Heteroaryl radicals. Part 1. Synthesis of linear pyridine-fused ring systems by *endo*-selective 2-pyridyl radical cyclizations †

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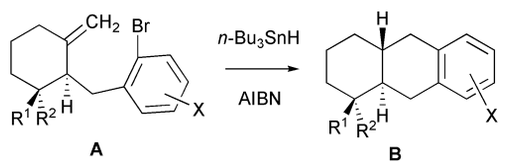
Bu_3SnH-induced 2-pyridyl radicals, derived from the 2-bromopyridinyl-substituted methylenecyclohexane **4** and also the vinyl- and the allyl-cyclohexanols **5** and **6**, undergo *endo*-selective cyclizations to give six-, seven- and eight-membered-ring annulated pyridines **7**, **11** and **12**.

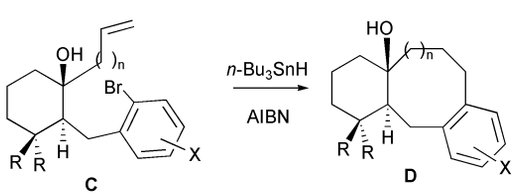
Organotin-mediated intramolecular aryl-radical cyclizations have emerged as useful synthetic methods for benzo-fused ring structures.[1] To a very limited extent such reactions involving heteroaryl radicals have also been successfully used to construct heteroaromatic-fused systems.[1c,d,2] Ring closures in aryl radicals, as in the case of alkyl radicals, readily proceed *via* 5-*exo* and 6-*exo* pathways, generating five- and six-membered rings.[1,3] However, the relatively small steric demand of an aryl radical coupled with its enhanced reactivity, compared with that of alkyl radicals,[4] allow it to enter into uncommon 6-*endo*-[4] and higher-order *exo*- and *endo*-ring annulated products also.[1c,d,5,6] Ghatak and co-workers reported[5a,7–11] a potentially useful route to certain linearly benzannulated six- to nine-membered ring structures through *endo-trig* aryl-radical cyclizations in *n*-Bu_3SnH-induced reactions. For example, radical cyclizations of methylenecyclohexanes **A** produced the *endo*-cyclization products **B** exclusively and in excellent yields[7] [equation (1)].



(1)

$R^1 = R^2$ = H/Me or R^1 = Me; R^2 = CO_2Me; X=H or OR

Similar regioselective aryl-radical cyclizations in cyclohexanols **C** at the terminal olefinic centre, through 7- and 8-*endo-trig* pathways, led to the respective seven[8]- and eight[9]-membered ring-fused tricyclic alcohols **D** [equation (2)]. We report herein



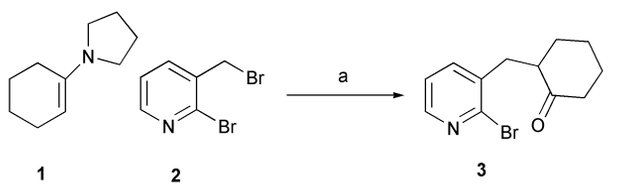
(2)

R = H or Me; X= H or OR; n=0, 1

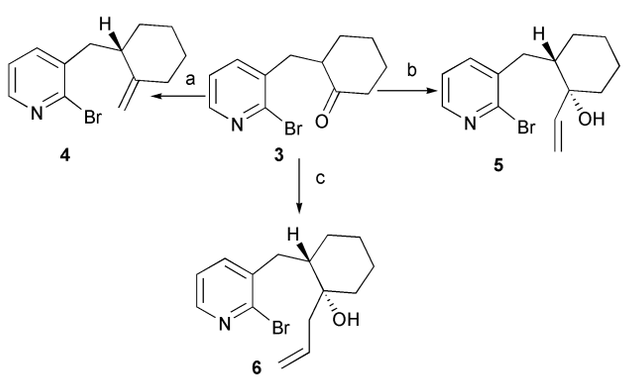
that similarly substituted 2-pyridyl radicals are equally effective in undergoing such cyclization, generating pyridine-fused six-, seven- and eight-membered-ring annulated derivatives.

Results and discussion

The key starting ketone **3** for the three olefinic precursors **4**, **5** and **6** was obtained by alkylation (Scheme 1) of the enamine **1** with 2-bromo-3-(bromomethyl)pyridine (**2**),[12] prepared by a modified route. Wittig olefination of **3** in THF in the presence of *n*-BuLi produced the *exo*-olefin **4** (Scheme 2).



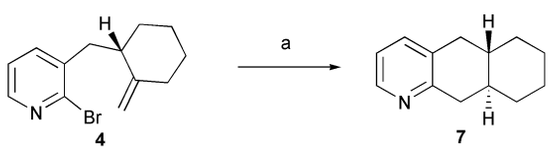
Scheme 1 (a) NaI, EtOH, reflux, 5 h, 65%.



