

Cathodic Cyclisation of *N*-(Oxoalkyl)pyridinium Salts – Formation of Tricyclic Indolizidine and Quinolizidine Derivatives in Aqueous Medium

Jens Heimann,^[a] Hans J. Schäfer,^{*[a]} Roland Fröhlich,^{[a],[‡]} and Birgit Wibbeling^[a]

Keywords: Cyclisation / Electrochemistry / Fused-ring systems / Heterocycles / Umpolung

The cathodic cyclisation of *N*-(oxoalkyl)pyridinium salts, derived from 4-methylpyridine and cyclic ketones, afforded functionalised tricyclic indolizidine and quinolizidine derivatives in high yields. Through systematic variation of the ring size of the ketone and the cyclised ring, a series of four cyclopenta-/cyclohexa[*a*]indolizidines and -quinolizidines was obtained. The cyclisation was also applied to the synthesis of a cyclohexa[*b*]quinolizidine derivative, which represents a substructure of the cevanine alkaloids. There is no obvious alternative route as short as this cathodic cyclisation to such indolizidines and quinolizidines. A detailed mechanism of

the cyclisation is proposed. In the key step, a hydroxyalkyl radical generated by reduction of the protonated ketone adds reversibly to the pyridinium ring. Semiempirical calculations indicate that only diastereomers resulting from the thermodynamically more stable cyclised intermediates are obtained. From these data and the $\Delta\Delta_f H^+$ value for the transition states of the cyclisation, thermodynamic rather than kinetic control seems to be more likely.

(© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2003)

Introduction

Since the pioneering work of Kolbe, organic electrochemistry has emerged as a powerful tool both for functional-group interconversions and for C–C bond-forming reactions.^[1] One important method of the latter class is the intramolecular cyclisation of acyclic precursors with two functional groups of the same polarity.^[2] This is achieved by selective reversal of the reactivity (“umpolung”) of one of these groups by electron transfer, which can render a nucleophilic group electrophilic by oxidation (e.g., enol ethers) or an electrophilic group nucleophilic by reduction (e.g., carbonyl groups), thus initiating the C–C bond coupling. This unique strategy provides simple routes to carbo- and heterocycles as documented by numerous anodic^[2,3] and cathodic cyclisations.^[2,4]

The following combinations of functional groups have recently been intramolecularly coupled at the cathode: alkyl halides with alkenes,^[5] two electron-deficient alkenes,^[6] α,β -unsaturated esters with allenes,^[7] ketones^[8] or aldehydes,^[9] diesters to give vicinal diketones,^[10] esters with alkenes to give secondary alcohols^[11] or two imines to piperazines^[12] and macrocycles.^[13] The coupling of ketones with alkenes,^[14] nitriles,^[15] vinylsilanes,^[16] *O*-methyl oximes^[17] and phenyl rings^[14a,18] was also studied recently.

A few years ago we showed that the cathodic cyclisation of arylalkanones,^[14a,18] can be extended to the cyclisation of *N*-(oxoalkyl)pyridinium salts to provide hydroxyindolizidine and -quinolizidine derivatives.^[19] The pyridinium salts are readily available by nucleophilic substitution of halogen ketones with pyridine. The sequence overall provides functionalised indolizidine and quinolizidine derivatives by a shorter route than achievable by existing methods.^[20] The radical cyclisation of *N*-(iodoalkyl)pyridinium salts^[21] and *N*-alkenyl-2-bromopyridinium salts^[22] is also reported to give indolizidines and quinolizidines. In comparison with the cathodic cyclisation, though, this method has drawbacks such as the use of tributyltin hydride for hydrogen atom transfer and the loss of functionality in the course of the cyclisation.

Here we report on the extension of the cathodic cyclisation to the synthesis of a series of tricyclic hydroxyindolizidine and -quinolizidine derivatives.^[23] The objectives were to examine the application of the reaction to more complex target structures and to gain a more detailed insight into the mechanism.

Results and Discussion

Preparation of the Pyridinium Salts

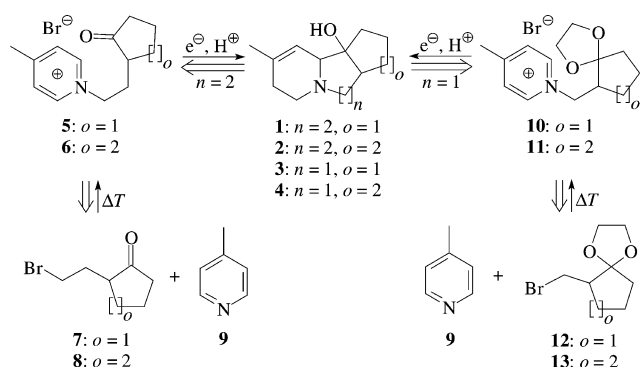
In order to demonstrate the potential for the construction of tricyclic indolizidines and quinolizidines by the way of cathodic cyclisation, compounds **1–4** were chosen as target compounds (Scheme 1). It was thought that the *N*-(4-

^[a] Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstraße 40, 48149 Münster, Germany
Fax: (internat.) + 49-251/8336523
E-mail: schafeh@uni-muenster.de

^[‡] Crystal structure determination.

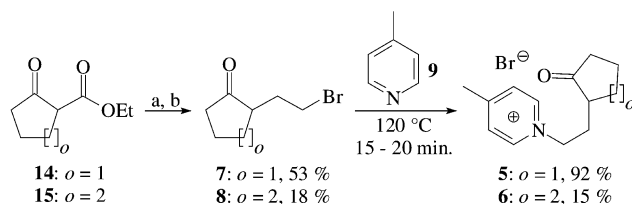
Supporting information for this article is available on the WWW under <http://www.eurjoc.org> or from the author.

oxoalkyl)pyridinium salts **5/6**, for the synthesis of the quinolizidines **1/2**, and the corresponding 3-oxo salts **10/11**, to provide the indolizidines **3/4**, should be available by alkylation of 4-methylpyridine (**9**) with the 4-bromo ketones **7/8** and the acetals of the 3-bromo ketones **12/13**, respectively. Protection of the carbonyl groups of the latter, which were deprotected in situ by the acidic electrolyte during cathodic reduction of the salts **10/11**, was necessary to prevent dehydrobromination in the alkylating step.



Scheme 1. Retrosynthetic analysis of the [a]-annelated indolizidines and quinolizidines **1–4**

The bromo ketone **7** was prepared by alkylation of the β -oxo ester **14** with 1,2-dibromoethane and potassium carbonate in refluxing acetone, followed by decarboxylation in hydrobromic acid^[24,25] (Scheme 2). Application of the same procedure to the synthesis of the bromo ketone **8**^[25,26] failed. With sodium hydride as base in DMF^[25] and subsequent treatment as above, the bromo ketone **8** was obtained as a rather unstable compound in 18% overall yield. Deprotonation of cyclohexanone with LDA, followed by the addition of dibromoethane in THF and heating until reflux, with or without added TMEDA, mainly gave aldol condensation products.



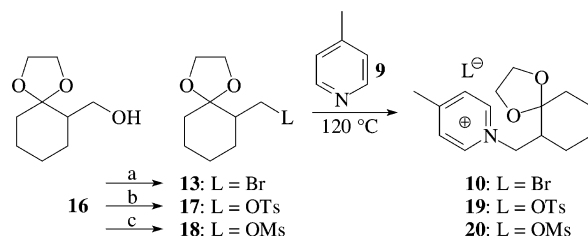
$\alpha = 1$: **a**) K_2CO_3 , $Br(CH_2)_2Br$, acetone, reflux 9 h, 65 %; **b**) 48 % HBr, reflux 30 min., 81 %. $\alpha = 2$: **a**) NaH, $Br(CH_2)_2Br$, DMF, reflux 30 min., not isolated; **b**) 48 % HBr, reflux 30 min..

Scheme 2. Synthesis of the salts **5** and **6**

For the preparation of the salts **5** and **6**, the bromo ketones **7** and **8** were heated to 120 °C with a 1.5-fold excess of 4-methylpyridine (**9**) without added solvent, similarly to the previously described procedure^[19] (Scheme 2). The resulting oils were washed with diethyl ether and dried to give white, powdery solids. These were not purified further, in

order to avoid losses due to their poor tendency to crystallise and because they are very hygroscopic. The yields and purities of **5** and **6** and all other salts reported (except for **10**, **19** and **20**, Table 1) were therefore determined reproducibly by 1H NMR spectroscopy with methyl 3-bromopropanoate as internal standard by integration of the NCH_2 signals of the salts and the CH_2 signals of the standard. The low yield of **6** in comparison to **5** results from 4-methylpyridine (**9**) acting more as a base than as a nucleophile in the case of the bromo ketone **8**, giving 4-methylpyridinium bromide as major product.

The alkylation precursor **13** was obtained by bromination of the hydroxy acetal **16** by a variant of the Mitsunobu reaction^[27] described by Falck^[28] with lithium bromide (Scheme 3). Since preliminary experiments to alkylate 4-methylpyridine (**9**) with **13** showed this compound to be less reactive than **7**, the corresponding tosylate **17**^[29] and mesylate **18**^[30] were also synthesised from the alcohol **16**.



a) DEAD, $P(Ph)_3$, LiBr, THF, 62 %; **b**) TsCl, pyridine, 80 %; **c**) MsCl, pyridine, 90 %.

Scheme 3. Synthesis of alkylation precursors from **16** and alkylation experiments

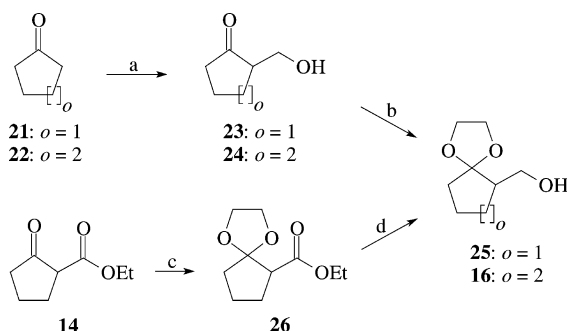
Table 1. Yields of the pyridinium salts **10**, **19** and **20**

Entry	1	2	3	4	5	6
Precursor	13	17	18	18	18	18
Time [min]	20	20	20	60	180	240
Yield ^[a]	< 1% 10	5% 19	5% 20	19% 20	33% 20	43% 20

^[a] Yields not corrected for purity.

The alcohol **16** was obtained by aldol addition of formaldehyde to cyclohexanone (**22**),^[31] followed by acetalisation of the resulting hydroxymethyl ketone **24** with ethylene glycol and PPTS catalysis^[32] in benzene (Scheme 4).^[33] In toluene instead of benzene, the dehydration product 6-methylene-1,4-dioxaspiro[4.5]decane was predominantly formed. Whilst the synthesis of (hydroxymethyl)cyclopentanone (**23**) by the same route was possible,^[31,34] the acetalisation resulted in a mixture of α,β -unsaturated methylenecyclopentanone and the corresponding acetal. The known procedure^[35] for acetalisation of the β -oxo ester **14** and subsequent hydride reduction to **25** was therefore employed.

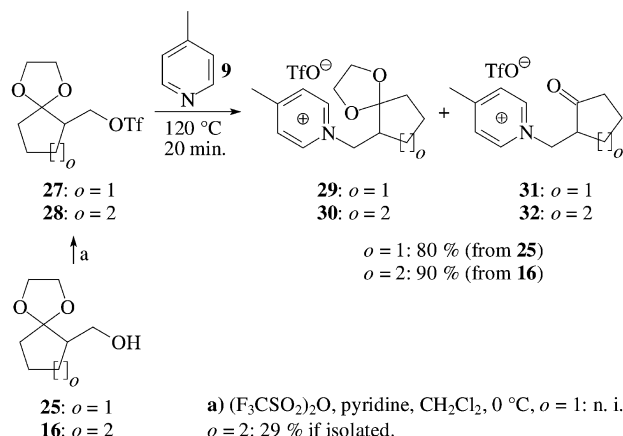
The alkylation of 4-methylpyridine (**9**) with **13**, **17** and **18** did not provide the precursor for the cyclisation in acceptable yields (Scheme 3, Table 1). This problem could finally be solved by the use of triflate as a leaving group (Scheme 5). The triflate **28** could be isolated by column



a) $\text{CH}_2\text{O}_{(\text{aq})}$, $\text{KOH}_{(\text{aq})}$, 3 h 35 °C, *o* = 1: 32 %, *o* = 2: 47 %; b) $\text{HO}(\text{CH}_2)_2\text{OH}$, PPTS, benzene, 1 h reflux, *o* = 1: n. i., *o* = 2: 82 %, c) $\text{HO}(\text{CH}_2)_2\text{OH}$, $\text{TsOH}\cdot\text{H}_2\text{O}$, CH_2Cl_2 , 4 d reflux, 56 %; d) LiAlH_4 , THF, 3 h reflux, 73 %.

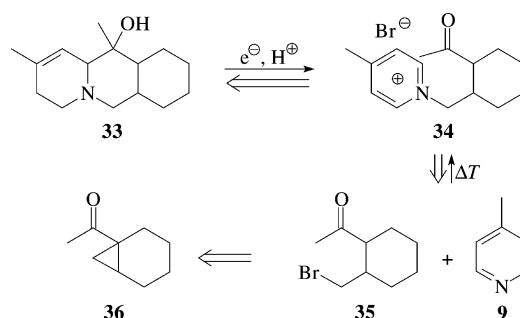
Scheme 4. Synthesis of **25** and **16**

chromatography and characterised, but the yield was low, so the alkylation was performed without isolation of the triflates. In this way, the cyclisation precursors **29** and **30** were obtained in high yields from the alcohols **25** and **16**. Some of the material was found to be deprotected, affording the salts **31** and **32**, respectively. For the determination of the yields by ^1H NMR as described above, solutions of the crude products in a mixture of D_2SO_4 , D_2O and CD_3CN were examined, resulting in the complete deprotection of the acetals to **31** and **32**, which was checked by ESI-MS.

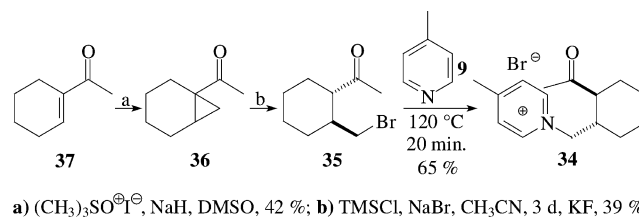
Scheme 5. Synthesis of the cyclisation precursors for the indolizidines from **25** and **16** via triflates

The synthesis of tricyclic [*b*]-anellated quinolizidines would be an important extension of the products accessible so far, because compound **33**, which was targeted as shown in Scheme 6, represents a substructure of the cevanine steroidal alkaloids.^[36,37] The salt **34** should arise from alkylation of 4-methylpyridine (**9**) with the bromo ketone **35**, which should in turn be accessible by nucleophilic ring-opening of the cyclopropyl ketone **36**.

The bicyclic ketone **36** was obtained by cyclopropanation of **37**^[38] (Scheme 7). The regioselective opening of the cyclopropyl ring in **36** with trimethylsilyl iodide has been reported.^[39] By using a combination of trimethylsilyl chlo-

Scheme 6. Retrosynthetic analysis of the cyclohexa[*b*]quinolizidine **33**

ride and sodium halide (I, Cl, Br) as nucleophile in acetonitrile it is possible to choose the halogen atom to be introduced.^[40] The intermediate trimethylsilyl ether is not isolated, but is cleaved during workup with fluoride solution. These conditions, when applied to **36**, afforded the bromo ketone **35** with *trans* stereochemistry, as was clearly confirmed by the coupling constants of the CHCOCH_3 proton ($2 \times J = 10.5$ Hz and $J = 3.7$ Hz). The alkylation of 4-methylpyridine (**9**) was accomplished as for the other salts. As in the case of **8**, significant amounts of 4-methylpyridinium bromide were formed as the main impurity in the product.

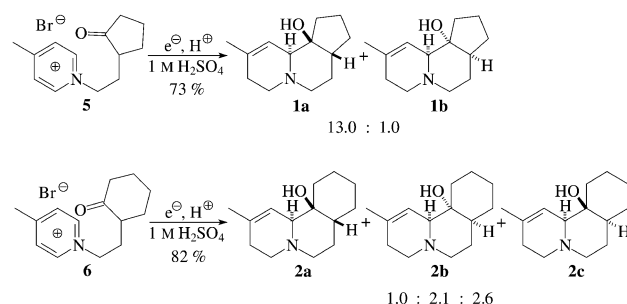
Scheme 7. Synthesis of the pyridinium salt **34**

Electrolysis

The electrolyses of the pyridinium salts were carried out in a divided beaker-type cell at a mercury pool cathode under constant current conditions, since this proved to result in higher yields of the cyclised products than obtainable by potential control conditions.^[19] The electrolyte was 1 M aqueous sulfuric acid, from which the products were easily extracted with diethyl ether and dichloromethane after the pH had been increased to about 10 with solid potassium carbonate.

