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STEREOREGULATION IN THE PREPARATION OF 1- AND 3-MONOSUBSTITUTED 1,2,3,4,6,7,12,12b-OCTAHYDROINDOLO[2,3-a]QUINOLIZINES.

MAURI LOUNASMAA*, REIJA JOKELA, BIRGIT TIRKKONEN AND TARJA TAMMINEN

Laboratory for Organic and Bioorganic Chemistry,
Technical University of Helsinki, SF-02150 Espoo, Finland

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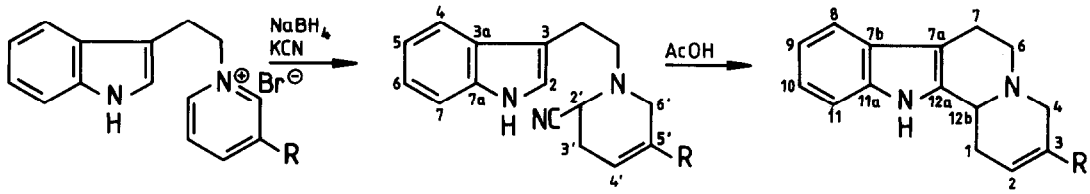
Abstract - Our recently developed method is successfully applied to the preparation of 1- and 3-monosubstituted 1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizines possessing the C(12b)H-C(1)H and C(12b)H-C(3)H relationship, respectively, cis or trans at will. Complete ^{13}C NMR data are presented for the prepared compounds.

We recently developed a new synthetic method[1] which permits the preparation of 2-monosubstituted 1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizines possessing at will the C(12b)H-C(2)H cis or trans relationship.
Here we explore the applicability of the method to the preparation of 1- and 3-monosubstituted 1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizines possessing the C(12b)H-C(1)H and C(12b)H-C(3)H relationship, respectively, cis or trans at will.

RESULTS AND DISCUSSION

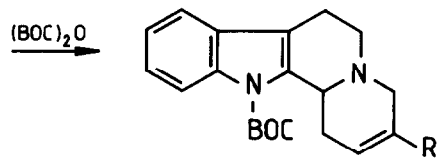
Alkylation of 3-ethylpyridine and methyl 3-pyridylacetate with tryptophyl bromide[2] afforded pyridinium salts 1 and 2, which, by $NaBH_4$ reduction and cyanide trapping,[3-8] were transformed to α-aminonitriles 3 and 4, respectively. When 3 and 4 were treated with AcOH, indolo[2,3-a]quinolizidines 5 and 6 were obtained. A part of compounds 5 and 6 was transformed with di-t-butyl dicarbonate [$(BOC)_2O$][9-12] to the corresponding BOC-protected indolo[2,3-a]-quinolizidines 7 and 8 (Scheme 1).