Scheme 2 (a) $MeP^+Ph_3I^-$, *n*-BuLi, THF, 0 °C to room temp., 88%, (b) CH_2=CHMgBr, THF, reflux, 5 h, 48%; (c) allyl bromide, indium, MeOH–H_2O (4 : 1), room temp., 24 h, 55%.

The crystalline cyclohexanols **5** and **6** were obtained by condensation of the ketone **3** in THF with vinylmagnesium bromide and allylmagnesium bromide, respectively; only one diastereoisomer was formed in each case (Scheme 2). The indium Barbier procedure[13] was also equally effective for the allylation of **3** and gave the same alcohol **6**. The assigned stereostructures are based upon analogy.[8,14]

Radical cyclization of the unsaturated bromopyridine **4** with *n*-Bu_3SnH and a catalytic amount of AIBN in refluxing benzene under high dilution afforded exclusively the cyclohexane-ring-annulated pyridine **7** (Scheme 3).



Scheme 3 (a) *n*-Bu_3SnH, AIBN, C_6H_6, reflux, 2 h, 90%.

† This paper has been dedicated to Professor U. R. Ghatak on the occasion of his 70th birthday.

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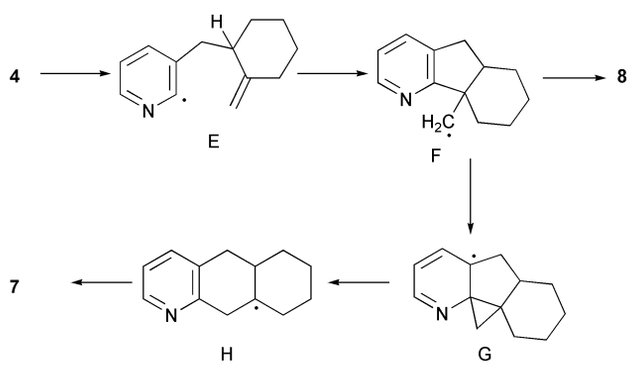
Table 1 Relative yields (%)[a] of products from cyclization of **4** in benzene

[Bu_3SnH], M	**7**[a]	**8**[a]	**9**[a]
0.1[b,d,f]	12	4	84
0.01[b,d,f]	67	8	25
0.002[b,e,f]	100		
0.1[c,d,g]	16	2	82
0.003[b,e,g]	61	1	38

[a] Determined by GC and based on the assumption that the total yield of **7**, **8** and **9** was 100%. [b] Reactions were carried out under reflux. [c] Reaction was carried out at room temperature. [d] *n*-Bu_3SnH was added in one lot. [e] *n*-Bu_3SnH in benzene solution was added dropwise. [f] AIBN was used as radical initiator. [g] Triethylborane was used as radical initiator.

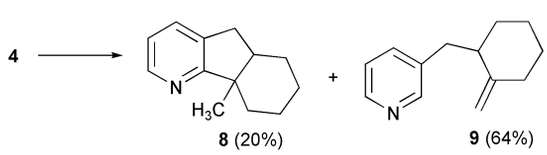
The assigned structure **7** was consistent with ^1H and ^{13}C NMR spectral data. The *trans*-geometry to the newly generated ring junction has been derived by analogy.[7]

To determine whether **7** originates directly by 6-*endo*-cyclization of the heteroaryl radical **E** and/or by an indirect route involving 5-*exo*-ring closure followed by neophyl rearrangement of the resulting radical **F** to radical **H** *via* a cyclopropyl intermediate **G** (Scheme 4), analogous to that



Scheme 4

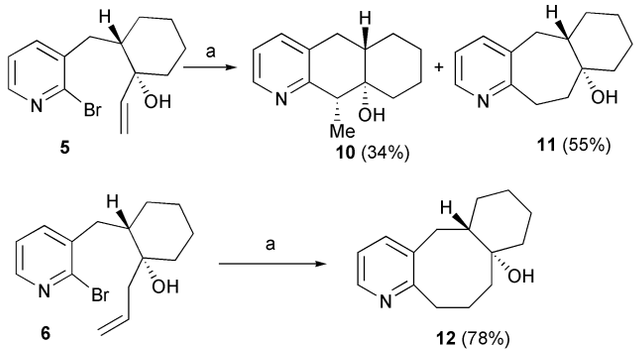
reported[4b,15] for a few aryl-radical cyclizations, some additional experiments were performed. To facilitate identification of the cyclized products, the 5-*exo*-ring-closed compound **8** was prepared by intramolecular Heck reaction of **4** in the presence of sodium formate[16] (Scheme 5). The assigned structure of



Scheme 5 5% $Pd(OAc)_2$, 20% Ph_3P, HCOONa (1 eq), DMF, 85–90 °C, 24 h.