The cyclisation of **5** had previously been reported to afford two isomeric products in a total yield of 46%.^[19] Meanwhile, the yield of this cyclisation was increased to 73% of two out of four possible diastereomeric products **1a** and **1b** by increasing the amount of charge transferred to a 2.6-fold excess (Scheme 8). The structure of the minor isomer **1b** was elucidated by X-ray crystallography (Figure 1), while the X-ray structure of the major isomer **1a** had been published before.^[19] The cyclisation of the salt **6** provided three diastereomeric quinolizidine^[41] derivatives **2a–2c** in a

combined yield of 82%, with much lower diastereoselectivity than seen in the case of **1** (Scheme 8). Again, the structures of all three products were corroborated by X-ray crystallography (Figure 1). The isomers **2a** and **2b** are structural analogues of **1a** and **1b**, respectively, whereas in the major isomer **2c** the former cyclohexanone and the new ring are *trans*-connected. (These two rings are *cis*-connected in all other isomers in this series.) The six-membered rings in all isomers **1** and **2** adopt the favoured chair conformation.



Scheme 8. Electrolysis of **5** and **6** to afford the quinolizidines **1** and **2**

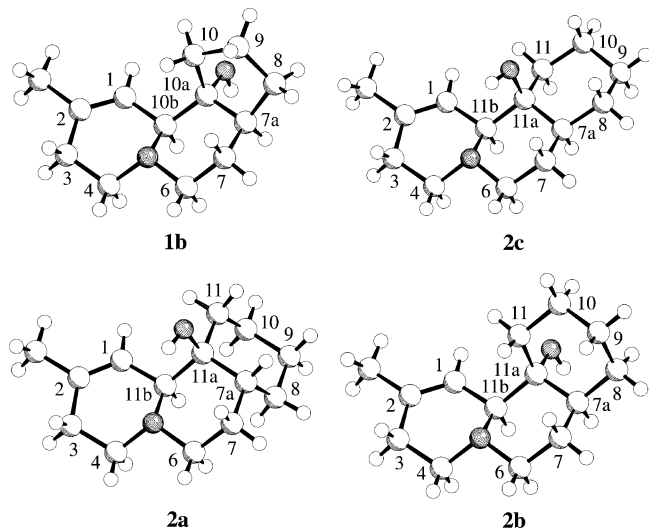
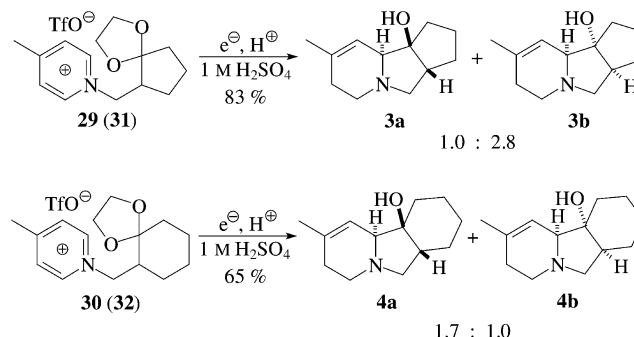


Figure 1. Crystal structures of the quinolizidines **1b** and **2a–2c**

The electrolysis of the pyridinium salts **29** and **30** provided two diastereomeric indolizidine^[42] derivatives in combined yields of 83 and 65% (Scheme 9). In all isomers, the former cycloalkanone and the new ring are *cis*-connected (analogues to **1a** and **1b**), no traces of the two other possible isomers with *trans*-connected rings being found. The diastereoselectivity of the cyclisation was low with respect to the observed isomers. Again, all structures were confirmed by X-ray crystallography (Figure 2). The indolizidine **4b** did not give crystals as a free base, but did so as a picrate salt (the picrate anion is omitted in Figure 2 for clarity). As in the case of the quinolizidines **1** and **2**, the six-membered rings in **4** adopt the chair conformation.



Scheme 9. Electrolysis of **29** and **30** to afford the indolizidines **3** and **4**

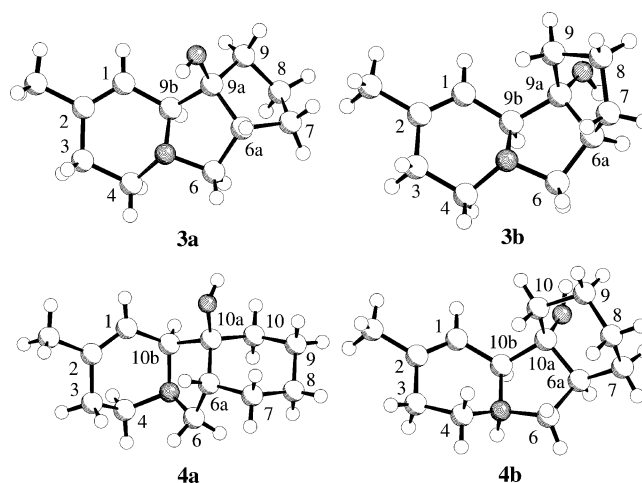
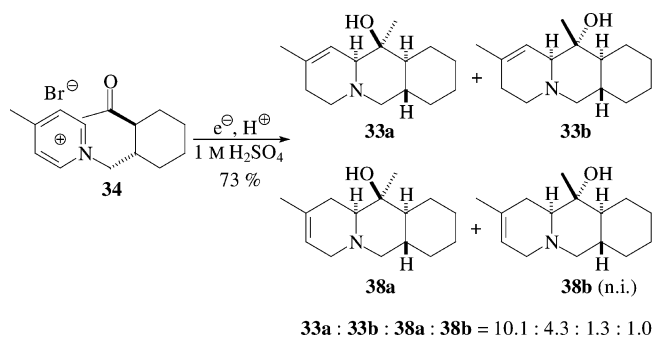


Figure 2. Crystal structures of the indolizidines **3a**, **3b**, **4a** and **4b**

Comparison of all crystal structures reveals that the indolizidine/quinolizidine core adopts a *trans* conformation (nitrogen lone pair and hydrogen atom 9b-H, 10b-H or 11b-H) in all cases except for the indolizidines **4** (Figure 1 and 2). This difference could also be deduced from the IR spectra, since all of these except for those of compounds **4** show strong Bohlmann absorptions^[43] of the NC–H stretch of the hydrogen atoms *trans* to the lone pair of the nitrogen atom in the 2700–2800 cm^{−1} region.

The cyclisation of the pyridinium salt **34** provided two sets – **33** and **38** – of two diastereomers of linear anellated cyclohexa[*b*]quinolizidines^[41] in a combined yield of 73% (**33a**, **33b**, **38a**) (Scheme 10). The two major products **33a** and **33b** represent two out of four possible diastereomers of **33** and differ in configuration at the former carbonyl carbon atom of compound **34**. The products **38a** and **38b** have the same stereochemistry as **33a** and **33b**, but the position of the remaining double bond of the former pyridinium ring is different. These kinds of regioisomers were observed previously in the case of bicyclic quinolizidines.^[19] The structures of **33b** and **38a** were elucidated by X-ray diffraction of appropriate crystals (Figure 3), and that of **33a** by NMR experiments demonstrating NOE effects between the C11–CH₃ and the C10a and C11a hydrogen atoms.^[44] The

IR spectrum of **33a** shows strong Bohlmann bands at 2818 and 2745 cm^{-1} and the signal of the 10a-H in the ^1H NMR spectrum shows two large couplings ($2 \times J = 11.2$, $J = 2.9$ Hz). These data suggest that in the case of **33a** – and also for **33b** and **38a** – all rings are *trans*-connected/in *trans* conformation. The structure of **38b**, which could not be isolated, is suggested to be that shown, as elucidated by comparison of the GC-MS data of the crude reaction mixture. The mass spectrum of **38b** is almost identical to that of **38a**, whereas the spectra of the isomers **33a** and **33b** are significantly different with respect to their peak intensities. In addition, the GC-MS showed that the cyclisation had also yielded the two other diastereomers of **33** in minor amounts (**33c** and **33d**, about 6% of all isomers, not isolated). The products **33** and **38** are of possible interest as they are substructures of some steroidal alkaloids of the cevanine type.^[36,37]



Scheme 10. Electrolysis of **34** to afford the [b]-annelated quinolizidines **33** and **38**

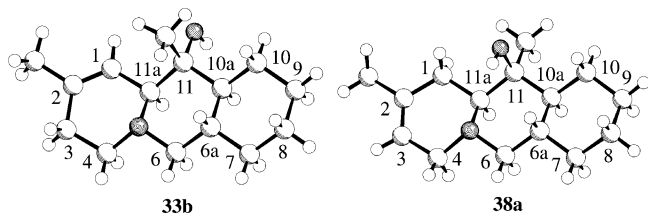


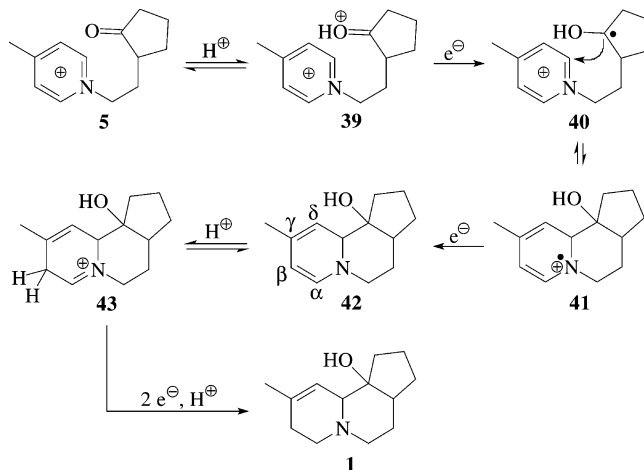
Figure 3. Crystal structures of the [b]-annelated quinolizidines **33b** and **38a**

Mechanistic Considerations

Differential pulse polarography of *N*-(4-oxopentyl)pyridinium chloride in aqueous sulfuric acid at pH = 1–4 showed one acidity-dependent potential shift from –1.91 to –1.53 V (vs. SCE) and a second, acidity-independent reduction potential at –1.43 V.^[19,45] The first reduction was attributed to the carbonyl group and the linear dependency on the pH to activation by protonation of the carbonyl oxygen atom at different acid concentrations. For 1 M aqueous sulfuric acid, the electrolyte used in the preparative electrolyses, the potential could not be measured directly, because the peak overlapped with that of the proton reduction from the electrolyte. By extrapolation from the potentials at higher pH, a value of –1.37 V for the carbonyl reduction

in 1 M aqueous sulfuric acid was obtained. The second potential was assigned to the pyridinium electrophore.

From these data, the mechanism presented in Scheme 11 is proposed. The carbonyl group in the salt **5** is activated by protonation and reduced by one electron to afford the nucleophilic hydroxyalkyl radical **40** (cathodic umpolung). The fact that the protonated carbonyl group is reduced, rather than the pyridinium ring, is further supported by the observation that no reduction of 4-methylpyridinium bromide, present as major impurity in the salts **6** and **34**, was observed during electrolysis. Only 4-methylpyridine (**9**), and no reduction products thereof, was found in the crude products in addition to the cyclised quinolizidine derivatives. The intermolecular coupling of acetone and *N*-ethylpyridinium bromide in sulfuric acid was also shown to proceed through the reduction of acetone rather than the pyridinium bromide.^[46] The hydroxyalkyl radical **40** adds intramolecularly to the electrophilic pyridinium ring, thus converting the distonic radical cation **40** into the delocalised radical cation **41**. This is further reduced to the neutral di-enamine **42**, which – after protonation to provide **43** – affords the indolizidine **1** after final reduction of the iminium group. No intermediates of the reaction can be observed by ESI-MS, which indicates that once the reaction is initiated by the reduction of **39** it proceeds directly to the final product, as all intermediates become reduced more anodically than **39**.

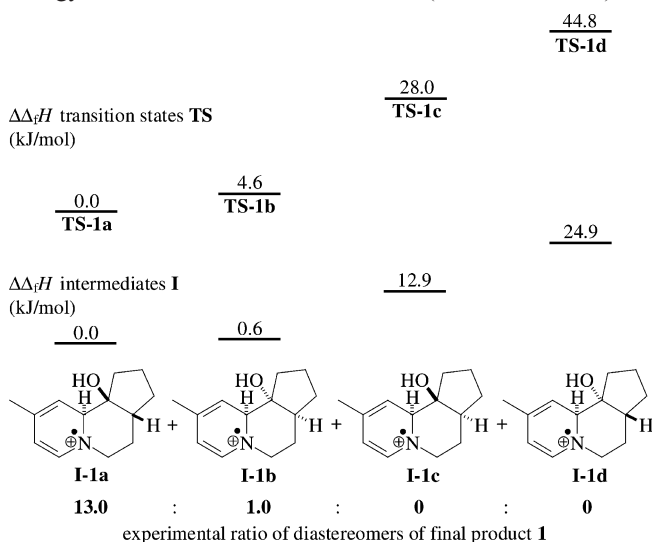


Scheme 11. Proposed mechanism of the cathodic cyclisation, shown for the synthesis of indolizidine **1** from the pyridinium salt **5**

The diastereoselectivity of the reaction is determined in the cyclisation step from **40** to **41**, as equilibration of the isomers by elimination of water and rehydration of the resulting alkenes was ruled out by control experiments. Stirring of the pure diastereomeric tertiary alcohols in 1 M aqueous sulfuric acid for 3 d left these unchanged. From the electrolysis of the salt **29**, only the two diastereomers with the thermodynamically strongly favoured *cis* connection of the two five-membered rings were isolated (Scheme 9). The cyclisation of the salt **6** yielded the isomer **2c** with *trans*-connected six-membered rings as major product, but also the isomers **2a** and **2b** with two *cis*-connected

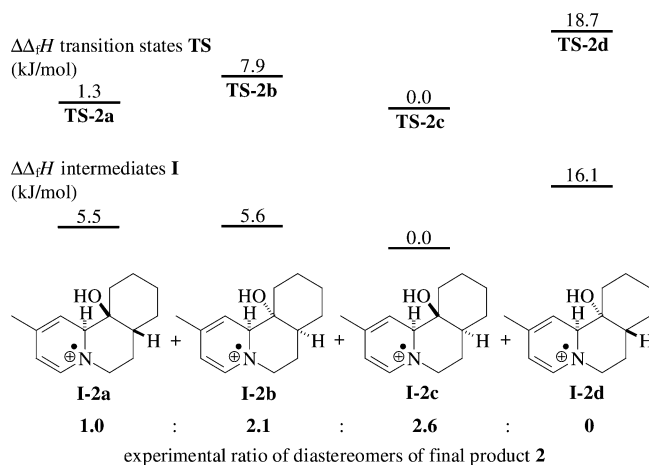
rings (Scheme 8). The product **2c** can be compared with *trans*-decalin, which is only slightly lower in energy than *cis*-decalin, being analogous to **2a** and **2b**. These observations suggest that the ring closure of **40** to **41** is reversible and that the diastereoselectivity is determined by the relative heats of formation of the isomeric intermediates **41** (thermodynamic control). Results obtained by Minisci on the intermolecular addition of radicals of different types to protonated heteroaromatic bases in various solvents^[47] additionally support the proposed reversible cyclisation.

