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Pyridine Radicals in Synthesis. Part 3: Cyclopentannulation of Pyridine via the 3-Pyridyl Radical and a Formal Synthesis of (±)-Oxerine

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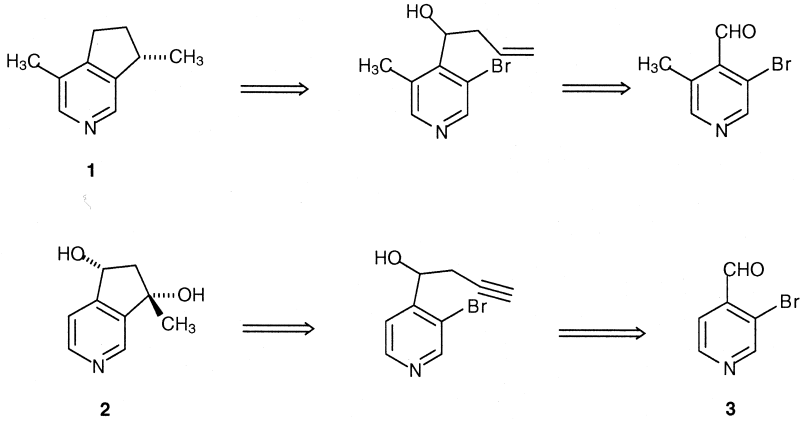
Abstract—The allylation and propargylation of 3-bromo-4-formylpyridine under zinc-mediated Barbier conditions is described. The homoallylic alcohols produced are cyclised via the derived 3-pyridyl radical to give cyclopentannulated pyridines. One of these bicyclic compounds is converted into an advanced intermediate in a previous synthesis of the monoterpene alkaloid (±)-oxerine.

As part of a programme of research designed to extend the use of aryl radicals in synthesis to the development and use of heteroaryl radicals, we have previously reported on the formation and cyclisation of radicals derived from 3-bromopyridines,[1] 2-bromopyridinium salts[2] and 2-bromoindoles.[3] In this paper we wish to describe in full our early work on the cyclisation of 3-pyridyl radicals which led to a formal synthesis of the alkaloid (±)-oxerine.[4] Prior to our work in this area, Snieckus and co-workers[5] reported the first cyclisation reaction involving 4-pyridyl radicals and Harrowven[6] reported on the cyclisation of the 2-pyridyl radical to ketenedithioacetals as a route to condensed thiophenes. Subsequent to our work, a recent report[7] describes the synthesis of tricyclic pyridones as $GABA_A$ receptor agonists via 3- and 4-pyridyl radical cyclisations. Our attention was attracted by the monoterpene alkaloids (−)-actinidine **1**[8] and (−)-oxerine **2**[9] which possess the cyclopentano[*c*]-pyridine ring system. Our retrosynthetic analysis of this bicyclic system is shown in Scheme 1. The key steps involve formation of the cyclopentane ring by a reductive 5-*exo* radical cyclisation leading to a methyl group in the correct position for both natural products, and allylation of



Scheme 1.

Keywords: pyridine radicals; cyclopentannulation; (±)-oxerine.
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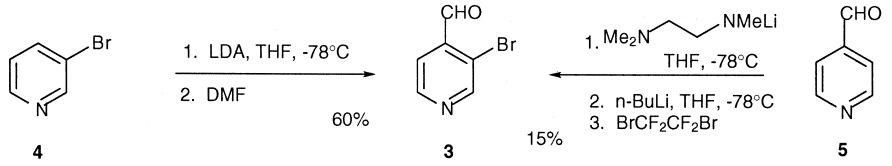
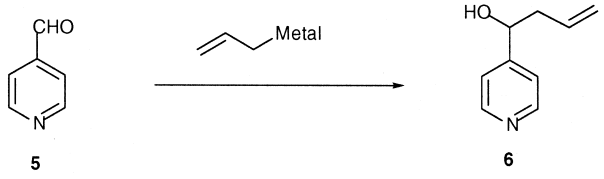
the known 3-bromo-4-formylpyridine **3**. In the case of actinidine **1** an extra methyl group is needed on the pyridine 5-position and reductive removal of the alcohol is required. Oxerine **2** requires a homopropargylic alcohol derived from propargylation of **3** in order to allow for the formation of the tertiary alcohol. We reported the synthesis of (±)-actinidine[1] recently and we would now like to report in detail on the allylation/propargylation reaction and its limitations, the radical cyclisation to create the cyclopentano[*c*]pyridine and the formal synthesis of (±)-oxerine.

The key starting material for all the work described in this paper is 3-bromo-4-formylpyridine **3**, the synthesis of which was described by Corey et al.[10] and involves ortholithiation and formylation of 3-bromopyridine **4** (Scheme 2). This reaction proved to be very sensitive to reaction conditions (especially temperature and the purity of the DMF used) and in our hands a yield of 60% was obtained rather than the 73% reported.[10] During the course of work on this reaction, an alternative was explored using the addition of lithium trimethylethylene diamine (LTMEDA) to 4-formylpyridine **5** followed by in situ ortholithiation and bromination.[11] This gave **3** in only 15% yield.



Scheme 2.

In order to explore the allylation, commercially available 4-formylpyridine **5** was used to test a variety of allylation reagents and conditions (Scheme 3, Table 1). The reaction of **5** with allylmagnesium bromide (entry 1) led to a low yield and some pyridine-4-methanol was also obtained. Allyltrimethylsilane and titanium (IV) chloride[12] gave a poor yield (entry 2) and although allyltributylstannane/boron trifluoride[13] gave a good yield (entry 3), the problems involved in separating the product **6** from the tin residues made this reaction practically difficult. The most successful and practically convenient method proved to involve Barbier-type reaction with an allyl zinc species.[14] Reaction of zinc and allyl bromide in THF followed by addition of **5** gave alcohol **6** in 73% yield.



Scheme 3.

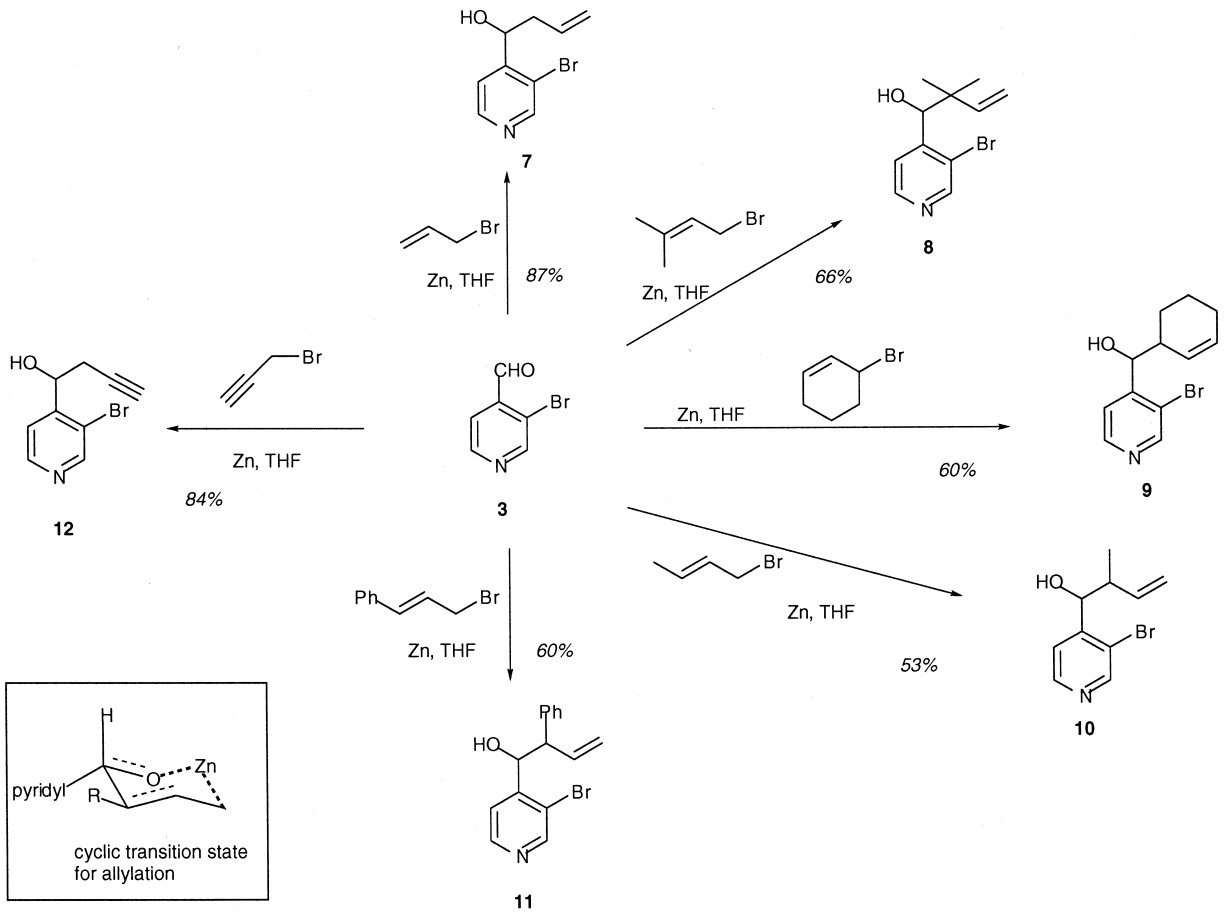
Table 1. Allylation of 4-formylpyridine **5**

