, 1373, 1291, 1044, 833; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32-8.28 (m, 1H, Ar-H), 7.82-7.79 (m, 1H, Ar-H), 7.42-7.39 (m, 2H, Ar-H), 7.14-7.11 (m, 4H, Ar-H), 5.42 (s, 1H, vinylic-H), 4.86 (s, 2H, -CH_2), 4.02 (s, 3H, -OCH_3), 3.87 (s, 3H, -OCH_3), 2.28 (s, 3H, -CH_3), 1.50 (s, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.0, 162.0, 161.7, 137.1, 134.0, 134.0, 131.9, 131.1, 129.5, 129.3, 129.1, 128.3, 128.1, 127.5, 127.2, 126.4, 126.0, 123.0, 122.8, 122.0, 120.3, 115.6, 55.2, 53.3, 52.8, 44.0, 29.7, 21.1; Anal. calcd. for $C_{30}H_{26}N_2O_5$; C: 72.86; H: 5.30; N: 5.66. Found: C: 72.81; H: 5.34; N: 5.69.

Dimethyl-9-bromo-4,4-dimethyl-2-(4-methylbenzyl)-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (10e): Reddish yellow solid (72%), mp. 233 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2955, 1711, 1588, 1373, 1291, 1044, 833; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.52 (d, *J* = 2.4 Hz, 1H, Ar-H), 7.86 (d, *J* = 9.3 Hz, 1H, Ar-H), 7.48 (dd, *J* = 9.3 Hz, *J* = 2.4 Hz, 1H, Ar-H), 7.07-7.01(m, 4H, Ar-H), 5.46 (s, 1H, vinylic-H), 4.85 (s, 2H, -CH_2), 4.00 (s, 3H, -OCH_3), 3.85 (s, 3H, -OCH_3), 2.24 (s, 3H, -CH_3), 1.50 (s, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.6, 164.4, 163.9, 137.2, 134.0, 132.8, 132.0, 130.5, 130.1, 129.5, 129.4, 129.3, 129.2, 128.7, 128.3, 127.4, 126.3, 125.2, 124.6, 123.4, 122.3, 120.5, 120.0, 119.2, 53.3, 52.1, 44.0, 42.4, 28.0, 21.0; Anal. calcd. for $C_{30}H_{25}BrN_2O_5$; C: 62.84; H: 4.39; N: 4.89. Found: C: 62.88; H: 4.36; N: 4.91.

Diethyl-2-butyl-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (10f): Yellow solid (74%), mp. 170-171 ºC (EtOAc); IR (KBr, υ cm^{-1}): 2999, 1713, 1598, 1503, 1355, 1260, 1044, 865, 735; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39-8.36 (m, 1H, Ar-H), 7.95-7.93 (m, 1H, Ar-H), 7.42-7.39 (m, 2H, Ar-H), 5.54 (s, 1H, vinylic-H), 4.50 (q, *J* = 6.9 Hz, 2H, -OCH_2), 4.34 (q, *J* = 6.9 Hz, 2H, -OCH_2), 3.37-3.69 (m, 2H, -NCH_2), 1.53 (s, 6H, -CH_3), 1.43-1.34 (m, 6H, -CH_3), 1.19 (t, *J* = 7.2 Hz, 2H, -CH_2), 0.93-0.88 (m, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.2, 164.2, 163.9, 134.1, 133.0, 131.1, 130.0, 127.2, 126.4, 126.2, 125.5, 123.0, 122.4, 120.8, 117.7, 62.6, 61.1, 42.4, 40.3, 31.2, 28.2, 20.2, 14.2, 14.0, 13.8; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for [$C_{28}H_{30}N_2O_5$Na]: 497.2047. Found 497.2068. Anal. calcd. for $C_{28}H_{30}N_2O_5$; C: 70.87; H: 6.37; N: 5.90. Found: C: 70.81; H: 6.41; N: 5.88.

