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Novel Routes to Indoles, Indolines, Quinolines and Tetrahydroquinolines from N-(Cyclohexylidene)amines

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Abstract : Cyclohexanones have been converted into a variety of bicyclic azaheterocycles of different oxidation level via a sequence of reactions involving (a) imination, (b) α -alkylation with N,N-disilyl-protected ω -bromoamines, (c) transimination, (d) α -chlorination of the resulting bicyclic imines and (e) dehydrochlorination and/or dehydrogenation. Appropriate choice of the reaction conditions selectively led the reactions to indoles, 7-chloroindoles, 7-chloroindolines, 4,5,6,7-tetrahydroindoles, 8-chloro-1,2,3,4-tetrahydroquinolines, 8-chloroquinolines or quinolines.

INTRODUCTION

Indoles, quinolines and their tetrahydro derivatives are very important compounds as they occur in a large number of natural products and display a variety of physiological activities.^{1,2} Many simple indole derivatives have been found to have antimicrobial or fungistatic activity,¹ while 7-halogenated indoles have been used as drug intermediates³ and as precursor of 7-substituted indole alkaloids.⁴ On the other hand, 1,2,3,4-tetrahydroquinoline derivatives are useful synthetic intermediates for drugs,⁵ agrochemicals⁶ and dyes.⁷

The construction of these skeletons by annelation of a pyrrole or pyridine moiety onto a cyclohexanone derivative is very attractive because of the ready availability of the latter, allowing the introduction of substituents of choice. Cyclic imines are accessible in a straightforward way from aldehydes or ketones via imination, subsequent α -alkylation with 1-(ω -bromoalkyl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentanes⁸ and following transimination.⁹ In the present report, this synthetic methodology is applied to cyclohexanones to give bicyclic imines, which are selectively converted via chlorination, dehydrochlorination or dehydrogenation processes into a large variety of functionalized indole and quinoline derivatives.

RESULTS AND DISCUSSION

Cyclohexanone (1a) and 4-methylcyclohexanone (1b) were converted into the corresponding N-isopropyl imines 2a,b by reaction with isopropylamine (4 equiv.) in the presence of titanium(IV) chloride (0.6 equiv.). Deprotonation of N-(cyclohexylidene)amines 2 with lithium diisopropylamide in THF at 0°C and subsequent reaction of the resulting 1-azaallylic anions with 1-(2-bromoethyl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane⁸ gave the corresponding α -alkylated imines, which underwent N-deprotection with potassium carbo-

nate in methanol under reflux. The transient γ -amino imines underwent spontaneous intramolecular transimination to afford 3,3a,4,5,6,7-hexahydro-2*H*-indoles 3 in 76-77% yield.

It proved to be advantageous to treat the reaction mixture with aqueous oxalic acid in a biphase system water diethyl ether in order to remove the organosilicon side product [MeOSi(Me₂)CH₂CH₂Si(Me₂)OMe] from the acidic extract. Basification with sodium hydroxide regenerated the bicyclic ketimines 3, which are stable compounds (contrary to 2,3,4,4a,5,6,7,8-octahydroquinolines 11; *vide infra*). Bicyclic ketimines 3 were smoothly α, α, α' -trichlorinated with excess of N-chlorosuccinimide in CCl₄ at room temperature to afford 3a,7,7-trichloro-3,3a,4,5,6,7-hexahydro-2H-indoles 4 in 49-60% yield after purification. Compound 4b consisted of a mixture of *cis*- and *trans*-isomers in a 54:46 ratio (or *vice versa*). These trichlorinated bicyclic imines 4 were converted into indolines and tetrahydroindoles by reaction with base (Scheme 1).

Reaction of 3a, 7, 7-trichloro-3, 3a, 4, 5, 6, 7-hexahydro-2H-indoles 4 with excess 2N sodium methoxide in methanol under reflux for 3h gave rise to either aromatization of the azaheterocyclic moiety or aromatization of the six-membered carbocyclic part. Under these conditions, compound 4a afforded a 1:1 mixture of 7,7-dimethoxy-4,5,6,7-tetrahydroindole (5a) and 7-chloroindoline (6a) (combined yield 78%). Upon flash chro-matography, acetal 5a was converted into the ketone, i.e. 7-oxo-4,5,6,7-tetrahydroindole (7a), which was cleanly separated from 7-chloroindoline (6a). On the other hand, the *cis*- and *trans*-4methyl-bicyclic imine 4b reacted with excess 2N sodium methoxide in methanol (reflux 3h) to afford a 7:3 mixture of acetal 5b and indoline 6b (combined yield 96%). This mixture led to 26% 7-chloro-5methylindoline (6b) and 63% 7-oxo-5-methyl-4,5,6,7-tetrahydroindole (7b) after flash chromatography.

7-Oxo-4,5,6,7-tetrahydroindole (7a) was converted in good yield into 4,5,6,7-tetrahydroindole (9a) with lithium aluminium hydride in tetrahydrofuran under reflux for 3 h. Oxidation of indoline 6a into 7-chloroindole (8a) was accomplished using either oxygen in methanol in the presence of salcomine (N,N'-bis(salicylidene)ethylenediaminocobalt (II))⁴ at room temperature or palladium on carbon (10%) in toluene at 135 °C for 15h. Not unexpectedly, 7-chloro-5-methylindoline (6b) did not give a straightforward oxidation with palladium on carbon in toluene or xylene under reflux for 3 days, as it resulted in the desired 7-chloro-5-methylindole (8b) and the dehalogenated 5-methylindole (10b) in a 4:1 ratio with toluene as solvent, and in a 3:2 ratio with o-xylene as solvent (Scheme 2). Both indoles 8b and 10b were separated by flash chromatography. A similar reaction with palladium on carbon has recently been reported in the literature. In the latter report, the hydrobromide salts of several substituted indolines were converted into the corresponding indole derivatives by reaction with palladium on carbon in aqueous alkaline solution in the presence of disodium fumarate.¹⁰ The direct conversion of bicyclic imine 3b into 5-methylindole (10b) with palladium on carbon in o-xylene for 2 days under reflux proceeded in poor yield giving the pure indole in only 17% after flash chromatography (Scheme 2). The dehydrochlorination of trichloroimine 4a with several bases under a variety of conditions led only to degradation products (selected reaction conditions : KOt-Bu, t-BuOH, reflux; K₂CO₄, DMSO, 90°C; NaOEt, EtOH, reflux; DBU, benzene, reflux; Et₃N, chlorobenzene, reflux), while the reaction with palladium on carbon in benzene (reflux 3 h) gave complete recovery of starting material. Also heating of compound 4a in chlorobenzene or 1,2-dichlorobenzene under reflux did not form cleanly aromatization products.