product **8** is based upon ^1H and ^{13}C NMR analysis, and the stereochemistry was deduced by analogy.[16] Cyclization of **4** was carried out with different concentrations of *n*-Bu_3SnH and the products analysed by GC (Table 1). This showed the formation of the *exo* product **8** (in minor amounts) and the debrominated olefin **9** besides the *endo* product **7**, the ratio being dependent on the concentrations employed. The cyclization of **4** with *n*-Bu_3SnH in higher concentration (0.1 M) in the presence of AIBN was found to yield **7**, **8** and **9** in the proportions *ca.* 12 : 4 : 84. Repeating the cyclization with Bu_3SnH in the presence of Et_3B[15] at room temperature gave virtually similar results, though **7** becomes the major product at high dilution. As the *exo*/*endo* ratio depends on the stannane concentration, it is conceivable that at least part of the *endo* product arises *via* rearrangement of the initially generated *exo*-radical **F** (Scheme 4), as suggested[4b] for the cyclization of some alkenyl-aryl radicals.

Cyclization of the vinyl alcohol **5** (Scheme 6) under high



Scheme 6 (a) *n*-Bu_3SnH, AIBN, C_6H_6, reflux, 5 h.

dilution led to a mixture of products from which pure 6- and 7-membered-ring annulated alcohols **10** and **11**, respectively, were isolated in the ratio 1 : 1.6 on chromatography in excellent total yield. The assigned structures of these alcohols are in agreement with the ^1H and ^{13}C NMR spectra. The stereochemistry shown for the benzylic methyl group in **10** has been assigned as it resonates at a downfield position (δ 1.48) comparable to that reported[15,17] in similar benzodecalin derivatives (δ 1.31–1.32; δ 1.10 for the epimer). Cyclization of the 2-pyridyl radical from **5** thus affords the 6-membered-ring product **10** in significant amounts besides the major 7-membered-ring product **11**, unlike that of the aryl radical which led only to 7-membered-ring products under comparable conditions.[8] This is not surprising as there are a number of examples in the aryl-radical cyclizations where subtle variation in the structures of the substrates lead to mixtures of 6-*exo* and 7-*endo* products or exclusively either of these.[5,6,9,16,18]

Reaction of the allyl alcohol **6** (Scheme 6) gave the new product **12** (78%) of the rare[6] 8-*endo* type as the only isolable material. Formation of the 8-*endo* product in preference to the 7-*exo* product parallels the earlier observations in alkyl-[19] and aryl-radical[6,8,11,20] cyclizations.

Conclusions

In conclusion, the intrinsic preference of intramolecular *n*-Bu_3SnH-mediated 2-pyridyl-radical cyclization of methylenecyclohexane or vinyl/allylcyclohexanols for the terminal olefinic carbon centre constitutes an efficient method of preparing pyridine-ring-fused six-, seven- and eight-membered-ring annulated polycyclic compounds which are not easily accessible by classical methodology. Further investigations on the generality of this type of *endo*-selective heteroaryl-radical cyclizations as a potential synthetic entry to a variety of new ring-fused heterocyclic structures of general interest are in progress.

Experimental

Mps recorded for the compounds are uncorrected. NMR spectra of $CDCl_3$ solutions were recorded with Bruker DPX-300 spectrometers. In all cases, chemical shifts are in δ (ppm) relative to TMS as internal standard; *J*-values are given in Hz, and multiplicity is indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, double doublet; br, broad; m, multiplet; *etc*. Protonation levels of the carbons indicated in ^{13}C NMR data were derived from DEPT spectra. Mass spectra were recorded using a JEOL AX-500 mass spectrometer. IR spectra were recorded using a JASCO FT/IR-410. All reagents were of commercial quality and used from freshly opened containers without purification. Organic solvents were dried by standard methods and distilled before use. All the reactions were

performed under N_2 atmosphere. Reaction progress was monitored by thin-layer chromatography (TLC) on precoated aluminium-backed plates (Merck Kieselgel $60F_{254}$) and the spots were visualized by UV light. Anhydrous Na_2SO_4 was used as drying agent during extraction processes. Silica gel (60–120 mesh) was used for column chromatography. Petroleum spirit used was of boiling range 60–80 °C. Bu_3SnH (1 M solution in hexane) was purchased from Aldrich. Ether refers to diethyl ether. Gas chromatographic analyses were performed on an HP-6890A machine using an HP-5 column (30 m × 0.32 mm; film thickness 0.25 μm) with N_2 as carrier gas and the temperature programme was as follows: 150 °C–5 min–2 °C min^{-1}–200 °C–5 min.