To demonstrate that only isomers resulting from thermodynamically favoured intermediates **41** were obtained, the heats of formation $\Delta_f H$ of all four diastereomeric intermediates **I-1a** to **I-1d** (Scheme 12) and **I-2a** to **I-2d** (Scheme 13) were calculated by use of MOPAC 93 (AM1).^[48] In the cyclisation of salt **5**, the intermediates **I-1a** and **I-1b**, with a *cis* connection of the five- and the six-membered ring, are lower in energy than the others, providing the isolated isomers (Scheme 12). For the cyclisation of **6**, the intermediate **I-2c** affording the major product **2c** is slightly lower in energy than **I-2a** and **I-2b**, thus also affording substantial portions of the products. In both cases, the intermediates **I-1d** and **I-2d** are significantly higher in energy than the corresponding *c* isomers, due to an unfavourable twist conformation that the central ring has to adopt. The fact that the isolated products only result from those intermediates that are lower in energy is also true for the cyclisation to the indolizidines **3** and **4**, as the *cis*-connected intermediates producing the afforded isomers are significantly lower in energy than the *trans*-connected ones (data not shown).^[48]



Scheme 12. Calculated $\Delta\Delta_f H$ values of the transition states TS and the cyclised intermediates **I** for the reduction of the salt **5** to the quinolizidine **1**

In the case of an irreversible cyclisation, the stereoselectivity should be governed by the relative energies of the transition states TSs between **40** and **41** (**I**) (kinetic control). The heats of formation $\Delta_f H$ of all transition states **TS-1a** to **TS-1d** and **TS-2a** to **TS-2d** were therefore also calculated by use of MOPAC 93 (AM1, TS algorithm with free op-



Scheme 13. Calculated $\Delta\Delta_f H$ values of the transition states TS and the cyclised intermediates **I** for the reduction of the salt **6** to the quinolizidine **2**

timisation of the geometries)^[48,49] (Schemes 12 and 13). From these data, it is not possible to differentiate clearly whether thermodynamic or kinetic control as more important, since the transition states **TS-1a**, **TS-1b** and **TS-2a** to **TS-2c**, producing the afforded isomers, are significantly lower in energy than the other. However, the heat of formation of the transition state **TS-2b** does not agree with the ratios of the observed diastereomers, thus suggesting that the cyclisation might not be kinetically controlled.

Overall, with the data obtained so far, a thermodynamically controlled reversible cyclisation, as also proposed by Minisci for related couplings,^[47] is suggested as the key step.

The position of the double bond in the final products is determined by the regioselectivity of the protonation of the dienamine (**42**) (either β -protonation as observed for **1-4** and **33**, or δ -protonation as occurred in the case of **38**), which produces isomeric eniminium ions, which are further reduced at the cathode. In dienamines the kinetically favoured site for protonation is the nitrogen atom, but at equilibrium the eniminium ions that occur by protonation at C- β and C- δ are dominant.^[50] It was deduced that weaker acids protonate more readily at the β -carbon atom while stronger acids afford the conjugated eniminium ions by protonation of the δ -carbon atom to a larger extent. However, as in the case of the related protonation of dienolate anions by water, the competition is also influenced strongly by steric and electronic factors. These are difficult to take into account to explain why the protonation is selective in most cases but not in the cyclisation of **34**.

Conclusion

The cathodic cyclisation of *N*-(oxoalkyl)pyridinium salts has successfully been extended to the synthesis of four cyclopenta-/cyclohexa[a]indolizidine (**3**, **4**) and -quinolizidine derivatives (**1**, **2**) in high yields, from 65 to 83%. One example of a cyclohexa[b]quinolizidine (**33/38**) is also pro-

vided. The pyridinium salts, which were completely converted into cyclised products, are easily available and need not to be purified. Another advantage of the method is the use of aqueous sulfuric acid as solvent, so that no supporting electrolyte is needed, which facilitates the workup. There is no alternative to this cathodic cyclisation that allows such a short synthesis of functionalised indolizidine and quinolizidine derivatives.

A mechanism has been developed to explain the observed diastereoselectivities, in terms of a reversible addition of an intermediate hydroxyalkyl radical to the pyridinium ring, as only diastereomers resulting from the thermodynamically more stable cyclised intermediates were obtained (thermodynamic control). This result might be useful for qualitative prediction, by simple semiempirical calculations, of which diastereomers of future synthetic targets should be accessible. However, from the data obtained so far, kinetic control could not be ruled out.

In due course, we will report on the extension of the method to the cyclisation of various pyridinium salts derived from aldehydes to demonstrate further the usefulness and scope of the reaction.

Experimental Section

General Remarks: For detailed synthetic procedures and analytical data for the known compounds **17**, **18**, **23**, **24**, **25**, **26** and **36**, and also the data for **16**, see the Supporting Information (see footnote on the first page of this article). Melting points were determined with a Kofler hot stage microscope and are not corrected. IR spectra were obtained with a Bruker IFS 28 FT-IR system. NMR spectra were recorded with Bruker ARX 300, Bruker AMX 400 and Varian Unity plus 600 instruments. Two-dimensional HH and CH correlations, as well as DEPT spectra, were recorded if necessary for the given assignments of the signals. A small letter “e” is used to assign equatorial protons, “a” is used for axial. Mass spectra (GC-MS) were recorded with a Finnigan-MAT 8230 (EI, 70 eV) in combination with a Varian GC 3400 and with the GC-MS iontrap system Varian Saturn II (EI, 70 eV). Data from the latter instrument is marked with an asterisk (*). In both systems, HP 5 capillary columns (25 m, 0.2 mm i.d., 0.33 μ m film) were used. ESI-MS data were recorded with a Micromass Quattro LC-Z machine equipped with nanospray inlet (capillary: 1.20 kV; cone: 20 V). The samples were applied as acetonitrile solutions. Exact mass (EMS) determinations were made with the MAT 8230 (reference PFK) and the Quattro LC-Z (reference PEG). Gas chromatography was carried out with a Hewlett–Packard HP 5890 Series II equipped with an HP5 capillary column (25 m, 0.2 mm i.d., 0.52 μ m film) and an FID detector. Preparative flash chromatography was carried out on silica gel 60 (40–63 μ m) purchased from Merck, with use of an excess pressure of 1 bar (argon). Diethyl ether and dichloromethane were distilled before use. Light petroleum refers to petroleum ether boiling at 30–50 °C and was purchased as p.a. quality. All other chemicals were used without further purification. The electrolyses were carried out in a divided beaker-type cell^[51] at a mercury pool cathode (18 cm²). A round platinum grid (5 cm²) served as anode and was placed in a glass tube (i.d. 3 cm), that was sealed at one end with a glass frit (D4) to separate the cell compartments. This anodic chamber was centred 1 cm above the mercury cathode so that the distance between the parallel electrodes was 1.5 cm. Both

electrodes were connected to the outside of the cell by platinum and copper wires that were sealed in glass to avoid contact with the solutions. The catholyte was stirred with a conventional Teflon-coated magnetic stirrer bar lying on top of the mercury. A Jaisle IMP 83 served as current source.

Preparation of the Pyridinium Salts

2-(2-Bromoethyl)cyclopentanone (7): A mixture of ethyl 2-oxocyclopentanecarboxylate (**14**, 11.71 g, 75.0 mmol), potassium carbonate (31.10 g, 225 mmol) and 1,2-dibromoethane (39.0 mL, 85.0 g, 453 mmol) was dissolved in acetone (200 mL, dried with molecular sieves 3 Å) and heated at reflux for 9 h, and then stirred at room temperature overnight. The suspension was filtered, the filtrate was concentrated, and excess 1,2-dibromoethane was distilled off at 10 mbar/60 °C. The residue was purified by flash chromatography (light petroleum/diethyl ether, 3:1, R_f = 0.29). Yield: 12.75 g (48.5 mmol, 65%) ethyl 1-(2-bromoethyl)-2-oxocyclopentanecarboxylate as a colourless oil. IR (film): $\tilde{\nu}$ = 2979 (m), 1748 (s, C=O, ester), 1726 (s, C=O, ketone), 1446 (m), 1404 (w), 1367 (w), 1298 (m), 1258 (s), 1235 (s), 1183 (s), 1159 (s), 1096 (m), 1028 (m), 860 (w) cm⁻¹. ¹H NMR (300.1 MHz, CDCl₃): δ = 1.26 (t, ³J = 7.2 Hz, 3 H, CH₃), 1.85–2.60 (m, 8 H), 3.31–3.40 (m, 1 H, CH_ABr), 3.47–3.56 (m, 1 H, CH_BBr), 4.18 (q, ³J = 7.2 Hz, 2 H, OCH₂) ppm. ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.0 (q, CH₃), 19.6 (t), 27.5 (t), 33.4 (t), 37.0 (t), 37.5 (t), 60.2 (s), 61.6 (t, OCH₂), 170.3 (s, COOEt), 213.4 (s, CO) ppm. MS (GC-MS): m/z (%) = 262/264 (2/2) [M⁺], 234/236 (52/52) [M⁺ – C₂H₄], 217/219 (24/24) [M⁺ – OCH₂CH₃], 207/209 (26/10), 205 (18), 182 (42) [M⁺ – HBr], 179 (22), 156 (100) [M⁺ – C₂H₃Br], 155 (22), 154 (64), 141 (24), 127 (14), 110 (36), 109 (52), 99 (44), 81 (70), 67 (22), 55 (34), 53 (30), 41 (25). C₁₀H₁₅BrO₃ (263.13): calcd. C 45.65, H 5.75; found C 45.81, H 5.67. Ethyl 1-(2-bromoethyl)-2-oxocyclopentanecarboxylate (10.00 g, 38.0 mmol) was dissolved in hydrobromic acid (48%, 40 mL) and the solution was heated at reflux for 30 min until the evolution of carbon dioxide ceased. The solution was cooled to room temperature, diluted with water (50 mL) and extracted with diethyl ether (100 mL). The aqueous phase was neutralised with solid sodium hydrogen carbonate and again extracted with diethyl ether (2 $\times$ 100 mL). The combined organic phases were washed with a saturated solution of sodium hydrogen carbonate (100 mL), dried (MgSO₄), filtered and concentrated. The residue was purified by flash chromatography (light petroleum/diethyl ether, 5:1, R_f = 0.24). Yield: 5.87 g (30.7 mmol, 81%) **7** as slightly yellow oil. IR (film): $\tilde{\nu}$ = 2964 (m), 2875 (m), 1739 (s, C=O), 1452 (w), 1431 (w), 1404 (w), 1274 (w), 1253 (w), 1221 (w), 1154 (m), 1086 (w), 928 (w), 804 (w) cm⁻¹. ¹H NMR (300.1 MHz, CDCl₃): δ = 1.40–1.60 (m, 1 H), 1.70–1.94 (m, 2 H), 1.96–2.20 (m, 2 H), 2.21–2.40 (m, 4 H), 3.41–3.51 (m, 1 H, CH_ABr), 3.54–3.62 (m, 1 H, CH_BBr) ppm. ¹³C NMR (75.5 MHz, CDCl₃): δ = 20.6 (t), 29.4 (t), 31.6 (t), 32.9 (t), 37.8 (t), 47.7 (d), 219.7 (s, C=O) ppm. MS (GC-MS): m/z (%) = 190/192 (4/4) [M⁺], 161/163 (2/2) [M⁺ – C₂H₅], 84 (100) [M⁺ – C₂H₃Br], 67 (6), 55 (50), 41 (21), 39 (10). C₇H₁₁BrO (191.07): calcd. C 44.00, H 5.80; found C 44.24, H 5.83.

4-Methyl-N-[2-(2-oxocyclopentyl)ethyl]pyridinium Bromide (5): 4-Methylpyridine (**9**, 2.92 mL, 2.79 g, 30.0 mmol) was added to 2-(2-bromoethyl)cyclopentanone (**7**, 3.82 g, 20.0 mmol), and the flask was closed with a paraffin bubbler. The mixture was heated to 120 °C for 20 min. The viscous liquid obtained was cooled to room temperature, and diethyl ether was added (80 mL). The mixture was stirred for 10 min and decanted. This procedure was repeated twice. Diethyl ether (80 mL) was then added, and the flask was stoppered and placed in a freezer at –20 °C until the pasty material solidified. The solid was pulverised under diethyl ether (because the

pyridinium salts are very hygroscopic) and stirred for 10 min. The diethyl ether was decanted and the salts were dried in vacuo. The purity and the yield of the salt were determined by ^1H NMR spectroscopy with methyl 3-bromopropanoate as internal standard by integration of the NCH_2 signals of the salt and the CH_2 signals of the standard. Yield: 5.46 g (purity: 96%, based on pure salt: 18.4 mmol, 92%) **5** as a powdery, white solid. M.p. 115 °C. IR (KBr): $\tilde{\nu}$ = 3047 (m), 2961 (m), 2878 (m), 1729 (s, C=O), 1643 (s), 1519 (m), 1475 (m), 1402 (w), 1380 (w), 1312 (w), 1275 (w), 1214 (w), 1173 (m), 1041 (w), 830 (m) cm^{-1} . ^1H NMR (400.1 MHz, CD_3CN): δ = 1.60–1.75 (m, 1 H), 1.78–1.91 (m, 1 H), 1.95–2.10 (m, 2 H), 2.11–2.43 (m, 5 H), 2.70 (s, 3 H, CH_3), 4.83 (t, 3J = 7.8 Hz, 2 H, NCH_2), 7.96 (d, 3J = 6.3 Hz, 2 H, NCHCH), 9.05 (d, 3J = 6.3 Hz, 2 H, NCH) ppm. ^{13}C NMR (100.6 MHz, CD_3CN): δ = 21.7 (t), 22.6 (q, CH_3), 30.6 (t), 32.7 (t), 38.6 (t), 47.0 (d), 60.3 (t, NCH_2), 130.0 (d, NCHCH), 145.3 (d, NCH), 161.1 (s, CCH_3), 220.8 (s, C=O) ppm. MS (ESI^+ -MS): m/z (%) = 204 (100) [M^+]. MS-MS (ESI^+ -MS, m/z = 204): m/z (%) = 204 (20) [M^+], 111 (100) [$\text{M}^+ - 9$], 94 (35) [$9 + \text{H}^+$], 83 (75), 55 (15). MS (ESI^- -MS): m/z (%) = 97/99 (10/10) [$\text{Br}^- + \text{H}_2\text{O}$], 79/81 (100/100) [Br^-]. EMS (ESI^+ -MS): calcd. ($\text{C}_{13}\text{H}_{18}\text{NO}^+$) 204.1388; found 204.1391.

2-(2-Bromoethyl)cyclohexanone (8): The alkylation was carried out under argon in dried glassware. Ethyl 2-oxocyclohexanecarboxylate (**15**, 15.00 g, 88.1 mmol) was added dropwise to a suspension of sodium hydride (60% in mineral oil, 3.60 g, 90.0 mmol) in DMF (100 mL, dried with molecular sieves 4 Å). The reaction mixture was stirred at room temperature until the evolution of hydrogen had ceased. 1,2-Dibromoethane (15.0 mL, 32.66 g, 174 mmol) was added, and the mixture was heated at reflux for 30 min. After the reaction mixture had been cooled to room temperature, it was poured into water (100 mL) and extracted with diethyl ether (4 × 80 mL). The combined organic phases were washed with saturated sodium hydrogen carbonate solution (150 mL) and subsequently with brine (2 × 150 mL), dried (MgSO_4), filtered and concentrated. Hydrobromic acid (48%, 50 mL) was added to the crude product, and the solution was heated at reflux for 30 min until the evolution of carbon dioxide had ceased. The solution was cooled to room temperature, poured into water (100 mL) and extracted with diethyl ether (4 × 100 mL). The combined organic phases were washed with a saturated solution of sodium hydrogen carbonate (200 mL), dried (MgSO_4), filtered and concentrated. The residue was purified by flash chromatography (pentane/diethyl ether, 5:1, R_f = 0.33) followed by a second purification (pentane/diethyl ether, 15:1, R_f = 0.16). Yield: 3.32 g (16.2 mmol, 18%) **8** as a colourless oil. IR (film): $\tilde{\nu}$ = 2935 (s), 2861 (m), 1710 (s, C=O), 1448 (m), 1371 (w), 1338 (w), 1312 (w), 1262 (w), 1224 (w), 1128 (m), 1065 (w), 828 (w), 715 (w) cm^{-1} . ^1H NMR (300.1 MHz, CDCl_3): δ = 1.37 (m , 1 H), 1.54–1.95 (m, 4 H), 2.02–2.19 (m, 2 H), 2.27–2.44 (m, 3 H), 2.57 (m , 1 H), 3.48 (t, 3J = 6.7 Hz, 2 H, CH_2Br) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 25.1 (t), 27.9 (t), 32.1 (t), 32.6 (t), 33.9 (t), 42.1 (t), 48.6 (d), 211.8 (s, C=O) ppm. MS (GC-MS): m/z (%) = 204/206 (3/3) [M^+], 161/163 (3/3) [$\text{M}^+ - \text{C}_2\text{H}_5$], 98 (100) [$\text{M}^+ - \text{C}_2\text{H}_5\text{Br}$], 81 (6), 70 (6), 55 (30), 41 (10). $\text{C}_8\text{H}_{13}\text{BrO}$ (205.10): calcd. C 46.85, H 6.39; found C 48.11, H 6.75. The compound is rather unstable, so that the exact mass had to be obtained: EMS (GC-MS): calcd. 204.0150/206.0129; found 204.0167/206.0149.

