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Synthesis and reactivity of hexahydropyrroloquinolines

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Abstract—Formal [4+2] cycloaddition of cyclic enamides with imines derived from aromatic amines gave the 4-arylhexahydropyrroloquinoline skeleton in one step as mixtures of diastereoisomers. Aromatic imines derived from formaldehyde and methylglyoxalate also participated in this chemistry, with the latter favouring formation of the *endo*-cycloadduct. The cycloadducts derived from methylglyoxalate were unstable and fragmented to give highly substituted quinolines under both neutral and basic conditions. Imines derived from 3-cyanoacrolein also underwent cycloaddition and gave an advanced potential precursor to martinellic acid, albeit with poor diastereoselectivity.

1. Introduction

Pyrroloquinolines, Fig. 1, form the central core of a number of biologically significant molecules. Antineoplastic agent **1**,[1] gastric (H^+/K^+) ATPase inhibitor **2**[2,3] and natural product, non-peptide Bradykinin inhibitor, martinellic acid **3**[4] all contain pyrroloquinolines in various oxidation states. Synthetic interest in martinellic acid has recently stimulated many new approaches to hexahydropyrroloquinolines.[5,6] Inter[7] and intramolecular[8–10] 1,3-dipolar cycloaddition of azomethine ylides, radical cyclisation[11,12] and transition metal catalysed cyclisation[13] have all been employed to give access to potential martinellic acid precursors. Despite this activity, to date no synthesis of martinellic acid has been accomplished. Hexahydropyrroloquinolines may be considered to be a sub-grouping of tetrahydroquinolines and a review on the synthesis of the latter class of compounds has recently been published.[14]

In recent studies directed towards the synthesis of martinellic acid, we[15] and others[16] reported a simple synthesis of hexahydropyrroloquinolines based on an imino Diels–Alder reaction. Imines derived from aromatic amines behaved as the diene and cyclic enamides as the dienophile component. The advantage of this approach was that all three chiral centres present in the hexahydropyrroloquinoline core were generated in one synthetic operation. There was therefore potential to control both the relative and absolute stereochemical outcome of this reaction by judicial choice of catalyst. The symmetry of the *para*-susbstituted aniline ensured the trisubstituted aromatic product was obtained with the correct regiochemistry. We now report full details on this chemistry and subsequent reactions of the hexahydropyrroloquinolines.

2. Results and discussion

Scheme 1 outlines the approach that was adopted. The cyclic enamides **5** and **26** were readily available from the

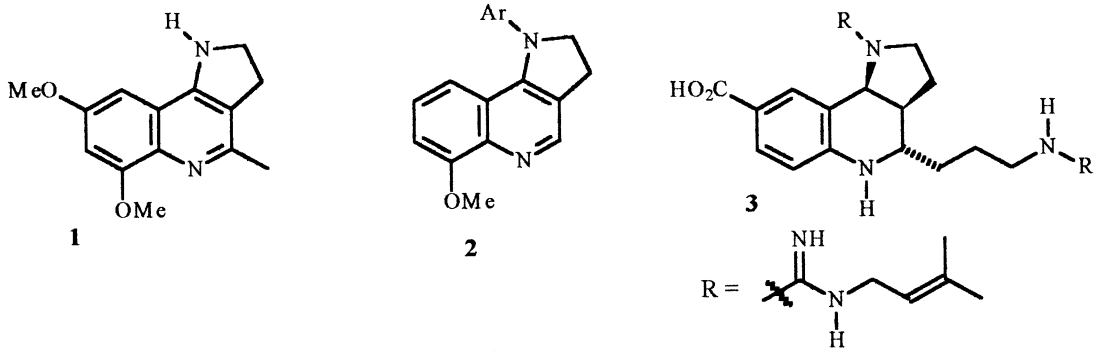

Figure 1.

Keywords: martinellic acid; martinelline; imino Diels–Alder reaction; cyclic enamide; indium trichloride.
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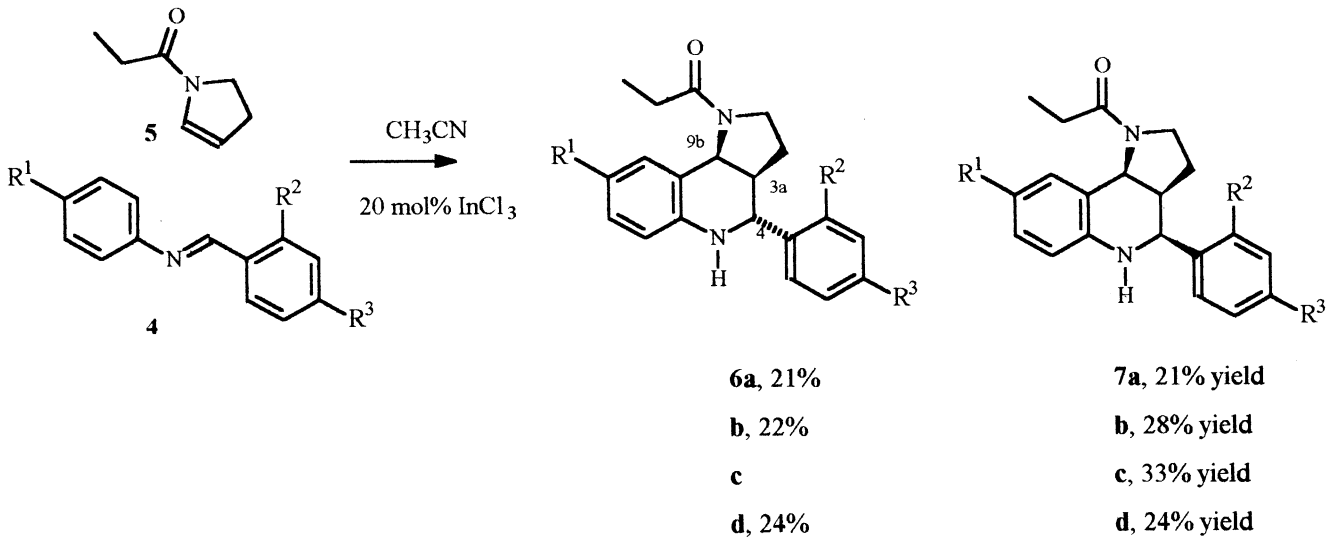


Scheme 1.

trimer of 3,4-dihydro-2-*H*-pyrrole,[17] but yields for this procedure were variable and generally low. The most reliable method for making these compounds was by dehydration of the corresponding amido hemiacetal using standard literature procedures.[18–20] Of these, it was found that the method of Correia was the most efficient. Reaction of cyclic enamide **5** with imines **4a**–**d** proceeded smoothly at room temperature in acetonitrile as solvent in the presence of 20 mol% indium trichloride and gave *exo*, *endo* cycloadducts **6** and **7**, respectively as mixtures of stereoisomers (Table 1, entries 1–4). The IUPAC numbering for pyrroloquinolines begins on the amide nitrogen and goes clockwise around the ring. For clarity positions 3a 4 and 9b are depicted on *exo*-isomer **6**, Scheme 1.

The reaction was completely regioselective giving only the isomers depicted in Scheme 1. In all cases investigated, the desired *exo*-selectivity was poor, but fortuitously these diastereoisomers were easily separated by flash chromatography. Although we could not find conditions to effect a purely thermal reaction with imines derived from aromatic aldehydes, other reagents such as scandium triflate and trifluoromethanesulphonic acid also catalysed this reaction. In our hands scandium triflate lost its catalytic activity on standing after the bottle was opened. The trifluoromethanesulphonic acid catalysed reaction, using one drop of acid per mmol of substrate, was as efficient as the indium catalysed reaction, both in terms of yield and diastereoselectivity. However, this procedure was always accompanied by some hydrolysis of the imine making it less than ideal. Protic acids have long been known to catalyse similar cycloaddition reactions.[21] Due to the reliability and reproducibility of indium trichloride this became the preferred catalyst for the cycloadditions.

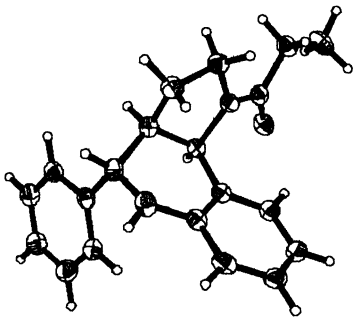
Table 1.

