Synthesis of Vinca Alkaloids and Related Compounds Part 94 [1]. Epimerization of Compounds with Aspidospermane and *D*-Secoaspidospermane Skeleton [§]

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The individual epimerization steps of vincadifformine (**1**), deethylvincadifformine isomers (**2,3**), their synthetic intermediates (**4-13**) as well as that of simpler compounds with *D*-secoaspidospermane skeleton (**15-17**) were studied **a)** in protic medium (boiling deuteroacetic acidic) and **b)** under reductive (with sodium borodeuteride in boiling acetic acid, or with sodium borohydride in boiling deuteroacetic acid) conditions.

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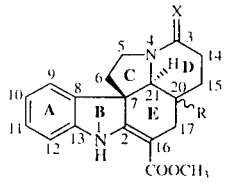
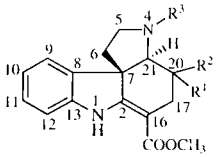
Introduction.

Over the last three decades the synthesis of most plant alkaloids having an aspidospermane skeleton and containing the anilinoacrylate structural unit had been achieved.

Up until now only alkaloids with substituents in *cis* steric position at C 20 and C 21 have been found in nature. However, in several syntheses the formation of molecules with different configurations at the above carbon atoms has been detected and there are examples of converting these products into the desired alkaloids [2,3].

In our earlier studies related to the convergent synthesis of aspidospermane [4,5], pseudoaspidospermane alkaloids [6] and some alkaloid-like compounds [7,8,9], we also observed in several cases partial or complete epimerization during the build-up of ring D in the presence of acids. Apart from the description of the experimental facts, the literature [10,11] offers only in a few cases some hints about the possible mechanism of the conversions; therefore we decided to conduct further research in order to find a plausible rationalization.





	R	X		R^1	R^2	R^3
1	αC_2H_5	H_2	7	αC_2H_5	$\beta[CH_2]_2$-$COOCH_3$	CH_2-C_6H_5
2	αH	H_2	8	βC_2H_5	$\alpha[CH_2]_2$-$COOCH_3$	CH_2-C_6H_5
3	βH	H_2	9	βH	$\alpha[CH_2]_2$-$COOCH_3$	CH_2-C_6H_5
4	αC_2H_5	O	10	βH	$\alpha[CH_2]_2$-O-CO-C_6H_5	CH_2-C_6H_5
5	αH	O	11	αH	$\beta[CH_2]_2$-O-CO-C_6H_5	H
6	βH	O	12	βH	$\alpha[CH_2]_2$-O-CO-C_6H_5	H
			13	βC_2H_5	$\alpha[CH_2]_2$-$COOCH_3$	H

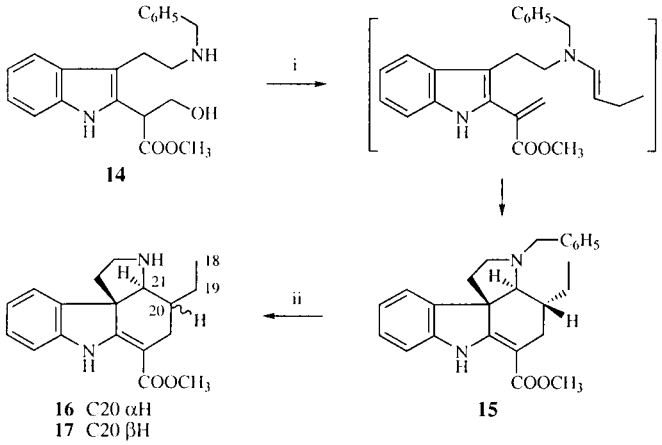
Figure 1

Results and discussions.

The selected compounds were vincadifformine (**1**) and the epimers (**2,3**) of 20-deethylvincadifformine, their synthetic intermediates (**4-13**) [4,7] (Figure 1) as well as some simple models prepared as follows.

The secondary amine [4] **14** was made to react with butanal. The stereoselective cyclization reaction gave the tertiary amine [12] **15**. Debenzylation in acetic acid, accompanied by partial epimerization, furnished a mixture of the secondary amines **16** and **17,** which were separated by thin layer chromatography. The ratio of the **16** : **17** isomers was 1:4 at room temperature and 1:2 at a reaction temperature of 70-75°C, (Scheme 1).

Scheme 1



16 C20 αH
17 C20 βH

Reagents and conditions: i, *n*-C_3H_7CHO, toluene/Δ; ii, Pd/C/H_2, CH_3COOH, room temperature or 70-75°C

We then studied the observable or detectable epimerization tendency of the selected compounds in *acidic medium*. It seemed promising to carry out these reactions in deuteroacetic acid instead of acetic acid, hoping that the

Table 1

Starting compound	Time of refluxing [q] (min.)	Structure of product(s) and their ratio [x]	Percentege of deuteriation at C 20	Percentage of isolated product(s)
1	120	**1**	0	35
2	15	**2**	0	32
3	15	**3**	0	33
4	60	**4**	0	33
5	30	**5**	0	31
6	30	**6**	0	33
7	60	**7**	0	30
8	60	**8**	0	31
9	120	**9**	100	48
10	120	**10**	>70	29
11	30	**11+12** (1:1)	~15 + ~15	16+17
12	30	**11+12** (1:1)	>20 + >20	14+14
13	180	**4**	0	33
15	15	**15**	~75	29
16	15	**16+17** (1:1)	0	32+31
17	15	**16+17** (1:2)	0	16+34

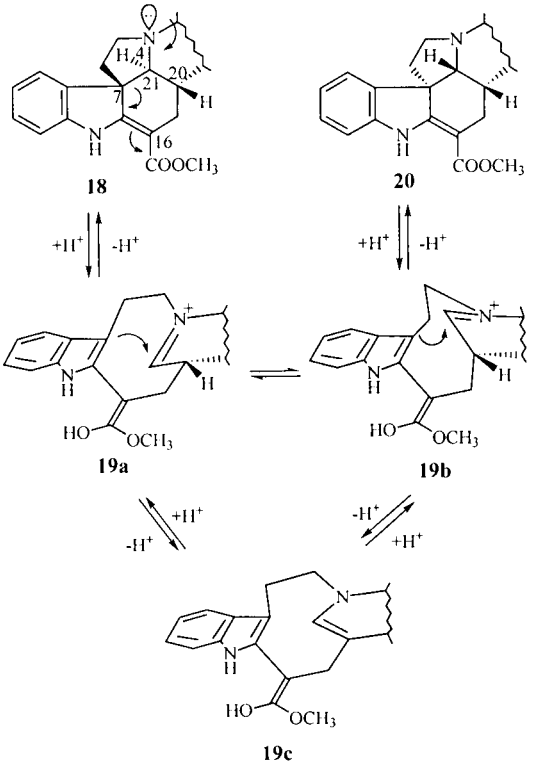
[q] 0.5 mmole of the starting compound was heated in 5 ml of deuteroacetic acid at reflux. Heating was continued until the decomposition observed during the reaction was not excessive. [x] In the formula of the products the introduced deuterium is not shown; if present, its place and its percentage are indicated in Column 4. (In all reactions the NH group of the compounds was deuterated).