4-Methyl-N-[2-(2-oxocyclohexyl)ethyl]pyridinium Bromide (6): 4-Methylpyridine (**9**, 2.92 mL, 2.79 g, 30.0 mmol) was added to 2-(2-bromoethyl)cyclohexanone (**8**, 4.10 g, 20.0 mmol) and the flask was closed with a paraffin bubbler. The mixture was heated to 120 °C for 15 min. The reaction mixture (two phases) was cooled to room temperature and treated as described for the synthesis of **5**. Yield:

3.57 g (purity: 25%, based on pure salt: 2.99 mmol, 15%) **6** as a powdery, white solid. IR (KBr): $\tilde{\nu}$ = 3048 (m), 2929 (m), 1701 (m, C=O), 1638 (s), 1610 (m), 1508 (m), 1440 (w), 1378 (w), 1310 (w), 1257 (w), 1200 (w), 1034 (w), 794 (m) cm^{-1} . ^1H NMR (400.1 MHz, CD_3CN): δ = 1.37 (m , 1 H), 1.50–1.90 (m, 4 H), 1.95–2.15 (m, 2 H), 2.18–2.58 (m, 4 H), 2.59 (s, 3 H, CH_3), 4.59 (t, 3J = 7.8 Hz, 2 H, NCH_2), 7.83 (d, 3J = 6.6 Hz, 2 H, NCHCH), 8.84 (d, 3J = 6.6 Hz, 2 H, NCH) ppm. ^{13}C NMR (100.6 MHz, CD_3CN): δ = 23.0 (q, CH_3), 26.1 (t), 29.0 (t), 32.7 (t), 35.4 (t), 43.1 (t), 48.6 (d), 60.5 (t, NCH_2), 130.1 (d, NCHCH), 145.2 (d, NCH), 161.0 (s, CCH_3), 213.1 (s, C=O) ppm. MS (ESI^+ -MS): m/z (%) = 218 (20) [M^+], 94 (100) [$9 + \text{H}^+$]. MS-MS (ESI^+ -MS, m/z = 218): m/z (%) = 218 (30) [M^+], 125 (100) [$\text{M}^+ - 9$], 94 (25) [$9 + \text{H}^+$]. MS (ESI^- -MS): m/z (%) = 97/99 (10/10) [$\text{Br}^- + \text{H}_2\text{O}$], 79/81 (100/100) [Br^-]. EMS (ESI^+ -MS): calcd. ($\text{C}_{14}\text{H}_{20}\text{NO}^+$) 218.1545; found 218.1551.

1,4-Dioxaspiro[4.5]dec-6-ylmethanol (16): 1,2-Ethanediol (38.73 g, 624 mmol) and pyridinium *para*-toluenesulfonate (PPTS, 7.84 g, 31.2 mmol) were added to a solution of 2-(hydroxymethyl)cyclohexanone (**24**, 20.00 g, 156 mmol) in benzene (400 mL) and the mixture was heated at reflux (1 h) in a Dean–Stark apparatus. Saturated sodium hydrogen carbonate solution (300 mL) was added and the layers were separated. The aqueous layer was extracted with diethyl ether (2 × 200 mL) and the combined organic phases were dried (MgSO_4), filtered and concentrated. The residue was distilled through a Vigreux column. The fraction boiling at 63 °C/0.06 mbar was collected to yield **16** (22.02 g, 128 mmol, 82%) as a colourless oil. Data: see Supporting Information.

6-(Bromomethyl)-1,4-dioxaspiro[4.5]decane (13): DEAD (4.42 mL, 4.95 g, 28.4 mmol) was added dropwise at 0 °C under argon, in dried glassware, to a solution of triphenylphosphane (7.61 g, 29.0 mmol) in dry THF (100 mL). After the mixture had been stirred for 20 min, lithium bromide (5.04 g, 58.1 mmol) was added, followed by alcohol **16** (2.00 g, 11.6 mmol). The orange solution was stirred at 0 °C for another hour and at room temperature for 4 h. The solvent was removed and the residue was poured into water (50 mL) and extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with brine (100 mL), dried (MgSO_4) and concentrated. Light petroleum (100 mL) was added to the residue, the mixture was stirred for 30 min and filtered, and the solvents were evaporated. The crude product was purified by flash chromatography (light petroleum/diethyl ether, 15:1, R_f = 0.38). Yield: 1.69 g (7.19 mmol, 62%) **13** as a colourless oil. IR (film): $\tilde{\nu}$ = 2939 (s), 2883 (m), 2862 (m), 1447 (w), 1353 (w), 1324 (w), 1278 (w), 1227 (w), 1184 (m), 1159 (s), 1139 (s), 1087 (s), 1061 (m), 1040 (w), 1015 (m), 948 (w), 926 (s), 872 (m) cm^{-1} . ^1H NMR (300.1 MHz, CDCl_3): δ = 1.20–1.80 (m, 7 H), 1.94–2.05 (m, 1 H), 2.10–2.20 (m, 1 H), 3.15 (dd, 3J = 10.5, 2J = 9.8 Hz, 1 H, CH_2OH), 3.72 (dd, 2J = 9.8, 3J = 3.1 Hz, 1 H, CH_2OH), 3.85–4.02 (m, 4 H) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 23.7 (t), 24.2 (t), 28.3 (t), 33.8 (t), 34.5 (t), 47.4 (d), 64.7 (2 t), 110.2 (s) ppm. MS (GC-MS*): m/z (%) = 234/236 (2/2) [M^+], 154 (100) [$\text{M}^+ - \text{HBr}$], 113 (15), 99 (20), 93 (5), 67 (6), 55 (30), 41 (16), 39 (20). $\text{C}_9\text{H}_{15}\text{BrO}_2$ (235.12): calcd. C 45.98, H 6.43; found C 46.11, H 6.68.

1,4-Dioxaspiro[4.5]dec-6-ylmethyl Trifluoromethanesulfonate (28): The reaction was carried out under argon in dried glassware. A solution of alcohol **16** (1.00 g, 5.81 mmol) and dry pyridine (0.52 mL, 510 mg, 6.44 mmol) in dry dichloromethane (5 mL) was added dropwise at 0 °C over 30 min to a solution of trifluoromethanesulfonic anhydride (1.00 mL, 1.72 g, 6.10 mmol) in dry dichloromethane (20 mL). The reaction mixture was stirred at 0 °C for a further 30 min and then poured into a mixture of ice and

saturated sodium hydrogen carbonate solution (50 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (2×50 mL). The combined organic phases were dried (MgSO_4), filtered and concentrated. The resulting suspension was filtered through a short column with silica gel (diethyl ether), then further purified by flash chromatography (light petroleum/diethyl ether, 1:1, $R_f = 0.56$). Yield: 511 mg (1.68 mmol, 29%) **28** as a colourless oil, which decomposed rapidly at room temperature. IR (film): $\tilde{\nu} = 2943$ (s), 2887 (m), 2867 (m), 1449 (m), 1413 (s), 1356 (w), 1339 (w), 1246 (s), 1206 (s), 1147 (s), 1098 (s), 1058 (m), 1017 (m), 987 (w), 940 (s), 867 (w), 821 (w), 762 (w) cm^{-1} . ^1H NMR (300.1 MHz, CDCl_3): $\delta = 1.20\text{--}1.85$ (m, 7 H), $1.90\text{--}2.00$ (m, 1 H), $2.10\text{--}2.25$ (m, 1 H), $3.85\text{--}4.08$ (m, 4 H), 4.37 (dd, $^2J = 9.5$, $^3J = 9.5$ Hz, 1 H, CH_2OS), 4.75 (dd, $^2J = 9.5$, $^3J = 4.3$ Hz, 1 H, CH_2OS) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): $\delta = 23.3$ (t), 24.0 (t), 26.8 (t), 34.2 (t), 44.1 (d), 64.4 (2 t), 77.3 (t), 108.8 (s), 118.7 (q, $^1J_{\text{C,F}} = 320$ Hz, CF_3) ppm. MS (GC-MS): m/z (%) = 304 (4) [M^+], 261 (68) [$\text{M}^+ - \text{C}_3\text{H}_7$], 217 (8), 171 (16) [$\text{M}^+ - \text{SO}_2\text{CF}_3$], 155 (100) [$\text{M}^+ - \text{SO}_3\text{CF}_3$], 125 (6), 113 (12), 99 (54), 86 (6), 55 (14), 41 (8). EMS (GC-MS): calcd. ($\text{C}_{10}\text{H}_{15}\text{F}_3\text{O}_5\text{S}$) 304.0592; found 304.0604.

***N*-(1,4-Dioxaspiro[4.5]dec-6-ylmethyl)-4-methylpyridinium Trifluoromethanesulfonate (30):** The reaction was carried out under argon in dried glassware. A solution of alcohol **16** (3.00 g, 17.4 mmol) and 4-methylpyridine (**9**, 1.70 mL, 1.63 g, 17.5 mmol) in dry diethyl ether (10 mL) was added dropwise at 0°C over 30 min to a solution of trifluoromethanesulfonic anhydride (2.71 mL, 4.66 g, 16.5 mmol) in dry diethyl ether (50 mL). The resulting suspension was stirred for a further 30 min at 0°C and then filtered (glass frit D4). 4-Methylpyridine (**9**, 2.55 mL, 2.44 g, 26.2 mmol) was added to the filtrate, and the diethyl ether was removed. The residue was heated to 120°C (flask closed with paraffin bubbler) for 20 min. The reaction mixture was cooled to room temperature, and diethyl ether (50 mL) was added. The mixture was stirred for 10 min and decanted. This procedure was repeated twice more. The residue was dissolved in water (100 mL) and repeatedly extracted with diethyl ether (100 mL) until the aqueous phase was only slightly yellow. The aqueous phase was concentrated and the residue was dried over P_2O_5 in vacuo. The viscous oil crystallised slowly on scratching, to provide a slightly yellow solid. Yield: 6.29 g (mixture of **30** and **32**). The purity was determined by NMR in $\text{D}_2\text{SO}_4/\text{D}_2\text{O}/\text{CD}_3\text{CN}$ to cleave all acetal **30** in the mixture to the ketone **32**: 83% **32**, based on pure salt **32**: 14.8 mmol, 90%. IR (KBr): $\tilde{\nu} = 3062$ (w), 2959 (m), 2902 (w), 2870 (w), 1645 (s), 1523 (m), 1481 (m), 1268 (s), 1224 (s), 1161 (s), 1093 (m), 1052 (m), 1032 (s), 1013 (m), 951 (m), 929 (m), 873 (w), 832 (m), 755 (w), 712 (w), 638 (m) cm^{-1} . ^1H NMR (400.1 MHz, CD_3CN): $\delta = 1.35\text{--}1.70$ (m, 3 H), $1.75\text{--}1.85$ (m, 1 H), $1.95\text{--}2.05$ (m, 2 H), 2.22 (m, 1 H), 2.33 (m, 1 H), 2.53 (s, 3 H, CH_3), 3.12 (m, 1 H, NCH_2CH), 4.32 (dd, $^2J = 13.8$, $^3J = 5.1$ Hz, 1 H, NCH_A), 4.70 (dd, $^2J = 13.8$, $^3J = 7.6$ Hz, 1 H, NCH_B), 7.75 (d, $^3J = 6.5$ Hz, 2 H, NCHCH), 8.55 (d, $^3J = 6.5$ Hz, 2 H, NCH) ppm. ^{13}C NMR (100.6 MHz, CD_3CN): $\delta = 21.3$ (q, CH_3), 24.2 (t), 27.5 (t), 31.5 (t), 41.6 (t), 50.6 (d), 59.9 (t, NCH_2), 120.3 (q, $^1J_{\text{C,F}} = 319$ Hz, CF_3), 128.6 (d, NCHCH), 144.1 (d, NCH), 160.3 (s, CCH_3), 213.3 (s, C=O) ppm. MS ($\text{ESI}^+\text{-MS}$): m/z (%) = 248 (100) [M^+], 204 (28) [$\text{M}^+ \text{32}$], 122 (15), 105 (10), 94 (14) [$\text{9} + \text{H}^+$]. MS-MS ($\text{ESI}^+\text{-MS}$, $m/z = 248$): m/z (%) = 248 (35) [M^+], 155 (100) [$\text{M}^+ - \text{9}$], 111 (12), 99 (10), 95 (10), 94 (12) [$\text{9} + \text{H}^+$], 93 (20), 83 (30), 73 (15), 55 (20). MS-MS ($\text{ESI}^+\text{-MS}$, $m/z = 204$): m/z (%) = 204 (35) [M^+], 111 (10), 94 (90) [$\text{9} + \text{H}^+$], 83 (45), 69 (15), 55 (100). MS ($\text{ESI}^-\text{-MS}$): m/z (%) = 149 (100) [CF_3SO_3^-]. EMS ($\text{ESI}^+\text{-MS}$): calcd. ($\text{C}_{15}\text{H}_{22}\text{NO}_2^+$) 248.1651; found 248.1677.

***N*-(1,4-Dioxaspiro[4.4]non-6-ylmethyl)-4-methylpyridinium Trifluoromethanesulfonate (29):** The reaction was carried out as described above for the salt **30**. Thus, a solution of alcohol **16** (3.16 g, 20.0 mmol) and 4-methylpyridine (**9**, 1.96 mL, 1.87 g, 20.1 mmol) in dry diethyl ether (10 mL) was added dropwise at 0°C over 30 min to a solution of trifluoromethanesulfonic anhydride (3.10 mL, 5.33 g, 18.9 mmol) in dry diethyl ether (50 mL). The resulting suspension was stirred at 0°C for a further 30 min, and was then filtered (glass frit D4). 4-Methylpyridine (**9**, 2.92 mL, 2.79 g, 30.0 mmol) was added to the filtrate, and the diethyl ether was removed. The subsequent procedure was identical to that used for **30**. Yield: 6.67 g of a mixture of **29** and **31**, which slowly crystallised to provide a slightly yellow solid. The purity was determined by NMR in $\text{D}_2\text{SO}_4/\text{D}_2\text{O}/\text{CD}_3\text{CN}$ to cleave all acetal **29** in the mixture to the ketone **31**: 77% **31**, based on pure salt **31**: 15.1 mmol, 80%. IR (KBr): $\tilde{\nu} = 3062$ (m), 2966 (m), 2892 (w), 1737 (m, C=O), 1644 (s), 1575 (w), 1520 (m), 1476 (m), 1263 (s), 1225 (s), 1158 (s), 1031 (s), 949 (m), 906 (w), 830 (m), 756 (m), 709 (w), 639 (s) cm^{-1} . ^1H NMR (400.1 MHz, CD_3CN): $\delta = 1.60$ (m, 1 H), 1.76 (m, 1 H), 1.92–1.98 (m, 1 H), 2.08–2.20 (m, 2 H), 2.25–2.34 (m, 1 H), 2.56 (s, 3 H, CH_3), 2.81 (m, 1 H, NCH_2CH), 4.50 (dd, $^2J = 13.8$, $^3J = 7.1$ Hz, 1 H, NCH_A), 4.66 (dd, $^2J = 13.8$, $^3J = 6.7$ Hz, 1 H, NCH_B), 7.79 (d, $^3J = 6.7$ Hz, 2 H, NCHCH), 8.53 (d, $^3J = 6.7$ Hz, 2 H, NCH) ppm. ^{13}C NMR (100.6 MHz, CD_3CN): $\delta = 20.2$ (t), 21.7 (q, CH_3), 27.3 (t), 38.0 (t), 49.9 (d), 60.1 (t, NCH_2), 120.7 (q, $^1J_{\text{C,F}} = 319$ Hz, CF_3), 129.1 (d, NCHCH), 144.1 (d, NCH), 161.0 (s, CCH_3), 219.7 (s, C=O) ppm. MS ($\text{ESI}^+\text{-MS}$): m/z (%) = 234 (100) [M^+], 190 (10) [$\text{M}^+ \text{31}$], 122 (20), 94 (10) [$\text{9} + \text{H}^+$]. MS-MS ($\text{ESI}^+\text{-MS}$, $m/z = 234$): m/z (%) = 234 (20) [M^+], 141 (70) [$\text{M}^+ - \text{9}$], 99 (100), 69 (10). MS-MS ($\text{ESI}^+\text{-MS}$, $m/z = 190$): m/z (%) = 190 (35) [M^+], 94 (100) [$\text{9} + \text{H}^+$], 69 (95), 55 (13), 41 (10). MS ($\text{ESI}^-\text{-MS}$): m/z (%) = 149 (100) [CF_3SO_3^-]. EMS ($\text{ESI}^+\text{-MS}$): calcd. ($\text{C}_{14}\text{H}_{20}\text{NO}_2^+$) 234.1494; found 234.1485.

