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Skeletal Wagner–Meerwein rearrangement of perhydro-3a,6;4,5-diepoxyisoindoles

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4,6-Epoxycyclopenta[*c*]pyridine

ABSTRACT

An investigation of a skeletal Wagner–Meerwein rearrangement of variously substituted or quinoline-annulated 3a,6;4,5-diepoxyisoindol-1-ones is reported. Optimum reaction conditions (Ac_2O, $BF_3 \cdot OEt_2$, rt) were discovered for the formation of the target 4,6-epoxycyclopenta[*c*]pyridines in 40–80% yields. It was shown that the direction of the sigmatropic rearrangement of 3a,6;4,5-diepoxyisoindol-1-ones depended dramatically on the carboxyl group position (*exo*-/*endo*-) in the oxabicyclo[2.2.1]heptane moiety. The spatial structure of previously unknown 7,9-epoxycyclopenta[4,5]pyrido[1,2-*a*]quinolines derived from Wagner–Meerwein rearrangement of 2,11b-epoxyoxireno[6,7]isoindolo[2,1-*a*]quinolines was established based on the X-ray analysis data. The skeletal rearrangement proceeded regio- and stereospecifically in all the cases examined due to the absence of the epimerization of the carbon atoms adjacent to the carbocation centres.

1. Introduction

7-Oxabicyclo[2.2.1]heptanes and -heptenes, available from Diels–Alder reaction between furans and the appropriate electron-deficient alkenes/alkynes, are valuable synthetic intermediates for organic synthesis including the synthesis of natural products.[1] The oxabicycloheptene moiety readily undergoes aromatization,[2] nucleophilic cleavage[3] and oxidation.[4] However, sigmatropic rearrangements of various types, of which cation-inducible skeletal Wagner–Meerwein rearrangement is the most thoroughly studied, are the most interesting and challenging routes for its transformation. The mechanism and products of the skeletal rearrangements of 7-oxabicyclo[2.2.1]heptanes were studied in detail by Vogel and co-workers,[5] as well as by some other research groups.[6] On the other hand, there have been no systematic study performed on similar rearrangements of the systems possessing 7-oxabicyclo[2.2.1]heptane fragment annulated with carbo- or heterocycles (which are easily available by IMDAF reaction[7]). The analysis of the few works on the sigmatropic rearrangements of annulated 7-oxabicyclo[2.2.1]heptanes showed that their results were often difficult to predict, as they depended on both the reaction conditions (catalyst, solvent) and the nature of the substituents in the heterocyclic core. This ambiguity impedes the preparative application of Wagner–Meerwein rearrangement of the aforementioned systems.

The most representative examples of Wagner–Meerwein rearrangement of isostructural analogues containing the 7-oxabicyclo[2.2.1]heptane fragment annulated with carbo- or heterocycles are depicted in the Schemes 1–3.

Cation-inducible skeletal rearrangements of hydrogenated 2,4a-epoxynaphthalenes under Woodward reaction conditions (I_2/AgOAc, aq AcOH, then aq Na_2CO_3) can proceed in two different directions leading to the formation of either hydrogenated 3,8a-methanochromenes or 2,4-epoxyazulenes depending on the nature of the substituents.[8a] In the case of their structural analogues—dinitrosubstituted[8b] 2,4a-epoxynaphthalenes—rearrangement does not proceed at all (Scheme 1).

There are only six original works[9] describing successful examples of the skeletal rearrangements of 7-oxabicyclo[2.2.1]heptanes annulated with nitrogen containing heterocycles four of which[9a–d] belong to this group.

As determined in earlier studies performed by this group,[9d] Lewis acids catalyzed sigmatropic rearrangement of spiroannulated 6,8a;7,8-diepoxyisoquinolines proceeded in two possible

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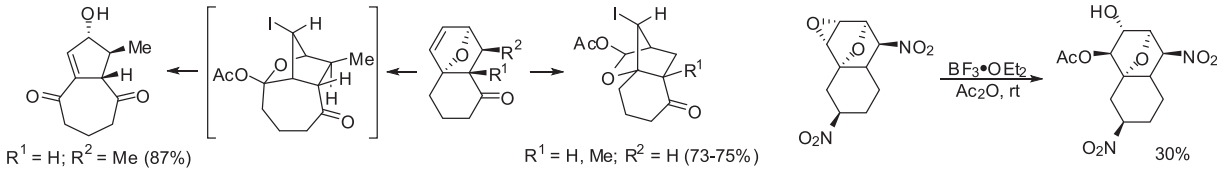
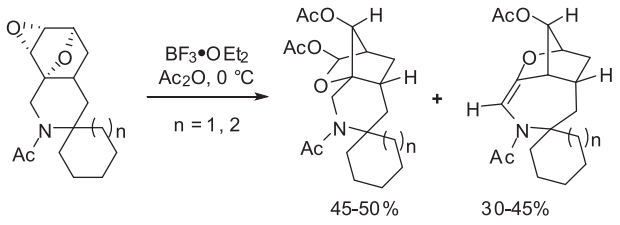
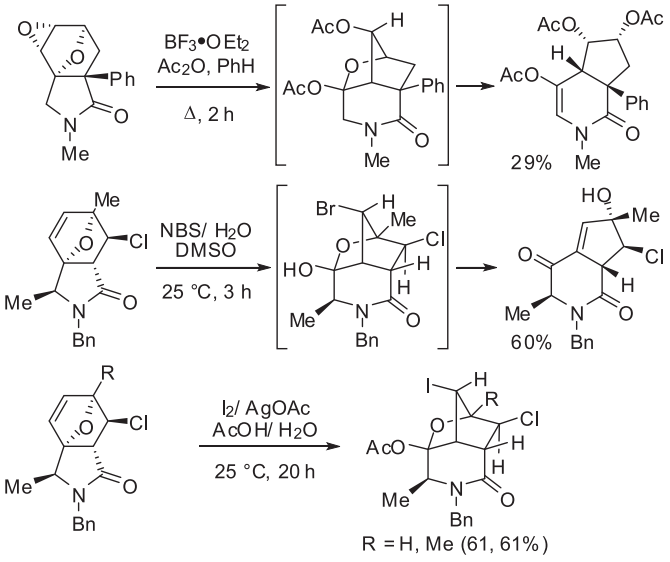


Scheme 1. 2,4a-Epoxynaphthalenes behaviour under the Wagner–Meerwein rearrangement conditions.



Scheme 2. Skeletal rearrangement of 6,8a;7,8-diepoxyisoquinolines.



Scheme 3. Transformations of 3a,6-epoxy- and 3a,6;4,5-diepoxyisoindoles in the presence of electrophilic agents.

directions (Scheme 2), as in the case of 2,4a-epoxynaphthalenes (Scheme 1).

The transformations of 3a,6;4,5-diepoxy- and 3a,6-epoxyisoindoles in the presence of various electrophilic agents (Scheme 3) were described in an early work by Gschwend[9g] and a short communication of Jung.[9e] The mechanisms of similar transformations are discussed further.

These solitary examples show clearly that there is currently no universal strategy for conducting sigmatropic rearrangements of annulated 7-oxabicyclo[2.2.1]heptanes whilst predicting their outcome beforehand. Thus, it is necessary to develop the unique reaction conditions as described here, in order to achieve acceptable yield and selectivity in each individual case. In this paper, we report a systematic study on the Wagner–Meerwein rearrangement of variously substituted or quinoline-annulated 3a,6;4,5-diepoxyisoindol-1-ones aimed to fulfil this gap.

2. Results and discussion

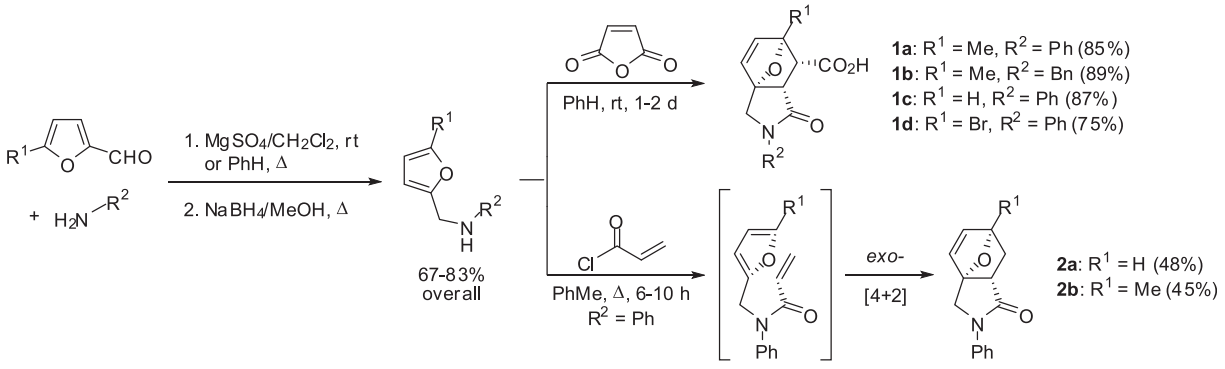
3a,6-Epoxyisoindoles, easily available by a known two-step reaction sequence (Scheme 4),[2d,10] were selected as the major target for our investigation.

The interaction of intermediate furfurylamines with maleic anhydride or acryloyl chloride proceeded smoothly and stereoselectively resulting in the formation of intramolecular Diels–Alder *exo*-adducts **1**, **2** in moderate to good yields.

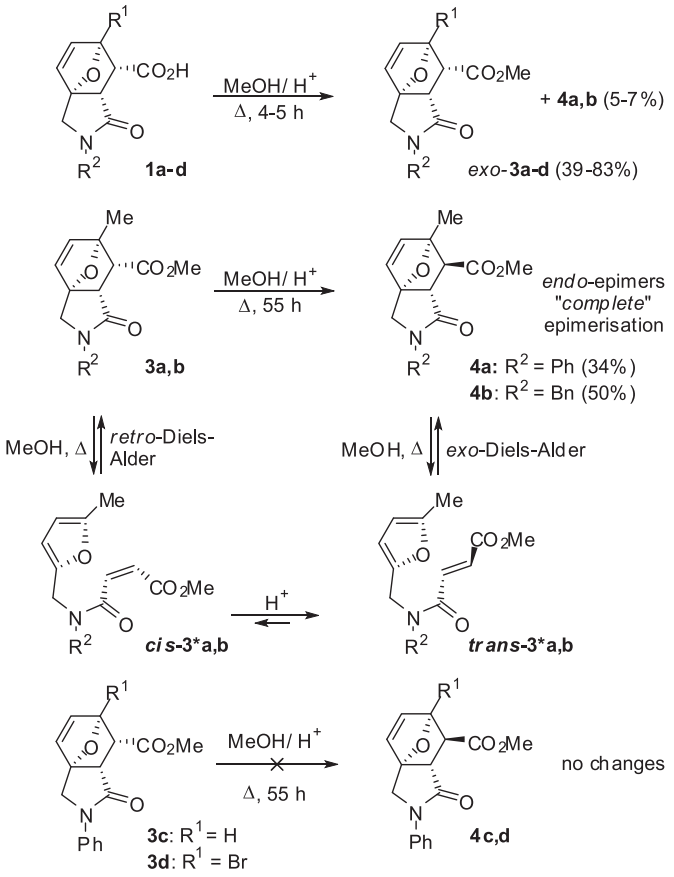
Carboxylic acids **1** were obtained as white fine-crystalline powders almost insoluble in common organic solvents (soluble reasonably in DMF and DMSO only). Thereupon, acids **1a**–**d** were transformed into soluble methylesters **3a**–**d** (Scheme 5) for further transformations.

Esterification was carried out in a classic manner yielding desired esters **3a**–**d** in moderate to good yields. However, GC–MS analysis of the reaction mixtures of 6-methyl substituted acids **1a**,**b** revealed the presence of minor products **4a**,**b** (5–7% after 4–5 h reflux in MeOH) along with the target esters **3a**,**b**. These minor products were isolated as individual compounds and analyzed in detail using NMR methods which allowed to assign a structure of 7-*endo*-methyl-3a,6-epoxyisoindole-7-carboxylates to them.

Prolonged reflux (50–60 h) of the starting carboxylic acids **1a**,**b** in methanol in the presence of catalytic amounts of sulfuric acid allowed to obtain 7-*endo*-epimers **4a**,**b** as pure products in 34–50% yield, while 7-*exo*-epimers **3a**,**b** were found only in trace amounts in the reaction mixtures (increased reaction time also resulted in the formation of some unidentified admixtures).



Scheme 4. Synthesis of starting 3a,6-epoxyisoindoles **1**, **2**.



Scheme 5. Esterification of *exo*-isoindolecarboxylic acids **1** and mechanism of epimers **4a**,**b** formation.

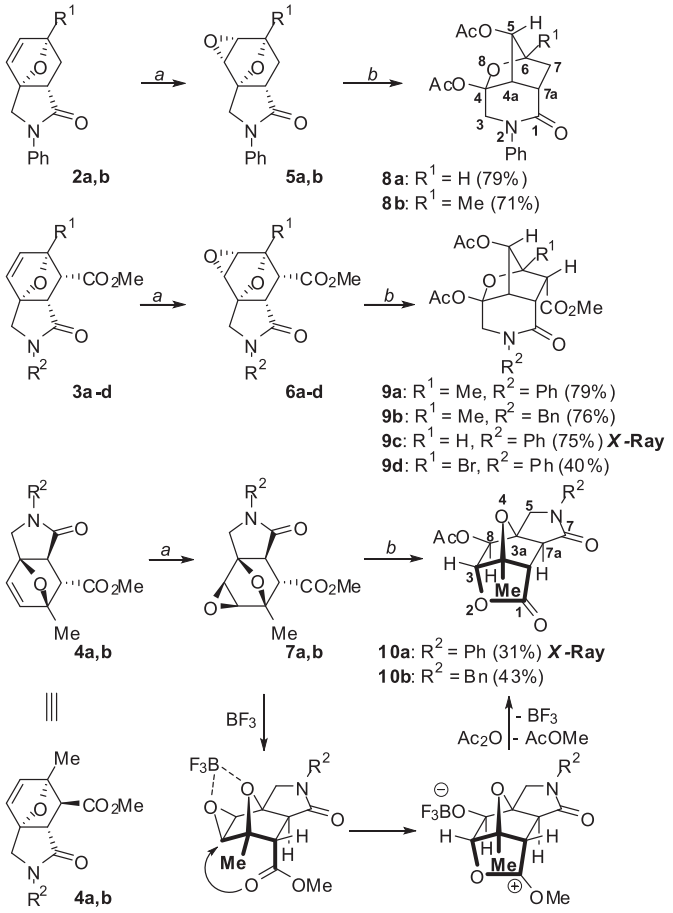
Individual 7-*exo*-esters **3a**,**b** epimerized completely into 7-*endo*-esters **4a**,**b** under similar conditions (Scheme 5).

The analysis of the literature data showed that such an epimerization was only observed in one of the early works,[10e] however, neither the mechanism of this transformation nor the spatial structure of the epimer formed were proposed.

We surmise that thermal retro Diels–Alder reaction of *exo*-esters **3a**,**b** is the most reasonable explanation of the *endo*-epimers **4a**,**b** formation. Thus, *N*-maleinamides *cis*-**3*a**,**b** formed by thermal retro Diels–Alder reaction of *exo*-**3a**,**b** transform into the more thermodynamically stable isomers *trans*-**3*a**,**b**,[11] which then undergo subsequent Diels–Alder reaction resulting in the formation of *endo*-epimers **4a**,**b**.

It is worth mentioning that the prolonged reflux of 6-H and 6-Br substituted 3a,6-epoxyisoindole-7-carboxylic acids **1c**,**d** in MeOH did not bring about the formation of the corresponding *endo*-methylesters **4c**,**d** (exclusively *exo*-methylesters **3c**,**d** were observed by GC–MS of the crude reaction mixtures and isolated). Apparently, in this case the first step of the epimerization, namely retro Diels–Alder reaction, did not occur at 65 °C. Thus, it was decided to investigate the behaviour of acids **1c**,**d** under the esterification by different alcohols to allow a gradual increase of the temperature of the reaction medium. First, switching from MeOH to EtOH did not make any difference as corresponding *exo*-ethylesters were formed exclusively. The temperature increase to ~100 °C (reflux in *n*-PrOH) gave full conversion of starting acids **1c**,**d** leading to the formation of the corresponding *exo*-propylesters accompanied by the minor admixtures of epimeric *endo*-propylesters (about 5–7% by GC–MS of the crude reaction mixtures) after 5 h. The esterification of acids **1c**,**d** in *n*-BuOH at reflux was completed after 2 h resulting in the exclusive formation of the corresponding *exo*-butylesters. However, the complete decomposition of intermediate butyl esters leading to the formation of corresponding starting furfurylamines and dibutylmaleate was observed after 15 h at reflux.

The oxidation of the oxabicyclo[2.2.1]heptene fragment of isoindolones **2**–**4** with *m*-CPBA gave the corresponding *exo*-oxiranes **5**–**7** in good (58–85%) yields (Scheme 6).[4c,9e,12]

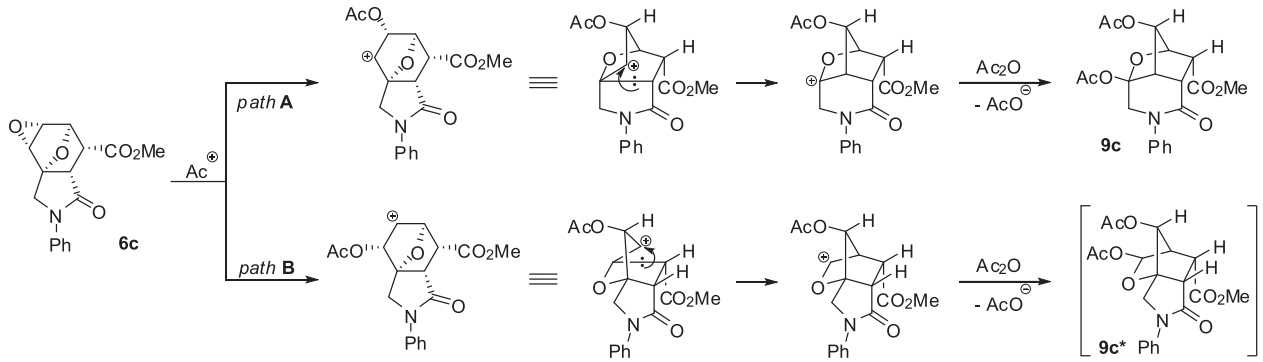


Scheme 6. Reagents and conditions: (a) *m*-CPBA/CH_2Cl_2, rt, 2 days; (b) $BF_3 \cdot OEt_2/Ac_2O$, 5→25 °C, 4 h.

In order to define the optimal reaction conditions for the cleavage of the oxirane ring of diepoxides **5**, **6**, a wide range of reagents and solvents combinations [$THF/BF_3 \cdot OEt_2$, $Ac_2O/BF_3 \cdot OEt_2$, $MeCN/BF_3 \cdot OEt_2$, CF_3CO_2H, $AcOH/H_2SO_4$, HBr (48%), $Ac_2O/AlCl_3$] was used. The best results were achieved using acetic anhydride as a reaction medium and boron trifluoride etherate as a homogenous electrophilic catalyst at rt (Scheme 6).

The cleavage of the oxirane ring of diepoxides **5**, **6** under the above conditions proceeded smoothly and was accompanied by the skeletal rearrangement (path **A**, Scheme 7) resulting in the formation of the Wagner–Meerwein rearrangement products—4,6-epoxycyclopenta[*c*]pyridines (**8**, **9**)—in good yields. It is vital to use acetic anhydride as a reaction medium to achieve good yields of the rearrangement products **8**, **9**. Apparently, this solvent neutralizes a carbocation centre during the last step of the rearrangement, thus preventing its further transformations which were observed in some earlier works (Schemes 1 and 3).[9g,e] In contrast, the use of acetic acid as a reaction medium resulted in the formation of a mixture of several unidentified products.

It is significant that although diepoxides **5**, **6** possess two alternative σ-bonds, both theoretically able to undergo sigmatropic



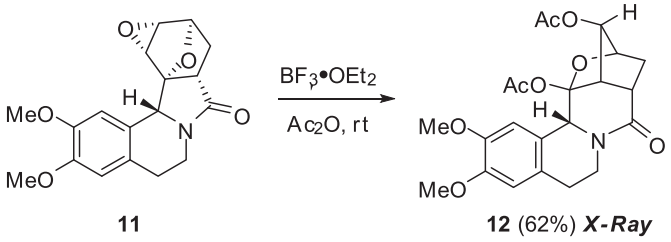
Scheme 7. Plausible mechanisms of the Wagner–Meerwein rearrangement of diepoxyisoindoles **5**, **6**.

rearrangement (paths **A** and **B**, Scheme 7), in fact, only one of them participates in the reaction, thus providing the realization of the path **A**. No alternative structures of type **9c***[8a,9d] were detected among the reaction products. Such a selectivity (path **A**) can be explained in terms of the higher strain and, therefore, lower strength of the σ-bond incorporated into the pyrrolidine ring (this σ-bond belongs to the both five-membered cycles) compared to the stronger alternative σ-bond belonging solely to the six-membered carbocycle (path **B**).

As expected, *endo*-esters **7a**,**b** epimeric to *exo*-esters **6a**,**b** did not undergo skeletal rearrangement under similar conditions (Ac_2O, $BF_3 \cdot OEt_2$, rt). In this case the strain of the three-membered oxirane ring was released by means of the intramolecular nucleophilic attack of the ester group[6b,f,e,13] (Scheme 6) leading to the formation of products of 3,4a-methanofuro[3′,4′:4,5]furo[2,3-*c*]pyrrole structural type (**10a**,**b**).