location of the introduced deuterium atom may provide some insight into the pathway of the reaction. The position and extent of deuteration can be unequivocally established by ^{1}H- and ^{13}C-nmr spectroscopy. The chosen compounds **1-13** and **15-17** were first heated in deuteroacetic acid at reflux whereupon unexpected results were obtained (see Table 1). In compounds having pentacyclic system **1-6** or tetracyclic system with the lack of C_{20}-H bond and with *N*-benzyl function **7-8** no change occurred, whereas the tetracyclic derivatives **9-13** and **15-17** suffered transformations. With *N*-benzyl derivatives **9**, **10** and **15** deuteration at C 20 took place in an unusual way, with *retention*, while in derivatives **11** and **12** (with NH group) the introduction of deuterium to C 20 was accompanied by partial epimerization. In compounds **16** and **17** (no ester group present at C 20 the side-chain) only partial epimerization was observed, in **13** (no C_{20}-H present and the lack of *N*-benzyl function) cyclization with epimerization occurred; in the latter three reactions *deuterium did not show up* in the products.

Published [10,11] and our aforementioned experimental results suggest the following mechanism for epimerization (see Scheme 2): in acid medium compound **18** gives the intermediate **19** as a consequence of the indicated electron shift, the splitting of the C 7/C 21 bond, and protonation; a loss of proton enables **19** to undergo a two-directional cyclization involving the reactive atoms C 7 and C 21 (→ **18** and → **20**). Our experimental results show that in the cases of compounds **9**, **10**, **11**, **12**, and **15** there must be an equilibration of the imminium salt with the corresponding enamine (**19c**). Compounds **1**, **4**, **7**, **8**, and **13** cannot form

Scheme 2

9-Member Ring Cycle Inversion



any enamine, as they have no proton at C 20, this might explain the absence of deuterium incorporation. Compounds **4-6** have no lone pair on the nitrogen (lactam) and therefore might behave their own way (probably no C/D bond splitting). Compounds **2-3** have no incorporated deuterium, owing to either no C/D bond splitting or a ring closure thermodinamically unfavourable enamine. Compound **13** must have been epimerized before the formation of the lactam, according to the fact that lactams **4-6** did not epimerize. Compounds **16-17** epimerization without deuterium introduction, seems to indicate that the formation of the enamine is not favourable, which might be related to the fact that the iminium is actually a protonated enamine(C=NH$^+$ *vs.* C=N$^+$-C in compounds **9-10**). If intramolecular reaction can give rise to the pentacyclic ring system the main product will be a molecule of type **20** with *cis* configuration (*e.g.* see the formation of compounds with the pseudoaspidospermane skeleton [6]). However, occasionally the presence of products of type **18**, derived from **20**, can also be found if tetracycles are formed (**11** → **11** + **12** and **16** → **16** + **17**). Compounds of type **19** (the intermediates of the suggested epimerization mechanism) were successfully trapped reductively and the structures of the products reported [11].

We could make the described mechanism more exact by effecting the reactions *under reductive conditions* in acetic acid with sodium borodeuteride, and in deuteroacetic acid with sodium borohydride as well.

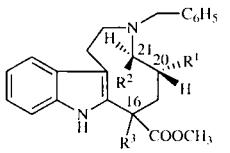
Both series of reactions were carried out with several molecules, and the results are summarized in Table 2.

Table 2

Reductive cleavage of C 7/C 21 bond.

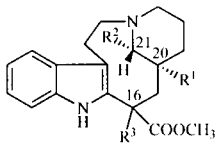
Starting Compound	Method	Structure of product(s)	Percentage of deuteration	Yield (%)
15	A	**21**	87	39
		22	100	14
15	B	**23**	90	38
		24	90	13
9	A	**25**	88	40
		26	95	14
9	B	**27**	92	38
		28	90	14
2	A	**29**	90	13
		30	100	8
2	B	**31**	50	13
		32	80	7
1	A	**33**	100	30
1	B	**34**	50	35
3	A	**35**	95 at C 2	65
3	B	**36**	90 at C-16	60

Depending on the starting compound, the reaction products were either the vincadine isomers (**33-34**) or the deethylvincadine isomers (**29-32**) and the corresponding *D*-seco derivatives (**21-28**) (see Figure 2, Figure 3).



Product	R^1	R^2	R^3
21	C_2H_5	D	αH
22	C_2H_5	D	βH
23	C_2H_5	H	αD
24	C_2H_5	H	βD
25	$[CH_2]_2$-$COOCH_3$	D	αH
26	$[CH_2]_2$-$COOCH_3$	D	αH
27	$[CH_2]_2$-$COOCH_3$	H	αD
28	$[CH_2]_2$-$COOCH_3$	H	βD

Figure 2



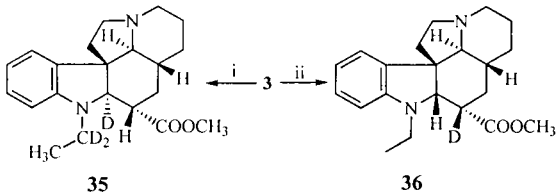
Product	R^1	R^2	R^3
29	H	D	αH
30	H	D	βH
31	H	H	αD
32	H	H	βD
33	C_2H_5	D	βH
34	C_2H_5	H	βH

Figure 3

The structures of the final products unequivocally show that in the cases of the tetracyclic compounds the treatment with sodium borodeuteride of the intermediates of type **19**, formed in hot acetic acid (Method A), resulted in their conversion into derivatives containing deuterium at C 21 (**21**, **22**, and **25**, **26**), whereas the reactions effected with sodium borohydride in deuteroacetic acid (Method B) gave products deuterated at C 16 (**23**, **24**, and **27**, **28**). In the former cases the deuteride anion always attacked the molecules on the β-face, while in the latter reactions the deutero cation was introduced into the products from both faces. In contrary, if the reductive ring cleavage was effected on the pentacyclic vincadifformine (**1**) and 20-deethyl-20-vincadifformine (**2**) the deuteride anion attacked C 21 from the α-face (leading to derivatives **29**, **30** and **33**), whereas the deutero cation attacked C 16 in the former case only from the β-face (leading to derivative **34**), and in the latter from both faces (leading to derivatives **31**, and **32**).

A reaction different from those described above was observed when 20-deethyl-20-epivincadifformine with β-H at C 20 (**3**) was allowed to react with the aforementioned deuterium-containing reactants. Compound **3** was split neither by sodium borodeuteride in acetic acid nor by sodium borohydride in deuteroacetic acid. In both cases the end products were N_1-ethylated pentacyclic molecules **35** and **36** (Scheme 3).

Scheme 3



35 **36**

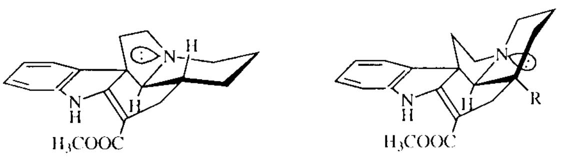
Reagents and conditions: i, $CH_3COOH/90°C + NaBD_4$; ii, $CH_3COOD/90°C + NaBH_4$

Conclusions.