***rac*-(1*S*,2*S*)-1-Acetyl-2-(bromomethyl)cyclohexane (35):** The reaction was carried out under argon in dried glassware. Trimethylsilyl chloride (9.14 mL, 7.86 g, 72.3 mmol) was added dropwise over a period of 5 min to a suspension of 1-acetylbicyclo[4.1.0]heptane (**36**, 5.00 g, 36.2 mmol) and sodium bromide (7.44 g, 72.3 mmol) in acetonitrile (100 mL, dried with molecular sieves $3 \text{ \AA}$). After stirring at room temperature for 3 d, the mixture was poured into sodium sulfite solution (5%, saturated with potassium fluoride, 200 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3×100 mL). The combined organic phases were washed with brine (200 mL), dried (MgSO_4), filtered and concentrated. The crude product was purified by flash chromatography (light petroleum/diethyl ether, 20:1, $R_f = 0.19$). Yield: 3.06 g (14.0 mmol, 39%) **35** as a colourless oil. IR (film): $\tilde{\nu} = 2933$ (s), 2857 (s), 1710 (s, C=O), 1448 (m), 1352 (m), 1300 (m), 1246 (m), 1219 (w), 1184 (w), 1159 (m), 954 (w) cm^{-1} . ^1H NMR (300.1 MHz, CDCl_3): $\delta = 1.18\text{--}1.42$ (m, 4 H), $1.72\text{--}2.03$ (m, 3 H), 2.19 (s, 3 H, CH_3), 2.55 (ddd, $^3J = 10.5$, $^3J = 10.5$, $^3J = 3.70$ Hz, 1 H, CHCOCH_3), 3.34 (dd, $^2J = 10.3$, $^3J = 2.6$ Hz, 1 H, CH_ABr), 3.43 (dd, $^2J = 10.3$, $^3J = 5.0$ Hz, 1 H, CH_BBr) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): $\delta = 25.2$ (t), 25.6 (t), 29.4 (t), 29.5 (q, CH_3), 29.7 (t), 38.9 (d, C-2), 39.5 (t, CH_2Br), 53.9 (d, C-1), 211.5 (s, C=O) ppm. MS (GC-MS): m/z (%) = 218/220 (4/6) [M^+], 163/165 (4/11), 139 (100) [$\text{M}^+ - \text{Br}$], 97 (20), 95 (40), 81 (24), 67 (16), 57 (10), 44 (15), 43 (16), 40 (36). $\text{C}_9\text{H}_{15}\text{BrO}$ (219.12): calcd. C 49.33, H 6.90; found C 49.66, H 6.90.

***rac*-*N*-{[(1*S*,2*S*)-2-Acetylcyclohexyl]methyl}-4-methylpyridinium Bromide (34):** 4-Methylpyridine (**9**, 1.46 mL, 1.40 g, 15.0 mmol) was added to 1-acetyl-2-(bromomethyl)cyclohexane (**35**, 2.19 g,

10.0 mmol), and the flask was closed with a paraffin bubbler. The mixture was heated to 120 °C for 20 min. The reaction mixture was cooled to room temperature and treated as described for the synthesis of the salt **5**. Yield: 2.55 g (purity: 65%, based on pure salt: 5.30 mmol, 53%) **34** as a powdery, white solid. IR (KBr): $\tilde{\nu}$ = 3048 (m), 2932 (s), 2858 (m), 1698 (s, C=O), 1640 (s), 1518 (m), 1475 (m), 1449 (m), 1360 (m), 1307 (w), 1249 (m), 1203 (w), 1175 (m), 1041 (w), 828 (m), 804 (m) cm^{-1} . ^1H NMR (400.1 MHz, CD_3CN): δ = 1.05–1.20 (m, 3 H), 1.25–1.35 (m, 1 H), 1.40–1.50 (m, 1 H), 1.65–1.80 (m, 2 H), 2.05–2.13 (m, 1 H), 2.15 (s, 3 H, COCH_3), 2.16–2.25 (m, 1 H), 2.54 (ddd, 3J = 11.6, 3J = 10.7, 3J = 3.8 Hz, 1 H, CHCOCH_3), 2.61 (s, 3 H, pyCH_3), 4.20 (dd, 2J = 13.3, 3J = 8.9 Hz, 1 H, NCH_A), 4.44 (dd, 2J = 13.3, 3J = 4.6 Hz, 1 H, NCH_B), 7.82 (d, 3J = 6.7 Hz, 2 H, NCHCH), 8.61 (d, 3J = 6.7 Hz, 2 H, NCH) ppm. ^{13}C NMR (100.6 MHz, CD_3CN): δ = 22.6 (q, pyCH_3), 25.8 (t), 26.5 (t), 29.2 (q, COCH_3), 29.7 (t), 30.8 (t), 40.6 (d, CHCH_2N), 54.6 (d, CHCOCH_3), 65.7 (t, NCH_2), 130.1 (d, NCHCH), 145.3 (d, NCH), 162.1 (s, CCH_3), 212.5 (s, C=O) ppm. MS (ESI^+ -MS): m/z (%) = 232 (100) [M^+], 94 (10) [$\text{9} + \text{H}^+$]. MS-MS (ESI^+ -MS, m/z = 232): m/z (%) = 232 (25) [M^+], 139 (100) [$\text{M}^+ - \text{9}$], 121 (12), 94 (30) [$\text{9} + \text{H}^+$], 81 (22), 57 (10), 43 (14). MS (ESI^- -MS): m/z (%) = 97/99 (20/20) [$\text{Br}^- + \text{H}_2\text{O}$], 79/81 (100/100) [Br^-]. EMS (ESI^+ -MS): calcd. ($\text{C}_{15}\text{H}_{22}\text{NO}^+$) 232.1701; found 232.1734.

Electrolyses

General Procedure: The pyridinium salt was dissolved in 1 M aqueous sulfuric acid and the solution was placed in the cathode compartment. The anode compartment was charged with 1 M aqueous sulfuric acid such that the levels of the liquids were equal. The electrolysis was carried out under constant current conditions (0.072 A, 4 mA/cm^2) at 20 °C. Typically, the cell voltage increased from 3.4 to 4.1 V during electrolysis. At the anode, the constant evolution of oxygen was clearly visible, at the cathode the evolution of hydrogen increased towards the end of the electrolysis. The catholyte was removed from the cell, made alkaline ($\text{pH} \geq 10$) and extracted with dichloromethane (3 $\times$ 60 mL) and diethyl ether (3 $\times$ 60 mL). The combined organic phases were dried (MgSO_4) and concentrated by rotary evaporation. To determine the isomeric ratios, a sample of the crude product was passed through a short pad of silica gel with diethyl ether/triethylamine (10:1) and analysed by gas chromatography.

Electrolysis of 4-Methyl-N-[2-(2-oxocyclopentyl)ethyl]pyridinium Bromide (5**):** The pyridinium salt **5** (1.71 g, 5.76 mmol based on pure salt) was dissolved in aqueous sulfuric acid (1 M, 30 mL) and electrolysed according to the General Procedure until 5789 C (2.6-fold excess) had been transferred. The crude product was analysed by GC: **1a/1b** = 13.0:1.0 and subjected to flash chromatography (diethyl ether/triethylamine, 10:1) to give two fractions of isomeric products **1b** (R_f = 0.80, 49 mg, slowly crystallising solid) and **1a** (R_f = 0.54, 827 mg, white crystalline solid). Combined yield: 876 mg (4.23 mmol, 73%).

rac-(7aS,10aR,10bS)-2-Methyl-3,4,6,7,7a,8,9,10,10a,10b-decahydrocyclopenta[a]quinolizin-10a-ol (1b**):** IR (KBr): $\tilde{\nu}$ = 3419 (s), 2930 (s), 2889 (s), 2809 (m, NC–H), 2745 (m, NC–H), 1638 (s), 1466 (s), 1444 (s), 1390 (m), 1346 (m), 1326 (s), 1282 (m), 1223 (w), 1188 (w), 1153 (m), 1139 (m), 1105 (s), 1071 (w), 1040 (m), 978 (m), 963 (m), 911 (m), 881 (w), 860 (w) cm^{-1} . ^1H NMR (599.0 MHz, CDCl_3): δ = 1.30–1.40 (m, 3 H, 7-H_A, 8-H_A, 10-H_A), 1.53 (m_c, 1 H, 7-H_B), 1.60–1.64 (m, 1 H, 7a-H), 1.65 (s, 3 H, CH_3), 1.68–1.80 (m, 3 H, 3-H_A, 9-H), 1.86 (m_c, 1 H, 10-H_B), 2.05 (m_c, 1 H, 8-H_B), 2.13 (ddd, 3J = 12.7, 2J = 11.5, 3J = 2.6 Hz, 1 H, 6-

H_A), 2.24–2.36 (m, 2 H, 3-H_B, 4-H_A), 2.48 (s, 1 H, 10b-H), 2.70 (ddd, 2J = 11.5, 3J = 4.1, 3J = 2.6 Hz, 1 H, 6-H_B), 2.79–2.83 (m, 1 H, 4-H_B), 5.50 (s, 1 H, 1-H) ppm. ^{13}C NMR (150.6 MHz, CDCl_3): δ = 20.5 (t, C-9), 22.9 (q, CH_3), 29.4 (t, C-8), 29.8 (t, C-7), 30.55 (t, C-3/C-10), 30.58 (t, C-3/C-10), 47.6 (d, C-7a), 52.4 (t, C-4), 55.1 (t, C-6), 67.6 (d, C-10b), 82.9 (s, C-10a), 119.6 (d, C-1), 133.0 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 206 (12) [$\text{M}^+ - \text{H}$], 192 (6), 122 (16) [$\text{M}^+ - \text{C}_5\text{H}_9\text{O}$], 110 (18) [$\text{M}^+ - \text{C}_6\text{H}_9\text{O}$], 96 (100) [$\text{M}^+ - \text{C}_7\text{H}_{11}\text{O}$], 94 (18), 81 (10), 80 (10), 67 (8), 55 (10), 41 (20), 39 (20). Because of the low quantity of slightly impure material obtained, the exact mass was determined instead of an elemental analysis. EMS (GC-MS): calcd. ($\text{C}_{13}\text{H}_{21}\text{NO}$) 207.1623; found 207.1635.

rac-(7aR,10aS,10bS)-2-Methyl-3,4,6,7,7a,8,9,10,10a,10b-decahydrocyclopenta[a]quinolizin-10a-ol (1a**):** M.p. 103 °C. IR (KBr): $\tilde{\nu}$ = 3552 (s), 3416 (s), 3345 (s), 2961 (s), 2927 (s), 2903 (s), 2878 (s), 2815 (s, NC–H), 2767 (s, NC–H), 1638 (w), 1618 (m), 1445 (m), 1398 (w), 1379 (m), 1365 (m), 1333 (s), 1315 (s), 1288 (s), 1215 (m), 1202 (m), 1128 (s), 1065 (s), 1037 (m), 1007 (m), 966 (m), 906 (m), 875 (s) cm^{-1} . ^1H NMR (300.1 MHz, CDCl_3): δ = 1.44–2.10 (m, 10 H), 1.72 (s, 3 H, CH_3), 2.25–2.40 (m, 3 H), 2.55–2.67 (m, 2 H), 2.75–2.85 (m, 1 H), 5.39 (s, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 19.5 (t), 23.2 (q, CH_3), 23.6 (t), 26.1 (t), 30.4 (t), 33.5 (t), 43.8 (d, C-7a), 51.3 (t), 52.5 (t), 63.2 (d, C-10b), 78.5 (s, C-10a), 118.5 (d, C-1), 135.8 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 207 (12) [M^+], 206 (16) [$\text{M}^+ - \text{H}$], 192 (7), 164 (3), 122 (21) [$\text{M}^+ - \text{C}_5\text{H}_9\text{O}$], 110 (33) [$\text{M}^+ - \text{C}_6\text{H}_9\text{O}$], 96 (100) [$\text{M}^+ - \text{C}_7\text{H}_{11}\text{O}$], 94 (31), 80 (13), 67 (10), 55 (13), 41 (24), 39 (24). $\text{C}_{13}\text{H}_{21}\text{NO}$ (207.32): calcd. C 75.32, H 10.21, N 6.76; found C 75.19, H 10.19, N 6.74.

Electrolysis of 4-Methyl-1-[2-(2-oxocyclohexyl)ethyl]pyridinium Bromide (6**):** The pyridinium salt **6** (3.57 g, 2.99 mmol based on pure salt) was dissolved in aqueous sulfuric acid (1 M, 30 mL) and electrolysed according to the General Procedure until 2975 C (2.6-fold excess) had been transferred. The crude product was analysed by GC: **2a/2b/2c** = 1.0:2.1:2.6 and subjected to flash chromatography (diethyl ether/triethylamine, 10:1) to give a mixture (544 mg, 2.46 mmol, 82%) of the three isomers. The diastereomers were separated by flash chromatography (light petroleum/triethylamine, 10:1): **2c** (R_f = 0.72, slowly crystallising white solid), **2a** (R_f = 0.50, white crystalline solid) and **2b** (R_f = 0.41, white crystalline solid).

rac-(7aS,11aS,11bS)-2-Methyl-3,4,6,7,7a,8,9,10,11a,11b-decahydro-[11H]-cyclohexa[a]quinolizin-11a-ol (2c**):** 41 M.p. 69 °C. IR (KBr): $\tilde{\nu}$ = 3422 (s), 3038 (w), 2924 (s), 2851 (s), 2809 (s, NC–H), 2758 (m, NC–H), 1681 (w), 1638 (m), 1618 (m), 1457 (m), 1382 (m), 1350 (m), 1310 (m), 1276 (s), 1254 (m), 1208 (s), 1149 (m), 1132 (m), 1105 (s), 1079 (m), 1039 (m), 1008 (m), 986 (m), 968 (m), 883 (s), 849 (m), 805 (w), 773 (w), 755 (w) cm^{-1} . ^1H NMR (599.0 MHz, CDCl_3): δ = 1.08 (ddd, 2J = 13.2, $^3J_{\text{aa}}$ = 13.2, J_{ac} = 4.6 Hz, 1 H_a, 11-H), 1.14–1.28 (m, 3 H, 7a-H, 8-H_e, 9-H_A), 1.31 (m_c, 1 H, 7-H_e), 1.39 (dddd, 2J = 12.9, $^3J_{\text{aa}}$ = 12.9, $^3J_{\text{aa}}$ = 12.9, $^3J_{\text{ac}}$ = 3.7 Hz, 1 H, 8-H_A), 1.52 (dddd, 2J = 13.2, $^3J_{\text{aa}}$ = 13.2, $^3J_{\text{aa}}$ = 13.2, $^3J_{\text{ac}}$ = 4.7 Hz, 1 H, 7-H_A), 1.55–1.66 (m, 3 H, 9-H_B, 10-H), 1.67 (s, 3 H, CH_3), 1.71 (m_c, 1 H, 3-H_A), 1.87 (m_c, 1 H, 11-H_e), 2.22 (ddd, $^3J_{\text{aa}}$ = 13.2, 2J = 11.2, $^3J_{\text{ac}}$ = 3.1 Hz, 1 H, 6-H_A), 2.20–2.90 (m, 1 H, 3-H_B), 2.31 (m_c, 1 H, 11b-H), 2.38 (ddd, 2J = 11.1, $^3J_{\text{aa}}$ = 11.1, $^3J_{\text{ac}}$ = 3.90 Hz, 1 H, 4-H_A), 2.72 (ddd, 2J = 11.1, $^3J_{\text{ee}}$ = 5.8, $^3J_{\text{ea}}$ = 1.0 Hz, 1 H, 4-H_e), 2.74 (ddd, 2J = 11.2, $^3J_{\text{ea}}$ = 4.7, $^3J_{\text{ee}}$ = 2.1 Hz, 1 H, 6-H_e), 2.80 (s, 1 H, OH), 5.38 (s, 1 H, 1-H) ppm. ^{13}C NMR (150.6 MHz, CDCl_3): δ = 21.7 (t, C-10), 23.5 (q, CH_3), 25.9 (t, C-9), 28.5 (t, C-8), 28.7 (t, C-7), 30.4 (t, C-3), 33.2 (t, C-11), 43.6 (d, C-7a), 52.1 (t, C-4), 55.8 (t, C-6), 69.3 (d, C-11b), 69.8 (s, C-11a),

