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Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2011, **9**, 7196

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PAPER

Intramolecular Povarov reactions involving 3-aminocoumarins†

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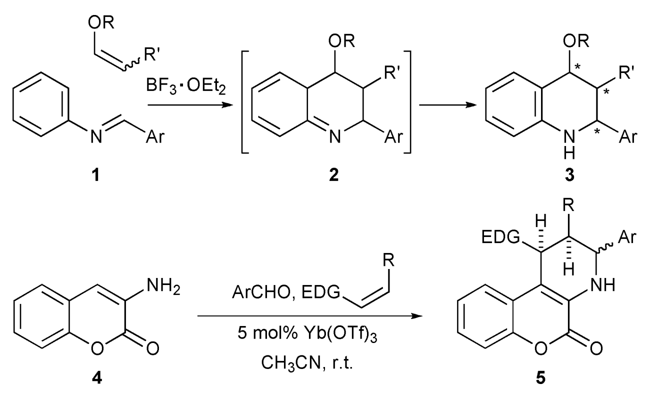
Received 1st June 2011, Accepted 18th July 2011
DOI: 10.1039/c1ob05867c

A series of pentacyclic heterocyclic systems (15 examples, 69–89%) have been synthesized using intramolecular Povarov reactions involving 3-aminocoumarins and *O*-cinnamylsalicylaldehydes. The Povarov adducts are formed with high selectivity for the *trans*,*trans* relative stereochemistry in the newly-formed [6,6] fused ring system. One example of a Povarov adduct featuring a new [6,5] fused ring system is reported. In this case, *cis*,*trans* relative stereochemistry was preferred.

Introduction

In its original form, the Povarov reaction involved a $BF_3 \cdot OEt_2$-catalysed formal inverse electron demand Diels–Alder (IEDDA) reaction between an aniline-derived imine **1** (a 2-azadiene) and a vinyl ether, followed by a double bond migration within the initial adduct **2** to afford a 1,2,3,4-tetrahydroisoquinoline **3** (Scheme 1).[1] Despite its impressive productivity (two new C–C bonds, one new ring and up to three new stereogenic centres are formed), it received only sporadic attention from the time of its discovery (1960s) until the 1990s, when a one-pot, three-component version involving *in situ* generation of the 2-azadiene **1** was developed.[2] Either as a two-step sequence or a multicomponent reaction, there are three points of diversity, which renders the Povarov reaction well-suited to diversity-oriented synthesis.[3] Over the past decade, various advances in the Povarov reaction have been reported,[4] including the broadening of its scope (with respect to all three components and the nature of the catalyst), progress toward the understanding of its mechanism and its application in total synthesis.[5]



Scheme 1 The Povarov reaction and examples involving 3-aminocoumarin (**4**).

We recently reported that 3-aminocoumarin (**4**) can function as the "aniline" component of the Povarov reaction, thereby giving rise to the formation of 1,2,3,4-tetrahydropyrido[2,3-*c*]coumarins such as **5** (Scheme 1).[6] We now report an intramolecular version of this reaction, which results in the efficient formation of pentacyclic heteroaromatic systems.

Results and discussion

The Povarov reaction can be rendered intramolecular by the tethering any two of the three components, or all three of them. To date, all reported intramolecular Povarov reactions involve the tethering of the dienophile and the aldehyde.[5b,7] However, as in the case of the intermolecular Povarov reaction, aromatic amines other than anilines have been used infrequently.[5b] The focus of this work was also the tethering of the aldehyde component and the dienophile component, but 3-aminocoumarins[8] were to be used as the aromatic amine. As such, it was envisioned that aldehydes of the general structure **6** would condense with 3-aminocoumarin (**4**) to afford 2-azadienes **7** bearing a pendant dienophile and then undergo a Type 1 intramolecular IEDDA reaction to afford, after double bond migration, polycyclic products **9** (Scheme 2).

For initial studies, 2-(allyloxy)benzaldehyde (**11**),[9] which was prepared in 87% yield by the *O*-alkylation of salicylaldehyde (**10**) with allyl bromide in the presence of anhydrous K_2CO_3 (Scheme 3), was chosen. Enal **11** was then subjected to reaction with 3-aminocoumarin[8] (**4**) in the presence of 5 mol% $Yb(OTf)_3$. No reaction was evident at room temperature (tlc analysis). This was not surprising because the C═C bond in the allyl group is electron neutral and would therefore not be expected to easily take part in an IEDDA reaction, even an intramolecular one. However, upon

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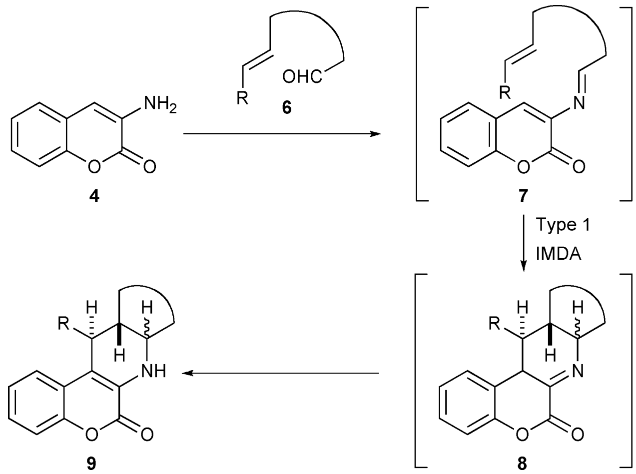
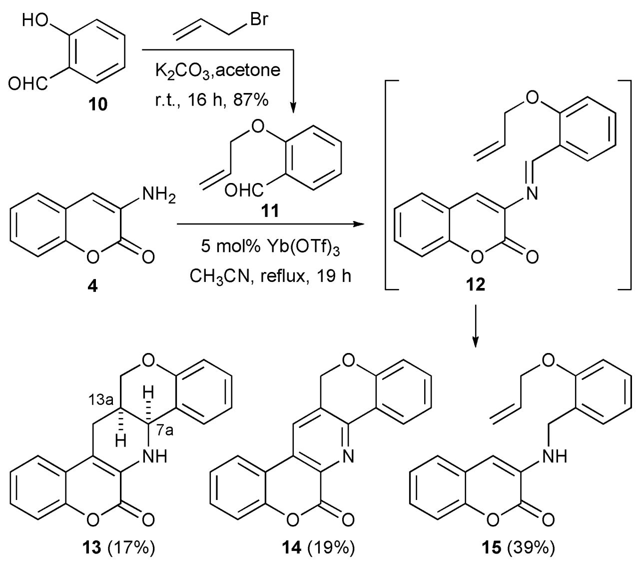
† Electronic supplementary information (ESI) available: experimental procedures and characterization data for compounds **23**, **32**, **33**, **35**, **37**, **54**, **59** and **60**; ^{1}H and ^{13}C spectra of all new compounds; CIF for **39**; COSY and HMQC spectra for compound **39**. CCDC reference number 828370. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob05867c



Scheme 2 Planned intramolecular Povarov reactions involving 3-aminocoumarin (**4**).



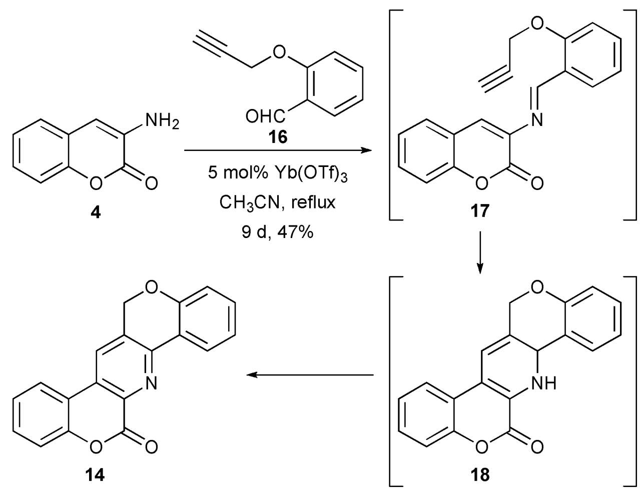
Scheme 3 Povarov reaction of 3-aminocoumarin (**4**) and enal **11**.

heating at reflux (CH_3CN, 19 h), three new products were isolated along with 23% recovery of 3-aminocoumarin (**4**) (Scheme 3).

One of these new products was determined to be the Povarov adduct **13** (17%). The *cis* relative stereochemistry was assigned on the basis of the small value of the coupling constant $J_{H(7a),H(13a)}$ (H(7a) is observed as a somewhat broad singlet, δ = 4.53) in conjunction with the value of the AM1-calculated dihedral angle (45–46°) for H(7a)–C(7a)–C(13a)–H(13a).[10] As described below, related systems with *trans* relative stereochemistry have coupling constants of *ca*. 11 Hz.

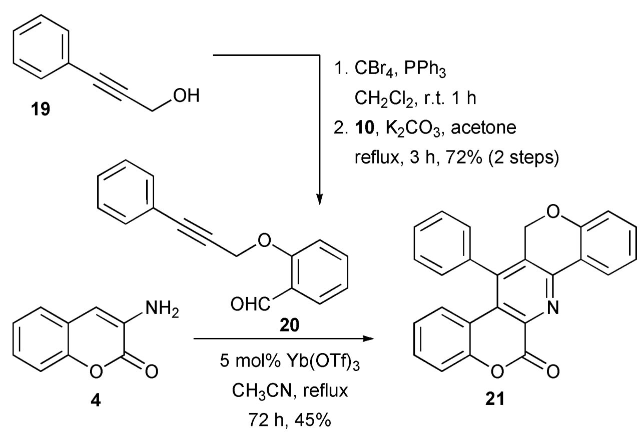
The other two products, **14** (19%) and **15** (39%), were determined to be an aromatized (dehydrogenated) version of **13** and a reduced form of the *in situ*-generated imine **12**, respectively. The observed 1 : 2 ratio for the yields of **14** and **15** is consistent with the notion that these two products are the result of transfer hydrogenation reactions from Povarov adduct **13** to the *in situ*-generated imine **12**. Similar transfer hydrogenations during Povarov reactions of aniline-derived 2-azadienes were reported recently.[11] Although the Povarov adduct **13** was isolated in only 17% yield, this result was encouraging, especially considering that the double bond in the allyl group is such a poor dienophile for the IEDDA reaction. Mechanistically, it is more likely that the IEDDA step of the Povarov reaction proceeds in a concerted fashion rather than a stepwise manner because the stepwise mechanism would require the intermediacy of a primary carbocation.