Even though the published mechanism [10,11] provides explanation for many acidic epimerization reactions described above, our observation shows that the results (*e.g.* retention, partial epimerization with or without deuteration) depend on subtle structural changes with the adducts (*e.g.* benzylated or not benzylated nitrogen). On the other hand our studies which were carried out in boiling deuteroacetic acid prove that in the cases of compounds **9**, **10**, **11**, **12**, and **15** there must be an equilibration of the imminium salt with the corresponding enamine.

The results of the reductive cleavage in a majority of the studied cases are also in harmony with the proposed mechanism. The lack of splitting of the ring C/D of compound **3**

must be related to the stereochemistry and conformation of the pentacyclic compound. *Trans* H/20-H/21 pentacyclic compound **3** has an equatorial C 7/C 21 bond unfavourable for splitting, whereas with *cis* derivatives **1** and **2** the bond opening processes as trans diaxial (see Figure 4).



3

1 R = C_2H_5
2 R = H

Figure 4

EXPERIMENTAL

General Experimental Procedures.

Melting points are uncorrected and were obtained using Hotstage microscope Boetius apparatus. Infrared spectra were obtained using a Specord JR-75 Spectrophotometer. ^{1}H and ^{13}C nmr spectra were obtained using a Varian VXL-400. Chemical shifts (in ppm) are relative to tetramethylsilane. Mutual ^{1}H-^{1}H couplings are given only once, at their first occurrance. Mass spectra were obtained using a VG-TRIO-2 quadrupol Mass Spectrometer. Column chromatography was accomplished using Merck Kieselgel 60 Mesh (0.063-0.200 mm). Preparative thin-layer chromatography was performed with Silica gel plates F254 (Merck). The organic layers were dried with magnesium sulfate.

(±)-2,16-Didehydro-16-methoxycarbonyl-3-phenyl-14,15-dinoraspidospermidine (**15**).

A solution of 1.00 g (14 mmoles) of butanal, 1.00 g (2.8 mmoles) of **14** and 10 mg of *p*-toluenesulfonic acid monohydrate was heated in 100 ml of anhydrous toluene at reflux under argon for 3 hours. The reaction mixture was extracted with brine (2 x 40 ml), and the combined brine washes were extracted with methylene chloride (2 x 20 ml). The combined organic layers were dried and evaporated *in vacuo*. The residue was purified by column chromatography (eluent: ether/hexane 1/1) to yield **15** (R_f = 0.78) (0.39 g, 36%): mp 88-90°C (from MeOH) (lit., [12] 92-94°C); ir (potassium bromide) 3480, 1730, 1685 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 0.75 (3H, t, J = 7.2 Hz ;18-H_3), 0.89 (2H, m; 19-H_2), 1.67 + 2.04 (2 x 1H, 2 x ddd, J_{gem} = 11.5, $J_{5,6}$ = 4.6 + < 1 and 12.0 + 6.2 Hz, respectively; 6-H_2), 1.77 (1H, tddd, $J_{19,20\beta}$ = 7.5, $J_{17\alpha,20\beta}$ = 3.0, $J_{17\beta,20\beta}$ = 3.5, $J_{20\beta,21\alpha}$ ~ 1 Hz; 20-H_β), 2.50 (1H, dd, J_{gem} = 15.2 Hz; 17-H_β), 2.64 + 2.90 (2 x 1H, 2 x ddd, J_{gem} = 8.9 Hz; 5-H_2), 2.69 (1H, ddd, $J_{17\alpha,21\alpha}$ = 1.7 Hz; 17-H_α), 2.93 (1H, br d; 21-H_α), 3.72 + 4.12 (2 x 1H, 2 x d, J_{gem} = 13.3 Hz; N-CH_2-Ph), 3.78 (3H, s; COOMe), 6.80 (1H, d, $J_{11,12}$ = 7.6 Hz; 12-H), 6.83 (1H, ddd, $J_{9,10}$ = 7.4, $J_{10,11}$ = 7.5, $J_{10,12}$ = 1.1 Hz; 10-H), 6.97 (1H, d; 9-H), 7.13 (1H, ddd, $J_{9,11}$ = 1.3 Hz; 11-H), 7.25-7.40 (5H, m; Ph), 8.94 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 11.91 (C18), 21.98 (C17), 23.83 (C19), 40.92 (C20), 42.25 (C6), 50.46 (C5), 50.94 (OMe), 55.14 (C7), 58.05 (NCH_2Ph) 71.62 (C21), 90.67 (C16), 109.12 (C12), 120.42 (C10), 122.25 (C9), 127.02 (C4'), 127.71 (C11), 128.28 (C3' + C5'), 128.95 (C2' + C6'), 138.08 (C8), 139.10 (C1'), 143.07 (C13), 165.23 (C2), 169.19 (COOMe); ms: m/z 388 (M^+, 5.0%), 357 (2.0), 255 (39.0), 174 (100.0), 154 (15.0), 91 (79.0), 65 (10.0).

Debenzylation of **15**.

Method I: A mixture of 1.00 g (2.5 mmoles) of **15** and 0.50 g of 10% palladium/charcoal in 20 ml of glacial acetic acid was hydrogenated for 1 hour at room temperature and then filtered. The filtrate was poured onto ice-water and neutralized with saturated Sodium carbonate solution. The solution was extracted with methylene chloride (3 x 30 ml), and the combined organic layers were dried and evaporated *in vacuo*. The two main components of the residue were separated by preparative thin-layer chromatography (eluent: hexane/acetone 1/5). The less polar compound (**16**, R_f = 0.66) was obtained as a yellow oil (0.10 g, 13%); ir (neat): 3400, 1685, 1620 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 0.98 (3H, t, J = 7.0 Hz; 18-H_3), 1.20 (1H, m; 20-H_α), 1.51 (2H, m; 19-H_2), 1.85 (2H, m; 6-H_2), 1.95 (1H, dd, J_{gem} = 15.0, $J_{17\beta,20\alpha}$ = 11.5 Hz; 17-H_β), 2.40 (1H, br; N4-H), 2.51 (1H, ddd, $J_{17\alpha,20\alpha}$ = 3.1, $J_{17\alpha,21\alpha}$ = 1.5 Hz; 17-H_α), 3.12 (2H, m; 5-H_2), 3.77 (3H, s; COOMe), 3.80 (1H, dd, $J_{20\alpha,21\alpha}$ = 4.9 Hz; 21-H_α), 6.83 (1H, d; 12-H), 6.89 (1H, dd; 10-H), 7.15 (1H, dd; 11-H), 7.25 (1H, d; 9-H), 8.93 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 12.38 (C18), 23.63 (C17 + C19), 43.92 (C20), 45.13 (C6), 45.91 (C5), 50.95 (OMe), 57.39 (C7), 62.11 (C21), 95.29 (C16), 109.21 (C12), 120.56 (C10), 121.74 (C9), 127.90 (C11), 137.32 (C8), 143.49 (C13), 166.17 (C2), 168.47 (COOMe); ms: m/z 298 (M^+, 18.0%), 255 (10.0), 215 (100.0), 167 (20.0), 154 (30.0), 84 (78.0).