1 R = CH_2CH_3
2 R = $CH_2CO_2CH_3$

3 R = CH_2CH_3
4 R = $CH_2CO_2CH_3$

5 R = CH_2CH_3
6 R = $CH_2CO_2CH_3$

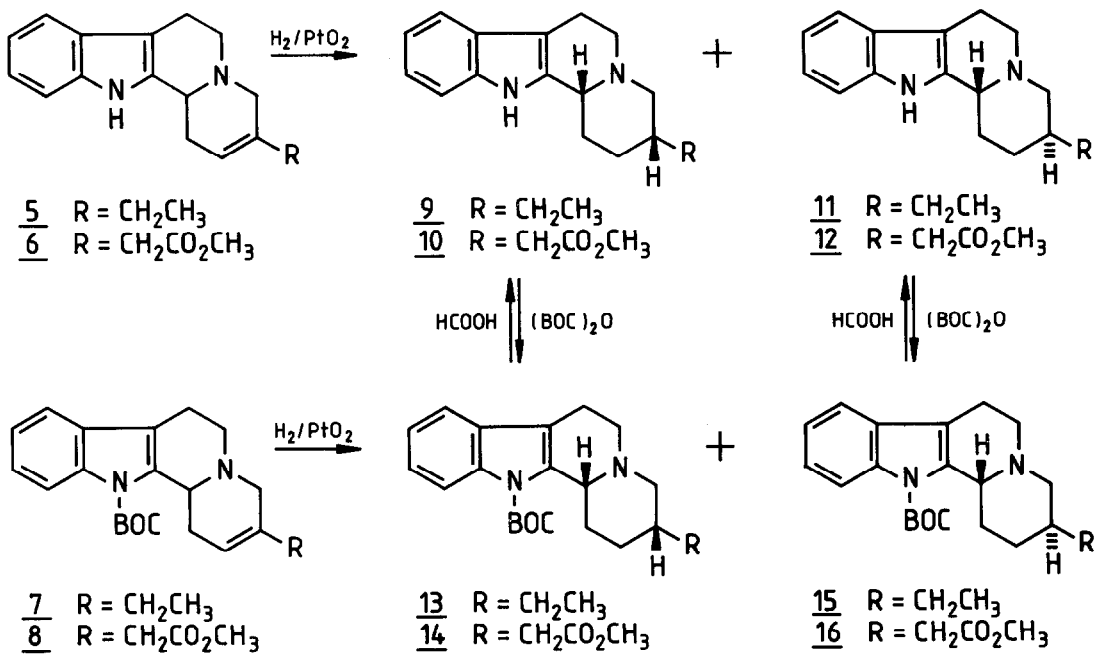


7 R = CH_2CH_3
8 R = $CH_2CO_2CH_3$

Scheme 1

Catalytic hydrogenation (PtO_2) of compounds 5 and 6 led to compounds 9 (60%) and 11 (5%), and 10 (75%) and 12 (15%), respectively, of which the main products (compounds 9 and 10) possess the C(12b)H-C(3)H *cis* configuration. Compounds 9, 10, 11 and 12 were transformed with $(BOC)_2O$ to the corresponding BOC-protected compounds 13, 14, 15 and 16, respectively. It was also verified that acid-induced cleavage (HCOOH) of the protective BOC-groups leads back to compounds 9, 10, 11 and 12 (Scheme 2).

By contrast, catalytic hydrogenation (PtO_2) of the BOC-protected compounds 7 and 8 led to compounds 13 (5%) and 15 (75%), and 14 (15%) and 16 (70%), respectively, of which the main products (compounds 15 and 16) possess the C(12b)H-C(3)H *trans* configuration. It was reverified (*vide supra*) that compounds 13, 14, 15 and 16 could be transformed to the corresponding non-protected compounds 9, 10, 11 and 12 by acid-induced cleavage (HCOOH) (Scheme 2).

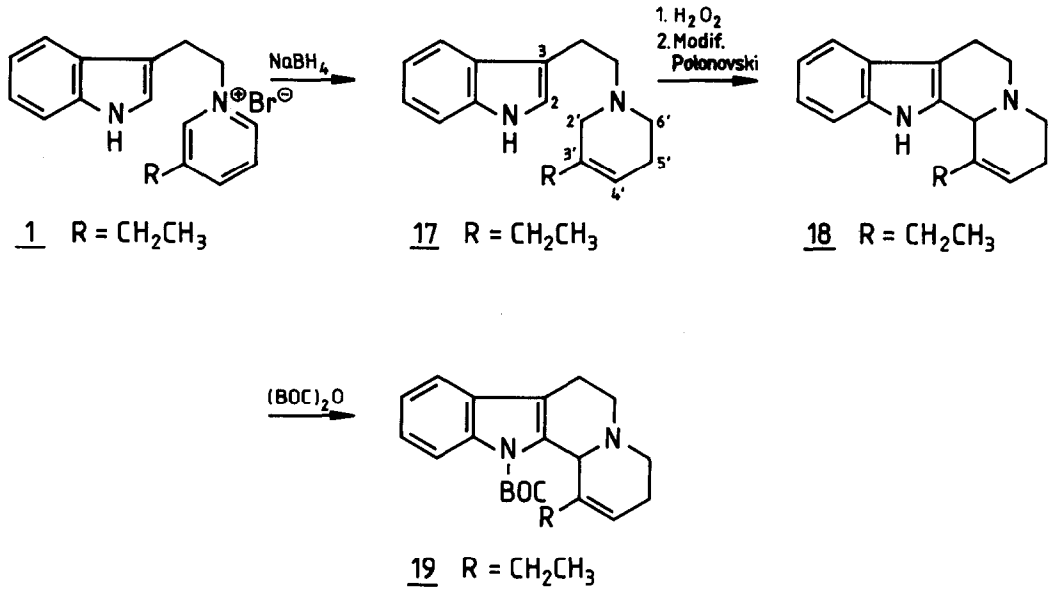


Scheme 2

$NaBH_4$ reduction of pyridinium salt 1 yielded compound 17, which by H_2O_2 oxidation and modified Polonovski reaction[6,13-15] was transformed to compound 18. A part of compound 18 was treated with $(BOC)_2O$ to afford the corresponding BOC-protected compound 19 (Scheme 3).

Catalytic hydrogenation (PtO_2) of compound 18 led to compound 20 possessing the C(12b)H-C(1)H cis configuration. Traces of the corresponding C(12b)H-C(1)H trans derivative (compound 23; vide infra) were detected by TLC. Compound 20 was transformed by $(BOC)_2O$ treatment to the corresponding BOC-protected compound 21, from which the non-protected compound 20 could be regenerated by acid-induced cleavage (HCOOH) (Scheme 4).

Again, in contrast to the above results, catalytic hydrogenation (PtO_2) of the BOC-protected compound 19 led to compound 22 possessing the C(12b)H-C(1)H trans configuration. Traces of the corresponding C(12b)H-C(1)H cis



