Tetrahedron 65 (2009) 8781–8785

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

# 2-Dienylphenacyloxazolones and an intramolecular Diels–Alder approach to the A–B–C ring system of phenanthridone alkaloids

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ARTICLE INFO

*Article history:*
Received 14 May 2009
Received in revised form 25 August 2009
Accepted 26 August 2009
Available online 31 August 2009

*Keywords:*
Synthesis
Alkaloid
Phenanthridones
Diels–Alder
Oxazolone

ABSTRACT

A general route to the A–B–C ring system of phenanthridone alkaloids is available by acylation of 2-oxazolone with a 2-butadienylbenzoic acid derivative, followed by an intramolecular Diels–Alder reaction and hydrolysis.



## 1. Introduction

The *Amaryllidaceae* alkaloids[1] are an important class of compounds characterized by a [1.3]dioxolophenanthridone skeleton. Pancratistatin[2] and lycoricidine[3] are well-known bioactive members of this family, which also includes narciclasine,[4] γ-lycorane,[5] and lycorine.[6] Glycoside alkaloids of this class are known, including kalbreclasine[7] (related to lycoricidine), pancratiside,[8] and telastaside.[9] Folk medicines based on extracts of *Amaryllidaceae* plants have been used for many years,[2c,7,10] and as a family these alkaloids exhibit a wide range of biological activity that has sparked considerable interest in their synthesis. Indeed, there are many total syntheses of various phenanthridone alkaloids.[11]

The goal of this work is to develop a general route to phenanthridone alkaloids that may eventually be applied to a synthesis of pancratistatin. However, there were several questions concerning the viability of our method, which is inspired by a synthesis of lycorine in which Stork assembled an enamide **1** and formed the B and C rings (see **2**) by an internal Diels–Alder reaction shown in Scheme 1.[12] Initial cyclization gave poor diastereoselectivity at the ring juncture, but Stork modified the approach to achieve greater stereoselectivity for the trans-B/C ring juncture.[13] Keck and coworkers introduced a variation of this strategy, generating a dienyl amide that allowed formation of the B and C rings of lycoricidine by an internal Diels–Alder reaction.[14]

We initially imagined a strategy similar to that of Stork (**1**→**2**), but with a modified structure that tethered a styrene derivative to a 5-vinyl-2-oxazolone, and would produce a key intermediate by an internal Diels–Alder reaction. We were unable to prepare the vinyl oxazolone, however, and modified the strategy to cyclize a 1-aryl-1,3-butadienyl-2-oxazolone (**3**) that would give **4**. This key step is an intramolecular Diels–Alder reaction of a phenacyloxazolone. Hartmann had reported earlier that *N*-acetyl 2-oxazolone reacted with both 1,3-butadiene and cyclopentadiene (160 °C, benzene, hydroquinone, autoclave, 24 h) to give greater than 70% yield of the corresponding cycloadduct.[15] In separate work, Deyrup reported similar results, and suggested that the reactivity of oxazolone was similar to that of vinylene carbonate.[16] Deyrup also showed that the unprotected 2-oxazolone decomposed upon vigorous heating, but the acyl derivative reacted smoothly with vinylene carbonate. The intramolecular version of this reaction was unknown when we began this work, but Fearnly has now reported an internal Diels–Alder of a tethered 2-oxazolone derivative **5** to give **6** in 65% yield, along with the trans ring juncture product **7** (see Scheme 2).[17]

## 2. Results and discussion

Our first problem was the preparation of 2-oxazolone (**11**), since it is no longer commercially available. 2-Oxazolidinone **8** is

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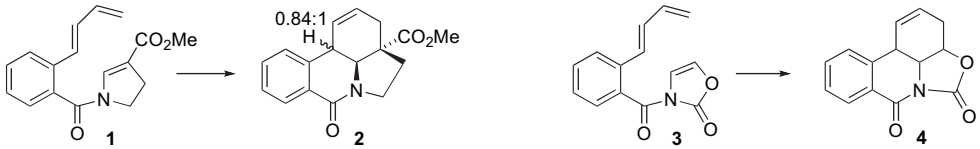
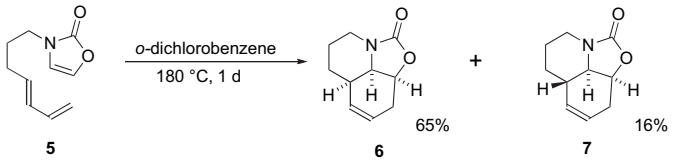
doi:10.1016/j.tet.2009.08.066