Entry	Product	R^1	R^2	R^3	Ratio **6**:**7**	Yield %
1	a	H	H	H	1:1	41
2	b	OMe	H	H	0.8:1	50
3	c	H	NO_2	H	1:2	33[a]
4	d	MeO_2C	H	H	1:1	48
5	e	H	H	OMe		0

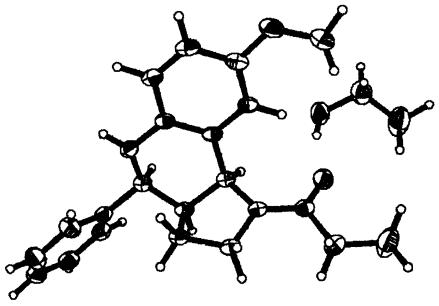
[a] Only the endo isomer **7c** isolated.

The stereochemistry at the ring junction in isomers **6a** and **7a** (Table 1, entry 1) was readily assigned as *cis* due to the axial–equatorial coupling constants J_{H3aH9b} of 6.7 and 6.2 Hz, respectively. This was further confirmed by nOe difference spectroscopy, where saturation of proton H9b gave enhancements of 6.0 and 6.8% onto H3a for the *endo* and *exo* isomers, respectively. Assigning *exo*, *endo* stereochemistry to each of the isomers **6a** and **7a** proved more difficult than initially anticipated, by proton NMR spectroscopy. This was because the *exo* isomers **6** adopted an unexpected conformation where the aryl group and the alkyl group of the pyrrolidine ring were *trans*-diaxial. Equatorial proton H3a, was antiperiplanar to the electronegative secondary aromatic amine and this resulted in a further decrease in the axial–equatorial vicinal coupling constant J_{H3aH4}.[22] As a result of these two effects, the vicinal coupling constants J_{H3aH4} for the *exo* and *endo* isomers **6a** and **7a** were remarkably similar at 2.7 and 2.5 Hz, respectively. Clearly these isomers cannot be distinguished from measurement of vicinal coupling constant J_{H3aH4}. Obtaining nOe difference experiments confirmed the stereochemistry of *endo*-adduct **7a**. Hence, saturation of proton H9b gave an enhancement onto H4 of 2% indicating these two protons were *cis* and also 1,3-diaxial. With the corresponding *exo*-isomer **6a** saturation of proton H9b resulted in an nOe enhancement onto the protons of the pendent aromatic ring of 2.0%. This confirmed the stereochemistry and indicated that both proton H9b and the phenyl group were 1,3-diaxial. This analysis of the stereochemistry and conformation in solution was further confirmed in the solid state by single crystal X-ray analysis of *exo* and *endo*-adducts **6a** and **7b**, respectively (Fig. 2).[†] It is clear from Fig. 2 that in the *exo*-adduct **6a**, two of the substituents are axial and one is

[†] A crystal structure of *endo* adduct **7d** was also recorded and the refined co-ordinates and bond distances have been deposited with the Cambridge Crystallographic Data Centre.



Exo-adduct **6a**



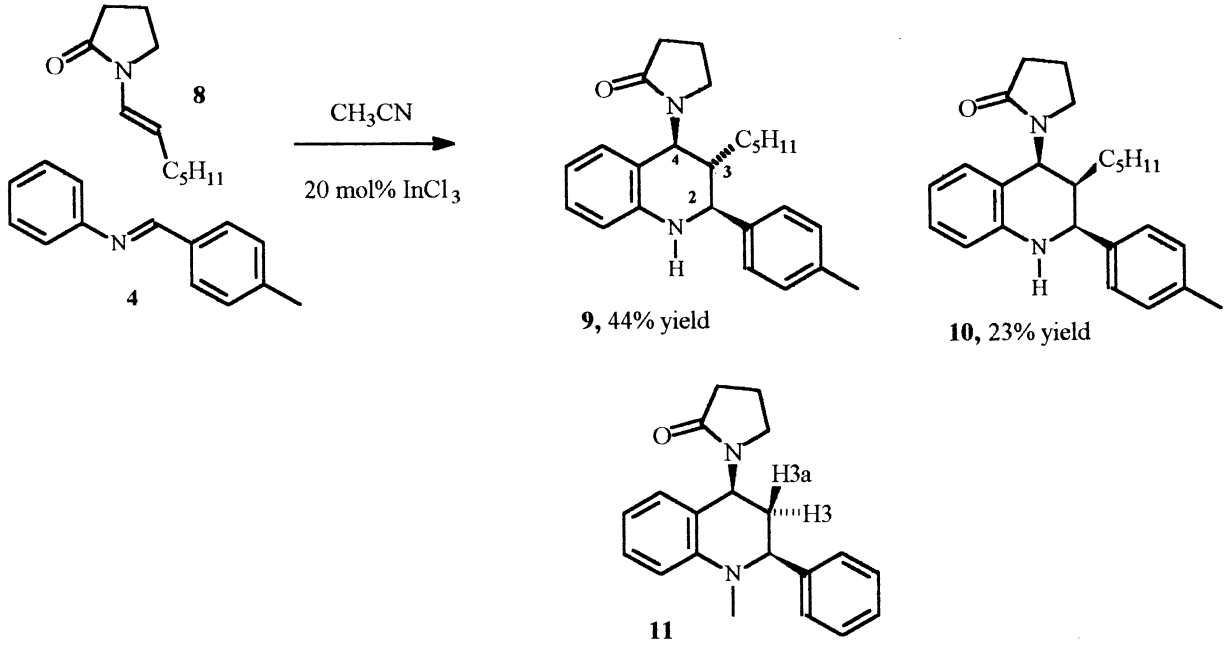
Endo-adduct **7b**

Figure 2. X-ray structures of *exo*, *endo* adducts **6a** and **7b**, respectively.

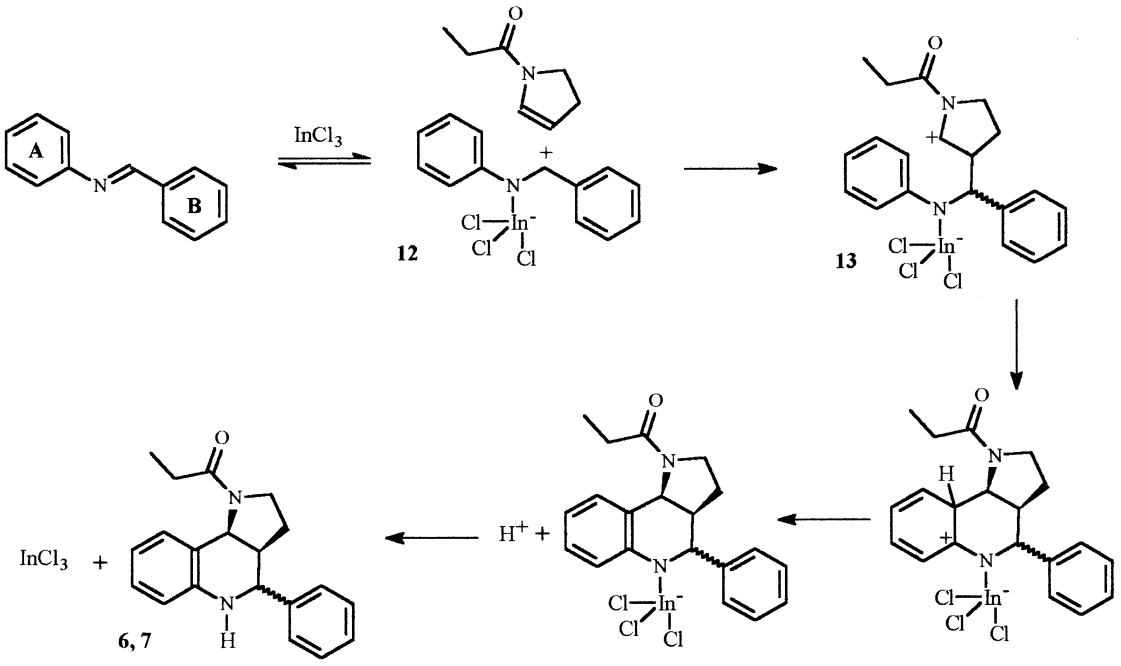
equatorial. Due to the similarity of our NMR data to that reported for martinelline,[4] it is likely that martinelline adopts a conformation similar to *exo*-adduct **6a**. In the crystal structure of the *endo*-adduct **7b** two of the substituents are equatorial and one is axial. This raises the interesting question as to which of the two isomers is thermodynamically more stable. It is noteworthy that when the bulk of the phenyl group was increased by introducing an *o*-nitro substituent (Table 1, entry 3) then the amount of *endo*-adduct substantially increased suggesting that this was the thermodynamically most stable isomer.