1 R = CH_2CH_3 17 R = CH_2CH_3 18 R = CH_2CH_3

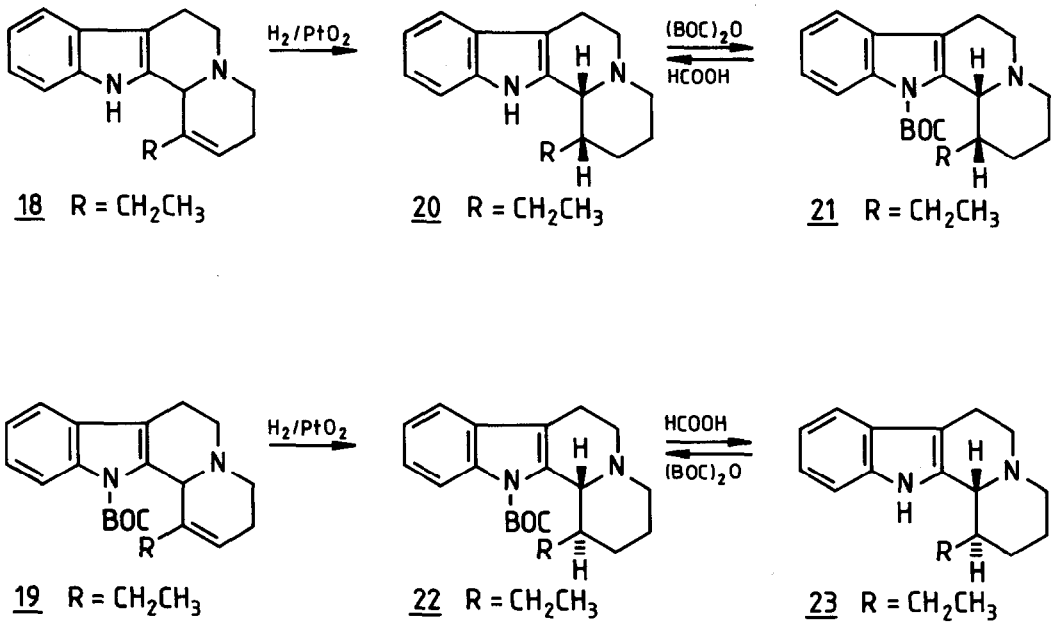
19 R = CH_2CH_3

Scheme 3

derivative (compound 21; vide supra) were detected by TLC. By acid-induced cleavage (HCOOH), compound 22 afforded the corresponding non-protected compound 23. It was also verified that the $(BOC)_2O$ treatment transformed compound 23 back to the BOC-protected compound 22 (Scheme 4).

We also became interested in the behaviour of the indolo[2,3-a]-quinolizidine skeleton possessing an exocyclic double bond at C-3 (present in many indole alkaloids) in the above described reduction conditions. For the compounds to be tested we chose (±)-deplancheine 24[16] and its BOC-protected counterpart 25, easily prepared from 24 by $(BOC)_2O$ treatment (Scheme 5).

Catalytic hydrogenation (PtO_2) of (±)-deplancheine 24 led almost exclusively to compound 11 possessing the C(12b)H-C(3)H trans configuration, whereas the same treatment of compound 25 afforded an equimolar mixture of compounds 13 and 15 possessing the C(12b)H-C(3)H cis and trans configurations, respectively (Scheme 5). Thus, even in these



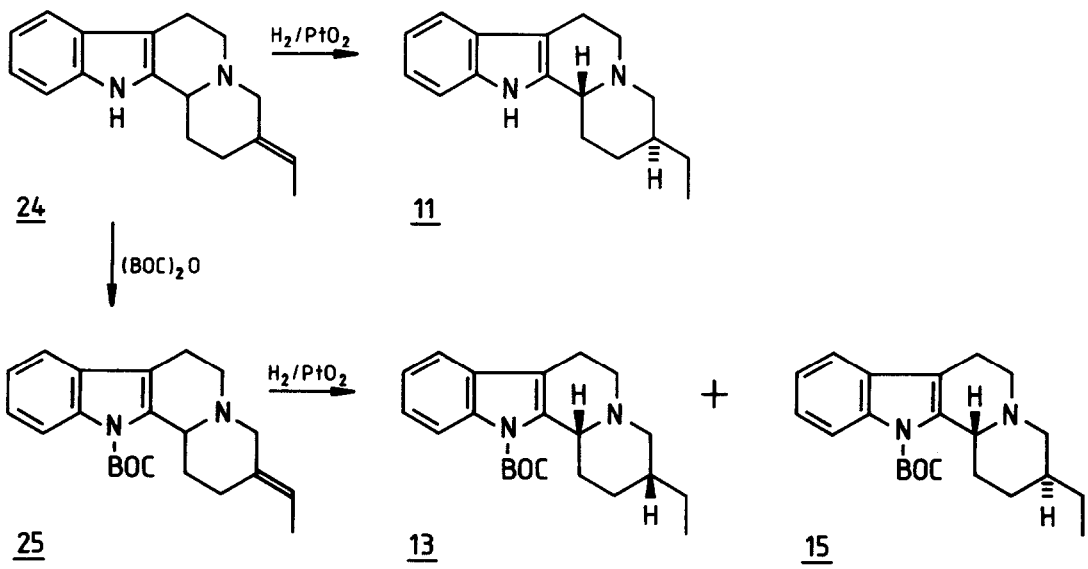
Scheme 4

cases the presence or absence of the BOC group in the indolo[2,3-a]quinolizidine skeleton has its effect on the stereochemistry of the resulting products, though in the opposite way to that described above.

The ^{13}C NMR data of compounds 4, 6, 8, 10, 12, 14, 16, 17, 18, 19, 21, 22, 24 and 25 are given in Fig. 1. For those of compounds 3, 5, 7, 9, 11, 13 and 15, see Ref. 6 (compounds 2, 3, 5, 8, 9, 11 and 12, respectively) and for those of compounds 20 and 23, see Ref. 17 (compounds 2 and 1, respectively).