In order to have access to functionalized quinolines and its derivatives, N-(cyclohexylidene)amines 2 were deprotonated with LDA, subsequently reacted with 1-(3-bromopropyl)-2,2,5,5-tetramethyl-1-aza-2,5-

disilacyclopentane,⁸ and N-desilylated with potassium carbonate in methanol to give a transient δ -amino imine

which underwent transimination to afford 2,3,4,4a,5,6,7,8-octahydroquinolines 11 in 74-78% yield. The bicyclic imine 11a proved to be very sensitive to oxygen as, on standing at room temperature, it was



spontaneously oxygenated at the α -position to produce the hydroxy derivative 12a,¹¹⁻¹³ which was already present for 10% in the initial reaction mixture. Compound 11a could not be purified by flash chromatography on silica gel as it was completely α -hydroxylated during the chromatography (isolated yield of 12a : 28%). Vacuum distillation gave access to the bicyclic imine 11a in low yield (24%). Therefore, the crude 11a was used as such in the next chlorination step. Reaction of crude 11a, i.e. containing 10% of α -hydroxy imine 12a, with excess (4 equiv.) N-chlorosuccinimide in CCl₄ at room temperature for 15h furnished a reaction





mixture containing mainly trichlorinated imine 13a and about 20% α,α -dichloro- α' -hydroxy imine 14a. The α -hydroxylation apparently went on during the α -chlorination process. Compounds 13a and 14a were separated by flash chromatography, yielding 51% of pure and stable trichlorinated imine 13a and 14% of pure α, α -dichloro- α' -hydroxy imine 14a (Scheme 3). The purified compounds 11a and 12a were also reacted, each separately, with excess N-chlorosuccinimide under the same reaction conditions as described above, affording 68% of trichloroimine 13a and 61% of dichloroimine 14a, respectively, after purification by flash chromatography.

In similar way, but without taking much notice of the presence of α -hydroxy imine 12b (10% contamination of imine 11b), the synthesis and purification of trichlorinated imine 13b was accomplished in 56% isolated yield. This compound consisted of a mixture of *cis*- and *trans*-isomers (ratio 88:12 or vice versa), which were not separated.

Trichlorinated bicyclic imines 13 were selectively converted into 1,2,3,4-tetrahydroquinolines 15 by reaction with excess potassium carbonate in dimethyl sulfoxide at 90°C for 2-4 h. No trace of any pyridine or quinoline derivative was observed, pointing to a selective dehydrochlorination process. Again here, bicyclic compound 13a afforded only degradation products on reaction with potassium t-butoxide, or did not give any reaction on treatment with palladium on carbon in benzene under reflux.

Surprisingly, 4a,8,8-trichloro-2,3,4,4a,5,6,7,8-octahydroquinoline (14a) is an extremely stable compound, which was left untouched on treatment with excess 2N sodium methoxide in methanol under reflux, or mesyl chloride in pyridine under reflux, or potassium carbonate in DMSO at 90°C, or p-toluenesulfonic acid in benzene at room temperature for 16h. However, it decomposes with potassium t-butoxide in THF under reflux to a mixture of unidentified compounds. 8-Chloro-1,2,3,4-tetrahydroquinoline (15a) was cleanly converted into 8-chloroquinoline (16a) on treatment with palladium on carbon in toluene under gentle reflux for one day. The 6-methyl analogue 15b underwent a similar oxidation into 8-chloro-6-methylquinoline (16b) (77%) under analogous reaction conditions (5 days reflux in toluene), but afforded the dechlorinated quinoline 16b upon reflux for three days in o-xylene (Scheme 3).



Finally, the use of ethyl 8,8-dichloro-2,3,4,4a,5,6,7,8-octahydroquinolyl-5-carboxylate (20) in the synthesis of azaheterocycles was verified. Compound 20 was synthesized from β -keto ester 17 via enamino ester

18. The alkylation of the latter compound with 1-(3-bromopropyl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane was executed as described above, except that aqueous oxalic acid was used in the N-deprotection and transimination step because the standard procedure utilizing potassium carbonate in methanol led to mixtures of ethyl and methyl esters by transesterification. Bicyclic compound **19** has also recently been synthesized



via an alkyl azide radical cyclization.¹⁴ The dichlorination of bicyclic imine **19** with excess N-chlorosuccinimide was executed in nearly quantitative yield. Ethyl 8,8-dichloro-2,3,4,4a,5,6,7,8-octahydroquinolyl-5-carboxylate (**20**) remained stable upon treatment with bases (selected reaction conditions : 4-6 equivalents of 2N NaOMe in MeOH, 4-20h reflux; 6 equivalents of K_2CO_3 in DMSO, 4h reflux).

EXPERIMENTAL

Melting points (mp, uncorrected) : Büchi 535 melting point determinator. TLC : Merck silicagel 60 F254, layer thickness 0.25 mm. Flash chromatography : Merck silicagel 60, particle size 40-63 μ m. IR spectra : Perkin Elmer 1310 spectrometer. Mass spectra (MS) : Varian MAT 112 mass spectrometer (70 eV) with GC-MS coupling, unless otherwise stated. ¹H- and ¹³C-NMR spectra : JEOL JNM-EX270 NMR spectrometer (270 MHz for ¹H-NMR, 68 MHz for ¹³C-NMR). The DEPT sequence and 2D H-C correlation spectroscopy was used for the ¹³C-NMR assignments. Dry solvents : dichloromethane and tetrachloromethane were dried over calciumhydride; ether was dried and distilled from sodium wire, while tetrahydrofuran (THF) was dried and distilled from sodium benzophenone ketyl.

<u>Preparation of N-(cyclohexylidene)amines 2^{15} .</u> The imination of cyclohexanones 1 with isopropylamine and titanium(IV) chloride was performed according to an earlier literature report.¹⁵ The reaction conditions

applied for the syntheses of imines 2 as well as the yields after distillation are given in Scheme 1.

General Procedure for the Preparation of 3.3a.4.5,6,7-hexahydro-2H-indoles 3 and 2.3.4.4a.5.6.7.8-octahydroquinolines 11. To a stirred, cooled (0°C) solution of disopropylamine (1.3 equivalents) in dry THF (10% w/v) was added n-BuLi (2.5 M solution in hexane; 1.2 equivalents) under a nitrogen atmosphere. A solution of one equivalent of N-(cyclohexylidene)amine 2 in THF was then added slowly via a syringe. The reaction mixture was subsequently stirred at 0° C for 30 minutes, after which a solution of one equivalent of 1-(ω -bromoalkyl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane⁸ in THF was added. Stirring was continued for a period of 5-6h, during which the mixture warmed up to room temperature. The solution was poured into a 0.5 N aqueous solution of NaOH and extracted three times with ether. After drying of the organic layers and evaporation of the solvent, the residue was dissolved in methanol (10% w/v), and after adding 3 equivalents of K_2CO_3 , the resulting suspension was stirred under gentle reflux for 3h. The reaction mixture was poured into water and extracted with dichloromethane. The organic layers were dried, the solvents evaporated, and the residue was dissolved in ether (10% w/v). After addition of a 10% (w/v) aqueous solution of oxalic acid dihydrate (one equivalent), the two layer system thus formed was shaken thoroughly in a separatory funnel, and the aqueous phase was isolated. After washing this phase two times more with ether, dichloromethane was added and solid NaOH pellets were added until alkaline. The two layer system was shaken thoroughly and the organic layer was isolated. After extraction of the aqueous phase with dichloromethane two times more, the combined organic layers were dried. Evaporation of the solvent afforded the crude bicyclic imines 3 and 11.