It was anticipated that the use of an alkyne-based dienophile for the intramolecular IEDDA reaction would more easily afford aromatized products because the Povarov adduct **18** (or the IEDDA adduct that precedes it) would only need to undergo one transfer hydrogenation step. Accordingly, 2-(propargyloxy)benzaldehyde (**16**)[12] was reacted with 3-aminocoumarin (**4**) in the presence of 5 mol% $Yb(OTf)_3$ in acetonitrile at reflux (Scheme 4). The reaction was sluggish, but the aromatized product **14** was isolated in 47% yield after 9 days of reaction. A substantial amount of 3-aminocoumarin (**4**) (19%) was recovered, but no reduced product corresponding to **15** was isolated. This may indicate that the oxidation of **18** (or the IEDDA adduct that precedes it) occurs by a process other than transfer hydrogenation.



Scheme 4 Povarov reaction of 3-aminocoumarin (**4**) and ynal **16**.

With the intention of facilitating the IEDDA step, aldehyde **20**,[13] which bears a pendant phenylethynyl dienophile, was synthesized in two steps from 3-phenylprop-2-yn-1-ol (**19**)[14] (Scheme 5). Ynol **19** was first converted into the corresponding bromide upon treatment with CBr_4/PPh_3[15] and the crude product was used to

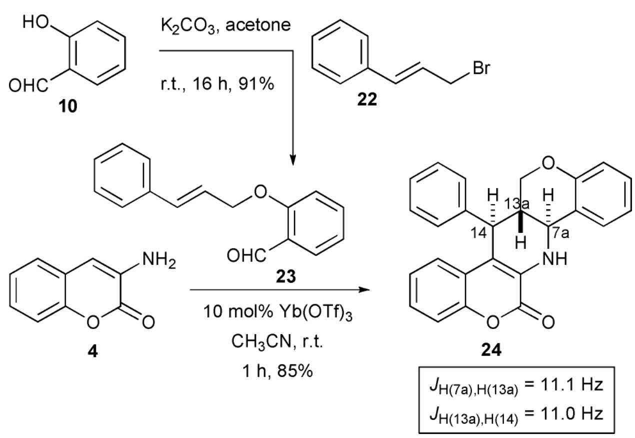


Scheme 5 Synthesis of aldehyde **20** and its Povarov reaction with 3-aminocoumarin (**4**).

O-alkylate salicylaldehyde (**10**). This afforded aldehyde **20** in 72% yield over 2 steps. Reaction of **20** with 3-aminocoumarin (**4**) in the presence of 10 mol% $Yb(OTf)_3$ resulted in no reaction after 3 h at room temperature (tlc analysis), so the reaction was heated. After 72 h at reflux, the aromatized product **21** (43%) was isolated along with 27% of recovered 3-aminocoumarin (**4**). No reduced product resulting from transfer hydrogenation was obtained.

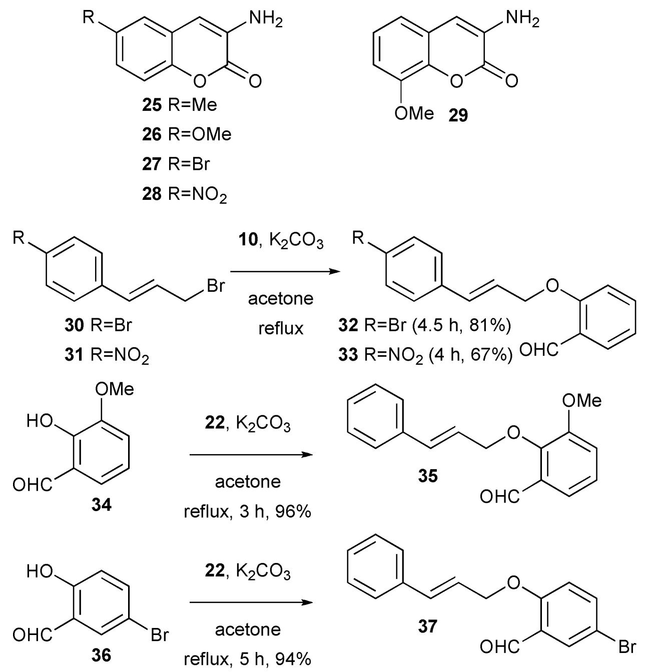
Despite the very limited benefit of adding a phenyl group to an acetylenic dienophile, the same tactic was used for the corresponding olefinic dienophile. This was predicated on the observation that, during our investigations on the intermolecular Povarov reactions,[6] styrenes were found to react well with preformed coumarin-fused 2-azadienes at room temperature with moderate to good levels of *endo*/*exo* selectivity.

2-(Cinnamyloxy)benzaldehyde (**23**) was prepared by the *O*-alkylation of salicylaldehyde (**10**) with cinnamyl bromide (**22**)[15] (Scheme 6). When **23** was subjected to reaction with 3-aminocoumarin (**4**) in the presence of 5 mol% $Yb(OTf)_3$ in acetonitrile at room temperature, pentacyclic Povarov adduct **24** was isolated in 56% yield after just 1 h. The yield could be improved to 85% by using 10 mol% of the catalyst. This reaction also had the practical advantage that the **24** precipitated as the reaction progressed. As a result, it could be isolated simply by suction filtration. The magnitude of the coupling constants around the newly-formed six-membered ring ($J_{H(7a),H(13a)}$ = 11.1 Hz, $J_{H(13a),H(14)}$ = 11.0 Hz) were key indicators of the *trans*,*trans* relative stereochemistry. Traces of what may be another diastereomer were observed in the ^{1}H NMR spectrum of the crude reaction mixture, but attempts to isolate this compound by flash chromatography were unsuccessful.



Scheme 6 Synthesis of aldehyde **23** and its Povarov reaction with 3-aminocoumarin (**4**).

As in the case of the intermolecular Povarov reaction, the intramolecular version described above offers three points of diversity, *i.e.* the 3-aminocoumarin unit, the salicyclaldehyde unit that connects the dienophile to diene and the cinnamyl unit (the dienophile). As described below, a series of pentacyclic heterocycles was generated using 3-aminocoumarins **4** and **25**–**29**, which were available from previous work in our group,[8] and aldehydes **23**, **32**, **33**, **35** and **37** (Scheme 7). Aldehydes **32**, **33**, **35** and **37** were synthesized in good to excellent yields using *O*-alkylation reactions involving cinnamyl bromides **22**, **30** and **31** and commercially available salicylaldehydes **10**, **34** and



Scheme 7 Synthesis of aldehydes **32**, **33**, **35** and **37**.

36 (Scheme 7). Although also commercially available, cinnamyl bromide (**22**) was prepared in two steps from ethyl cinnamate using literature procedures.[16] Cinnamyl bromides **30** and **31** were prepared from 4-bromobenzaldehyde and 4-nitrobenzaldehyde, respectively, in three steps using published procedures.[16,17,18]

The results of the intramolecular Povarov reactions are summarized in Table 1. As with the parent reaction (Scheme 6 and Table 1, Entry 1), the reaction between 3-aminocoumarin (**4**) and aldehyde **32** (Table 1, Entry 2) proceeded smoothly at room temperature to afford **38** as a single diastereoisomer (84%). The slightly longer reaction time is consistent with the mild electron withdrawing effect of the bromo group on any developing positive charge at the transition state of the IEDDA step. By the same token, the replacement of the bromo substituent with a much stronger electron withdrawing group (NO_2) (Table 1, Entry 3) caused the reaction time to increase to 5 days with a small decrease in the yield (**39**, 72%). When the reaction of **4** and nitroaldehyde **33** was conducted at reflux, the starting materials were consumed after 16 h and **39** was isolated in 49% yield.

A single crystal X-ray structure determination of **39** confirmed the NMR-based assignment of the *trans*,*trans* relative stereochemistry. The pentacyclic skeleton is relatively flat and the molecules are grouped into hydrogen bonded pairs of enantiomers (Fig. 1). More specifically, the H–N–C–C=O unit of one enantiomer hydrogen bonds in a complementary fashion with that of its antipode. In the resulting box-like arrangement of the interacting O and H atoms, the intermolecular O–H distances (2.29(3) Å) are almost the same as the intramolecular O–H distances (2.38(3) Å). The N(1)–H(1)–O(2′) bond angle is 167(3)°.