Comparison of the chemical shifts found for compounds 6, 8, 10, 12, 14, 16, 18, 19, 21, 22, 24 and 25 with those given earlier,[1,6,17] taking into account the conformational considerations relevant for indolo[2,3-a]quinolizidines,[1,5] provides clear evidence of the stereostructures depicted in the formulae. Drastic changes are seen in the shift values for C(6), C(7a), C(9), C(10), C(11) and C(12a) in the BOC-protected indolo[2,3-a]quinolizidines 8, 14, 16, 19, 21, 22 and 25 relative to their non-protected counterparts 6, 10, 12, 18, 20, 23 and 24. The shift value of ~

47 ppm found for C(6) in the spectra of compounds 8, 16 and 25, and that of 51.3 ppm found in the spectrum of compound 14, are in agreement with the earlier results.[6]



24 11 25 13 15

Scheme 5

The clear difference between the C(6) signals (51.8 vs. 42.9 ppm) in the spectra of compounds 21 and 22 indicates a pronounced change in the contribution of different conformations of the indolo[2,3-a]quinolizidine skeleton to the conformational equilibrium of these two compounds. For a more detailed general discussion of this subject, see Refs. 1, 5 and 6.

CONCLUSIONS

The results clearly demonstrate the value of our method for the stereoselective preparation of 1- and 3-monosubstituted 1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizines with the C(12b)H-C(1)H and C(12b)H-C(3)H relationship, respectively, cis or trans at will.