Entry	Metal	Solvent	*T* (°C)	Yield of **6** (%)
1	MgBr	Ether	25	35
2	Me_3Si[a]	Dichloromethane	25	19
3	*n*-Bu_3Sn[b]	Dichloromethane	−78	60
4	ZnBr[c]	Tetrahydrofuran	25	73

[a] 1 molar equivalent of freshly distilled $TiCl_4$ was used as Lewis acid catalyst.[12]
[b] 1 molar equivalent of BF_3 etherate was used as catalyst.[13]
[c] Barbier procedure was used (see Experimental).[14]

The zinc Barbier procedure was applied to the allylation of 3-bromo-4-formylpyridine **3** and gave the homoallylic alcohol **7** in 87% yield (Scheme 4). Pyridine **7** was also obtained in 13% yield by ortholithiation of alcohol **6** with 2 molar equivalents of *t*-BuLi followed by bromination with 1,2-dibromotetrafluoroethane. The use of *s*-BuLi in this reaction led to addition of the organolithium to the 2-position of the pyridine. Reaction with other allylic bromides under similar conditions also gave satisfactory yields of homoallylic alcohols. Thus reaction of **3** with prenyl bromide gave the dimethyl-substituted homoallylic alcohol **8** in 66% yield via an allylic rearrangement.[15] Reaction with the symmetrical allyl bromide, 3-bromocyclohexene, gave rise to the expected product **9** as a mixture of diastereoisomers in a 2:1 ratio. Similarly, reaction with crotyl bromide gave **10** as a 7:6 mixture of diastereoisomers in 53% yield and reaction with cinnamyl bromide gave **11** in 60% yield as a 5:1 mixture of diastereoisomers. Although we did not assign the stereochemistry to the diastereoisomers of **9**, **10** and **11**, the fact that allylic rearrangement had occurred would suggest the reaction proceeds via a cyclic transition state. Assuming that the pyridine and the substituent on the allylic double bond are pseudo-equatorial in such a transition state would allow a tenuous assignment of stereochemistry. However, the only evidence for assignment of stereochemistry, the vicinal coupling constant of the benzylic proton, was either not discernible in the ^{1}H NMR (compound **10**), had the same value for both diastereoisomers (compound **9**, J=4 Hz) or differed by a small amount (compound **11**, J=6 Hz for major isomer and J=4 Hz for minor isomer). Finally, the reaction of **3** with propargyl bromide was carried out in the same way leading to the homopropargyl alcohol **12** in 84% yield.

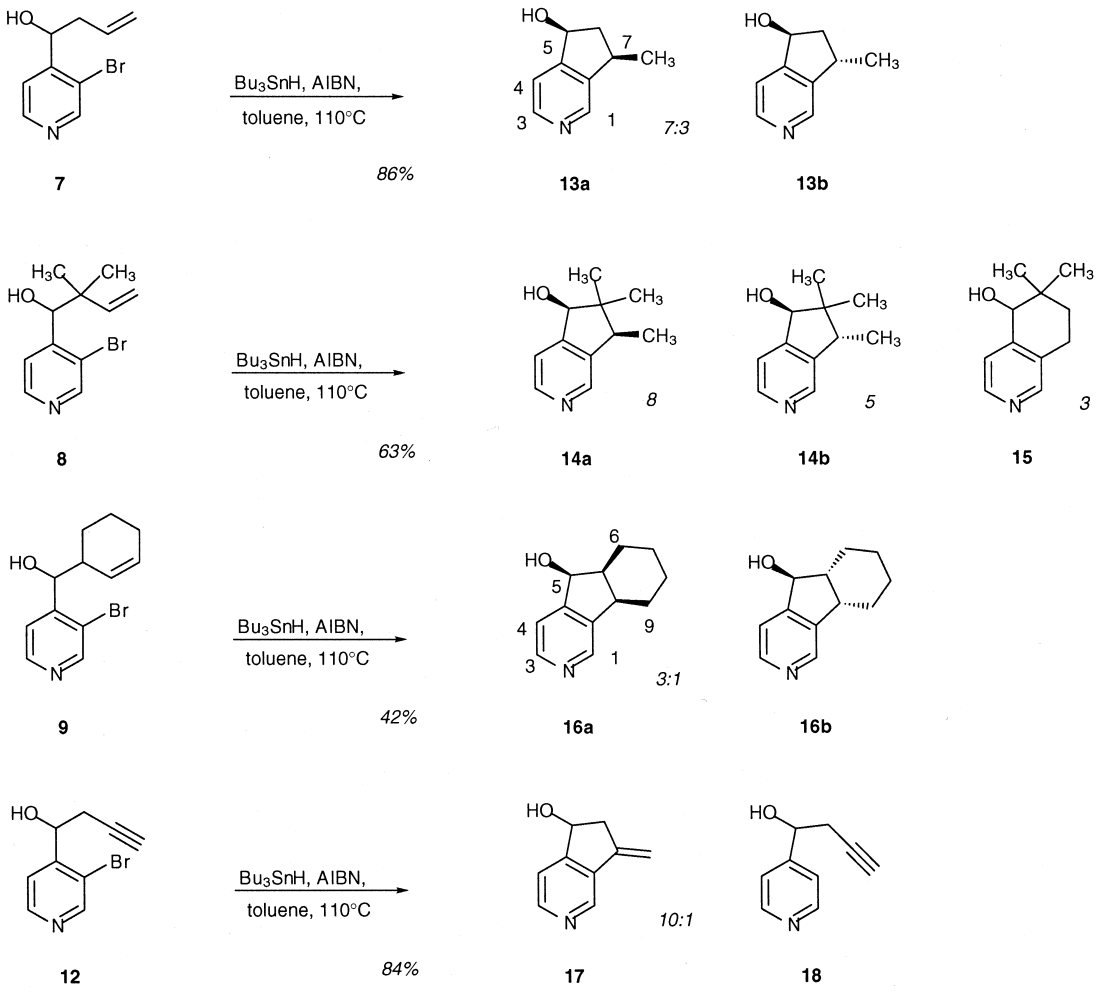
Radical cyclisation of this range of unsaturated bromopyridine alcohols was now investigated using the standard conditions of tributyltin hydride (TBTH) in refluxing toluene at low concentration with azobisisobutyronitrile (AIBN) as the initiator.[16] Reaction of **7** under these conditions gave rise to cyclopentannulated pyridines **13a** and **13b** in a combined yield of 86% (Scheme 5). The assignment of the structure was clear from ^{1}H NMR as the olefinic protons were lost and replaced by a doublet for the



Scheme 4.