The more polar compound (**17**, R_f = 0.49) was obtained as a yellow oil (0.40 g, 52%): ir (neat): 3400, 1685, 1600 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 0.77 (3H, t, J = 7.3 Hz; 18-H_3), 0.95 (2H, m; 19-H_2), 1.65 (1H, m; 20-H_β), 1.82 + 1.89 (2 x 1H, 2 x ddd, J_{gem} = 12.0, $J_{5,6}$ = 5.0 + 1.7 and 11.0 + 6.9 Hz, respectively; 6-H_2), 2.22 (1H, br; N4-H), 2.26 (1H, dd, J_{gem} = 15.4, $J_{17\beta,20\beta}$ = 3.6 Hz; 17-H_β), 2.71 (1H, ddd, $J_{17\alpha,20\beta}$ = 2.9, $J_{17\alpha,21\alpha}$ = 1.6 Hz; 17-H_α), 3.11 + 3.15 (2 x 1H, 2 x ddd, J_{gem} = 10.5 Hz; 5-H_2), 3.47 (1H, br s; 21-H_α), 3.78 (3H, s; COOMe), 6.83 (1H, d; 12-H), 6.89 (1H, dd; 10-H), 7.16 (1H, ddd; 11-H), 7.24 (1H, d; 9-H), 9.02 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 11.81 (C18), 21.68 (C17), 24.42 (C19), 42.85 (C20), 44.58 (C6), 45.38 (C5), 50.96 (OMe), 55.93 (C7), 66.77 (C21), 90.04 (C16), 109.19 (C12), 120.70 (C10), 121.89 (C9), 127.83 (C11), 137.76 (C8), 143.18 (C13), 165.51 (C2), 169.01 (COOMe); ms: m/z 298 (M^+, 21.0%), 255 (11.0), 215 (100.0), 167 (19.0), 154 (28.0), 84 (82.0).

Method II: A mixture of 1.00 g (2.5 mmoles) of **15** and 0.50 g of 10% palladium/charcoal in 20 ml of glacial acetic acid was hydrogenated for 5 minutes at 70-75°C and then filtered. The two main products were separated as described above to yield **16** (0.15 g, 19%) and **17** (0.30 g, 39%).

Epimerization studies of **16** and **17**.

Method I: A solution of 0.1 g (0.33 mmole) of **17** was heated in 2 ml of glacial acetic acid at reflux for 5 minutes. The reaction mixture was poured onto ice-water and neutralized with saturated sodium carbonate solution. The solution was extracted with methylene chloride (3 x 10 ml), and the combined organic layers were dried and evaporated *in vacuo*. The two main components of the residue were separated by preparative thin-layer chromatography (eluent: hexane/acetone 1/5) to yield **16** (0.16 g, 16%) and **17** (0.34 g, 34%).

Method II: A solution of 0.1 g (0.33 mmole) of **16** was heated in 2 ml of glacial acetic acid at reflux for 5 minutes. The two main products were separated as described above to yield **16** (0.31 g, 31%) and **17** (0.32 g, 32%).

General procedure for reactions carried out in boiling deuteroacetic acid (Table 1).

The 5 mmoles of starting compound (**1-17**) was heated in 5 ml of deuteroacetic acid at reflux. The reaction mixture was poured onto ice-water and neutralized with saturated Sodium carbonate solution. The solution was extracted with methylene chloride (3 x 10 ml), and the combined organic layers were dried and evaporated *in vacuo*. The residue was purified by thin-layer chromatography. The structure of products, the percentage of deuteration at C20 and the percentage of the isolated products can be found in Table 1.

General procedure for reductive cleavage of C7-C21 bond with deuterium-containing reactants (Table 2).

Method A: 0.5 mmole of starting compound (**1**, **2**, **3**, **9**, and **15**) was heated in 5 ml of glacial acetic acid at 90°C and 0.2 g (4.8 mmoles) of sodium borodeuteride was added in portions. After addition of the reducing agent, the mixture was poured onto ice-water and neutralized with saturated Sodium carbonate solution. The solution was extracted with methylene chloride (3 x 10 ml), and the combined organic layers were dried and evaporated *in vacuo*. The residue was purified by thin-layer chromatography (eluents were either methylene chloride /MeOH 100/1 [a] or 10/1 [b]). The structure of products, the percentage of deuteration and the yields can be found in Table 2.

Method B: 0.5 mmole of starting compound (**1**, **2**, **3**, **9**, and **15**) was heated in 5 ml of deuteroacetic acid at 90°C and 0.2 g (5.2 mmoles) of sodium borohydride was added in portions. After addition of reducing agent the products were separated as described above. The structure of products, the percentage of deuteration and the yields can be found in Table 2.

Spectral data of products:

Compound **21**: R_f = 0.65 [a]; ^{1}H nmr (deuteriochloroform): δ 0.67 (3H, t, J = 7.3 Hz; 18-H_3), 0.90-1.10 (3H, m; 19-H_2 + 20-H_β), 1.54 + 1.97 (2 x 1H, 2 x ddd, J_{gem} = 13.0, $J_{16,17}$ = 4.6 and 12.0, $J_{17,20}$ = 10.0 and 16 Hz, respectively; 17-H_2), 2.30 (1H, d, $J_{20,21}$ = 10.8 Hz; 21-H_α), 2.43 + 2.86 (2 x 1H, 2 x m; 5-H_2), 2.61 + 2.84 (2 x 1H, 2 x m; 6-H_2), 3.65 + 3.85 (2 x 1H, 2 x d, J_{gem} = 12.8 Hz; NCH_2Ph), 3.77 (3H, s; COOMe), 5.65 (1H, dd; 16-H_α), 7.06 (1H, ddd, 10-H), 7.13 (1H, ddd; 11-H), 7.20-7.50 (7H, m; 12-H + 9-H + Ph), 8.72 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 11.40 (C18), 24.97 (C6), 26.77 (C19), 34.78 (C20), 39.80 (C17), 41.68 (C16), 52.10 (OMe), 55.83 (C5), 61.07 ($^1J_{C,D}$ = 19.4 Hz; C21), 63.19 (NCH_2Ph), 110.75 (C12), 114.30 (C7), 117.78 (C9), 118.83 (C10), 121.23 (C11), 126.91 (C4'), 128.05 (C8), 128.22 (C3' + C5'), 129.47 (C2' + C6'), 131.79 (C2), 135.59 (C13), 139.79 (C1'), 176.20 (COOMe).

NOE: 5.65 (16-H_α) → 1.54 (17-H_α), 2.61 (6-H_α), 2.30 (21-H_α), 1.00 (19-H_2); 2.30 (21-H_α) → 1.00 (19-H_2), 0.67 (18-H_3), 1.54 (17-H_α), 5.65 (16-H_α), 2.61 (6-H_α); 1.97 (17-H_β) → 1.54 (17-H_α), ~1.00 (20-H_β + 19-H_2), 0.67 (18-H_3), 8.72 (NH) 7.46 (9-H) → 7.06 (10-H), 2.84 (6-H_β); 8.72 (NH) → 7.32 (12-H), 1.97 (17- H_β).