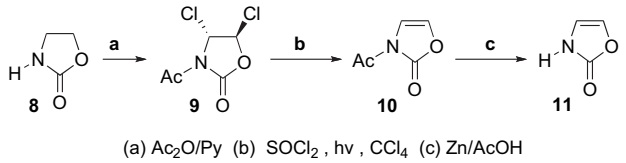



**Scheme 1.** Intramolecular Diels–Alder reactions.




**Scheme 2.** The fearnly cyclization of tethered 2-oxazolone derivatives.

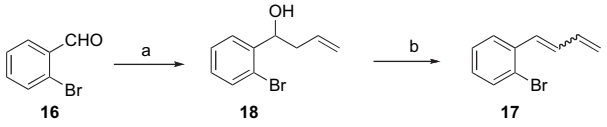
available, and Hartmann and co-worker's Organic Syntheses procedure described a sequence of acetylation followed by chlorination with chlorine gas, thermal dehalogenation to give **10**, and deprotection in refluxing methanol gave **11**.[15] Deyrup and Gingrich also prepared **11** by this method.[16] In our hands, the literature methods for the synthesis of **11** gave yields in the 5–35% range, which limited subsequent synthetic efforts. The scale of our reactions prevented us from weighing chlorine gas. Our efforts to control the stoichiometry of chlorine gas were only modestly successful, and mixtures of chlorinated products were common, which led to poor yields of **10**. These problems led us to develop an alternative synthesis of **11** via reaction of *N*-acetyl-2-oxazolidinone with sulfuryl chloride to give *trans*-4,5-dichloro compound **9**, as shown in Scheme 3.[18] Subsequent warming of **9** with Zn/AcOH gave *N*-acetyl-2-oxazolone **10** in 58% yield, providing a reliable source of this key component.



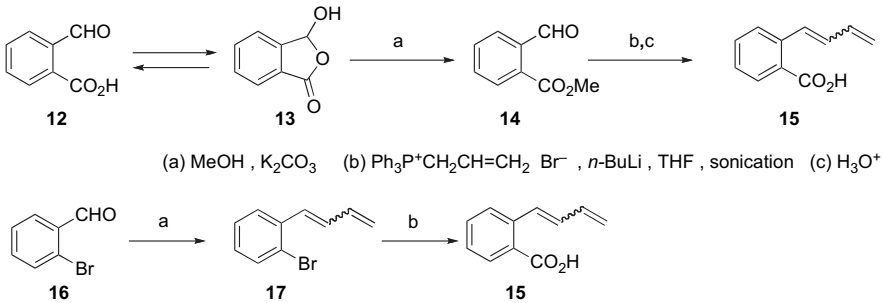

**Scheme 3.** Synthesis of 2-oxazolone.

With a reliable source of **10** now available, we confronted several key questions. The preparation of the requisite dienyl benzoic acid was the first issue. Conversion to the oxazolone derivative and the viability of the internal Diels–Alder reaction were the second and third. Issues of stereochemistry for the cycloaddition and hydrolysis of the targeted oxazolidinone cycloadduct were also important. We therefore targeted **3** as a key intermediate that contained the A–B–C ring system of the phenanthridone alkaloids. We initially explored a general route to **15** from 2-formylbenzoic acid (**12**), which exists in equilibrium with lactone **13**. Treatment of **13** with methanol in dry acetone in the presence of potassium carbonate[19] gave the methyl ester (**14**) in 98% yield. Subsequent Wittig reaction with allyltriphenylphosphonium bromide and *n*-butyllithium proved to be a very poor reaction. Despite the observation that benzaldehyde reacted with this reagent to give 1-phenyl-1,3-butadiene in 98% yield when ultrasound was employed,[20] similar reaction with **14** followed by aqueous acid hydrolysis gave less than 15% yield of **15**, as shown in Scheme 4. Both Wittig[21] or Horner–Wadsworth–Emmons[22] conditions were examined, but poor yields and competitive cyclization to what appeared to be an allyl phthalide proved unavoidable. These problems prompted us to abandon this approach.