117.8 (d, C-1), 153.3 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 221 (6) $[M^+]$, 220 (11) $[M^+ - H]$, 206 (3), 122 (15) $[M^+ - C_6H_{11}O]$, 110 (23) $[M^+ - C_7H_{11}O]$, 96 (100) $[M^+ - C_8H_{13}O]$, 94 (23), 81 (11), 67 (8), 55 (12), 41 (20), 39 (18). $C_{14}H_{23}NO$ (221.34): calcd. C 75.97, H 10.47, N 6.33; found C 75.73, H 10.64, N 6.34.

rac-(7aR,11aS,11bS)-2-Methyl-3,4,6,7,8,9,10,11a,11b-decahydro[11H]-cyclohexa[a]quinolizin-11a-ol (2a):^[41] M.p. 90 °C. IR (KBr): $\tilde{\nu}$ = 3412 (s), 3036 (w), 2956 (s), 2928 (s), 2908 (s), 2859 (s), 2816 (s, NC-H), 2772 (m, NC-H), 1638 (w), 1618 (w), 1465 (m), 1447 (m), 1398 (w), 1380 (w), 1349 (m), 1317 (s), 1288 (m), 1268 (m), 1229 (w), 1198 (m), 1171 (w), 1130 (s), 1112 (m), 1047 (s), 1011 (m), 952 (w), 923 (w), 880 (m), 859 (m), 809 (w), 762 (w) cm^{-1} . 1H NMR (300.1 MHz, $CDCl_3$): δ = 1.20–1.50 (m, 5 H), 1.55–1.82 (m, 5 H), 1.71 (s, 3 H, CH_3), 2.02–2.08 (m, 1 H), 2.23–2.40 (m, 2 H), 2.41–2.52 (m, 2 H), 2.60 (m_c, 1 H), 2.78 (m_c, 1 H), 3.05 (s, 1 H, 11b-H), 3.63 (s, 1 H, OH), 5.39 (s, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 22.7 (t, C-10), 23.5 (q, CH_3), 26.3, 27.4, 28.4 (3 t, C-7, C-8, C-9), 30.4 (t, C-3), 34.2 (t, C-11), 42.7 (d, C-7a), 51.5, 52.3 (2 t, C-4, C-6), 60.4 (d, C-11b), 71.2 (s, C-11a), 117.7 (d, C-1), 135.8 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 221 (6) $[M^+]$, 220 (11) $[M^+ - H]$, 206 (3), 122 (16) $[M^+ - C_6H_{11}O]$, 110 (23) $[M^+ - C_7H_{11}O]$, 96 (100) $[M^+ - C_8H_{13}O]$, 94 (25), 81 (11), 67 (10), 55 (13), 41 (20), 39 (21). $C_{14}H_{23}NO$ (221.34): calcd. C 75.97, H 10.47, N 6.33; found C 76.02, H 10.57, N 6.45.

rac-(7aS,11aR,11bS)-2-Methyl-3,4,6,7,8,9,10,11a,11b-decahydro[11H]-cyclohexa[a]quinolizin-11a-ol (2b):^[41] M.p. 146 °C. IR (KBr): $\tilde{\nu}$ = 3413 (s), 3029 (w), 2932 (s), 2914 (s), 2858 (s), 2814 (s, NC-H), 2742 (w, N-CH), 1638 (m), 1618 (m), 1464 (m), 1439 (m), 1397 (w), 1350 (m), 1321 (m), 1271 (m), 1207 (s), 1186 (m), 1142 (m), 1130 (m), 1113 (s), 1085 (w), 1068 (w), 1043 (m), 1014 (m), 992 (m), 962 (w), 891 (s), 865 (w) cm^{-1} . 1H NMR (300.1 MHz, $CDCl_3$): δ = 1.26–1.60 (m, 9 H), 1.69 (s, 3 H, CH_3), 1.70–1.85 (m, 2 H), 1.90–2.05 (m, 2 H), 2.12–2.38 (m, 4 H), 2.75–2.90 (m, 2 H), 5.49 (s, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.3, 21.4, 23.0 (q, CH_3), 26.8, 26.9, 27.8, 30.5 (6 t, C-3, C-7, C-8 to C-11), 42.8 (d, C-7a), 52.5, 56.1 (2 t, C-4, C-6), 71.4 (d, C-11b), 72.2 (s, C-11a), 119.1 (d, C-1), 133.4 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 221 (6) $[M^+]$, 220 (15) $[M^+ - H]$, 206 (3), 122 (21) $[M^+ - C_6H_{11}O]$, 110 (28) $[M^+ - C_7H_{11}O]$, 96 (100) $[M^+ - C_8H_{13}O]$, 94 (26), 81 (10), 80 (11), 67 (8), 55 (12), 41 (21), 39 (20). $C_{14}H_{23}NO$ (221.34): calcd. C 75.97, H 10.47, N 6.33; found C 75.69, H 10.74, N 6.55.

Electrolysis of *N*-(1,4-Dioxaspiro[4.4]non-6-ylmethyl)-4-methylpyridinium Trifluoromethanesulfonate (29): The pyridinium salt **29** (2.55 g, 5.77 mmol based on pure salt **30**) was dissolved in aqueous sulfuric acid (1 M, 30 mL) and electrolysed according to the General Procedure until 5160 C (2.3-fold excess) had been transferred. The crude product was analysed by GC (**3a/3b** = 1.0:2.8) and subjected to flash chromatography (diethyl ether/triethylamine, 10:1) to give two fractions of isomeric products **3b** (R_f = 0.73, 659 mg, slowly crystallising white solid) and **3a** (R_f = 0.40, 267 mg, white crystalline solid). Combined yield: 926 mg (4.79 mmol, 83%).

rac-(6aR,9aS,9bR)-2-Methyl-3,4,6,6a,7,8,9a,9b-octahydro-9H-cyclopenta[a]indolizin-9a-ol (3b): M.p. 35 °C. IR (KBr): $\tilde{\nu}$ = 3409 (s), 3322 (s), 2944 (s), 2906 (s), 2862 (m), 2806 (s, NC-H), 2727 (m, NC-H), 1666 (w), 1638 (w), 1618 (w), 1446 (m), 1377 (m), 1321 (s), 1281 (s), 1209 (m), 1187 (s), 1132 (m), 1102 (m), 1085 (m), 1041 (m), 1017 (s), 980 (m), 936 (m), 915 (w), 865 (s), 835 (w) cm^{-1} . 1H NMR (300.1 MHz, $CDCl_3$): δ = 1.22–1.38 (m, 1 H), 1.55–1.68 (m, 4 H), 1.69 (s, 3 H, CH_3), 1.80–1.91 (m, 1 H), 2.05–2.20 (m, 2 H), 2.22–2.45 (m, 3 H), 2.50–2.65 (m, 3 H), 2.95 (m_c, 1 H, 9b-

H), 5.49 (s, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 23.1 (q, CH_3), 26.5 (t), 30.2 (t), 34.0 (t), 37.0 (t), 48.4 (t, C-4), 51.2 (d, C-6a), 58.4 (t, C-6), 71.5 (d, C-9b), 90.5 (s, C-9a), 119.3 (d, C-1), 134.3 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 194 (9) $[M^+ + H]$, 192 (10) $[M^+ - H]$, 178 (5), 109 (100) $[M^+ - C_5H_8O]$, 96 (20) $[M^+ - C_6H_9O]$, 94 (19), 81 (21), 67 (6), 55 (6), 41 (18), 39 (20). $C_{12}H_{19}NO$ (193.29): calcd. C 74.57, H 9.91, N 7.25; found C 74.38, H 10.04, N 7.24.

rac-(6aR,9aS,9bS)-2-Methyl-3,4,6,6a,7,8,9a,9b-octahydro-9H-cyclopenta[a]indolizin-9a-ol (3a): M.p. 85 °C. IR (KBr): $\tilde{\nu}$ = 3470 (m), 3407 (m), 3356 (s), 3232 (s), 3042 (w), 2937 (s), 2921 (s), 2905 (s), 2886 (s), 2869 (s), 2852 (s), 2794 (m, NC-H), 2776 (s, NC-H), 2724 (m, NC-H), 1638 (w), 1618 (w), 1467 (m), 1445 (m), 1395 (m), 1372 (m), 1329 (m), 1311 (s), 1290 (s), 1262 (m), 1244 (m), 1217 (m), 1196 (m), 1174 (m), 1149 (s), 1128 (m), 1079 (s), 1064 (s), 1044 (m), 911 (m), 875 (s), 836 (m), 694 (m) cm^{-1} . 1H NMR (300.1 MHz, $CDCl_3$): δ = 1.30–1.40 (m, 1 H), 1.50–1.70 (m, 2 H), 1.72 (s, 3 H, CH_3), 1.73–2.00 (m, 5 H), 2.25–2.42 (m, 4 H, 4-H, 6-H_A, 6a-H), 2.75 (s, 1 H, OH), 3.00–3.10 (m, 1 H, 9b-H), 3.26 (dd, 3J = 8.6, 2J = 8.6 Hz, 1 H, 6-H_B), 5.49 (s, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 23.0 (q, CH_3), 25.5 (t), 30.1 (t), 30.9 (t), 36.2 (t), 48.5 (t, C-4), 51.6 (d, C-6a), 59.6 (t, C-6), 70.1 (d, C-9b), 89.8 (s, C-9a), 118.1 (d, C-1), 135.9 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 192 (6) $[M^+ - H]$, 178 (4), 150 (3), 109 (100) $[M^+ - C_5H_8O]$, 96 (30) $[M^+ - C_6H_9O]$, 94 (25), 81 (31), 67 (10), 55 (10), 41 (24), 39 (25). $C_{12}H_{19}NO$ (193.29): calcd. C 74.57, H 9.91, N 7.25; found C 74.50, H 9.98, N 7.59.

Electrolysis of *N*-(1,4-Dioxaspiro[4.5]dec-6-ylmethyl)-4-methylpyridinium Trifluoromethanesulfonate (30): The pyridinium salt **30** (2.41 g, 5.69 mmol based on pure salt **32**) was dissolved in aqueous sulfuric acid (1 M, 30 mL) and electrolysed according to the General Procedure until 5775 C (2.6-fold excess) had been transferred. The crude product was analysed by GC (**4a/4b** = 1.7:1.0) and subjected to short path flash chromatography (diethyl ether/triethylamine, 10:1) to give a mixture (771 mg, 3.72 mmol, 65%) of the two isomers. The diastereomers were separated over a longer column (diethyl ether/triethylamine, 10:1): **4a** (R_f = 0.30, white crystalline solid), **4b** (R_f = 0.13, white amorphous solid).

rac-(6aR,10aS,10bS)-2-Methyl-3,4,6,6a,7,8,9,10,10a,10b-decahydrocyclohexa[a]indolizin-10a-ol (4a):^[42] M.p. 119 °C. IR (KBr): $\tilde{\nu}$ = 3416 (m), 3052 (s), 2971 (s), 2928 (s), 2853 (s), 2825 (m, NC-H), 1638 (w), 1618 (w), 1492 (m), 1441 (s), 1377 (w), 1345 (m), 1306 (s), 1262 (m), 1224 (m), 1212 (m), 1200 (w), 1160 (s), 1141 (s), 1078 (m), 1047 (m), 1032 (m), 1003 (m), 984 (m), 963 (w), 842 (m), 801 (m), 717 (m) cm^{-1} . 1H NMR (300.1 MHz, $CDCl_3$): δ = 1.18–1.43 (m, 3 H), 1.50–2.00 (m, 7 H), 1.76 (s, 3 H, CH_3), 2.10–2.25 (m, 1 H, 6a-H), 2.39 (dd, 2J = 9.3, 3J = 3.3 Hz, 1 H, 6-H_A), 2.64–2.73 (m_c, 1 H, 4-H_A), 2.88–2.95 (m_c, 1 H, 4-H_B), 3.15 (dd, 2J = 9.3, 3J = 7.2 Hz, 1 H, 6-H_B), 3.24 (m_c, 1 H, 10b-H), 5.39 (s, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 22.4 (t), 23.6 (q, CH_3), 23.8 (t), 29.4 (t), 30.2 (t), 31.9 (t), 45.0 (d, C-6a), 48.2 (t, C-4), 57.3 (t, C-6), 62.9 (d, C-10b), 78.3 (s, C-10a), 117.5 (d, C-1), 138.0 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 207 (2) $[M^+]$, 206 (5) $[M^+ - H]$, 159 (4), 109 (100) $[M^+ - C_6H_{10}O]$, 96 (20) $[M^+ - C_7H_{11}O]$, 94 (22), 81 (36), 67 (8), 55 (8), 41 (20), 39 (25). $C_{13}H_{21}NO$ (207.32): calcd. C 75.32, H 10.21, N 6.76; found C 75.11, H 10.38, N 6.91.

rac-(6aR,10aS,10bR)-2-Methyl-3,4,6,6a,7,8,9,10,10a,10b-decahydrocyclohexa[a]indolizin-10a-ol (4b):^[42] M.p. 104 °C. IR (KBr): $\tilde{\nu}$ = 3412 (m), 3097 (s), 2971 (s), 2925 (s), 2836 (s, NC-H), 1638 (w), 1618 (w), 1449 (s), 1427 (s), 1374 (m), 1350 (s), 1319 (s), 1282

(m), 1217 (m), 1201 (m), 1164 (m), 1150 (s), 1119 (s), 1080 (m), 1053 (s), 1031 (m), 1015 (m), 980 (m), 929 (w), 891 (w), 841 (m), 797 (m), 769 (m), 698 (m) cm^{-1} . ^1H NMR (599.0 MHz, CDCl_3): δ = 1.28–1.49 (m, 7 H, 7- H_A , 8-H, 9-H, 10-H), 1.61–1.65 (m, 1 H, 7- H_B), 1.66 (s, 3 H, CH_3), 1.91–2.05 (m, 2 H, 3-H), 2.08–2.12 (m, 1 H, 6a-H), 2.58 (dd, 3J = 9.2, 2J = 9.2 Hz, 1 H, 6- H_A), 2.68–2.76 (m, 2 H, 4-H), 2.93 (dd, 3J = 9.2, 2J = 9.2 Hz, 1 H, 6- H_B), 3.16 (m, 1 H, 10b-H), 5.40 (m, 1 H, 1-H) ppm. ^{13}C NMR (150.6 MHz, CDCl_3): δ = 20.9, 21.1 (2 t, C-8, C-9), 23.5 (q, CH_3), 24.0 (t, C-7), 29.1 (t, C-3), 30.7 (t, C-10), 43.6 (d, C-6a), 48.3 (t, C-4), 54.8 (t, C-6), 69.1 (d, C-10b), 77.1 (s, C-10a), 118.8 (d, C-1), 134.2 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 206 (5) [M^+ – H], 192 (4), 187 (5), 159 (7), 144 (3), 109 (100) [M^+ – $\text{C}_6\text{H}_{10}\text{O}$], 96 (15) [M^+ – $\text{C}_7\text{H}_{11}\text{O}$], 94 (21), 81 (27), 67 (10), 55 (10), 41 (20), 39 (23). $\text{C}_{13}\text{H}_{21}\text{NO}$ (207.32): calcd. C 75.32, H 10.21, N 6.76; found C 74.95, H 10.21, N 6.60.

Electrolysis of *rac*-N-[(1S,2S)-2-Acetylcyclohexylmethyl]-4-methylpyridinium Bromide (34): The pyridinium salt **34** (1.87 g, 3.90 mmol based on pure salt) was dissolved in aqueous sulfuric acid (1 M, 30 mL) and electrolysed according to the General Procedure until 5789 C (3.8-fold excess) had been transferred. The crude product was analysed by GC: **33a/33b/33c/33d/38a/38b** = 10.1:4.3:0.2:0.7:1.3:1.0 and subjected to short path flash chromatography (light petroleum/triethylamine, 10:1) to give a mixture of isomers (672 mg, 2.86 mmol, 73%). Isomers **33a**, **33b** and **38a** were isolated by repeated flash chromatography (light petroleum/triethylamine, 10:1): **33a** (R_f = 0.60, slowly solidifying colourless oil), **38a** (R_f = 0.54, white crystalline solid), **33b** (R_f = 0.38, white crystalline solid).