Compound **22**: R_f = 0.34 [a]; ^{1}H nmr (deuteriochloroform): δ 0.84 (3H, t, J = 7.3 Hz; 18-H_3), 1.10 (2H, m; 19-H_2), 1.72 (1H, m, 20-H_β), 1.89 + 2.28 (2 x 1H, 2 x ddd, J_{gem} = 13.6, $J_{16,17}$ = 9.4 and 1.5, $J_{17,20}$ = 11.3 and 5.2 Hz, respectively; 17-H_2), 2.27 (1H, d, $J_{20,21}$ = 7.5 Hz; 21-H_α), 2.33 + 2.70 (2 x 1H, 2 x ddd, J_{gem} = 12.5, $J_{5,6}$ = 10.5 + 2.3 and 3.8 + 3.5 Hz, respectively; 5-H_2), 2.76 + 2.83 (2 x 1H, 2 x ddd, J_{gem} = 14.0 Hz, 6-H_2), 3.36 + 3.78 (2 x 1H, 2 x d, J_{gem} = 13.6 Hz; NCH_2Ph), 3.75 (3H, s; OMe), 5.06 (1H, dd; 16-H_β), 7.05 (1H, ddd; 10-H), 7.14 (1H, ddd; 11-H), 7.20-7.45 (7-H, m; 12-H + 9-H + Ph), 8.60 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 11.46 (C18), 26.23 (C6), 28.51 (C19), 40.14 (C20), 39.13 (C17), 40.38 (C16), 52.27 (OMe), 52.41 (C5), 59.12 ($^1J_{C,D}$ = 18.5 Hz; C21), 61.10 (NCH_2Ph), 110.72 (C12), 111.66 (C7), 118.17 (C9), 119.04 (C10), 121.61 (C11), 126.80 (C4'), 127.78 (C8), 128.27 (C3' + C5'), 128.63 (C2' + C6'), 134.09 (C2), 135.95 (C13), 140.46 (C1'), 175.56 (COOMe).

NOE: 1.72 (20-H_β) → 5.06 (16-H_β), 2.27 (21-H_α), 2.28 (17-H_β), 0.84+ 1.10 (Et); 5.06 (16-H_β) → 1.72 (20-H_β), 2.76 (6-H_β), 2.28 (17-H_β); 1.89 (17-H_α) → 2.28 (17-H_β), 8.60 (NH), 0.84+1.10 (Et); 0.84 (18-H_3) → 1.10 (19-H_2), 1.72 (20-H_β), 2.27 (21-H_α); 8.60 (NH) → 7.34 (12-H), 1.89 (17-H_α).

Compound **23**: R_f = 0.65 [a]; ^{1}H nmr (deuteriochloroform): δ 0.67 (3H, t, J = 7.3 Hz; 18-H_3), 0.90-1.10 (3H, m; 19-H_2 + 20-H_β), 1.53 + 1.96 (2 x 1H, 2 x dd, J_{gem} = 13.0, $J_{17,20}$ 10.0 and 1.5 Hz, respectively; 17-H_2), 2.33 + 2.36 (2 x 1H, 2 x dd, J_{gem} = 12.5, $J_{20,21}$ = 10.0 and 3 Hz, respectively; 21-H_2), 2.43 + 2.86 (2 x 1H, 2 x m, 5-H_2), 2.61 + 2.84 (2 x 1H, 2 x m, 6-H_2), 3.64 + 3.85 (2 x 1H, 2 x d, J_{gem} = 12.8 Hz; NCH_2Ph), 3.77 (3H, s; OMe), 7.06 (1H, ddd; 10-H_β), 7.13 (1H, ddd; 11-H), 7.20-7.50 (7-H, m; 12-H + 9-H + Ph), 8.72 (1H, br s; N1-H).

NOE: 1.53 (17-H_α) → 1.96 (17-H_β), 2.33 (21-H_α), 1.00 (19-H_2); 2.61 (6-H_α) → 2.85 (6-H_β+5-H_α), 1.00 (19-H_2).

Compound **24**: R_f = 0.34 [a]; ^{1}H nmr (deuteriochloroform): δ 0.84 (3H, t, J = 7.3 Hz; 18-H_3), 1.10 (2H, m; 19-H_2), 1.73 (1H, m; 20-H_β), 1.88 + 2.28 (2 x 1H, 2 x dd, J_{gem} = 13.8, $J_{17,20}$ = 11.3 and 5.2 Hz, respectively; 17-H_2), 2.26 + 2.29 (2 x 1H, 2 x dd, J_{gem} = 12.7, $J_{20,21}$ = 2.8 and 8.5 Hz, respectively; 21-H_2), 2.33 + 2.70 (2 x 1H, 2 x ddd, J_{gem} = 13.0, $J_{5,6}$ = 11.0 and 2.5 and 4.0 + 3.5 Hz, respectively; 5-H_2), 2.76 + 2.83 (2 x 1H, 2 x ddd, J_{gem} = 15.0 Hz; 6-H_2), 3.36 + 3.78 (2 x 1H, 2 x d, J_{gem} = 13.6 Hz; NCH_2Ph), 3.75 (3H, s; OMe), 7.06 (1H, ddd; 10-H), 7.14 (1H, ddd; 11-H), 7.20-7.45 (7H, m; 12-H + 9-H + Ph), 8.60 (1H, br s; N1-H).

Compound **25**: R_f = 0.67 [a]; ^{1}H nmr (deuteriochloroform): δ 1.00 (1H, m; 20-H_β), 1.27 + 1.34 (2 x 1H, 2 x dddd, J_{gem} = 13.8, $J_{14,15}$ = 9.1 + 6.3 and 9.2 + 6.2, $J_{15,20}$ = 7.2 and 6.0 Hz, respectively; 15-H_2), 1.54 + 1.94 (2 x 1H, 2 x ddd, J_{gem} = 13.0, $J_{16,17}$ = 4.6 and 12.0, $J_{17,20}$ = 10.5 and 2.0 Hz, respectively; 17-H_2), 2.06 + 2.11 (2 x 1H, 2 x ddd, J_{gem} = 15.5 Hz; 14-H_2), 2.31 (1H, d; $J_{20\beta,21\alpha}$ = 11.6 Hz; 21-H_α), 2.39 + 2.89 (2 x 1H, 2 x m; 5-H_2), 2.61 + 2.85 (2 x 1H, 2 x m; 6-H_2), 3.37 (3H, s; 14-COOMe), 3.63 + 3.84 (2 x 1H, 2 x d, J_{gem} = 12.8 Hz; NCH_2Ph), 3.76 (3H, s; 16-COOMe), 5.60 (1H, dd; 16-H_α), 7.04 (1H, ddd; 10-H), 7.12 (1H, ddd; 11-H), 7.20-7.50 (7H, m; 9-H + 12-H + Ph), 8.70 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 24.90 (C6), 28.89 (C15), 31.75 (C14), 33.05 (C20), 39.55 (C17), 41.57 (C16), 51.32 (C3-OMe), 52.13 (16-COOMe) 56.01 (C5), 60.92 ($^1J_{C,D}$ = 19.6 Hz; C21), 63.04 (NCH_2Ph), 110.77 (C12), 114.37 (C7), 117.77 (C9), 118.89 (C10), 121.34 (C11), 126.98 (C4'), 127.88 (C8), 128.24 (C3' + C5'), 129.44 (C2' + C6'), 131.35 (C2), 135.64 (C13), 139.52 (C1'), 173.74 (C3), 175.79 (16-COOMe).