A second synthesis shown in Scheme 4 reacted the ylide derived from allyltriphenylphosphonium bromide with 2-bromobenzaldehyde (**16**) to give **17** in up to 62% yield, although yields were variable. Subsequent reaction of 1-(2-bromophenyl)-1,3-butadiene (**17**) with magnesium followed by quenching with carbon dioxide and an aqueous acid workup gave 2-(1,3-butadienyl)benzoic acid (**15**) in 50% yield. A more reliable route to the diene is shown in Scheme 5, in which **16** is converted to 1-(2-bromophenyl)-but-3-en-1-ol (**18**) by reaction with either allylmagnesium bromide (prepared in situ) in 82% yield,[23a] or by an indium–boron trifluoride diethyl etherate mediated substitution with allyl bromide in 87% yield.[23b] Conversion of the alcohol to 1-(2-bromophenyl)-1,3-butadiene **17** was accomplished in 83% yield by a one-pot conversion to the bromide using carbon tetrabromide and triphenylphosphine with triethylamine.[23a] With carboxylic acid **15** in hand, heating with oxalyl chloride formed the acid chloride, which was concentrated and heated with 2-oxazolone (**11**) in acetonitrile without further purification using triethylamine as a base. The isolated yield of **19** was



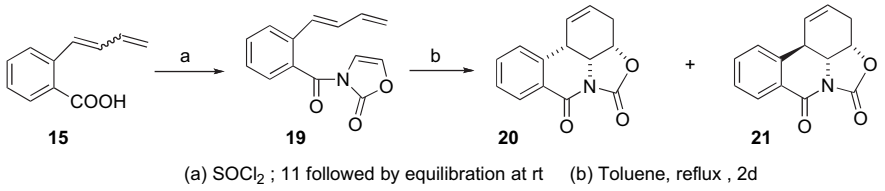

**Scheme 5.** Synthesis of 1-(2-bromophenyl)-1,3-butadiene.




**Scheme 4.** Synthesis of methyl 2-butadienylbenzoic acid.

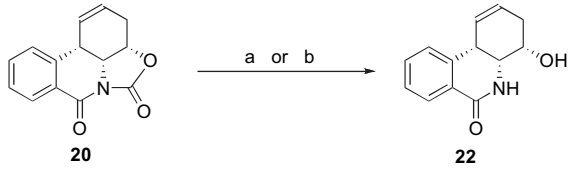
88%. Interestingly, **19** was isolated as a 2:1 *E*/*Z* mixture, but complete equilibration to the *E*-alkene occurred after standing at room temperature for about 48 h. Heating a chloroform solution of **19** accelerated the equilibration.

Initial attempts at the intramolecular Diels–Alder reaction involved the reflux of **19** in toluene for 3 days. Filtration and removal of the toluene was followed by dissolution of the resulting oil in dichloromethane/ethyl acetate, and flash chromatography gave a 40% yield of product. Analysis by GC–MS indicated a 4:1 mixture of isomeric products **20** and **21** in the initial version of the reaction. Analysis by COSY and NOESY NMR showed that the major isomer was **20** with a cis-B/C ring juncture. The minor product was confirmed as **21**, with the trans-B/C ring juncture. One or more of the products is somewhat soluble in toluene, evidenced by the observation of a coating of one or more products on the stirbar during the course of the reaction. An improved isolation technique washed the flask and stirbar with dichloromethane/ethyl acetate after filtration, and all solvents were combined and evaporated in vacuo. The resulting oil was dissolved in dichloromethane/ethyl acetate and added directly to silica gel for flash chromatography. We also observed improved yields by shortening the reaction time. The reflux of **19** in toluene for 2 days, followed by the modified isolation procedure led a 2:1 mixture of **20** and **21** in 80% yield, as shown in Scheme 6.