methyl group. No trace of reduced product (i.e. debrominated **7**) was detected, indicating an efficient cyclisation reaction, and there was also no sign of the product arising from 6-*endo* cyclisation. The ratio of diastereoisomers **13a** and **13b** was found to be 7:3 and they proved to be inseparable by flash chromatography. The assignment of the *trans*-stereochemistry to the minor isomer **13b** was based on an nOe between the proton adjacent to the alcohol and the methyl group in the nOesy spectrum of the mixture. That the major isomer **13a** has the *cis*-arrangement of alcohol and methyl group is in accord with the Beckwith model for radical cyclisations.[17] Reaction of pyridine **8** under the same conditions led to an inseparable mixture of three compounds derived via radical cyclisation in overall 63% yield and in a ratio of 8:5:3. The major compound proved to be the cyclopentannulated pyridine **14a** with *cis*-stereochemistry. The *trans*-isomer **14b** was the intermediate compound and the minor compound was assigned the tetrahydroisoquinoline structure **15** owing to the presence of two CH_2 peaks in the ^{13}C NMR. Compound **15** clearly arises from a 6-*endo* cyclisation of the pyridine radical and is in marked contrast to the result obtained for cyclisation of pyridine **7**. Presumably, the presence of the gem-dimethyl group both creates some hindrance to 5-*exo* cyclisation and enhances 6-*endo* cyclisation via a Thorpe–Ingold effect.[18] Cyclisation of cyclohexenylpyridine **9** gave two products in 42% yield as an inseparable mixture of diastereoisomers. Although this cyclisation substrate is already a mixture of diastereoisomers and another stereogenic centre is generated in the cyclisation, only two diastereoisomeric products were obtained. We believe that this is because in both products, the cyclohexane unit is *cis*-fused to the newly created cyclopentane. Inspection of molecular models and literature precedent[19] indicates the more favourable nature of *cis*-ring fusion in this case. Further, the major product **16a** showed a vicinal coupling constant of 8 Hz for the proton adjacent to the alcohol which fits well for the all *cis*-structure based upon a dihedral angle of 0–10° between the coupled protons. The minor product **16b** was assigned the stereostructure shown on the basis of a 6 Hz vicinal coupling constant for the same hydrogen. Models indicate a dihedral angle of about 130° in this isomer which is reasonably consistent with a coupling constant of this value. However, these assignments must be treated as tentative and owing to the fact that an inseparable mixture was obtained, further information could not be gleaned from spectroscopic experiments. The assignment of **16a** as the structure of the major product might cast light on the stereochemical nature of the starting material **9** but such inferences must be treated with caution.

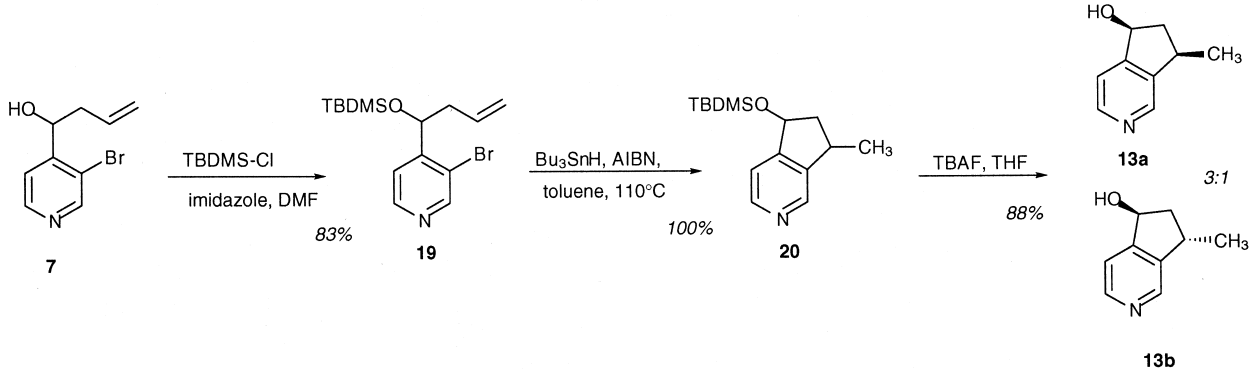
Cyclisation of pyridines **10** and **11** followed by chromatography led to material assigned the cyclopentanopyridine skeleton in 68 and 70% yield, respectively. However in both cases a large number of diastereoisomers was obtained and structure assignment by spectroscopic techniques was not



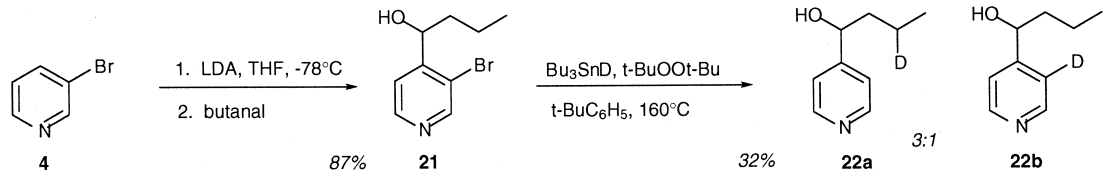
Scheme 5.

possible. With a synthesis of oxerine **2** in mind, the cyclisation of the propargyl alcohol **12** was studied. It is known that alkynes are not as good radical acceptors as alkenes[20] and that addition of TBTH across the unprotected triple bond can occur.[21] We were delighted to find that reaction under the usual conditions gave a 10:1 mixture of cyclised material **17** and reduced product **18** in a combined yield of 84%. Although not separable by chromatography, **17** could be obtained pure by recrystallisation in 57% yield from **12** (Scheme 5).

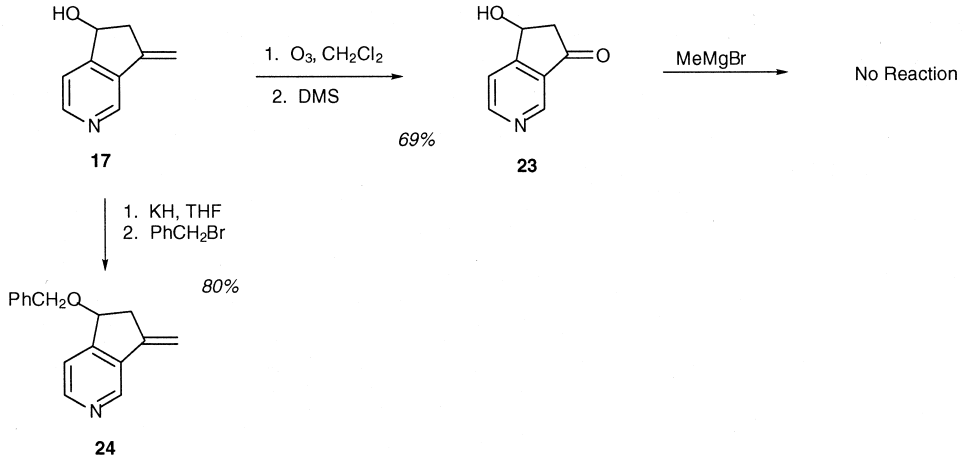
Two more radical reactions were carried out to further explore the properties of the pyridyl radical. The first involved introducing a bulky silyl-group onto the alcohol function of **7**. The radical reactions do not need OH-protection but we wanted to explore the change in ratio of the diastereoisomers produced in the cyclisation reaction with a bulky group at this position. Silylation of **7** under the usual conditions with *tert*-butyldimethylsilyl chloride (TBDMSCl) proceeded to give silyl ether **19** in 83% yield (Scheme 6). Cyclisation of **19** under the same conditions as



Scheme 6.



Scheme 7.



Scheme 8.

used for the other cyclisation reactions gave **20** as a 3:1 mixture of diastereoisomers in quantitative yield. The assignment of stereochemistry was carried out by deprotecting **20** in 88% yield to give **13a** and **13b** as a 3:1 mixture. Thus, a bulky group produces a slightly enhanced ratio of *cis*:*trans* isomers as predicted by the Beckwith model.

The final radical reaction involved exploring the ability of the 3-pyridyl radical to carry out [1,5]-hydrogen atom abstraction on a saturated side-chain at C-4 with a view to investigating whether the alkyl radical so generated would add to the pyridine based on the chemistry published by Storey and Beckwith.[22] Reaction of 3-bromopyridine **4** with LDA at low temperature followed by quenching with butanal gave the saturated alcohol **21** in 87% yield (Scheme 7). Reaction of **21** under the conditions of Storey and Beckwith using tributyltin deuteride delivered by syringe pump over 10 h in *tert*-butylbenzene at 160°C gave in 32% combined yield **22a** and **22b** in a ratio of 3:1 favouring the product in which the initial 3-pyridyl radical has abstracted a hydrogen atom from the side-chain prior to reduction. Although the yield is low, this demonstrates the feasibility of [1,5]-hydrogen atom abstraction using pyridyl radicals. However, there was no sign of addition of this side-chain radical to the pyridine and presumably stabilising groups would be required to achieve this process.