The structure of the products **9c** and **10a** was established unambiguously based on their X-ray analysis data (see Figs. 1 and 3 and text below).

As was shown earlier by this group,[9b] hydrogenated 2,11c-epoxyoxireno[6,7]isoindolo[1,2-*a*]isoquinolines (**11**) underwent similar rearrangement in the presence of Lewis acids resulting in the formation of pentacycles of type **12** (Scheme 8).



Scheme 8.

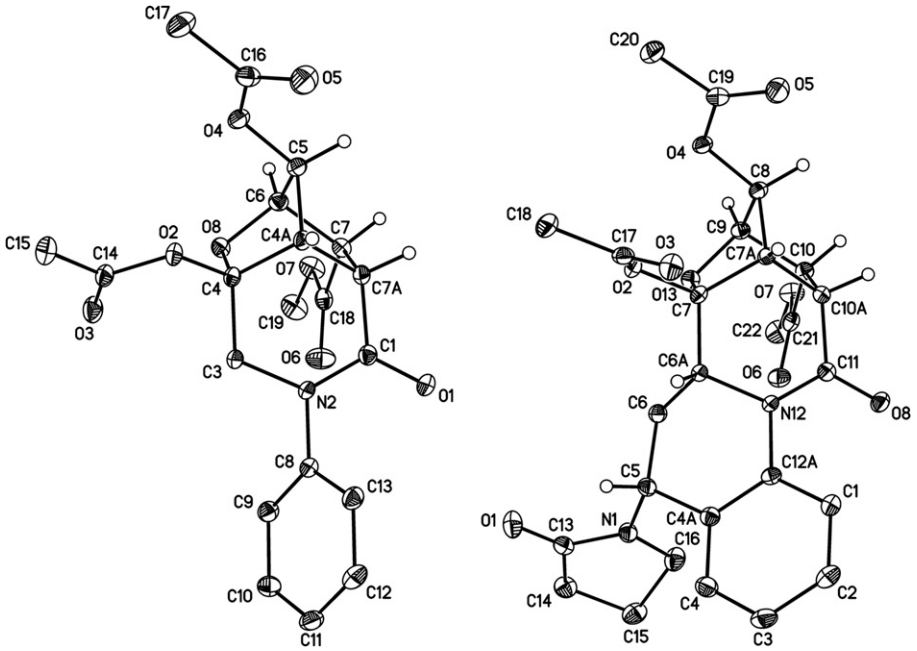
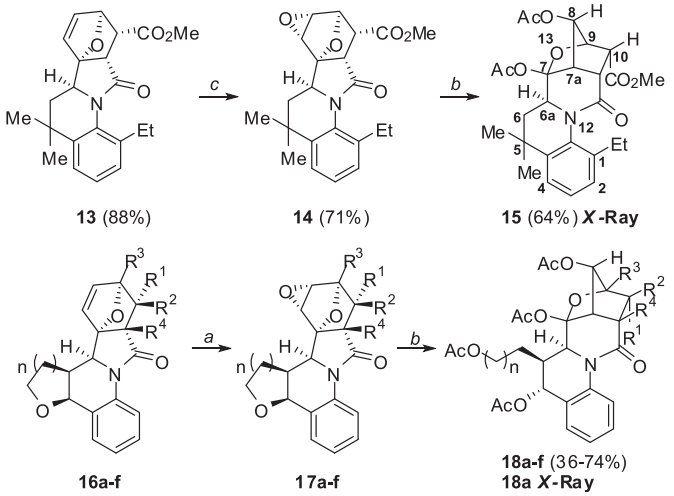


Fig. 1. Molecular structure of **9c** (on the left) and **21g** (on the right). Displacement ellipsoids are depicted at the 50% probability level. Only hydrogen atoms at the asymmetric centres are presented. The solvate ethanol molecule is not shown for **9c** and the solvate water molecules are not shown for **21g**.

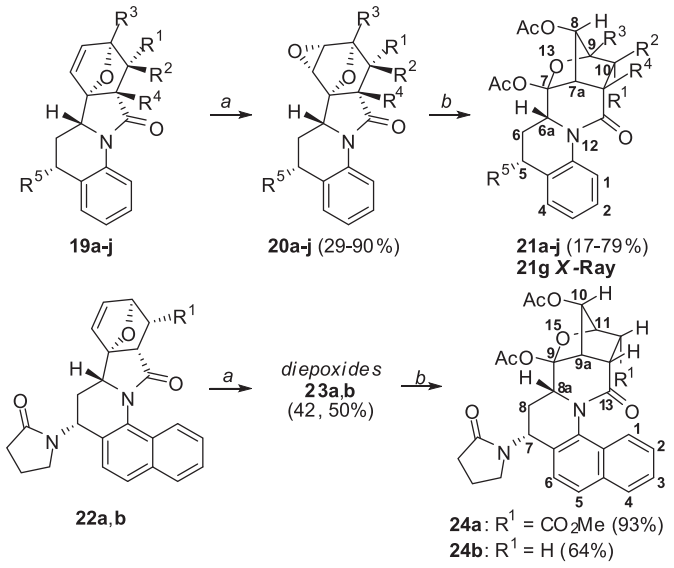
With the Wagner–Meerwein methodology polished for uncomplicated systems—3a,6;4,5-diepoxyisoindoles (**5**, **6**)—in hand, we turned our attention to the more sophisticated structures. The leitmotif of the further study was the investigation of the scope and limitations of Wagner–Meerwein rearrangement applied to 3a,6;4,5-diepoxyisoindoles condensed with other heterocycles.

6b,9-Epoxyisoindolo[2,1-*a*]quinolines **13**, **16**, **19**, **22** (Schemes 9, 10) easily available by a two-step reaction sequence[14] involving Povarov reaction[15] turned out to be the most suitable objects for the investigation of the influence of the substituents

in the 3a,6;4,5-diepoxyisoindoles core on the rearrangement outcome. This synthetic approach allows a broad variation in the nature of the substituents both in isoindole and quinoline fragments.



Scheme 9. Reagents and conditions: (a) *m*-CPBA/CH_2Cl_2, rt, 2 d; (b) BF_3OEt_2/Ac_2O, 0→25 °C, 4–24 h; (c) H_2O_2 (50%)/$HCO_2H/(CH_2Cl)_2$, Δ, 20 h.



Scheme 10. Reagents and conditions: (a) *m*-CPBA/CH_2Cl_2, rt, 2 d; (b) BF_3OEt_2/Ac_2O, 0→25 °C, 2–24 h.

Epoxyisoindolo[2,1-*a*]quinoline **13**[10c] easily underwent oxidation by performic acid to form the corresponding diepoxide **14**. This diepoxide was converted with a good yield into 7,9-epoxycyclo[4,5]pyrido[1,2-*a*]quinoline **15** under the sigmatropic rearrangement conditions (Scheme 9).

The rearrangement of diepoxides **17**[14a] annulated with furan (**17a**–**e**) or pyran (**17f**) ring at the side [*c*] (prepared by the oxidation of 11,13a-epoxyfuro-(or pyrano-) [3,2-*c*]isoindolo[2,1-*a*]quinolines **16**[14a,d]) proceeded as a more complex process (Scheme 9). Thus, in the case of substrates **17a**–**f** nucleophilic cleavage of the furan (pyran) ring was observed along with the expected sigmatropic rearrangement. Apparently, this cleavage proceeded via a S_N2 mechanism with the complete inversion of configuration at C3a (for **17a**–**e**, *n*=1) or C4a (for **17f**, *n*=2) atom.

On the other hand, the *N*-pyrrolidine (R^5) fragment of diepoxyisoindoloquinolines **20**, **23**[14e] (prepared by the oxidation of isoindoloquinolines **19**,[14c] **22**[14b]) appeared to be robust under the reaction conditions and did not undergo substitution by the acetoxy group (Scheme 10).

The structure of the products **15**, **18a** and **21g** was established unambiguously based on their X-ray analysis data (see Figs. 1 and 2 and text below).

The analysis of the data summarized in the Table 1 allowed concluding that neither steric nor electronic effects of the substituents (R^1–R^5) in the molecules of starting diepoxyisoindoloquinolines **14**, **17**, **20**, **23** influenced the direction of the Wagner–Meerwein rearrangement. The yields of target rearrangement products varied (30–79%) for different substrates, however, we did not manage to reveal the rule describing a functional dependence yield/substituent.

It is significant that no products of epimerization at C6a (for compounds **15**, **18**, **21**) or C8a (for **24**) atoms adjacent to the 'carbocation centre' (see mechanism depicted in the Scheme 7) were observed in the reaction mixtures. We suppose this fact to be the evidence of a concerted rather than a stepwise mechanism of the rearrangement.

Since there were almost no spectral data of octahydro-4,6-epoxycyclopenta[*c*]pyrans presented in the previously published short communications,[8a,9e,g] we are reporting certain reference NMR signals and key structural motives of this class of compounds here.

The signals of the C7 (for **18**, **21**) or C4 (for **8**, **9**) or C9 (for **24**) atom at 103.2–106.9 ppm and C8 (for **18**, **21**) or C5 (for **8**, **9**) or C10 (for **24**) atom at 75.4–79.2 ppm are the most identifiable signals of octahydro-4,6-epoxycyclopenta[*c*]pyrans in their ^{13}C NMR spectra. The most characteristic feature of their ^1H NMR spectra is the presence of a triplet or doublet-doublet signal of the bridged hydrogen atom H8 (for **18**, **21**) or H5 (for **8**, **9**) at ~5 ppm with coupling constant $^3J_{7a,8}$–$^3J_{8,9}$=0.9–2.1 Hz.

According to X-ray data the molecules **9c**, **12**, **15**, **18a** and **21g** comprise a fused tricyclic system of 4,6-epoxycyclopenta[*c*]pyridine (Figs. 1–3). The general geometrical features of this system in **9c**, **12**, **15**, **18a** and **21g** are determined by the direction of the Wagner–Meerwein rearrangement and, consequently, are similar. The five-membered rings have usual *envelope* conformation. The two *O*-carboxylate substituents occupying the same positions (at the C4 and C5 for **9c**, the C12 and C11 for **12**, the C7 and C8 for **21g** and **18a**, and the C7 and C5 for **15** carbon atoms) are in the sterically unfavourable *syn*-periplanar configuration relative to the tetrahydrofuran ring. Furthermore, the third *C*-carboxylate substituent of the system in **9c**, **15**, **18a** and **21g** is disposed in identical fashion. Thus, the relative configuration of the asymmetric centres in the bicyclo[2.2.1]heptane fragment of the tricyclic system is kept unchanged, i.e., 4*R**,4a*R**,5*R**,6*S**,7*S**,7a*R** in the case of **9c** (the corresponding atom labels should be applied for **12**, **15**, **18a** and **21g**).

However, the conformation of the six-membered tetrahydropyridinone ring of the tricyclic system in **9c**, **12**, **15**, **18a** and **21g** is distinguished depending on different substituents at the N – C_{sp^3} bond as well as the configuration of additional asymmetric centre within the system. So, in the absence of substituents at the C3 carbon atom in **9c**, it adopts the flattened *twist-boat* conformation.

The presence of fused cyclic substituents at the N – C_{sp^3} bond and the *S** configuration of the C12a carbon atom in **12** and C6a carbon atom in **21g** relative to the aforementioned configurations of the asymmetric centres in the bicyclo[2.2.1]heptane fragment give rise to the *sofa* and *boat* conformation of this ring, respectively. The presence of fused cyclic substituents at the N – C_{sp^3} bond and the *R** configuration of the C6a and C8 carbon atoms in **18a** and **15**, respectively, relative to the aforementioned configurations of the

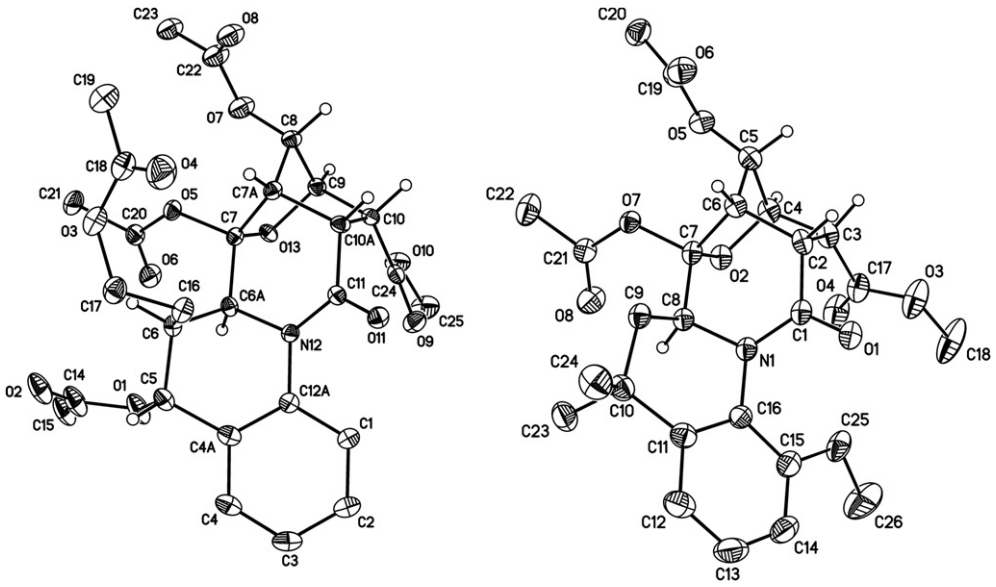


Fig. 2. Molecular structure of **18a** (on the left) and **15** (on the right). Displacement ellipsoids in case of **18a** are depicted at the 50% probability level. The alternative positions of the smaller occupancies for the two disordered carboxylate substituents at the C5 and C8 carbon atoms are not shown for **18a**. Displacement ellipsoids in case of **15** are depicted at the 40% probability level. Only hydrogen atoms at the asymmetric centres are presented.

asymmetric centres in the bicyclo[2.2.1]heptane fragment results in the distorted *chair* conformation of the tetrahydropyridinone ring.

The conformation of the tetrahydropyridine ring in **12**, **15**, **18a** and **21g** is the distorted nonsymmetrical *half-chair*. The dihedral angle between the planes of the tetrahydropyridinone and benzene rings is 57.7, 50.0, 38.8, 32.0 and 49.9° for **9c**, **12**, **15**, **18a** and **21g**, respectively.

The crystals of **9c**, **12**, **18a** and **21g** are racemic, while the crystal of **15** is enantiomeric. Evidently, this substance crystallizes as a conglomerate and it is capable of spontaneous enantiomeric separation by Pasteur. Nevertheless, it is impossible to determine unambiguously the absolute configuration of the asymmetric centres in **15** due to the absence of the heavy atoms with $Z>14$ (Si) in its composition. The configurations of additional asymmetric centres out of the described tricyclic system are 5*S**,6*R** in **18a** and 5*S** in **21g** relative to the aforementioned configurations of the asymmetric centres in the bicyclo[2.2.1]heptane fragment.

Compound **10a** comprises a fused tetracyclic system of octahydro-3,4a-methanofuro[3′,4′:4,5]furo[2,3-*c*]pyrrole (Fig. 3). All the rings adopt the usual *envelope* conformation. The crystal of **10a** is racemic and consists of enantiomeric pairs with the following relative configuration of the centres: *rac*-3*R**,3a*R**,4a*R**,7a*S**,7b*S**,8*R**.

In summary, we have investigated the mechanism of the skeletal Wagner–Meerwein rearrangement of 3a,6;4,5-diepoxy isoindol-1-ones and 2,11b-epoxyoxireno[6,7]isoindolo[2,1-*a*]quinolines. It was shown that irrespective of the nature of the substituents in an oxabicyclo[2.2.1]heptane fragment the rearrangement proceeded only in one direction affording substituted or annulated with the quinoline ring 4,6-epoxycyclopenta[*c*]pyridines. The synthetic protocol developed for the Wagner–Meerwein rearrangement is of considerable interest from a preparative viewpoint due to a relative availability of starting materials, mild reaction conditions, straightforward experimental procedures and stereo- and regiospecificity.

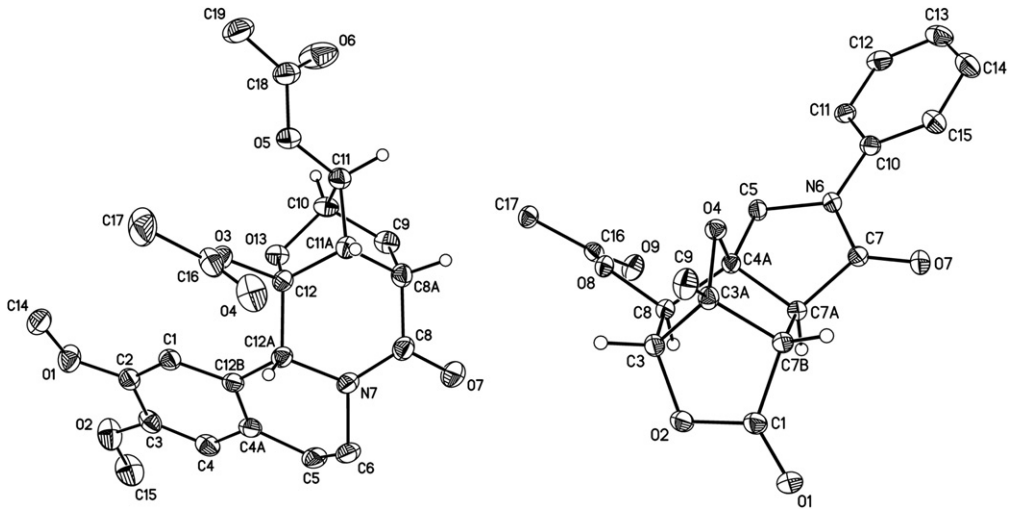


Fig. 3. Molecular structure of **12** (on the left) and **10a** (on the right). Displacement ellipsoids are depicted at the 40% probability level. Only hydrogen atoms at the asymmetric centres are presented.

Table 1
Substituents and yields[a] (%) of 7,9-epoxycyclopenta[4,5]pyrido[1,2-*a*]quinolines **18**, **21**

Prod.	R^1	R^2	R^3	R^4	*n* or R^5	Yield
18a	CO_2Me	H	H	H	1	48
18b	CO_2Me	H	Me	H	1	70
18c	CO_2Me	Me	H	H	1	61
18d	H	H	H	Me	1	41
18e	H	Ph	H	H	1	74
18f	CO_2Me	H	H	H	2	36
21a	H	H	H	H	2-Oxopyrrolidin-1-yl	47
21b	H	H	Me	H	2-Oxopyrrolidin-1-yl	60
21c	H	H	H	Me	2-Oxopyrrolidin-1-yl	34
21d	H	Me	H	H	2-Oxopyrrolidin-1-yl	79
21e	H	Ph	H	H	2-Oxopyrrolidin-1-yl	59
21f	H	H	H	H	NMeAc	59
21g	CO_2Me	H	H	H	2-Oxopyrrolidin-1-yl	30
21h	CO_2Me	H	Me	H	2-Oxopyrrolidin-1-yl	66
21i	CO_2Me	Me	H	H	2-Oxopyrrolidin-1-yl	34
21j	CO_2Me	H	H	H	NMeAc	77

[a] Yields of isolated after recrystallization products are given.

3. Experimental

3.1. General

All reagents were purchased from Acros Chemical Co. All solvents were used without further purification. Melting points were determined using a Stuart SMP30 melting point apparatus and are uncorrected. IR spectra were obtained in KBr pellets for solids or in thin films for oils using an IR-Fourier spectrometer Infralum FT-801. NMR spectra were recorded on a Bruker AMX 400 or an Jeol JNM-ECA 600 spectrometers (400 or 600 MHz for ^{1}H, 100.6 or 150.9 MHz for ^{13}C) for 5–10% solutions in $CDCl_3$ or DMSO-d_6 at 27 °C. Residual chloroform (^{1}H NMR δ 7.26 ppm and ^{13}C NMR δ 77.16 ppm) or DMSO-d_5H (^{1}H NMR δ 2.49 ppm and ^{13}C NMR δ 39.43 ppm) were used as the internal standards. Mass spectra were taken either on Thermo Focus DSQ II (electron ionization, 70 eV, ion source temperature 200 °C, gas chromatographic inlet with Varian FactorFour VF-5ms column) or Thermo Trace DSQ (electron ionization, 70 eV, ion source temperature was 200 °C, direct inlet probe) spectrometers. High-resolution mass spectra (HRMS) were taken on a JEOL AccuTOF JMS-T100LP spectrometer using direct analysis in real time (DART) ionization method (helium was used as DART gas, gas flow rate was 1 L/min, flow *T* 300 °C, discharge electrode was set to +4000 V, the mass scale was calibrated using PEG 600). This method was used when no molecular ions were observed in the electron ionization mass spectra. The purity of the substances obtained and the composition of the reaction mixtures were monitored by TLC (Sorbfile plates) or, if possible, by GC–MS. The purification of the final products was carried out either by column chromatography on Al_2O_3 (activated, neutral, 50–200 mesh) and SiO_2 (40–100 mesh) or by fractional crystallization. Microanalyses were performed for C, H, N on an elemental analysis system GmbH Vario Macro CHN/CHNS and were within ±0.4% of theoretical values (the data were obtained in Centre for collective use (CPU PFUR)).