**Scheme 6.** Intramolecular Diels–Alder reaction of 2-butadienylphenacyl-2-oxazolone.

The final step in this sequence required hydrolysis of the oxazolidinone ring to liberate the hydroxy lactam, as shown in Scheme 7. The reaction of **20** with Amberlyst A-21 gave alcohol **22** in 79% yield after 20–25 h. An alternative procedure hydrolyzed the oxazolidinone ring by stirring with sodium hydroxide (or potassium hydroxide) and methanol for an hour, giving **22** in 89% yield. Phenanthridone **22** has the A–B–C ring system of the targeted alkaloids, and functionality that allows elaboration of the C ring.




**Scheme 7.** Hydrolysis of the oxazolidinone cycloadduct.

This model study constitutes a proof-of-principle demonstration of the viability of the dienylphenacyloxazolone strategy to assemble the phenanthridone ABC ring system from readily available starting materials via an intramolecular Diels–Alder reaction. The yield of cycloadduct is reasonable, although the diastereoselectivity for the all cis diastereomer is modest. We are currently examining alternative routes to improve the selectivity. The oxazolone ring system is a useful amino-alcohol or amido-alcohol surrogate since the oxazolidinone product is efficiently hydrolyzed in high yield under relatively mild conditions. The phenacyloxazolone route offers a rapid and potentially versatile route for the synthesis of several important alkaloids.

## 3. Experimental section

### 3.1. General

All solvents were dried according to standard procedures. THF was distilled from sodium benzophenone, methylene chloride, toluene, and benzene were distilled from $CaH_2$ and DMF was vacuum distilled from $CaH_2$. Unless otherwise noted, all reactions were carried out under nitrogen gas. All chemicals were purchased from Aldrich Chemical Company and used without further purification. Thin-layer chromatography was done on 0.2 mm layer thickness Fluka aluminum-backed TLC plates with a fluorescent indicator. Column chromatography was done using 60 Å porosity, 32–63 μm silica gel. $^1H$ and $^{13}C$ NMR were recorded on a Brüker Avance 300 (300.13 MHz $^1H$, 75.48 MHz $^{13}C$) or a Brüker DRX-400 [400.144 MHz $^1H$, 100.65 MHz $^{13}C$]. Chemical shifts are reported in ppm ($\delta$) downfield from TMS. IR data were collected on a Brüker IFS 66 v/S FT-IR spectrometer. Mass spectroscopy data were collected on a Hewlett Packard 5970B GC/MSD mass spectrometer with an HP-1 column and high-resolution mass spectrometry was done on a Micromass VB-QTOF tandem mass spectrometer. 2-Oxazolidinone (**8**), *n*-butyllithium, 2-bromobenzaldehyde (**16**), benzoic acid 2-carboxaldehyde (**12**), and allyltriphenylphosphonium bromide were purchased from the Aldrich Chemical Co. 2-Oxazolone (**11**) was prepared using our published sulfuryl chloride procedure.[18]

*3.1.1. Methyl 2-formylbenzoate,* ***14****.* Iodomethane (17.58 g, 123.89 mmol), 2-formylbenzoic acid (**12**, 10.00 g, 66.61 mmol), and potassium carbonate (4.97 g, 35.97 mmol) were refluxed in DMF (50 mL) for 1 h. The reaction mixture was diluted with water (100 mL) and extracted with $CH_2Cl_2$ (100 mL). The organic layer was washed with 10% aqueous HCl (50 mL), saturated aqueous $NaHCO_3$ (50 mL), dried over $MgSO_4$, decolorized with activated carbon, filtered, and concentrated in vacuo to yield 10.77 g (65.6 mmol, 98%) of **14** as a pale yellow oil.[19] Bp 115–123 °C at 2 mmHg. $^1H$ NMR ($CD_2Cl_2$): $\delta$ 10.62 (s, 1H), 7.98 (m, 2H), 7.66 (m, 2H), 3.98 (s, 3H).