***rac*-(6aS,10aS,11S,11aS)-2,11-Dimethyl-3,4,6,6a,7,8,9,10,11,11a-decahydro-10aH-cyclohexa[b]quinolizin-11-ol (33a):**^[41] M.p. 61 °C. IR (KBr): $\tilde{\nu}$ = 3466 (s), 3403 (s), 3036 (w), 2993 (m), 2914 (s), 2852 (s), 2818 (m, NC–H), 2745 (m, NC–H), 1682 (w), 1638 (w), 1618 (w), 1459 (m), 1449 (m), 1381 (m), 1356 (m), 1334 (m), 1304 (m), 1287 (s), 1220 (m), 1176 (m), 1152 (m), 1121 (s), 1102 (m), 1058 (s), 1025 (m), 980 (m), 952 (m), 867 (s), 845 (w), 702 (w) cm^{-1} . ^1H NMR (599.0 MHz, CDCl_3): δ = 0.80 (ddd, $^3J_{aa}$ = 11.2, $^3J_{ab}$ = 11.2, $^3J_{ac}$ = 2.9 Hz, 1 H, 10a-H), 0.83–0.92 (m, 1 H, 7- H_A), 1.11 (s, 3 H, C11– CH_3), 1.17–1.22 (m, 3 H, 8- H_A , 9- H_A , 10- H_A), 1.44–1.59 (m, 2 H, 6a-H, 7- H_B), 1.60–1.63 (m, 1 H, 8- H_B), 1.67 (s, 3 H, C2– CH_3), 1.72 (m, 1 H, 3- H_A), 1.74–1.80 (m, 2 H, 9- H_B , 10- H_B), 1.90 (dd, 2J = 12.3, $^3J_{aa}$ = 12.3 Hz, 1 H, 6- H_A), 2.20–2.28 (m, 1 H, 3- H_B), 2.28 (ddd, 2J = 11.3, $^3J_{aa}$ = 11.3, $^3J_{ac}$ = 4.0 Hz, 1 H, 4- H_A), 2.28 (s, 1 H, 11a-H), 2.60 (s, 1 H, OH), 2.63 (dd, 2J = 12.3, $^3J_{ca}$ = 3.9 Hz, 1 H, 6- H_C), 2.73 (ddd, 2J = 11.3, $^3J_{ca}$ = 6.0, $^3J_{ce}$ = 1.2 Hz, 1 H, 4- H_C), 5.44 (s, 1 H, 1-H) ppm. ^{13}C NMR (150.6 MHz, CDCl_3): δ = 20.4 (q, C11– CH_3), 23.5 (q, C2– CH_3), 24.9, 25.7, 26.5 (3 t, C-8, C-9, C-10), 30.3 (t, C-3), 30.7 (t, C-7), 37.0 (d, C-6a), 50.9 (d, C-10a), 52.1 (t, C-4), 62.5 (t, C-6), 69.6 (d, C-11a), 70.7 (s, C-11), 118.7 (d, C-1), 135.5 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 234 (10) [M^+ – H], 220 (3) [M^+ – CH_3], 138 (6), 110 (35) [M^+ – $\text{C}_8\text{H}_{13}\text{O}$], 96 (100) [M^+ – $\text{C}_9\text{H}_{15}\text{O}$], 94 (20), 81 (12), 67 (10), 55 (8), 43 (25), 41 (18), 39 (15). $\text{C}_{15}\text{H}_{25}\text{NO}$ (235.37): calcd. C 76.55, H 10.71, N 5.95; found C 76.70, H 10.82, N 5.96.

***rac*-(6aS,10aS,11S,11aS)-2,11-Dimethyl-1,6,6a,7,8,9,10,10a,11,11a-decahydro-4H-cyclohexa[b]quinolizin-11-ol (38a):**^[41] M.p. 132 °C. IR (KBr): $\tilde{\nu}$ = 3383 (s), 2956 (s), 2921 (s), 2854 (s), 2812 (m, NC–H), 2762 (m, NC–H), 1638 (w), 1444 (m), 1403 (w), 1380 (m), 1351 (m), 1338 (m), 1320 (m), 1301 (m), 1290 (m), 1252 (m), 1229 (w), 1216 (w), 1178 (m), 1152 (m), 1122 (s), 1060 (m), 1027 (m), 998 (m), 967 (m), 792 (s), 605 (m) cm^{-1} . ^1H NMR

(300.1 MHz, CDCl_3): δ = 0.80–1.30 (m, 6 H), 1.06 (s, 3 H, C11– CH_3), 1.45–1.85 (m, 5 H), 1.71 (s, 3 H, C2– CH_3), 1.86–2.00 (m, 1 H), 2.01–2.10 (m, 1 H), 2.30–2.47 (m, 2 H), 2.69 (m, 1 H), 2.79 (dd, J = 11.2, J = 3.8 Hz, 1 H), 3.22 (m, 1 H), 5.33 (m, 1 H, 3-H) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 20.4 (q, C11– CH_3), 22.9 (q, C2– CH_3), 24.7, 25.6, 26.5 (3 t, C-8, C-9, C-10), 30.0, 31.0 (2 t, C-1, C-7), 35.5 (d, C-6a), 50.5 (d, C-10a), 54.9 (t, C-4), 62.8 (t, C-6), 65.4 (d, C-11a), 70.9 (s, C-11), 117.1 (d, C-3), 132.3 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 235 (40) [M^+], 234 (95) [M^+ – H], 220 (22) [M^+ – CH_3], 216 (8), 202 (8), 192 (10), 190 (9), 136 (8), 124 (11), 120 (7), 110 (100) [M^+ – $\text{C}_8\text{H}_{13}\text{O}$], 96 (95) [M^+ – $\text{C}_9\text{H}_{15}\text{O}$], 94 (80), 81 (32), 67 (42), 55 (20), 43 (80), 41 (60), 39 (45). Due to the low quantity of the material the exact mass was determined instead of an elemental analysis. EMS (GC-MS): calcd. ($\text{C}_{15}\text{H}_{25}\text{NO}$) 235.1936; found 235.1934.

***rac*-(6aS,10aS,11R,11aS)-2,11-Dimethyl-3,4,6,6a,7,8,9,10,11,11a-decahydro-10aH-cyclohexa[b]quinolizin-11-ol (33b):**^[41] M.p. 132 °C. IR (KBr): $\tilde{\nu}$ = 3412 (s), 3327 (s), 2932 (s), 2857 (s), 2801 (s, NC–H), 2741 (m, NC–H), 1638 (w), 1618 (w), 1463 (m), 1450 (m), 1405 (m), 1371 (m), 1354 (m), 1323 (m), 1298 (m), 1276 (s), 1242 (m), 1224 (m), 1179 (m), 1165 (m), 1154 (m), 1122 (s), 1108 (s), 1063 (m), 1045 (w), 930 (s), 883 (m) cm^{-1} . ^1H NMR (300.1 MHz, CDCl_3): δ = 0.85–1.95 (m, 13 H), 1.01 (s, 3 H, C11– CH_3), 1.71 (s, 3 H, C2– CH_3), 2.18–2.38 (m, 3 H), 2.70 (dd, J = 11.0, J = 4.1 Hz, 1 H), 2.78 (m, 1 H), 5.53 (s, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 16.9 (q, C11– CH_3), 23.0 (q, C2– CH_3), 25.0, 25.9, 26.4 (3 t, C-8, C-9, C-10), 30.4 (t, C-3), 30.8 (t, C-7), 38.2 (d, C-6a), 52.3 (t, C-4), 53.7 (d, C-10a), 62.9 (t, C-6), 71.6 (d, C-11a), 73.2 (s, C-11), 119.4 (d, C-1), 133.5 (s, C-2) ppm. MS (GC-MS*): m/z (%) = 234 (12) [M^+ – H], 220 (5) [M^+ – CH_3], 136 (6), 110 (36) [M^+ – $\text{C}_8\text{H}_{13}\text{O}$], 96 (100) [M^+ – $\text{C}_9\text{H}_{15}\text{O}$], 94 (20), 81 (12), 67 (10), 55 (6), 43 (22), 41 (17), 39 (15). $\text{C}_{15}\text{H}_{25}\text{NO}$ (235.37): calcd. C 76.55, H 10.71, N 5.95; found C 76.16, H 10.67, N 5.76.

X-ray Crystallographic Studies: Data sets were collected with Enraf Nonius CAD4 and Nonius Kappa CCD diffractometers. Programs used: data collection EXPRESS (Nonius B. V., 1994) and COLLECT (Nonius B.V., 1998), data reduction MoLEN (K. Fair, Enraf–Nonius B. V., 1990) and Denzo-SMN (Z. Otwinowski, W. Minor, *Methods Enzymol.*, **1997**, 276, 307–326), absorption correction for CCD data SORTAV (R. H. Blessing, *Acta Crystallogr.* **1995**, A51, 33–37; R. H. Blessing, *J. Appl. Crystallogr.* **1997**, 30, 421–426), structure solution SHELXS-97 (G. M. Sheldrick, *Acta Crystallogr.* **1990**, A46, 467–473), structure refinement SHELXL-97 (G. M. Sheldrick, Göttingen, **1997**), graphics SCHAKAL (E. Keller, Freiburg, **1997**). CCDC-204763 (**1b**), -204762 (**2a**), -204761 (**2b**), -204760 (**2c**), -204767 (**3a**), -204766 (**3b**), -204764 (**4a**), -204765 (**4b**), -204768 (**33b**) and -204769 (**38a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

X-ray Crystal Structure Analysis of 1b: Formula $\text{C}_{13}\text{H}_{21}\text{NO}$, M = 207.31, colourless crystal $0.15 \times 0.10 \times 0.10$ mm, a = 32.050(6), b = 5.373(1), c = 20.653(2) Å, V = 3556.5(10) Å³, $\rho_{\text{calcd.}}$ = 1.161 g cm^{-3} , μ = 5.60 cm^{-1} , empirical absorption correction through ψ -scan data ($0.921 \leq T \leq 0.946$), Z = 4, orthorhombic, space group $Pna2_1$ (no. 33), λ = 1.54178 Å, T = 223 K, $\omega/2\theta$ scans, 3743 reflections collected ($-h$, $-k$, $+l$), $[(\sin\theta)/\lambda]$ = 0.62 Å^{−1}, 3743 independent (R_{int} = 0.000) and 2267 observed reflections [$I \geq 2 \sigma(I)$], 413 refined parameters, R = 0.048, wR^2 = 0.102, max. residual electron

density $0.20 (-0.20) \text{ e} \cdot \text{\AA}^{-3}$, Flack parameter $0.0(4)$, three independent molecules in the asymmetric unit, ratio of enantiomers 2:1, hydrogen atoms calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of 2a: Formula $\text{C}_{14}\text{H}_{23}\text{NO}$, $M = 221.33$, colourless crystal $0.20 \times 0.15 \times 0.10 \text{ mm}$, $a = 7.027(1)$, $b = 9.445(1)$, $c = 9.852(1) \text{ \AA}$, $\alpha = 96.08(1)$, $\beta = 102.76(1)$, $\gamma = 99.50(1)^\circ$, $V = 622.06(13) \text{ \AA}^3$, $\rho_{\text{calcd.}} = 1.182 \text{ g cm}^{-3}$, $\mu = 5.63 \text{ cm}^{-1}$, no absorption correction ($0.896 \leq T \leq 0.946$), $Z = 2$, triclinic, space group $P\bar{1}$ (no. 2), $\lambda = 1.54178 \text{ \AA}$, $T = 223 \text{ K}$, $\omega/2\theta$ scans, 2748 reflections collected ($+h, \pm k, \pm l$), $[(\sin\theta)/\lambda] = 0.62 \text{ \AA}^{-1}$, 2533 independent ($R_{\text{int}} = 0.063$) and 2031 observed reflections [$I \geq 2 \sigma(I)$], 148 refined parameters, $R = 0.045$, $wR^2 = 0.126$, max. residual electron density $0.25 (-0.18) \text{ e} \cdot \text{\AA}^{-3}$, hydrogen atoms calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of 2b: Formula $\text{C}_{14}\text{H}_{23}\text{NO}$, $M = 221.33$, colourless crystal $0.50 \times 0.40 \times 0.20 \text{ mm}$, $a = 5.420(1)$, $b = 6.612(1)$, $c = 18.136(1) \text{ \AA}$, $\alpha = 81.79(1)$, $\beta = 85.03(1)$, $\gamma = 73.20(1)^\circ$, $V = 615.12(15) \text{ \AA}^3$, $\rho_{\text{calcd.}} = 1.195 \text{ g cm}^{-3}$, $\mu = 5.69 \text{ cm}^{-1}$, empirical absorption correction through ψ -scan data ($0.764 \leq T \leq 0.895$), $Z = 2$, triclinic, space group $P\bar{1}$ (no. 2), $\lambda = 1.54178 \text{ \AA}$, $T = 223 \text{ K}$, $\omega/2\theta$ scans, 2722 reflections collected ($\pm h, -k, \pm l$), $[(\sin\theta)/\lambda] = 0.62 \text{ \AA}^{-1}$, 2493 independent ($R_{\text{int}} = 0.023$) and 2366 observed reflections [$I \geq 2 \sigma(I)$], 148 refined parameters, $R = 0.045$, $wR^2 = 0.147$, max. residual electron density $0.31 (-0.19) \text{ e} \cdot \text{\AA}^{-3}$, hydrogen atoms calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of 2c: Formula $\text{C}_{14}\text{H}_{23}\text{NO}$, $M = 221.33$, colourless crystal $0.30 \times 0.20 \times 0.10 \text{ mm}$, $a = 7.792(1)$, $b = 15.819(2)$, $c = 10.550(1) \text{ \AA}$, $\beta = 104.05(1)^\circ$, $V = 1261.5(3) \text{ \AA}^3$, $\rho_{\text{calcd.}} = 1.165 \text{ g cm}^{-3}$, $\mu = 5.55 \text{ cm}^{-1}$, empirical absorption correction through ψ -scan data ($0.851 \leq T \leq 0.947$), $Z = 4$, monoclinic, space group $P2_1/n$ (no. 14), $\lambda = 1.54178 \text{ \AA}$, $T = 223 \text{ K}$, $\omega/2\theta$ scans, 5414 reflections collected ($-h, \pm k, \pm l$), $[(\sin\theta)/\lambda] = 0.62 \text{ \AA}^{-1}$, 2573 independent ($R_{\text{int}} = 0.038$) and 1683 observed reflections [$I \geq 2 \sigma(I)$], 148 refined parameters, $R = 0.048$, $wR^2 = 0.123$, max. residual electron density $0.26 (-0.24) \text{ e} \cdot \text{\AA}^{-3}$, hydrogens calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of 3a: Formula $\text{C}_{12}\text{H}_{19}\text{NO}$, $M = 193.28$, colourless crystal $0.20 \times 0.20 \times 0.20 \text{ mm}$, $a = 19.521(1)$, $b = 12.832(1)$, $c = 9.425(1) \text{ \AA}$, $\beta = 113.01(1)^\circ$, $V = 2173.1(3) \text{ \AA}^3$, $\rho_{\text{calcd.}} = 1.182 \text{ g cm}^{-3}$, $\mu = 5.77 \text{ cm}^{-1}$, empirical absorption correction via ψ -scan data ($0.893 \leq T \leq 0.893$), $Z = 8$, monoclinic, space group $C2/c$ (no. 15), $\lambda = 1.54178 \text{ \AA}$, $T = 223 \text{ K}$, $\omega/2\theta$ scans, 2365 reflections collected ($\pm h, -k, +l$), $[(\sin\theta)/\lambda] = 0.62 \text{ \AA}^{-1}$, 2223 independent ($R_{\text{int}} = 0.032$) and 1829 observed reflections [$I \geq 2 \sigma(I)$], 130 refined parameters, $R = 0.045$, $wR^2 = 0.118$, max. residual electron density $0.32 (-0.23) \text{ e} \cdot \text{\AA}^{-3}$, hydrogen atoms calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of 3b: Formula $\text{C}_{12}\text{H}_{19}\text{NO}$, $M = 193.28$, colourless crystal $0.30 \times 0.20 \times 0.10 \text{ mm}$, $a = 9.849(1)$, $b = 12.794(2)$, $c = 17.851(1) \text{ \AA}$, $V = 2249.4(2) \text{ \AA}^3$, $\rho_{\text{calcd.}} = 1.141 \text{ g cm}^{-3}$, $\mu = 5.58 \text{ cm}^{-1}$, empirical absorption correction via ψ -scan data ($0.851 \leq T \leq 0.946$), $Z = 8$, orthorhombic, space group $P2_12_12_1$ (no. 19), $\lambda = 1.54178 \text{ \AA}$, $T = 223 \text{ K}$, $\omega/2\theta$ scans, 5034 reflections collected ($+h, +k, \pm l$), $[(\sin\theta)/\lambda] = 0.62 \text{ \AA}^{-1}$, 4565 independent ($R_{\text{int}} = 0.025$) and 3104 observed reflections [$I \geq 2 \sigma(I)$], 257 refined parameters, $R = 0.055$, $wR^2 = 0.141$, Flack parameter $0.3(3)$, max. residual electron density $0.32 (-0.25) \text{ e} \cdot \text{\AA}^{-3}$, two almost identical molecules in the asymmetric unit, hydrogen atoms calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of 4a: Formula $\text{C}_{13}\text{H}_{21}\text{NO}$, $M = 207.31$, colourless crystal $0.40 \times 0.40 \times 0.20 \text{ mm}$, $a = 17.339(1)$,