3,3a,4,5,6,7-Hexahydro-2H-indole (3a). Yield : 77%. The crude bicyclic imine **3a** (purity 97%; GC, ¹Hand ¹³C-NMR) was purified by flash chromatography (CH₂Cl₂ : MeOH 96:4; Rf 0.23). MS m/z (%) : 123 (M⁺, 92); 122 (50); 96(24); 95(100); 94(33); 67(42); 55(56); 41(30). IR (NaCl) : 1650 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : δ 1.0-2.7 (11H, m, (CH₂)₄CHCH₂); 3.4-3.9 (2H, m, CH₂N). ¹³C-NMR (CDCl₃) : δ 25.39, 26.76, 29.70, 31.81 and 34.64 (each CH₂); 48.01 (CH); 59.01 (NCH₂); 179.66 (C=N).

5-Methyl-3,3a,4,5,6,7-hexahydro-2H-indole (3b). Yield : 76%. The crude material (purity 96%; GC, ¹H and ¹³C-NMR) was purified by flash chromatography (CH₂Cl₂ : MeOH 95:5; Rf 0.27). MS m/z (%) : 137 (M⁺, 77); 122 (36); 109(41); 95(77); 94(32); 81(34); 67(45); 55(100); 41(45). IR (NaCl) : 1653 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : δ 0.95 (3H, d, J=6.6 Hz, Me); 1.1-1.5, 1.6-2.3 and 2.6-2.7 (10H, m); 3.6-3.7 and 3.8-4.0 (2H, m, NCH₂). ¹³C-NMR (CDCl₃) : δ 22.35 (Me); 30.40 and 31.71 (each CH₂); 32.45 (CHMe); 35.63 and 43.55 (each CH₂); 48.31 (CHC=N); 60.03 (NCH₂); 180.19 (C=N).

2,3,4,4a,5,6,7,8-Octahydroquinoline (11a). The crude residue consisted of 90% **11a** (yield 74%) and 10% 2,3,4,4a,5,6,7,8-octahydroquinoline-4a-ol (**12a**) (yield 8%). Bicyclic imine **11a** could be purified by distillation (yield 24%). Bp. 22-25°C/0.04 mmHg (Lit.¹⁶ bp. 35-40°C/0.2 mmHg). IR (NaCl) : 1659 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : δ 1.2-2.4 (12H, m); 3.3-3.6 (2H, m, NCH₂). ¹³C-NMR (CDCl₃) : δ 21.33, 25.91, 27.46, 27.89 and 34.95 (each CH₂); 38.71 (CH); 39.23 (CH₂); 49.54 (NCH₂); 173.73 (C=N).

2,3,4,4a,5,6,7,8-Octahydroquinoline-4a-ol (12a). 1-Hydroxyimine **12a** was isolated from the crude reaction mixture by flash chromatography (CH₂Cl₂ : MeOH 13:2; Rf 0.23; Yield 28%). Mp. 110°C (Lit.¹⁶ mp. 115-115,5°C). MS m/z (%) : 153 (M⁺, 100); 136(75); 125(50); 97(42); 96(44); 83(40); 68(59); 67(40); 58(90); 55(48); 44(43); 43(65); 41(85). IR (NaCl) : 3000-3600 (OH); 1655 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : δ 1.4-

2.0 (10H, m); 2.1-2.3 and 2.5-2.8 (2H, m, $CH_2C=N$); 2.8-3.7 (3H, m, CH_2N and OH). ¹³C-NMR (CDCl₃) : δ 19.34, 21.08, 27.28, 35.15, 36.62 and 40.77 (each CH₂); 49.65 (NCH₂); 67.49 (O-Cquat); 173.31 (C=N).

6-Methyl-2,3,4,4a,5,6,7,8-octahydroquinoline (11b). The crude residue consisted mainly of bicyclic imine **11b** (yield 78%), contaminated with 10% of hydroxy imine **12b** (yield 9%). The pure bicyclic imine **11b** could be obtained by vacuum distillation. Bp. 29°C/0,04 mmHg. IR (NaCl) : 1657 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : δ 0.95 (3H, d, J=6.0 Hz, Me); 1.0-2.5 (12H, m); 3.4-3.8 (2H, m, NCH₂). ¹³C-NMR (CDCl₃) : δ 21.42 (CH₂); 21.83 (Me); 27.92 (CH₂); 32.27 (CH); 35.69 (CH₂); 37.74 (CH); 38.78 and 43.36 (each CH₂); 49.69 (NCH₂); 172.67 (C=N).

Preparation of Ethyl 2-(Isopropylamino)-1-cyclohexene-1-carboxylate (18). β -Enamino ester 18 was synthesized following an analogous procedure described in the literature.¹⁶ To a solution of 5.10 g (30 mmol) of β -keto ester 17 in 100 mL of benzene was added 8.85 g (150 mmol) of isopropylamine and 0.29 g (1.5 mmol) of p-toluenesulfonic acid. The flask was equipped with a Dean Stark apparatus, and the reaction mixture was stirred under gentle reflux for 20h. In order to avoid amide formation, the temperature of the oil bath was kept below 100°C. After evaporation of the solvent, the residue was dissolved in 100 mL of ether and dried with MgSO₄. After filtration and evaporation, the crude β -enamino ester was distilled, which yielded 5.40 g of pure β -enamino ester 18 (yield 85%). Bp. 68-75°C/0.04 mmHg.

Ethyl 2-(Isopropylamino)-1-cyclohexene-1-carboxylate (18). MS m/z (%) : 211 (M⁺, 38); 196(19); 182(13); 168(28); 166(25); 164(27); 150(100); 138(57); 122(26); 96(22); 94(14); 81(21); 79(14); 67(14); 58(17); 41(23). IR (NaCl) : 3200-3300 (NH); 1645 (C=O); 1594 cm⁻¹ (C=C). ¹H-NMR (CDCl₃) : δ 1.18 (3H, d, J=6.6 Hz, Me); 1.19 (3H, d, J=6.3 Hz, Me); 1.26 and 1.27 (each 3H, each t, each J=7.10 Hz, each OCH₂CH₃); 1.5-1.7 (4H, m, (CH₂)₂); 2.27 (2H, t, J=5.94 Hz, CH₂C=); 2.35 (2H, t, J=6.1 Hz, CH₂C=); 3.6-3.75 (1H, m, NHC<u>H</u>); 4.11 and 4.12 (each 2H, each q, each J=7.10 Hz, each OCH₂); 8.92 (1H, broad d, J=7.59 Hz, NH). ¹³C-NMR (CDCl₃) : δ 14.74 (OCH₂CH₃); 22.43, 22.82 and 23.86 (each CH₂); 24.42 (Me₂); 26.25 (CH₂); 43.20 (CHNH); 58.54 (OCH₂); 89.06 (C_{quat}-COOEt); 158.72 (=C-NH); 170.92 (<u>C</u>OOEt).