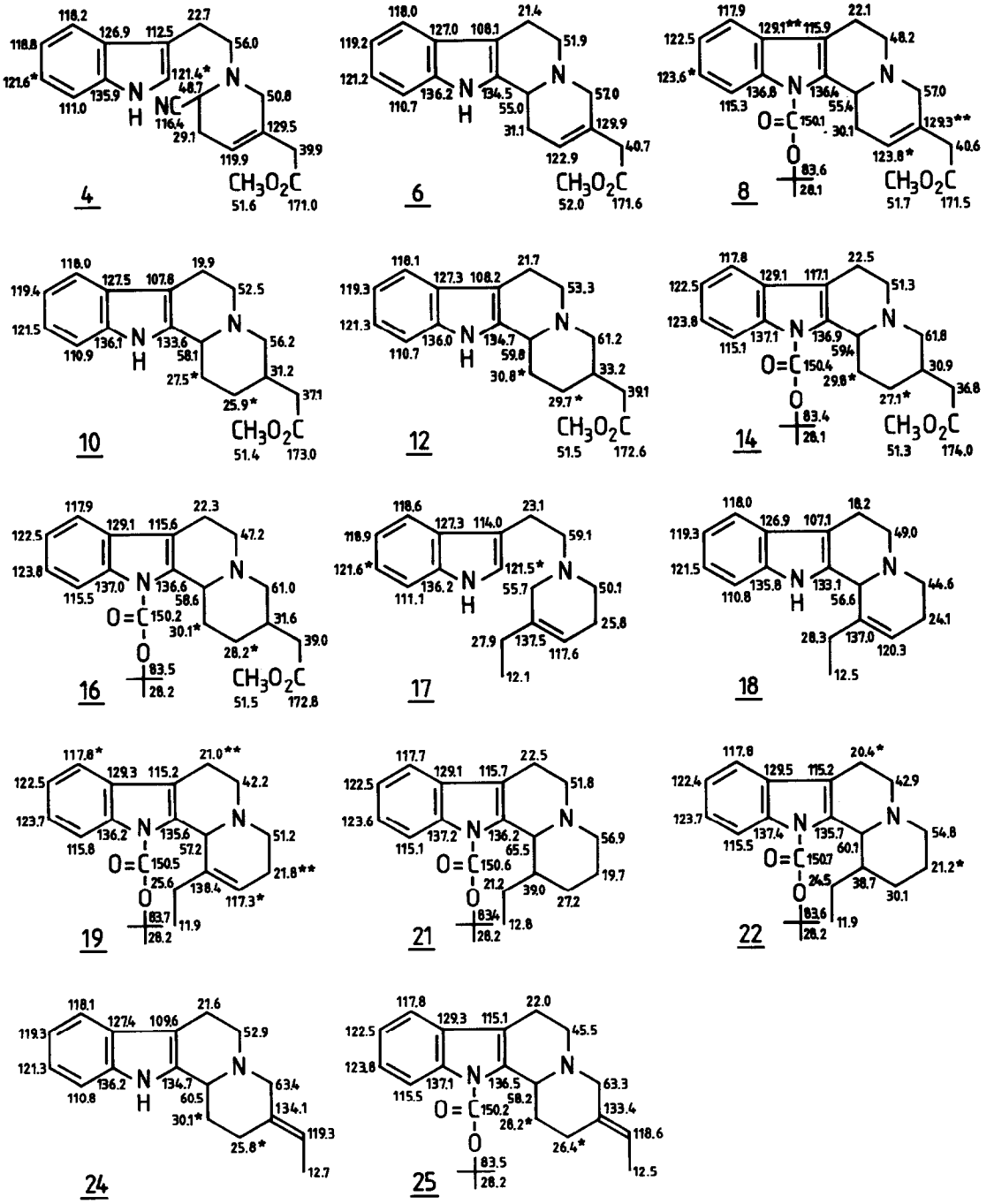


Fig. 1

EXPERIMENTAL

IR spectra were recorded with a Perkin-Elmer 700 spectrophotometer in $CHCl_3$, if not otherwise stated. ^1H and ^{13}C NMR spectra were measured with a Jeol JNM-FX 60 spectrometer working at 59.80 MHz (^1H NMR) and 15.04 MHz (^{13}C NMR). The spectra were recorded in $CDCl_3$. Chemical shift data are given in ppm downfield from TMS. Abbreviations s, d, t, m, br and def are used to designate singlet, doublet, triplet, multiplet, broad and deformed, respectively. For the ^{13}C NMR data of compounds 3, 5, 7, 9, 11, 13 and 15, see Ref. 6 (compounds 2, 3, 5, 8, 9, 11 and 12, respectively) and for the data of compounds 20 and 23, see Ref. 17 (compounds 2 and 1, respectively). For the other ^{13}C NMR data, see Fig. 1. Mass spectrometry (EIMS and HRMS) was done on a Jeol DX 303/DA 5000 instrument.

Preparation of compound 3

Hydrochloric acid (6 N, 1.5 ml) was added dropwise to a stirred solution of KCN (1.13 g, 17.4 mmol) in H_2O (1.5 ml), layered with Et_2O (9 ml), and kept at 0°C (Ar atm). Pyridinium salt 1[17] (1.00 g, 3.02 mmol) prepared by alkylation of 3-ethylpyridine with tryptophyl bromide[2], was dissolved in MeOH (2.4 ml), and $NaBH_4$ (127 mg, 3.32 mmol) was added during 0.5 h. The mixture was stirred at rt for 3.5 h. The Et_2O layer was separated and the aqueous layer was extracted several times with Et_2O. The combined ethereal extracts were dried (Na_2SO_4) and evaporated to give compound 3.

Y. 90%. Viscous oil.

Analytical data were identical with those described earlier.[6]

Preparation of compound 4

Reaction of pyridinium salt 2[11,18] (1.13 g, 3.02 mmol), prepared by alkylation of methyl 3-pyridylacetate with tryptophyl bromide[2], with KCN (1.13 g, 17.4 mmol) and $NaBH_4$ (127 mg, 3.32 mmol) using the procedure described for compound 3 (*vide supra*) afforded compound 4.

Y. 92%. Amorphous material.

IR: 3450 (NH), 1740 (C=O).

^1H NMR: 3.63 (3H, s, $-CO_2CH_3$), 5.57 (1H, br s, H-4'), 6.89 (1H, d, J=1.8 Hz, H-2), 7.17-7.65 (4H, m, arom. H), 8.47 (1H, br s, NH).

MS: 323 (M^+), 296, 237, 193, 179, 166, 165, 151, 144 (100%), 130; exact mass: 323.1624 (calc. for $C_{19}H_{21}N_3O_2$: 323.1634).

Preparation of compound 5

Compound 3 (0.76 g, 2.72 mmol) was dissolved in 80 ml of 50% HOAc and the solution was stirred at rt (N_2 atm) for 3 d. It was then evaporated and shaken with 2N Na_2CO_3. Extraction with CH_2Cl_2 and drying (Na_2SO_4) yielded the crude product of 5[6,19], which was purified by column chromatography (silica, CH_2Cl_2-MeOH, 95:5).

Y. 45%. Mp. 146-148°C (EtOH) (lit. Mp. 147-148°C[4], 146-148°C[6], 143-145°C[20]).

Analytical data were identical with those described earlier.[6]

Preparation of compound 6

Compound 4 (0.88 g, 2.72 mmol) was dissolved in 90 ml of 50% HOAc and the solution was stirred at rt (Ar-atm) for 23 h. Usual work-up afforded the crude product of compound 6[18], which was purified by column chromatography (alumina, CH_2Cl_2-MeOH, 99.5:0.5).

Y. 42%. Mp. 133°C (MeOH) (lit.[18] amorphous material).

IR: 3450 (NH), 1730 (C=O).

^1H NMR: 3.69 (3H, s, $-CO_2CH_3$), 5.64 (1H, br s, H-2), 6.99-7.54 (4H, m, arom. H), 8.14 (1H, br s, NH).

MS: 298 (M^+), 283, 237, 220 (100%), 182; exact mass: 298.2338 (calc. for $C_{18}H_{20}N_2O_2$: 296.1525).

Preparation of compound 7

To compound 5 (116 mg, 0.46 mmol) in 1 ml of abs. CH_2Cl_2 was added p-dimethylamino pyridine (DMAP) (6 mg, 0.1 equiv.) and di-t-butyl dicarbonate [$(BOC)_2O$] (120 mg, 1.2 equiv.) with stirring at rt (Ar atm). After 2 h the mixture was evaporated and purified by column chromatography (silica, CH_2Cl_2-MeOH-Et_3N, 97.75:2:0.25) to afford compound 7.