*3.1.2. 2-(1,3-Butadienyl)benzoic acid,* ***15****.* A solution of 2-(1,3-butadienyl)bromobenzene (**17**, 2.43 g, 11.63 mmol) in dry THF (25 mL) was added to a flame-dried, three-neck flask that contained magnesium turnings (0.31 g, 12.79 mmol). The reaction was refluxed for 3 h, and then cooled to room temperature. Dry $CO_2$ was bubbled through the gray solution for three more hours. The reaction was acidified with diluted HCl, extracted with EtOAc (2×25 mL), and the combined organic extracts were washed with dilute NaOH (3×25 mL). The combined basic aqueous washes were acidified with concentrated HCl and extracted with EtOAc (3×25 mL). The combined organic extracts were washed with water, brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to yield 1.01 g (5.8 mmol, 50%) of **15** as a white solid.[22] Mp 86–88 °C. $^1H$ NMR ($CDCl_3$): $\delta$ 11.75 (br s, 1H), 8.05 (d, 1H, $J$=6.9 Hz), 7.64 (d, 1H, $J$=7.8 Hz), 7.51 (m, 2H), 7.32 (t, 1H, $J$=7.5 Hz), 6.65 (m, 2H), 5.37 (d, 1H, $J$=15.6 Hz), 5.23 (d, 1H, $J$=9 Hz); $^{13}C$ NMR ($CDCl_3$): $\delta$ 173.4, 139.8, 137.4, 133.0, 132.7, 131.6, 131.3, 127.3, 127.1, 118.7; IR: 3011(br), 2649,

1685, 1597, 1563, 1405, 1271, 1003, 905, 751 $cm^{-1}$. MS *m*/*z*: 174 (P, 24), 130 (13), 129 (100), 128 (59), 127 (28), 115 (11), 77 (16), 63 (10), 51 (18).

*3.1.3. 1-(2-Bromophenyl)1,3-butadiene,* ***17****. Wittig protocol.* A solution of 2.2 M *n*-butyllithium in hexanes (10 mL, 22 mmol) was added dropwise to a sonicated suspension (in a sonic cleaning bath) of commercial prop-2-enyltriphenylphosphonium bromide (7.66 g, 20 mmol) in dry THF under nitrogen. After 15 min, 2-bromobenzaldehyde (**16**, 3.7 g, 20 mmol) was added to the red reaction at ambient temperature over 3 h, and stirred for 3 h without sonication until consumption of the aldehyde was complete, as monitored by TLC. The solvent was removed in vacuo and the residue triturated with ether to precipitate triphenylphosphine oxide. The mixture was filtered through a silica gel pad, the filtrate concentrated in vacuo, and purified by flash column chromatography (silica; hexane/$CH_2Cl_2$=95:5) to give 2.6 g (12.43 mmol, 62%) of **17** as a mixture of *E* and *Z* isomers.[23a] $^1H$ NMR ($CDCl_3$): $\delta$ 5.21, 5.38, 6.36, 6.51, 6.78 (sets of dd), 6.93, 7.28, 7.36, 7.58; $^{13}C$ NMR ($CDCl_3$): $\delta$ 119.1, 120.5, 124.2, 126.8, 127.1, 127.7, 128.9, 129.0, 130.1, 131.4, 131.5, 132.0, 132.4, 132.9, 133.0, 133.3, 137.0, 137.2, 137.4; IR (film): 3085, 3057, 1815, 1596, 1558, 1464, 1432, 1025, 1000, 946, 906, 750, 734 $cm^{-1}$; MS *m*/*z*: 210(P+2, 5), 208 (P, 5), 129 (100), 128 (77), 127 (30), 102 (11), 75 (11), 64 (13), 63 (18), 51 (28), 50 (16).