NOE: 1.00 (20-H_β) → 1.94 (17-H_β), 2.39 (5-H_β), 1.27+1.34 (15-H_2); 5.60 (16-H_α) → 1.54 (17-H_α), 2.61 (6-H_α), 2.31 (21-H_α); 8.70 (NH) → 7.32 (12-H), 1.94 (17-H_α).

Compound **26**: R_f = 0.35 [a]; ^{1}H nmr (deuteriochloroform): δ 1.41 (2H, m; 15-H_2), 1.82 (1H, m; 20-H_β), 1.92 (1H, m; 17-H_α), 2.20-2.40 (5H, m; 14-H_2 + 17-H_β + 21-H_α + 5-H_α), 2.65-2.90 (3H, m; 5-H_β + 6-H_2), 3.37 + 3.76 (2 x 1H, 2 x d, J_{gem} = 13.6 Hz; NCH_2Ph), 3.62 (3H, s; 14-COOMe), 3.74 (3H, s; 16-COOMe), 5.05 (1H, dd, $J_{16,17}$ = 9.2 + 1.0 Hz; 16-H_β) 7.05 (1H, ddd; 10-H), 7.14 (1H, ddd; 11-H), 7.20-7.45 (7H, m; 9-H + 12-H + Ph), 8.59 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 26.15 (C6), 30.64 (C15), 31.48 (C14), 37.72 (C20), 38.83 (C17), 40.26 (C16), 51.61 (C3-OMe), 52.30 (16-COOMe) 52.41 (C5), 59.07 ($^1J_{C,D}$ = 19.5 Hz; C21), 61.09 (NCH_2Ph), 110.74 (C12), 111.71 (C7), 118.17 (C9), 119.09 (C10), 121.70 (C11), 126.85 (C4'), 127.73 (C8), 128.28 (C3' + C5'), 128.59 (C2' + C6'), 133.76 (C2), 135.95 (C13), 140.15 (C1'), 173.84 (C3), 175.22 (16-COOMe).

NOE: 5.05 (16-H_β) → 1.82 (20-H_β), 2.27 (17-H_β), 2.75 (6-H_β).

Compound **27**: R_f = 0.67 [a]; ^{1}H nmr (deuteriochloroform): δ 1.01 (1H, m; 20-H_β), 1.27 + 1.35 (2 x 1H, 2 x dddd; J_{gem} = 13.5, $J_{14,15}$ = 9.3 + 6.5 and 9.2 + 6.2, $J_{15,20}$ = 7.2 and 6.0 Hz, respectively; 15-H_2), 1.53 + 1.93 (2 x 1H, 2 x dd, J_{gem} = 13.0, $J_{17,20}$ = 10.5 and 2.0 Hz, respectively; 17-H_2), 2.06 + 2.11 (2 x 1H, 2 x ddd, J_{gem} = 15.5 Hz, 14-H_2), 2.34 (2H, m; 21-H_2), 2.39 + 2.89 (2 x 1H, 2 x m, 5-H_2), 2.62 + 2.85 (2 x 1H, 2 x m; 6-H_2), 3.37 (3H, s; 14-COOMe), 3.64 + 3.85 (2 x 1H, 2 x d, J_{gem} = 12.8 Hz; NCH_2Ph), 3.77 (3H, s; 16-COOMe), 7.05 (1H, ddd; 10-H), 7.12 (1H, ddd; 11-H), 7.2-7.5 (7H, m; 9-H + 12-H + Ph), 8.68 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 24.90 (C6), 28.93 (C15), 31.77 (C14), 33.16 (C20), 39.53 (C17), 41.33 ($^1J_{C,D}$ = 20.0 Hz; C16), 51.34 (C3-OMe), 52.13 (16-COOMe), 56.10 (C5), 61.38 (C21), 63.09 (NCH_2Ph), 110.78 (C12), 114.37 (C7), 117.79 (C9), 118.91 (C10), 121.36 (C11), 127.00 (C4'), 127.90 (C8), 128.26 (C3' + C5'), 129.46 (C2' + C6'), 131.31 (C2), 135.65 (C13), 139.53 (C1'), 173.75 (C3), 175.81 (16-COOMe).

Compound **28**: R_f = 0.35 [a]; ^{1}H nmr (deuteriochloroform): δ 1.42 (2H, m; 15-H_2), 1.83 (1H, m; 20-H_β), 1.91 (1H, dd; J_{gem} = 13.5, $J_{17\alpha,20}$ = 11.5 Hz; 17-H_α), 2.20-2.40 (6H, m; 14-H_2 + 17-H_β + 21-H_2 + 5-H_α), 2.65-2.90 (3H, m; 5-H_β + 6-H_2), 3.37 + 3.77 (2 x 1H, 2 x d, J_{gem} = 13.6 Hz; NCH_2Ph), 3.62 (3H, s; 14-COOMe), 3.74 (3H, s; 16-COOMe), 7.05 (1H, ddd; 10-H), 7.14 (1H, ddd; 11-H), 7.20-7.45 (7H, m; 9-H + 12-H + Ph), 8.60 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 26.18 (C6), 30.70 (C15), 31.49 (C14), 37.78 (C20), 38.84 (C17), 39.95 ($^1J_{C,D}$ ~ 20.0 Hz; C16), 51.62 (C3-OMe), 52.30 (16-COOMe); 52.43 (C5), 59.61 (C21), 61.15 (NCH_2Ph), 110.75 (C12), 111.71 (C7), 118.19 (C9), 119.11 (C10), 121.72 (C11), 126.87 (C4'), 127.75 (C8), 128.30 (C3' + C5'), 128.62 (C2' + C6'), 133.77 (C2), 135.98 (C13), 140.16 (C1'), 173.85 (C3), 175.25 (16-COOMe).

Compound **29**: R_f = 0.91 [a]; ^{1}H nmr (deuteriochloroform): δ 1.45 + 1.60 (2 x 1H, 2 x dm, J_{gem} = 12.5 Hz; 15-H_2), 1.51 + 1.91 (2 x 1H, 2 x m; 14-H_2), 1.75 (1H, m; 20-H_α), 1.97 + 2.50 (2 x 1H, 2 x ddd, J_{gem} = 14.5, $J_{16,17}$ = 1.5 and 11.6, $J_{17,20}$ = 1.5 and 8.4 Hz, respectively; 17-H_2), 2.19 (1H, ddd, J = 1.5 + 1.5 + 1.5 Hz; 21-H_β), 2.27 + 2.58 (2 x 1H, 2 x m; 5-H_2), 2.52 + 2.97 (2 x 1H, 2 x dm; J_{gem} = 10.5 Hz; 3-H_2), 2.80-2.92 (2H, m; 6-H_2), 3.68 (3H, s; OMe), 5.57 (1H, dd; 16-H_β), 7.07 (1H, ddd, $J_{9,10}$ = 7.9, $J_{10,11}$ = 7.0, $J_{10,12}$ = 1.2 Hz; 10-H), 7.13 (1H, ddd, $J_{9,11}$ = 1.4, $J_{11,12}$ = 8.1 Hz; 11-H), 7.32 (1H, dd; 12-H), 7.49 (1H, dd; 9-H), 8.62 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 24.07 (C14), 26.56 (C6), 30.94 (C20), 32.29 (C15), 38.95 (C17), 41.57 (C16), 52.07 (OMe), 53.98 (C5), 54.37 (C3), 54.96 ($^1J_{C,D}$ = 19.5 Hz; C21), 110.64 (C12), 111.59 (C7), 118.17 (C9) 118.90 (C10), 121.41 (C11), 127.78 (C8), 133.92 (C2), 135.81 (C13), 175.70 (COOMe).