3.2. X-ray structure determination

The X-ray analysis data for compounds **9c**,[9c] **12**,[9b] **21g**[9a] were published previously in *Acta Crystallographica Section E*.

The crystal of **10a** ($C_{18}H_{17}NO_6$, M=343.33) is monoclinic, space group $P2_1/c$, at T=120 K: a=8.6758(5) Å, b=19.6319(12) Å, c=10.0853(6) Å, β=114.932(1)°, V=1557.67(16) Å^3, Z=4, d_{calc}=1.464 g/cm^3, F(000)=720, μ=0.111 mm^{-1}. 15842 total reflections (3758 unique reflections, R_{int}=0.029) were measured on a three-circle Bruker SMART 1K CCD diffractometer (λ(Mo Kα)-radiation, graphite monochromator, φ and ω scan mode, $2\theta_{max}$=56°). The structure was determined by direct methods and refined by full-matrix least squares technique with anisotropic displacement parameters for non-hydrogen atoms. The hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters [U_{iso}(H)=1.5U_{eq}(C) for the CH_3-groups and U_{iso}(H)=1.2U_{eq}(C) for the other groups]. The final divergence factors were R_1=0.059 for 3002 independent reflections with $I>2\sigma(I)$ and wR_2=0.153 for all independent reflections, S=1.002. All calculations were carried out using the SHELXTL program.[16]

The crystal of **15** ($C_{26}H_{31}NO_8$, M=485.52) is orthorhombic, space group $P2_12_12_1$, at T=293 K: a=6.909(2) Å, b=15.184(4) Å, c=22.756(5) Å, V=2387.2(11) Å^3, Z=4, d_{calc}=1.351 g/cm^3, F(000)=1032, μ=0.100 mm^{-1}. 3033 total reflections (2969 unique reflections, R_{int}=0.069) were measured on a four-circle Enraf Nonius CAD-4 diffractometer (λ(Mo Kα)-radiation, graphite monochromator, $\omega/2\theta$ scan mode, $2\theta_{max}$=54°). The structure was determined by direct methods and refined by full-matrix least squares technique with anisotropic displacement parameters for non-hydrogen atoms. The hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters [U_{iso}(H)=1.5U_{eq}(C) for the CH_3-groups and U_{iso}(H)=1.2U_{eq}(C) for the other groups]. The final divergence factors were R_1=0.053 for 1957 independent reflections with $I>2\sigma(I)$ and wR_2=0.152 for all independent reflections, S=1.001. All calculations were carried out using the SHELXTL program.[16]

The crystal of **18a** ($C_{28}H_{31}NO_{12}$, M=573.54) is orthorhombic, space group $Pna2_1$, at T=100 K: a=11.6523(4) Å, b=22.5174(8) Å, c=10.3206(4) Å, V=2707.91(17) Å^3, Z=4, d_{calc}=1.407 g/cm^3, F(000)=1208, μ=0.111 mm^{-1}. 34049 total reflections (4131 unique reflections, R_{int}=0.043) were measured on a three-circle Bruker SMART APEX II CCD diffractometer (λ(Mo Kα)-radiation, graphite monochromator, φ and ω scan mode, $2\theta_{max}$=60°). The structure was determined by direct methods and refined by full-matrix least squares technique with anisotropic displacement parameters for non-hydrogen atoms. The two carboxylate substituents at the C5 and C8 carbon atoms are disordered over two sites each with the occupancies of 0.6:0.4 and 0.7:0.3, respectively. The hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters [U_{iso}(H)=1.5U_{eq}(C) for the CH_3-groups and U_{iso}(H)=1.2U_{eq}(C) for the other groups]. The final divergence factors were R_1=0.054 for 3813 independent reflections with $I>2\sigma(I)$ and wR_2=0.138 for all independent reflections, S=1.001. All calculations were carried out using the SHELXTL program.[16]

Crystallographic data for the investigated compounds have been deposited with the Cambridge Crystallographic Data Center, CCDC 758210 (**9c**), CCDC 819025 (**10a**), CCDC 694217 (**12**), CCDC 787856 (**15**), CCDC 787855 (**18a**) and CCDC 766860 (**21g**). Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk).

3.3. Synthesis of the starting acids 1a–d

The starting 2-R^2-6-R^1-1-oxo-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole-7-carboxylic acids (**1**) were obtained and characterized earlier: **1a**,**b**,**d**,[17] **1c**.[2d]

3.4. Synthesis of tetrahydro-3a,6-epoxyisoindol-1-ones (2). Typical procedure

The corresponding furfurylamine (0.06 mol) was dissolved in toluene (100 mL) and triethylamine (16.7 mL, 0.12 mol) was added

in one portion to the solution followed by a rapid dropwise addition of acryloyl chloride (7.36 mL, 0.09 mol). The reaction mixture was heated to reflux for 6–10 h (TLC monitoring), cooled to rt, diluted with water (200 mL) and extracted with ethyl acetate (3×70 mL). The extract was dried over $MgSO_4$ and concentrated in vacuo. The residue solidified on standing and further recrystallization from a hexane–ethyl acetate mixture afforded the corresponding isoindolone **2a**,**b** as white crystals.

3.4.1. (3aR,6R*,7aS*)-2-Phenyl-2,3,7,7a-tetrahydro-3a,6-epoxyisoindol-1(6H)-one (**2a**).* Colourless plates; yield 6.54 g (48%); mp 125–126 °C; IR (KBr): 1687 (NC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 227 (11), 198 (3), 172 (3), 104 (5), 91 (9), 81 (100), 77 (23), 65 (6), 55 (33); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.61 (2H, d, $J_{2',3'}$ 8.2 Hz, H-2′(H-6′)), 7.35 (2H, dd, $J_{3',4'}$ 7.6, $J_{2',3'}$ 8.2 Hz, H-3′(H-5′)), 7.13 (1H, t, $J_{3',4'}$=$J_{5',4'}$=7.6 Hz, H-4′), 6.44 (1H, d, $J_{5,4}$ 5.5 Hz, H-4), 6.40 (1H, dd, $J_{5,4}$ 5.5, $J_{5,6}$ 1.7 Hz, H-5), 5.06 (1H, dd, $J_{5,6}$ 1.7, $J_{6,7A}$ 4.8 Hz, H-6), 4.41 (1H, d, $J_{3A,3B}$ 11.7 Hz, H-3A), 4.10 (1H, d, $J_{3A,3B}$ 11.7 Hz, H-3B), 2.59 (1H, dd, $J_{7a,7A}$ 3.4, $J_{7a,7B}$ 8.9 Hz, H-7a), 2.28 (1H, ddd, $J_{7a,7A}$ 3.4, $J_{6,7A}$ 4.8, $J_{7A,7B}$ 12.4 Hz, H-7A), 1.64 (1H, dd, $J_{7a,7B}$ 8.9, $J_{7A,7B}$ 12.4 Hz, H-7B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.3 (C_1), 139.4 ($C_{1'}$), 137.2 (C_4), 132.9 (C_5), 128.7 ($C_{3'}$($C_{5'}$)), 124.4 ($C_{4'}$), 119.9 ($C_{2'}$($C_{6'}$)), 87.9 (C_{3a}), 79.0 (C_6), 50.6 (C_3), 48.6 (C_{7a}), 28.8 (C_7). Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.21; H, 5.60; N, 6.32.

3.4.2. (3aR,6R*,7aS*)-6-Methyl-2-phenyl-2,3,7,7a-tetrahydro-3a,6-epoxyisoindol-1(6H)-one (**2b**).* White needles; yield 6.51 g (45%); mp 135–136 °C; IR (KBr): 1687 (NC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 241 (35), 198 (5), 148 (4), 95 (100), 77 (11), 65 (11), 55 (51); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.58 (2H, d, $J_{2',3'}$ 7.6 Hz, H-2′(H-6′)), 7.30 (2H, t, $J_{2',3'}$=$J_{3',4'}$=7.6 Hz, H-3′(H-5′)), 7.08 (1H, t, $J_{3',4'}$=$J_{5',4'}$=7.6 Hz, H-4′), 6.42 (1H, d, $J_{5,4}$ 5.5 Hz, H-4), 6.22 (1H, d, $J_{5,4}$ 5.5 Hz, H-5), 4.35 (1H, d, $J_{3A,3B}$ 11.7 Hz, H-3A), 4.04 (1H, d, $J_{3A,3B}$ 11.7 Hz, H-3B), 2.68 (1H, dd, $J_{7a,7A}$ 3.4, $J_{7a,7B}$ 8.2 Hz, H-7a), 1.98 (1H, dd, $J_{7a,7A}$ 3.4, $J_{7A,7B}$ 11.7 Hz, H-7A), 1.71 (1H, dd, $J_{7a,7B}$ 8.2, $J_{7A,7B}$ 11.7 Hz, H-7B), 1.60 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.1 (C_1), 140.6 (C_4), 139.4 ($C_{1'}$), 133.5 (C_5), 128.8 ($C_{3'}$($C_{5'}$)), 124.5 ($C_{4'}$), 120.1 ($C_{2'}$($C_{6'}$)), 87.7 (C_{3a}), 87.4 (C_6), 51.9 (C_{7a}), 51.0 (C_3), 35.0 (C_7), 18.7 (Me). Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81. Found: C, 74.35; H, 6.56; N, 6.38.

3.5. Esterification of the carboxylic acids (1). Typical procedure

The corresponding acid **1** (0.03 mol) was heated to reflux in methanol (100 mL) for 4–5 h (TLC monitoring) in the presence of a catalytic amount of concentrated H_2SO_4 (~0.1 mL). Upon completion, the reaction mixture was cooled to rt, poured into 300 mL of water and extracted with chloroform (3×100 mL). The extract was dried over $MgSO_4$ and concentrated in vacuo. The solid residue was recrystallized from hexane–ethyl acetate mixture to afford pure corresponding ester **3a**–**d** as white crystals.

3.5.1. Methyl (3aS,6R*,7S*,7aR*)-6-methyl-1-oxo-2-phenyl-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole-7-carboxylate (**3a**).* Colourless plates; yield 3.86 g (43%); mp 139–140 °C; IR (KBr): 1696 (NC=O), 1722 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 299 (6), 267 (5), 240 (4), 186 (27), 113 (11), 95 (100), 77 (14), 59 (10), 43 (13); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.58 (2H, dd, $J_{2',4'}$ 1.2, $J_{2',3'}$ 8.7 Hz, H-2′(H-6′)), 7.35 (2H, dd, $J_{3',4'}$ 7.5, $J_{2',3'}$ 8.7 Hz, H-3′(H-5′)), 7.14 (1H, t, $J_{3',4'}$=$J_{5',4'}$=7.5 Hz, H-4′), 6.60 (1H, d, $J_{5,4}$ 5.6 Hz, H-5), 6.26 (1H, d, $J_{5,4}$ 5.6 Hz, H-4), 4.39 (1H, d, $J_{3A,3B}$ 11.8 Hz, H-3A), 4.19 (1H, d, $J_{3A,3B}$ 11.8 Hz, H-3B), 3.78 (3H, s, OMe), 3.01 (1H, d, $J_{7,7a}$ 8.7 Hz, H-7), 2.85 (1H, d, $J_{7,7a}$ 8.7 Hz, H-7a), 1.67 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.0 (C_1), 170.3 (*C*O_2Me), 139.2 ($C_{1'}$), 140.5 (C_5), 136.4 (C_4), 128.9 ($C_{3'}$($C_{5'}$)), 124.9 ($C_{4'}$), 120.5 ($C_{2'}$($C_{6'}$)), 89.5 (C_6), 87.2 (C_{3a}), 55.6 (C_{7a}), 52.0 (CO_2*Me*), 50.5 (C_3), 49.2 (C_7), 16.0 (Me). Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.72; N, 4.68. Found: C, 68.57; H, 5.32; N, 5.06.

3.5.2. Methyl (3aS,6R*,7S*,7aR*)-2-benzyl-6-methyl-1-oxo-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole-7-carboxylate (**3b**).* Transparent plates; yield 3.66 g (39%); mp 122 °C; IR (KBr): 1679 (NC=O), 1724 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 313 (6), 254 (4), 222 (25), 200 (17), 190 (15), 113 (47), 95 (100), 85 (14), 65 (14), 43 (5); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.26 (5H, m, C_6H_5), 6.45 (1H, d, $J_{5,4}$ 5.5 Hz, H-5), 6.16 (1H, d, $J_{5,4}$ 5.5 Hz, H-4), 4.63 (1H, d, $J_{CH2A,CH2B}$ 15.1 Hz, CH_2A), 4.30 (1H, d, $J_{CH2A,CH2B}$ 15.1 Hz, CH_2B), 3.73 (3H, s, OMe), 3.72 (1H, d, $J_{3A,3B}$ 11.7 Hz, H-3A), 3.61 (1H, d, $J_{3A,3B}$ 11.7 Hz, H-3B), 2.81 (1H, d, $J_{7,7a}$ 8.9 Hz, H-7), 2.74 (1H, d, $J_{7,7a}$ 8.9 Hz, H-7a), 1.61 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.9 (C_1), 170.8 (*C*O_2Me), 139.9 (C_5), 136.3 (C_4), 135.9 ($C_{1'}$), 128.6 ($C_{2'}$($C_{6'}$)), 127.8 ($C_{3'}$($C_{5'}$)), 127.4 ($C_{4'}$), 88.9 (C_{3a}), 87.8 (C_6), 54.4 (C_{7a}), 51.6 (CO_2*Me*), 48.4 (C_3), 48.2 (C_7), 46.5 (CH_2), 15.8 (Me). Anal. Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 69.34; H, 6.30; N, 4.49.

3.5.3. Methyl (3aS,6R*,7S*,7aR*)-1-oxo-2-phenyl-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole-7-carboxylate (**3c**).* White powder; yield 6.95 g (83%); mp 130–131 °C; IR(KBr): 1702 (NC=O), 1735 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 285 (2), 172 (40), 113 (14), 104 (6), 81 (100), 53 (27), 41 (4); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.58 (2H, br d, $J_{2',3'}$ 8.1 Hz, H-2′(H-6′)), 7.36 (2H, dd, $J_{3',4'}$ 7.5, $J_{2',3'}$ 8.1 Hz, H-3′(H-5′)), 7.15 (1H, t, $J_{3',4'}$=$J_{5',4'}$=7.5 Hz, H-4′), 6.58 (1H, d, $J_{5,4}$ 5.4 Hz, H-4), 6.50 (1H, dd, $J_{5,4}$ 5.4, $J_{5,6}$ 1.9 Hz, H-5), 5.21 (1H, d, $J_{5,6}$ 1.9 Hz, H-6), 4.43 (1H, d, $J_{3A,3B}$ 11.2 Hz, H-3A), 4.22 (1H, d, $J_{3A,3B}$ 11.2 Hz, H-3B), 3.81 (3H, s, OMe), 2.99 (1H, d, $J_{7,7a}$ 9.0 Hz, H-7), 2.83 (1H, d, $J_{7,7a}$ 9.0 Hz, H-7a); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.1 (C_1), 169.9 (*C*O_2Me), 139.1 ($C_{1'}$), 137.0 (C_4), 135.1 (C_5), 128.7 ($C_{3'}$($C_{5'}$)), 124.7 ($C_{4'}$), 120.2 ($C_{2'}$($C_{6'}$)), 87.5 (C_{3a}), 81.5 (C_6), 52.1 (C_{7a}), 52.0 (CO_2*Me*), 49.8 (C_3), 45.5 (C_7). Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.74; H, 5.61; N, 5.12.

3.5.4. Methyl (3aS,6S*,7R*,7aR*)-6-bromo-1-oxo-2-phenyl-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole-7-carboxylate (**3d**).* Colourless needles; yield 8.08 g (74%); mp >186 °C (decomp.); IR (KBr): 1712 (NC=O), 1744 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 363 (for ^{79}Br) (3), 250 (36), 188 (9), 170 (19), 161 (93), 143 (17), 131 (81), 113 (100), 104 (24), 91 (29), 85 (74), 77 (95), 59 (78), 51 (77), 39 (25); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.54 (2H, dd, $J_{2',4'}$ 1.2, $J_{2',3'}$ 8.7 Hz, H-2′(H-6′)), 7.37 (2H, dd, $J_{3',4'}$ 7.5, $J_{2',3'}$ 8.7 Hz, H-3′(H-5′)), 7.17 (1H, t, $J_{3',4'}$=$J_{5',4'}$=7.5 Hz, H-4′), 6.67 (1H, d, $J_{5,4}$ 5.6 Hz, H-5), 6.49 (1H, d, $J_{5,4}$ 5.6 Hz, H-4), 4.44 (1H, d, $J_{3A,3B}$ 11.8 Hz, H-3A), 4.23 (1H, d, $J_{3A,3B}$ 11.8 Hz, H-3B), 3.83 (3H, s, OMe), 3.25 (1H, d, $J_{7,7a}$ 8.7 Hz, H-7), 3.10 (1H, d, $J_{7,7a}$ 8.7 Hz, H-7a); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.0 (C_1), 168.9 (*C*O_2Me), 141.2 (C_4), 138.7 ($C_{1'}$), 136.9 (C_5), 129.0 ($C_{3'}$($C_{5'}$)), 125.4 ($C_{4'}$), 120.7 ($C_{2'}$($C_{6'}$)), 89.6 (C_6), 86.8 (C_{3a}), 55.0 (C_7), 52.5 (C_{7a}), 52.4 (CO_2*Me*), 50.1 (C_3). Anal. Calcd for $C_{16}H_{14}NO_4Br$: C, 52.89; H, 3.86; N, 3.86. Found: C, 52.63; H, 4.01; N, 3.58.

3.6. Epimerization of the esters 3a,b. Typical procedure

The corresponding acid **1a**,**b** (or ester **3a**,**b**) (0.017 mol) was heated to reflux in methanol (100 mL) for 44–60 h (GC–MS monitoring) in the presence of a catalytic amount of concentrated H_2SO_4 (~0.1 mL). Upon completion, the reaction mixture was cooled to rt, diluted with 200 mL of water and extracted with chloroform (3×70 mL). The extract was dried over $MgSO_4$ and concentrated in vacuo. The residual viscous brown oil was purified by column chromatography on SiO_2 using hexane–ethyl acetate mixture as eluent.

3.6.1. Methyl (3aS,6R*,7R*,7aR*)-6-methyl-1-oxo-2-phenyl-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole-7-carboxylate (**4a**).* Colourless prismatic crystals; R_f 0.50 (hexane–ethyl acetate, 1:1); yield 1.73 g (34%); mp 130–131 °C; IR (KBr): 1694 (NC=O), 1736 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 299 (12), 267 (12), 240 (9), 186 (59), 113 (3), 95 (100), 77 (11), 59 (8), 43 (16); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.62 (2H, dd, $J_{2',4'}$ 1.3, $J_{2',3'}$ 8.8 Hz, H-2′(H-6′)), 7.37 (2H, dd, $J_{3',4'}$ 7.5, $J_{2',3'}$ 8.8 Hz, H-3′(H-5′)), 7.15 (1H, t, $J_{3',4'}=J_{5',4'}$=7.5 Hz, H-4′), 6.59 (1H, d, $J_{5,4}$ 5.6 Hz, H-5), 6.22 (1H, d, $J_{5,4}$ 5.6 Hz, H-4), 5.21 (1H, d, $J_{5,6}$ 1.9 Hz, H-6), 4.39 (1H, d, $J_{3A,3B}$ 11.8 Hz, H-3A), 4.10 (1H, d, $J_{3A,3B}$ 11.8 Hz, H-3B), 3.70 (3H, s, OMe), 3.22 (1H, d, $J_{7,7a}$ 3.7 Hz, H-7), 3.21 (1H, d, $J_{7,7a}$ 3.7 Hz, H-7a), 1.78 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.0 (C_1), 171.0 (*C*O_2Me), 139.3 ($C_{1'}$), 138.6 (C_5), 135.1 (C_4), 128.9 ($C_{3'}$($C_{5'}$)), 124.8 ($C_{4'}$), 120.1 ($C_{2'}$($C_{6'}$)), 89.5 (C_6), 88.3 (C_{3a}), 56.0 (CO_2*Me*), 52.3 (C_{7a}), 52.2 (C_7), 50.9 (C_3), 18.4 (Me). Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.72; N, 4.68. Found: C, 68.53; H, 5.47; N, 4.91.

3.6.2. Methyl (3aS,6R*,7R*,7aR*)-2-benzyl-6-methyl-1-oxo-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole-7-carboxylate (**4b**).* Viscous pale-yellow oil; R_f 0.49 (hexane–ethyl acetate, 1:2); yield 2.66 g (50%); IR (neat): 1679 (NC=O), 1723 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 313 (24), 254 (11), 222 (62), 200 (30), 190 (19), 110 (100), 91 (51), 85 (14), 65 (5), 43 (9); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.32 (2H, t, $J_{3',4'}=J_{2',3'}$=7.6 Hz, H-3′(H-5′)), 7.26 (1H, t, $J_{3',4'}=J_{5',4'}$=7.6 Hz, H-4′), 7.22 (2H, d, $J_{2',3'}$ 7.6 Hz, H-2′(H-6′)), 6.45 (1H, d, $J_{5,4}$ 5.5 Hz, H-5), 6.14 (1H, d, $J_{5,4}$ 5.5 Hz, H-4), 4.70 (1H, d, $J_{CH2A,CH2B}$ 15.1 Hz, CH_2A), 4.30 (1H, d, $J_{CH2A,CH2B}$ 15.1 Hz, CH_2B), 3.78 (1H, d, $J_{3A,3B}$ 11.7 Hz, H-3A), 3.67 (3H, s, OMe), 3.48 (1H, d, $J_{3A,3B}$ 11.7 Hz, H-3B), 3.14 (1H, d, $J_{7,7a}$ 3.7 Hz, H-7), 3.03 (1H, d, $J_{7,7a}$ 3.7 Hz, H-7a), 1.75 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.4 (C_1), 171.0 (*C*O_2Me), 138.1 (C_5), 135.9 ($C_{1'}$), 135.0 (C_4), 128.6 ($C_{2'}$($C_{6'}$)), 127.8 ($C_{3'}$($C_{5'}$)), 127.5 ($C_{4'}$), 89.1 (C_{3a}), 89.1 (C_6), 54.7 (C_{7a}), 52.0 (CO_2*Me*), 51.4 (C_7), 48.9 (C_3), 46.6 (CH_2), 18.3 (Me). Anal. Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.42; H, 5.97; N, 4.13.