*3.1.4. 1-(2-Bromophenyl)but-3-en-1-ol,* ***18****.* Magnesium turnings (0.83 g, 34.26 mmol) in dry $Et_2O$ (10 mL) were added to a flame-dried, three-neck flask, fitted with a reflux condenser and addition funnel. A solution of allyl bromide (3.0 mL, 34.26 mmol) in $Et_2O$ (20 mL) was added dropwise, and the reaction was refluxed for 5 h. After cooling to room temperature, a solution of 2-bromobenzaldehyde (**16**, 2.0 mL, 17.13 mmol) in $Et_2O$ (20 mL) was added dropwise, and then the reaction was refluxed overnight. The reaction was quenched with saturated $NH_4Cl$ and extracted with $Et_2O$ (3×50 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (25% EtOAc/Hex; $R_f$=0.50) to yield 3.21 g (14.1 mmol, 82%) of **18** as a pale yellow oil.[23a] $^1H$ NMR ($CDCl_3$): $\delta$ 7.54 (m, 2H), 7.34 (td, 1H, *J*=1.1, 7.5 Hz), 7.13 (td, 1H, *J*=1.7, 7.6 Hz), 5.89 (m, 1H), 5.21 (m, 1H), 5.17 (d, 1H, *J*=1.1 Hz), 5.10 (dd, 1H, *J*=3.4, 8.3 Hz), 2.65 (m, 1H), 2.36 (m, 1H), 2.16 (s, 1H); $^{13}C$ NMR ($CDCl_3$): $\delta$ 142.9, 134.4, 132.9, 129.0, 127.8, 127.5, 122.0, 118.8, 72.0, 42.3; MS (ES) *m*/*z* 227 (14), 225 (17), 185 (87), 183 (100).

## 3.2. Indium-mediated procedure[23b]

A suspension of indium metal (4.72 g, 41.12 mmol) was stirred at 35 °C overnight under $N_2$ in a solution of 2-bromobenzaldehyde (**16**, 6.0 mL, 51.40 mmol), boron trifluoride etherate (6.5 mL, 51.40 mmol), and allyl bromide (4.4 mL, 51.40 mmol) in dry THF (80 mL). The reaction mixture was diluted with water (50 mL) and extracted with EtOAc (2×75 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to yield a thick colorless oil. Flash column chromatography (15% EtOAc/Hex) yielded 10.15 g (44.6 mmol, 87%) of **18** as a colorless oil.

*3.2.1. 2-(1,3-Butadienyl)bromobenzene,* ***17****. Bromination–elimination protocol.* A solution of 1-(2-bromophenyl)but-3-en-1-ol (**18**, 3.21 g, 14.13 mmol), triphenylphosphine (4.45 g, 16.96 mmol), hydroquinone (0.28 g, 2.54 mmol), and carbon tetrabromide (5.62 g, 16.96 mmol) were refluxed in dry THF (30 mL) for 30 min. Triethylamine (7.9 mL, 56.52 mmol) was added dropwise and the reaction was refluxed overnight. Water (75 mL) was added to the reaction mixture, which was extracted with hexanes (3×100 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, 100% hexanes) to yield 2.45 g (11.72 mmol, 83%) of **17** as a yellow oil.[23a] $^1H$ NMR ($CDCl_3$): $\delta$ 7.56 (m, 2H), 7.26 (m, 1H), 7.07 (td, 1H, *J*=1.7, 7.6 Hz), 6.92 (d, 1H, *J*=15.4 Hz), 6.74 (m, 1H), 6.57 (m, 1H), 5.38 (dd, 1H, *J*=1.4, 16.5 Hz), 5.24 (dd, 1H, *J*=1.4, 9.7 Hz); $^{13}C$ NMR ($CDCl_3$): $\delta$ 137.0, 131.9, 131.2, 130.3, 128.6, 127.6, 126.5, 125.4, 117.6, 116.6; MS (ES) *m*/*z* 210 (10), 208 (10), 129 (100).