With unsaturated alcohol **17** in hand, we believed that addition of water to the *exo*-methylene group would lead to a short synthesis of (±)-oxerine **2**. However, under a wide variety of conditions (mercuric acetate, sodium borohydride; mercuric trifluoroacetate, sodium borohydride; epoxidation with peracids) the double bond proved to be resistant to reaction. This could be caused by the electron-withdrawing pyridine reducing the usual reactivity of the double bond. Ozonolysis of the double bond proceeded smoothly to give ketone **23** in 69% yield (Scheme 8). However, reaction with MeMgBr[23] in an attempt to create the desired tertiary alcohol resulted only in starting material being recovered. Finally, we abandoned the plan of directly producing oxerine from **17** and instead benzylated the alcohol to give ether **24** which had been used in the previous synthesis of (±)-oxerine **2**.[24] The spectral data of **24** were in agreement with that reported apart from a typographical error in the previous report.[25]

In conclusion, we have shown that pyridine radicals can be generated, and react in the same manner as radicals derived from halobenzenes. This methodology provides a valuable method for the intramolecular creation of carbon/carbon bonds to pyridine and in particular the formation of the cyclopentanopyridine skeleton. To exemplify this chemistry, we have achieved a formal synthesis of the alkaloid (±)-oxerine.

Experimental

General details

All reactions were carried out under argon and solutions dried with magnesium sulphate. Diethyl ether, tetrahydrofuran (THF) and toluene were distilled from sodium benzophenone ketyl immediately before use. Zinc was activated by washing with 10% hydrochloric acid. Sodium and potassium hydride were washed with petrol or hexane (which was discarded) at least three times before use. Column chromatography was performed with silica gel

(Merck 7734) using the flash chromatography technique. Thin layer chromatographic analysis was performed using plastic-backed silica plates (Merck 5735). Components were visualised by either UV or phosphomolybdic acid dip. All melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1605 FT-IR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM360 spectrometer operating at 360 MHz for proton and 90 MHz for carbon. Tetramethylsilane (TMS) was adopted as the internal standard for ^{1}H NMR spectra and the solvent peaks for ^{13}C NMR spectra. Chemical shifts (δ_H and δ_C) values are reported as parts per million (ppm). The multiplicity of a ^{1}H NMR signal is designated by one of the following abbreviations: s=singlet, d=doublet, t=triplet, q=quartet, br=broad and m=multiplet. High resolution mass spectra were performed at the Chemistry Department, King's College London. Elemental analysis of compounds was carried out at the Chemistry Department, University College London.

3-Bromopyridine-4-carbaldehyde (3). To a THF solution (50 ml) of LDA, prepared from diisopropylamine (1.57 ml, 12 mmol) and *n*-BuLi (4 ml of 2.5 M solution in hexane, 10 mmol), 3-bromopyridine (0.96 ml, 10 mmol) in THF solution (5 ml) was added dropwise at −78°C under argon. The resulting solution was stirred for 10 min at this temperature. A THF solution (10 ml) of DMF (2.32 ml, 30 mmol) was then added. The mixture was stirred for 1 h at −78°C, warming to room temperature over 1 h. The reaction was poured into cold stirred 5% $NaHCO_3$ (50 ml), diluted with diethyl ether (100 ml) and the organic layer was separated. The aqueous layer was extracted with diethyl ether (3×50 ml). The combined organic solution was washed with brine (2×100 ml), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was chromatographed (ethyl acetate:hexane 3:2) to give the *aldehyde* **1** (1.12 g, 60%) as a solid, which was recrystallised from hexane to give white needles, mp 80–82°C (lit.,[10] 82°C). R_f 0.7 (ethyl acetate:hexane 3:2); ν_{max}/cm^{-1} 1693 (CO); δ_H($CDCl_3$) 7.36 (1H, d, *J*=5 Hz, C(5)H), 8.7 (1H, d, *J*=5 Hz, C(6)H), 8.92 (1H, s, C(2)H), 10.37 (1H, s, CHO); δ_C($CDCl_3$) 122.1 (C(5)H), 122.8 (C(3)Br), 138.7 (C(4)), 149.4 (C(6)H), 154.0 (C(2)H), 190.7 (CO); *m*/*z* 187/185 (60%, M^+), 106 (100%, M^+-Br).

3-Bromo-4-(but-3-en-1-ol)pyridine (7) (general procedure). 3-Bromo-pyridine-4-carbaldehyde **3** (0.372 g, 2 mmol) was added to a stirred mixture of allylbromide (0.43 ml, 5 mmol) and activated zinc powder (0.523 g, 8 mmol) in THF (10 ml). The reaction was stirred for 3 h at room temperature, quenched with saturated $NaHCO_3$ and filtered through a celite plug which was washed with diethyl ether. The aqueous layer was extracted with diethyl ether (3×50 ml) and the combined organic extracts were washed with brine (2×50 ml), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was chromatographed (ethyl acetate:-hexane 2:1) to give the *alcohol* **7** (0.397 g, 87%) as a brown-red oil. R_f 0.52 (ethyl acetate:hexane 2:1); ν_{max}/cm^{-1} 3290 (OH), 1641 (C=C), 1587 (pyr-C=C); δ_H($CDCl_3$) 2.31 (1H, m, C(2′)H), 2.66 (1H, m, C(2′)H, 5.04 (1H, dd, *J*=8 and 3 Hz, C(1′)H), 5.20 (2H, m, C(4′)H), 5.86 (1H, m, C(3′)H), 7.53 (1H, d, *J*=5 Hz, C(5)H), 8.49 (1H, d, *J*=5 Hz, C(6)H), 8.6 (1H, s, C(2)H); δ_C($CDCl_3$) 41.3 (C(2′)H), 70.8 (C(1′)H), 119.5 (C(4′)H), 119.9 (C(3)Br), 122.2 (C(5)H), 133.3 (C(3′)H, 148.5 (C(6)H), 151.6 (C(2)H), 151.8 (C(4)); *m*/*z* 229/227 (73%, M^+), 188/186 (100%, $M^+-CH_2CH=CH_2$), 148 (55%, M^+-Br); Found: M^+, 228.9927. $C_9H_{10}{}^{81}BrON$ requires M^+, 228.9927.

3-Bromo-4-(2,2-dimethyl-but-3-en-1-ol)pyridine (8). 3-Bromo-pyridine-4-carbaldehyde **3** (0.2 g, 1.07 mmol) was added to a stirred mixture of prenyl bromide (0.25 ml, 2.15 mmol) and activated zinc powder (0.4 g, 6.15 mmol) in THF (10 ml) following the same procedure for **7**. The residue was purified by flash chromatography (ethyl acetate: hexane 2:1) to give the *title compound* **8** (0.180 g, 66%) as an oil. R_f 0.55 (ethyl acetate:hexane 2:1); ν_{max}/cm^{-1} 3300 (OH), 1637 (C=C), 1580 (pyr-C=C); δ_H($CDCl_3$) 0.93 (3H, s, C(2′)CH_3), 1.03 (3H, s, C(2′)CH_3), 4.83 (1H, s, C(1′)H), 4.86 (1H, dd, *J*=17.5 and 1.1 Hz, C(4′)H), 5.00 (1H, dd, *J*=10.7 and 1.1 Hz, C(4′)H), 5.88 (1H, dd, *J*=10.7 and 1.1 Hz, C(3′)H), 7.32 (1H, dd, *J*=5 Hz, C(5)H), 8.20 (1H, d, *J*=5 Hz, C(6)H), 8.37 (1H, s, C(2)H); δ_C($CDCl_3$) 21.9 (C(2′)CH_3), 24.2 (C(2′)CH_3), 43.1 (C(2′)), 76.8 (C(1′)H), 114.0 (C(4′)H), 122.4 (C(3)Br), 124.8 (C(5)H), 143.5 (C(3′)H), 147.0 (C(6)H), 150.7 (C(2)H), 151.1 (C(4)); *m*/*z* 257/255 (35%, M^+), 188/186 (100%, $M^+-CMe_2CH=CH_2$); Found: M^+, 255.0261. $C_{11}H_{14}{}^{79}BrON$ requires M^+, 255.0259.