In *exo*, *endo* isomers **6a** and **7a** the chemical shift of proton H9b was 5.17 and 5.75 ppm, respectively and the ^{13}C shifts for C3 were 27.6 and 22.7 ppm, respectively. These large differences in chemical shift for proton H9b and carbon C3 in *exo*, *endo* isomers **6** and **7** listed in Table 1 are quite general and could be reliably used to assign the stereochemistry of all subsequent new hexahydropyrroloquinolines that were prepared.

One example of an acyclic enamide was investigated. 2-Pyrrolidinone and heptanal condensed with azeotropic removal of water and gave exclusively the *E*-enamide **8**.[23,24] Reaction of imine **4** with enamide **8** proceeded smoothly at room temperature and gave a mixture of two diastereoisomers, in the ratio 2:1 and 67% combined yield, Scheme 2. The numbering used for tetrahydroquinolines is indicated on structure **9**. The diastereoisomers were separated by flash chromatography and proton NMR analysis confirmed the major product was the *exo*-adduct **9**, with the stereochemistry of the enamide preserved, relative stereochemistry-2*S**3*R**4*S**. In particular, the large pseudo diaxial coupling constants J_{H3H4} and J_{H3H2} of 10.8 and 10.1 Hz, respectively, showed that all three substituents on the saturated ring were pseudo equatorial. Assignment of relative stereochemistry to the minor isomer **10** proved a little more problematic. The coupling constant J_{H3H4} of 7.0 Hz is indicative of an equatorial–axial arrangement of protons H3 and H4 and strongly suggests that the two substituents attached at C3 and C4 are *cis*. Coupling constant J_{H3H2} of 4.0 Hz seemed a little small to be an



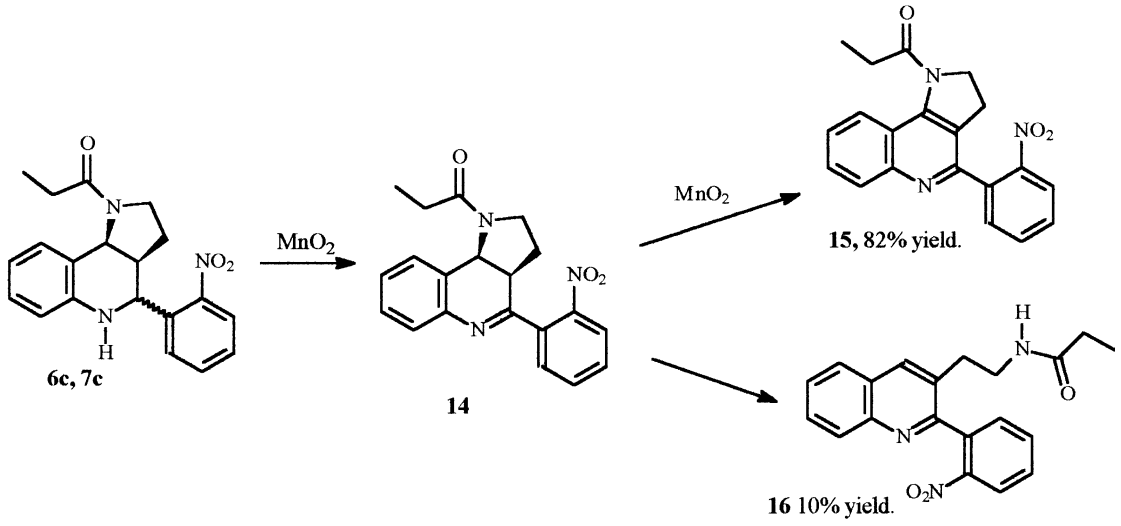
Scheme 2.



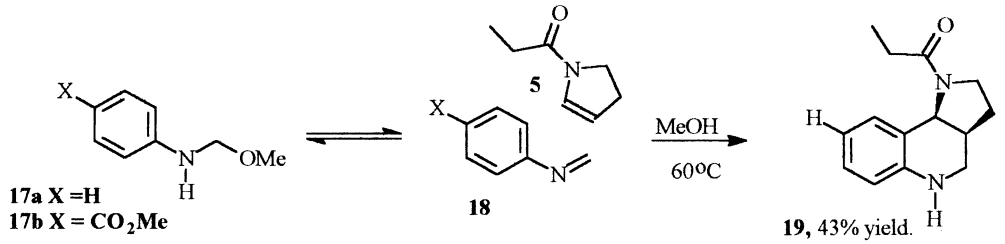
Scheme 3.

axial–equatorial coupling. However, in a closely related system **11**, devoid of the 3-pentyl group, assignment of the relative stereochemistry at C2 and C4 was trivial due to the large pseudo diaxial couplings of J_{H3aH2} 10.5 Hz and J_{H3aH4} 11.4 Hz, respectively.[25] Of particular note was that the axial–equatorial coupling constant J_{H3H2} in compound **11** was 4.2 Hz. This confirms that our value for J_{H3H2} of 4.0 Hz is due to an axial–equatorial coupling and the relative stereochemistry of the minor isomer is therefore 2*S**3*S**4*S**, i.e. *endo* with the stereochemistry of the enamide reversed. This result indicates that adduct **10** was formed by a non-concerted process.

The cycloaddition reaction appears to be general and both electron-donating and electron-withdrawing groups are tolerated on the amine component of the imine (Scheme 3, ring A). However the reaction failed when a strong electron releasing component was present on the aldehyde end of the imine, ring B (Table 1, entry 5). This effect has also been noted in similar imino Diels–Alder reactions using enol ethers as the dienophile.[26] The imino Diels–Alder reactions of aromatic imines with alkenes is well documented,[27–32] and it is generally accepted that this is a stepwise process involving ionic intermediates. In our case, the stepwise mechanism is supported by the formation of adduct **10** in which the stereochemistry of the double bond is not conserved in the cycloadduct. The mechanism for the reaction is depicted in Scheme 3. The first step is co-ordination of the imine to the Lewis acid to give the iminium salt **12**. This then reacts with the electron-rich enamide to give the stabilised *N*-acyl iminium ion **13**, hence controlling the regioselectivity of the addition. Intramolecular cyclisation



Scheme 4.



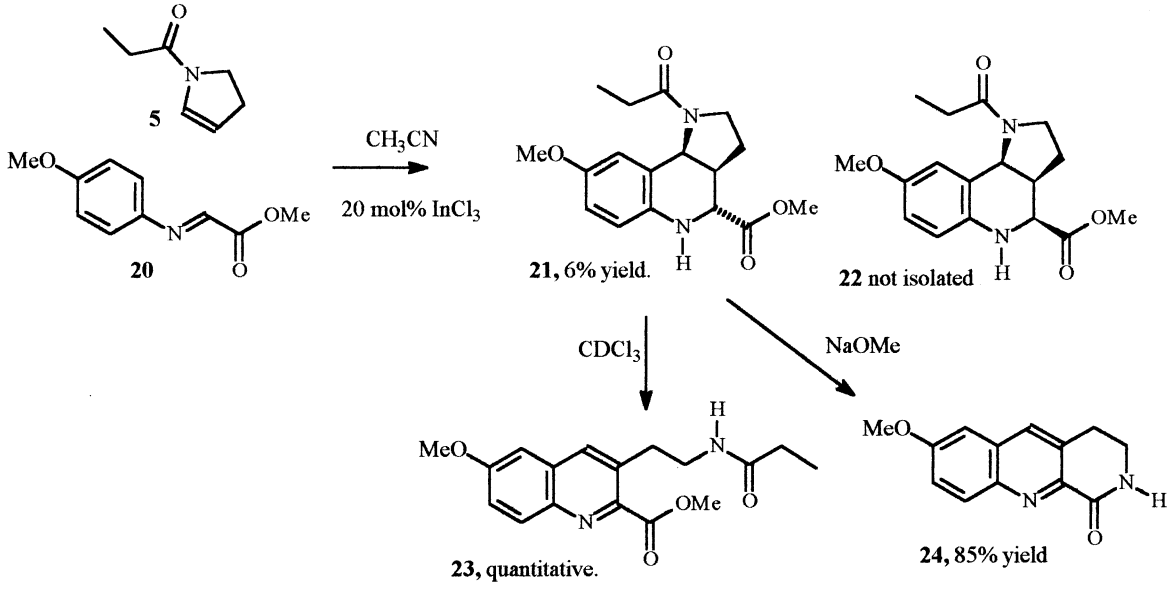
Scheme 5.

followed by proton transfer gave adducts **6** and **7** after release of the indium catalyst. The fact that a strong electron-releasing group on ring B gave no cycloadduct (Table 1, entry 5) whilst electron-withdrawing groups on ring A do not have any detrimental effect, suggests that the first carbon–carbon bond forming reaction, i.e. **12→13** is the slow step in the process.