Synthesis of Ethyl 2.3.4,4a,5.6,7,8-Octahydroquinolyl-5-carboxylate (19). The alkylation of ethyl 2-(isopropylamino)cyclohex-1-ene-1-carboxylate (18) with 1-(3-bromopropyl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane¹³ was executed as described above for the syntheses of bicyclic imines 11. The alkylating reagent was added in a slight excess (1.2 equivalents) in order to obtain complete alkylation. In the following N-deprotection step, aqueous oxalic acid was used instead of the usual methanolysis. The residue obtained after alkylation was therefore dissolved in ether (10% w/v), and an aqueous 10% (w/v) solution of oxalic acid dihydrate (1.7 equivalents) was added. The resulting two layer system was refluxed for 30 minutes under vigourous stirring, after which it was stirred at room temperature for 15h. The aqueous layer was isolated, washed two times more with ether, and was subsequently basified with sodium hydroxide pellets. The resulting aqueous phase was extracted three times with dichloromethane, after which the combined dichloromethane layers were dried. Evaporation of the solvent afforded bicyclic imine 19 (purity 98%; GC, ¹H- and ¹³C-NMR) in 54% yield. Ethyl 2,3,4,4a,5,6,7,8-Octahydroquinolyl-5-carboxylate (19). Bicyclic imine 19 was purified by flash chromatography (CH₂Cl₂ : MeOH 9:1; Rf 0.39). MS m/z (%) : 209 (M⁺, 7); 137(15); 136(100); 108(8); 68(9); 67(14); 55(10); 49(7); 44(12); 41(17). IR (NaCl) : 1720 (C=O); 1654 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : δ 1.27 (3H, t, J=7.26 Hz, Me); 1.4-2.0 and 2.3-2.4 (12H, m); 3.4-3.7 (2H, m, CH₂N); 4.21 (2H, q, J=7.26 Hz, OCH₂). ¹³C-NMR (CDCl₃) : δ 14.25 (Me); 19.32, 23.41, 27.22, 33.44, 38.10 and 38.22 (each CH₂); 49.38 (<u>C</u>-COOEt); 49.47 (NCH₂); 61.06 (OCH₂); 169.38 (C=N); 174.19 (<u>COOEt</u>).

General Procedure for the Preparation of Chlorinated Bicyclic Imines 4, 13, 14a and 20. To a stirred, cooled (0°C) solution of bicyclic imine (3, 11, 12a or 19; 1 equivalent) in dry CCl_4 was added, portionwise, N-chlorosuccinimide (4 equivalents for imines 3, 11 and 12a; 3 equivalents for imine 19). The resulting suspension was stirred at room temperature for 15h, after which stirring was stopped and the mixture was cooled to 0°C. Succinimide was filtered off and washed twice with cold CCl_4 (0°C). Evaporation of the filtrate afforded the crude chlorinated imines (4, 13, 14a or 20). The latter imines were purified by flash chromatography in order to eliminate all traces of residual succinimide, present in the crude reaction mixture (5-10%).

3a,7,7-Trichloro-3,3a,4,5,6,7-hexahydro-2*H***-indole (4a). Yield after flash chromatography : 49% (hexane : EtOAc; 7:3; Rf 0.30). Mp. 69°C. MS m/z (%) : 225/27/29/31 (M⁺, 24); 190/2/4(100); 154/6(67); 127 (14); 119(13); 118(33); 93(12); 91(27); 89(13); 65(14); 53(15); 41(15). IR (KBr) : 1630 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : \delta 1.8-3.0 (8H, m); 3.98 (1H, dxdxd, J₁=16.50 Hz, J₂=9.24 Hz, J₃=5.94 Hz, CH_AH_BN); 4.20 (1H, dxd, J₁=16.50 Hz, J₂=7.76 Hz, CH_AH_BN). ¹³C-NMR (CDCl₃) : \delta 20.13, 40.90, 44.85, 48.10 and 57.09 (each CH₂); 73.26 and 82.28 (each C_{quat}); 171.44 (C=N). Anal. calcd. for C₈H₁₀Cl₃N : Cl, 46.95; N, 6.18. Found : Cl, 46.83; N, 6.07.**

3a,7,7-Trichloro-5-methyl-3,3a,4,5,6,7-hexahydro-2H-indole (4b) c/t. Yield after flash chromatography : 60% (hexane : EtOAc 4:1; Rf_1 0.25, Rf_2 0.21). Isomer with higher Rf (Rf₁ 0.25) : MS m/z (%) : direct inlet : 239/41/3/5 (M⁺, 31); 204/6/8(100); 168/70(82); 132(68); 117(24); 107(17); 105(18); 91(26); 89(30); 81(20); 79(19); 77(28); 65(28); 63(19); 55(24); 53(51); 51(24); 41(39). IR (NaCl) : 1638 cm⁻¹ (C=N). ¹H-NMR (CDCl₃): δ 1.20 (3H, d, J=6.60 Hz, Me); 2.0-2.2 (3H, m, C<u>H</u>Me, <u>C</u>H₂ and C<u>H</u>₄H₄.); 2.59 (1H, dxd, $J_1 = 14.19 \text{ Hz}, J_2 = 5.45 \text{ Hz}, C\underline{H}_BH_B$; 2.72 (1H, dxd, $J_1 = 14.19 \text{ Hz}, J_2 = 4.45 \text{ Hz}, CH_B\underline{H}_B$; 2.96 (1H, dxd, $J_1 = 14.51$ Hz, $J_2 = 10.89$ Hz, CH_AH_A ; 4.06 (1H, dxdxd, $J_1 = 16.49$ Hz, $J_2 = 8.91$ Hz, $J_3 = 5.28$ Hz, $NCH_{c}H_{c}$); 4.19 (1H, dxd, $J_1 = 16.49$ Hz, $J_2 = 7.59$ Hz, $NCH_{c}H_{c}$). ¹³C-NMR (CDCl₃) : δ 21.74 (Me); 25.77 (CHMe); 42.86, 44.87 and 49.52 (each CH₂); 58.06 (NCH₂); 73.51 (CCIC=N); 80.16 (CCI₂); 173.98 (C=N). Isomer with lower Rf (Rf₂ 0.21) : mp. 48.5-50°C. MS m/z (%) : 239/41/3/5 (M⁺, 29); 204/6/8 (100); 169/71(18); 168/70 (77); 132(53); 117(21); 107(18); 105(16); 91(19); 89(25); 81(17); 79(16); 77(21); 65(21); 55(18); 53(39); 51(18); 41(28). IR (KBr) : 1630 cm^{-1} (C=N). ¹H-NMR (CDCl₃) : δ 1.07 (3H, d, J=6.60 Hz, Me); 1.54 (1H, dxd, $J_1=14.52$ Hz, $J_2=11.88$ Hz, CH_AH_A); 2.1-2.3 (2H, m, CH_BH_B and $CH_{c}H_{c}$; 2.5-2.7 (3H, m, $CH_{A}H_{A'}$, CHMe and $CH_{c}H_{c}$; 2.85 (1H, dxt, $J_1=14.19$ Hz, $J_2=2.64$ Hz, $CH_{B}H_{B'}$; 4.00 (1H, dxdxd, $J_{1} = 16.49$ Hz, $J_{2} = 9.23$ Hz, $J_{3} = 5.61$ Hz, $NCH_{D}H_{D'}$); 4.22 (1H, dxd, $J_{1} = 16.49$ Hz, $J_2 = 7.58$ Hz, NCH_DH_D.). ¹³C-NMR (CDCl₃) : δ 19.93 (Me); 26.67 (CHMe); 44.98, 48.86, 55.83 and 57.39 (each CH₂); 73.01 (<u>CCIC=N</u>); 81.62 (CCl₂); 171.26 (C=N). Cis:trans ratio 54:46 (or vice versa). Anal. calcd. for $C_9H_{12}Cl_3N$: Cl, 44.22. Found : Cl, 44.34.