3-Bromo-4-(cyclohex-2-enyl-methanol)pyridine (9). 3-Bromo-pyridine-4-carbaldehyde **3** (0.15 g, 0.8 mmol) was added to a stirred mixture of 3-bromocyclohexene (0.184 g, 1.6 mmol) and activated zinc powder (0.3 g, 4.28 mmol) in THF (10 ml) following the same procedure for as **7**. The residue was purified by flash chromatography (ethyl acetate:hexane 2:1) to give the *title compound* **9** (0.132 g, 60%) as a 2:1 mixture of diastereoisomers. R_f 0.55 (ethyl acetate:hexane 2:1); ν_{max}/cm^{-1} 3280 (OH), 1645 (C=C), 1588 (pyr-H); *m*/*z* 269/267 (28%, M^+), 188/186 (100%, $M^+-C_6H_9$); Found: M^+, 267.0250. $C_{12}H_{14}{}^{79}BrON$ requires M^+, 267.0259. *Major isomer:* δ_H($CDCl_3$) 1.52–1.75 (4H, m, C(6′)H and C(7′)H), 1.96 (2H, m, C(5′)H), 2.66 (1H, m, C(2′)H), 4.95 (1H, d *J*=4 Hz, C(1′)H), 5.48 (1H, m, C(4′)H), 5.93 (1H, m, C(3′)H), 7.44 (1H, d, *J*=5 Hz, C(5)H), 8.43 (1H, d, *J*=5 Hz, C(6)H), 8.57 (1H, s, C(2)H); δ_C($CDCl_3$) 21.3, 22.1 and 25.1 (cyclohexene), 40.0 (C(2′)H), 74.4 (C(1′)H), 120.4 (C(3)Br), 123.4 (C(5)H), 127.5 and 132.5 (C(4′)H and C(3′)H), 148.2 (C(6)H), 150.4 (C(4)), 151.8 (C(2)H). *Minor isomer:* δ_H($CDCl_3$) 1.52–1.75 (4H, m, C(6′)H and C(7′)H), 1.96 (2H, m, C(5′)H), 2.56 (1H, m, C(2′)H), 4.81 (1H, d *J*=4 Hz, C(1′)H), 5.42 (1H, m, C(3′)H), 5.93 (1H, m, C(3′)H), 7.38 (1H, d, *J*=5 Hz, C(5)H), 8.44 (1H, d, *J*=5 Hz, C(6)H), 8.58 (1H, s, C(2)H); δ_C($CDCl_3$) 21.7, 25.1 and 26.7 (cyclohexene), 40.6 (C(2′)H), 74.9 (C(1′)H), 122.9 (C(3)Br), 124.1 (C(5)H), 127.5 (C(4′)H), 132.5 (C(3′)H, 148.4 (C(6)H), 150.0 (C(4)), 151.9 (C(2)H).

3-Bromo-4-(2-methyl-but-3-en-1-ol)pyridine (10). 3-Bromo-pyridine-4-carbaldehyde **3** (0.1 g, 0.53 mmol) was added to a stirred mixture of 1-bromo-2-butene (0.15 ml, 1.34 mmol) and activated zinc powder (0.4 g, 6.15 mmol) in THF (5 ml)

following the same procedure as for **7**. The residue was purified by flash chromatography (ethyl acetate:hexane 2:1) to give the *title compound* **10** (0.100 g, 53%) as a 7:6 mixture of diastereoisomers. R_f 0.47 (ethyl acetate:hexane 2:1); ν_{max}/cm^{-1} 3250 (OH), 1632 (C=C), 1591 (pyr-C=C); *m/z* 243/241 (45%, M^+), 188/186 (100%, $M^+-C_4H_7$); Found: M^+, 241.0103. $C_{10}H_{12}{}^{79}BrNO$ requires M^+, 241.0102. *Major isomer:* $\delta_H(CDCl_3)$ 0.94 (3H, d *J*=7 Hz, C(2′)CH_3), 2.72 (1H, m, C(2′)H), 4.87–5.15 (3H, m, C(1′)H and C(4′)H), 5.95 (1H, m, C(3′)H), 7.49 (1H, d, *J*=5 Hz, C(5)H), 8.44 (1H, d *J*=5 Hz, C(6)H), 8.59 (1H, s, C(2)H); $\delta_C(CDCl_3)$ 12.1 (C(2′)CH_3), 41.8 (C(2′)H), 74.2 (C(1′)H), 117.6 (C(4′)H), 120.9 (C(3)Br), 123.3 (C(5)H), 137.9 (C(3′)H), 147.9 (C(6)H), 151.2 (C(4)), 151.5 (C(2)H). *Minor isomer:* $\delta_H(CDCl_3)$ 1.12 (3H, d, *J*=7 Hz, C(2′)CH_3), 2.70 (1H, m, C(2′)H), 4.87–5.15 (3H, m, C(1′)H and C(4′)H), 5.73 (1H, m, C(3′)H), 7.40 (1H, d, *J*=5 Hz, C(5)H), 8.44 (1H, d, *J*=5 Hz, C(6)H), 8.58 (1H, s, C(2)H); $\delta_C(CDCl_3)$ 16.8 (C(2′)CH_3), 43.9 (C(2′)H), 74.8 (C(1′)H), 116.1 (C(4′)H), 120.6 (C(3)Br), 123.5 (C(5)H), 140.1 (C(3′)H), 148.0 (C(6)H), 151.2 (C(4)), 151.4 (C(2)H).

3-Bromo-4-(2-phenyl-but-3-en-1-ol)pyridine (11). 3-Bromopyridine-4-carbaldehyde **3** (0.1 g, 0.53 mmol) was added to a stirred mixture of 1-bromo-3-phenyl-2-propene (0.234 g, 1.34 mmol) and activated zinc powder (0.4 g, 6.15 mmol) in THF (5 ml) following the same procedure as for **7**. The residue was purified by flash chromatography (ethyl acetate:hexane 2:1) to give the *title compound* **11** (0.097 g, 60%) as a 5:1 mixture of diastereoisomers. R_f 0.41 (ethyl acetate:hexane 2:1); *m/z* 305/303 (22%, M^+), 188/186 (30%, $M^+-C_9H_9$), 117 (100%); Found: M^+, 303.0234. $C_{15}H_{14}{}^{79}BrNO$ requires M^+, 303.0259. *Major isomer:* $\delta_H(CDCl_3)$ 3.76 (1H, m, C(2′)H), 4.87–5.11 (2H, m, C(4′)H), 5.24 (1H, d, *J*=4 Hz, C(1′)H), 6.25 (1H, m, C(3′)H), 7.22–7.32 (5H, m, C(Ar)H), 7.47 (1H, d, *J*=5 Hz, C(5)H), 8.43 (1H, d, *J*=5 Hz, C(6)H), 8.55 (1H, s, C(2)H); $\delta_C(CDCl_3)$ 54.6 (C(2′)), 75.2 (C(1′)H), 119.4 (C(4′)H), 120.8 (C(3)Br), 123.7 (C(5)H), 127.2–129.1 (5×C(Ar)H), 134.3 (C(3′)H), 140.9 (C(Ar)), 147.8 (C(6)H), 150.6 (C(4)), 151.3 (C(2)H). *Minor isomer:* $\delta_H(CDCl_3)$ 3.77 (1H, m, C(2′)H), 4.87–5.11 (2H, m, C(4′)H), 5.37 (1H, d, *J*=6 Hz, C(1′)H), 6.20 (1H, m, C(3′)H), 7.11–7.16 (5H, m, C(Ar)H), 7.38 (1H, d, *J*=6 Hz, C(5)H), 8.30 (1H, d, *J*=6 Hz, C(6)H), 8.59 (1H, s, C(2)H); $\delta_C(CDCl_3)$ 54.5 (C(2′)), 75.3 (C(1′)H), 119.5 (C(4′)H), 120.6 (C(3)Br), 123.3 (C(5)H), 127.2–129.1 (5×C(Ar)H), 133.8 (C(3′)H), 140.7 (C(Ar)), 147.6 (C(6)H), 150.7 (C(4)), 151.2 (C(2)H).