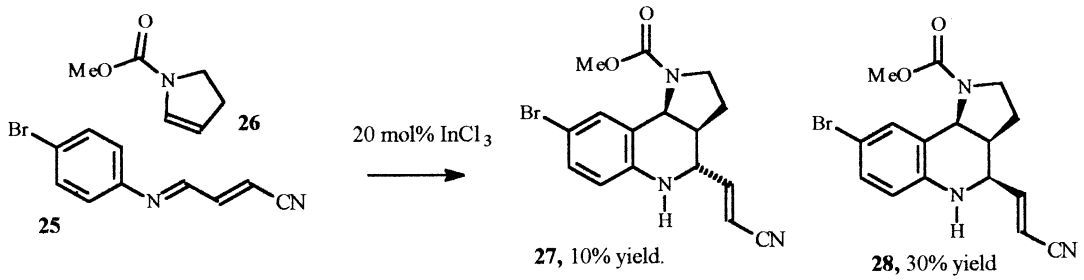
Given the biological importance of dihydropyrroloquinolines, oxidation of the hexahydropyrroloquinolines **6c** and **7c** to dihydropyrroloquinolines was attempted. It has previously been shown that 4-aminodihydroquinolines of the type **14** are unstable and will readily eliminate to give the corresponding quinoline.[33] Therefore, there are two competitive pathways after initial oxidation to **14**, namely further oxidation to **15** or elimination of amide to give **16**, Scheme 4. Using a large excess of battery grade manganese dioxide (50 equiv.) in refluxing benzene for 8 h gave exclusively **15** in 80% yield. This indicated that the second oxidation was indeed faster than the competing elimination. When the reaction was repeated using 25 equiv. of manganese dioxide and stopped after three hours, NMR analysis of the crude reaction mixture revealed 37% starting material, 50% of adduct **15** and 13% of elimination product **16**. These experiments demonstrate that dihydroquinoline **14**, in which the nitrogen functionality at the 4-position is amide, is much more stable than the corresponding amine derivatives.

The cycloaddition failed for imines derived from aliphatic aldehydes, with only intractable materials being produced. However, when methoxymethylphenylamine **17a**, a known precursor of imine **18**,[34] was treated with a two fold excess of cyclic enamide **5** in boiling methanol, the parent C4 unsubstituted hexahydropyrroloquinoline **19** was formed in 43% yield, Scheme 5. Neither Lewis nor protic acid was required to effect this transformation. When an electron withdrawing carbomethoxy group was present at the *p*-position of the imine **16b**, this substrate failed to participate in the cycloaddition, suggesting that this process may be mechanistically different to the Lewis acid catalysed reaction of the aromatic imines.

For martinellic acid synthesis, a phenyl group at the 4-position is not particularly useful functionality. In order to have the potential to chain extend at this position imine **20** derived from methyl glyoxalate was briefly investigated. The cycloaddition of imine **20** was not as clean as the previously investigated phenyl imines and a 2:1 mixture of *endo*, *exo* adducts **22** and **21** was produced as determined by proton NMR spectroscopy, Scheme 6. However, flash chromatography gave only the *endo*-adduct **22** in a miserable 6% isolated yield. This low yield can in part be attributed to imine instability, but it soon became clear that product **22** was also very unstable. On standing in deuterochloroform overnight adduct **22** was quantitatively converted to quinoline **23**. This process requires elimination of amide and an oxidation, presumably by oxygen, though it is not clear in which order these events occur. Synthesis of



Scheme 6.



Scheme 7.

quinolines from 4-ethoxytetrahydroquinoline by loss of ethanol and oxidation by oxygen is well known.[35] The instability of adducts **21** and **22** make them less than ideal to work with.

When cyclic enamides were employed, in all cases in where one of the cycloadducts predominated it was the *endo* isomer. In an attempt to distinguish which isomer **21** or **22** was thermodynamically more stable, an attempt was made to epimerise freshly prepared adduct **22** using sodium methoxide as base. Hexahydropyrroloquinoline **21** proved to be base sensitive and fragmented to give an unusual tricyclic compound **24** in 85% yield. This elimination–oxidation requires a carbomethoxy group at the 4-position to proceed cleanly. The previously prepared 4-phenyl substituted products **6** and **7** decomposed when treated under both acidic and basic conditions.

It was clear from these feasibility studies that products derived from glyoxalate esters were never going to be suitable precursors to martinellic acid. The problem remained as to how to modify this chemistry to put a three carbon side chain at C4. To this end imine **25**, derived from 3-cyanoacrolein,[36] was investigated, Scheme 7. There are a number of possible sites of diene reactivity in substrate **25**. It was therefore gratifying that reaction of imine **25** with carbamate **26** produced the desired chemoselectivity and gave a 1:3 mixture of *exo*, *endo* adducts **27** and **28** in 40% combined yield. Despite the problems with this chemistry, particularly the lack of *exo*-selectivity, it is remarkable that the hexahydropyrroloquinoline skeleton **27**, containing the correct functionality for elaboration to martinellic acid can be assembled in one step from very readily available starting materials.

3. Experimental

3.1. General

Melting points were recorded using a Kofler hot stage apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer Model 983G instrument coupled to a Perkin–Elmer 3700 Data Station as potassium bromide (KBr) disks, or films (liquids). ^{1}H nuclear magnetic resonance (NMR) spectra were recorded at 300 MHz using General Electric QE300, Bruker DPX 300 and at 500 MHz using a Bruker DRX500 NMR spectrometers. Chemical shifts are given in parts per million (δ) down field from tetramethylsilane as internal standard and coupling constants are given in Hertz. A 2 Hz line broadening was used to process the proton NMR spectra. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet and br=broad. Mass spectra were recorded using Double Focusing Triple Sector VG Auto Spec and accurate molecular masses were determined by the peak matching method using perfluorokerosene as standard reference and were accurate to within +/−0.0006 a.m.u. Analytical TLC was carried out on Merck Kielselgel 60_{254} plates and the spots visualised using a Hanovia Chromatolite UV lamp. Flash chromatography was effected using Merck Kielselgel 60 (230–400 mesh).

3.2. General procedure for preparation of imines

All imines were prepared by mixing equimolar portions of aldehyde and amine in dichloromethane over magnesium sulphate or molecular sieves. When the reaction was deemed to be complete by NMR spectroscopy, the drying agent and solvent were removed to provide the imine which was used crude for the next step. Imines derived from ethyl gyloxalate and 3-cyanoacrolein were found to be unstable and could not be stored.

3.3. General procedure for indium trichloride catalysed cycloadditions of imines to enamides

To a stirred solution of the imine (1 mmol) and cyclic enamide (1 mmol) in dry acetonitrile (5 ml) under a nitrogen atmosphere was added indium trichloride (0.2 mmol). After 30 min dichloromethane (10 ml) was added followed by saturated sodium carbonate solution and stirring was continued for 10 min. The organic layer was separated, dried over magnesium sulphate and concentrated to provide an *exo*, *endo* mixture of the cycloadducts. In all cases the *endo*-isomer had a higher chemical shift for proton H9b than the *exo*-isomer in the proton NMR spectra. The *exo*, *endo* ratios were quantified by comparing the integrations of these signals. Solvents quoted with the R_f values were the ones that were used for performing flash chromatography.