Aldehydes **35** and **37**, which bear substituents on the benzaldehyde moiety, reacted with 3-aminocoumarin (**4**) to afford Povarov adducts **40** (Table 1, Enty 4, 89%) and **41** (Table 1, Entry 5, 69%), respectively. A series of 3-aminocoumarin derivatives **25**–**29** was then reacted with aldehydes **23** and **35** to afford Povarov adducts

Table 1 Intramolecular Povarov reactions leading to pentacyclic compounds **24** and **38–51**[a]

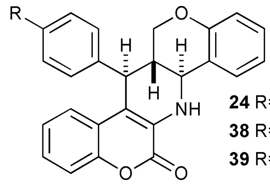
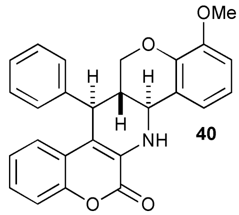
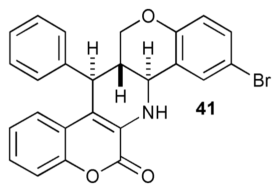
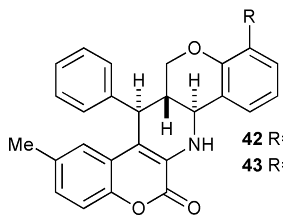
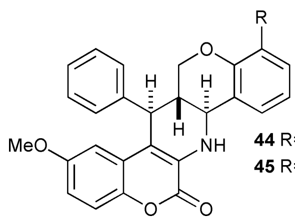
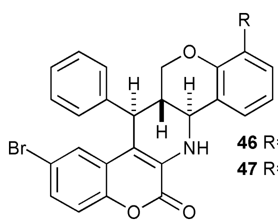
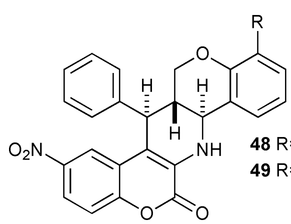
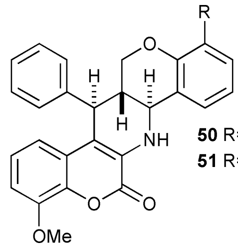
Entry	Reactants	Time (h)	Product	Yield (%)[b]
1	**4**, **23**	1	 **24** R=H, **38** R=Br, **39** R=NO_2	85
2	**4**, **32**	2	 **40**	84
3	**4**, **33**	120[c]		72[c]
4	**4**, **35**	1		89
5	**4**, **37**	2	 **41**	69
6	**25**, **23**	2	 **42** R=H, **43** R=OMe	87
7	**25**, **35**	2	 **44** R=H, **45** R=OMe	84
8	**26**, **23**	2		84
9	**26**, **35**	2	 **46** R=H, **47** R=OMe	85
10	**27**, **23**	1		78
11	**27**, **35**	1	 **48** R=H, **49** R=OMe	75
12	**28**, **23**	0.5		82

Table 1 (*Contd.*)

Entry	Reactants	Time (h)	Product	Yield (%)[b]
13	**28**, **35**	0.5	 **50** R=H, **51** R=OMe	78
14	**29**, **23**	2		86
15	**29**, **35**	2		86

[a] See Scheme 6 for reaction conditions. [b] Isolated yields. [c] 16 h reaction time and 49% yield when conducted at reflux.

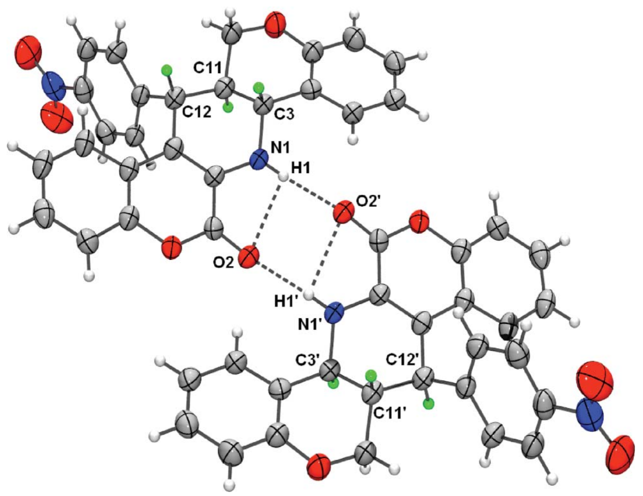
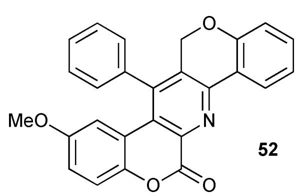


Fig. 1 ORTEP representation (50% thermal ellipsoids) of **39** in the crystal. C(3), C(11) and C(12) (crystallograhpic numbering) correspond to C(7a), C(13a) and C(14), respectively (systematic numbering).

42–51 (Table 1, Entries 6–15) in 75–87% yield. As before, the *trans*,*trans* product could be isolated by suction filtration of the reaction mixture. On only one occasion, very small amounts of two minor products were isolated by flash chromatography of the filtrate (Entry 8). One of these products was identified (^{1}H NMR, IR, MS) as the aromatized product **52** (2%). A ^{13}C NMR spectrum of this compound could not be obtained due to its low solubility in common organic solvents. Only traces (<1 mg, <1%) of the other product were isolated. LC–MS (APCI(+)) analysis (m/z = 412, M$^+$ + 1) suggested that it was an isomer of **44**.



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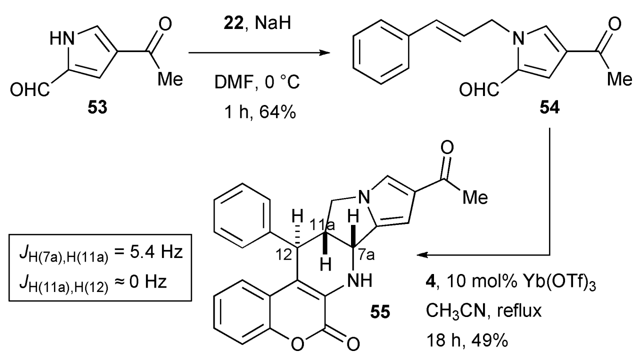
With regard to the mechanism, the *trans*,*trans* relative stereochemistry of the products is consistent with either a highly *endo*/*exo*-selective,[19] concerted IEDDA step or a stepwise ring closure that leads very selectively to the most stable product. In this case, a stepwise mechanism is reasonable because it involves the intermediacy of a secondary benzylic carbocation.

In all of the above examples, a new fused [6,6] ring system is formed. To gain access to fused [6,5] ring systems, diene–dienophile combinations with a one atom shorter tether would be required. Accordingly, pyrrole-based aldehyde **53**[20] was *N*-alkylated with cinnamyl bromide (**22**) in the presence of NaH in DMF at 0 °C to afford ketoaldehyde **54** (64%) (Scheme 8). Inferior results were obtained using other base/solvent combinations, *i.e.* KOH/CH_2Cl_2, reflux, 72 h (10%); NaH/THF, reflux, 4 h (16%); KOH/DMF, r.t., 24 h (33%).

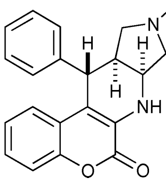
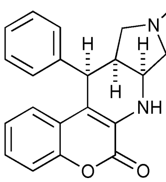
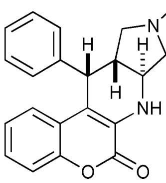
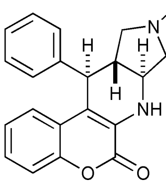


Scheme 8 Synthesis of ketoaldehyde **54** and its intramolecular Povarov reaction with 3-aminocoumarin (**4**).

Reaction of ketoaldehyde **54** with 3-aminocoumarin (**4**) under the standard Povarov reaction conditions was slow at room temperature, but went to completion upon heating at reflux for 18 h. Povarov adduct **55** was isolated in 49% yield (Scheme 8). In contrast to all of the previous examples, which have *trans*,*trans* relative stereochemistry, **55** has *cis*,*trans*[21] relative stereochemistry. The stereochemical outcome is consistent either with a concerted IEDDA step, in which the *endo*/*exo* selectivity[19] is opposite to that of the previous examples, or a stepwise ring closure leading to the most stable product (see below).

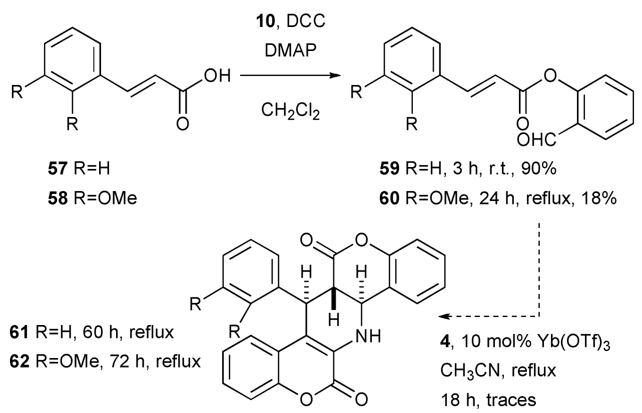
The *cis*,*trans* relative stereochemistry in **55** was assigned on the basis of AM1-calculated structures of model system **56** (compound **55** without the acetyl group) and the observed values of the coupling constants around the newly-formed six-membered ring (Table 2). Of the four possible diastereomers of **56**,[21] *cis*,*trans*-**56**

Table 2 AM1-calculated relative energies of the four possible diastereomers of **56**

		Dihedral Angles (°)	
Isomer	Relative Energy (kcal mol^{-1})	H(7a)–C(7a)–C(11a)–H(11a)	H(11a)–C(11a)–C(12)–H(12)
 *cis,trans*-**56**	0.0	−12.6	−91.4
 *cis,cis*-**56**	5.4	19.6	−28.6
 *trans,cis*-**56**	9.1	165.0	50.5
 *trans,trans*-**56**	9.8	164.0	173.7

is about 5 kcal mol^{-1} lower in energy than *cis*,*cis*-**56** and 9–10 kcal mol^{-1} lower in energy than *trans*,*cis*-**55** and *trans*,*trans*-**56**. The calculated H(7a)–C(7a)–C(11a)–H(11a) and H(11a)–C(11a)–C(12)–H(12) dihedral angles (−12.6° and −91.4°, respectively) for *cis*,*trans*-**56** are much more consistent with the observed coupling constants ($J_{H(7a),H(11a)}$ = 5.4 Hz and $J_{H(11a),H(12)} \approx 0$ Hz) than for any of the other three isomers of **56**.