Y. 90%. Viscous oil.

Analytical data were identical with those described earlier.[6]

Preparation of compound 8

Reaction of compound 6 (166 mg, 0.56 mmol) with DMAP (7 mg, 0.1 equiv.) and $(BOC)_2O$ (220 mg, 1.8 equiv.) using the procedure described for compound 7 (vide supra) gave the crude product of 8, which was purified by column chromatography (silica, CH_2Cl_2-MeOH-Et_3N, 99:0.75:0.25).

Y. 85%. Viscous oil.

IR: 1725 (C=O).

^1H NMR: 1.66 (9H, s, $-C(CH_3)_3$), 3.69 (3H, s, $-CO_2CH_3$), 5.67 (1H, br s, H-2), 7.14-7.52 (3H, m, H-8, 9, 10), 8.07 (1H, m, H-11).

MS: 396 (M^+), 339, 295, 281, 214, 170 (100%), 169, 168; exact mass: 396.2058 (calc. for $C_{23}H_{28}N_2O_4$: 396.2049).

Preparation of compounds 9 and 11

Hydrogenation (MeOH, PtO_2, 25 h) of compound 5 (230 mg, 0.91 mmol) followed by separation by column chromatography (silica, CH_2Cl_2-MeOH, 95:5) yielded compounds 9 and 11.

Compound 9:

Y. 60%. Viscous oil.

Analytical data were identical with those described earlier.[6,17,21,22]

Compound 11:

Y. 5%. Mp. 159-161°C (EtOH) (lit. Mp. 159-161°C[6], 160-161°C[22], 157°C[23]).

Analytical data were identical with those described earlier.[6,17,21-23]

Preparation of compounds 10 and 12

Hydrogenation (MeOH, PtO_2, 25 h) of compound 6 (224 mg, 0.76 mmol) followed by separation by column chromatography (silica, CH_2Cl_2-MeOH, 97:3) yielded compounds 10 and 12.

Compound 10:

Y. 75%. Mp. 180-182°C (MeOH).

Analytical data were identical with those described earlier.[11]

Compound 12:

Y. 15%. Mp. 164-165°C (MeOH) (lit.[18] Mp. 168°C).

IR: 3420 (NH), 1740 (C=O).

^1H NMR: 3.68 (3H, s, $-CO_2CH_3$), 7.00-7.55 (4H, m, arom. H), 7.81 (1H, br s, NH).

MS 298 (M^+), 297 (100%), 283, 267, 225, 197, 184, 170, 169; exact mass: 298.1683 (calc. for $C_{18}H_{22}N_2O_2$: 298.1681).

Preparation of compound 13

Reaction of compound 9 (133 mg, 0.52 mmol) with DMAP (6 mg, 0.1 equiv.) and $(BOC)_2O$ (204 mg, 1.8 equiv.) using the procedure described for compound 7 (*vide supra*) afforded the crude product of compound 13, which was purified by column chromatography (silica, CH_2Cl_2-MeOH, 97:3).

Y. 90%. Viscous oil.

Analytical data were identical with those described earlier.[6]

Preparation of compound 14

Reaction of compound 10 (90 mg, 0.30 mmol) with DMAP (4 mg, 0.1 equiv.) and $(BOC)_2O$ (120 mg, 1.8 equiv.) using the procedure described for compound 7 (vide supra) gave the crude product of compound 14, which was purified by column chromatography (silica, CH_2Cl_2-MeOH, 99:1).

Y. 90%. Viscous oil.

IR: 1730 (C=O).

^1H NMR: 1.64 (9H, s, $-C(CH_3)_3$), 3.66 (3H, s, $-CO_2CH_3$), 7.13-7.50 (3H, m, H-8, 9, 10), 8.08 (1H, m, H-11).

MS: 398 (M^+), 342, 341 (100%), 297, 269, 170, 169; exact mass: 398.2219 (calc. for $C_{23}H_{30}N_2O_4$: 398.2206).

Preparation of compound 15

Reaction of compound 11 (35 mg, 0.14 mmol) with DMAP (1.7 mg, 0.1 equiv.) and $(BOC)_2O$ (53 mg, 1.8 equiv.) using the procedure described for compound 7 (vide supra) afforded the crude product of compound 15, which was purified by flash chromatography (alumina, CH_2Cl_2).

Y. 85%. Viscous oil.

Analytical data were identical with those described earlier.[6]

Preparation of compound 16

Reaction of compound 12 (22 mg, 0.08 mmol) with DMAP (0.8 mg, 0.1 equiv.) and $(BOC)_2O$ (28 mg, 1.8 equiv.) using the procedure described for compound 7 (vide supra) afforded the crude product of compound 16, which was purified by flash chromatography (alumina, CH_2Cl_2).

Y. 50%. Viscous oil.

IR: 1730 (C=O).

^1H NMR: 1.65 (9H, s, $-C(CH_3)_3$), 3.68 (3H, s, $-CO_2CH_3$), 7.13-7.40 (3H, m, H-8, 9, 10), 8.09 (1H, m, H-11).

MS: 398 (M^+), 342, 341 (100%), 297, 269, 170, 169; exact mass: 398.2232 (calc. for $C_{23}H_{30}N_2O_4$: 398.2206).

Preparation of compounds 13 and 15

Hydrogenation (MeOH, PtO_2, 17 h) of compound 7 (150 mg, 0.43 mmol) followed by separation by column chromatography (silica, CH_2Cl_2-MeOH, 97:3) afforded compounds 13 and 15.