*3.2.2. 3-(2-Buta-1,3-dienyl-benzoyl)-3H-oxazol-2-one,* ***20****.* 1-(1,3-Butadienyl)benzoic acid (**15**, 0.50 g, 2.87 mmol) was added to oxalyl chloride (5 mL). Evolution of gas started immediately, and after 10 min heat was applied. The mixture was refluxed under $N_2$ for 5 h. The reaction was concentrated in vacuo, a sample analyzed by MS and IR to confirm the presence of the acid chloride, and it was used without further purification. MS (EI) *m*/*z*: 194 (P+2, 9), 192 (P, 21), 157 (100), 129 (100), 128 (86), 127 (43), 102 (19), 77 (14), 75 (10), 63 (14), 51 (19); IR: 1770, 1650, 1595, 1560, 1469, 1183, 1102, 1002, 867, 649 $cm^{-1}$. Triethylamine (0.70 mL, 5.03 mmol) was added dropwise to a solution of 2-(1,3-butadienyl)benzoyl chloride (0.75 g, 3.89 mmol) and 2-oxazolone (**11**, 0.43 g, 5.03 mmol) in acetonitrile (25 mL). The reaction mixture was stirred at room temperature overnight, concentrated, and the residue added to a mixture of water (25 mL) and $Et_2O$ (25 mL). The layers were separated and the aqueous layer extracted with $Et_2O$ (2×25 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to yield 0.83 g (3.44 mmol, 88%) of **19**. $^1H$ NMR ($CDCl_3$): $\delta$ 7.66 (d, 1H, *J*=6 Hz), 7.52 (m, 1H), 7.30–7.44 (m, 3H), 6.90 (d, 1H, *J*=3 Hz), 6.72 (m, 2H), 6.47 (m, 1H), 5.38 (d, 1H, *J*=18 Hz), 5.25 (d, 1H, *J*=9.0 Hz); $^{13}C$ NMR ($CDCl_3$): $\delta$ 166.2, 150.3, 136.6, 135.9, 133.3, 131.5, 130.7, 130.3, 128.2, 128.0, 127.1, 126.0, 119.4, 112.4; IR ($cm^{-1}$): 3155, 2925, 1788, 1701, 1598, 1481, 1357, 1281, 1226, 1181, 1117, 1067, 1027, 1005, 933, 867, 750, 697, 663; MS (ES) *m*/*z* 241 (8), 157 (100), 129 (100), 102 (11), 77 (16); HRMS ($ES^+$) *m*/*z* calcd for $C_{14}H_{11}NO_3$: $[M+H]^+$, 242.0812; found: $[M+H]^+$, 242.0819.

*3.2.3. 3,3a,10b,10c-Tetrahydro-4-oxa-5a-aza-acephenanthrylene-5,6-dione,* ***20*** *and* ***21****.* A solution of 3-(2-buta-1,3-dienyl-benzoyl)-3*H*-oxazol-2-one (**19**, 0.40 g, 1.66 mmol) was refluxed in dry toluene (10 mL) for 2 days under $N_2$. After cooling, the toluene was filtered and the stirbar and flask washed with EtOAc to dissolve all residues that coated those surfaces. The EtOAc was added to the toluene, all solvents were removed in vacuo. The residue was taken up in dichloromethane/ethyl acetate and added directly to silica gel, which allowed purification by flash column chromatography (gradient 25% EtOAc/Hex to 100% EtOAc) to give 0.22 g (0.91 mmol, 55%) of **20** (all cis) as a white solid, $R_f$=0.32 (100% EtOAc). $^1H$ NMR ($CDCl_3$): $\delta$ 8.12 (d, 1H, *J*=8 Hz), 7.55 (t, 1H, *J*=8 Hz), 7.40 (t, 1H, *J*=8 Hz), 7.28 (d, 1H, *J*=8 Hz), 5.95 (m, 1H), 5.59 (d, 1H, *J*=8 Hz), 5.01 (t, 1H, *J*=4 Hz), 4.84 (t, 1H, *J*=4 Hz), 3.46 (s, 1H), 2.60 (dd, 1H, *J*=8, 16 Hz), 2.27 (d, 1H, *J*=16 Hz); $^{13}C$ NMR ($CDCl_3$): $\delta$ 172.5, 160.0, 150.9, 139.4, 133.4, 128.7, 127.8, 127.5, 127.0, 125.2, 70.6, 54.0, 35.7, 26.8; MS *m*/*z*: 241 (P, 44), 198 (13), 197 (54), 196 (16), 181 (10), 180 (38), 170 (11), 157 (95), 156 (49), 141 (15), 129 (100), 128 (82), 127 (33), 115 (28), 102 (10), 89 (15), 77 (21), 76 (12), 75 (10), 63 (21), 51 (20), 50 (13); HRMS ($ES^+$) *m*/*z* calcd for $C_{14}H_{11}NO_3$: $[M+H]^+$, 242.0812; found: $[M+H]^+$, 242.0811. In addition, 0.10 g (0.42 mmol, 25%) of the **21** (trans) was obtained as a tan solid, $R_f$=0.48 (100% EtOAc). $^1H$ NMR ($CDCl_3$): $\delta$ 8.11 (d, 1H, *J*=6 Hz), 7.58 (m, 1H), 7.44 (m, 2H), 6.50 (m, 1H), 6.09 (m, 1H), 4.70 (m, 1H), 3.96 (t, 1H, *J*=18 Hz), 3.65 (d, 1H, *J*=12 Hz), 3.07 (m, 1H), 2.28 (m, 1H); $^{13}C$ NMR ($CDCl_3$): $\delta$ 29.4, 38.6, 58.7, 71.3, 123.6, 126.8, 127.8, 128.0, 129.1, 130.7, 134.0, 138.7, 151.1, 161.2; IR: 2977, 1790 (str), 1678, 1603, 1354, 1303, 1274, 1185, 1025, 749, 676, 662, 541 $cm^{-1}$; MS *m*/*z*: 242 (P+1, 11), 241 (P, 70), 198 (15), 197 (100), 196 (65), 182 (18), 180 (10), 170 (13), 169 (23), 168 (28), 167 (13), 157 (77), 156 (70), 144 (13), 141 (21), 140 (11), 130 (10), 129