As a final avenue of investigation, the possibility of conducting intramolecular Povarov reactions with electron deficient dienophiles was investigated. This was prompted by the observation that aldehyde **33**, which has a somewhat electron deficient dienophile, still participated in the Povarov reaction, albeit slowly. 2-Formylphenyl cinnamate (**59**), which differs from **33** by virtue of the carbonyl group adjacent to the double bond, was selected for initial studies. It was synthesized (90%) from salicylaldehyde (**10**) and *trans*-cinnamic acid (**56**) using slightly modified literature conditions (Scheme 9),[22] but its reaction with **4** did not show any signs of progress after 3 h at room temperature. After heating the reaction at reflux for 60 h, tlc analysis showed the presence of traces of a new compound and a small amount of a white precipitate had formed. LC–MS (APCI(+)) analysis of this precipitate (~5 mg) showed a peak (*m*/*z* = 395) corresponding to the molecular ion of the expected Povarov adduct **61**, but the ^{1}H NMR spectrum of this precipitate was complicated due to the apparent presence of more than one compound. Nevertheless, it clearly showed the presence



Scheme 9 Attempted intramolecular Povarov reaction of aldehydes **59** and **60** with 3-aminocoumarin (**4**).

of signals attributable to the expected Povarov adduct **61** with *trans*,*trans* relative stereochemistry. The characteristic signals in the ^{1}H NMR spectrum were observed at *δ* 5.56 (s, 1H), 4.99 (d, *J* = 10.0 Hz, 1H), 4.45 (d, *J* = 10.9 Hz, 1H) and 3.18 (m, 1H). Attempts to purify this poorly-soluble compound were unsuccessful.

In an effort to facilitate the IEDDA step of the Povarov reaction and also enhance the solubility of the product, 2,3-dimethoxycinnamic acid (**58**) was converted into its

2-formylphenyl ester **60** upon reaction with salicylaldehyde (**10**), albeit at low yield (Scheme 9). However, the presence of the methoxy groups did not appear to have any beneficial effect on the attempted Povarov reaction. As before, the reaction did not show any signs of progress at room temperature and, after heating at reflux for 72 h, only traces of a new product were observed (tlc analysis). It may be that any benefit from the electron-donating methoxy groups may be mitigated to some extent by steric crowding. A small amount (~5 mg) of a poorly-soluble white product was again isolated by suction filtration and it showed LC–MS (APCI(+)) (m/z = 455) and ^{1}H NMR signals (4.75 (d, J = 10.0 Hz), 4.44 (d, J = 10.0 Hz) and 3.39 (br m) that are consistent with the expected Povarov adduct **62** with *trans*,*trans* relative stereochemistry. The low solubility again precluded purification.

Conclusions

Intramolecular Povarov reactions involving a variety of 3-aminocoumarins and benzaldehydes bearing a pendant dienophile were found to proceed under mild conditions and with high *endo*/*exo* selectivity. Using this methodology, fifteen new heterocycles with a common pentacyclic core were synthesized.

Experimental section

General methods

All reactions were carried out without inert gas protection, unless otherwise mentioned. THF was dried and distilled over sodium/benzophenone. All other chemicals, including solvents, were used as received, without further purification. Thin layer chromatography (tlc) was performed on MN PolyGram precoated silica gel plates using 254 nm UV visualization. Flash chromatography was performed on silica gel columns. Melting points were recorded on Fisher–Johns apparatus and are uncorrected. All proton and carbon assignments are based on 2-D experiments (COSY, HMQC, HMBC, see ESI for a representative example). ^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE spectrometer at 500.133 MHz and 125.770 MHz, respectively. Peaks reported are relative to internal standards: TMS (δ = 0.00) for ^{1}H and $CDCl_3$ (δ = 77.23), CD_2Cl_2 (δ = 54.00) or DMSO-d_6 (δ = 39.51) for ^{13}C spectra. Reported multiplicities are apparent. Infrared spectra were obtained on Bruker Tensor 27 instrument using neat samples. Low-resolution mass spectra were obtained using Agilent 1100 series LC/MS chromatographic system and high-resolution mass spectra were obtained using a Waters GCT Permier Micromass mass spectrometer using neat samples. The X-ray crystal structure of **39** was obtained on an AFC8-Saturn single crystal X-ray diffractometer.

1. Synthesis of 3-(2-Allyloxybenzylamino)chromen-2-one (15), (7a*S,13a*R**)-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (13) and 5,6,12,13-tetrahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (14).** To a clear, colorless solution of enal **11** (0.087 g, 0.54 mmol) in acetonitrile (5.0 mL) was added 3-aminocoumarin (**4**) (0.082 g, 0.51 mmol) at room temperature followed by the addition of $Yb(OTf)_3$ (0.016 g, 0.026 mmol). The clear, colorless solution turned into a clear yellow solution instantaneously. The reaction mixture was stirred at room temperature for 3 h and then heated at reflux for 19 h. The solvent was removed under reduced pressure and the yellow residue was subjected to flash chromatography (0–10% ethyl acetate/petroleum ether) to afford **15** (0.061 g, 39%) as a pale yellow gum, **13** (0.026 g, 17%) as an off-white solid, **14** (0.029 g, 19%) as a white solid and recovered **25** (0.014 g, 17%) as an off-white solid.

15: $\delta_H(CDCl_3)$ = 7.29–7.24 (m, 4H), 7.22–7.15 (m, 2H), 6.95–6.90 (m, 2H), 6.38 (s, 1H, H-4), 6.13–6.06 (m, 1H, H-9′), 5.44 (dd, J = 16.8, 1.3 Hz, 1H, H-10′ *trans* to H-9′), 5.36 (br s, 1H, H-1′), 5.31 (dd, J = 10.8, 1.7 Hz, 1H, H-10′ *cis* to H-9′), 4.62 (dd, J = 3.6, 1.8 Hz, 2H, H-2′), 4.43 (d, J = 5.6 Hz, 2H, H-8′) ppm; $\delta_C(CDCl_3)$ = 159.9 (C-6), 156.5, 148.1, 133.3, 133.2, 128.94, 128.89, 125.8, 125.2, 124.7, 122.0, 121.0, 117.8, 116.2 (C-4), 111.9, 105.5, 69.0 (C-2′), 42.7 (C-8′) ppm; IR ν = 3412 (w), 1705 (s), 1627 (m), 1602 (w), 1574 (w), 1504 (m), 1456 (m), 1355 (w), 1287 (m), 1239 (m), 1167 (m), 1117 (w) cm^{-1}; MS m/z (relative intensity) = 308 (M^++1, 21), 147 (M^+−160, 100); HRMS [M^+] calcd for $C_{19}H_{17}NO_3$ 307.1208 found 307.1211. **13**: mp = 212–214 °C (ethyl acetate/hexanes); $\delta_H(CDCl_3)$ = 7.38–7.37 (m, 1H), 7.29–7.25 (m, 3H), 7.24–7.21 (m, 2H), 6.93 (t, J = 7.0 Hz, 1H), 8.87 (d, J = 8.0 Hz, 1H), 5.07 (s, 1H, H-7), 4.53 (s, 1H, H-7a), 4.22–4.14 (m, 2H, H-13), 3.03 (dd, J = 18.3, 6.8 Hz, 1H, H-14β), 2.72 (dd, J = 18.5, 4.5 Hz, 1H, H-14α), 2.68–2.64 (m, 1H, H-13a) ppm; $\delta_C(CDCl_3)$ = 158.3 (C-6), 153.9, 148.1, 129.9, 129.1, 126.5, 126.2, 124.8, 122.6, 121.5, 121.3, 121.1, 117.1, 116.7, 114.6, 66.7 (C-13), 47.5 (C-7a), 28.7 (C-14), 22.8 (C-13a) ppm; IR ν = 3331 (m), 1701 (s), 1612 (w), 1578 (m), 1501 (w), 1484 (m), 1469 (w), 1431 (m), 1339 (w), 1322 (w), 1289 (m), 1255 (m), 1232 (m), 1195 (s), 1127 (w), 1074 (w), 1029 (m), 1009 (w) cm^{-1}; MS m/z (relative intensity) = 307 (M^++2, 21), 306 (M^++1, 100), 304 (14), 302 (72), 174 (17); HRMS [M^+] calcd for $C_{19}H_{15}NO_3$ 305.1052 found 305.1048. **14**: mp = 222–224 °C; δ_H(DMSO-d_6) = 8.79 (s, 1H), 8.30 (m, 1H), 8.24 (dd, J = 7.6, 1.0 Hz, 1H), 7.64–7.61 (m, 1H), 7.48–7.46 (m, 3H), 7.21 (t, J = 8.0 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 5.50 (s, 2H) ppm; δ_C(DMSO) = 157.9 (C-6), 156.6, 150.5, 149.1, 137.3, 132.6, 132.1, 131.2, 130.8, 127.6, 124.8, 123.8, 122.6, 121.6, 117.3, 117.1, 116.9, 67.2 (C-13) ppm; IR ν = 1742 (s), 1608 (m), 1509 (s), 1432 (m), 1339 (s), 1177 (w), 1026 (s) cm^{-1}; MS m/z (relative intensity) = 303 (M^++2, 23), 302 (M^++1, 100); HRMS [M^+] calcd for $C_{19}H_{11}NO_3$ 301.0739 found 301.0741.

2. Synthesis of 5,6,12,13-tetrahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (14). To a clear, colorless solution of 3-aminocoumarin (**4**) (0.161 g, 1.00 mmol) in acetonitrile (10.0 mL) was added ynal **16** (0.168 g, 1.05 mmol) followed by $Yb(OTf)_3$ (0.031 g, 5 mol%). The reaction mixture was heated at reflux for 9 d, during which time the reaction mixture became a yellow suspension. After cooling to room temperature, the reaction mixture was subjected to suction filtration and the solids were washed with cold dichloromethane and air-dried to afford **14** as a yellow solid (0.111 g, 37%). The filtrate was concentrated and purified by flash chromatography on silica gel (20% ethyl acetate/light petroleum ether) to afford a second batch of **14** (0.029 g, 10%) as an off-white solid and recovered 3-aminocoumarin (**4**) (0.030 g, 19%) as an off-white solid. Combined yield of **14** = 0.140 g (47%).