Diethyl-9-bromo-2-butyl-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (10g): Yellow solid (72%), mp. 183 ºC (EtOAc); IR (KBr, υ cm^{-1}): 3005, 1711, 1662, 1505, 1288, 1054, 963, 750; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46 (d, *J* = 1.8 Hz, 1H, Ar-H), 7.87 (d, *J* = 9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 9 Hz, *J* = 2.1 Hz, 1H, Ar-H), 5.58 (s, 1H, vinylic-H), 4.46 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.33 (q, *J* = 7.2 Hz, 2H, -OCH_2), 3.69 (t, *J* = 6.9 Hz, 2H, -NCH_3), 1.59 (s, 6H, -CH_3), 1.38-1.28 (m, 6H, -CH_3), 1.19-1.15 (m, 4H, -CH_2), 0.93-0.88 (m, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.7, 164.0, 163.4, 132.9, 131.8, 130.8, 129.9, 128.5, 125.5, 124.6, 124.6, 123.0, 121.4, 120.7, 119.8, 119.2, 107.8, 62.6, 61.2, 42.4, 40.2, 31.1, 28.1, 20.1, 14.0, 13.9, 13.8; Anal. calcd. for $C_{28}H_{29}BrN_2O_5$; C: 60.76; H: 5.28; N: 5.06. Found: C: 60.83; H: 5.27; N: 4.02.

Diethyl-2-cyclohexyl-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (10h): Yellow solid (68%), mp. 213-214 ºC (EtOAc); IR (KBr, υ cm^{-1}): 3012, 1715, 1608, 1364, 1199, 1014, 833, 742; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.70 (d, *J* = 6.6 Hz, 1H, Ar-H), 8.12 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.87-7.72 (m, 2H, Ar-H), 5.90 (s, 1H, vinylic-H), 4.84-4.25 (m, 4H, -OCH_2), 4.04-3.99 (m, 1H, -NCH), 2.13-1.99 (m, 6H, -CH_2), 1.86-1.79 (m, 4H, -CH_2), 1.55 (s, 6H, -CH_3), 1.52-1.42 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.2, 166.3, 154.3, 142.7, 131.8, 130.9, 130.5, 129.8, 129.3, 128.7, 127.5, 124.8, 124.0, 122.6, 117.7, 60.8, 60.4, 48.8, 42.8, 37.1, 31.0, 27.8, 25.4, 13.3, 13.1; Anal. calcd. for $C_{30}H_{32}N_2O_5$; C: 71.98; H: 6.44; N: 5.60. Found: C: 71.91; H: 6.41; N: 5.56.

Diethyl-9-bromo-2-cyclohexyl-4,4-dimethyl-1-oxo-2,4-dihydro-1H-2,6a-diazacyclopenta[fg]aceanthrylene-5,6-dicarboxylate (10i): Yellow solid (67%), mp. 232 ºC (EtOAc); IR (KBr, υ cm^{-1}): 3004, 1713, 1622, 1444, 1249, 1135, 952, 743; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.52 (d, *J* = 2.4 Hz, 1H, Ar-H), 8.26 (d, *J* = 9 Hz, 1H, Ar-H), 7.86 (d, *J* = 9 Hz, 1H, Ar-H), 5.86 (s, 1H, vinylic-H), 4.47 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.34 (q, *J* = 7.2 Hz, 2H, -OCH_2), 4.22-4.18 (m, 1H, -NCH), 1.87-1.84 (m, 6H, -CH_2), 1.73 (s, 4H, -CH_2), 1.53 (s, 6H, -CH_3), 1.43-1.33 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.2, 166.3, 154.3, 142.7, 134.3, 133.5, 129.9, 126.4, 123.4, 119.1, 118.4, 62.7, 61.2, 48.9, 42.5, 31.9, 29.7, 26.4, 25.4, 14.2, 14.1, 14.0; Anal. calcd. for $C_{30}H_{31}BrN_2O_5$; C: 62.18; H: 5.39; N: 4.83. Found: C: 62.11; H: 5.37; N: 4.86.

4,4-Dimethyl-2-p-tolyl-4,5-dihydro-2H-pyrrolo[2,3,4-kl]acridin-1-one (Intermediate **D** of **9a):**Light yellow solid; m.p. 223 °C (EtOAc); IR (KBr, υ cm^{-1}): 3075, 2957, 1719, 1466, 1354, 1141, 837, 732, 479; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.73 (d, *J* = 7.8 Hz, 1H, Ar-H), 8.17 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.78-7.72 (m, 1H, Ar-H), 7.68-7.63 (m, 1H, Ar-H), 7.40-7.33 (m, 4H, Ar-H), 5.59 (s, 1H, vinylic-H), 3.21 (s, 2H, -CH_2), 2.44 (s, 3H, -CH_3), 1.32 (s, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.8, 154.6, 149.7, 137.4, 133.6, 132.1, 130.0, 129.9, 129.4, 127.7, 126.4, 126.4, 126.3, 126.2, 125.1, 124.3, 122.6, 118.1, 44.2, 37.0, 30.9, 21.2; Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23%. Found: C, 81.18; H, 5.93; N, 8.24%.

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