4a,8,8-Trichloro-2,3,4,4a,5,6,7,8-octahydroquinoline (13a). Yield after flash chromatography : 68% (CH₂Cl₂ : MeOH 96:4; Rf 0.78). Mp. 114-116°C. MS m/z (%) : 239/41/3/5 (M⁺, 21); 204/6/8(100); 176/8/80(16); 168/70(78); 132(14); 105(10); 99(17); 79(12); 77(22); 75(13); 69(11); 67(14); 65(14); 59(14); 58(12); 56(15); 53(17); 51(21); 45(12); 43(34); 41(34). IR (KBr) : 1650 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : δ 1.6-2.6 and 2.9-3.1 (10H, m); 3.81 (1H, dxdxd, J₁=19.80 Hz, J₂=11.55 Hz, J₃=5.94 Hz, NCH_AH_A.); 4.22 (1H, dxd, J₁=19.80 Hz, J₂=5.94 Hz, NCH_AH_A.). ¹³C-NMR (CDCl₃) : δ 18.01, 18.51, 37.97, 40.58, 47.22 and 50.55 (each CH₂); 61.47 and 87.65 (each C_{quat}.); 162.21 (C=N). Anal. Calcd. for C₉H₁₂Cl₃N : Cl, 44.22; N, 5.82. Found : Cl, 44.40; N, 5.72.

4a,8,8-Trichloro-6-methyl-2,2,4,4a,5,6,7,8-octahydroquinoline (13b) (c/t). Yield after flash chromatography : 56% (CH₂Cl₂ : MeOH 99:1; Rf 0.66). Mp. (c/t) 108.5-109.5°C. MS m/z (%) : 253/5/7/9 (M⁺, 13); 218/20/2(79); 182/4(100); 146(42); 91(28); 77(41); 67(35); 65(35); 55(30); 53(42); 44(87); 41(91). IR (KBr) : 1642 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : δ 1.05 (3H, d, J=6.93 Hz, Me of major isomer); 1.24 (3H, d, J=6.60 Hz, Me of minor isomer); 1.53 (1H, dxd, J₁=14.69 Hz, J₂=11.72 Hz, CH_AH_A.); 1.5-2.4 and 2.6-3.0 (8H, m); 3.83 (1H, dxdxd, J₁=19.80 Hz, J₂=11.55 Hz, J₂=5.94 Hz, NCH_BH_B.); 4.23 (1H, dxd, J₁=19.80 Hz, J₂=5.94 Hz, NCH_BH_B.); 4.23 (1H, dxd, J₁=19.80 Hz, J₂=5.94 Hz, NCH_BH_B.); 1.62.20 (Me); 24.98 (CHMe); 38.04, 50.03 and 50.62 (each CH₂); 56.19 (NCH₂); 60.66 (C-Cl); 87.60 (CCl₂); 161.45 (C=N); δ minor isomer : 17.68 (CH₂); 22.57 (Me); 24.22 (CHMe); 37.21, 41.26 and 48.01 (each CH₂); 50.22 (NCH₂); 60.75 (C-Cl); 85.70 (CCl₂); 164.76 (C=N). *Cis:trans* ratio 88:12 (or *vice versa*). Anal. Calcd. for C₁₀H₁₄Cl₃N : Cl, 41.78. Found : Cl, 41.67.

8,8-Dichloro-2,3,4,4a,5,6,7,8-octahydroquinoline-4a-ol (14a). Yield after flash chromatography : 61% (hexane : EtOAc 3:2; Rf 0.28). Mp. 61-63 °C. MS m/z (%) : 221/3/5 (M⁺, 17); 186/8(30); 185/7(20); 168 (70); 158 (39); 150(31); 132(30); 130(20); 97(27); 80(24); 77(26); 69(22); 67(29); 57(26); 56(28); 55(71); 53(33); 44(100); 43(53); 42(53); 41(100). IR (NaCl) : 3100-3600 (OH); 1640 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : δ 1.4-2.5 (8H, m); 2.8-3.0 (2H, m, CH₂CCl₂); 3.67 (1H, dxdxd, J₁=19.14 Hz, J₂=11.55 Hz, J₃=5.28 Hz, NCH_AH_A.); 4.13 (1H, dxd broad, J₁=19.14 Hz, J₂=5.28 Hz, NCH_AH_A.); OH invisible. ¹³C-NMR (CDCl₃) : δ 18.04, 18.36, 35.79, 39.57, 48.32 and 51.21 (each CH₂); 68.32 (C-OH); 90.46 (CCl₂); 163.88 (C=N). Anal. Calcd. for C₉H₁₃Cl₂NO : N, 6.31. Found : N, 6.19.

Ethyl 8,8-Dichloro-2,3,4,4a,5,6,7,8-octahydroquinolyl-5-carboxylate (20). Yield after flash chromatography : 66% (hexane : EtOAc 4:1, Rf 0.23). MS m/z (%) : 277/9/81 (M⁺, 2); 242/4(8); 241/3(9); 168/70 (100); 140(5); 134(12); 132(12); 79(7); 77(8); 68(6); 67(6); 54(5); 53(5); 44(8); 41(13). IR (NaCl) : 1729 (C=O); 1660 cm⁻¹ (C=N). ¹H-NMR (CDCl₃) : δ 1.20 (3H, t, J=7.26 Hz, Me); 1.3-2.4 (8H, m); 2.42 (1H, dxm, J=13.86 Hz, CH_AH_A·CCl₂); 3.6-3.8 (1H, m, NCH_BH_{B'}); 3.9-4.2 (3H, m, NCH_BH_B and OCH₂). ¹³C-NMR (CDCl₃) : δ 13.98 (Me); 18.40, 20.20, 34.36, 35.87, 48.09 and 49.79 (each CH₂); 47.03 (C_{quat}); 61.40 (OCH₂); 90.96 (<u>C</u>Cl₂); 161.74 (C=N); 172.23 (<u>C</u>OOEt). Anal. Calcd. for C₁₂H₁₇Cl₂NO₂ : Cl, 25.49; N, 5.04. Found : Cl, 25.41; N, 5.10.