3. Synthesis of 14-Phenyl-5,6,12,13-tetrahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (21). To a clear, colorless solution of 3-aminocoumarin (**4**) (0.081 g, 0.50 mmol) in acetonitrile (5.0 mL) was added ynal **20** (0.125 g, 0.525 mmol) and $Yb(OTf)_3$ (0.031 g, 10 mol%). The resulting yellow suspension was stirred at room temperature for 3 h. The reaction mixture was then heated at reflux for 72 h. The mixture was cooled to room temperature. The precipitate was isolated by suction filtration, washed with acetonitrile and air-dried to afford **21** as a white solid (0.085 g, 43%). mp = 277–279 °C (decomp); $\delta_H(CD_2Cl_2)$ = 8.35 (d, *J* = 7.8 Hz, 1H), 7.55–7.54 (m, 3H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.28–7.27 (m, 2H), 7.23–7.22 (m, 2H), 7.10 (t, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 6.77–6.72 (m, 2H), 4.94 (s, 2H) ppm; $\delta_C(CD_2Cl_2)$ = 159.3 (C-6), 157.2, 151.6, 150.2, 144.6, 139.2, 136.8, 133.2, 131.6, 130.9, 130.8, 130.0, 129.5, 128.5, 127.9, 126.3, 124.3, 123.3, 122.6, 118.3, 118.1, 117.5, 66.7 (C-13) ppm; MS *m/z* (relative intensity) = 379 (M^++2, 29), 378 (M^++1, 100); HRMS [M^+] calcd for $C_{25}H_{15}NO_3$ 377.1052 found 377.1049.

4. Synthesis of (7a*R,13a*R**,14*S**)-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (24).** To a clear colorless solution of 3-aminocoumarin (**4**) (0.097 g, 0.60 mmol) in acetonitrile (6.0 mL) was added enal **23** (0.15 g, 0.63 mmol) followed by $Yb(OTf)_3$ (0.037 g, 10 mol%). The resulting clear yellow solution was stirred at room temperature for 1 h. The reaction turned into a pale yellow suspension over the course of the reaction. The product was isolated by suction filration to afford **24** as a white solid (0.195 g, 85%). mp = 268–269 °C; $\delta_H(CD_2Cl_2)$ = 7.36 (d, *J* = 7.7 Hz, 1H), 7.30–7.28 (m, 2H), 7.27–7.26 (m, 2H), 7.25–7.23 (m, 3H), 7.21–7.19 (m, 1H), 7.07–7.05 (m, 1H), 6.98–6.95 (m, 2H), 6.85 (d, *J* = 7.4 Hz, 1H), 5.49 (s, 1H, H-7), 4.42 (d, *J* = 11.1 Hz, 1H, H-7a), 4.36 (dd, *J* = 10.6, 3.1 Hz, 1H, H-13α), 4.11 (t, *J* = 10.6 Hz, 1H, H-β), 3.98 (d, *J* = 11.0 Hz, 1H, H-14), 2.44–2.39 (m, 1H, H-13a) ppm; $\delta_C(CD_2Cl_2)$ = 159.1 (C-6), 154.4, 150.5, 149.0, 142.5, 132.1, 129.5, 129.4, 129.1, 126.7, 125.7, 125.5, 124.7, 124.2, 121.5, 121.2, 120.8, 117.3, 116.7, 66.9 (C-12), 52.0 (C-7), 45.0 (C-13a), 44.0 (C-14) ppm; IR *ν* = 3334 (m), 1702 (s), 1618 (w), 1581 (w), 1492 (m), 1475 (w), 1445 (w), 1347 (m), 1322 (m), 1287 (w), 1252 (m), 1229 (m), 1191 (s), 1129 (w), 1116 (w), 1074 (w), 1050 (m), 1028 (w), 1012 (w) cm^{-1}; MS *m/z* (relative intensity) = 383 (M^++2, 14), 382 (M^++1, 53), 380 (29), 379 (29), 378 (100); HRMS [M^+] calcd for $C_{25}H_{19}NO_3$ 381.1365, found 381.1371.

5. General procedure for the intramolecular Povarov reactions. To a solution of 3-aminocoumarin in acetonitrile (~0.1 M solution) was added enal (1.05 equiv) and $Yb(OTf)_3$ (10 mol%) at room temperature. The resulting mixture was stirred at room temperature or heated at reflux as specified until complete consumption of the starting material (3-aminocoumarin) was observed by tlc analysis. The resulting slurry was subjected to suction filtration and the solids were washed with cold acetonitrile and air-dried to afford the product. The filtrate was subjected to flash chromatography depending upon the result of LC/MS analysis.

6. Synthesis of (7a*R,13a*R**,14*S**)-14-(4-bromophenyl)- 5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (38).** According to the general procedure, 3-aminocoumarin (**4**) (0.135 g, 0.840 mmol), enal **32** (0.28, 0.88 mmol) and $Yb(OTf)_3$ (0.052 g, 10 mol%) afforded **38** as a white solid (0.32 g, 84%). mp = 276–278 °C; $\delta_H(CD_2Cl_2)$ = 7.48 (d, *J* = 7.1 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.26–7.22 (m, 2H), 7.16–7.15 (m, 2H), 7.07 (t, *J* = 6.9 Hz, 1H), 7.01–6.98 (m, 2H), 6.87 (d, *J* = 7.1 Hz, 1H), 5.51 (s, 1H, H-7), 4.43 (d, *J* = 10.8 Hz, 1H, H-7a), 4.34 (dd, *J* = 10.4 Hz, 2.7 Hz, 1H, H-13α), 4.10 (*t*, *J* = 10.4 Hz, 1H, H-13β), 3.97 (d, *J* = 10.9 Hz, 1H, H-14), 2.41–2.34 (m, 1H) ppm; due to very low solubility of this compound, a satisfactory ^{13}C NMR spectrum could not be obtained; the following major signals were observed: $\delta_C(CD_2Cl_2)$ = 141.7, 132.6, 132.0, 129.5, 126.8, 125.4, 124.5, 124.4, 121.3, 117.3, 116.8, 66.7 (C-13), 51.9 (C-7a), 44.9 (C-13a), 43.4 (C-14) ppm; IR *ν* = 3389 (w), 1704 (s), 1628 (m), 1555 (w), 1462 (m), 1457 (w), 1428 (w), 1346 (m), 1322 (w), 1281 (w), 1260 (w), 1238 (m), 1189 (m), 1172 (m), 1051 (m) cm^{-1}; HRMS [M^+] calcd for $C_{25}H_{18}NO_3Br$ 459.0470, found 459.0471.

7. Synthesis of (7a*R,13a*R**,14*S**)-14-(4-nitrophenyl)- 5,6,7,7a,12,13,13a,14-octahydro-5,12–dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (39).** According to the general procedure, 3-aminocoumarin (**4**) (0.055 g, 0.34 mmol), enal **33** (0.10 g, 0.36 mmol) and $Yb(OTf)_3$ (0.021 g, 10 mol%) afforded **39** as a pale yellow solid (0.104 g, 72%). mp = 239–240 °C; $\delta_H(CD_2Cl_2)$ = 8.17 (m, 2H), 7.43–7.41 (m, 3H), 7.34 (d, *J* = 7.4 Hz, 1H), 7.25–7.18 (m, 2H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.94 (t, *J* = 7.2 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 2H), 5.55 (s, 1H, H-7), 4.45 (d, *J* = 10.7 Hz, 1H, H-7a), 4.29 (dd, *J* = 10.3, 3.2 Hz, 1H, H-13α), 4.13–4.09 (m, 2H), 2.39–2.35 (m, 1H, H-13a) ppm; $\delta_C(CD_2Cl_2)$ = 159.0 (C-6), 154.4, 150.5, 149.2, 147.9, 132.7, 129.9, 129.6, 127.2, 125.7, 125.0, 124.7, 124.3, 121.7, 121.2, 120.4, 119.5, 117.6, 117.2, 66.7 (C-12), 52.1 (C-7a), 44.9 (C-13a), 44.0 (C-14) ppm; IR *ν* = 3401 (w), 1705 (s), 1629 (m), 1552 (m), 1489 (m), 1448 (w), 1431 (m), 1327 (w), 1277 (w), 1258 (w), 1236 (m), 1181 (m), 1176 (w), 1042 (m) cm^{-1}; HRMS [M^+] calcd for $C_{25}H_{18}N_2O_5$ 426.1216, found 426.1211.

8. Synthesis of (7a*R,13a*R**,14*S**)-11-methoxy-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (40).** According to the general procedure, 3-aminocoumarin (**4**) (0.040 g, 0.25 mmol), enal **35** (0.070 g, 0.26 mmol) and $Yb(OTf)_3$ (0.016 g, 10 mol%) afforded **40** as a white solid (0.092 g, 89%). mp = 261–262 °C; $\delta_H(CD_2Cl_2)$ = 7.30–7.27 (m, 3H), 7.26–7.24 (m, 1H), 7.22–7.19 (m, 3H), 7.01–6.96 (m, 4H), 6.88 (d, *J* = 6.9 Hz, 1H), 5.42 (s, 1H, H-7), 4.42–4.38 (m, 2H, H-7a, H-13α), 4.06 (t, *J* = 11.0 Hz, 1H, H-13β), 3.94 (d, *J* = 11.1 Hz, 1H, H-14), 3.79 (s, 3H, C-11-O*CH₃*), 2.41–2.35 (m, 1H, H-13a) ppm; $\delta_C(CD_2Cl_2)$ = 159.3 (C-6), 149.23, 149.21, 144.2, 142.6, 132.4, 129.6, 128.7, 127.8, 126.8, 124.9, 124.4, 122.3, 121.3, 121.1, 121.0, 117.2, 116.9, 111.7, 67.2 (C-13), 56.4 (C-11-OCH_3), 52.2 (C-7a), 45.1 (C-13a), 44.2 (C-14) ppm; IR *ν* = 3396 (w), 1717 (s), 1616 (w), 1598 (w), 1580 (w), 1494 (m), 1483 (m), 1457 (m), 1442 (m), 1342 (m), 1269 (m), 1216 (m), 1198 (m), 1181 (m), 1130 (m), 1115 (w), 1091 (m), 1063 (m) cm^{-1}; MS *m/z* (relative intensity) = 413 (M^++2, 24), 412 (M^++1, 97), 411 (42), 410 (100); HRMS [M^+] calcd for $C_{26}H_{21}NO_4$ 411.1471 found 411.1461.