2-Bromo-3-(bromomethyl)pyridine (2)

(2-Bromopyridin-3-yl)methanol (2 g, 10.63 mmol), prepared through the $NaBH_4$ reduction of 2-bromopyridine-3-carbaldehyde,[21] was dissolved in CH_2Cl_2 (100 mL). To this solution was added carbon tetrabromide (4.23 g, 12.76 mmol) at −10 °C and the mixture was stirred for 10 minutes. Triphenylphosphine (3.35 g, 12.75 mmol) was then added to it portionwise during 15 minutes at the same temperature. The reaction mixture was further stirred for 30 minutes at −10 °C to complete the reaction (TLC monitor). The reaction mixture was decomposed with saturated aq. NaCl (60 mL) at 0 °C. The organic layer was separated and the aqueous layer was further extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layer was washed with brine, dried, and the solvent was evaporated under reduced pressure. The residual product was chromatographed (EtOAc–petroleum spirit, 4–6%) to give dibromide **2** (2.4 g, 90%) as a colourless oil, which solidified on refrigeration; mp 33–34 °C [reported[12] as an oil, bp 90–91 °C (1 mmHg)]; δ_H 4.56 (2H, s), 7.29 (1H, dd, *J* 7.5 and 4.7 Hz), 7.78 (1H, dd, *J* 7.5 and 1.9 Hz), 8.32 (1H, dd, *J* 4.8 and 1.8 Hz).

2-(2-Bromopyridin-3-ylmethyl)cyclohexanone (3)

A mixture of enamine **1** (4.74 g, 31 mmol), bromide **2** (7.16 g, 28 mmol) and NaI (121 mg, 0.8 mmol) in dry ethanol (75 mL) was heated under reflux for 5 h. Ethanol was removed in a rotary evaporator under reduced pressure, and the residue was diluted with water and extracted with CH_2Cl_2 (50 mL × 3). The combined organic layer was washed with brine, dried, and concentrated. The residual product was chromatographed (EtOAc–petroleum spirit, 5–10%) to give ketone **3** (5 g, 65%); mp 55–56 °C; IR (KBr) ν_{max} 1708 cm^{-1}; δ_H (300 MHz) 1.43–1.49 (1H, m), 1.62–1.73 (2H, m), 1.87–1.90 (1H, m), 2.06–2.13 (2H, m), 2.32–2.40 (2H, m), 2.54 (1H, dd, *J* 14.0 and 6.6 Hz), 2.72–2.78 (1H, m), 3.28 (1H, dd, *J* 13.9 and 6.6 Hz), 7.18 (1H, dd, *J* 7.4 and 4.7 Hz), 7.64 (1H, dd, *J* 7.4 and 1.7 Hz), 8.21 (1H, dd, *J* 4.6 and 1.8 Hz); δ_C (75 MHz) 25.3 (CH_2), 28.1 (CH_2), 34.2 (CH_2), 35.1 (CH_2), 42.3 (CH_2), 50.2 (CH), 122.6 (CH), 137.2 (C), 140.1 (CH), 144.4 (C), 147.8 (CH), 211.7 (CO); MS (EI) *m*/*z* 268 (M^+), 189 (100%), 188, 172, 170, 146, 130, 120, 117, 108; Found: C, 53.94; H, 5.39; N, 4.98. $C_{12}H_{14}BrNO$ requires C, 53.75; H, 5.26; N, 5.22%.

2-Bromo-3-(2-methylenecyclohexylmethyl)pyridine (4)

n-BuLi (1.5 mL of 1.6 M solution in hexane, 3 mmol) was added to a solution of methyltriphenylphosphonium iodide (1.4 g, 3.5 mmol) in dry THF (10 mL) at 0 °C, and the mixture was stirred at the same temperature for 2.5 h. To this solution was added a solution of ketone **3** (268 mg, 1 mmol) in dry THF (10 mL), and the mixture was stirred at 0 °C for 30 minutes and at room temperature for 2 h. Saturated aq. ammonium chloride (20 mL) was added to the reaction mixture and THF was removed in a rotary evaporator under reduced pressure. The residue was extracted with CH_2Cl_2 (20 mL × 3) and the combined organic layer was washed with brine, dried, and concentrated. The crude material was chromatographed on silica gel (EtOAc–petroleum spirit, 1–2%) to give bromoalkene **4** (235 mg, 88%) as a white crystalline solid; mp 53–54 °C; IR (KBr) ν_{max} 1639, 1558 cm^{-1}; δ_H (300 MHz) 1.28–1.73 (6H, m), 2.05–2.14 (1H, m), 2.30–2.38 (1H, m), 2.45–2.51 (1H, m), 2.78 (1H, dd, *J* 13.9 and 8.2 Hz), 3.05 (1H, dd, *J* 13.9 and 6.4 Hz), 4.54 (1H, s), 4.70 (1H, s), 7.17 (1H, dd, *J* 7.4 and 4.6 Hz), 7.43 (1H, dd, *J* 7.5 and 1.6 Hz), 8.21 (1H, dd, *J* 4.4 and 1.8 Hz); δ_C (75 MHz) 24.4 (CH_2), 28.5 (CH_2), 33.1 (CH_2), 35.0 (CH_2), 38.0 (CH_2), 42.5 (CH), 106.6 (CH_2), 122.4 (CH), 137.8 (C), 139.1 (CH), 144.8 (C), 147.5 (CH), 151.3 (C); MS (EI) *m*/*z* 267 (M^+ + 1), 265, 186 (100%), 173, 171, 103; Found: C, 58.54; H, 6.24; N, 5.04. $C_{13}H_{16}BrN$ requires C, 58.66; H, 6.06; N, 5.26%.