Reaction of Trichloroimines 4 with Sodium Methoxide in Methanol. As a typical procedure the reaction of trichloroimine 4a with NaOMe in methanol is described. 4 ML (8 mmol) of a 2N solution of NaOMe in methanol was added dropwise to 0.45 g (2 mmol) of 3a,7,7-trichloro-3,3a,4,5,6,7-hexahydro-2H-indole (4a). The resulting solution was stirred under reflux for 3h, after which the mixture was poured into 20 mL of water and extracted three times with 5 mL of dichloromethane. The extracts were dried, and evaporation

of the solvent afforded 0.26 g of a 1:1 mixture of 7,7-dimethoxy-4,5,6,7-tetrahydroindole (5a) and 7-chloroindoline (6a) (combined yield 78%). Without full characterization of the intermediate dimethoxy compound 5a, the crude reaction mixture was subjected to flash chromatography, which led to the isolation of 40 mg of 7-chloroindoline (6a) and 70 mg of 7-oxo-4,5,6,7-tetrahydroindole (7a). The reaction of trichloroimine 4b with NaOMe in methanol was performed in a completely similar way, leading to a 7:3 reaction mixture of compounds 5b and 6b, respectively, in a combined crude yield of 96%. Flash chromatography of the latter reaction mixture afforded the pure bicyclic compounds 6b and 7b.

7-Chloroindoline (6a). Yield after flash chromatography : 13% (hexane : EtOAc 4:1; Rf 0.51). MS m/z (%) : 153/5 (M⁺, 79); 152/4(92); 151(14); 118(24); 117(100); 116(15); 91(10); 90(14); 89(27); 63(17); 58 (40); 44(10). IR (NaCl) : ν_{max} : 3120-3420 (NH); 1606; 1467; 1130; 755 cm⁻¹. ¹H-NMR (CDCl₃) : δ 3.09 (2H, t, J=8.58 Hz, CH₂); 3.60 (2H, t, J=8.58 Hz, NCH₂); 6.61 (1H, t, J=7.75 Hz, CH=CH-CCl); 6.9-7.0 (2H, m, CH=CH-CH=CCl); NH invisible. ¹³C-NMR (CDCl₃) : δ 30.55 (CH₂); 47.08 (NCH₂); 114.90 (C_{quat}); 119.26, 122.77 and 126.97 (each CH=); 130.80 and 148.64 (each C_{quat}). The ¹H-NMR and IR spectral data were in complete accordance with literature data.⁴

7-Oxo-4,5,6,7-tetrahydroindole (7a). Yield after flash chromatography : 26% (hexane : EtOAc 4:1; Rf 0.18). Mp. 97°C (Lit.¹⁷ mp. 95°C). MS m/z (%) : 135 (M⁺, 100); 120(12); 118(12); 107(42); 106(16); 93(30); 80(14); 79(95); 77(11); 53(16); 52(34); 51(19). IR (KBr) : 3100-3350 (NH); 1623 cm⁻¹ (C=O). ¹H-NMR (CDCl₃) : δ 2.12 (2H, pent., J=6.11 Hz, CH₂); 2.77 and 2.51 (each 2H, each t, each J=6.11 Hz, CH₂C=O and CH₂C=C); 6.11 (1H, ~t, CH=); 7.03 (1H, t, J=2.64 Hz, =C<u>H</u>-NH); 9.97 (1H, broad s, NH). ¹³C-NMR (CDCl₃) : δ 23.31, 25.28 and 37.75 (each CH₂); 108.61 and 125.71 (each CH=); 128.08 and 137.34 (each =C_{qual}); 188.86 (C=O).

7-Chloro-5-methylindoline (6b). Yield after flash chromatography : 29% (hexane : EtOAc 4:1; Rf 0.41). MS m/z (%) : 167/9 (M⁺, 100); 166/8(92); 132(26); 131(83); 130(55); 77(19); 64(37); 51(22); 44(79). IR (NaCl) : ν_{max} : 3150-3440 (NH); 2910; 2850; 1582; 1488; 1472; 1323; 1260; 1106; 850 cm⁻¹. ¹H-NMR (CDCl₃) : δ 2.22 (3H, s, Me); 3.06 (2H, t, J=8.25 Hz, CH₂CH₂N); 3.59 (2H, t, J=8.25 Hz; CH₂CH₂N); 6.82-6.83 (2H, m, =CH's); NH invisible. ¹³C-NMR9X(CDCl₃) δ 20.58 (Me); 30.64 (CH₂); 47.26 (NCH₂); 114.91 (C_{quar}); 123.75 and 127.11 (each =CH); 129.45 and 131.18 (each =C_{quar}); 145.91 (=C_{quar} Cl). Anal. Calcd. for C₉H₁₀ClN : N, 8.36. Found : N, 8.47.

5-Methyl-7-oxo-4,5,6,7-tetrahydroindole (7b). Yield after flash chromatography : 63% (hexane : EtOAc 4:1; Rf 0.15). Mp. 142.5°C. MS m/z (%) : 149 (M⁺, 84); 134(10); 132(10); 107(52); 106(16); 80(36); 79(90); 53(13); 52(24); 51(12); 44(100); 42(15). IR (KBr) : ν_{max} : 3220; 1630; 1404; 1121; 1048; 778 cm⁻¹. ¹H-NMR (CDCl₃) : δ 1.13 (3H, d, J=4.95 Hz, Me); 2.2-2.9 (5H, m, CH₂CHMeCH₂); 6.07 (1H, broad s, CH=CHN); 7.07 (1H, t, J=2.64 Hz, NCH=); 10.92 (1H, broad s, NH). ¹³C-NMR (CDCl₃) : δ 21.35 (Me); 31.75 (CH₂); 33.19 (CH); 46.04 (CH₂C=O); 108.43 (=CH); 126.63 (NCH=); 127.80 and 137.32 (each=C_{quat}); 188.68 (C=O). Anal. Calcd. for C₉H₁₁NO : C, 72.46; H, 7.43; N, 9.39. Found : C, 72.31; H, 7.49; N, 9.45.