3.3.1. *exo*-1-(4-Phenyl-2,3,3a,4,5,9b-hexahydropyrrolo[3,2-*c*]quinolin-1-yl)propan-1″-one 6a. Reaction according to the general procedure gave the *titled compound* (64 mg, 21%), as a white solid mp 185–186°C R_f 0.38, (ether:pet. ether 90:10). ($C_{20}H_{22}N_2O$ Requires M^+ 306.1732. Found 306.1735); ν_{max} (KBr)/cm^{-1} 3333.2, 2971.9, 1617.8. δ_H ($CDCl_3$, 500 MHz) 1.19 (3H, t, J=7.1 Hz, CH_3CH_2), 2.13 (2×1H, 2×m, 3-*H*), 2.24 (2×1H, 2×m, CH_3CH_2), 2.47 (1H,

m, 3a-*H*), 3.45 (2×1H, 2×m, 2-*H*), 4.27 (1H, br, N*H*), 4.35 (1H, d, *J*=2.5 Hz, 4-*H*), 5.17 (1H, d, *J*=6.7 Hz, 9a-*H*), 6.50 (1H, d, *J*=7.3 Hz, 6-*H*), 6.61 (1H, t, *J*=7.3 Hz, 8-*H*), 7.04 (1H, t, *J*=7.3 Hz, 7-*H*), 7.10–7.30 (5H, 5×m, Ph*H*), 7.36 (1H, d, *J*=7.3 Hz, 9-*H*). δ_C ($CDCl_3$, 125 MHz) 9.3(C3″), 27.6(C3), 28.7(C2″), 43.1(C3a), 45.3(C2), 51.7(C4), 55.7(C9b), 113.3(C6), 117.9(C8), 120.9(C7), 125.7(C9a), 127.2(C4′), 128.2(2×C3′), 128.7(2×C2′), 130.5(C9), 142.3(C5a), 144.8(C1′), 173.9(C1″). *m/z* 306 (M^+, 30%), 277 (11), 249 (19), 206 (100), 91 (16).

3.3.2. *endo*-1-(4-Phenyl-2,3,3a,4,5,9b-hexahydropyrrolo-[3,2-*c*]quinolin-1-yl)propan-1″-one 7a. Reaction according to the general procedure gave the *titled compound* (64 mg, 21%), as a white solid mp 153–154°C R_f 0.48, (ether:pet. ether 90:10). ($C_{20}H_{22}N_2O$ Requires M^+ 306.1732. Found 306.1735); ν_{max} (KBr)/cm^{-1} 3312.8, 2975.6, 1629.2. δ_H ($CDCl_3$, 500 MHz) 1.19 (3H, t, *J*=7.4 Hz, C*H*$_3$CH$_2$), 1.64 (1H, m, 3-*H*), 2.30 (3×1H, 3×m, CH$_3$C*H*$_2$ and 3-*H*), 2.49 (1H, m, 3a-*H*), 3.33 (1H, dt, *J*=9.6 Hz, 7.7, 2-*H*), 3.48 (1H, t, *J*=9.6 Hz, 2-*H*), 3.90 (1H, br, N*H*), 4.73 (1H, d, *J*=2.7 Hz, 4-*H*), 5.77 (1H, d, *J*=6.1 Hz, 9b-*H*), 6.58 (1H, d, *J*=7.1 Hz, 6-*H*), 6.74 (1H, t, *J*=7.1 Hz, 8-*H*), 7.06 (1H, t, *J*=7.1 Jz, 7-*H*), 7.30–7.46 (5H, m, Ph–*H*), 7.63 (1H, d, *J*=7.1 Hz, 9-*H*). δ_C ($CDCl_3$, 125 MHz) 9.1(C3″), 22.0(C3), 27.6(C2″), 44.0(C3a), 45.2(C2), 55.8(C4), 56.4(C9b), 114.7(C6), 119.1(C8), 122.2(C7), 126.6(C9a), 127.8(C4′), 128.0(2×C3′), 128.7(2×C2′), 130.9(C9), 141.8(C5a), 143.7(C1′), 174.0(C1″). *m/z* 306 (M^+, 100%), 277 (60), 249 (59), 206 (95), 91 (32).

3.3.3. *exo*-1-(8-Methoxy-4-phenyl-2,3,3a,4,5,9b-hexahydropyrrolo[3,2-*c*]quinolin-1-yl)propan-1″-one 6b. Reaction according to the general procedure gave the *titled compound* (74 mg, 22%) as a white solid. mp 153–154°C, R_f 0.48, (ether). ($C_{21}H_{24}N_2O_2$ Requires M^+ 336.1837. Found 336.1843). ν_{max} (KBr)/cm^{-1} 3345.7, 2937.9, 1625.1, 1503.5. δ_H ($CDCl_3$, 500 MHz) 1.18 (3H, t, *J*=7.1 Hz, C*H*$_3$CH$_2$), 2.19 (2×1H, m, 3-*H*), 2.32 (2×1H, 2×m, CH$_3$C*H*$_2$), 2.56 (1H, m, 3a-*H*), 3.53 (2×1H, m, 2-*H*), 3.71 (3H, s, C*H*$_3$O), 3.72 (1H, br, N*H*), 4.67 (1H, br, 4-*H*), 5.21 (1H, br, 9b-*H*), 6.70 (1H, dd, *J*=7.1 Hz, 2.8, 6-*H*), 6.70 (1H, dd, *J*=7.1 Hz, 2.8, 7-*H*), 7.10 (1H, d, *J*=2.8 Hz, 9-*H*), 7.25 (5H, m, Ph–*H*,). δ_C ($CDCl_3$, 125 MHz) 9.4(C3″), 27.8(C3), 28.7(C2″), 43.4(C3a), 45.5(C2), 52.3(OCH$_3$), 55.7(C4), 56.1(C9b), 114.5(C6), 114.6(C7), 115.5(C9), 121.5(C9a), 125.9(C4′), 127.3 (2×C3′), 128.8(2×C2′), 136.6(C5a), 144.9(C1′), 152.4(C8), 173.9(C1″). *m/z* (M^+, %), 336 (M^+, 66%), 307 (8), 279 (15), 236 (100), 91 (14).

3.3.4. *endo*-1-(8-Methoxy-4-phenyl-2,3,3a,4,5,9b-hexahydropyrrolo[3,2-*c*]quinolin-1-yl)propan-1″-one 7b. Reaction according to the general procedure gave the *titled compound* (93.4 mg, 28%) as a white solid mp 157.0–158.2°C, R_f 0.53, (ether). ($C_{21}H_{24}N_2O_2$ Requires M^+ 336.1837. Found 336.1844). ν_{max} (KBr)/cm^{-1}; 3360.7, 2974.0, 1638.8, 1504.0. δ_H ($CDCl_3$, 500 MHz) 1.28 (3H, t, *J*=7.1 Hz, C*H*$_3$CH$_2$), 1.63 (1H, m, 3-*H*), 2.31 (3×1H, 3×m, CH$_3$C*H*$_2$ and 3-*H*), 2.48 (1H, m, 3a-*H*), 3.35 (1H, dt, *J*=9.7 Hz, 7.3, 2-*H*), 3.49 (1H, t, *J*=9.7 Hz, 2-*H*), 3.72 (3H, s, C*H*$_3$O), 3.73 (1H, br, N*H*), 4.67 (1H, d, *J*=2.5 Hz, 4-*H*), 5.75 (1H, d, *J*=7.3 Hz, 9b-*H*), 6.51 (1H, d, *J*=8.5 Hz, 6-*H*), 6.68 (1H, dd, *J*=8.5, 3.0 Hz, 7-*H*), 7.30-7.46 (6H, m, Ph–*H* and 9-*H*). δ_C ($CDCl_3$, 125 MHz) 9.2(C3″), 22.7(C3), 27.7(C2″), 44.1(C3a), 45.6(C2), 55.7(OCH$_3$), 56.1(C9b), 56.8(C4), 114.5(C7), 115.6(C9a), 115.8(C6), 123.2(C9), 126.6(2×C3′), 127.7(C4′), 128.6(2×C2′), 137.7(C5a), 142.0(C1′), 153.0(C8), 174.0(C1″). *m/z* (M^+, %); 336 (M+, 100%), 307 (19), 279 (38), 236 (55), 91 (24).