2-(2-Bromopyridin-3-ylmethyl)-1-vinylcyclohexanol (5)

A solution of vinyl bromide (9.8 mL of 1 M solution in THF, 10 mmol) was added dropwise to a suspension of magnesium (77.6 mg, 3.2 mg-atm) in dry THF (5 mL) at 0–5 °C during 10 minutes and the mixture was stirred at room temperature until all the magnesium was dissolved. To this solution was added a solution of ketone **3** (280 mg, 1.04 mmol) in dry THF (5 mL) at 0–5 °C during 20 minutes. The reaction mixture was stirred at room temperature for 1 h and then heated under reflux for 5 h. Saturated aq. NH_4Cl (20 mL) was added and THF was removed in a rotary evaporator under reduced pressure. The residual part was extracted with ether (10 mL × 3). The combined organic part was washed with brine, dried, and concentrated. The crude product was chromatographed over silica gel (EtOAc–petroleum sprit, 10–20%) to furnish alcohol **5** (148 mg, 48%) as a white solid; mp 80–81 °C; IR (KBr) ν_{max} 3389, 1653, 1578, 995, 921 cm^{-1}; δ_H (300 MHz) 1.10–1.18 (1H, m), 1.31–1.41 (2H, m), 1.55–1.79 (7H, m), 2.38 (1H, dd, *J* 13.5 and 11.1 Hz), 3.02 (1H, dd, *J* 13.5 and 3.0 Hz), 5.17 (1H, d, *J* 10.8 Hz), 5.35 (1H, d, *J* 17.3 Hz), 6.03 (1H, dd, *J* 17.3 and 10.8 Hz), 7.16 (1H, dd, *J* 7.5 and 4.7 Hz), 7.42 (1H, dd, *J* 4.6 and 1.9 Hz), 8.20 (1H, dd, *J* 7.5 and 1.8 Hz); δ_C (75 MHz) 21.3 (CH_2), 25.6 (CH_2), 26.1 (CH_2), 36.0 (CH_2), 39.4 (CH_2), 43.5 (CH), 74.4 (C), 112.2 (CH_2), 122.4 (CH), 138.1 (C), 139.9 (CH), 144.7 (C), 145.5 (CH), 147.5 (CH); MS (EI) *m*/*z* 297 (M^+ + 1), 295, 242, 240, 227, 225, 216 (100%), 200, 198, 186, 184, 173, 171, 134, 130, 189; Found: C, 56.64; H, 5.91; N, 4.86. $C_{14}H_{18}BrNO$ requires C, 56.77; H, 6.13; N, 4.73%.

1-Allyl-2-(2-bromopyridin-3-ylmethyl)cyclohexanol (6)

Allyl bromide (0.13 mL, 1.5 mmol) was added to a solution of ketone **3** (200 mg, 0.74 mmol) and indium powder (103 mg, 0.9 mg-atom) in MeOH–H_2O (1 : 4; 10 mL) and the mixture was stirred at room temperature for 24 h. Again, identical amounts of allyl bromide and indium powder were added and the mixture was further stirred for another 24 h at room temperature. The reaction mixture was poured into aq. KH_2PO_4 (5%; 50 mL) and was then extracted with EtOAc (50 mL × 3). The combined organic layer was washed with brine, dried, and concentrated. The residue was chromatographed over silica gel (EtOAc–petroleum spirit, 10–12%) to give alcohol **6** (127 mg, 55%) as a white solid; mp 74–75 °C; IR (KBr) ν_{max} 3350, 1639, 1560, 984, 906 cm^{-1}; δ_H (300 MHz) 1.10–1.13 (1H, m), 1.22–1.31 (2H, m), 1.43–1.69 (6H, m), 1.75–1.83 (1H, m), 2.39–2.60 (3H, m), 3.18 (1H, dd, *J* 13.5 and 3.5 Hz), 5.17 (2H, m), 5.87–6.01 (1H, m), 7.18 (1H, dd, *J* 7.4 and 4.6 Hz), 7.46 (1H, dd, *J* 7.4 and 1.8 Hz), 8.20 (1H, dd, *J* 4.6 and 1.8 Hz); δ_C (75 MHz) 21.9 (CH_2), 25.5 (CH_2), 26.8 (CH_2), 35.2 (CH_2), 37.4 (CH_2), 43.5 (CH), 45.4 (CH_2), 73.2 (C), 119.3 (CH_2), 122.9 (CH), 134.0 (CH), 138.6 (C), 140.3 (CH), 145.2 (C), 148.0 (CH); MS (EI) *m*/*z* 311 (M^+ + 1), 309, 268, 270 (100%), 188, 172, 170, 95, 88, 55; Found: C, 57.92; H, 6.21; N, 4.67. $C_{15}H_{20}BrNO$ requires C, 58.07; H, 6.50; N, 4.51%.