9. Synthesis of (7a*R,13a*R**,14*S**)-9-bromo-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (41).** According to the general procedure, 3-aminocoumarin (**4**) (0.040 g, 0.25 mmol), enal **37** (0.082 g, 0.26 mmol) and $Yb(OTf)_3$ (0.016 g, 10 mol%) afforded **41** as a white solid 0.10 g, 89%). mp = 271–272 °C; $\delta_H(CDCl_3)$ = 7.51 (s, 1H), 7.32–7.23 (m, 5H), 7.19–7.13 (m, 3H), 6.97–6.90 (m, 2H), 6.71 (d, 1H, *J* = 8.8 Hz), 5.41 (s, 1H, H-7), 4.44–4.33 (m, 2H, H-7a, H-13α), 4.05 (t, *J* = 10.7 Hz, 1H, H-13β), 3.90 (d, *J* = 10.6 Hz, 1H, H-14), 2.40–2.11 (m, 1H, H-13a) ppm; $\delta_C(CDCl_3)$ = 159.0 (C-6), 153.1, 148.7, 141.7, 132.2, 131.4, 129.4, 128.0, 127.6, 126.7, 124.5, 124.2, 123.0, 121.2, 120.2, 119.0, 116.6, 113.1, 66.7 (C-13), 51.4 (C-7a), 44.2 (C-13a), 43.8 (C-14) ppm (one carbon signal fewer than expected); IR ν = 3357 (w), 1720 (s), 1630 (m), 1602 (w), 1501 (m), 1484 (m), 1461 (m), 1451 (s), 1404 (w), 1367 (m), 1322 (m), 1292 (w), 1256 (m), 1234 (m), 1198 (s), 1176 (m), 1137 (w), 1116 (w), 1091 (w), 1072 (w), 1047 (m), 1034 (s) cm^{-1}; MS m/z (GC-MS) (relative intensity) = 461 ($M^{+(81)}$, 94), 459 ($M^{+(79)}$, 100); HRMS [M^+] calcd for $C_{25}H_{18}BrNO_3$ 459.0470 found 459.0476.

10. Synthesis of (7a*R,13a*R**,14*S**)-2-methyl-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (42).** According to the general procedure, 3-amino-6-methylcoumarin (**25**) (0.105 g, 0.600 mmol), enal **23** (0.15 g, 0.63 mmol) and $Yb(OTf)_3$ (0.037 g, 10 mol%) afforded **42** as an off-white solid (0.206 g, 87%). mp = 228–229 °C; $\delta_H(CD_2Cl_2)$ = 7.24–7.21 (m, 2H), 7.19–7.17 (m, 2H), 7.15–7.11 (m, 3H), 7.10–7.07 (m, 1H), 6.94–6.91 (m, 1H), 8.86–6.83 (m, 1H), 6.62 (d, J = 8.4 Hz, 1H), 5.43 (s, 1H, H-7), 4.34 (d, J = 10.8 Hz, 1H, H-7a), 4.29 (dd, J = 10.7, 3.5 Hz, 1H, H-13α), 3.96 (t, J = 11.0 Hz, 1H, H-13β), 3.88 (d, J = 11.1 Hz, 1H, H-14), 2.32–2.24 (m, 1H, H-13a), 2.23 (s, 3H, C-2-CH_3) ppm; $\delta_C(CD_2Cl_2)$ = 159.4 (C-6), 152.3, 149.3, 142.7, 132.4, 130.9, 130.3, 129.6, 128.7, 127.8, 126.8, 125.9, 124.9, 124.4, 121.4, 121.2, 121.0, 117.2, 116.9, 67.1 (C-13), 52.2 (C-7a), 45.3 (C-13a), 44.3 (C-14), 20.8 (C-2-CH_3) ppm; IR ν = 3366 (w), 1727 (s), 1699 (w), 1684 (w), 1652 (w), 1628 (m), 1558 (m), 1541 (w), 1499 (s), 1465 (m), 1340 (m), 1323 (m), 1287 (w), 1257 (m), 1222 (m), 1192 (m), 1180 (m), 1117 (m), 1073 (w), 1048 (m), 1036 (m) cm^{-1}; MS m/z (relative intensity) = 397 (M^++2, 28), 396 (M^++1, 100), 395 (16), 394 (22), 392 (47). HRMS [M^+] calcd for $C_{26}H_{21}NO_3$ 395.1521 found 395.1520.

11. Synthesis of (7a*R,13a*R**,14*S**)-11-methoxy-2-methyl-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (43).** According to the general procedure, 3-amino-6-methylcoumarin (0.044 g, 0.25 mmol) (**25**), enal **35** (0.070 g, 0.26 mmol) and $Yb(OTf)_3$ (0.016 g, 10 mol%) afforded **43** as a white solid (0.089 g, 84%). mp = 230–232 °C; $\delta_H(CD_2Cl_2)$ = 7.24 (t, J = 7.0 Hz, 2H), 7.18 (d, J = 6.8 Hz, 1H), 7.14–7.13 (m, 2H), 7.06 (d, J = 8.4 Hz, 1H), 6.94–6.87 (m, 3H), 6.77 (d, J = 7.8 Hz, 1H), 6.73 (s, 1H), 5.32 (s, 1H, H-7), 4.33 (dd, J = 11.3, 3.5 Hz, 1H, H-13α), 4.30 (d, J = 10.9 Hz, 1H, H-7a), 3.98 (t, J = 11.5 Hz, 1H, H-13β), 3.84 (d, J = 10.8 Hz, 1H, H-14), 3.72 (s, 3H, C-11-OCH_3), 2.31 (m, 1H, H-13a), 2.00 (s, 3H, C-2-CH_3) ppm; $\delta_C(CD_2Cl_2)$ = 159.5 (C-6), 149.2, 147.3, 144.2, 142.7, 134.0, 132.3, 129.6, 128.7, 127.8, 125.1, 122.4, 121.5, 121.1, 120.6, 117.2, 116.5, 111.7 (C-10), 67.2 (C-13), 56.4 (C-11-OCH_3), 52.1 (C-7a), 44.8 (C-13a), 44.1 (C-14), 28.6 (C-2-CH_3) ppm (one carbon signal fewer than expected); IR ν = 3358 (w), 1701 (s), 1678 (w), 1650 (w), 1613 (m), 1501 (s), 1469 (m), 1345 (w), 1312 (w), 1281 (w), 1252 (m), 1219 (m), 1191 (m), 1172 (w), 1119 (m), 1065 (w), 1033 (m) cm^{-1}; MS m/z (relative intensity) = 427 (M^++2, 30), 426 (M^++1, 100), 425 (18), 424 (32), 422 (11); HRMS [M^+] calcd for $C_{27}H_{23}NO_4$ 425.1627, found 425.1623.

12. Synthesis of (7a*R,13a*R**,14*S**)-2-methoxy-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (44) and 2-methoxy-14-phenyl-5,6,12,13-tetrahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (52).** According to the general procedure, 3-amino-6-methoxycoumarin (**26**) (0.076 g, 0.40 mmol), enal **23** (0.10 g, 0.42 mmol) and $Yb(OTf)_3$ (0.025 g, 10 mol%) afforded **44** as an off-white solid (0.14 g, 84%). Additionally, flash chromatography (ethyl acetate) of the filtrate afforded **52** as a white solid (0.003 g, 2%). **44**: mp = 228–229 °C. $\delta_H(CD_2Cl_2)$ = 7.41 (d, J = 7.1 Hz, 1H, H-8), 7.35–7.32 (m, 2H), 7.28 (d, J = 7.0 Hz, 1H), 7.26–7.20 (m, 3H), 7.17 (d, J = 8.8 Hz, 1H, H-4), 7.02 (t, J = 7.4 Hz, 1H, H-9), 6.82 (d, J = 8.4 Hz, 1H, H-11), 6.73 (dd, J = 8.9, 2.1 Hz, 1H, H-3), 6.42 (d, J = 2.0 Hz, 1H, H-1), 5.49 (s, 1H, H-7), 4.41 (d, J = 10.2 Hz, 1H, H-7a), 4.32 (dd, J = 10.7, 3.0 Hz, 1H, H-13α), 4.07 (t, J = 11.1 Hz, 1H, H-13β), 3.91 (d, J = 11.3 Hz, 1H, H-14), 3.42 (s, 3H, C-2-OCH_3), 2.41 (m, 1H, H-13a) ppm; $\delta_C(CD_2Cl_2)$ = 159.3 (C-6), 156.2, 154.6, 143.5, 142.7, 132.5, 129.7, 129.6, 128.7, 127.9, 125.6 (C-8), 121.6, 121.5 (C-9), 121.4, 120.9, 117.7, 117.5 (C-11), 114.4 (C-3), 107.9 (C-1), 67.2 (C-13), 55.9 (C-2-OCH_3), 52.1 (C-7a), 44.8 (C-14), 44.4 (C-13a) ppm; IR ν = 3360 (w), 1702 (s), 1614 (w), 1560 (w), 1499 (m), 1467 (w), 1451 (w), 1426 (w), 1343 (m), 1319 (w), 1282 (w), 1258 (w), 1234 (w), 1187 (m), 1170 (m), 1050 (m) cm^{-1}; MS m/z (relative intensity) = 413 (M^++2, 30), 412 (M^++1, 100), 411 (39), 410 (69), 408 (65). HRMS [M^+] calcd for $C_{26}H_{21}NO_4$ 411.1471, found 411.1465. **52**: mp = 273–274 °C (decomp); $\delta_H(CDCl_3)$ = 8.54 (dd, J = 7.6, 2.4 Hz, 1H), 7.68–7.65 (m, 2H), 7.59 (d, J = 7.3 Hz, 1H), 7.40–7.38 (m, 1H), 7.35 (d, J = 6.5 Hz, 1H), 7.27–7.26 (m, 1H), 7.18 (t, J = 7.6 Hz, 1H), 6.94–6.90 (m, 2H), 6.47 (d, J = 7.0 Hz, 1H), 4.98 (s, 2H), 3.29 (s, 3H) ppm; $\delta_C(CDCl_3)$ = due to small quantity and low solubility of this compound, ^{13}C NMR data could not be obtained. IR ν = 1734 (s), 1597 (w), 1561 (w), 1499 (m), 1465 (s), 1431 (m), 1376 (m), 1294 (m), 1252 (m), 1215 (s), 1190 (m), 1153 (s), 1110 (m), 1085 (w), 1061 (w), 1039 (s), 1020 (m) cm^{-1}; MS m/z (relative intensity) = 409 (M^++2, 26), 408 (M^++1, 100); HRMS [M^+] calcd for $C_{26}H_{17}NO_4$ 407.1158, found 407.1160