3.3.5. *endo*-1-[4-(2′-Nitrophenyl)-2,3,3a,4,5,9b-hexahydropyrrolo[3,2-*c*]quinolin-1-yl]propan-1″-one 7c. Reaction according to the general procedure followed by stirring overnight resulted in precipitation of an orange solid which was recrystallised from dichloromethane hexane to give the *titled compound* (117 mg, 33%) as a orange solid R_f 0.50, (ether:hexane 90:10), mp >270°C. ($C_{20}H_{21}N_3O_3$ Requires M^+ 351.1583. Found 351.1584). ν_{max} (KBr)/cm^{-1} 3333.0, 2972.0, 1623.4, 1586.9. δ_H ($CDCl_3$, 500 MHz) 1.20 (3H, t, *J*=7.1 Hz, C*H*$_3$CH$_2$), 1.62 (1H, m, 3-*H*), 2.31 (3×1H, 3×m, CH$_3$C*H*$_2$ and 3-*H*), 2.85 (1H, m, 3a-*H*), 3.38 (1H, dt, *J*=9.9, 7.6 Hz, 2-*H*), 3.51 (1H, t, *J*=9.9 Hz, 2-*H*), 3.73 (1H, br, N*H*), 5.23 (1H, d, *J*=2.8 Hz, 4-*H*), 5.81 (1H, d, *J*=7.0 Hz, 9b-*H*) 6.57 (1H, d, *J*=7.0 Hz, 6-*H*), 6.80 (1H, t, *J*=7.0 Hz, 8-*H*), 7.06 (1H, t, *J*=7.0 Hz, 7-*H*), 7.48 (1H, t *J*=7.5 Hz, 5′-*H*), 7.68 (2×1H, 2×m, 3′-*H* and 4′-*H*), 7.95 (1H, d, *J*=7.5 Hz, 9-*H*), 8.05 (1H, d, *J*=7.5 Hz, 6′-*H*). δ_C ($CDCl_3$, 125 MHz) 9.0(C3″), 23.2(C3), 27.6(C2″), 41.3(C3a), 45.5(C2), 51.5(C4), 55.7(C9b), 115.0(C6), 119.8(C8), 122.7(C9a), 124.8(C3′), 128.00(C7), 128.6(C4′), 128.7(C9), 131.1(C6′), 133.1(C5′), 136.4(C1′), 143.2(C5a), 149.0(C2′), 174.0(C1″). *m/z* (M^+, %), 351 (M^+, 25%), 260 (100), 91 (14).

3.3.6. *exo*-4-Phenyl-1-propionyl-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline-8-carboxylic acid methyl ester 6d. Reaction according to the general procedure gave the *titled compound* (87 mg, 24%) as a white solid R_f 0.18, (ether), mp 170–171°C ($C_{22}H_{24}N_2O_3$ Requires M^+ 364.1774. Found 364.1780). ν_{max} (KBr)/cm^{-1}; 3314.4, 2971.0, 1700.0, 1632.3, 1608.3. δ_H ($CDCl_3$, 500 MHz) 1.21 (3H, t, *J*=7.1 Hz, C*H*$_3$CH$_2$), 2.18 (2H, m, 3-*H*), 2.32 (2H, q, *J*=7.1 Hz, CH$_3$C*H*$_2$), 2.52 (1H, m, 3a-*H*), 3.51 (2×1H, 2×m, 2-*H*), 3.81 (3H, s, C*H*$_3$O), 4.32 (1H, br, N*H*) 4.50 (1H, br, 4-*H*), 5.26 (1H, d, *J*=6.4 Hz, 9b-*H*), 6.50 (1H, d, *J*=8.2 Hz, 6-*H*), 7.24 (5H, m, Ph–*H*), 7.80 (1H, d, *J*=8.2 Hz, 7-*H*), 8.05 (1H, s, 9-*H*). δ_C ($CDCl_3$, 125 MHz) 9.3(C3″), 27.7(C3), 28.7(C2″), 42.8(C3a), 45.2(C2), 51.3(C4), 51.6(OCH$_3$), 55.4(C9b), 112.8(C6), 119.5(C9a), 119.7(C8), 125.5(2×C3′), 127.6(C4′), 129.0(2×C2′), 130.4(C7), 132.5(C9), 144.1(C1′), 146.3(C5a), 167.3(*C*OCH$_3$), 173.9(C1″). *m/z* (M^+, %), 364 (M^+, 7%), 264 (15), 91 (37), 57 (100).

3.3.7. *endo*-4-Phenyl-1-propionyl-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline-8-carboxylic acid methyl ester 7d. Reaction according to the general procedure gave the *titled compound* (87 mg, 24%) as a white solid R_f 0.28, (ether), mp 192–193°C. ($C_{22}H_{24}N_2O_3$ Requires M^+ 364.1787. Found 364.1780). ν_{max} (KBr)/cm^{-1} 3372.4, 2979.6, 1705.2, 1644.4, 1608.6. δ_H ($CDCl_3$, 300 MHz) 1.28 (3H, t, *J*=7.1 Hz, C*H*$_3$CH$_2$), 1.64 (1H, m, 3-*H*), 2.17 (1H, m, 3-*H*), 2.32 (2H, q, *J*=7.1 Hz, CH$_3$C*H*$_2$), 2.50 (1H, m, 3a-*H*), 3.35 (1H, td, *J*=10.2, 7.7 Hz, 2-*H*), 3.48 (1H, m, 2-*H*), 3.89 (3H, s, C*H*$_3$O), 4.34 (1H, br, N*H*), 4.82 (1H, d, *J*=2.7 Hz, 4-*H*), 5.76 (1H, d, *J*=7.3 Hz, 9b-*H*), 6.60

(1H, d, J=8.5 Hz, 6-*H*), 7.40 (5H, m, *Ph–H*), 7.74 (1H, d, J=8.5 Hz, 7-*H*), 8.19 (1H, s, 9-*H*). δ_C ($CDCl_3$, 125 MHz) 9.2(C3″), 23.4(C3), 27.6(C2″), 43.4(C3a), 45.4(C2), 51.7(OCH_3), 55.3(C9b), 56.0(C4), 114.1(C6), 120.5(C9a), 120.9(C8), 126.5(2×C3′), 128.3(C4′), 128.9(2×C2′), 130.0(C7), 132.7(C9), 141.0(C1′), 147.5(C5a), 167.2(*C*OCH_3), 174.1(C1″). *m/z* (M^+, %), 364 (M^+, 17%), 307 (10), 210 (100).

3.3.8. 1′-(3-Pentyl-2-*p*-tolyl-1,2,3,4-tetrahydroquinolin-4-yl)pyrrolidin-2′-ones 9 and 10. Imine (500 mg, 2.56 mol, 1 equiv.), and enamide (460 mg, 2.54 mmol, 1 equiv.) were reacted according to the general procedure to give a 2:1 mixture of **9** and **10** by proton NMR spectroscopy. Flash chromatography provided compound **9** (424 mg, 44%), as an oil which slowly solidified to give a white solid mp 145–146°C, R_f 0.44 (hexane:ether 1:4). ($C_{25}H_{32}N_2O$ requires M^+ 376.2515 Found M^+ 376.2501). ν_{max} (KBr)/cm^{-1} 3364, 2929, 1856, 1671, 1408, 1344, 1268. δ_H (500 MHz, $CDCl_3$) 0.67 (3H, t, J=7.2 Hz, CH_2CH_3), 1.96 (8H, m, methylene envelope), 1.94 (2H, m, CH_2CH_2CO), 2.01 (3H, s, ArCH_3), 2.10 (1H, ddt, J=10.8, 10.4, 4.4 Hz, 3-H), 2.44 (2H, m, CH_2CH_2CO), 3.09 (2×1H, 2×m, NCH_2CH_2), 3.99 (1H, s, N*H*), 4.34 (1H, d, J=10.1 Hz, 2-H), 5.37 (1H, d, J=10.8 Hz, 4-H), 6.55 (1H, d, J=8.0 Hz, 8-H), 6.66 (1H, t, J=7.4 Hz, 7-H), 6.77 (1H, d, J=7.8 Hz, 5-H), 7.20 (1H, t, J=7.6 Hz, 6-H), 7.55 (2H, d, J=8.6 Hz, Ar*H*), 8.15 (2H, d, J=8.4 Hz, Ar*H*). δ_H (125 MHz, $CDCl_3$) 12.9, 16.4, 17.3, 21.3, 23.9, 27.4, 29.0, 31.0, 39.9, 41.4, 56.1, 60.7, 113.6, 115.3, 117.7, 122.7, 126.2, 2×126.9, 2×128.5, 144.1, 146.7, 148.3, 175.2. *m/z* (M^+, %) 376(M^+34), 291(34), 220(100), 195(40), 124(83), 86(51), 41(51).