General procedure for radical cyclization of the olefins 4–6

To a gently stirred refluxing solution of the appropriate olefin **4**–**6** (0.203 mmol) in degassed dry benzene (80 mL) was added a solution of Bu_3SnH (1.5 eq) and AIBN (6 mg, 0.037 mmol) in degassed dry benzene (20 mL) slowly over a period of *ca.* 3.5 h. After complete addition, the mixture was further refluxed for an additional 2 h. Benzene was removed in a rotary evaporator under reduced pressure. The residual product was taken up in ether (50 mL) – saturated aq. KF (50 mL) and the reaction mixture was stirred vigorously at room temperature for 10 h. The organic phase was separated and the aqueous phase was further extracted with ether. The combined organic phase was washed with brine, dried, and concentrated to give the crude product, which on chromatography (EtOAc–petroleum spirit) yielded pure cyclized product **7**; **10** and **11**; or **12**, respectively.

5,5a,6,7,8,9,9a,10-Octahydrobenzo[*g*]quinoline (7). Following the general procedure, olefin **4** (54 mg, 0.203 mmol) was treated with Bu_3SnH (0.3 mL of 1 M solution in hexane, 0.30 mmol) in the presence of AIBN (6 mg, 0.037 mmol). After work-up, the crude product was chromatographed (EtOAc–petroleum spirit, 3–4%) to give tricycle **7** (34 mg, 90%) as white crystals; mp 44–45 °C; IR (KBr) ν_{max} 2924, 2847, 1572, 1443, 1414, 785 cm^{-1}; δ_H (300 MHz) 1.05–1.25 (2H, m), 1.26–1.57 (4H, m), 1.78 (2H, d, *J* 6.6 Hz), 1.89 (2H, t, *J* 12.4 Hz), 2.41–2.59 (2H, m), 2.75 (1H, dd, *J* 16.7 and 4.6 Hz), 2.98 (1H, dd, *J* 17.3 and 4.6 Hz), 7.01 (1H, dd, *J* 7.5 and 4.6 Hz), 7.31 (1H, d, *J* 7.5 Hz), 8.33 (1H, d, *J* 4.5 Hz); δ_C (75 MHz) 26.0 (CH_2), 26.2 (CH_2), 33.5 (CH_2), 33.7 (CH_2), 36.6 (CH_2), 38.2 (CH), 38.6 (CH), 40.2 (CH_2), 120.8 (CH), 131.8 (C), 136.1 (CH), 146.7 (CH), 157.1 (C); MS (EI) *m*/*z* 187 (M^+, 100%), 172, 158, 144, 130, 118, 107, 91; Found: C, 83.49; H, 9.08; N, 7.52. $C_{13}H_{17}N$ requires C, 83.37; H, 9.15; N, 7.48%.

10-Methyl-5,6,7,8,9,10-hexahydro-5a*H*-benzo[*g*]quinolin-9a-ol (10) and 5,5a,6,7,8,9,10,11-octahydrobenzo[4,5]cyclohepta-[1,2-*b*]pyridin-9a-ol (11). Following the general procedure, olefin **5** (60 mg, 0.203 mmol) was treated with Bu_3SnH (0.3 mL of 1 M solution in hexane, 0.304 mmol) in the presence of AIBN (6 mg, 0.037 mmol). After work-up, the crude product was chromatographed on silica gel. First fraction (EtOAc–petroleum spirit, 20–30%) gave alcohol **10** (15 mg, 34%) as a white solid; mp 144–145 °C; IR (KBr) ν_{max} 3328, 2930, 2863, 1579, 1443, 1387, 1195, 951, 786 cm^{-1}; δ_H (300 MHz) 1.18 (1H, br s), 1.25–1.45 (3H, m), 1.48 (3H, d, *J* 7.0 Hz), 1.52–1.80 (5H, m), 2.13 (1H, br d, *J* 13.6 Hz), 2.57 (1H, dd, *J* 16.8 and 5.3 Hz), 2.71–2.81 (2H, m), 7.03 (1H, dd, *J* 7.5 and 4.7 Hz), 7.33 (1H, d, *J* 7.8 Hz), 8.42 (1H, d, *J* 4.6 Hz); δ_C (75 MHz) 11.1 (CH_3), 21.6 (CH_2), 25.6 (CH_2), 28.8 (CH_2), 32.4 (CH_2), 36.8 (CH_2), 40.1 (CH), 46.7 (CH), 71.2 (C), 120.9 (CH), 131.0 (C), 135.9 (CH), 147.1 (CH), 158.5 (C); MS (FAB) *m*/*z* 218 (M^+ + 1, 100%), 200, 154, 137, 121, 107; Found: C, 77.19; H, 8.96; N, 6.17. $C_{14}H_{19}NO$ requires C, 77.38; H, 8.81; N, 6.45%.