3-Bromo-4-(but-3-yn-1-ol)pyridine (12). 3-Bromo-4-formylpyridine (**3**, 0.93 g, 5 mmol) was added to a stirred mixture of propargyl bromide (1.39 ml, 12.5 mmol) and activated zinc powder (1.3 g, 20 mmol) in THF (25 ml) following the same procedure as for **7**. The residue was purified by flash chromatography (ethyl acetate:hexane 2:1) to give the *alcohol* **12** (0.928 g, 82%) as a solid, which was recrystallised from hexane–ethyl acetate to give colourless cubes, mp 91–92°C. R_f 0.39 (ethyl acetate:hexane 2:1); ν_{max}/cm^{-1} 3238 (CCH), 3140 (OH), 1587 (pyr-C=C); $\delta_H(CDCl_3)$ 2.11 (1H, t, *J*=2 Hz, C(4′)H), 2.55 (1H, ddd, *J*=17, 7 and 2 Hz, C(2′)H), 2.84 (1H, ddd, *J*=17, 4 and 2 Hz, C(2′)H), 5.16 (1H, dd, *J*=7 and 4 Hz, C(1′)H), 7.60 (1H, d, *J*=5 Hz, C(5)H), 8.50 (1H, d, *J*=5 Hz, C(6)H), 8.60 (1H, s, C(2)H); $\delta_C(CDCl_3)$ 27.1 (C(2′)H), 69.8 (C(4′)H), 71.8 (C(1′)H), 79.2 (C(3′)), 119.8 (C(3)Br), 122.4 (C(5)H), 148.4 (C(6)H), 150.4 (C(4)H), 151.5 (C(2)H); *m/z* 225 (42%, M^+) 186 (100%, M^+-CH_2CCH); Found: M^+, 226.9769. $C_9H_8{}^{81}BrNO$ requires M^+, 226.9770. Found: C, 47.51; H, 3.86; N, 6.02. C_9H_8BrNO requires C, 47.82; H, 3.57; N, 6.20.

6,7-Dihydro-7-methyl-5*H*-[2]pyrindin-5-ol (13) (general procedure). Tributyltin hydride (0.14 ml, 0.53 mmol) was added to a solution of **7** (100 mg, 0.44 mmol) in toluene (20 ml) and heated to 110°C under argon. AIBN (10% in mole) was added and the mixture heated under reflux under argon for 3 h. After cooling, the toluene was removed under reduced pressure. The crude product was purified by flash chromatography (hexane followed by hexane:ethyl acetate 1:2) to give the *cyclised product* **13** (56 mg, 86%) as a 3:1 mixture of diastereoisomers. R_f 0.26 (ethyl acetate); ν_{max}/cm^{-1} 3149 (OH), 1605 (pyr-C=C); *m/z* 149 (79%, M^+), 148 (67%, M^+-H), 132 (77%, M^+-OH), 116 (100%); Found: M^+, 149.0839. $C_9H_{11}NO$ requires M^+, 149.0841. **13a**: $\delta_H(CDCl_3)$ 1.36 (3H, d, *J*=7 Hz, C(7)CH_3), 1.54 (1H, m, C(6)H), 2.75 (1H, m, C(6)H), 3.11 (1H, dd, *J*=16 and 7 Hz, C(7)H), 5.18 (1H, t, *J*=8 Hz, C(5)H), 7.35 (1H, d, *J*=5 Hz, C(3)H), 8.41 (2H, br, C(2)H and C(4)H); $\delta_C(CDCl_3)$ 19.5 (C(7)CH_3), 34.8 (C(7)H), 45.5 (C(6)H), 74.0 (C(5)H), 119.0 (C(3)H), 142.6 (C(7a)), 144.7 (C(4)H), 147.3 (C(2)H), 155.0 (C(5a)). **13b**: $\delta_H(CDCl_3)$ 1.28 (3H, d, *J*=7 Hz, C(7)CH_3), 2.02 (1H, m, C(6)H), 2.26 (1H, m, C(6)H), 3.46 (1H, q, *J*=7 Hz, C(7)H), 5.29 (1H, dd, *J*=7 and 4 Hz, C(5)H), 7.35 (1H, d, *J*=5 Hz, C(3)H), 8.41 (2H, br, C(2)H and C(4)H); $\delta_C(CDCl_3)$ 20.5 (C(7)CH_3), 35.4 (C(7)H), 44.2 (C(6)H), 74.0 (C(5)H), 119.7 (C(3)H), 144.0 (C(7a)), 145.5 (C(6)H), 147.4 (C(2)H), 153.8 (C(5a)).

6,7-Dihydro-6,6,7-trimethyl-5*H*-[2]pyrindin-5-ol (14) and 6,6-dimethyl-5-hydroxy-5,6,7,8-tetrahydroisoquinoline (15). Tributyltin hydride (0.10 ml, 0.40 mmol) and AIBN (10% in mole) was added to a solution of **8** (84 mg, 0.33 mmol) in refluxing toluene (15 ml) for 3 h following the same procedure as for **13**. The crude product was purified by flash chromatography (hexane followed by hexane:ethyl acetate 1:2) to give the *cyclised products* **14** and **15** (oil, 37 mg, 63%) as a mixture of diastereoisomers and regioisomers in a ratio 8:5:3. R_f 0.18 (ethyl acetate:hexane 2:1); ν_{max}/cm^{-1} 3290 (OH), 1582 (pyr-C=C); *m/z* 177 (88%, M^+), 144 (100%, $M^+-(H_2O+CH_3)$), 134 (89%, $M^+-C_3H_7$); Found: M^+, 177.1153. $C_{11}H_{15}NO$ requires M^+, 177.1153. **14a**: $\delta_H(CDCl_3)$ 0.94 (3H, s, C(6)CH_3), 1.07 (3H, s, C(6)CH_3), 1.17 (3H, d, *J*=7.2 Hz, C(7)CH_3), 3.03 (1H, q, *J*=7.2 Hz, C(7)H), 4.68 (1H, s, C(5)H), 7.30 (1H, d, *J*=4.5 Hz, C(3)H), 8.34 (1H, s, C(2)H), 8.38 (1H, d, *J*=4.5 Hz, C(4)H); $\delta_C(CDCl_3)$ 14.1 (C(7)CH_3), 21.3 (C(6)CH_3), 21.4 (C(6)CH_3), 44.9 (C(7)H), 50.9 (C(6)), 81.7 (C(5)H), 119.9 (C(3)), 143.0 (C(7a)), 145.6 (C(4)H), 147.8 (C(2)H), 152.9 (C(5a)). **14b**: $\delta_H(CDCl_3)$ 0.65 (3H, s, C(6)CH_3), 1.24 (3H, s, C(6)CH_3), 1.24 (3H, d, *J*=7.2 Hz, C(7)CH_3), 2.73–3.81 (1H, m, C(7)H), 4.74 (1H, s, C(5)H), 7.28 (1H, d, *J*=4.5 Hz, C(3)H), 8.29 (1H, s, C(2)H), 8.39 (1H, d, *J*=4.5 Hz, C(4)H); $\delta_C(CDCl_3)$ 11.7 (C(7)CH_3), 14.4 (C(6)CH_3), 24.1 (C(6)CH), 44.4 (C(7)H), 50.9 (C(6)), 82.3 (C(5)H), 118.5 (C(3)H), 140.4 (C(7a)), 144.1 (C(4)H), 147.7 (C(2)H), 153.7 (C(5a)). **15**: $\delta_H(CDCl_3)$

0.92 (3H, s, C(6)CH_3), 1.05 (3H, s, C(6)CH_3), 1.57–1.65 (2H, m, C(7)H), 1.75–1.82 (1H, m, C(8)H), 2.73–2.81 (1H, m, C(8)H), 4.68 (1H, s, C(5)H), 7.42 (1H, d, J=5 Hz, C(3)H), 8.31 (1H, s, C(2)H), 8.38 (1H, d, J=5 Hz, C(4)H); δ_C($CDCl_3$) 20.3 (C(6)CH_3), 22.9 (C(7)H), 26.7 (C(6)CH_3), 32.9 C(8)H), 33.9 (C(6)), 75.4 (C(5)H), 122.6 (C(3)H), 131.6 (C(8a)), 146.8 (C(4)H), 146.9 (C(2)H), 149.6 (C(5a)).