3.7. Epoxidation of the isoindolones 2–4. Typical procedure

A solution of the corresponding isoindolone **2a**,**b**, **3a**–**d**, **4a**,**b** (8.3 mmol) and *m*-CPBA 4.3 g (25 mmol) in CH_2Cl_2 (50 mL) was stirred at rt for 2 days (TLC monitoring). Upon completion, the reaction mixture was poured into 100 mL of water and basified with satd aq $NaHCO_3$ to pH 9–10. The organic layer was separated and the water layer was extracted with CH_2Cl_2 (3×50 mL). The combined organic layers were washed with water (2×40 mL), dried over $MgSO_4$ and concentrated in vacuo. The solid residue was recrystallized from a hexane–ethyl acetate mixture to provide corresponding diepoxide **5a**,**b**, **6a**–**d**, **7a**,**b** as white crystals.

3.7.1. (1aR,2R*,3aS*,6aR*,6bR*)-5-Phenylhexahydro-2,6a-epoxyoxireno[e]isoindol-4(2H)-one (**5a**).* White powder; yield 1.37 g (68%); mp 208–209 °C; IR (KBr): 1689 (NC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 243 (100), 214 (14), 186 (15), 119 (12), 105 (57), 95 (21), 77 (94), 51 (28), 39 (48); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.57 (2H, d, $J_{2',3'}$ 7.6 Hz, H-2′(H-6′)), 7.36 (2H, t, $J_{3',4'}=J_{2',3'}$=7.6 Hz, H-3′(H-5′)), 7.17 (1H, t, $J_{3',4'}=J_{5',4'}$=7.6 Hz, H-4′), 4.62 (1H, d, $J_{2,3B}$ 4.4 Hz, H-2), 4.29 (1H, d, $J_{6A,6B}$ 11.4 Hz, H-6A), 4.12 (1H, d, $J_{6A,6B}$ 11.4 Hz, H-6B), 3.50 (1H, d, $J_{1a,6b}$ 3.4 Hz, H-1a), 3.43 (1H, d, $J_{1a,6b}$ 3.4 Hz, H-6b), 2.81 (1H, dd, $J_{3A,3a}$ 9.6, $J_{3B,3a}$ 4.4 Hz, H-3a), 2.28 (1H, dt, $J_{2,3B}=J_{3B,3a}$=4.4, $J_{3B,3A}$ 13.1 Hz, H-3B), 1.89 (1H, dd, $J_{3A,3a}$ 9.6, $J_{3B,3A}$ 13.1 Hz, H-3A); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.3 (C_4), 139.2 ($C_{1'}$), 129.1 ($C_{3'}$($C_{5'}$)), 125.0 ($C_{4'}$), 120.3 ($C_{2'}$($C_{6'}$)), 84.1 (C_{6a}), 75.7 (C_2), 50.4 (C_{1a}), 50.2 (C_{6b}), 49.6 (C_6), 49.0 (C_{3a}), 31.8 (C_3). Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.14; H, 5.35; N, 5.76. Found: C, 69.27; H, 5.48; N, 5.12.

3.7.2. (1aS,2R*,3aS*,6aR*,6bR*)-2-Methyl-5-phenylhexahydro-2,6a-epoxyoxireno[e]isoindol-4(2H)-one (**5b**).* Colourless plates; yield 1.81 g (85%); mp 186–187 °C; IR (KBr): 1688 (NC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 257 (27), 214 (14), 186 (11), 156 (9), 130 (9), 104 (60), 95 (32), 77 (78), 67 (24), 55 (24), 43 (100); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.55 (2H, d, $J_{2',3'}$ 7.6 Hz, H-2′(H-6′)), 7.33 (2H, t, $J_{3',4'}=J_{2',3'}$=7.6 Hz, H-3′(H-5′)), 7.12 (1H, t, $J_{3',4'}=J_{5',4'}$=7.6 Hz, H-4′), 4.24 (1H, d, $J_{6A,6B}$ 11.4 Hz, H-6A), 4.06 (1H, d, $J_{6A,6B}$ 11.4 Hz, H-6B), 3.54 (1H, d, $J_{1a,6b}$ 3.4 Hz, H-1a), 3.43 (1H, d, $J_{1a,6b}$ 3.4 Hz, H-6b), 2.84 (1H, dd, $J_{3A,3a}$ 9.6, $J_{3B,3a}$ 4.4 Hz, H-3a), 1.97 (1H, dd, $J_{3B,3a}$ 4.4, $J_{3B,3A}$ 13.1 Hz, H-3B), 1.92 (1H, dd, $J_{3A,3a}$ 9.6, $J_{3B,3A}$ 13.1 Hz, H-3A), 1.57 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.4 (C_4), 139.0 ($C_{1'}$), 128.8 ($C_{3'}$($C_{5'}$)), 124.7 ($C_{4'}$), 119.9 ($C_{2'}$($C_{6'}$)), 83.7 (C_{6a}), 83.4 (C_2), 52.7 (C_{1a}), 51.7 (C_{6b}), 50.4 (C_{3a}), 49.6 (C_6), 37.3 (C_3), 16.2 (Me). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.04; H, 5.84; N, 5.45. Found: C, 69.80; H, 6.06; N, 5.22.

3.7.3. Methyl (1aS,2R*,3R*,3aS*,6aR*,6bR*)-2-methyl-4-oxo-5-phenyloctahydro-2,6a-epoxyoxireno[e]isoindole-3-carboxylate (**6a**).* Fine colourless crystalline aggregates; yield 2.14 g (82%); mp 210–211 °C; IR (KBr): 1708 (NC=O), 1735 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 315 (61), 240 (45), 212 (57), 184 (29), 156 (14), 124 (37), 104 (36), 91 (20), 77 (85), 51 (30), 43 (100); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.55 (2H, dd, $J_{2',4'}$ 1.2, $J_{2',3'}$ 8.6 Hz, H-2′(H-6′)), 7.36 (2H, dd, $J_{3',4'}$ 7.5, $J_{2',3'}$ 8.6 Hz, H-3′(H-5′)), 7.14 (1H, br t, $J_{3',4'}=J_{5',4'}$=7.5 Hz, H-4′), 4.28 (1H, d, $J_{6A,6B}$ 11.8 Hz, H-6A), 4.16 (1H, d, $J_{6A,6B}$ 11.8 Hz, H-6B), 3.76 (3H, s, OMe), 3.59 (1H, d, $J_{1a,6b}$ 3.1 Hz, H-1a), 3.30 (1H, d, $J_{1a,6b}$ 3.1 Hz, H-6b), 3.13 (1H, d, $J_{3,3a}$ 9.3 Hz, H-3), 2.97 (1H, d, $J_{3,3a}$ 9.3 Hz, H-3a), 1.58 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.3 (C_4), 169.2 (*C*O_2Me), 138.9 ($C_{1'}$), 128.9 ($C_{3'}$($C_{5'}$)), 125.1 ($C_{4'}$), 120.3 ($C_{2'}$($C_{6'}$)), 85.5 (C_{6a}), 83.2 (C_2), 55.4 (C_{1a}), 52.6 (C_{6b}), 51.9 (C_{3a}), 51.9 (CO_2*Me*), 51.1 (C_6), 49.3 (C_3), 13.8 (Me). Anal. Calcd for $C_{17}H_{17}NO_5$: C, 64.75; H, 5.43; N, 4.44. Found: C, 64.60; H, 5.04; N, 4.13.

3.7.4. Methyl (1aR,2S*,3R*,3aR*,6aS*,6bS*)-5-benzyl-2-methyl-4-oxooctahydro-2,6a-epoxyoxireno[e]isoindole-3-carboxylate (**6b**).* Colourless rhombuses; yield 2.23 g (82%); mp 145–146 °C; IR (KBr): 1679 (NC=O), 1731 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 329 (19), 298 (6), 226 (11), 187 (4), 118 (6), 91 (100), 65 (11), 43 (12); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.26 (5H, m, C_6H_5), 4.50 (1H, d, $J_{CH2A,CH2B}$ 15.1 Hz, CH_2A), 4.43 (1H, d, $J_{CH2A,CH2B}$ 15.1 Hz, CH_2B), 3.71 (3H, s, OMe), 3.62 (1H, d, $J_{6A,6B}$ 11.7 Hz, H-6A), 3.59 (1H, d, $J_{6A,6B}$ 11.7 Hz, H-6B), 3.48 (1H, d, $J_{1a,6b}$ 3.4 Hz, H-1a), 3.25 (1H, d, $J_{1a,6b}$ 3.4 Hz, H-6b), 2.97 (1H, d, $J_{3,3a}$ 9.6 Hz, H-3), 2.89 (1H, d, $J_{3,3a}$ 9.6 Hz, H-3a), 1.54 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.8 (C_4), 169.3 (*C*O_2Me), 135.6 ($C_{1'}$), 128.6 ($C_{2'}$($C_{6'}$)), 127.7 ($C_{3'}$($C_{5'}$)), 127.4 ($C_{4'}$), 85.1 (C_{6a}), 83.9 (C_2), 54.3 (C_{1a}), 52.2 (C_{6b}), 51.6 (CO_2*Me*), 51.1 (C_{3a}), 50.9 (C_3), 47.3 (C_6), 46.4 (CH_2), 13.6 (Me). Anal. Calcd for $C_{18}H_{19}NO_5$: C, 65.65; H, 5.77; N, 4.25. Found: C, 65.80; H, 5.55; N, 4.43.

3.7.5. Methyl (1aR,2R*,3R*,3aS*,6aR*,6bR*)-4-oxo-5-phenyloctahydro-2,6a-epoxyoxireno[e]isoindole-3-carboxylate (**6c**).* White powder; yield 1.72 g (69%); mp 213–214 °C; IR (KBr): 1700 (NC=O), 1729 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M^+ 301 (42), 207 (18), 172 (13), 130 (18), 119 (23), 104 (43), 91 (23), 77 (100), 65 (18), 59 (45), 51 (68), 39 (44); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.55 (2H, dd, $J_{2',4'}$ 1.2, $J_{2',3'}$ 8.7 Hz, H-2′(H-6′)), 7.36 (2H, dd, $J_{3',4'}$ 7.5, $J_{2',3'}$ 8.7 Hz, H-3′(H-5′)), 7.17 (1H, t, $J_{3',4'}=J_{5',4'}$=7.5 Hz, H-4′), 4.81 (1H, s, H-2), 4.29 (1H, d, $J_{6A,6B}$ 11.5 Hz, H-6A), 4.19 (1H, d, $J_{6A,6B}$ 11.5 Hz, H-6B), 3.78 (3H, s, OMe), 3.56 (1H, d, $J_{1a,6b}$ 3.7 Hz, H-1a), 3.45 (1H, d, $J_{1a,6b}$ 3.7 Hz, H-6b), 3.18 (1H, d, $J_{3,3a}$ 9.3 Hz, H-3), 3.00 (1H, d, $J_{3,3a}$ 9.3 Hz, H-3a); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.4 (C_4), 168.9 (*C*O_2Me), 138.9 ($C_{1'}$), 129.0 ($C_{3'}$($C_{5'}$)), 125.2 ($C_{4'}$), 120.4 ($C_{2'}$($C_{6'}$)), 83.8 (C_{6a}), 78.1 (C_2), 54.2 (C_{1a}), 52.3 (C_{6b}), 49.3 (C_{3a}), 49.0 (CO_2*Me*), 48.9 (C_6), 48.5 (C_3). Anal. Calcd for $C_{16}H_{15}NO_5$: C, 63.78; H, 5.02; N, 4.65. Found: C, 63.11; H, 5.44; N, 5.12.

3.7.6. Methyl (1aR,2R*,3R*,3aR*,6aS*,6bS*)-2-bromo-4-oxo-5-phenyloctahydro-2,6a-epoxyoxireno[e]isoindole-3-carboxylate*

(***6d***). White powder; yield 1.82 g (58%); mp >258 °C (decomp.); IR 1709 (KBr): (NC=O), 1740 (OC=O) cm^{-1}; EIMS (70 eV) *m/z* (rel intensity): M^+ 379 (for ^{79}Br) (100), 350 (3), 300 (9), 268 (100), 252 (11), 240 (16), 212 (12), 201 (22), 161 (12), 153 (16), 130 (13), 119 (49), 104 (47), 94 (13), 76 (37), 59 (27), 43 (39); ^1H NMR (DMSO, 400 MHz) δ 7.60 (2H, d, $J_{2',3'}$ 7.5 Hz, H-2′(H-6′)), 7.39 (2H, t, $J_{3',4'}=J_{2',3'}=7.5$ Hz, H-3′(H-5′)), 7.17 (1H, t, $J_{3',4'}=J_{5',4'}=7.5$ Hz, H-4′), 4.48 (1H, d, $J_{6A,6B}$ 11.8 Hz, H-6A), 4.05 (1H, d, $J_{6A,6B}$ 11.8 Hz, H-6B), 4.01 (1H, d, $J_{1a,6b}$ 3.1 Hz, H-1a), 3.99 (1H, d, $J_{1a,6b}$ 3.1 Hz, H-6b), 3.64 (3H, s, OMe), 3.58 (2H, br s, H-3 and H-3a); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 168.6 (C_4), 167.9 (CO_2Me), 138.8 ($C_{1'}$), 128.7 ($C_{3'}(C_{5'})$), 124.5 ($C_{4'}$), 119.7 ($C_{2'}(C_{6'})$), 88.3 (C_2), 83.6 (C_{6a}), 54.8 (C_{1a}), 54.0 (C_{6b}), 53.3 (C_{3a}), 51.6 (CO_2Me), 51.3 (C_3), 48.3 (C_6). Anal. Calcd for $C_{16}H_{14}NO_5Br$: C, 50.66; H, 3.69; N, 3.69. Found: C, 50.78; H, 3.91; N, 3.29.

3.7.7. Methyl (1aR,2S*,3R*,3aR*,6aS*,6bS*)-2-methyl-4-oxo-5-phenyloctahydro-2,6a-epoxyoxireno[e]isoindole-3-carboxylate* (***7a***). Colourless needles; yield 2.20 g (84%); mp 219–221 °C; IR (KBr): 1692 (NC=O), 1731 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m/z* (rel intensity): M^+ 315 (100), 284 (8), 239 (14), 212 (26), 184 (8), 124 (8), 104 (9), 77 (17), 59 (22), 43 (21); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.58 (2H, d, $J_{2',3'}$ 7.9 Hz, H-2′(H-6′)), 7.37 (2H, t, $J_{3',4'}=J_{2',3'}=7.9$ Hz, H-3′(H-5′)), 7.14 (1H, t, $J_{3',4'}=J_{5',4'}=7.9$ Hz, H-4′), 4.28 (1H, d, $J_{6A,6B}$ 11.7 Hz, H-6A), 4.10 (1H, d, $J_{6A,6B}$ 11.7 Hz, H-6B), 3.78 (3H, s, OMe), 3.65 (1H, d, $J_{1a,6b}$ 3.1 Hz, H-1a), 3.38 (1H, d, $J_{3,3a}$ 4.1 Hz, H-3), 3.36 (1H, d, $J_{1a,6b}$ 3.1 Hz, H-6b), 3.20 (1H, d, $J_{3,3a}$ 4.1 Hz, H-3a), 1.68 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.4 (C_4), 169.9 (CO_2Me), 139.2 ($C_{1'}$), 128.8 ($C_{3'}(C_{5'})$), 124.3 ($C_{4'}$), 119.4 ($C_{2'}(C_{6'})$), 84.6 (C_{6a}), 83.9 (C_2), 55.1 (C_{1a}), 54.5 (C_{6b}), 52.4 (C_{3a}), 50.4 (CO_2Me), 49.6 (C_3), 49.1 (C_6), 16.0 (Me). Anal. Calcd for $C_{17}H_{17}NO_5$: C, 64.75; H, 5.43; N, 4.44. Found: C, 64.34; H, 5.11; N, 4.76.

3.7.8. Methyl (1aS,2R*,3R*,3aS*,6aR*,6bR*)-5-benzyl-2-methyl-4-oxooctahydro-2,6a-epoxyoxireno[e]isoindole-3-carboxylate* (***7b***). White powder; yield 2.02 g (74%); mp 119–121 °C; IR (KBr): 1687 (NC=O), 1739 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m/z* (rel intensity): M^+ 329 (37), 254 (7), 226 (6), 106 (7), 91 (100), 65 (11), 43 (13); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.32 (2H, t, $J_{3',4'}=J_{2',3'}=7.6$ Hz, H-3′(H-5′)), 7.26 (1H, t, $J_{3',4'}=J_{5',4'}=7.6$ Hz, H-4′), 7.21 (2H, d, $J_{2',3'}$ 7.6 Hz, H-2′(H-6′)), 4.62 (1H, d, $J_{CH2A,CH2B}$ 15.1 Hz, CH_2A), 4.33 (1H, d, $J_{CH2A,CH2B}$ 15.1 Hz, CH_2B), 3.76 (3H, s, OMe), 3.66 (1H, d, $J_{6A,6B}$ 11.7 Hz, H-6A), 3.52 (1H, d, $J_{1a,6b}$ 3.4 Hz, H-1a), 3.49 (1H, d, $J_{6A,6B}$ 11.7 Hz, H-6B), 3.30 (1H, d, $J_{1a,6b}$ 3.4 Hz, H-6b), 3.22 (1H, d, $J_{3,3a}$ 4.1 Hz, H-3), 3.12 (1H, d, $J_{3,3a}$ 9.6 Hz, H-3a), 1.65 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.7 (C_4), 170.3 (CO_2Me), 135.6 ($C_{1'}$), 128.8 ($C_{2'}(C_{6'})$), 128.0 ($C_{3'}(C_{5'})$), 127.8 ($C_{4'}$), 85.1 (C_{6a}), 85.1 (C_2), 55.1 (C_{1a}), 53.8 (C_{6b}), 52.5 (CO_2Me), 51.3 (C_{3a}), 50.3 (C_3), 47.9 (C_6), 46.9 (CH_2), 16.1 (Me). Anal. Calcd for $C_{18}H_{19}NO_5$: C, 65.65; H, 5.77; N, 4.25. Found: C, 65.34; H, 5.92; N, 4.48.

3.8. Wagner–Meerwein rearrangement of the diepoxyisoindolones 5, 6. Typical procedure

$BF_3 \cdot OEt_2$ (0.39 mL, 3.0 mmol) was added to a solution of the corresponding diepoxyisoindolones **5a**,**b** or **6a**–**d** (1.50 mmol) in 10 mL of acetic anhydride at 5 °C. Then the reaction mixture was allowed to warm up to rt and stirred for 4 h (TLC monitoring). Upon completion, the reaction mixture was diluted with water (60 mL), basified with satd aq $NaHCO_3$ to pH 9–10 and extracted with chloroform (3×50 mL). The combined organic layers were washed with water (2×30 mL), dried over $MgSO_4$ and concentrated in vacuo. The residual viscous oil was triturated in Et_2O (5 mL) to give corresponding product **8a**,**b**, **9a**,**c**–**d** as a white powder. Subsequent recrystallization from a hexane–ethyl acetate mixture provided analytically pure samples. In the case of **9b**, it turned impossible to crystallize the residue after solvent evaporation, thus the target product was isolated by flash chromatography on alumina (hexane–ethyl acetate). A single crystal of the compound **9c** for X-ray analysis was obtained by slow crystallization from an ethanol–DMF mixture.