<u>Synthesis of 4,5,6,7-Tetrahydroindole (9a)</u>. To a stirred, cooled (0°C) solution of 0.20 g (1.5 mmol) 7-oxo-4,5,6,7-tetrahydroindole (7a) in 3 mL of dry THF was added 0.11 g (3 mmol) of lithium aluminium hydride. After stirring of the resulting suspension under reflux for 3h, 0.17 g of water was added very slowly under vigourous stirring at 0°C. The slurry thus formed was filtered, washed twice with THF, and the filtrate was dried. Evaporation of the solvent afforded 0.18 g of 4,5,6,7-tetrahydroindole (**9a**) (yield 88%; purity 96%; ¹H- and ¹³C-NMR). Flash chromatography yielded the pure compound **9a** (hexane : EtOAc 95:5; Rf 0.12). **4,5,6,7-Tetrahydroindole (9a**). MS m/z (%) : 121 (M⁺, 51); 120(15); 118(8); 117(5); 103(5); 93(100); 91 (7); 80(8); 77(6); 66(6); 65(8); 58(7); 53(5); 52(6); 51(6); 44(16). IR (NaCl) : ν_{max} : 3360; 2910; 2838; 1442; 1313; 1087; 711 cm⁻¹. ¹H-NMR (CDCl₃) : δ 1.6-1.8 (4H, m, (CH₂)₂); 2.4-2.5 (4H, m, 2xCH₂C=); 5.89 (1H, t, J=2.64 Hz, C<u>H</u>=CHN); 6.50 (1H, t, J=2.64 Hz, =CH-N); 7.4-7.6 (1H, broad s, NH). ¹³C-NMR (CDCl₃) : δ 22.66, 22.81, 23.38 and 23.78 (each CH₂); 107.22 (d, J=4.8 Hz, HC=); 115.54 (d, J=4.8 Hz, NCH=); 116.69 and 126.79 (each =C_{qual}). The ¹H-NMR and IR spectral data were consistent with literature data.¹⁸

<u>Preparation of 1,2,3,4-Tetrahydroquinolines 15</u>. To a solution of trichlorinated bicyclic imine 13 (1 equivalent) in dimethyl sulfoxide (5% w/v) was added K_2CO_3 (6 equivalents). The suspension was stirred at 90°C for a period of 2-4h, after which it was poured into water and extracted three times with ether. After drying of the organic layers and evaporation of the solvent, the crude 1,2,3,4-tetrahydroquinolines 15 were obtained, which were purified by flash chromatography.

8-Chloro-1,2,3,4-tetrahydroquinoline (15a). Yield after flash chromatography : 74% (hexane : EtOAc 95:5; Rf 0.37). MS m/z (%) : 167/9 (M⁺, 95); 166/8(100); 132(36); 131(52); 130(50); 117(28); 77(30); 65(35); 64(43); 51(28); 44(23). IR (NaCl) : ν_{max} : 3400-3420 (NH); 1600; 1498; 1355; 1299 cm⁻¹. ¹H-NMR (CDCl₃) : δ 2.00 (2H, ~pent., J=5.94 Hz, CH₂); 2.84 (2H, t, J=6.27 Hz, CH₂C=); 3.45 (2H, txd, J₁=5.45 Hz, J₂=2.31 Hz, CH₂N); 4.01 (1H, broad s, NH); 6.57 (1H, t, J=7.59 Hz, =C<u>H</u>-CH=C_{qual}); 6.91 (1H, d, J=7.25 Hz, CH=C_{qual}); 7.12 (1H, dxt, J₁=7.92 Hz, J₂=0.66 Hz, CH=C_{qual}). ¹³C-NMR (CDCl₃) : δ 21.62 (CH₂); 27.19 (CH₂C=); 41.78 (CH₂N); 116.24 (CH=); 118.02 and 122.60 (each =C_{qual}); 126.75 and 127.64 (each H<u>C</u>=C_{qual}); 140.70 (=CCl). Lit.¹⁹ bp. 95-110°C.

8-Chloro-6-methyl-1,2,3,4-tetrahydroquinoline (15b). Yield after flash chromatography : 48% (hexane : MeOH 99:1; Rf 0.19). MS m/z (%) : 181/3 (M⁺, 100); 180/2(74); 146(22); 145(32); 144(35); 131(23); 130(16); 115(9); 91(13); 89(15); 77(9); 71(29); 65(14); 58(11); 51(11); 44(36). IR (NaCl) : ν_{max} : 3380-3430 (NH); 2918; 2835; 1500; 1322; 1298; 1188. ¹H-NMR (CDCl₃) : δ 2.03 (2H, ~pent., J=5.61 Hz, CH₂); 2.29 (3H, s, Me); 2.85 (2H, t, J=6.27 Hz, CH₂C=); 3.46 (2H, t, J=5.61 Hz, NCH₂); 4.2 (1H, broad s, NH); 6.79 and 7.00 (each 1H, each broad s, each =CH). ¹³C-NMR (CDCl₃) : δ 20.13 (Me); 21.94 and 27.19 (each CH₂); 41.89 (NCH₂); 117.91, 122.55 and 125.71 (each =C_{quar}); 127.04 and 128.41 (each CH=); 138.36 (=C_{quar} Cl). Anal. Calcd. for C₁₀H₁₂ClN : N, 7.71. Found : N, 7.79.

General Procedure for the Reaction of Azabicyclic Compounds 3b, 6, 13 and 15 with Palladium on Carbon (Pd/C). To a solution of azabicyclic compound (3b, 6, 13 or 15) in toluene or xylene (10% w/v) was added a catalytic amount of palladium, 10% on carbon. This suspension was stirred under very gentle reflux for several days. The exact reaction conditions (solvent, reaction period) are given in schemes 1, 2 and 3. The warm reaction mixture was filtered and washed two times with dichloromethane, after which the solvents of the filtrate were evaporated. The resulting residue was analyzed by ¹H- and ¹³C-NMR spectrometry, and purified by flash chromatography.

7-Chloroindole (8a). Yield after flash chromatography : 66% (CH₂Cl₂ : hexane 1:1; Rf 0.48). This compound was also synthesized utilizing a methodology reported in the literature⁴ by bubbling a stream of oxygen through a methanolic solution of **6a** containing a catalytic amount of salcomine (yield after flash chromatography 65%). MS m/z (%) : 151/3 (M⁺, 100); 124/6(12); 116(24); 115(20); 114(8); 89(29); 88(10); 75(17); 63(15); 62(11); 57(10). IR (NaCl) : ν_{max} : 3395-3400 (NH); 1900; 1705; 1617; 1663; 1486; 1432; 1330; 1190; 1140; 1063; 938; 781; 721. ¹H-NMR (CDCl₃) : δ 6.51 (dxd, J₁=3.14 Hz, J₂=2.15 Hz, HC₅=); 6.94-7.00 and 7.10-7.17 (3H, m, HC₃=, HC₄= and HC₆=); 7.47 (1H, d, J=7.92 Hz, NCH=); 8.27 (1H, broad s, NH). ¹³C-NMR (CDCl₃) : δ 103.65 (HC=); 116.55 (=C_{quat}); 119.32, 120.54 and 121.29 (each =CH); 129.25 and 133.12 (each =C_{quat}). The ¹H-NMR spectra were consistent with reported literature data.⁴