Second fraction (EtOAc–petroleum spirit, 40%) yielded alcohol **11** (24 mg, 55%) as a white solid; mp 169–170 °C; IR (KBr) ν_{max} 3242, 2922, 2852, 1580, 1439, 1100, 919, 794, 762, 710 cm^{-1}; δ_H (300 MHz) 1.20–1.42 (4H, m), 1.49–1.63 (6H, m), 1.69–1.86 (2H, m), 2.02 (1H, d, *J* 14.3 Hz), 2.78 (1H, dd, *J* 14.3 and 6.7 Hz), 3.28 (1H, dd, *J* 14.2 and 10.7 Hz), 3.52 (1H, t, *J* 13.2 Hz), 7.00 (1H, dd, *J* 7.4 and 4.9 Hz), 7.35 (1H, d, *J* 7.1 Hz), 8.26 (1H, d, *J* 4.9 Hz); δ_C (75 MHz) 21.6 (CH_2), 26.5 (CH_2), 30.9 (CH_2), 32.7 (CH_2), 37.3 (CH_2), 41.2 (CH_2), 41.6 (CH_2), 45.8 (CH), 72.5 (C), 121.7 (CH), 136.5 (CH), 137.6 (C), 146.6 (CH), 163.3 (C); MS (FAB) *m*/*z* 218 (M^+ + 1, 100%), 200, 154, 137, 107; Found: C, 77.52; H, 8.61; N, 6.41. $C_{14}H_{19}NO$ requires C, 77.38; H, 8.81; N, 6.45%.

6,7,8,9,10,11,11a,12-Octahydro-5*H*-benzo[4,5]cycloocta[1,2-*b*]pyridin-7a-ol (12). Following the general procedure, olefin **6** (63 mg, 0.203 mmol) was treated with Bu_3SnH (0.3 mL of 1 M solution in hexane, 0.304 mmol) in the presence of AIBN (6 mg, 0.037 mmol). After work-up, the crude product was chromatographed (EtOAc–petroleum spirit, 25–30%) to give alcohol **12** (42 mg, 78%) as white crystals; mp 129 °C; IR (KBr) ν_{max} 3250, 2923, 2852, 1582, 1453, 1272, 1218, 962, 789 cm^{-1}; δ_H (300 MHz) 1.10–1.19 (2H, m), 1.25–1.59 (8H, m), 1.68–1.74 (3H, m), 2.02–2.13 (1H, m), 2.32 (1H, d, *J* 14.3 Hz), 2.82–2.89 (1H, m), 2.98 (1H, dd, *J* 13.5 and 10.4 Hz), 3.21–3.31 (1H, m), 7.05 (1H, dd, *J* 7.5 and 4.8 Hz), 7.42 (1H, dd, *J* 7.6 and 1.2 Hz), 8.38 (1H, dd, *J* 4.7 and 1.4 Hz); δ_C (75 MHz) 21.7 (CH_2), 25.3 (CH_2), 26.1 (CH_2), 31.3 (CH_2), 34.2 (CH_2), 37.4 (CH_2), 38.1 (CH_2), 43.5 (CH_2), 51.1 (CH), 72.9 (C), 121.3 (CH), 136.7 (C), 136.9 (CH), 147.3 (CH), 160.2 (C); MS (FAB) *m*/*z* 232 (M^+ + 1, 100%), 154, 107; Found: C, 78.03; H, 9.24; N, 5.81. $C_{15}H_{21}NO$ requires C, 77.88; H, 9.15; N, 6.05%.

9a-Methyl-5a,6,7,8,9,9a-hexahydro-5*H*-indeno[1,2-*b*]pyridine (8) and 3-(2-methylenecyclohexylmethyl)pyridine (9)