3.8.1. (4S,4aS*,5R*,6R*,7aR*)-1-Oxo-2-phenyloctahydro-4H-4,6-epoxycyclopenta[c]pyridine-4,5-diyl diacetate* (***8a***). Transparent colourless plates; yield 0.41 g (79%); mp 179–180 °C; IR (KBr): 1674 (NC=O), 1737 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m/z* (rel intensity): M^+ 345 (1), 285 (15), 257 (3), 215 (5),193 (7), 104 (28), 83 (6), 77 (14), 66 (11), 43 (100); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.38 (2H, dd, $J_{3',4'}$ 7.6, $J_{2',3'}$ 8.2 Hz, H-3′(H-5′)), 7.26 (1H, t, $J_{3',4'}=J_{5',4'}=7.6$ Hz, H-4′),7.23 (2H, d, $J_{2',3'}$ 8.2 Hz, H-2′(H-6′)), 4.85 (1H, br s, H-6), 4.84 (1H, br s, H-5), 4.25 (1H, d, $J_{3A,3B}$ 13.1 Hz, H-3A), 4.16 (1H, d, $J_{3A,3B}$ 13.1 Hz, H-3B), 3.65 (1H, dd, $J_{5,4a}$ 1.4, $J_{4a,7a}$ 4.8 Hz, H-4a), 3.06 (1H, dt, $J_{7endo,7a}=J_{4a,7a}=4.8$, $J_{7exo,7a}$ 11.7 Hz, H-7a), 2.33 (1H, dd, $J_{7exo,7a}$ 11.7, $J_{7,7}$ 13.1 Hz, H-7*exo*), 2.11 (3H, s, OAc), 2.05 (3H, s, OAc), 1.80 (1H, dd, $J_{7endo,7a}$ 4.8, $J_{7,7}$ 13.1 Hz, H-7*endo*); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.9 (C_1), 169.3, 168.8 (OCOMe×2), 141.0 ($C_{1'}$), 129.2 ($C_{3'}(C_{5'})$), 127.2 ($C_{4'}$), 126.1 ($C_{2'}(C_{6'})$), 103.9 (C_4), 79.7 (C_6), 77.9 (C_5), 54.2 (C_3), 43.0 (C_{4a}), 36.3 (C_{7a}), 34.2 (C_7), 21.7, 20.7 (OCO*Me*×2). Anal. Calcd for $C_{18}H_{19}NO_6$: C, 62.60; H, 5.55; N, 4.06. Found: C, 62.25; H, 5.24; N, 4.48.

3.8.2. (4S,4aS*,5R*,6R*,7aR*)-6-Methyl-1-oxo-2-phenyloctahydro-4H-4,6-epoxycyclopenta[c]pyridine-4,5-diyl diacetate* (***8b***). White whiskers needles; yield 0.38 g (71%); mp 130–131 °C; IR (KBr): 1670 (NC=O), 1741 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m/z* (rel intensity): M^+ 359 (2), 299 (28), 271 (21), 257 (91), 212 (20), 188 (42), 106 (100), 97 (26), 77 (46), 43 (70); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.37 (2H, t, $J_{3',4'}=J_{2',3'}=7.6$ Hz, H-3′(H-5′)), 7.25 (1H, t, $J_{3',4'}=J_{5',4'}=7.6$ Hz, H-4′),7.22 (2H, d, $J_{2',3'}$ 7.6 Hz, H-2′(H-6′)), 4.77 (1H, br s, H-5), 4.19 (1H, d, $J_{3A,3B}$ 13.1 Hz, H-3A), 4.11 (1H, d, $J_{3A,3B}$ 13.1 Hz, H-3B), 3.61 (1H, dd, $J_{5,4a}$ 1.4, $J_{4a,7a}$ 4.8 Hz, H-4a), 3.04 (1H, dt, $J_{7endo,7a}=J_{4a,7a}=4.8$, $J_{7exo,7a}$ 11.7 Hz, H-7a), 2.33 (1H, dd, $J_{7exo,7a}$ 11.7, $J_{7,7}$ 13.7 Hz, H-7*exo*), 2.11 (3H, s, OAc), 2.03 (3H, s, OAc), 1.79 (1H, dd, $J_{7endo,7a}$ 4.8, $J_{7,7}$ 13.7 Hz, H-7*endo*); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.8 (C_1), 169.5, 168.8 (OCOMe×2), 141.1 ($C_{1'}$), 129.2 ($C_{3'}(C_{5'})$), 127.2 ($C_{4'}$), 126.1 ($C_{2'}(C_{6'})$), 104.1 (C_4), 86.8 (C_6), 78.5 (C_5), 54.6 (C_3), 44.4 (C_{4a}), 39.5 (C_7), 36.2 (C_{7a}), 21.8, 20.7 (OCO*Me*×2), 14.9 (Me). Anal. Calcd for $C_{19}H_{21}NO_6$: C, 63.50; H, 5.89; N, 3.90. Found: C, 63.73; H, 5.97; N, 3.53.

3.8.3. (4R,4aR*,5R*,6S*,7S*,7aS*)-Methyl 4,5-bis(acetyloxy)-6-methyl-1-oxo-2-phenyloctahydro-1H-4,6-epoxycyclopenta[c]pyridine-7-carboxylate* (***9a***). Colourless needles; yield 0.49 g (79%); mp 207 °C; IR (KBr): 1666 (NC=O), 1745 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m/z* (rel intensity): M^+417 (1), 357 (3), 315 (4), 187 (6), 104 (7), 77 (16), 43 (100); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.40 (4H, m, H–Ar), 7.28 (1H, m, H-4′), 4.84 (1H, d, $J_{5,4a}$ 1.3 Hz, H-5), 4.48 (1H, d, $J_{3A,3B}$ 13.4 Hz, H-3A), 3.98 (1H, d, $J_{3A,3B}$ 13.4 Hz, H-3B), 3.74 (3H, s, OMe), 3.66 (1H, dd, $J_{5,4a}$ 1.3, $J_{4a,7a}$ 4.4 Hz, H-4a), 3.31 (1H, dd, $J_{4a,7a}$ 4.4, $J_{7,7a}$ 11.2 Hz, H-7a), 3.15 (1H, d, $J_{7,7a}$ 11.2 Hz, H-7), 2.15 (3H, s, OAc), 2.05 (3H, s, OAc), 1.47 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.9 (C_1), 168.7 (CO_2Me), 168.2, 167.3 (OCOMe×2), 141.5 ($C_{1'}$), 129.4 ($C_{3'}(C_{5'})$), 127.5 ($C_{4'}$), 126.7 ($C_{2'}(C_{6'})$), 104.9 (C_4), 88.6 (C_6), 77.9 (C_5), 57.8 (C_3), 52.2 (CO_2Me), 50.1 (C_7), 45.2 (C_{4a}), 39.3 (C_{7a}), 21.7, 20.8 (OCO*Me*×2), 14.5 (Me). Anal. Calcd for $C_{21}H_{23}NO_8$: C, 60.43; H, 5.55; N, 3.36. Found: C, 60.15; H, 5.21; N, 3.78.

3.8.4. (4R,4aR*,5R*,6S*,7S*,7aS*)-Methyl 4,5-bis(acetyloxy)-2-benzyl-6-methyl-1-oxooctahydro-1H-4,6-epoxycyclopenta[c]pyridine-7-carboxylate* (***9b***). Viscous pale-yellow oil; R_f 0.57 (ethyl acetate); yield 0.49 g (76%); IR (neat): 1658 (NC=O), 1739 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m/z* (rel intensity): M^+ 431 (2), 371 (10), 329 (8), 311 (6), 242 (5), 201 (16), 138 (5), 91 (99), 65 (9), 43 (100);

^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.26 (5H, m, C_6H_5), 5.06 (1H, d, $J_{CH2A,CH2B}$ 14.8 Hz, CH_2A), 4.73 (1H, br s, H-5), 4.03 (1H, d, $J_{CH2A,CH2B}$ 14.8 Hz, CH_2B), 3.99 (1H, d, $J_{3A,3B}$ 13.5 Hz, H-3A), 3.60 (3H, s, OMe), 3.53 (1H, d, $J_{3A,3B}$ 13.5 Hz, H-3B), 3.42 (1H, br d, $J_{4a,7a}$ 4.1 Hz, H-4a), 3.23 (1H, dd, $J_{4a,7a}$ 4.1, $J_{7,7a}$ 11.0 Hz, H-7a), 3.05 (1H, d, $J_{7,7a}$ 11.0 Hz, H-7), 2.06 (3H, s, OAc), 1.92 (3H, s, OAc), 1.37 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.4 (C_1), 168.1 (CO_2Me), 167.8, 166.7 (OCOMe×2), 135.7 ($C_{1'}$), 128.2 ($C_{2'}$($C_{6'}$)), 127.9 ($C_{3'}$($C_{5'}$)), 127.1 ($C_{4'}$), 104.4 (C_4), 87.9 (C_6), 77.5 (C_5), 53.1 (C_3), 51.6 (CO_2*Me*), 49.5 (CH_2), 49.4 (C_7), 44.6 (C_{4a}), 38.6 (C_{7a}), 21.3, 20.3 (OCO*Me*×2), 14.0 (Me). Anal. Calcd for $C_{22}H_{25}NO_8$: C, 61.25; H, 5.84; N, 3.25. Found: C, 60.79; H, 6.19; N, 3.58.

3.8.5. (4R,4aR*,5R*,6S*,7S*,7aS*)-Methyl 4,5-bis(acetyloxy)-1-oxo-2-phenyloctahydro-1H-4,6-epoxycyclopenta[c]pyridine-7-carboxylate (**9c**).* Colourless prisms; yield 0.45 g (75%); mp 190–191 °C; IR (KBr): 1665 (NC=O), 1738 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M$^+$ 403 (1), 343 (5), 256 (4), 230 (5), 188 (16), 168 (6), 124 (20), 104 (17), 77 (22), 43 (100); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (4H, m, H–Ar), 7.28 (1H, m, H-4′), 4.90 (1H, d, $J_{5,4a}$ 1.3 Hz, H-5), 4.84 (1H, s, H-6), 4.47 (1H, d, $J_{3A,3B}$ 13.4 Hz, H-3A), 4.01 (1H, d, $J_{3A,3B}$ 13.4 Hz, H-3B), 3.73 (3H, s, OMe), 3.65 (1H, m, H-4a), 3.29 (1H, d, $J_{7,7a}$ 11.4 Hz, H-7a), 3.28 (1H, d, $J_{7,7a}$ 11.4 Hz, H-7), 2.11 (3H, s, OAc), 2.04 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.1 (C_1), 168.8 (CO_2Me), 168.3, 166.9 (OCOMe×2), 141.5 ($C_{1'}$), 129.4 ($C_{3'}$($C_{5'}$)), 127.5 ($C_{4'}$), 126.7 ($C_{2'}$($C_{6'}$)), 104.5 (C_4), 82.2 (C_6), 76.6 (C_5), 57.6 (C_3), 52.5 (CO_2*Me*), 46.2 (C_7), 44.8 (C_{4a}), 39.0 (C_{7a}), 21.7, 20.8 (OCO*Me*×2). Anal. Calcd for $C_{20}H_{21}NO_8$: C, 59.55; H, 5.25; N, 3.47. Found: C, 60.12; H, 5.00; N, 4.01.

3.8.6. (4R,4aR*,5R*,6R*,7S*,7aS*)-Methyl 4,5-bis(acetyloxy)-6-bromo-1-oxo-2-phenyloctahydro-1H-4,6-epoxycyclopenta[c]pyridine-7-carboxylate (**9d**).* White powder; yield 0.29 g (40%); mp 169–171 °C; IR (KBr): 1679 (NC=O), 1708, 1740, 1755 (OC=O) cm^{-1}; LCMS *m*/*z*: MH$^+$ 484; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37 (5H, m, H–Ar), 5.16 (1H, d, $J_{5,4a}$ 1.4 Hz, H-5), 4.52 (1H, d, $J_{3A,3B}$ 13.4 Hz, H-3A), 3.98 (1H, d, $J_{3A,3B}$ 13.4 Hz, H-3B), 3.78 (3H, s, OMe), 3.65 (1H, dd, $J_{4a,5}$ 1.4, $J_{4a,7a}$ 4.7 Hz, H-4a), 3.52 (1H, d, $J_{7,7a}$ 11.8 Hz, H-7), 3.44 (1H, dd, $J_{4a,7a}$ 4.7, $J_{7,7a}$ 11.4 Hz, H-7a), 2.07 (3H, s, OAc),2.07 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.5 (C_1), 168.5 (CO_2Me), 166.8, 166.1 (OCOMe×2), 141.0 ($C_{1'}$), 129.6 ($C_{3'}$($C_{5'}$)), 128.0 ($C_{4'}$), 126.8 ($C_{2'}$($C_{6'}$)), 105.8 (C_6), 90.7 (C_4), 78.5 (C_5), 57.1 (C_3), 53.2 (C_7), 52.7 (CO_2*Me*), 42.8 (C_{4a}), 40.5 (C_{7a}), 21.7, 20.8 (OCO*Me*×2). Anal. Calcd for $C_{20}H_{20}NO_8Br$: C, 49.90; H, 4.16; N, 2.91. Found: C, 50.13; H, 3.87; N, 2.72.

3.9. Lactonisation of the diepoxyisoindolones 7. Typical procedure

$BF_3\cdot OEt_2$ (0.39 mL, 3.0 mmol) was added to a solution of the corresponding diepoxyisoindolone **7a**,**b** (1.50 mmol) in 10 mL of acetic anhydride at 5 °C. Then the reaction mixture was allowed to warm up to rt and stirred for 12–24 h (TLC monitoring). Upon completion, the reaction mixture was diluted with water (60 mL), basified with satd aq $NaHCO_3$ to pH 9–10 and extracted with chloroform (3×30 mL). The combined organic layers were washed with water (2×30 mL), dried over $MgSO_4$ and concentrated in vacuo. The residual viscous oil was triturated in Et_2O (5 mL) to give corresponding product **10a**,**b** as a white powder. Subsequent recrystallization from a hexane–ethyl acetate mixture provided analytically pure samples. A single crystal of the compound **10a** for X-ray analysis was obtained by slow crystallization from an ethanol–DMF mixture.

3.9.1. (3R,3aR*,4aR*,7aS*,7bS*,8R*)-3a-Methyl-1,7-dioxo-6-phenyloctahydro-3,4a-methanofuro[3′,4′:4,5]furo[2,3-c]pyrrol-8-yl acetate (**10a**).* Colourless prisms; yield 0.17 g (31%); mp >260 °C; IR (KBr): 1704 (NC=O), 1704, 1797 (OC=O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M$^+$ 343 (100), 283 (6), 272 (17), 244 (47), 212 (32), 184 (13), 175 (19), 154 (7), 125 (18), 104 (27), 77 (11), 59 (32), 43 (34); ^{1}H NMR (DMSO, 600 MHz) δ 7.65 (2H, d, $J_{2',3'}$ 8.2 Hz, H-2′(H-6′)), 7.37 (2H, dd, $J_{3',4'}$ 7.5, $J_{2',3'}$ 8.2 Hz, H-3′(H-5′)), 7.14 (1H, t, $J_{3',4'}$=$J_{5',4'}$=7.5 Hz, H-4′), 5.16 (1H, s, H-8), 4.60 (1H, s, H-3), 4.25 (1H, d, $J_{5A,5B}$ 11.7 Hz, H-5A), 4.06 (1H, d, $J_{5A,5B}$ 11.7 Hz, H-5B), 3.72 (1H, d, $J_{7a,7b}$ 1.7 Hz, H-7a), 2.88 (1H, d, $J_{7a,7b}$ 1.7 Hz, H-7b), 2.06 (3H, s, OAc), 1.58 (3H, s, Me); ^{13}C NMR (DMSO, 100.6 MHz) δ 174.0 (C_7), 169.7 (CO_2), 169.1 (OCOMe), 138.8 ($C_{1'}$), 128.9 ($C_{3'}$($C_{5'}$)), 124.5 ($C_{4'}$), 119.4 ($C_{2'}$($C_{6'}$)), 89.1 (C_{3a}), 87.2 (C_3), 87.0 (C_{4a}), 77.1 (C_8), 54.3 (C_{7b}), 48.2 (C_5), 47.7 (C_{7a}), 20.6 (OCO*Me*), 15.1 (Me). Anal. Calcd for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.96; N, 4.08. Found: C, 62.70; H, 5.12; N, 3.68.

3.9.2. (3R,3aR*,4aR*,7aS*,7bS*,8R*)-6-Benzyl-3a-methyl-1,7-dioxooctahydro-3,4a-methanofuro[3′,4′:4,5]furo[2,3-c]pyrrol-8-yl acetate (**10b**).* Colourless rhombuses; yield 0.23 g (43%); mp 243–244 °C; IR (KBr): 1693 (NC=O), 1744, 1796 (OC=O) cm^{-1}; GC–MS (EI, 70 eV) *m*/*z* (rel intensity): M$^+$ 357 (47), 269 (3), 201 (3), 188 (5), 132 (5), 106 (8), 91 (100), 65 (8), 43 (41); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.33 (2H, t, $J_{3',4'}$=$J_{2',3'}$=7.5 Hz, H-3′(H-5′)), 7.28 (1H, t, $J_{3',4'}$=$J_{5',4'}$=7.5 Hz, H-4′), 7.20 (2H, d, $J_{2',3'}$ 8.2 Hz, H-2′(H-6′)), 5.01 (1H, s, H-8), 4.51 (1H, d, $J_{CH2A,CH2B}$ 15.1 Hz, CH_2A), 4.47 (1H, d, $J_{CH2A,CH2B}$ 15.1 Hz, CH_2B), 4.33 (1H, s, H-3), 3.64 (1H, d, $J_{5A,5B}$ 11.7 Hz, H-5A), 3.41 (1H, d, $J_{5A,5B}$ 11.7 Hz, H-5B), 3.01 (1H, d, $J_{7a,7b}$ 2.1 Hz, H-7a), 2.99 (1H, d, $J_{7a,7b}$ 2.1 Hz, H-7b), 2.07 (3H, s, OAc),1.69 (3H, s, Me); ^{13}C NMR (DMSO, 100.6 MHz) δ 173.5 (C_7), 169.8 (CO_2), 169.1 (OCOMe), 135.4 ($C_{1'}$), 128.9 ($C_{2'}$($C_{6'}$)), 127.9 ($C_{3'}$($C_{5'}$)), 127.9 ($C_{4'}$), 89.1 (C_{3a}), 88.4 (C_{4a}), 87.9 (C_3), 77.7 (C_8), 54.0 (C_{7b}), 47.5 (C_{7a}), 47.1 (C_5), 46.9 (CH_2), 20.5 (OCO*Me*), 15.6 (Me). Anal. Calcd for $C_{19}H_{19}NO_6$: C, 63.87; H, 5.32; N, 3.92. Found: C, 63.66; H, 5.13; N, 4.24.

3.9.3. Methyl (6aR,6bR*,9S*,10R*,10aS*)-1-ethyl-5,5-dimethyl-11-oxo-6,6a,9,10,10a,11-hexahydro-5H-6b,9-epoxyisoindolo[2,1-a]quinoline-10-carboxylate (**13**).* The corresponding isoindoloquinoline acid **10c** (2.06 g, 5.8 mmol) was heated to reflux in methanol (30 mL) for 2 h in the presence of a catalytic amount of concentrated H_2SO_4 (~0.1 mL) (TLC monitoring). Upon completion, the reaction mixture was cooled to rt, poured into 150 mL of water and extracted with chloroform (3×70 mL). The extract was dried over $MgSO_4$ and concentrated in vacuo. The crude product was recrystallized from a hexane–ethyl acetate mixture to give ester **13** as white crystals (1.89 g, 88%); mp 162.5–164 °C; IR (KBr): 1695 (NC=O), 1715 (OC=O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M$^+$ 367 (42), 352 (7), 336 (5), 254 (100), 240 (20), 226 (14), 212 (9), 198 (14), 186 (10), 172 (14), 160 (26), 144 (15), 130 (12), 113 (60), 103 (5), 85 (20), 77 (17), 59 (34), 53 (15), 40 (31); ^{1}H NMR (DMSO, 400 MHz) δ 7.22–7.16 (3H, m, Ar), 6.64 (1H, d, $J_{8,7}$ 5.8 Hz, H-7), 6.50 (1H, dd, $J_{8,9}$ 1.7, $J_{8,7}$ 5.8 Hz, H-8), 5.24 (1H, d, $J_{9,8}$ 1.7 Hz, H-9), 4.23 (1H, dd, $J_{6eq,6a}$ 2.8, $J_{6ax,6a}$ 12.8 Hz, H-6a), 3.79 (3H, s, OMe), 2.87 (1H, d, $J_{10,10a}$ 9.0 Hz, H-10a,), 2.78 (1H, d, $J_{10,10a}$ 9.0 Hz, H-10), 2.67 (2H, m, $J_{CH2,Me}$7.5 Hz, C*H*$_2$Me), 2.13 (1H, dd, $J_{6eq,6a}$ 2.8, $J_{6eq,6ax}$ 12.8 Hz, H-6eq), 1.87 (1H, t, $J_{6eq,6ax}$=$J_{6ax,6a}$=12.8 Hz, H-6ax), 1.45 (3H, s, Me), 1.36 (3H, s, Me), 1.17 (3H, t, $J_{CH2,Me}$ 7.5 Hz, *Me*CH$_2$); ^{13}C NMR (DMSO, 100.6 MHz) δ 171.2 (CO_2Me), 168.7 (C_4), 138.7 (C_{5a} and C_{9a}), 136.7 (C_{1a}), 134.1 (C_{11c}), 132.2 (C_6), 126.2 (C_7), 125.7 (C_8), 124.0 (C_9), 90.6 (C_{11b}), 81.3 (C_2), 55.1 (CO_2*Me*), 49.3 (C_3), 45.2 (C_{3a} and C_{11a}), 40.5 (C_{11}), 33.9 (C_{10}), 33.1 and 31.5 (C*Me*×2), 24.4 (*C*H$_2$Me), 13.9 (CH$_2$*Me*). Anal. Calcd for $C_{22}H_{25}NO_4$: C, 71.91; H, 6.86; N, 3.81. Found: C, 71.54; H, 6.89; N, 3.51.