5a,6,7,8,9,9a-Hexahydro-5*H*-ideno[2]-pyridin-5-ol (16). Tributyltin hydride (0.11 ml, 0.44 mmol) and AIBN (10% in mole) was added to a solution of **9** (100 mg, 0.37 mmol) in refluxing toluene (10 ml) for 3 h following the same procedure as for **13**. The crude product was purified by flash chromatography (hexane followed by hexane:ethyl acetate 1:2) to give the *cyclised product* **16** (oil, 30 mg, 42%) as a 3:1 mixture of diastereoisomers. R_f 0.14 (ethyl acetate:hexane 2:1); ν_{max}/cm^{-1} 3300 (OH), 1580 (pyr-C=C); *m*/*z* 189 (15%, M^+), 171 (20%), 143 (42%), 113 (40%), 100 (100%); Found: M^+, 189.1155. $C_{12}H_{15}NO$ requires M^+, 189.1153. **16a**: δ_H($CDCl_3$) 1.18–1.67 (8H, m, cyclohexane), 2.27 (1H, m, C(9a)H), 3.17–3.23 (1H, m, C(5a)H), 5.00 (1H, d, J=7.8 Hz, C(5)H), 7.36 (1H, d, J=5 Hz, C(3)H), 8.44 (1H, s, C(2)H), 8.46 (1H, d J=5 Hz, C(4)H); δ_C($CDCl_3$) 21.1, 22.9, 23.4 and 29.1 (C(cyclohexane)), 38.9 (C9(a)), 48.2 (C(5a)), 75.5 (C(5)H), 118.7 (C(3)H), 143.0 (C(2a)), 144.1 (C(4)H), 147.0 (C(2)H), 152.3 (C(3a)). **16b**: δ_H($CDCl_3$) 1.18–1.67 (8H, m, cyclohexane), 2.27 (1H, m, C(9a)H), 3.17–3.23 (1H, m, C(5a)H), 5.15 (1H, d, J=6 Hz, C(5)H), 7.35 (1H, d, J=4 Hz, C(3)H), 8.41 (1H, s, C(2)H), 8.49 (1H, d, J=4 Hz, C(4)H); δ_C($CDCl_3$) 20.6, 23.0, 24.1 and 25.8 (C(cyclohexane)), 38.1 (C(9a)), 45.6 (C(5a)), 76.3 (C(5)H), 118.0 (C(3)H), 143.4 (C(2a)), 144.5 (C(4)H), 146.9 (C(2)H), 152.3 (C(3a)).

6,7-Dihydro-7-methylene-5*H*-[2]pyrindin-5-ol (17). Tributyltin hydride (0.52 ml, 1.87 mmol) was added to a solution of **12** (0.352 g, 1.55 mmol) in toluene (70 ml) and after being heated to 110°C under argon, AIBN (10% in mole) was added and the mixture continued to be refluxed under argon for 2 h, following the same procedure as for **13**. Purification by flash chromatography (hexane followed by hexane:ethyl acetate 1:3) give the *cyclised product* and reduced starting material **18** (0.192 g, 84%, 10:1 mixture). Recrystallisation from hexane–ethyl acetate give pure **17** (0.131 g, 57%) as colourless needles, mp 99–100°C. R_f 0.2 (ethyl acetate:hexane 3:1); ν_{max}/cm^{-1} 3152 (OH), 1645 (C=C), 1602 (pyr-C=C); δ_H($CDCl_3$) 2.68 (1H, ddt, J=17, 5 and 2 Hz, C(6)H), 3.19 (1H, ddt, J=17, 7 and 2 Hz, C(6)H), 5.19 (1H, t, J=2 Hz, C(7)CH_2), 5.28 (1H, dd, J=7 and 5 Hz, C(5)H), 5.60 (1H, t, J=2 Hz, C(7)CH_2), 7.39 (1H, d, J=5 Hz, C(3)H), 8.38 (1H, d, J=5 Hz, C(4)H), 8.66 (1H, s, C(2)H); δ_C($CDCl_3$) 42.3 (C(6)H), 72.7 (C(5)H), 106.5 (C(7)CH_2), 120.0 (C(3)H), 135.9 (C(7)), 143.1 (C(4)H), 143.8 (C(7a)), 148.7 (C(2)H), 155.2 (C(3a)); *m*/*z* 147 (100%, M^+), 130 (14%, M^+-OH); Found: M^+, 147.0697. C_9H_9NO requires M^+, 147.0684; Found: C, 73.33; 6.10; N, 9.33. C_9H_9NO requires C, 73.45; H, 6.16; N, 9.52.

3-Bromo-4-(1-*tert*-butyldimethylsilyloxy-but-3-enyl)-pyridine (19). A mixture of **7** (0.228 g, 1 mmol), *tert*-butyldimethylsilyl chloride (0.19 g, 1.2 mmol) and imidazole (0.17 g, 2.5 mmol) in DMF (5 ml) was stirred at room temperature for 4 days. The reaction mixture was poured into water and extracted with diethyl ether (3×50 ml). The organic layer was washed with brine (2×50 ml), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was chromatographed (hexane:ethyl acetate 2:1) to give the *protected alcohol* **19** (0.285 g, 83%) as a yellow oil. R_f 0.58 (hexane:ethyl acetate 2:1); ν_{max}/cm^{-1} 1640 (C=C), 1577 (pyr-C=C); δ_H($CDCl_3$) −0.98 (3H, s, $(CH_3)_2$Si), 0.07 (3H, s, $(CH_3)_2$Si), 0.89 (9H, s, $(CH_3)_3$C), 2.28–2.37 (1H, m, C(2′)H), 2.45 (1H, m, C(2′)H), 4.99–5.01 (3H, m, C(4′)H) and C(1′)H), 5.82 (1H, m, C(3′)H), 7.47 (1H, d, J=5 Hz, C(5)H), 8.49 (1H, d, J=5 Hz, C(6)H), 8.63 (1H, s, C(2)H); δ_C ($CDCl_3$) −4.9 ((CH_3)$_2$Si), 18.1 ((CH_3)$_3$C–Si), 25.7 ((CH_3)$_3$C–Si), 42.4 (C(2′)H), 72.5 (C(1′)H), 118.1 (C(4′)H), 119.2 (C(3)Br), 122.9 (C(5)H), 133.7 (C(3′)H), 148.2 (C(6)H), 151.5 (C(2)H), 152.7 (C(4)); *m*/*z* 343/341 (13%, M^+), 302/300 (85%, $M^+-CH_2CH=CH_2$), 286/284 (100%, $M^+-C(CH_3)_3$); Found: M^+, 341.0799. $C_{15}H_{24}{}^{79}BrNOSi$ requires M^+, 341.0811.

6,7-Dihydro-7-methyl-5-*tert*-butyldimethylsilyloxy-5*H*-[2]pyrindine (20). Tributyltin hydride (0.14 ml, 0.55 mmol) was added to a solution of **19** (156 mg, 0.46 mmol) in toluene (20 ml) and after being heated to 110°C under argon, AIBN (10% in mole) was added and the mixture continued to be refluxed under argon for 3 h, following the same procedure as for **13**. The crude product was purified by flash chromatography (hexane followed by hexane:ethyl acetate 2:1) to give the *cyclised product* **20** (120 mg, 0.46 mmol, quantitative yield) as an inseparable mixture. R_f 0.37 (hexane:ethyl acetate 2:1); ν_{max}/cm^{-1} 1600 (pyr-C=C); *m*/*z* 206 (94%, $M^+-(CH_3)_3C$), 132 (100%, M^+-TBDMSO). *cis*-**20**: δ_H($CDCl_3$) 0.16 (6H, s, Si$(CH_3)_2$), 0.97 (9H, s, $(CH_3)_3$C), 1.39 (3H, d, J=7 Hz, C(7)CH_3), 1.60 (1H, m, C(6)H), 2.65 (1H, m, C(6)H), 3.10 (1H, m, C(7)H), 5.14 (1H, t, J=8 Hz, C(5)H), 7.22 (1H, d, J=5 Hz, C(3)H), 8.48 (2H, br, C(2)H and C(4)H); δ_C($CDCl_3$) 13.6 (Si(CH_3)$_2$), 18.2 (Si$C(CH_3)_3$), 19.3 (C(7)CH_3), 25.8 ((CH_3)$_3$C), 34.7 (C(7)H), 46.0 (C(6)H), 74.7 (C(5)H), 118.6 (C(3)H), 142.7 (C(7a)), 145.1 (C(4)H), 147.8 (C(2)H), 154.6 (C(5a)). *trans*-**20**: δ_H($CDCl_3$) 0.19 (6H, s, Si$(CH_3)_2$), 0.93 (9H, s, $(CH_3)_3$C), 1.27 (3H, d, J=7 Hz, C(7)CH_3), 2.03 (1H, m, C(6)H), 2.18 (1H, m, C(6)H), 3.46 (1H, m, C(7)H), 5.30 (1H, t, J=8 Hz, C(5)H), 7.22 (1H, d, J=5 Hz, C(3)H), 8.48 (2H, br, C(2)H and C(4)H); δ_C($CDCl_3$) 13.6 (Si(CH_3)$_2$), 18.2 (Si$C(CH_3)_3$), 21.0 (C(7)CH_3), 25.9 ((CH_3)$_3$C), 35.4 (C(7)H), 44.6 (C(6)H), 74.8 (C(5)H), 118.8 (C(3)H), 142.6 (C(7a)), 145.9 (C(4)H), 147.9 (C(2)H), 154.8 (C(5a)).