A stirred mixture of the olefin **4** (200 mg, 0.752 mmol), $Pd(OAc)_2$ (8.4 mg, 0.039 mmol), PPh_3 (394 mg, 0.15 mmol) and HCOONa (51 mg, 0.752 mmol) in dry DMF (12 mL), was heated at 85–90 °C for 24 h. The cooled reaction mixture was diluted with water (30 mL) and extracted with ether (30 × 3 mL). The combined organic layer was washed with brine, dried, and evaporated. GC of the crude product showed **8** and **9** to be present in the ratio 1 : 3. The crude product was chromatographed on silica gel. The first fraction (EtOAc–petroleum spirit, 2–4%) gave tricycle **8** (28 mg, 20%) as a colourless oil; IR (neat) ν_{max} 2925, 2853, 1576, 1420, 1371, 1157, 1092, 785 cm^{-1}; δ_H (300 MHz) 1.29 (3H, s), 1.32–1.56 (6H, m), 1.72–1.79 (2H, m), 2.05–2.17 (1H, m), 2.65 (1H, dd, *J* 15.6 and 7.1 Hz), 2.87 (1H, dd, *J* 15.6 and 7.1 Hz), 7.01 (1H, t, *J* 6.0 Hz), 7.49 (1H, d, *J* 7.4 Hz), 8.36 (1H, d, *J* 4.7 Hz); δ_C (75 MHz) 22.5 (CH_2), 23.1 (CH_2), 24.6 (CH_3), 27.4 (CH_2), 33.6 (CH_2), 34.2 (CH_2), 45.2 (CH), 46.0 (C), 121.4 (CH), 133.4 (CH), 136.0 (C), 147.6 (CH), 171.9 (C); MS (EI) *m*/*z* 187 (M^+), 172 (100%), 144, 132, 130; Found: C, 83.65; H, 8.94; N, 7.23. $C_{13}H_{17}N$ requires C, 83.37; H, 9.15; N, 7.48%.

The second fraction (EtOAc–petroleum spirit, 6–10%) gave alkene **9** (90 mg, 64%) as a colourless oil; IR (neat) ν_{max} 2927, 2854, 1643, 1575, 1477, 1424, 1026, 886, 792, 713 cm^{-1}; δ_H (300 MHz) 1.17–1.77 (5H, m), 1.97–2.43 (4H, m), 2.55 (1H, dd *J* 13.7 and 6.2 Hz), 2.99 (1H, dd, *J* 13.7 and 6.2 Hz), 4.56 (1H, s), 4.69 (1H, s), 7.20–7.26 (1H, m), 7.49 (1H, d, *J* 7.8 Hz), 8.44 (2H, d, *J* 4.5 Hz); δ_C (75 MHz) 24.4 (CH_2), 28.5 (CH_2), 32.9 (CH_2), 35.1 (CH_2), 35.9 (CH_2), 44.3 (CH), 106.2 (CH_2), 123.1 (CH), 136.3 (CH), 136.5 (C), 147.2 (CH), 150.4 (CH), 151.8 (C); MS (EI) *m*/*z* 187 (M^+), 103, 101 (100%); Found: C, 83.21; H, 9.63; N, 7.16. $C_{13}H_{17}N$ requires C, 83.37; H, 9.15; N, 7.48%.

Radical cyclization of 4 with Bu_3SnH at 0.1 M concentration

To a solution of **4** (50 mg, 0.188 mmol) in degassed dry benzene (2 mL) were added Bu_3SnH (60 mg, 0.207 mmol) and AIBN (5 mg, 0.02 mmol) and the mixture was heated under reflux for 9 h. After evaporation of the solvent in a rotary evaporator under reduced pressure, ether (20 mL) and saturated aq. KF (20 mL) were added to the residue, and the whole mixture was stirred at room temperature for 24 h. The organic phase was separated, washed with brine, dried, and concentrated. GC analysis of the crude product showed it to be a mixture of **7** (t_R 10.48), **8** (t_R 6.28) and **9** (t_R 8.47) in the proportions 12 : 4 : 84.

Radical cyclization of 4 with Bu_3SnH at 0.01 M concentration

To a solution of **4** (50 mg, 0.188 mmol) in degassed dry benzene (20 mL) were added Bu_3SnH (60 mg, 0.207 mmol) and AIBN (5 mg, 0.02 mmol) and the mixture was heated under reflux for 9 h. After usual work-up, GC analysis of the crude product showed the presence of **7**, **8** and **9** in the proportions 67 : 8 : 25.

Radical cyclization of 4 with Bu_3SnH–Et_3B at room temperature

To a solution of **4** (50 mg, 0.188 mmol) and Bu_3SnH (71 mg, 0.24 mmol) in degassed dry benzene (2.8 mL) was added Et_3B (0.75 ml of 1 M solution in THF, 0.752 mmol) at room temperature. The reaction mixture was stirred at the same temperature for 48 h. After usual work-up, GC analysis of the crude product showed the presence of **7**, **8** and **9** in the proportions 16 : 2 : 82.

Radical cyclization of 4 with Bu_3SnH–Et_3B at reflux

To a gently stirred refluxing solution of the olefin **4** (25 mg, 0.094 mmol) in degassed dry benzene (30 mL) was added a solution of a mixture of Bu_3SnH (0.125 mL of 1 M solution in hexane) and Et_3B (0.38 mL of 1 M solution in THF) in degassed dry benzene (17 mL) slowly over a period of *ca* 3 h. After complete addition, the mixture was further refluxed for an additional 3 h. After usual work-up, GC analysis of the crude product showed the presence of **7**, **8** and **9** in the proportions 61 : 1 : 38.

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