3.9.4. Methyl (1aR,2R*,3R*,3aS*,11aR*,11bR*,11cR*)-6-ethyl-10,10-dimethyl-4-oxo-1a,2,3,3a,4,11,11a,11c-octahydro-10H-2,11b-epoxyoxireno[6,7]isoindolo[2,1-a]quinoline-3-carboxylate (**14**).* A mixture of 1.0 mL (27.3 mmol) of formic acid and 2.0 mL (35.4 mmol) of 50%

hydrogen peroxide was added to a solution of ester **13** 1.00 g (2.7 mmol) in 40 mL of dichloroethane and the reaction mixture was stirred at reflux for 20 h (TLC monitoring). Upon completion, the reaction mixture was diluted with water (100 mL), basified with satd aq $NaHCO_3$ to pH 9–10 and extracted with chloroform (4×50 mL). The combined organic layers were washed with satd aq $NaHCO_3$ (50 mL), water (50 mL), dried over $MgSO_4$ and concentrated in vacuo. The solid residue was recrystallized from an *i*-PrOH–DMF mixture to afford diepoxide **14** as white crystals (0.73 g, 71%); mp 241.5–243 °C; IR (KBr): 1685 (NC=O), 1730 (OC=O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+ 383 (100), 366 (18), 353 (7), 294 (20), 280 (5), 266 (9), 254 (9), 214 (16), 186 (12), 172 (11), 157 (6), 144 (6), 130 (3), 113 (3). ^{1}H NMR (DMSO, 400 MHz) δ 7.29 (1H, dd, $J_{7,9}$ 1.1, $J_{7,8}$ 7.7 Hz, H-7), 7.15 (1H, t, $J_{7,8}$=$J_{8,9}$=7.7 Hz, H-8), 4.04 (1H, dd, $J_{11eqv,11a}$ 2.5, $J_{11ax,11a}$ 12.8 Hz, H-11a), 3.75 (1H, d, $J_{11c,1a}$ 3.4 Hz, H-11c), 3.62 (1H, d, $J_{11c,1a}$ 3.4 Hz, H-1a), 3.58 (3H, s, OMe), 3.29 (1H, d, $J_{3,3a}$ 9.6 Hz, H-3a), 3.03 (1H, d, $J_{3,3a}$ 9.6 Hz, H-3), 2.49–2.41 (2H, m, $J_{CH2,Me}$7.5 Hz, C*H*$_2$Me), 2.11 (1H, dd, $J_{11eqv,11a}$ 2.5, $J_{11eqv,11ax}$ 13.2 Hz, H-11eqv), 1.91 (1H, br t, H-11ax, $J_{11eqv,11ax}$=$J_{11ax,11a}$=13.0), 1.38 (3H, s, Me), 1.29 (3H, s, Me), 1.08 (3H, t, $J_{CH2,Me}$ 7.5 Hz, *Me*CH$_2$); ^{13}C NMR (DMSO, 100.6 MHz) δ 170.3 (*C*O$_2$Me), 167.8 (C_4), 138.8 (C_{5a}), 138.7 (C_{9a}), 131.9 (C_6), 126.3 (C_7), 125.9 (C_8), 124.0 (C_9), 86.9 (C_{11b}), 77.7 (C_2), 54.2 (CO$_2$*Me*), 51.4 (C_{1a}), 51.2 (C_{11c}), 48.7 (C_3), 48.0 (C_{3a}), 46.6 (C_{11a}), 40.6 (C_{11}), 33.9 (C_{10}), 33.1 and 31.4 (C*Me*×2), 24.4 (*C*H$_2$Me), 14.1 (CH$_2$*Me*). Anal. Calcd for $C_{22}H_{25}NO_5$: C, 68.91; H, 6.57; N, 3.65. Found: C, 68.75; H, 6.39; N, 3.51.

3.10. Wagner–Meerwein rearrangement of the annulated diepoxyisoindolones 14, 17, 20, 23. Typical procedure

$BF_3 \cdot OEt_2$ (0.38 mL, 3.0 mmol) was added to a solution of the corresponding diepoxyisoindoloquinoline **14**, **17a**–**f**,[15a] **20a**–**j**,[14e] **23a**,**b**[14e] (1.50 mmol) in 10 mL of acetic anhydride at 0 °C. The reaction mixture was stirred at room temperature for 4–24 h (at 60 °C for 0.5 h for compound **15**) (TLC monitoring). Upon completion, the reaction mixture was diluted with water (60 mL), basified with satd aq $NaHCO_3$ to pH 9–10 and extracted with chloroform (4×40 mL). The combined organic layers were washed with water (2×30 mL), dried over $MgSO_4$ and concentrated in vacuo. The residual viscous oil was triturated in Et_2O (5 mL) to give corresponding polycycle **15**, **18a**–**f**, **21a**–**j**, **24a**,**b** as a white powder. Subsequent recrystallization from ethyl acetate provided analytically pure samples. A single crystal of the compound **15** for X-ray analysis was obtained by slow crystallization from acetone, single crystals of the compounds **18a** and **21g**—from an ethanol–DMF mixture.

3.10.1. Methyl (6aS,7R*,7aS*,8S*,9R*,10R*,10aR*)-7,8-bis(acetyloxy)-1-ethyl-5,5-dimethyl-11-oxo-5,6,6a,7,7a,8,9,10,10a,11-decahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-10-carboxylate (**15**).* Colourless plates; yield 0.23 g (64%); mp 206.5–208 °C (decomp.); IR (KBr): 1672 (NC=O), 1752 (OC=O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+ 485 (8), 456 (4), 443 (13), 425 (2), 401 (7), 214 (12), 188 (10), 157 (6), 130 (4), 113 (4), 59 (4), 43 (100); ^{1}H NMR (DMSO, 400 MHz) δ 7.24 (1H, dd, $J_{2,4}$ 1.5, $J_{3,4}$ 7.6 Hz, H-4), 7.18 (1H, t, $J_{3,4}$=$J_{2,3}$=7.6 Hz, H-3), 7.07 (1H, dd, $J_{2,4}$ 1.5, $J_{2,3}$ 7.6 Hz, H-2), 4.97 (1H, br s, H-8), 4.81 (1H, br s, H-9), 4.55 (1H, dd, $J_{6a,6A}$ 4.5, $J_{6a,6B}$ 11.0 Hz, H-6a), 3.55 (1H, d, $J_{10,10a}$ 11.8 Hz, H-10), 3.48 (1H, br d, $J_{7a,10a}$ 4.9 Hz, H-7a), 3.42 (1H, dd, $J_{10,10a}$ 11.8, $J_{7a,10a}$ 4.9 Hz, H-10a), 3.62 (3H, s, OMe), 2.20 (1H, dd, $J_{CHA,Me}$ 7.5, $J_{A,B}$ 16.0 Hz, C*H*$_A$Me), 2.14 (1H, dd, $J_{CHB,Me}$ 7.5, $J_{A,B}$ 16.0 Hz, C*H*$_B$Me), 2.10 (3H, s, OAc), 2.03 (3H, s, OAc), 1.95 (1H, dd, $J_{6a,6B}$ 11.0, $J_{6A,6B}$ 13.6 Hz, H-6B), 1.86 (1H, dd, $J_{6a,6A}$ 4.5, $J_{6A,6B}$ 13.6 Hz, H-6A), 1.21 (3H, s, Me-5A), 1.18 (3H, s, Me-5B), 1.06 (3H, t, $J_{CH2,Me}$ 7.5 Hz, *Me*CH$_2$); ^{13}C NMR (DMSO, 100.6 MHz) δ 169.9 and 168.8 (OCOMe×2), 167.9 (*C*O$_2$Me), 164.3 (C_4), 140.7 (C_{12a}), 139.7 (C_1), 136.1 (C_{4a}), 126.6 (C_4), 125.2 (C_2), 123.5 (C_3), 105.4 (C_7), 80.6 (C_9), 75.9 (C_8), 55.6 (C_{6a}), 51.4 (CO$_2$*Me*), 45.4 (C_{10}), 43.9 (C_6), 43.3 (C_{7a}), 40.1 (C_{10a}), 33.4 (C_5), 31.7 and 31.4 (C*Me*×2), 22.9 (*C*H$_2$Me), 21.9 and 20.6 (OCO*Me*×2), 13.6 (CH$_2$*Me*). Anal. Calcd for $C_{26}H_{31}NO_8$: C, 64.33; H, 6.39; N, 2.89. Found: C, 64.45; H, 6.80; N, 3.18.

3.10.2. Methyl (5S,6R*,6aR*,7R*,7aR*,8R*,9S*,10S*,10aR*)-5,7,8-triacetoxy-6-(2-acetoxyethyl)-11-oxo-5,6,6a,7,7a,8,9,10,10a,11-decahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-10-carboxylate (**18a**).* Colourless plates; yield 0.41 g (48%); mp 263–264 °C (decomp.); IR (KBr): 1670 (NC=O), 1751 (OC=O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+ 573 (1), 513 (5), 471 (28), 453 (14), 426 (100), 411 (15), 384 (35), 366 (16), 342 (26), 255 (27), 216 (99), 156 (49), 130 (21), 113 (13), 43 (68); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91 (1H, dd, $J_{1,3}$ 1.2, $J_{1,2}$ 8.5 Hz, H-1), 7.33 (1H, ddd, $J_{2,4}$ 1.7, $J_{2,3}$ 7.2, $J_{1,2}$ 8.5 Hz, H-2), 7.22 (1H, dd, $J_{2,4}$ 1.7, $J_{3,4}$ 7.8 Hz, H-4), 7.13 (1H, ddd, $J_{1,3}$ 1.2, $J_{2,3}$ 7.2, $J_{3,4}$ 7.8 Hz, H-3), 5.62 (1H, d, $J_{5,6}$ 2.1 Hz, H-5), 5.09 (1H, s, H-6a), 4.88 (1H, br s, H-9), 4.87 (1H, d, $J_{7a,8}$ 1.3 Hz, H-8), 4.18 (2H, m, H-2′), 3.66 (3H, s, OMe), 3.36 (1H, dd, $J_{7a,10a}$ 4.4, $J_{10,10a}$ 11.3 Hz, H-10a), 3.32 (1H, dd, $J_{7a,8}$ 1.3, $J_{7a,10a}$ 4.4 Hz, H-7a), 3.30 (1H, d, $J_{10,10a}$ 11.3 Hz, H-10), 2.15 (1H, m, H-6), 2.09 (3H, s, OAc), 2.03 (3H, s, OAc), 2.02 (3H, s, OAc), 2.00 (3H, s, OAc), 1.70 (1H, m, H-1′A), 1.33 (1H, m, H-1′B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.6, 170.3, 169.8, 167.6 (OCOMe×4), 167.4 (*C*O$_2$Me), 166.2 (C_{11}), 138.1 (C_{12a}), 130.9 (C_4), 128.7 (C_2), 125.3 (C_3), 124.9 (C_1), 123.3 (C_{4a}), 103.9 (C_7), 80.1 (C_9), 76.7 (C_8), 70.5 (C_5), 61.4 ($C_{2'}$), 58.4 (C_{6a}), 52.4 (CO$_2$*Me*), 46.6 (C_{10}), 45.9 (C_{7a}), 39.4 (C_{10a}), 37.1 (C_6), 24.2 ($C_{1'}$), 21.6, 21.0, 20.7, 20.6 (OCO*Me*×4). Anal. Calcd for $C_{28}H_{31}NO_{12}$: C, 58.64; H, 5.45; N, 2.44. Found: C, 58.56; H, 5.51; N, 2.36.

3.10.3. Methyl (5S,6R*,6aR*,7R*,7aR*,8R*,9S*,10S*,10aR*)-5,7,8-triacetoxy-6-(2-acetoxyethyl)-9-methyl-11-oxo-5,6,6a,7,7a,8,9,10,10a,11-decahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-10-carboxylate (**18b**).* Colourless druses; yield 0.61 g (70%); mp 244–246 °C (decomp.); IR (KBr): 1660 (NC=O), 1747 (OC=O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+ 587 (1), 485 (62), 440 (91), 398 (34), 356 (27), 315 (44), 288 (66), 259 (27), 216 (100), 156 (43), 113 (23), 76 (36), 60 (87), 43 (97); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (1H, d, $J_{1,2}$ 8.2 Hz, H-1), 7.37 (1H, ddd, $J_{2,4}$ 0.8, $J_{2,3}$ 7.7, $J_{1,2}$ 8.2 Hz, H-2), 7.27 (1H, dd, $J_{2,4}$ 0.8, $J_{3,4}$ 7.7 Hz, H-4), 7.18 (1H, t, $J_{2,3}$=$J_{3,4}$=7.7 Hz, H-3), 5.66 (1H, d, $J_{5,6}$ 0.9 Hz, H-5), 5.10 (1H, s, H-6a), 4.78 (1H, s, H-8), 4.22 (2H, m, H-2′), 3.73 (3H, s, OMe), 3.41 (1H, dd, $J_{7a,10a}$ 4.7, $J_{10,10a}$ 11.3 Hz, H-10a), 3.38 (1H, br d, $J_{7a,10a}$ 4.7 Hz, H-7a), 3.20 (1H, d, $J_{10,10a}$ 11.3 Hz, H-10), 2.19 (1H, m, H-6), 2.19 (3H, s, OAc), 2.07 (3H, s, OAc), 2.07 (3H, s, OAc), 2.06 (3H, s, OAc), 1.75 (1H, m, H-1′A), 1.55 (3H, s, Me), 1.40 (1H, m, H-1′B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.7, 170.4, 169.8, 167.7 (OCOMe×4), 167.5 (*C*O$_2$Me), 166.2 (C_{11}), 138.4 (C_{12a}), 131.1 (C_4), 128.7 (C_2), 125.4 (C_3), 124.7 (C_1), 123.7 (C_{4a}), 104.7 (C_7), 86.8 (C_9), 78.4 (C_8), 70.7 (C_5), 61.6 ($C_{2'}$), 58.8 (C_{6a}), 52.3 (CO$_2$*Me*), 50.2 (C_{10}), 46.0 (C_{7a}), 40.1 (C_{10a}), 37.2 (C_6), 24.4 ($C_{1'}$), 21.9, 21.2, 20.8, 20.7 (OCO*Me*×4), 14.2 (*Me*). Anal. Calcd for $C_{29}H_{33}NO_{12}$: C, 59.28; H, 5.66; N, 2.38. Found: C, 59.21; H, 5.43; N, 2.43.

3.10.4. Methyl (5S,6R*,6aR*,7R*,7aR*,8R*,9S*,10S*,10aR*)-5,7,8-triacetoxy-6-(2-acetoxyethyl)-10-methyl-11-oxo-5,6,6a,7,7a,8,9,10,10a,11-decahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-10-carboxylate (**18c**).* Colourless plates; yield 0.54 g (61%); mp 227–228 °C; IR (KBr): 1678 (NC=O), 1751 (OC=O) cm^{-1}; HRMS (DART) *m*/*z* (rel intensity): 588.205(2) $[M+H]^+$ (100) (exact mass for $C_{29}H_{34}NO_{12}$ 588.2081), 589.21 (32), 590.21 (7), 591.22 (1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (1H, d, $J_{1,2}$ 7.6 Hz, H-1), 7.34 (1H, t, $J_{2,3}$= $J_{1,2}$=7.6 Hz, H-2), 7.24 (1H, d, $J_{3,4}$ 7.6 Hz, H-4), 7.15 (1H, t, $J_{2,3}$=$J_{3,4}$=7.6 Hz, H-3), 5.62 (1H, br s, H-5), 5.12 (1H, s, H-6a), 5.02 (1H, br s, H-8), 4.66 (1H, s, H-9), 4.18 (2H, m, H-2′), 3.67 (3H, s,

OMe), 3.41 (1H, br s, H-7a), 2.97 (1H, d, $J_{7a,10a}$ 4.1 Hz, H-10a), 2.14 (1H, m, H-6), 2.12 (3H, s, OAc), 2.05 (3H, s, OAc), 2.04 (3H, s, OAc), 2.02 (3H, s, OAc), 1.71 (1H, m, H-1′A), 1.55 (3H, s, Me), 1.34 (1H, m, H-1′B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.3, 170.6, 170.3, 170.1 (OCOMe×4), 167.7 (CO_2Me), 166.6 (C_{11}), 138.3 (C_{12a}), 131.0 (C_4), 128.7 (C_2), 125.3 (C_3), 125.0 (C_1), 123.3 (C_{4a}), 103.2 (C_7), 83.9 (C_9), 75.4 (C_8), 70.6 (C_5), 61.5 ($C_{2'}$), 58.6 (C_{6a}), 54.0 (C_{10}), 52.7 (CO_2Me), 48.7 (C_{7a}), 46.0 (C_{10a}), 37.3 (C_6), 26.0 (*Me*), 24.3 ($C_{1'}$), 21.7, 21.1, 20.8, 20.7 (OCO*Me*×4). Anal. Calcd for $C_{29}H_{33}NO_{12}$: C, 59.28; H, 5.66; N, 2.38. Found: C, 59.42; H, 5.49; N, 2.47.

3.10.5. (5S,6R*,6aR*,7R*,7aR*,8R*,9S*,10aR*)-6-(2-Acetoxyethyl)-10a-methyl-11-oxo-6,6a,7a,8,9,10,10a,11-octahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-5,7,8(5H)-triyl triacetate (**18d**).* Colourless druses; yield 0.32 g (41%); mp 193–194 °C (decomp.); IR (KBr): 1679 (NC═O), 1747 (OC═O) cm^{-1}; HRMS (DART) *m*/*z* (rel intensity): 530.204(7) $[M+H]^+$ (100) (exact mass for $C_{27}H_{32}NO_{10}$ 530.2026), 531.21 (30), 532.21 (6), 533.21 (1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03 (1H, d, $J_{1,2}$ 8.1 Hz, H-1), 7.28 (1H, d, $J_{3,4}$ 7.5 Hz, H-4), 7.27 (1H, dd, $J_{2,3}$ 7.5, $J_{1,2}$ 8.1 Hz, H-2), 7.06 (1H, t, $J_{2,3}$=$J_{3,4}$=7.5 Hz, H-3), 5.78 (1H, d, $J_{5,6}$ 1.9 Hz, H-5), 5.09 (1H, s, H-6a), 4.62 (1H, br s, H-9), 4.57 (1H, br s, H-8), 4.13 (2H, m, H-2′), 3.72 (1H, br s, H-7a), 2.41 (1H, m, H-6), 2.23 (1H, m, H-1′A), 2.21 (1H, d, $J_{10A,10B}$ 13.7 Hz, H-10A), 2.06 (3H, s, OAc), 2.02 (3H, s, OAc), 1.98 (3H, s, OAc), 1.95 (3H, s, OAc), 1.72 (1H, d, $J_{10A,10B}$ 13.7 Hz, H-10B),1.13 (1H, m, H-1′B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.2, 171.1, 170.1, 169.6 (OCOMe×4), 169.1 (C_{11}), 137.8 (C_{12a}), 132.1 (C_4), 129.2 (C_2), 125.0 (C_3), 123.5 (C_{4a}), 123.3 (C_1), 106.9 (C_7), 80.6 (C_9), 76.8 (C_8), 71.3 (C_5), 62.8 ($C_{2'}$), 55.4 (C_{6a}), 47.7 (C_{7a}), 42.6 (C_{10a}), 42.2 (C_{10}), 35.3 (C_6), 26.1 (*Me*), 24.8 ($C_{1'}$), 21.8, 21.3, 21.0, 21.0 (OCO*Me*×4). Anal. Calcd for $C_{27}H_{31}NO_{10}$: C, 61.24; H, 5.90; N, 2.65. Found: C, 61.46; H, 6.02; N, 2.75.

3.10.6. (5S,6R*,6aR*,7R*,7aR*,8R*,9S*,10S*,10aS*)-6-(2-Acetoxyethyl)-11-oxo-10-phenyl-6,6a,7a,8,9,10,10a,11-octahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-5,7,8(5H)-triyl triacetate (**18e**).* Colourless plates; yield 0.66 g (74%); mp 221–222 °C; IR 1671 (NC═O), 1745 (OC═O) cm^{-1}; HRMS (DART) *m*/*z* (rel intensity): 592.220(7) $[M+H]^+$ (100) (exact mass for $C_{32}H_{34}NO_{10}$ 592.2183), 593.22 (35), 594.22 (8), 595.23 (1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.42 (1H, d, $J_{1,2}$ 8.2 Hz, H-1), 7.55 (2H, d, $J_{2'',3''}$ 7.6 Hz, H-2″(H-6″)), 7.36 (m, 4H, H-4, H-4″, H-3″and H-5″), 7.25 (1H, dd, $J_{2,3}$ 7.6, $J_{1,2}$ 8.2 Hz, H-2), 7.16 (1H, t, $J_{2,3}$=$J_{3,4}$=7.6 Hz, H-3), 5.88 (1H, d, $J_{5,6}$ 2.1 Hz, H-5), 5.13 (1H, s, H-6a), 5.09 (1H, d, $J_{9,10}$ 2.1 Hz, H-9), 4.67 (1H, br s, H-8), 4.23 (2H, m, H-2′), 4.16 (1H, dd, $J_{9,10}$ 2.1, $J_{10,10a}$ 4.8 Hz, H-10), 3.38 (1H, br d, $J_{7a,10a}$ 4.8 Hz, H-7a), 3.33 (1H, t, $J_{7a,10a}$=$J_{10,10a}$=4.8 Hz, H-10a), 2.52 (1H, m, H-6), 2.38 (1H, m, H-1′A), 2.14 (3H, s, OAc), 2.11 (3H, s, OAc), 2.04 (3H, s, OAc), 2.02 (3H, s, OAc), 1.26 (1H, m, H-1′B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.9, 170.1, 169.4, 169.3 (OCOMe×4), 169.0 (C_{11}), 139.5 (C_{12a}), 137.7 ($C_{1''}$), 132.2 (C_4), 129.3 ($C_{4''}$), 129.0 ($C_{3''}$($C_{5''}$)), 127.2 (C_2), 126.9 ($C_{2''}$($C_{6''}$)), 125.2 (C_3), 123.4 (C_{4a}), 122.9 (C_1), 106.8 (C_7), 82.2 (C_9), 76.2 (C_8), 71.3 (C_5), 62.7 ($C_{2'}$), 56.2 (C_{6a}), 50.7 (C_{10}), 46.4 (C_{7a}), 41.7 (C_{10a}), 35.2 (C_6), 24.9 ($C_{1'}$), 21.6, 21.2, 20.9, 20.8 (OCO*Me*×4). Anal. Calcd for $C_{32}H_{33}NO_{10}$: C, 64.97; H, 5.62; N, 2.37. Found: C, 64.75; H, 5.43; N, 2.36.