NOE: 1.75 (20-H_α) → 2.19 (21-H_β), 2.50 (17-H_α), 1.45 (15-H_α), 1.97 (17-H_β), 1.60 (15-H_β); 5.57 (16-H_β) → 2.19 (21-H_β), 2.86 (6-H_β), 1.97 (17-H_β), 1.91 (14-H_β), 1.60 (15-H_β); 8.62 (NH) → 7.32 (12-H), 2.50 (17-H_α), 2.19 (21- H_β).

Compound **30**: R_f = 0.49 [a]; ^{1}H nmr (deuteriochloroform): δ 1.19 (1H, m; 14-H_α), 1.37 (1H, m; 15-H_α), 1.45-1.60 (2H, m; 14-H_β + 15-H_β), 1.97 (1H, m; 20-H_α), 1.98 + 2.30 (2 x 1H, 2 x ddd, J_{gem} = 16.0, $J_{16,17}$ = 1.5 and 6.0, $J_{17,20}$ = 7.5 and 12.8 Hz, respectively; 17-H_2), 2.25 + 2.49 (2 x 1H, 2 x ddd, J_{gem} = 11.0, $J_{5,6}$ = 10.5 + 6.5 and 4.0 + 2.2 Hz, 5-H_2), 2.35 (2H, m; 3-H_2), 2.89 + 2.92 (2 x 1H, 2 x ddd, J_{gem} = 15.0 Hz; 6-H_2), 3.47 (1H, m; 21-H_β), 3.74 (3H, s; OMe), 3.93 (1H, dd; 16-H_α), 7.06 (1H, ddd; 10-H), 7.12 (1H, ddd,11-H), 7.32 (1H, dd; 12-H), 7.49 (1H, dd; 9-H), 8.97 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 21.24 (C14), 22.05 (C6), 29.23 (C15), 33.03 (C20), 35.99 (C17), 39.08 (C16), 50.28 ($^1J_{C,D}$ = 19.5 Hz; C21), 52.28 (OMe), 52.57 (C5), 55.30 (C3), 109.78 (C7), 110.72 (C12), 117.70 (C9) 118.76 (C10), 120.94 (C11), 127.96 (C8), 135.13 (C2), 135.28 (C13), 176.51 (COOMe).

NOE: 3.93 (16-H_α) → 3.47 (21-H_β), 2.92 (6-H_α), 1.98 (17-H_α), 1.97 (20-H_α); 3.47 (21-H_β) → 3.93 (16-H_α), 2.92 (6-H_α), 1.97 (20-H_α); 8.97 (NH) → 7.32 (12-H), 16-COOMe.

Compound **31**: R_f = 0.91 [a]; ^{1}H nmr (deuteriochloroform): δ 1.45 + 1.59 (2 x 1H, 2 x dm, J_{gem} = 12.8 Hz; 15-H_2), 1.51 + 1.91 (2 x 1H, 2 x m; 14-H_2), 1.75 (1H, m; 20-H_α), 1.96 (1H, ddd, Jgem = 14.5, $J_{17\beta,20\alpha}$ = 1.5, $J_{17\beta,21\alpha}$ = 1.0 Hz, 17-H_β), 2.19 + 2.22 (2 x 1H, 2 x dddd, J_{gem} = 11.5, $J_{20,21}$ = 3.0 and 1.5, $J_{longrange}$ = 1.0 + 0.5 and 1.5 + 1.5 Hz, respectively; 21-H_2), 2.27 (1H, m; 5-H_α), 2.45-2.61 (3H, m; 17-H_β + 5-H_β + 3-H_α), 2.80-2.92 (2H, m; 6-H_2), 2.97 (1H, m; 3-H_β), 3.68 (3H, s; OMe), 7.06 (1H, ddd; 10-H), 7.12 (1H, ddd,11-H), 7.32 (1H, dd; 12-H), 7.49 (1H, dd; 9-H), 8.62 (1H, br s; N1-H).

NOE: 2.19 (21-H_α) → 1.75 (20- H_α), 1.45 (15-H_α), 2.51 (3-H_α); 2.97 (3-H_β) → 2.51 (3-H_α), 2.58 (5-H_β) 1.91 (14-H_β).

Compound **32**: R_f = 0.49 [a]; ^{1}H nmr (deuteriochloroform): δ 1.19 (1H, m; 14-H_α), 1.37 (1H, m; 15-H_α), 1.45-1.60 (2H, m; 14-H_β + 15-H_β), 1.95 + 3.49 (2 x 1H, 2 x dm, J_{gem} = 12.0 Hz, 21-H_2), 1.97 + 2.30 (2 x 1H, 2 x dd, J_{gem} = 16.0, $J_{17,20}$ = 7.5 and 12.9 Hz, respectively; 17-H_2), 1.98 (1H, m; 20-H_α), 2.25 + 2.49 (2 x 1H, 2 x ddd, J_{gem} = 11.0, $J_{5,6}$ = 10.5 + 6.5 and 4.1 + 2.2 Hz; 5-H_2), 2.35 (2H, m; 3-H_2), 2.89 + 2.93 (2 x 1H, 2 x ddd, J_{gem} = 15.0 Hz; 6-H_2), 3.74 (3H, s; OMe), 7.05 (1H, ddd; 10-H), 7.12 (1H, ddd,11-H), 7.32 (1H, dd; 12-H), 7.49 (1H, dd; 9-H), 8.96 (1H, br s; N1-H).