(44), 128 (46), 127 (25), 116 (13), 115 (54), 114 (11), 102 (15), 101 (18), 89 (15), 77 (21), 76 (15), 75 (20), 74 (10), 65 (10), 63 (21), 51 (28), 50 (15); HRMS ($ES^+$) *m/z* calcd for $C_{14}H_{11}NO_3$: $[M+H]^+$, 242.0812; found: $[M+H]^+$, 242.0831.

*3.2.4. 3,4,4a,5-Tetrahydro-4-hydroxyphenanthridin-6-(10bH)-one,* ***22****.* A solution of **20** (0.07 g, 0.29 mmol) in absolute MeOH (0.75 mL) and THF (0.25 mL) was stirred in the presence of Amberlyst A-21 resin (0.37 g) for 6 days. The resin was filtered and rinsed with EtOAc. The filtrate was concentrated and purified by flash column chromatography (100% EtOAc) to yield 0.05 g (0.23 mmol, 79%) of **22** as an amorphous white solid. $^1H$ NMR ($CDCl_3$): $\delta$ 7.98 (d, 1H, $J$=8 Hz), 7.62 (br s, 1H), 7.44 (t, 1H, $J$=8 Hz), 7.30 (t, 1H, $J$=8 Hz), 7.18 (d, 1H, $J$=8 Hz), 5.55 (m, 1H), 5.20 (d, 1H, $J$=8 Hz), 4.17 (s, 1H), 4.09 (m, 1H), 3.59 (s, 1H), 2.33 (m, 2H); $^{13}C$ NMR ($CDCl_3$): $\delta$ 166.6, 140.6, 133.0, 128.1, 127.5, 127.4, 126.9, 124.6, 67.9, 53.5, 39.9, 28.9; MS (EI) *m/z* 215 (29), 197 (100), 184 (85), 166 (20), 156 (13), 146 (18), 129 (44), 115 (8), 89 (21); HRMS ($ES^+$) *m/z* calcd for $C_{13}H_{13}NO_2$: $[M+H]^+$, 216.1019; found: $[M+H]^+$, 216.1024.

An alternative hydrolysis procedure stirred a mixture of **20** (0.34 g, 1.41 mmol) and sodium hydroxide (0.17 g, 4.23 mmol) in absolute MeOH (20 mL) for 1 h. The reaction was neutralized with saturated aqueous $NH_4Cl$ and extracted with EtOAc (3×15 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated to yield 0.27 g (1.25 mmol, 89%) of **22** as a pale yellow solid.

## Acknowledgements

We thank Dr. Dennis Hill and Ms. Tzipporah Kertesz for obtaining the high-resolution mass spectral data.

## Supplementary data

The proton and carbon NMR spectra for compounds **15** and **17**–**22** are provided. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.08.066.

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