Compound 13:

Y. 5%. Viscous oil.

Analytical data were identical with those of compound 13 described above.

Compound 15:
Y. 75%. Viscous oil.
Analytical data were identical with those of compound 15 described above.

Preparation of compounds 14 and 16
Hydrogenation (MeOH, PtO_2, 22 h) of compound 8 (160 mg, 0.40 mmol) followed by separation by column chromatography (silica, CH_2Cl_2-MeOH, 99:1) afforded compounds 14 and 16.
Compound 14:
Y. 15%. Viscous oil.
Analytical data were identical with those of compound 14 described above.

Compound 16:
Y. 70%. Viscous oil.
Analytical data were identical with those of compound 16 described above.

Preparation of compounds 9 and 11 by BOC cleavage
Compound 13 or 15 (88 mg, 0.25 mmol) was dissolved in HCOOH (3.7 ml). The reaction mixture was stirred for 28 h at rt (Ar atm). It was then evaporated and shaken with 10% aq. Na_2CO_3. Extraction with CH_2Cl_2 and drying (Na_2SO_4) afforded the crude product of compound 9 or compound 11, respectively, which was purified by column chromatography (silica, CH_2Cl_2-MeOH, 95:5).
Compound 9:
Y. 80%. Viscous oil.
Analytical data were identical with those described earlier.[6,17,21,22]
Compound 11:
Y. 80%. Mp. 159-161°C (EtOH) (lit. Mp. 159-161°C[6], 160-161°C[22], 157°C[23]).
Analytical data were identical with those described earlier.[6,17,21-23]

Preparation of compounds 10 and 12 by BOC cleavage
Treatment of compounds 14 and 16 (88 mg, 0.22 mmol) with HCOOH following the procedure described for compounds 9 and 11 (*vide supra*) gave the crude products of compounds 10 and 12, respectively, which were purified by preparative TLC (silica, CH_2Cl_2-MeOH, 90:10).
Compound 10:
Y. 80%. Mp. 180-182°C (MeOH).
Analytical data were identical with those described earlier.[11]

Compound 12:
Y. 80%. Mp. 164-165°C (MeOH).
Analytical data were identical with those of compound 12 described above.

Preparation of compound 17
Pyridinium salt 1 (3.00 g, 9.06 mmol) (vide supra) was dissolved in MeOH:H_2O (9:1, 150 ml), and $NaBH_4$ (4.13 g, 0.11 mol) was added during 30 min at 0°C (Ar atm). The mixture was stirred for 4 h at rt. Usual work-up afforded compound 17.
Y. 99%. Mp. 122°C (benzene-hexane) (lit.[24] Mp. 122°C).
IR (KBr): 3440 (NH).
^1H NMR: 1.02 (3H, t, J=7.2 Hz, $-CH_2\underline{CH_3}$), 5.47 (1H, br s, H-4'), 6.92 (1H, d, J=1.8 Hz, H-2), 7.18-7.68 (4H, m, arom. H), 8.54 (1H, br s, NH).
MS: 254 (M^+), 124 (100%); exact mass: 254.1775 (calc. for $C_{17}H_{22}N_2$: 254.1783).

Preparation of compound 18
Compound 17 (1.51 g, 5.95 mmol) was reacted with H_2O_2 (30%, 1.7 ml) in $CHCl_3$:MeOH (1:1, 30 ml) to afford after the usual work-up the corresponding N-oxide (1.59 g, 99%). The N-oxide in trifluoroacetic acid (32 ml) was stirred at 0°C (Ar atm) and trifluoroacetic anhydride (8 ml, 9.6 equiv.) was added during 15 min. After 1 h at rt, 2N HCl (48 ml) was added carefully and the mixture was kept at 70°C for 20 min. Neutralization with $NaHCO_3$ (s) in CH_2Cl_2 followed by usual work-up and purification by flash chromatography (alumina, CH_2Cl_2) afforded compound 18.
Y. 20%. Mp. 108-112°C (benzene-hexane) (lit.[25] Mp. 115-116°C).
IR: 3480 (NH).
^1H NMR: 1.13 (3H, t, J=7.4 Hz, $-CH_2\underline{CH_3}$), 4.57 (1H, m, H-12b), 5.60 (1H, m, H-2), 7.00-7.55 (4H, arom. H), 8.17 (1H, br s, NH).
MS: 252 (M^+, 100%), 251, 237, 223; exact mass: 252.1601 (calc. for $C_{17}H_{20}N_2$: 252.1626).

Preparation of compound 19
Reaction of compound 18 (34 mg, 0.14 mmol) with DMAP (2 mg, 0.1 equiv.) and $(BOC)_2O$ (53 mg, 1.8 equiv.) following the procedure described for compound 7 (vide supra) afforded the crude product of compound 19, which was purified by column chromatography (alumina, CH_2Cl_2).
Y. 90%. Viscous oil.
IR: 1730 (C=O).

^{1}H NMR: 0.80 (3H, t, J=7.3 Hz, $CH_2\underline{CH_3}$), 1.66 (9H, s, $-CH(CH_3)_3$), 5.51 (1H, m, H-2), 7.14-7.41 (3H, m, H-8, 9, 10), 8.11 (1H, m, H-11).
MS: 352 (M^+), 323, 295 (100%), 267, 251; exact mass: 352.2168 (calc. for $C_{22}H_{28}N_2O_2$: 352.2151).