13. Synthesis of (7a*R,13a*R**,14*S**)-2,11-dimethoxy-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo-[*a*,*h*]anthracen-6-one (45).** According to the general procedure, 3-amino-6-methoxycoumarin (0.048 g, 0.25 mmol) (**26**), enal **35** (0.070 g, 0.26 mmol) and $Yb(OTf)_3$ (0.016 g, 10 mol%) afforded **45** as a white solid (0.094 g, 85%). mp = 258–260 °C; $\delta_H(CD_2Cl_2)$ = 7.25 (t, J = 7.4 Hz, 2H), 7.19 (d, J = 7.4 Hz, 1H, H-4), 7.09–7.08 (m, 2H), 7.08 (d, J = 9.1 Hz, 1H), 6.93–6.87 (m, 2H), 6.76 (d, J = 7.7 Hz, 1H, H-10), 6.64 (dd, J = 9.0, 3.1 Hz, 1H, H-3), 6.34 (d, J = 2.9 Hz, 1H, H-1), 5.37 (s, 1H, H-7), 4.34–4.30 (m, 2H, H-7a, H-13α), 3.97 (t, J = 11.1 Hz, 1H, H-13β), 3.83 (d, J = 10.2 Hz, 1H, H-14), 3.71 (s, 3H, C-11-OCH_3), 3.33 (s, 3H, C-2-OCH_3), 2.32 (m, 1H, H-13a) ppm; $\delta_C(CD_2Cl_2)$ = 159.3 (C-6), 156.2, 149.2, 144.2, 143.5, 142.7, 132.5, 129.7, 128.7 (C-4), 127.9, 122.3, 121.5, 121.1, 120.8, 117.6, 117.2, 114.3 (C-3), 111.7 (C-10), 107.9 (C-1), 67.2 (C-13), 56.4 (C-11-OCH_3), 55.9 (C-2-OCH_3), 52.1 (H-7a), 44.7 (H-13a), 44.4 (H-14) ppm; IR ν = 3365 (w), 1699 (s), 1619 (w), 1555 (m), 1501 (m), 1468 (w), 1421 (m), 1329 (m), 1302 (w), 1285 (w), 1257 (w), 1232 (m), 1182 (m), 1169 (m), 1029 (m) cm^{-1}; MS m/z (relative intensity) = 443 (M^++2, 32), 442 (M^++1, 100), 441 (24), 440 (48), 438 (26); HRMS [M^+] calcd for $C_{27}H_{23}NO_5$ 441.1576, found 441.1577.

14. Synthesis of (7a*R,13a*R**,14*S**)-2-bromo-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (46).** According to the general procedure, 3-amino-6-bromocoumarin (**27**) (0.072 g, 0.30 mmol), enal **23** (0.075 g, 0.32 mmol) and $Yb(OTf)_3$ (0.019 g, 10 mol%) afforded **46** as a white solid (0.11 g, 78%). mp = 273–274 °C; δ_H(DMSO-d_6) = 7.68 (dd, J = 7.2, 2.6 Hz, 1H, H-3), 7.40–7.37 (m, 3H), 7.34–7.30 (m, 4H), 7.24 (m, 1H), 7.22–7.21 (m, 1H), 7.19 (dd, J = 7.8, 2.8 Hz, 1H), 6.68 (d, J = 8.4 Hz, 1H, H-11), 6.08 (s, 1H, H-7), 4.42 (d, J = 10.2 Hz, 1H, H-7a), 4.29–4.04 (m, 3H), 2.13–2.05 (m, 1H, H-13a) ppm; δ_C(CD_2Cl_2) = 159.1 (C-6), 154.5, 150.4, 149.2, 147.9, 131.6, 130.0, 129.7, 127.2, 125.6, 125.0, 124.8, 124.4, 121.6, 121.3 (C-9), 120.4, 119.6, 117.5, 117.2 (C-11), 66.7 (13), 52.1 (C-7a), 44.9 (C-14), 44.0 (C-13a) ppm; IR ν = 3392 (w), 1703 (s), 1620 (m), 1595 (w), 1583 (w), 1559 (w), 1488 (s), 1458 (m), 1410 (m), 1343 (s), 1310 (m), 1275 (m), 1254 (w), 1230 (w), 1217 (m), 1201 (s), 1137 (w), 1077 (m), 1048 (s), 1024 (m), 1009 (m) cm^{-1}; HRMS [M$^+$] calcd for $C_{25}H_{18}NO_3Br$ 459.0470, found 459.0468.

15. Synthesis of (7a*R,13a*R**,14*S**)-2-bromo-11-methoxy-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (47).** According to the general procedure, 3-amino-6-bromocoumarin (0.060 g, 0.25 mmol) (**27**), enal **35** (0.070 g, 0.26 mmol) and $Yb(OTf)_3$ (0.016 g, 10 mol%) afforded **47** as an off-white solid (0.092 g, 75%). mp = 253–255 °C; δ_H(CD_2Cl_2) = 7.28–7.26 (m, 2H), 7.22 (m, 1H), 7.17 (dd, J = 9.2, 1.8 Hz, 1H, H-3), 7.13 (m, 2H), 7.07 (d, J = 8.1 Hz, 1H, H-4), 7.02 (d, J = 2.1 Hz, 1H, H-1), 6.93–6.88 (m, 2H), 6.78 (d, J = 7.4 Hz, 1H, H-10), 5.44 (s, 1H, H-7), 4.35 (d, J = 11.5 Hz, 1H, H-7a), 4.31 (dd, J = 10.9 Hz, J = 3.9 Hz, 1H, H-13α), 3.97 (t, J = 11.3 Hz, 1H, H-13β), 3.80 (d, J = 11.1 Hz, 1H, H-14), 3.72 (s, 3H, C-11-*OCH₃*), 2.31 (m, 1H, H-13a) ppm; δ_C(CD_2Cl_2) = 158.7 (C-6), 149.3, 148.0, 142.2, 141.9, 132.8, 129.8, 129.3 (C-3), 128.1, 127.5 (C-1), 122.9, 122.0, 121.2, 119.4, 118.5 (C-4), 117.2, 117.1, 111.8 (C-10), 67.2 (C-13), 56.4 (C-11-OCH_3), 52.1 (C-7a), 44.8 (C-13a), 44.1 (C-14) ppm (one carbon signal fewer than expected); IR ν = 3351 (m), 1710 (s), 1614 (w), 1584 (w), 1497 (m), 1482 (s), 1455 (m), 1407 (w), 1345 (m), 1316 (w), 1263 (s), 1229 (s), 1214 (m), 1203 (m), 1122 (w), 1091 (w), 1077 (w), 1059 (w), 1037 (s) cm^{-1}; HRMS [M$^+$] calcd for $C_{26}H_{20}BrNO_4$ 489.0576, found 489.0574.

16. Synthesis of (7a*R,13a*R**,14*S**)-2-nitro-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (48).** According to the general procedure, 3-amino-6-nitrocoumarin (**28**) (0.062 g, 0.30 mmol), enal **23** (0.075 g, 0.32 mmol) and $Yb(OTf)_3$ (0.019 g, 10 mol%) afforded **48** as a pale yellow solid (0.105 g, 82%). mp = 262–263 °C; δ_H(CD_2Cl_2) = 8.00 (dd, J = 9.0 Hz, 1.8 Hz, 1H, H-3), 7.82 (d, J = 2.4 Hz, 1H, H-1), 7.41–7.36 (m, 4H), 7.33–7.18 (m, 4H), 7.04 (t, J = 7.8 Hz, 1H, H-10), 6.82 (t, J = 7.3 Hz, 1H, H-9), 5.61 (s, 1H, H-7), 4.49 (d, J = 10.4 Hz, 1H, H-7a), 4.29 (dd, J = 10.3, 3.2 Hz, 1H, H-13α), 4.04 (t, J = 10.3 Hz, 1H, H-13β), 3.99 (d, J = 10.6 Hz, 1H, H-14), 2.48–2.40 (m, 1H, H-13a) ppm; δ_C(CD_2Cl_2) = 158.7 (C-6), 152.3 151.2, 144.0, 140.9, 132.4, 130.0, 129.8, 128.4, 128.3, 128.0, 125.4, 121.6, 121.5, 120.5, 120.4, 119.4, 119.2, 117.5, 67.8 (C-13), 52.2 (C-7a), 42.1 (C-13a), 41.9 (C-14) ppm; IR ν = 3354 (m), 1718 (s), 1583 (w), 1527 (s), 1490 (s), 1336 (s), 1254 (m), 1234 (w), 1185 (m), 1105 (w), 1049 (m) cm^{-1}; HRMS [M$^+$] calcd for $C_{25}H_{18}N_2O_5$ 426.1216, found 426.1215.