3.10.7. Methyl (5S,6R*,6aR*,7R*,7aR*,8R*,9S*,10S*,10aR*)-5,7,8-triacetoxy-6-(3-acetoxypropyl)-11-oxo-5,6,6a,7,7a,8,9,10,10a,11-decahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-10-carboxylate (**18f**).* Colourless plates; yield 0.32 g (36%); mp 282–283 °C (decomp.); IR 1667 (NC═O), 1732 and 1749 (OC═O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+ 587 (3), 527 (7), 485 (31), 426 (100), 384 (27), 342 (11), 255 (13), 230 (66), 170 (7), 130 (15), 113 (8), 43 (52); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.94 (1H, d, $J_{1,2}$ 8.3 Hz, H-1), 7.35 (1H, dd, $J_{2,3}$ 7.6, $J_{1,2}$ 8.3 Hz, H-2), 7.23 (1H, d, $J_{3,4}$ 7.6 Hz, H-4), 7.16 (1H, t, $J_{2,3}$=$J_{3,4}$=7.6 Hz, H-3), 5.62 (1H, s, H-5), 5.09 (1H, s, H-6a), 4.91 (1H, br s, H-8), 4.87 (1H, s, H-9), 4.05 (2H, m, H-3′), 3.69 (3H, s, OMe), 3.38 (1H, dd, $J_{7a,10a}$ 4.5, $J_{10,10a}$ 11.5 Hz, H-10a), 3.31 (1H, br d, $J_{7a,10a}$ 4.5 Hz, H-7a), 3.29 (1H, d, $J_{10,10a}$ 11.5 Hz, H-10), 2.12 (3H, s, OAc), 2.06 (3H, s, OAc), 2.05 (3H, s, OAc), 2.01 (3H, s, OAc), 1.82 (1H, m, H-6), 1.60 (2H, m, H-2′), 1.41 (1H, m, H-1′A), 1.13 (1H, m, H-1′B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.1, 170.8, 170.1, 167.9 (OCOMe×4), 167.5 (CO_2Me), 166.3 (C_{11}), 138.3 (C_{12a}), 131.1 (C_4), 128.9 (C_2), 125.5 (C_3), 125.1 (C_1), 123.7 (C_{4a}), 104.2 (C_7), 80.2 (C_9), 76.9 (C_8), 70.7 (C_5), 63.4 ($C_{3'}$), 58.8 (C_{6a}), 52.7 (CO_2Me), 46.8 (C_{10}), 46.3 (C_{7a}), 39.7 (C_{10a}), 39.5 (C_6), 25.5 ($C_{1'}$), 21.9, 21.3, 20.9, 20.8 (OCO*Me*×4), 21.0 ($C_{2'}$). Anal. Calcd for $C_{29}H_{33}NO_{12}$: C, 59.28; H, 5.66; N, 2.38. Found: C, 59.42; H, 5.31; N, 2.50.

3.10.8. (5R,6aR*,7S*,7aS*,8S*,9R*,10aR*)-11-Oxo-5-(2-oxopyrrolidin-1-yl)-6,6a,7a,8,9,10,10a,11-octahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-7,8(5H)-diyl diacetate (**21a**).* Colourless druses; yield 0.32 g (47%); mp 234–236 °C (decomp.); IR 1687, 1662 (NC═O), 1735 (OC═O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+ 454 (1), 394 (88), 351 (17), 338 (26), 305 (35), 281 (26), 267 (25), 250 (55), 238 (27), 222 (91), 196 (21), 156 (17), 130 (100), 43 (55); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.95 (1H, dd, $J_{1,3}$ 1.2, $J_{1,2}$ 8.5 Hz, H-1), 7.18 (1H, ddd, $J_{2,4}$ 1.8, $J_{2,3}$ 7.2, $J_{1,2}$ 8.5 Hz, H-2), 7.06 (1H, ddd, $J_{1,3}$ 1.2, $J_{2,3}$ 7.2, $J_{3,4}$ 7.8 Hz, H-3), 6.98 (1H, br d, $J_{3,4}$ 7.8 Hz, H-4), 5.55 (1H, dd, $J_{5,6A}$ 7.5, $J_{5,6B}$ 11.8 Hz, H-5), 4.88 (1H, d, $J_{7a,8}$ 1.9 Hz, H-8), 4.59 (1H, br s, H-9), 4.27 (1H, dd, $J_{6a,6A}$ 1.5, $J_{6a,6B}$ 11.8 Hz, H-6a), 3.93 (1H, dd, $J_{7a,8}$ 1.9, $J_{7a,10a}$ 4.9 Hz, H-7a), 3.18 (1H, m, H-5′A), 3.18 (1H, m, H-10a), 2.98 (1H, m, H-5′B), 2.43 (2H, m, H-3′), 2.40 (1H, ddd, $J_{6a,6A}$ 1.5, $J_{5,6A}$ 7.5, $J_{6A,6B}$ 13.4 Hz, H-6A), 2.24 (1H, ddd, $J_{9,10A}$ 1.4, $J_{10A,10a}$ 12.0, $J_{10A,10B}$ 13.7 Hz, H-10A), 2.06 (3H, s, OAc), 2.06 (3H, s, OAc), 2.02 (1H, dt, $J_{6a,6B}$=$J_{5,6B}$=11.8, $J_{6A,6B}$ 13.4 Hz, H-6B), 1.95 (2H, m, H-4′), 1.66 (1H, ddd, $J_{9,10B}$ 1.5, $J_{10B,10a}$ 4.1, $J_{10A,10B}$ 13.7 Hz, H-10B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.6 ($C_{2'}$), 169.3 and 169.8 (OCOMe×2), 168.0 (C_{11}), 137.7 (C_{12a}), 127.4 (C_2), 127.3 (C_4), 125.9 (C_{4a}), 125.5 (C_3), 124.6 (C_1), 105.7 (C_7), 79.4 (C_9), 77.3 (C_8), 58.3 (C_{6a}), 47.9 (C_5), 42.1 ($C_{5'}$), 40.2 (C_{7a}), 36.4 (C_{10a}), 33.6 (C_{10}), 31.0 ($C_{3'}$), 27.4 (C_6), 20.7 and 21.8 (OCO*Me*×2), 17.8 ($C_{4'}$). Anal. Calcd for $C_{24}H_{26}N_2O_7$: C, 63.43; H, 5.77; N, 6.16. Found: C, 63.29; H, 5.85; N, 6.31.

3.10.9. (5R,6aR*,7S*,7aS*,8S*,9R*,10aR*)-9-Methyl-11-oxo-5-(2-oxopyrrolidin-1-yl)-6,6a,7a,8,9,10,10a,11-octahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-7,8(5H)-diyl diacetate (**21b**).* Colourless druses; yield 0.42 g (60%); mp 259–260 °C (decomp.); IR (KBr): 1679, 1654 (NC═O), 1741 (OC═O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+ 468 (3), 408 (37), 349 (100), 295 (14), 282 (23), 264 (84), 236 (94), 211 (22), 196 (11), 180 (11), 130 (63), 78 (22), 69 (30), 55 (74), 43 (93); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00 (1H, dd, $J_{1,3}$ 1.0, $J_{1,2}$ 8.4 Hz, H-1), 7.23 (1H, ddd, $J_{2,4}$ 1.0, $J_{2,3}$ 7.5, $J_{1,2}$ 8.4 Hz, H-2), 7.10 (1H, dt, $J_{1,3}$ 1.0, $J_{2,3}$=$J_{3,4}$=7.5 Hz, H-3), 7.03 (1H, dd, $J_{2,4}$ 1.0, $J_{3,4}$ 7.5 Hz, H-4), 5.59 (1H, dd, $J_{5,6A}$ 7.6, $J_{5,6B}$ 11.9 Hz, H-5), 4.94 (1H, d, $J_{7a,8}$ 1.8 Hz, H-8), 4.29 (1H, dd, $J_{6a,6A}$ 1.4, $J_{6a,6B}$ 11.8 Hz, H-6a), 3.94 (1H, dd, $J_{7a,8}$ 1.8, $J_{7a,10a}$ 4.5 Hz, H-7a), 3.25 (1H, m, H-5′A), 3.21 (1H, dt, $J_{7a,10a}$=$J_{10B,10a}$=4.5, $J_{10A,10a}$ 12.2 Hz, H-10a), 3.04 (1H, m, H-5′B), 2.49 (2H, m, H-3′), 2.43 (1H, ddd, $J_{6a,6A}$ 1.4, $J_{5,6A}$ 7.6, $J_{6A,6B}$ 13.4 Hz, H-6A), 2.24 (1H, dd, $J_{10A,10a}$ 12.2, $J_{10A,10B}$ 13.3 Hz, H-10A), 2.13 (3H, s, OAc), 2.10 (3H, s, OAc), 2.04 (1H, dt, $J_{6a,6B}$=$J_{5,6B}$=11.8, $J_{6A,6B}$ 13.4 Hz, H-6B), 2.01 (2H, m, H-4′), 1.69 (1H, dd, $J_{10B,10a}$ 4.5, $J_{10A,10B}$ 13.3 Hz, H-10B), 1.55 (3H, m, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.9 ($C_{2'}$), 169.6 and 169.8 (OCOMe×2), 168.5 (C_{11}), 137.9 (C_{12a}), 127.7 (C_2), 127.5 (C_4), 126.2 (C_{4a}), 125.7 (C_3), 124.9 (C_1), 106.1 (C_7), 87.0 (C_9), 77.9 (C_8), 58.6 (C_{6a}), 48.2 (C_5), 42.4 ($C_{5'}$), 41.8 (C_{7a}), 39.1 (C_{10}), 36.7 (C_{10a}), 31.2 ($C_{3'}$), 27.6 (C_6), 22.2 and 20.9 (OCO*Me*×2), 18.0 ($C_{4'}$), 15.1 (*Me*). Anal. Calcd for $C_{25}H_{28}N_2O_7$: C, 64.09; H, 6.02; N, 5.98. Found: C, 63.89; H, 5.97; N, 6.20.

3.10.10. (5R,6aR*,7S*,7aS*,8S*,9R*,10aR*)-10a-Methyl-11-oxo-5-(2-oxopyrrolidin-1-yl)-6,6a,7a,8,9,10,10a,11-octahydro-7,9-*

*epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-7,8(5H)-diyl diacetate (**21c**).* Colourless druses; yield 0.24 g (34%); mp 269–270 °C (decomp.); IR (KBr): 1691, 1659 (NC=O), 1740 (OC=O) cm^{-1}; HRMS (DART) *m/z* (rel intensity): 469.199(1) $[M+H]^+$ (100) (exact mass for $C_{25}H_{29}N_2O_7$ 469.1975), 470.20 (27), 471.20 (5); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.85 (1H, d, $J_{1,2}$ 8.2 Hz, H-1), 7.21 (1H, br t, $J_{1,2}=J_{2,3}=8.2$ Hz, H-2), 7.10 (1H, t, $J_{2,3}=J_{3,4}=8.2$ Hz, H-3), 7.02 (1H, br d, $J_{3,4}$ 8.2 Hz, H-4), 5.57 (1H, dd, $J_{5,6A}$ 6.9, $J_{5,6B}$ 11.7 Hz, H-5), 5.16 (1H, d, $J_{7a,8}$ 2.1 Hz, H-8), 4.62 (1H, br s, H-9), 4.34 (1H, dd, $J_{6a,6A}$ 1.4, $J_{6a,6B}$ 11.9 Hz, H-6a), 3.73 (1H, br s, H-7a), 3.23 (1H, m, H-5′A), 3.06 (1H, m, H-5′B), 2.50 (2H, m, H-3′), 2.49 (1H, br d, $J_{10A,10B}$ 13.1 Hz, H-10A), 2.42 (1H, ddd, $J_{6a,6A}$ 1.4, $J_{5,6A}$ 6.9, $J_{6A,6B}$ 13.4 Hz, H-6A), 2.12 (3H, s, OAc), 2.11 (3H, s, OAc), 2.03 (1H, m, H-6B), 2.00 (2H, m, H-4′), 1.78 (1H, d, $J_{10A,10B}$ 13.1 Hz, H-10B), 1.62 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.8 ($C_{2'}$), 171.7 and 170.0 (OCOMe×2), 169.5 (C_{11}), 138.0 (C_{12a}), 127.5 (C_2), 127.5 (C_4), 126.3 (C_{4a}), 125.6 (C_3), 125.1 (C_1), 105.7 (C_7), 80.0 (C_9), 77.6 (C_8), 57.7 (C_{6a}), 48.0 (C_5), 46.4 (C_{7a}), 42.7 (C_{10}), 42.3 ($C_{5'}$), 41.2 (C_{10a}), 31.2 ($C_{3'}$), 27.4 (C_6), 25.9 (*Me*), 22.1 and 20.9 (OCO*Me*×2), 18.0 ($C_{4'}$). Anal. Calcd for $C_{25}H_{28}N_2O_7$: C, 64.09; H, 6.02; N, 5.98. Found: C, 63.87; H, 5.86; N, 6.11.

3.10.11. (5R,6aR*,7S*,7aS*,8S*,9R*,10S*,10aR*)-10-Methyl-11-oxo-5-(2-oxopyrrolidin-1-yl)-6,6a,7a,8,9,10,10a,11-octahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-7,8(5H)-diyl diacetate (**21d**).* Colourless plates; yield 0.55 g (79%); mp 233–234 °C (decomp.); IR (KBr): 1692, 1665 (NC=O), 1732 (OC=O) cm^{-1}; HRMS (DART) *m/z* (rel intensity): 469.200(3) $[M+H]^+$ (100) (exact mass for $C_{25}H_{29}N_2O_7$ 469.1975), 470.20 (27), 471.20 (5); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.02 (1H, d, $J_{1,2}$ 8.2 Hz, H-1), 7.23 (1H, dd, $J_{2,3}$ 7.6, $J_{1,2}$ 8.2 Hz, H-2), 7.11 (1H, t, $J_{2,3}=J_{3,4}=7.6$ Hz, H-3), 7.03 (1H, br d, $J_{3,4}$ 7.6 Hz, H-4), 5.59 (1H, dd, $J_{5,6A}$ 7.6, $J_{5,6B}$ 11.7 Hz, H-5), 5.08 (1H, d, $J_{7a,8}$ 2.1 Hz, H-8), 4.35 (1H, br s, H-9), 4.29 (1H, dd, $J_{6a,6A}$ 1.2, $J_{6a,6B}$ 11.5 Hz, H-6a), 3.98 (1H, dd, $J_{7a,8}$ 1.9, $J_{7a,10a}$ 4.9 Hz, H-7a), 3.21 (1H, m, H-5′A), 3.01 (1H, m, H-5′B), 2.70 (1H, t, $J_{7a,10a}=J_{10,10a}=4.9$ Hz, H-10a), 2.47 (1H, m, H-6A), 2.45 (2H, m, H-3′), 2.12 (3H, s, OAc), 2.11 (3H, s, OAc), 2.03 (1H, m, H-6B), 2.02 (1H, m, H-10), 1.99 (2H, m, H-4′), 1.23 (3H, d, $J_{10,Me}$ 6.9 Hz, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.7 ($C_{2'}$), 170.0 and 169.4 (OCOMe×2), 167.9 (C_{11}), 138.1 (C_{12a}), 127.5 (C_2), 127.5 (C_4), 126.2 (C_{4a}), 125.6 (C_3), 124.8 (C_1), 105.2 (C_7), 83.5 (C_9), 76.0 (C_8), 58.7 (C_{6a}), 48.2 (C_5), 45.4 (C_{10a}), 42.8 (C_{10}), 42.2 ($C_{5'}$), 40.9 (C_{7a}), 31.1 ($C_{3'}$), 28.0 (C_6), 21.9 and 20.8 (OCO*Me*×2), 18.4 (*Me*), 18.0 ($C_{4'}$). Anal. Calcd for $C_{25}H_{28}N_2O_7$: C, 64.09; H, 6.02; N, 5.98. Found: C, 64.22; H, 6.15; N, 5.73.

3.10.12. (5R,6aR*,7S*,7aS*,8S*,9R*,10R*,10aR*)-11-Oxo-5-(2-oxopyrrolidin-1-yl)-10-phenyl-6,6a,7a,8,9,10,10a,11-octahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-7,8(5H)-diyl diacetate (**21e**).* Colourless needles; yield 0.47 g (59%); mp 251–252 °C (decomp.); IR (KBr): 1688, 1664 (NC=O), 1750 (OC=O) cm^{-1}; HRMS (DART) *m/z* (rel intensity): 531.215(7) $[M+H]^+$ (100) (exact mass for $C_{30}H_{31}N_2O_7$ 531.2131), 532.22 (33), 533.22 (6), 534.22 (1); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.06 (1H, dd, $J_{1,3}$ 1.0, $J_{1,2}$ 8.5 Hz, H-1), 7.50 (2H, d, $J_{2'',3''}$ 7.5 Hz, H-2″(H-6″)), 7.33 (2H, t, $J_{2'',3''}=J_{4'',3''}=7.5$ Hz, H-3″(H-5″)), 7.24 (m, 2H, H-2 and H-4″), 7.12 (1H, t, $J_{2,3}=J_{3,4}=7.5$ Hz, H-3), 7.04 (1H, d, $J_{3,4}$ 7.5 Hz, H-4), 5.62 (1H, dd, $J_{5,6A}$ 7.5, $J_{5,6B}$ 11.8 Hz, H-5), 5.09 (1H, d, $J_{7a,8}$ 1.9 Hz, H-8), 5.03 (1H, br s, H-9), 4.37 (1H, dd, $J_{6a,6A}$ 1.2, $J_{6a,6B}$ 11.7 Hz, H-6a), 4.08 (1H, dd, $J_{7a,8}$ 1.9, $J_{7a,10a}$ 3.7 Hz, H-7a), 3.21 (3H, m, H-5′A, H-10 and H-10a), 3.05 (1H, m, H-5′B), 2.48 (1H, m, H-6A), 2.48 (2H, m, H-3′), 2.13 (1H, m, H-6B), 2.12 (3H, s, OAc), 2.12 (3H, s, OAc), 1.99 (2H, m, H-4′); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.8 ($C_{2'}$), 170.2 and 169.6 (OCOMe×2), 168.1 (C_{11}), 139.5 ($C_{1''}$), 137.9 (C_{12a}), 128.9 ($C_{3''}$($C_{5''}$)), 127.6 (C_2), 127.6 ($C_{4''}$), 127.2 (C_4), 126.8 ($C_{2''}$($C_{6''}$)), 126.3 (C_{4a}), 125.8 (C_3), 124.9 (C_1), 105.8 (C_7), 81.6 (C_9), 77.2 (C_8), 58.7 (C_{6a}), 51.0 (C_{10}), 48.2 (C_5), 45.6 (C_{10a}), 42.4 ($C_{5'}$), 40.8 (C_{7a}), 31.2 ($C_{3'}$), 27.9 (C_6), 22.0 and 20.9 (OCO*Me*×2), 18.0 ($C_{4'}$). Anal. Calcd for $C_{30}H_{30}N_2O_7$: C, 67.91; H, 5.70; N, 5.28. Found: C, 67.31; H, 5.58; N, 5.39.

3.10.13. (5R,6aR*,7S*,7aS*,8S*,9R*,10aR*)-5-[Acetyl(methyl)amino]-11-oxo-6,6a,7a,8,9,10,10a,11-octahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-7,8(5H)-diyl diacetate (**21f**).* Colourless plates; yield 0.39 g (59%); mp 221–222 °C (decomp.); IR (KBr): 1650 (NC=O), 1734 (OC=O) cm^{-1}; EIMS (70 eV) *m/z* (rel intensity): 401 $[M-41]^+$ (2), 382 (43), 367 (71), 339 (16), 297 (16), 281 (34), 267 (21), 250 (22), 222 (32), 187 (37), 168 (21), 159 (18), 130 (49), 101 (13), 76 (24), 56 (100), 43 (59); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.76 (1H, dd, $J_{1,3}$ 1.2, $J_{1,2}$ 8.2 Hz, H-1), 7.15 (2H, m, H-2 and H-3), 6.98 (1H, br d, $J_{3,4}$ 7.6 Hz, H-4), 5.93 (1H, dd, $J_{5,6A}$ 7.8, $J_{5,6B}$ 10.8 Hz, H-5), 4.93 (1H, d, $J_{7a,8}$ 1.8 Hz, H-8), 4.57 (1H, br s, H-9), 4.24 (1H, dd, $J_{6a,6A}$ 1.1, $J_{6a,6B}$ 11.9 Hz, H-6a), 3.81 (1H, dd, $J_{7a,8}$ 1.8, $J_{7a,10a}$ 4.5 Hz, H-7a), 3.20 (1H, m, H-10a), 2.51 (3H, s, NMe), 2.31 (1H, ddd, $J_{6a,6A}$ 1.1, $J_{5,6A}$ 7.8, $J_{6A,6B}$ 13.1 Hz, H-6A), 2.22 (1H, m, H-10A), 2.06 (3H, s, OAc), 2.04 (3H, s, OAc), 1.99 (3H, s, NAc), 1.92 (1H, m, H-6B), 1.51 (1H, dd, $J_{10B,10a}$ 4.0, $J_{10A,10B}$ 13.5 Hz, H-10B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.8 (NCOMe), 170.1 and 169.6 (OCOMe×2), 168.3 (C_{11}), 138.4 (C_{12a}), 127.8 (C_2), 127.5 (C_4), 126.9 (C_{4a}), 125.8 (C_3), 124.9 (C_1), 106.0 (C_7), 79.7 (C_9), 77.6 (C_8), 58.6 (C_{6a}), 50.3 (C_5), 40.5 (C_{7a}), 36.7 (C_{10a}), 33.9 (C_{10}), 31.2 (NMe), 27.6 (C_6), 22.1 and 22.1 (OCO*Me*×2), 21.0 (NCO*Me*). Anal. Calcd for $C_{23}H_{26}N_2O_7$: C, 62.43; H, 5.92; N, 6.33. Found: C, 62.46; H, 5.81; N, 6.12.