Preparation of compound 20
Hydrogenation (MeOH, PtO_2, 5h) of compound 18 (61 mg, 0.24 mmol) afforded after usual work-up compound 20.
Y. 90%. Mp. 216-217°C (benzene-hexane) (lit. Mp. 116-119°C[21], 61-70°C[26]).
Analytical data were identical with those described earlier.[17]

Preparation of compound 21
Reaction of compound 20 (41 mg, 0.16 mmol) with DMAP (2 mg, 0.1 equiv.) and $(BOC)_2O$ (64 mg, 1.8 equiv.) following the procedure described for compound 7 (vide supra) afforded the crude product of compound 21, which was purified by flash chromatography (alumina, CH_2Cl_2-MeOH, 99.5:0.5).
Y. 80%. Viscous oil.
IR: 1720 (C=O).
^{1}H NMR: 0.75 (3H, def, $-CH_2\underline{CH_3}$), 1.65 (9H, s, $-C(CH_3)_3$), 3.74 (1H, m, H-12b), 7.13-7.40 (3H, m, H-8, 9, 10), 8.06 (1H, m, H-11).
MS: 354 (M^+), 298, 297 (100%), 253, 170, 169; exact mass: 354.2315 (calc. for $C_{22}H_{30}N_2O_2$: 354.2307).

Preparation of compound 20 by BOC cleavage
Treatment of compound 21 (32 mg, 0.09 mmol) with HCOOH following the procedure described for compounds 9 and 11 (vide supra) afforded after normal work-up compound 20.
Y. 95%. Mp. 216-217°C (benzene-hexane) (lit. Mp. 116-119°C[21], 61-70°C[26]).
Analytical data were identical with those of compound 20 described above.

Preparation of compound 22
Hydrogenation (MeOH, PtO_2, 60 h) of compound 19 (83 mg, 0.24 mmol) followed by purification by flash chromatography (alumina, CH_2Cl_2) afforded compound 22.
Y. 35%. Viscous oil.
IR: 1730 (C=O).
^{1}H NMR: 0.90 (3H, def, $-CH_2\underline{CH_3}$), 1.66 (9H, s, $-C(CH_3)_3$) 4.64 (1H, m, H-12b), 7.11 - 7.41 (3H, m, H-8, 9, 10), 8.07 (1H, m, H-11).

MS: 354 (M^+), 298, 297 (100%), 253, 170, 169; exact mass: 354.2346 (calc. for $C_{22}H_{30}N_2O_2$: 354.2307).

Preparation of compound 23 by BOC cleavage

Treatment of compound 22 (32 mg, 0.09 mmol) with HCOOH following the procedure described for compounds 9 and 11 (vide supra) gave after normal work-up compound 23.

Y. 95%. Mp. 123-125°C (benzene-hexane) (lit. Mp. 90-93°C[21], 113-114°C[26]).

Analytical data were identical with those described earlier.[17]

Preparation of compound 22 from compound 23

Reaction of compound 23 (23 mg, 0.09 mmol) with DMAP (1.1 mg, 0.1 equiv.) and $(BOC)_2O$ (35 mg, 1.8 equiv.) following the procedure described for compound 7 (vide supra) afforded the crude product of compound 22, which was purified by flash chromatography (alumina, CH_2Cl_2).

Y. 45%. Viscous oil.

Analytical data were identical with those of compound 22 described above.

Preparation of compound 11 from (±)-deplancheine 24

Hydrogenation (MeOH, PtO_2, 20 h) of (±)-deplancheine 24[16] (21 mg, 0.08 mmol) gave after normal work-up compound 11.

Y. 99%. Mp. 159-161°C (EtOH) (lit. Mp. 159-161°C[6], 160-161°C[22], 157°C[23]).

Analytical data were identical with those described earlier.[17,21-23]

Preparation of compound 25

Reaction of (±)-deplancheine 24[16] (28 mg, 0.11 mmol) with DMAP (1.4 mg, 0.1 equiv.) and $(BOC)_2O$ (44 mg, 1.8 equiv.) following the procedure described for compound 7 gave compound 25. The crude product was purified by flash chromatography (alumina, CH_2Cl_2).

Y. 75%. Viscous oil.

IR: 1735 (C=O).

^1H NMR: 1.68 (9H, s, $-C(CH_3)_3$), 4.41 (1H m, H-12b), 5.34 (1H, m, $=\underline{CH}CH_3$), 7.13-7.50 (3H, m, H-8,9,10), 8.11 (1H, m, H-11).

MS: 352 (M^+), 296, 295 (100%), 281, 251, 170, 169; exact mass: 352.2162 (calc. for $C_{22}H_{28}N_2O_2$: 352.2151).

Preparation of compounds 13 and 15 from compound 25

Hydrogenation (MeOH, PtO_2, 20 h) of compound 25 (29 mg, 0.08 mmol)

followed by purification by flash chromatography (alumina, CH_2Cl_2) afforded a 1:1 mixture of compounds 13 and 15.

Y. 50%.

For the analytical data, see above.

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