17. Synthesis of (7a*R,13a*R**,14*S**)-11-methoxy-2-nitro-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]anthracen-6-one (49).** According to the general procedure, 3-amino-6-nitrocoumarin (0.052 g, 0.25 mmol) (**28**), enal **35** (0.070 g, 0.26 mmol) and $Yb(OTf)_3$ (0.016 g, 10 mol%) afforded **49** as a pale yellow solid (0.089 g, 78%). mp = 257–259 °C; δ_H(CD_2Cl_2) = 7.89 (dd, J = 8.7, 2.3 Hz, 1H), 7.82 (d, J = 2.7 Hz, 1H), 7.29–7.26 (m, 3H), 7.21–7.19 (m, 3H), 6.93–6.89 (m, 2H), 6.78 (dd, J = 7.2, 1.5 Hz, 1H), 5.53 (s, 1H, H-7), 4.41 (d, J = 10.7 Hz, 1H, H-7a), 4.31 (dd, J = 10.7 Hz, 3.2 Hz, 1H, H-13α), 3.98 (t, J = 11.5 Hz, 1H, H-13β), 3.90 (d, J = 11.3 Hz, 1H, H-14), 3.72 (s, 3H, C-11-OCH_3), 2.36 (m, 1H, H-13a) ppm; δ_C(CD_2Cl_2) = 163.2 (C-6), 158.1, 152.4, 149.3, 144.5, 144.3, 141.4, 133.2, 130.0, 128.3, 121.74, 121.67, 121.4, 121.3, 120.7, 119.2, 117.8, 117.0, 111.9, 67.1 (C-13), 56.5 (C-11-OCH_3), 52.1 (C-7a), 44.5 (C-13a), 44.1 (C-14) ppm; IR ν = 3395 (w), 1725 (s), 1629 (m), 1560 (m), 1499 (m), 1467 (w), 1451 (w), 1426 (w), 1343 (m), 1319 (w), 1282 (w), 1258 (w), 1234 (w), 1187 (m), 1170 (m), 1050 (m) cm^{-1}; MS m/z (relative intensity) = 457 (M$^+$+1, 14), 456 (M$^+$, 52), 455 (100), 419 (26), 214 (56); HRMS [M$^+$] calcd for $C_{26}H_{20}N_2O_6$ 456.1321 found 456.1325.

18. Synthesis of (7a*R,13a*R**,14*S**)-4-Methoxy-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo[*a*,*h*]-anthracen-6-one (50).** According to the general procedure, 3-amino-8-methoxycoumarin (0.076 g, 0.40 mmol) (**29**), enal **23** (0.10 g, 0.42 mmol) and $Yb(OTf)_3$ (0.025 g, 10 mol%) afforded **50** as an off-white solid (0.141 g, 86%). mp = 276–278 °C; δ_H(CD_2Cl_2) = 7.33 (d, J = 7.6 Hz, 1H), 7. 23 (m, 2H), 7.16 (m, 1H), 7.12 (m, 3H), 6.93 (t, J = 7.3 Hz, 1H), 6.78 (t, J = 7.8 Hz, 1H), 6.74 (d, J = 7.8 Hz, 1H), 6.69 (d, J = 8.2 Hz, 1H), 6.51 (d, J = 8.3 Hz, 1H), 5.37 (s, 1H, H-7), 4.30 (d, J = 10.3 Hz, 1H, H-7a), 4.24 (dd, J = 10.7, 3.3 Hz, 1H, H-13α), 3.98 (t, J = 11.0 Hz, 1H, H-13β), 3.84 (d, J = 10.5 Hz, 1H, H-14), 3.83 (s, 3H, C-4-OCH_3), 2.29 (m, 1H, H-13a) ppm; δ_C(CD_2Cl_2) = 158.9 (C-6), 154.6, 147.8, 142.9, 138.8, 132.5, 129.6, 128.7, 127.8, 125.7, 124.1, 121.8, 121.7, 121.6, 121.4, 117.5, 116.7, 109.4, 67.1 (C-13), 56.7 (C-4-OCH_3), 52.2 (C-7a), 45.2 (C-13a), 44.4 (C-14) ppm (one carbon signal fewer than expected) ppm; IR ν = 3332 (m), 1682 (s), 1622 (w), 1600 (w), 1575 (m), 1483 (m), 1452 (m), 1345 (m), 1281 (m), 1260 (w), 1223 (m), 1212 (m), 1197 (m), 1179 (s), 1133 (w), 1108 (w), 1063 (w), 1050 (w), 1028 (m), 1003 (m) cm^{-1}; MS m/z (relative intensity) = 413 (M$^+$+2, 27), 412 (M$^+$+1, 100), 411 (25), 410 (48), 408 (43); HRMS [M$^+$] calcd for $C_{26}H_{21}NO_4$ 411.1471, found 411.1474.

19. Synthesis of (7a*R,13a*R**,14*S**)-4,11-dimethoxy-14-phenyl-5,6,7,7a,12,13,13a,14-octahydro-5,12-dioxa-7-azadibenzo-[*a*,*h*]anthracen-6-one (51).** According to the general procedure, 3-amino-8-methoxycoumarin (0.048 g, 0.25 mmol) (**29**), enal **35** (0.070 g, 0.26 mmol) and $Yb(OTf)_3$ (0.016 g, 10 mol%) afforded **51** as an off-white solid (0.095 g, 86%). mp = 265–266 °C; δ_H(CD_2Cl_2) = 7.31–7.29 (m, 2H), 7.26–7.23 (m, 1H), 7.19–7.18 (m, 2H), 7.01 (d, J = 7.8 Hz, 1H), 6.97 (t, J = 8.3 Hz, 1H), 6.87–6.84 (m, 2H), 6.77 (d, J = 7.5 Hz, 1H), 6.60 (d, J = 7.7 Hz, 1H), 5.43 (s, 1H, H-7), 4.41–4.37 (m, 2H, H-7a, H-13α), 4.05 (t, J = 11.0 Hz, 1H, H-13β), 3.92–3.91 (m, 4H, H-14), 3.79 (s, 3H), 2.36 (m, 1H, H-13a) ppm; δ_C(CD_2Cl_2) = 158.8, 149.2, 147.8, 144.2, 142.8, 138.7, 132.5, 129.6, 128.6, 127.7, 124.0, 122.3, 121.8, 121.5, 121.1, 117.2, 116.7, 111.7, 109.3, 67.1, 56.7, 56.4, 52.1, 45.1, 44.3 ppm; IR ν = 3345 (m), 1681 (s), 1602 (w), 1576 (m), 1558 (w), 1483 (m), 1439 (m), 1337 (m), 1258 (m), 1205 (s), 1175 (s), 1133 (m), 1109 (m), 1090 (m), 1064 (s) cm^{-1}; MS m/z (relative intensity) = 443 (M$^+$+2, 32), 442 (M$^+$+1, 100), 440 (12); HRMS [M$^+$] calcd for $C_{27}H_{23}NO_5$ 441.1576 found 441.1583.

20. Synthesis of (7a*S,11a*S**,12*R**)-9-acetyl-12-phenyl-7,7a,10a,11,11a,12-hexahydro-6*H*-chromeno[3,4-*b*]pyrrolizino[2,1-*e*]pyridin-6-one (55).** According to the general procedure, 3-aminocoumarin (**4**) (0.040 g, 0.25 mmol), enal **54** (0.066 g, 0.26 mmol) and $Yb(OTf)_3$ (0.016 g, 10 mol%) were reacted at rt for 6 h and then heated at reflux for 18 h. The precipitate was suction filtered and the solids were washed with cold acetonitrile to afford **55** as a pale yellow solid (0.038 g, 38%). The solvent was removed from filtrate under reduced pressure and the residue was subjected to flash chromatography (30% ethyl acetate/hexanes) to afford **55** as a pale yellow solid (0.011 g, 11%). Combined yield = 0.049 g, 49%. mp = 265–266 °C; $\delta_H(CDCl_3)$ = 7.36–7.33 (m, 4H), 7.30–7.26 (m, 2H), 7.24 (s, 1H), 7.22–7.18 (m, 2H), 7.12–7.08 (m, 1H), 6.47 (s, 1H), 4.93 (s, 1H, H-7), 4.65 (d, *J* = 5.4 Hz, 1H, H-7a), 4.30 (s, 1H, H-12), 4.23 (dd, *J* = 10.8, 7.4 Hz, 1H, H-11α), 3.84 (t, *J* = 10.8 Hz, 1H, H-11β), 3.40–3.35 (m, 1H, H-11a), 2.35 (s, 3H, CO*CH₃*) ppm; $\delta_C(CDCl_3)$ = 193.4 (*CO*CH₃), 158.2 (C-6), 148.0, 142.5, 138.7, 129.8, 129.5, 128.5, 127.8, 127.5, 126.2, 124.9, 121.6, 120.8, 116.7, 112.0, 102.3, 50.1 (C-11), 49.4 (C-11a), 46.7 (C-7a), 38.9 (C-12), 27.2 (CO*CH₃*) ppm; MS *m/z* (relative intensity) = 400 (M^++2, 21), 399 (100); HRMS [M^+] calcd for $C_{25}H_{20}N_2O_3$ 396.1474 found 396.1479.

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