3.10.14. (5R,6aR*,7S*,7aS*,8S*,9R*,10R*,10aS*)-7,8-Bis(acetyloxy)-11-oxo-5-(2-oxopyrrolidin-1-yl)-5,6,6a,7,7a,8,9,10,10a,11-decahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-10-carboxylate (**21g**).* Colourless needles; yield 0.23 g (30%); mp 187–189 °C (decomp.); IR (KBr): 1673 (NC=O), 1744 (OC=O) cm^{-1}; EIMS (70 eV) *m/z* (rel intensity): M^+ 512 (3), 452 (100), 397 (38), 363 (32), 308 (31), 280 (55), 265 (28), 248 (22), 213 (47), 196 (25), 130 (86), 43 (62); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.87 (1H, dd, $J_{1,3}$ 1.2, $J_{1,2}$ 8.4 Hz, H-1), 7.18 (1H, ddd, $J_{2,4}$ 2.0, $J_{2,3}$ 6.9, $J_{1,2}$ 8.4 Hz, H-2), 7.06 (1H, ddd, $J_{1,3}$ 1.2, $J_{2,3}$ 6.9, $J_{3,4}$ 7.9 Hz, H-3), 7.02 (1H, dd, $J_{2,4}$ 2.0, $J_{3,4}$ 7.9 Hz, H-4), 5.56 (1H, dd, $J_{5,6A}$ 8.2, $J_{5,6B}$ 11.3 Hz, H-5), 4.93 (1H, d, $J_{7a,8}$ 1.9 Hz, H-8), 4.76 (1H, br s, H-9), 4.22 (1H, dd, $J_{6a,6A}$ 1.7, $J_{6a,6B}$ 12.0 Hz, H-6a), 4.05 (1H, dd, $J_{7a,8}$ 1.9, $J_{7a,10a}$ 4.7 Hz, H-7a), 3.59 (3H, s, OMe), 3.33 (1H, m, H-5′A), 3.23 (1H, dd, $J_{9,10}$ 1.3, $J_{10,10a}$ 11.3 Hz, H-10), 3.18 (1H, dd, $J_{7a,10a}$ 4.7, $J_{10,10a}$ 11.3 Hz, H-10a), 3.00 (1H, m, H-5′B), 2.54 (1H, ddd, $J_{6a,6A}$ 1.7, $J_{5,6A}$ 8.2, $J_{6A,6B}$ 13.3 Hz, H-6A), 2.43 (2H, m, H-3′), 2.07 (3H, s, OAc), 2.05 (3H, s, OAc), 2.02 (1H, ddd, $J_{5,6B}$ 11.3, $J_{6a,6B}$ 12.0, $J_{6A,6B}$ 13.3 Hz, H-6B), 1.94 (2H, m, H-4′); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.5 ($C_{2'}$), 169.1 and 169.7 (OCOMe×2), 168.3 (CO_2Me), 165.0 (C_{11}), 137.9 (C_{12a}), 127.6 (C_4), 127.3 (C_2), 126.4 (C_{4a}), 125.5 (C_3), 125.1 (C_1), 106.2 (C_7), 81.4 (C_9), 76.3 (C_8), 58.5 (C_{6a}), 52.1 (CO_2*Me*), 47.6 (C_5), 46.4 (C_{10}), 42.0 ($C_{5'}$), 41.3 (C_{7a}), 39.3 (C_{10a}), 31.1 ($C_{3'}$), 25.2 (C_6), 20.6 and 21.7 (OCO*Me*×2), 17.8 ($C_{4'}$). Anal. Calcd for $C_{26}H_{28}N_2O_9$: C, 60.93; H, 5.51; N, 5.47. Found: C, 61.15; H, 5.80; N, 5.31.

3.10.15. Methyl (5R,6aR*,7S*,7aS*,8S*,9R*,10R*,10aS*)-7,8-diacetoxy-9-methyl-11-oxo-5-(2-oxopyrrolidin-1-yl)-5,6,6a,7,7a,8,9,10,10a,11-decahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-10-carboxylate (**21h**).* Colourless needles; yield 0.23 g (66%); mp 211–213 °C (decomp.); IR (KBr): 1674 (NC=O), 1746 (OC=O) cm^{-1}; EIMS (70 eV) *m/z* (rel intensity): $[M^+-31]$ 495 (3), 466 (100), 423 (19), 411 (26), 395 (17), 378 (27), 347 (46), 322 (26), 294 (56), 263 (17), 236 (16), 213 (27), 130 (26), 59 (22), 43 (53); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.88 (1H, dd, $J_{1,3}$ 1.3, $J_{1,2}$ 8.4 Hz, H-1), 7.22 (1H, ddd, $J_{2,4}$ 1.4, $J_{2,3}$ 7.7, $J_{1,2}$ 8.4 Hz, H-2), 7.11 (1H, dt, $J_{1,3}$ 1.3, $J_{2,3}=J_{3,4}=7.7$ Hz, H-3), 7.08 (1H, dd, $J_{2,4}$ 1.4, $J_{3,4}$ 7.7 Hz, H-4), 5.60 (1H, dd, $J_{5,6A}$ 8.2, $J_{5,6B}$ 11.6 Hz, H-5), 5.02 (1H, d, $J_{7a,8}$ 1.8 Hz, H-8), 4.24 (1H, dd, $J_{6a,6A}$ 1.6, $J_{6a,6B}$ 12.6 Hz, H-6a), 4.05 (1H, dd, $J_{7a,8}$ 1.8, $J_{7a,10a}$ 4.9 Hz, H-7a), 3.64 (3H, s, OMe), 3.43 (1H, dd, $J_{7a,10a}$ 4.9, $J_{10,10a}$ 11.3 Hz, H-10a), 3.15 (1H, d, $J_{10,10a}$ 11.3 Hz, H-10), 3.07 (1H, m,

H-5′A), 3.03 (1H, m, H-5′B), 2.74 (1H, ddd, $J_{6a,6A}$ 1.6, $J_{5,6A}$ 8.2, $J_{6A,6B}$ 13.2 Hz, H-6A), 2.48 (2H, m, H-3′), 2.31 (1H, ddd, $J_{5,6B}$ 11.6, $J_{6a,6B}$ 12.6, $J_{6A,6B}$ 13.2 Hz, H-6B), 2.14 (3H, s, OAc), 2.10 (3H, s, OAc), 2.00 (2H, m, H-4′), 1.40 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.7 ($C_{2'}$), 169.5 and 169.7 (OCOMe×2), 168.4 (CO_2Me), 165.9 (C_{11}), 138.0 (C_{12a}), 127.9 (C_4), 127.5 (C_2), 126.8 (C_{4a}), 125.7 (C_3), 125.3 (C_1), 106.6 (C_7), 88.4 (C_9), 77.3 (C_8), 58.7 (C_{6a}), 52.1 (CO_2*Me*), 50.6 (C_5), 47.9 (C_{10}), 42.2 ($C_{5'}$), 42.2 (C_{7a}), 40.0 (C_{10a}), 31.4 ($C_{3'}$), 25.1 (C_6), 20.8 and 22.1 (OCO*Me*×2), 18.0 ($C_{4'}$), 14.4 (*Me*). Anal. Calcd for $C_{27}H_{30}N_2O_9$: C, 61.59; H, 5.74; N, 5.32. Found: C, 61.51; H, 5.81; N, 5.21.

3.10.16. Methyl (5R,6aR*,7S*,7aS*,8S*,9R*,10R*,10aS*)-7,8-diacetoxy-10-methyl-11-oxo-5-(2-oxopyrrolidin-1-yl)-5,6,6a,7,7a,8,9,10,10a,11-decahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-10-carboxylate (**21i**).* White powder; yield 0.26 g (34%); mp 276 °C (decomp.); IR (KBr): 1673 (NC=O), 1751 (OC=O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+526 (9), 466 (100), 411 (26), 395 (16), 377 (17), 322 (18), 294 (19), 262 (11), 234 (16), 213 (21), 195 (12), 130 (64), 86 (9), 43 (63); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (1H, dd, $J_{1,3}$ 1.0, $J_{1,2}$ 8.2 Hz, H-1), 7.26 (1H, ddd, $J_{2,4}$ 1.0, $J_{2,3}$ 7.0, $J_{1,2}$ 8.2 Hz, H-2), 7.13 (1H, ddd, $J_{1,3}$ 1.0, $J_{2,3}$ 7.0, $J_{3,4}$ 7.8 Hz, H-3), 7.08 (1H, dd, $J_{2,4}$ 1.0, $J_{3,4}$ 7.8 Hz, H-4), 5.62 (1H, br d, $J_{5,6A}$=$J_{5,6B}$=9.5 Hz, H-5), 5.23 (1H, br s, H-8), 4.67 (1H, br s, H-9), 4.24 (1H, dd, $J_{6a,6A}$ 1.1, $J_{6a,6B}$ 11.9 Hz, H-6a), 4.05 (1H, br d, $J_{7a,10a}$ 2.0 Hz, H-7a), 3.69 (3H, s, OMe), 3.34 (1H, m, H-5′A), 3.05 (1H, d, $J_{7a,10a}$ 2.0 Hz, H-10a), 3.03 (1H, m, H-5′B), 2.51 (2H, m, H-3′), 2.74 (1H, ddd, $J_{6a,6A}$ 1.1, $J_{5,6A}$ 9.5, $J_{6A,6B}$ 13.5 Hz, H-6A), 2.15 (1H, ddd, $J_{5,6B}$ 9.5, $J_{6a,6B}$ 11.9, $J_{6A,6B}$ 13.5 Hz, H-6B), 2.14 (3H, s, OAc), 2.11 (3H, s, OAc), 2.00 (2H, m, H-4′), 1.58 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.6 ($C_{2'}$), 171.4 and 170.0 (OCOMe×2), 169.3 (CO_2Me), 165.1 (C_{11}), 138.5 (C_{12a}), 127.8 (C_4), 127.5 (C_2), 126.4 (C_{4a}), 125.6 (C_3), 125.4 (C_1), 105.6 (C_7), 86.0 (C_9), 74.5 (C_8), 59.0 (C_{6a}), 54.3 (C_{10}), 52.3 (CO_2*Me*), 48.7 (C_{10a}), 47.9 (C_5), 42.3 ($C_{5'}$), 42.0 (C_{7a}), 31.4 ($C_{3'}$), 25.6 (C_6), 24.5 (*Me*), 22.0 and 20.9 (OCO*Me*×2), 18.2 ($C_{4'}$). Anal. Calcd for $C_{27}H_{30}N_2O_9$: C, 61.59; H, 5.74; N, 5.32. Found: C, 61.72; H, 5.67; N, 5.44.

3.10.17. Methyl (5R,6aR*,7S*,7aS*,8S*,9R*,10R*,10aS*)-7,8-diacetoxy-5-[acetyl(methyl)amino]-11-oxo-5,6,6a,7,7a,8,9,10,10a,11-decahydro-7,9-epoxycyclopenta[4,5]pyrido[1,2-a]quinoline-10-carboxylate (**21j**).* White powder; yield 0.58 g (77%); mp 213–215 °C (decomp.); IR (KBr): 1662 (NC=O), 1745 (OC=O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+500 (2), 459 (7), 441 (55), 425 (100), 398 (32), 367 (14), 339 (36), 280 (18), 159 (11), 130 (31), 69 (14), 56 (58), 43 (26); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91 (1H, dd, $J_{1,3}$ 0.9, $J_{1,2}$ 8.4 Hz, H-1), 7.23 (1H, ddd, $J_{2,4}$ 0.9, $J_{2,3}$ 7.7, $J_{1,2}$ 8.4 Hz, H-2), 7.10 (1H, dt, $J_{1,3}$ 0.9, $J_{2,3}$=$J_{3,4}$=7.7 Hz, H-3), 7.09 (1H, dd, $J_{2,4}$ 0.9, $J_{3,4}$ 7.7 Hz, H-4), 6.14 (1H, dd, $J_{5,6A}$ 8.3, $J_{5,6B}$ 11.0 Hz, H-5), 4.98 (1H, d, $J_{7a,8}$ 1.8 Hz, H-8), 4.82 (1H, br s, H-9), 4.27 (1H, dd, $J_{6a,6A}$ 1.6, $J_{6a,6B}$ 12.1 Hz, H-6a), 4.10 (1H, dd, $J_{7a,8}$ 1.8, $J_{7a,10a}$ 4.8 Hz, H-7a), 3.41 (1H, dd, $J_{7a,10a}$ 4.8, $J_{10,10a}$ 11.3 Hz, H-10a), 3.28 (1H, dd, $J_{9,10}$ 0.8, $J_{10,10a}$ 11.3 Hz, H-10), 2.76 (3H, s, NMe), 2.53 (1H, ddd, $J_{6a,6A}$ 1.6, $J_{5,6A}$ 8.3, $J_{6A,6B}$ 13.4 Hz, H-6A), 2.35 (1H, ddd, $J_{5,6A}$ 11.0, $J_{6a,6A}$ 12.1, $J_{6A,6B}$ 13.4 Hz, H-6B), 2.19 (3H, s, OAc), 2.13 (3H, s, OAc), 2.11 (3H, s, NAc), 1.51 (1H, dd, $J_{10B,10a}$ 4.0, $J_{10A,10B}$ 13.5 Hz, H-10B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.2 (NCOMe), 166.9 and 167.4 (OCOMe×2), 166.1 (CO_2Me), 162.8 (C_{11}), 136.0 (C_{12a}), 125.5 (C_4), 124.9 (C_{4a}), 124.8 (C_2), 123.2 (C_3), 122.8 (C_1), 104.0 (C_7), 79.2 (C_8), 74.0 (C_9), 56.3 (CO_2*Me*), 49.7 (C_{6a}), 47.4 (C_5), 44.1 (C_{10}), 39.0 (C_{7a}), 37.0 (C_{10a}), 28.7 (N*Me*), 22.7 (C_6), 19.6 and 19.5 (OCO*Me*×2), 18.3 (NCO*Me*). Anal. Calcd for $C_{25}H_{28}N_2O_9$: C, 59.99; H, 5.64; N, 5.60. Found: C, 60.13; H, 5.82; N, 5.87.

3.10.18. Methyl (7R,8aR*,9S*,9aS*,10S*,11R*,12R*,12aS*)-9,10-diacetoxy-13-oxo-7-(2-oxopyrrolidin-1-yl)-7,8,8a,9,9a,10,11,12,12a,13-decahydro-9,11-epoxybenzo[h]cyclopenta[4,5]pyrido[1,2-a]quinoline-12-carboxylate (**24a**).* White powder; yield 0.78 g (93%); mp 177–179 °C; IR (KBr): 1672 (NC=O), 1738 (OC=O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+ 562 (5), 502 (27), 349 (33), 246 (23), 181 (24), 180 (100), 127 (12), 85 (34), 60 (55), 45 (45); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75 (1H, dd, $J_{1,3}$ 2.2, $J_{1,2}$ 6.6 Hz, H-1), 7.70 (1H, d, $J_{5,6}$ 8.5 Hz, H-5), 7.60 (1H, dd, $J_{2,4}$ 1.7, $J_{3,4}$ 7.6 Hz, H-4), 7.45 (2H, m, H-2 and H-3), 7.14 (1H, d, $J_{5,6}$ Hz, H-6), 5.76 (1H, t, $J_{7,8A}$=$J_{7,8B}$=9.0 Hz, H-7), 5.02 (2H, m, H-10 and H-8a), 4.86 (1H, br s, H-11), 3.90 (3H, s, OMe), 3.58 (2H, m, H-9a and H-12), 3.36 (1H, d, $J_{12,12a}$ 11.5 Hz, H-12a), 3.15 (1H, m, H-5′A), 2.94 (1H, m, H-5′B); 2.52 (1H, m, H-8A), 2.45 (2H, m, H-3′), 2.11 (3H, s, OAc), 2.07 (3H, s, OAc), 1.95 (1H, m, H-8B), 1.88 (2H, m, H-4′); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.6 ($C_{2'}$), 170.2 (CO_2Me), 168.9 and 168.0 (OCOMe×2), 165.8 (C_{11}), 136.9 (C_{14a}), 133.3 (C_{4a}), 128.6 (C_4), 128.3 (C_{14b}), 128.0 (C_3), 127.0 (C_{6a}), 126.4 (C_2), 126.0 (C_5), 125.0 (C_1 and C_6), 105.4 (C_9), 80.7 (C_{11}), 76.2 (C_{10}), 58.4 (C_{8a}), 52.5 (CO_2*Me*), 48.1 (C_7), 46.8 (C_{12}), 44.0 (C_{9a}), 42.5 ($C_{5'}$), 41.1 (C_{12a}), 33.3 ($C_{3'}$), 31.2 (C_8), 22.2 and 20.7 (OCO*Me*×2), 17.9 ($C_{4'}$). Anal. Calcd for $C_{30}H_{30}N_2O_9$: C, 64.05; H, 5.38; N, 4.98. Found: C, 64.27; H, 5.79; N, 5.16.

3.10.19. (7R,8aR*,9S*,9aS*,10S*,11R*,12aR*)-13-Oxo-7-(2-oxopyrrolidin-1-yl)-8,8a,9a,10,11,12,12a,13-octahydro-9,11-epoxybenzo[h]cyclopenta[4,5]pyrido[1,2-a]quinoline-9,10(7H)-diyl diacetate (**24b**).* Colourless plates; yield 0.48 g (64%); mp 278–279 °C (decomp.); IR (KBr): 1677 (NC=O), 1739 (OC=O) cm^{-1}; EIMS (70 eV) *m*/*z* (rel intensity): M^+ 504 (5), 445 (60), 402 (22), 401 (43), 292 (12), 291 (38), 181 (33), 180 (100), 127 (7), 107 (15), 69 (37), 59 (47), 43 (40); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.81 (1H, dd, $J_{1,3}$ 2.5, $J_{1,2}$ 6.2 Hz, H-1), 7.73 (1H, d, $J_{5,6}$ 8.7 Hz, H-5), 7.49 (3H, m, H–Ar), 7.20 (1H, d, $J_{5,6}$ 8.7 Hz, H-6), 5.85 (1H, br t, $J_{7,8A}$=$J_{7,8B}$=9.0 Hz, H-7), 5.02 (1H, dd, $J_{8a,8A}$ 1.9, $J_{8a,8B}$ 12.5 Hz, H-8a), 4.87 (1H, br s, H-10), 4.80 (1H, br s, H-11), 3.44 (1H, br d, $J_{9a,12a}$ 3.7 Hz, H-9a), 3.19 (1H, m, H-12a), 3.11 (1H, m, H-5′A), 2.97 (1H, m, H-5′B), 2.53 (2H, m, H-3′), 2.47 (1H, m, H-8A), 2.26 (1H, ddd, $J_{11,12A}$ 1.5, $J_{12A,12a}$ 4.9, $J_{12A,12B}$ 13.7 Hz, H-12A), 2.14 (3H, s, OAc), 2.12 (1H, m, H-8B), 2.10 (3H, s, OAc), 1.94 (m, 2H, H-4′), 1.90 (1H, br dd, $J_{12a,12B}$ 4.4, $J_{12A,12B}$ 13.7 Hz, H-12B); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.4 ($C_{2'}$), 170.9 and 170.3 (OCOMe×2), 168.2 (C_{11}), 136.5 (C_{14a}), 133.3 (C_{4a}), 128.4 (C_4), 128.3 (C_3), 128.0 (C_{14b}), 127.0 (C_{6a}), 126.5 (C_2 and C_5), 125.1 (C_6), 123.3 (C_1), 104.9 (C_9), 80.1 (C_{11}), 78.0 (C_{10}), 59.5 (C_{8a}), 48.2 (C_7), 43.4 (C_{9a}), 42.4 ($C_{5'}$), 37.5 (C_{12a}), 34.3 (C_{12}), 33.0 ($C_{3'}$), 31.2 (C_8), 22.1 and 20.8 (OCO*Me*×2), 17.9 ($C_{4'}$). Anal. Calcd for $C_{28}H_{28}N_2O_7$: C, 66.66; H, 5.59; N, 5.55. Found: C, 66.39; H, 5.81; N, 5.31.

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