Collection of further fractions provided compound **10** as a brown oil (221 mg, 23%). R_f 0.29 (hexane:ether 1:4) ν_{max} (KBr)/cm^{-1} 3410, 2928, 1671, 1345. δ_H (500 MHz, $CDCl_3$) 0.74 (3H, t, J=7.3 Hz, CH_2CH_3), 1.08 (8H, m, methylene envelope), 1.29 (2×1H, 2×m, CH_2CH_2CO), 1.92 (2×1H, 2×m, CH_2CH_2CO), 2.23 (1H, qd, J=6.8 Hz, 4.0, 3-H), 2.43 (3H, s, ArCH_3), 3.04 (1H, ddd, J=9.7, 7.8, 5.8 Hz, NCH*H*CH_2), 3.16 (1H, ddd, J=9.8, 7.9, 6. 0Hz, NC*H*HCH_2), 4.26 (1H, s, N*H*), 4.60 (1H, d, J=4.0 Hz, 2-H), 4.97 (1H, d, J=7.0 Hz, 4-H), 6.58 (1H, d, J=7.3 Hz, 8-H), 6.70 (1H, dd, J=7.4 Hz, 7-H), 6.9(1H, d, J=7.3 Hz, 5-H), 7.05 (1H, d J=7.3 Hz, 6-H), 7.35 (2H, d, J=10.0 Hz, Ar*H*), 8.10 (2H, d, J=10.0 Hz, Ar*H*); δ_C (75 MHz, $CDCl_3$) 12.9, 17.6, 21.5, 25.3, 25.8, 25.9, 30.5, 30.7, 40.3, 43.9, 49.4, 54.9, 113.6, 116.2, 117.4, 123.1, 126.3, 2×127.9, 2×128.7, 143.3, 146.3, 148.3, 174.4. *m/z* (M^+, %) 376 (M^+34), 291(34), 220(100), 195(40), 124(83), 86(51), 41(51).

3.3.9. 1-[4-(2′-Nitrophenyl)-2,3-dihydropyrrolo[3,2-*c*]-quinolin-1-yl]propan-1″-one 15. Battery grade manganese dioxide (activated by heating in an oven at 85°C overnight) (1.216 g, 14 mmol), was added to a mixture of precipitated *endo*/*exo*-1-[4-(2′-nitrophenyl)-2,3,3a,4,5,9b-hexahydropyrrolo[3,2-*c*]quinolin-1-yl]-1″-propanone (100 mg, 0.14 mmol) in dry benzene (15 ml) and refluxed under a nitrogen atmosphere for 16 h. The solution was then filtered through celite and the residue washed with methanol (2×10 ml). The methanol and benzene solutions were then combined and concentrated under reduced pressure and the residue purified by flash chromatography to yield the *titled compound* (80 mg, 82%) as clear oil R_f 0.3 (ether). ($C_{20}H_{17}N_3O_3$ Requires M^+ 347.1270 Found 347.1256); ν_{max} (KBr)/cm^{-1} 2963.9, 1680.0, 1527.6. δ_H ($CDCl_3$, 500 MHz) 1.34 (3H, t, J=7.2 Hz, CH_3CH_2), 2.65 (2H, q, J=7.2 Hz, CH_3CH_2), 3.02 (2H, t, J=8.0 Hz, 3-*H*), 4.24 (2H, t, J=8.0 Hz, 2-*H*), 7.52 (1H, t, J=8.0 Hz, 7-*H*), 7.55 (1H, d, J=7.6 Hz, 6′-*H*), 7.62 (1H, t, J=7.8 Hz, 4′-*H*), 7.67 (1H, t, J=8.0 Hz, 8-*H*), 7.74 (1H, t, J=7.6 Hz, 5′-*H*), 8.04 (2×1H, 2×d, J=8.0 Hz, 6-*H* and 9-*H*), 8.14 (1H, d, J=7.8 Hz, 3′-H); δ_C ($CDCl_3$, 125 MHz) 8.6, 27.0, 29.0, 50.0, 119.3, 123.7, 124.3, 124.6, 125.2, 128.4, 2×128.6, 130.4, 132.4, 134.8, 147.8, 148.2, 149.1, 153.1, 173.4; *m/z* (M^+, %), 347(M^+, 6%), 149 (100), 91 (45), 57 (97).

3.3.10. *N*-{2′-(2″-Nitrophenyl)quinolin-3-ylethyl}propanamide 16. Battery grade manganese dioxide (activated by heating in an oven at 85°C overnight) (608 mg, 7 mmol), was added to a mixture of precipitated *endo*/*exo*-1-[4-(2-nitrophenyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]-quinolin-1-yl]-1-propanone (100 mg, 0.28 mmol,) in dry benzene (15 ml) and this was refluxed under a nitrogen atmosphere for 3 h. The solution was then filtered through celite and the residue washed with methanol (2×10 ml). The methanol and benzene solutions were then combined and concentrated under reduced pressure and the residue purified by P.L.C (ether). This provided a 1:1 mixture of two compounds (10 mg, 10%), R_f 0.1(ether), **16** and a compound which may be the imine **14**. On standing in $CDCl_3$ overnight the mixture became homogenous affording the *titled compound* **16**, (10 mg, 10%) as a clear oil R_f 0.1 (ether). ($C_{20}H_{19}N_3O_3$ Requires M^+ 349.1426 Found 349.1428). ν_{max} (KBr)/cm^{-1} 3926.8, 2935.6, 1650.0, 1526.4. δ_H ($CDCl_3$, 300 MHz) 0.97 (3H, t, J=7.5 Hz, CH_3CH_2), 1.99 (2H, m, CH_3CH_2), 2.83 (2H, t, J=6.6 Hz, 1′-H), 3.36 (2H, m, 2′), 5.48 (1H, br, N*H*), 7.52 (1H, d, J=7.6 Hz, 6″-*H*), 7.57 (1H, t, J=7.8 Hz, 7-*H*), 7.60 (1H, t, J=7.6 Hz, 4″-*H*), 7.70 (1H, t, J=7.8 Hz, 6-*H*), 7.75 (1H, t, J=7.6 Hz, 5″-*H*), 7.83 (1H, d, J=7.8 Hz, 5-*H*), 8.01 (1H, d, J=7.8 Hz, 8-*H*), 8.10 (1H, s, 4-*H*), 8.18 (1H, d, J=7.6 Hz, 3″-*H*). δ_C ($CDCl_3$, 125 MHz) 8.9, 28.7, 31.3, 37.7, 125.0, 125.15, 127.18, 127.6, 129.1, 129.5, 129.6, 129.9, 131.3, 133.5, 135.8, 136.7, 146.4, 148.4, 157.2, 174.0. *m/z* (M^+, %), 349, (M^+, 10%), 263 (10), 149 (64), 57 (75), 28 (100).

3.3.11. 1-(3,3a,4,5,9b-hexahydropyrrolo[3,2,*c*]quinolin-1-yl)propan-1′-one 19. A solution of methoxymethylphenylamine **17a** (55 mg, 0.4 mmol) and 1-(2,3-dihydropyrrol-1-yl)propan-1-one **5** (100 mg, 0.8 mmol) in methanol 10 ml was boiled under reflux for 18 h. The solvent was removed under reduced pressure and flash chromatography gave the *titled compound* (40 mg, 43%) as a white solid mp 99–101°C R_f 0.35 (ether), $C_{14}H_{18}N_2O$ requires M^+ 230.1419 found M^+ 230.1410. $\nu_{max.}$ (KBr)/cm^{-1} 3334, 2925, 2855, 1734, 1371, 1300. δ_H(500 MHz, $CDCl_3$) 1.13 (3H, t, J=7.5 Hz, CH_3), 1.94 (2×1H, 2×m, H3), 2.24 (2×1H, 2×m, CH_3CH_2), 2.41 (1H, m, H3a), 3.11 (1H, dd, J=11.8, 2.4 Hz, H4′), 3.43 (3×1H, 3×m, H2, and H4), 5.46 (1H, d, J=7.4 Hz, H9b), 6.40 (1H, d, J=7.7 Hz, H6), 6.59 (1H, t, J=7.7 Hz, H8), 6.93 (1H, t, J=7.7 Hz, H7), 7.91 (1H, d, J=7.7 Hz, H9). δ_C (75 MHz, $CDCl_3$) 8.1(C3′), 23.9(C3), 25.2(C2′), 33.6(C4) 40.8(C3a),

44.7(C2), 53.3(C9b), 113.3(C6), 117.5(C8), 121.4(C9a), 126.8(C7), 130.0(C9), 142.6(C5a), 172.9(C1′). *m/z* (M^+, %) 230(59), 201(89), 173(39), 145(43), 130(100).