6,7-Dihydro-7-methyl-5*H*-[2]pyrindin-5-ol (13) from 20. Tetra-*n*-butylammonium fluoride (0.46 ml of a 1 M solution in THF, 0.45 mmol) was added to a solution of **20** (60 mg, 0.23 mmol) in THF (5 ml) at 0°C under argon. The mixture was stirred for 15 min at that temperature and at 25°C overnight. The reaction was quenched with water (5 ml), extracted with diethyl ether (3×10 ml), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography (2:1 ethyl acetate:hexane) to give the *deprotected alcohol* **13** (30 mg, 88%) as a 3:1 mixture of diastereoisomers (see above for spectral data).

3-Bromo-4-(butan-1-ol)pyridine (21). To a THF solution (50 ml) of LDA, prepared from diisopropylamine (1.57 ml, 12 mmol) and *n*-BuLi (4 ml of 2.5 M solution in hexane, 10 mmol), 3-bromopyridine **4** (0.96 ml, 10 mmol) in THF solution (5 ml) was added dropwise at −78°C under argon. The resulting solution was stirred for 10 min at this temperature. A THF solution (10 ml) of butyraldehyde (2.7 ml, 30 mmol) was then added. The mixture was stirred for 1 h at −78°C, warming to room temperature over 1 h. The reaction was poured into cold stirred 5% $NaHCO_3$ (50 ml), diluted with diethyl ether (100 ml) and the organic layer was separated. The aqueous layer was extracted with ethyl acetate (3×50 ml). The combined organic solution was washed with brine (2×100 ml), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was chromatographed (ethyl acetate:hexane 2:1) to give the *alcohol* **21** (2.00 g, 87%) as a brown/red oil. R_f 0.53 (ethyl acetate:-hexane 2:1); ν_{max}/cm^{-1} 3333 (OH), 1583 (pyr-C=C); $\delta_H(CDCl_3)$ 0.97 (3H, t, *J*=7 Hz, C(4′)H), 1.49–1.66 (2H, m, C(3′)H), 1.69–1.75 (2H, m, C(2′)H), 5.00 (1H, dd, *J*=5 and 4 Hz, C(1′)H), 7.52 (1H, d, *J*=5 Hz, C(5)H), 8.45 (1H, d, *J*=5 Hz, C(6)H), 8.58 (1H, s, C(2)H); $\delta_C(CDCl_3)$ 13.8 (C(4′)H), 18.8 (C(3′)H), 39.2 (C(2′)H), 71.6 (C(1′)H), 120.0 (C(3)Br), 122.2 (C(5)H), 148.4 (C(6)H), 151.5 (C(2)H), 153.2 (C(4)); *m*/*z* 232 (15%, M^++1), 186 (13%, $M^+-CH_2CH_2CH_3$); Found: M^+, 231.0101. $C_9H_{12}{}^{81}BrON$ requires M^+, 231.0082.

5,6-Dihydro-7-hydroxy-5*H*-[2]pyrindin-7-one (23). 7-Methylene-6,7-dihydro-5*H*-[2]pyrindin-5-ol **17** (221 mg, 1.5 mmol) in 5:1 dichloromethane:methanol (90 ml) was ozonised at −78°C. The reaction was monitored by TLC and judged complete after 4 h at −78°C. Dimethyl sulfide (8 ml) was added to the reaction mixture, which was slowly warmed to room temperature overnight. The solvent was then removed under reduced pressure to give a residue, which was dissolved in acetone (2×50 ml). The acetone solution was filtered and evaporated in vacuo. The residue was chromatographed (chloroform:methanol 9:1) to give the *ketone* **23** (154 mg, 69%) as a solid, mp 105–106°C (decomp). R_f 0.31 (chloroform:methanol 9:1); ν_{max}/cm^{-1} 3318 (OH), 1723 (CO), 1602 (pyr-C=C); δ_H(acetone-d_6) 2.54 (1H, dd, *J*=19 and 3 Hz, C(6)H), 3.10 (1H, dd, *J*=19 and 7 Hz, C(6)H), 5.47 (1H, dd, *J*=7 and 3 Hz, C(5)H), 7.78 (1H, d, *J*=5 Hz, C(3)H), 8.82 (1H, d, *J*=5 Hz, C(4)H), 8.87 (1H, s, C(2)H); δ_C(acetone-d_6) 47.4 (C(6)H), 68.3 (C(5)H), 122.1 (C(3)H), 132.6 (C(7a)), 145.8 (C(4)H), 155.1 (C(2)H), 164.7 (C(5a)), 202.7 (C(7)); *m*/*z* 149 (100%, M^+), 132 (21%, M^+-OH); Found: M^+, 149.0472. $C_8H_7NO_2$ requires M^+ 149.0477.

5-Benzyloxy-6,7-dihydro-7-methylene-5*H*-[2]pyrindine (24). 7-Methylene-6,7-dihydro-5*H*-[2]pyrindin-5-ol **17** (100 mg, 0.68 mmol) in THF (2 ml) was added at 0°C to a THF (3 ml) suspension of 35% KH (93 mg, 0.81 mmol) under argon. After the mixture was stirred for 1 h, benzyl bromide (0.12 ml, 1 mmol) was added dropwise. The resulting mixture was stirred at 0°C for 2 h. The mixture was quenched with saturated NH_4Cl (5 ml) and diluted with diethyl ether (5 ml). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (2×10 ml). The combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed (ethyl acetate:hexane 4:3) to give the *protected alcohol* **24**[24] (129 mg, 80%) as an oil. R_f 0.59 (ethyl acetate:hexane 4:3); ν_{max}/cm^{-1} 1647 (C=C), 1597 (pyr-C=C); $\delta_H(CDCl_3)$ 2.82 (1H, ddt, *J*=16,4 and 2 Hz, C(6)H), 3.10 (1H, ddt, *J*=16, 7 and 2 Hz, C(6)H), 4.62 (1H, ABq, *J*=12 Hz, $PhCH_2$), 4.68 (1H, ABq, *J*=12 Hz, $PhCH_2$), 5.07 (1H, dd, *J*=7 and 4 Hz, C(5)H), 5.20 (1H, t, *J*=2 Hz, C(7)CH_2), 5.64 (1H, t, *J*=2 Hz, C(7)CH_2), 7.28–7.39 (6H, m, C(3)H and C(Ar)H), 8.50 (1H, d, *J*=5 Hz, C(4)H), 8.83 (1H, s, C(2)H); $\delta_C(CDCl_3)$ 39.0 (C(6)H), 71.3 (CH_2O), 78.9 (C(5)H), 106.3 (C(7)CH_2), 120.4 (C(3)H), 127.8 (2×C(Ar)H), 127.9 (C(Ar)H), 128.5 (2×C(Ar)H), 136.2 (C(7)), 137.8 (C(Ar)), 144.0 (C(7a)), 148.9(C(2)H), 152.9 (C(5a)).

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