Compound **33**: R_f = 0.31 [a]; ^{1}H nmr (deuteriochloroform): δ 0.66 (3H, t, J = 7.3 Hz; 18-H_3), 0.98 (2H, m; 19-H_2), 1.03 + 1.60 (2 x 1H, 2 x m; 15-H_2), 1.55 + 1.86 (2 x 1H, 2 x m; 14-H_2), 1.85 + 2.19 (2 x 1H, 2 x dd, J_{gem} = 14.5, $J_{16,17}$ = 1.8 and 11.8 Hz, respectively; 17-H_2), 2.10 (1H, br s; 21-H_β), 2.27 + 2.62 (2 x 1H, 2 x dm, J_{gem} = 13.0 Hz; 5-H_2), 2.45 + 2.98 (2 x 1H, 2 x dm, J_{gem} = 10.0 Hz; 3-H_2), 2.80-2.92 (2H, m; 6-H_2), 3.69 (3H, s; OMe), 5.63 (1H, dd; 16-H_β), 7.07 (1H, ddd; 10-H), 7.13 (1H, ddd,11-H), 7.33 (1H, dd; 12-H), 7.50 (1H, dd; 9-H), 8.62 (1H, br s; N1-H); ^{13}C nmr (deuteriochloroform): δ 7.35 (C18), 23.60 (C14), 26.24 (C6), 35.48 (C20), 35.59 (C19), 37.23 (C15), 40.89 (C16), 42.89 (C17), 52.07 (OMe), 53.89 (C5), 54.01 (C3), 60.47 ($^1J_{C,D}$ = 19.0 Hz; C21), 110.71 (C12), 111.67 (C7), 118.11 (C9), 118.87 (C10), 121.32 (C11), 127.75 (C8), 133.90 (C2), 135.85 (C13), 175.88 (COOMe).

Compound **34**: R_f = 0.31 [a]; ^{1}H nmr (deuteriochloroform): δ 0.67 (3H, t, J = 7.3 Hz; 18-H_3), 0.98 (2H, m; 19-H_2), 1.03 + 1.60

(2 x 1H, 2 x m; 15-H_2), 1.55 + 1.87 (2 x 1H, 2 x m; 14-H_2), 1.79 + 2.12 (2 x 1H, 2 x d, J_{gem} = 11.8 Hz; 21-H_2), 1.84 + 2.19 (2 x 1H, 2 x d, J_{gem} = 14.5 Hz; 17-H_2), 2.27 + 2.62 (2 x 1H, 2 x dm, J_{gem} = 13.0 Hz; 5-H_2), 2.45 + 2.98 (2 x 1H, 2 x dm, J_{gem} = 10 Hz; 3-H_2), 2.80-2.92 (2H, m; 6-H_2), 3.69 (3H, s; OMe), 7.08 (1H, ddd; 10-H), 7.14 (1H, ddd, 11-H), 7.33 (1H, dd; 12-H), 7.50 (1H, dd; 9-H), 8.61 (1H, br s; N1-H).

Compound **35** R_f = 0.57 [b]; ^1H nmr (deuteriochloroform): δ 0.97 (3H, s; NCD_2CH_3), 1.15 + 1.72 (2 x 1H, 2 x m; 15-H_2), 1.28 (1H, m; 20-H_β), 1.40 + 1.77 (2 x 1H, 2 x m; 14-H_2), 1.67 + 1.71 (2 x 1H, 2 x m; 17-H_2), 2.11 + 2.25 (2 x 1H, 2 x ddd, J_{gem} = 13.5, $J_{5,6}$ = 10.8 + 4.8 and 9.3 + 5.4 Hz, respectively; 6-H_2), 2.42 (1H, br d, $J_{20,21}$ = 11.0 Hz; 21-H_α), 2.70 (1H, dd, $J_{16,17}$ = 10.5 + 4.5 Hz; 16-H_β), 2.98 + 3.03 (2 x 1H, 2 x dm, J_{gem} = 14 Hz; 3-H_2), 3.13 + 3.40 (2 x 1H, 2 x ddd, J_{gem} = 9.5 Hz; 5-H_2), 3.71 (3H, s; OMe), 6.49 (1H, dd; 12-H), 6.74 (1H, ddd; 10-H), 7.11 (1H, ddd, 11-H), 7.24 (1H, dd; 9-H);

NOE: 2.70 (16-H_β) → 1.28 (20-H_β), 2.10 (6-H_β), 3.71 (OMe); 2.42 (21-H_α) → 1.15 (15-H_α) 1.67 (17-H_α), 2.98 (3-H_α), 7.24 (9-H); 0.97 (NCD_2CH_3) → 6.49 (12-H), 3.71 (OMe); 3.71 (OMe) → 0.97 (NCD_2CH_3), 2.70 (16-H_β).

^{13}C nmr (deuteriochloroform): δ 8.79 (NCD_2CH_3), 20.63 (C14), 26.78 (C17), 30.20 (C15), 31.11 (C6), 33.29 (C20), 39.83 (NCD_2), 43.61 (C16), 46.55 (C5), 47.90 (C3), 51.65 (OMe), 53.83 (C7), 67.30 (C2), 70.38 (C21), 107.74 (C12), 118.28 (C10), 123.00 (C9), 127.76 (C11), 137.08 (C8), 149.40 (C13), 175.04 (COOMe).

Compound **36** R_f = 0.57 [b]; ^1H nmr (deuteriochloroform): δ 0.99 (3H, t, J = 7.2 Hz; NCH_2CH_3), 1.11 + 1.70 (2 x 1H, 2 x m; 15-H_2), 1.23 (1H, m; 20-H_β), 1.30 + 1.73 (2 x 1H, 2 x m; 14-H_2), 1.61 + 1.65 (2 x 1H, 2 x dd, J_{gem} = 13, $J_{17,20}$ = 10 and 4.5 Hz, respectively; 17-H_2), 2.05 + 2.21 (2 x ddd, J_{gem} = 13.5, $J_{5,6}$ = 10.6 + 4.6 and 9.3 + 5.6 Hz, respectively; 6-H_2), 2.23 (1H, br d, $J_{20,21}$ ~ 10 Hz; 21-H_α), 2.88 + 2.98 (2 x 1H, 2 x m; 3-H_2), 2.88 + 3.25 (2 x 1H, 2 x dq, J_{gem} = 15.5, J_{vic} = 7.0 and 7.4 Hz, respectively; NCH_2CH_3), 3.10 + 3.18 (2 x 1H, 2 x m; 5-H_2), 3.72 (3H, s; OMe), 3.96 (1H, s; 2-H_β), 6.50 (1H, dd; 12-H), 6.74 (1H, ddd; 10-H), 7.10 (1H, ddd,11-H), 7.19 (1H, br d; 9-H);

^{13}C nmr (deuteriochloroform): δ 9.14 (NCH_2CH_3), 20.82 (C14), 26.81 (C17), 30.82 (C15), 31.54 (C6), 33.08 (C20), 40.61 (NCH_2CH_3), 43.50 (C16), 46.29 (C5), 47.78 (C3), 51.58 (OMe), 53.83 (C7), 67.44 (C2), 70.73 (C21), 107.63 (C12), 118.23 (C10), 122.94 (C9), 127.44 (C11), 138.20 (C8), 149.48 (C13), 175.31 (COOMe).

NOE: 3.96 (2-H_β) → 0.99 (NCH_2CH_3), 2.05 (6-H_β), 2.21 (6-H_α), 2.88 + 3.25 (NCH_2CH_3), 1.23 (20-H_β); 2.05 (6-H_β) → 3.96 (2-H_β), 1.23 (20-H_β), 3.09 (5-H_β); 3.72 (OMe) → 0.99 (NCH_2CH_3), 2.88 ($NCH_\alpha CH_\beta$).

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[§] The compounds described in this paper are racemates, but only one of the antipodes, in general the more rational representation, is shown.