3.3.12. *endo*-8-Methoxy-1-propionyl-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline-4-carboxylic acid methyl ester 22. Imine **20** and enamide **5** reacted according to the general procedure to give a 2:1 *endo*:*exo* mixture of diastereoisomers by NMR spectroscopy. Separation by flash chromatography provided only the *endo*-isomer as an orange oil (21 mg, 6%), R_f 0.25, (ether). As compound **22** rapidly aromatises, it could only be characterised by proton NMR spectroscopy. δ_H ($CDCl_3$, 300 MHz) 1.23 (3H, t, *J*=7.2 Hz, CH_3CH_2), 1.90 (2H, m, 3-*H*), 2.40 (3H, overlapping m, CH_3CH_2 and 3a-*H*), 3.35–3.50 (2×1H, 2×m, 2-H), 3.81 (3H, s, CH_3O), 4.08 (4H, s overlapping with m, CH_3O and 4-*H*), 5.64 (1H, d, *J*=8.8 Hz, 9b-H), 6.88 (1H, dd, *J*=8.8, 0.9 Hz, 7-H), 7.01 (1H, d, *J*=0.9 Hz, 9-*H*), 7.60 (1H, d, *J*=8.6 Hz, 6-*H*).

3.3.13. 6-Methoxy-3-[2-(propionylamino)ethyl]quinoline-2-carboxylic acid methyl ester 23. *endo*-8-Methoxy-1-propionyl-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline-4-carboxylic acid methyl ester **22** (80 mg, 0.25 mmol) was allowed to stand overnight in deuterochloroform (1 ml) in a capped NMR tube. Proton NMR spectroscopy showed complete consumption of the starting material. The solvent was then removed under reduced pressure to provide the pure *titled compound* (79 mg, 100%) as an orange oil. ($C_{17}H_{20}N_2O_4$ Requires M^+ 316.1423. Found 316.1422). ν_{max} (KBr)/cm^{-1} 2972.4, 1726.2, 1637.9, 1542.3. δ_H ($CDCl_3$, 500 MHz) 1.08 (3H, t, *J*=7.6 Hz, CH_3CH_2), 2.14 (2H, q, *J*=7.6 Hz, CH_3CH_2), 3.23 (2H, t, *J*=7.2 Hz, 1′-H), 3.65 (2H, q, *J*=7.2 Hz, 2′-*H*), 3.95 (3H, s, CH_3O), 4.06 (3H, s, CH_3O), 6.21 (1H, br, N*H*), 7.03 (1H, d, *J*=2.7 Hz, 5-*H*), 7.38 (1H, dd, *J*=9.4, 2.7 Hz, 7-*H*), 8.01 (1H, s, 4-*H*), 8.07 (1H, d, *J*=9.4 Hz, 8-*H*). δ_C ($CDCl_3$, 125 MHz) 10.2, 30.0, 32.5, 41.4, 53.5, 56.1, 104.4, 123.8, 130.8, 131.8, 132.8, 137.7, 142.7, 146.2, 159.9, 167.8, 174.4. *m/z* (M^+, %), 316 (M^+, 75%), 257 (57), 231 (95), 171 (100).

3.3.14. 7-Methoxy-3,4-dihydro-2*H*-benzo[*b*][1,7]naphthyridin-1-one 24. Sodium methoxide (11 mg, 0.2 mmol) was added to *endo*-8-methoxy-1-propionyl-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline-4-carboxylic acid methyl ester (64 mg, 0.2 mmol) in methanol and the solution was refluxed for 3 h. The methanol was removed under reduced pressure, the residue dissolved in DCM (10 ml) washed with water (2×10 ml) dried over magnesium and concentrated. The residue was purified by flash chromatography to afford the *titled compound* (39 mg, 85%) as a white solid mp >270°C, R_f 0.5 ($CHCl_3$:MeOH, 90:10). ($C_{13}H_{12}N_2O_2$ requires M^+ 228.0899. Found 228.0907). ν_{max} (KBr)/cm^{-1} 3205.2, 2950.2, 1676.8, 1619.8; δ_H ($CDCl_3$, 300 MHz) 3.22 (2H, t, *J*=6.3 Hz, 4-*H*), 3.68 (2H, td, *J*=6.3, 3.1 Hz, 3-*H*), 3.95 (3H, s, CH_3O), 7.07 (1H, d, *J*=2.6 Hz, 6-*H*), 7.16 (1H, br, N*H*), 7.38 (1H, dd, *J*=9.3, 2.6 Hz, 8-*H*), 7.92 (1H, s, 5-*H*), 8.27 (1H, d, *J*=9.3 Hz, 9-*H*). δ_C ($CDCl_3$, 125 MHz) 28.6, 40.0, 56.6, 104.0, 122.8, 130.6, 131.6, 132.6, 133.0, 143.9, 144.3, 159.4, 164.9. *m/z* (M^+, %), 228(M^+, 94%), 199 (16), 171 (100), 128 (22).

3.3.15. *endo*-8-Bromo-4-(2′-cyanovinyl)-2,3,3a,4,5,9b-hexahydropyrrolo[3,2-*c*]quinoline-1-carboxylic acid methyl ester 28. General procedure gave *titled compound* (108 mg, 30%) as a clear oil R_f 0.69 (ether). ($C_{16}H_{16}BrN_3O_2$ requires M^+ 361.0425. Found 361.0438). ν_{max} (KBr)/cm^{-1} 3305.1, 2956.0, 2224.9, 1657.3. δ_H ($CDCl_3$, 300 MHz) 1.90 (2×1H, br, 3-*H*), 2.41 (1H, br, 3a-*H*), 3.30 (2×1H, br, 2-*H*), 3.70 (3H, s, CH_3O), 4.21 (1H, br, 4-*H*), 5.05 (0.33H, br, 9b-*H*), 5.20 (0.67H, br, 9b-*H*), 5.62 (1H, d, *J*=16.4 Hz, 2′-*H*), 6.37 (1H, d, *J*=8.5 Hz, 6-*H*), 6.70 (1H, dd, *J*=16.4, 5.4 Hz, 1′-*H*), 7.06 (1H, d, *J*=8.4 Hz, 7-*H*), 7.40 (0.33H, br, 9-*H*), 7.63 (0.67H, br, 9-*H*). δ_C ($CDCl_3$, 75 MHz) 22.7, 40.2, 44.4, 52.6, 53.1, 55.6, 101.1, 111.7, 116.3, 116.6, 131.1, 132.0, 132.8, 140.7, 153.1, 156.7. *m/z* (M^+, %) 361(M+, 35), 264 (37), 128 (100).

Collection of further fractions gave *exo*-8-bromo-4-(2′-cyanovinyl)-2,3,3a,4,5,9b-hexahydropyrrolo[3,2-*c*]quinoline-1-carboxylic acid methyl ester **27** (36 mg, 10%) as a clear oil R_f 0.27 (ether). ($C_{16}H_{16}BrN_3O_2$ requires M^+ 361.0425. Found 361.0432). ν_{max} (KBr)/cm^{-1} 3305.1, 2956.0, 2224.9, 1657.3. δ_H ($CDCl_3$, 300 MHz) 2.05 (2×1H, br, 3-*H*), 2.41 (1H, br, 3a-*H*), 3.30 (1H, br, 2-H), 3.40 (1H, br, 2-*H*), 3.75 (3H, s, CH_3O), 4.05 (1H, br, 4-*H*), 4.16 (1H, br, N*H*), 4.95 (1H, br, 9b-*H*), 5.52 (1H, d, *J*=16.3 Hz, 2′-*H*), 6.40 (1H, d, *J*=8.6 Hz, 6-*H*), 6.75 (1H, dd, *J*=16.3, 5.1 Hz, 1′-*H*), 7.10 (1H, d, *J*=8.6 Hz, 7-*H*), 7.50 (1H, br, 9-*H*). *m/z* (M^+, %), 361(M+, 35), 264 (37), 128 (100).

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