$b = 6.342(1)$, $c = 10.264(1) \text{ \AA}$, $\beta = 91.98(1)^\circ$, $V = 1128.0(2) \text{ \AA}^3$, $\rho_{\text{calcd.}} = 1.221 \text{ g cm}^{-3}$, $\mu = 5.88 \text{ cm}^{-1}$, empirical absorption correction via ψ -scan data ($0.799 \leq T \leq 0.891$), $Z = 4$, monoclinic, space group $P2_1/c$ (no. 14), $\lambda = 1.54178 \text{ \AA}$, $T = 223 \text{ K}$, $\omega/2\theta$ scans, 2428 reflections collected ($\pm h, -k, -l$), $[(\sin\theta)/\lambda] = 0.62 \text{ \AA}^{-1}$, 2287 independent ($R_{\text{int}} = 0.054$) and 2111 observed reflections [$I \geq 2 \sigma(I)$], 138 refined parameters, $R = 0.057$, $wR^2 = 0.170$, max. residual electron density $0.30 (-0.38) \text{ e} \cdot \text{\AA}^{-3}$, hydrogen atoms calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of 4b: Formula $\text{C}_{13}\text{H}_{22}\text{NO} \times \text{C}_6\text{H}_2\text{N}_3\text{O}_7$, $M = 436.42$, yellow crystal $0.40 \times 0.10 \times 0.05 \text{ mm}$, $a = 7.283(1)$, $b = 25.682(1)$, $c = 10.658(1) \text{ \AA}$, $V = 1993.5(3) \text{ \AA}^3$, $\rho_{\text{calcd.}} = 1.454 \text{ g cm}^{-3}$, $\mu = 9.73 \text{ cm}^{-1}$, empirical absorption correction via SORTAV ($0.697 \leq T \leq 0.953$), $Z = 4$, orthorhombic, space group $Pna2_1$ (no. 33), $\lambda = 1.54178 \text{ \AA}$, $T = 223 \text{ K}$, ω and scans, 7516 reflections collected ($\pm h, \pm k, \pm l$), $[(\sin\theta)/\lambda] = 0.59 \text{ \AA}^{-1}$, 3092 independent ($R_{\text{int}} = 0.025$) and 2531 observed reflections [$I \geq 2 \sigma(I)$], 282 refined parameters, $R = 0.037$, $wR^2 = 0.088$, Flack parameter $0.5(2)$, max. residual electron density $0.14 (-0.19) \text{ e} \cdot \text{\AA}^{-3}$, hydrogen atoms calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of 33b: Formula $\text{C}_{15}\text{H}_{25}\text{NO}$, $M = 235.36$, colourless crystal $0.50 \times 0.40 \times 0.30 \text{ mm}$, $a = 5.372(1)$, $b = 11.295(1)$, $c = 22.434(1) \text{ \AA}$, $\beta = 96.37(1)^\circ$, $V = 1352.8(3) \text{ \AA}^3$, $\rho_{\text{calcd.}} = 1.156 \text{ g cm}^{-3}$, $\mu = 5.45 \text{ cm}^{-1}$, empirical absorption correction through ψ scan data ($0.772 \leq T \leq 0.854$), $Z = 4$, monoclinic, space group $P2_1/n$ (No. 14), $\lambda = 1.54178 \text{ \AA}$, $T = 223 \text{ K}$, $\omega/2\theta$ scans, 3055 reflections collected ($+h, -k, \pm l$), $[(\sin\theta)/\lambda] = 0.62 \text{ \AA}^{-1}$, 2754 independent ($R_{\text{int}} = 0.027$) and 2440 observed reflections [$I \geq 2 \sigma(I)$], 158 refined parameters, $R = 0.045$, $wR^2 = 0.139$, max. residual electron density $0.31 (-0.17) \text{ e} \cdot \text{\AA}^{-3}$, hydrogens calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of 38a: Formula $\text{C}_{15}\text{H}_{25}\text{NO}$, $M = 235.36$, colourless crystal $0.30 \times 0.30 \times 0.20 \text{ mm}$, $a = 8.895(1)$, $b = 11.849(2)$, $c = 12.710(1) \text{ \AA}$, $\beta = 93.94(1)^\circ$, $V = 1336.4(3) \text{ \AA}^3$, $\rho_{\text{calcd.}} = 1.170 \text{ g cm}^{-3}$, $\mu = 5.51 \text{ cm}^{-1}$, empirical absorption correction through ψ -scan data ($0.852 \leq T \leq 0.898$), $Z = 4$, monoclinic, space group $P2_1/n$ (no. 14), $\lambda = 1.54178 \text{ \AA}$, $T = 223 \text{ K}$, $\omega/2\theta$ scans, 2839 reflections collected ($\pm h, +k, -l$), $[(\sin\theta)/\lambda] = 0.62 \text{ \AA}^{-1}$, 2718 independent ($R_{\text{int}} = 0.028$) and 2331 observed reflections [$I \geq 2 \sigma(I)$], 158 refined parameters, $R = 0.038$, $wR^2 = 0.107$, max. residual electron density $0.23 (-0.16) \text{ e} \cdot \text{\AA}^{-3}$, hydrogen atoms calculated and refined as riding atoms.

- [1] [1a] *Rodd's Chemistry of Carbon Compounds*, vol. 5 (Topical Volumes, "Organic Electrochemistry") (Ed.: M. Sainsbury), 2nd ed., Elsevier, Amsterdam, Boston, London, New York, Oxford, Paris, San Diego, San Francisco, Singapore, Sydney, Tokyo, 2002. [1b] *Organic Electrochemistry* (Eds.: H. Lund, O. Hammerich), 4th ed., Marcel Dekker, New York, Basel, 2001. [1c] H. J. Schäfer, in *Radicals in Organic Synthesis*, vol. 1 (Basic Principles) (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, New York, Chichester, Brisbane, Singapore, Toronto, 2001. [1d] J. Grimshaw, *Electrochemical Reactions and Mechanisms in Organic Chemistry*, Elsevier, Amsterdam, Lausanne, New York, Oxford, Shannon, Singapore, Tokyo, 2000. [1e] *Novel Trends in Electroorganic Synthesis* (Ed.: S. Torii), Springer-Verlag, Tokyo, Berlin, Heidelberg, New York, 1998. [1f] J. Volke, F. Liska, *Electrochemistry in Organic Synthesis*, Springer-Verlag, Berlin, Heidelberg, New York, London, Paris, Tokyo, Hong Kong, Barcelona, Budapest, 1994. [1g] D. Kyriacou, *Modern Electroorganic Chemistry*, Springer-Verlag, Berlin, Heidelberg, New York, 1994.

- [12] R. D. Little, K. D. Moeller, *Electrochem. Soc. Interface* **2002**, 11, 36–42.
- [13] Reviews: [3a] K. D. Moeller, *Top. Curr. Chem.* **1997**, 185, 49–86. [3b] K. D. Moeller, *Tetrahedron* **2000**, 56, 9527–9554. [3c] H. J. Schäfer, in ref.^[1b], p. 883–967.
- [14] Reviews: [4a] R. D. Little, *Chem. Rev.* **1996**, 96, 93–114. [4b] R. D. Little, M. K. Schwaebe, *Top. Curr. Chem.* **1997**, 185, 1–48. [4c] M. Folmer Nielsen, J. H. P. Utley in ref.^[1b], p. 795–882.
- [15] E. Dunach, A. P. Esteves, A. M. Freitas, M. J. Medeiros, S. Olivero, *Tetrahedron Lett.* **1999**, 40, 8693–8696.
- [16] H. E. Bode, C. G. Sowell, R. D. Little, *Tetrahedron Lett.* **1990**, 31, 2525–2528.
- [17] S. Torii, H. Okumoto, M. A. Rashid, M. Mohri, *Synlett* **1992**, 721–722.
- [18] [8a] A. J. Fry, R. D. Little, J. Leonetti, *J. Org. Chem.* **1994**, 59, 5017–5026. [8b] D. P. Fox, R. D. Little, M. M. Baizer, *J. Org. Chem.* **1985**, 50, 2202–2204. [8c] M. Schwaebe, R. D. Little, *J. Org. Chem.* **1996**, 61, 3240–3244.
- [19] G. L. Carroll, R. D. Little, *Org. Lett.* **2000**, 2, 2873–2876.
- [10] S. Kashimura, Y. Murai, C. Washika, D. Yoshihara, Y. Kataoka, H. Murase, T. Shono, *Tetrahedron Lett.* **1997**, 38, 6717–6720.
- [11] S. Kashimura, Y. Murai, M. Ishifune, H. Masuda, M. Shimomura, H. Murase, T. Shono, *Acta Chem. Scand.* **1999**, 53, 949–951.
- [12] T. Shono, N. Kise, E. Shirakawa, H. Matsumoto, E. Okazaki, *J. Org. Chem.* **1991**, 56, 3063–3067.
- [13] N. Kise, H. Oike, E. Okazaki, M. Yoshimoto, T. Shono, *J. Org. Chem.* **1995**, 60, 3980–3992.
- [14] [14a] A. K. Yadav, A. Singh, *Synlett* **2000**, 1999–1201. [14b] T. Shono, I. Nishiguchi, H. Ohmizu, M. Mitani, *J. Am. Chem. Soc.* **1978**, 100, 545–550.
- [15] T. Shono, N. Kise, T. Fujimoto, N. Tominaga, H. Morita, *J. Org. Chem.* **1992**, 57, 7175–7187.
- [16] S. Kashimura, M. Ishifune, Y. Murai, N. Moriyoshi, T. Shono, *Tetrahedron Lett.* **1995**, 36, 5041–5044.
- [17] T. Shono, N. Kise, T. Fujimoto, A. Yamanami, R. Nomura, *J. Org. Chem.* **1994**, 59, 1730–1740.
- [18] N. Kise, T. Suzumoto, T. Shono, *J. Org. Chem.* **1994**, 59, 1407–1413.
- [19] R. Gorny, H. J. Schäfer, R. Fröhlich, *Angew. Chem.* **1995**, 107, 2188–2191; *Angew. Chem. Int. Ed. Engl.* **1995**, 34, 2007–2009.
- [20] [20a] J. P. Michael, *Nat. Prod. Rep.* **2002**, 19, 719–741. [20b] D. J. Hart, in *Radicals in Organic Synthesis*, vol. 2 (Applications) (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, New York, Chichester, Brisbane, Singapore, Toronto, **2001**, 279–302. [20c] T. Fujii, M. Ohba, *Heterocycles* **1998**, 47, 525–539. [20d] S. Laschat, *Liebigs Ann./Recueil* **1997**, 1–11.
- [21] J. A. Murphy, M. S. Sherburn, *Tetrahedron* **1991**, 47, 4077–4088.
- [22] A. P. Dobbs, K. Jones, K. T. Veal, *Tetrahedron Lett.* **1997**, 38, 5383–5386.
- [23] The synthesis and some of the data for one of the products, **1a**, were communicated previously; see ref.^[19]
- [24] [24a] K. Jarowicki, T. Jaworski, *Monatsh. Chem.* **1984**, 115, 605–612. [24b] V. A. Dombrovskii, D. Y. Fonskii, T. M. Filipova, V. A. Mironov, *J. Org. Chem. USSR* **1986**, 22, 1471–1480.
- [25] J. K. Crandall, R. J. Seidewand, *J. Org. Chem.* **1970**, 35, 697–701.
- [26] [26a] G. A. Molander, J. A. McKie, *J. Org. Chem.* **1993**, 58, 7216–7227. [26b] P. Dowd, S.-C. Choi, *J. Am. Chem. Soc.* **1987**, 109, 6548–6549.
- [27] D. L. Hughes, *Org. React.* **1992**, 42, 335–656.
- [28] S. Manna, J. R. Falck, *Synth. Commun.* **1985**, 15, 663–668.
- [29] W. Kirmse, S. Schneider, *Chem. Ber.* **1969**, 102, 2440–2448.
- [30] [30a] J. J. Gajewski, G. C. Paul, *J. Org. Chem.* **1991**, 56, 1986–1989. [30b] R. C. Gadwood, R. M. Lett, *J. Org. Chem.* **1982**, 47, 2268–2275.
- [31] N. V. Elagina, N. S. Martinkova, B. A. Kazanskii, *Zh. Obshch. Khim.* **1959**, 29, 3969–3971.
- [32] R. Sterzycki, *Synthesis* **1979**, 724–725.
- [33] Compound **16** was also prepared by reduction of the oxolane obtained from **15**, for example: S. R. Hitchcock, F. Perron, V. A. Martin, K. F. Albizati, *Synthesis* **1990**, 1059–1061.
- [34] C. L. Penney, B. Belleau, *Can. J. Chem.* **1978**, 56, 2396–2404.
- [35] R. J. K. Taylor, K. Wiggins, D. H. Robinson, *Synthesis* **1990**, 589–590.
- [36] Alkaloids of the cevanine type were also classified as cerveratrum-type steroidal alkaloids.
- [37] See for example: [37a] Atta-ur-Rahman, M. I. Choudhary, in *The Alkaloids, Chemistry and Biology* (Ed.: G. A. Cordell), Academic Press, San Diego, London, Boston, New York, Sydney, Tokyo, Toronto, **1998**, vol. 50, p. 61–108. [37b] Atta-ur-Rahman, M. N. Akhtar, M. I. Choudhary, Y. Tsuda, B. Sener, A. Khalid, M. Parvez, *Chem. Pharm. Bull.* **2002**, 50, 1013–1016. [37c] G. Lin, P. Li, S.-L. Li, S.-W. Chan, *J. Chromatogr. A* **2001**, 935, 321–338. [37d] Y. Tezuka, T. Kikuchi, W. Zhao, J. Chen, Y. Guo, *J. Nat. Prod.* **1998**, 61, 1397–1399.
- [38] E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1965**, 87, 1353–1364.
- [39] R. D. Miller, D. R. McKean, *J. Org. Chem.* **1981**, 46, 2412–2414.
- [40] R. K. Dieter, S. Pounds, *J. Org. Chem.* **1982**, 47, 3174–3177.
- [41] According to the IUPAC rules the products **2**, **33** and **38** should be named as isoquinolines rather than quinolizidines (hydroquinolizines). For clarity this was not followed.
- [42] According to the IUPAC rules the products **4** should be named as isoindoles rather than indolizidines (hydroindolizines). For clarity this was not followed.
- [43] [43a] F. Bohlmann, *Chem. Ber.* **1958**, 91, 2157–2167. [43b] H. S. Aaron, C. P. Rader, G. E. Wicks, Jr., *J. Org. Chem.* **1966**, 31, 3502–3507. [43c] H. M. Garaffo, L. D. Simon, J. W. Daly, T. F. Spande, *Tetrahedron* **1994**, 50, 11329–11338.
- [44] For details concerning the NOE data of **33a** see Supporting Information.
- [45] R. Gorny, Dissertation, Westfälische Wilhelms-Universität, Münster, **1995**.
- [46] T. Koizumi, T. Fuchigami, Z. E.-S. Kandeel, N. Sato, T. Nonaka, *Bull. Chem. Soc., Jpn.* **1986**, 59, 757–762.
- [47] [47a] A. Citterio, A. Gentile, F. Minisci, M. Serravalle, S. Ventura, *Tetrahedron* **1985**, 41, 617–620. [47b] F. Minisci, E. Vismara, F. Fontana, *Heterocycles* **1989**, 28, 489–519.
- [48] For details of all calculations see Supporting Information.
- [49] For graphical representation of the structures see Supporting Information.
- [50] [50a] J. R. Keefe, A. J. Kresge, in *The chemistry of enamines Part 2* (Ed.: Z. Rappoport), John Wiley & Sons, Chichester, New York, Brisbane, Toronto, Singapore, **1994**, p. 1062–1063. [50b] P. W. Hickmott in ref.^[50a], p. 1536–1537, 1542–1545.
- [51] For a graphical representation of the cell see ref.^[1c], p. 258 (no Luggin capillary was used).

Received March 17, 2003