7-Chloro-5-methylindole (8b). Crude yield : 56% (toluene) - 43% (xylene). Indole **8b** was separated from the dehalogenated compound **10b** by flash chromatography (CH₂Cl₂ : hexane 1:4; Rf 0.24). MS m/z (%) : 165/7 (M⁺, 100); 164/6(59); 130(96); 128(16); 102(13); 101(16); 77(13); 64(13); 51(16). IR (NaCl) : ν_{max} : 3350-3500 (NH); 1568; 1332; 1321; 867; 842; 722 cm⁻¹. ¹H-NMR (CDCl₃) : δ 2.39 (3H, s, Me); 6.46 (1H, t, J=2.64 Hz, CH=CHN); 7.02 (1H, broad s, CH=CMe); 7.10 (1H, t, J=2.64 Hz, CH=CHN); 8.12 (1H, broad s, NH). ¹³C-NMR (CDCl₃) : δ 21.20 (Me); 103.05 (CH=); 116.03 (=C_{quat}); 119.03, 122.77 and 124.87 (each HC=); 129.41, 130.22 and 131.43 (each =C_{quat}). Lit.²⁰ bp. 130-134°C/14 mmHg.

5-Methylindole (10b). Crude yield from **6b** : 14% (toluene) - 29% (xylene); from **3b** : 17% (xylene). Indole **10b** was isolated by flash chromatography (CH₂Cl₂ : hexane 1:4; Rf 0.12). Mp. 58.3-60.2°C (Lit.²¹ mp. 58.5°C). MS m/z (%) : 131 (M⁺, 88); 130(100); 103(12); 102(6); 77(16); 65(6); 64(6); 52(5); 51(8). IR (NaCl) : ν_{max} : 3250-3500 (NH); 1578; 1415; 1321; 1093; 802 cm⁻¹. ¹H-NMR (CDCl₃) : δ 2.43 (3H, s, Me); 6.42 (1H, broad s, C<u>H</u>=CHN); 6.97-7.05 (2H, m, CH=C<u>H</u>N and CH=C<u>H</u>-C_{quat} Me); 7.17 (1H, d, J=8.25 Hz, C<u>H</u>=CH-C_{quat} Me); 7.41 (1H, broad s, =C<u>H</u> C_{quat} Me); 7.83 (1H, broad s, NH). ¹³C-NMR (CDCl₃) : 21.40 (Me); 101.89, 110.69, 120.27, 123.52 and 124.27 (each =CH); 128.05, 128.89 and 134.03 (each =C_{quat}).

8-Chloroquinoline (16a). Crude yield : 41% (toluene). 8-Chloroquinoline (**16a**) was purified by flash chromatography (CH₂Cl₂ : hexane 4:1; Rf 0.19). MS m/z (%) : 163/5 (M⁺, 100); 136/8(9); 128(30); 127(13); 101(13); 75(13); 74(9); 68(11); 51(9); 50(12); 44(51). IR (NaCl) : ν_{max} : 1593; 1490; 1459; 1380; 1304; 1209; 1062; 980; 823; 784 cm⁻¹. ¹H-NMR (CDCl₃) : δ 7.4-7.5 (2H, m, =C₃H and =C₆H); 7.77 (1H, dxd, J₁=8.25 Hz, J₂=0.99 Hz, =C₄H); 7.86 (1H, dxd, J₁=7.59 Hz, J₂=1.32 Hz, =C₇H); 8.21 (1H, dxd, J₁=8.25 Hz, J₂=1.65 Hz, =C₃H); 9.07 (1H, dxd, J₁=4.29 Hz, J₂=1.65 Hz, =C₂H). ¹³C-NMR (CDCl₃) : δ 121.91, 126.49, 126.95, 129.54 and 129.58 (each =CH); 133.42 (=C_{quat}); 136.51 (=CH); 144.42 (=C_{quat} N); 151.00 (NCH=). Lit.¹⁹ bp. 110°C/1 mmHg.

8-Chloro-6-methylquinoline (16b). Crude yield : 77% (toluene). Quinoline **16b** was purified by flash chromatography (hexane : EtOAc 7:3; Rf 0.29). MS m/z (%) : 177/9 (M⁺, 1); 143(100); 142(54); 141(10); 140 (5); 117(5); 116(7); 115(17); 114(4); 89(7); 72(7); 71(6); 63(6); 59(9); 58(4); 51(4). IR (NaCl) : ν_{max} : 2910; 1592; 1484; 1360; 1322; 1262; 990; 917; 861; 782; 732 cm⁻¹. ¹H-NMR (CDCl₃) : δ 2.54 (3H, s, Me); 7.48 (1H, dxd, J₁=8.25 Hz, J₂=4.29 Hz, NCH=C<u>H</u>); 7.55 (1H, s, C<u>H</u>=CCl); 7.73 (1H, d, J=1.65 Hz, C_{quat}C<u>H</u>CMe); 8.15 (1H, dxd, J₁=8.24 Hz, J₂=1.65 Hz, NCHCHC<u>H</u>); 9.03 (1H, dxd, J₁=4.29 Hz, J₂=1.65 Hz, NC<u>H</u>). ¹³C-NMR (CDCl₃) : δ 21.42 (Me); 121.94 and 125.91 (each =CH); 125.98, 128.53 and 129.58 (each =C_{quat}); 131.98 and 136.37 (each =CH); 137.03 (=C_{quat}); 149.95 (NCH=).

6-Methylquinoline (17b). Crude yield : 38%. 6-Methylquinoline (17b) was purified by flash chromatography (CH₂Cl₂ : hexane 9:1; Rf 0.19). MS m/z (%) : 143 (M⁺, 100); 142(47); 115(29); 89(23); 71(20); 63 (20); 57(29); 55(18); 44(26); 43(39); 41(27). IR (NaCl) : ν_{max} : 1655; 1590; 1554; 1497; 1114; 828 cm⁻¹. ¹H-NMR (CDCl₃) : δ 2.54 (3H, s, Me); 7.36 (1H, dxd, J₁=8.25 Hz, J₂=4.29 Hz, =C₃H); 7.53-7.57 (2H, m, =C₈H and =C₄H); 8.00 (1H, d, J=8.57 Hz, =C₇H); 8.07 (1H, d, J=8.25 Hz, =C₄H); 8.85 (1H, ~d, J=3.30 Hz, NC₂H=). ¹³C-NMR (CDCl₃) : δ 21.58 (Me); 121.08, 126.59, 129.07, 131.77 and 135.42 (each CH=); 128.32; 136.40 and 146.84 (each =C_{quart}); 149.50 (CH=N). Lit.²¹ bp. 240-257°C/760 mmHg.

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