Chiral Polymethine Dyes, VII[+]

Synthesis and UV/Vis Spectroscopic Properties of Chiral Symmetrical Pentamethinium Cyanine Dyes with 1′,2′,3′,4′,10,11-Hexahydroquinin-1′-yl and -Hexahydroquinidin-1′-yl End Groups

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Starting from the 1′,2′,3′,4′,10,11-hexahydroquinines **3a–c** (Schemes 1 and 3) and 1′,2′,3′,4′,10,11-hexahydroquinidine **6c** (Scheme 2), we have synthesized the new chiral, symmetrical pentamethinium streptocyanine dyes **11a–c** (Scheme 4) and **12c** (Scheme 5). These products have a total of ten stereogenic centers in the two heterocyclic end groups, the absolute configurations of eight of which are known from the natural starting material, i.e. (–)-quinine **1a**, (–)-10,11-dihydroquinine **2a**, (+)-quinidine **4a**, and (+)-10,11-dihydroquinidine **5a**. The latter four compounds were hydrogenated at 70 bar and 70 °C in the presence of Raney nickel as catalyst to give the hexahydroquinine **3c** and the hexahydroquinidine **6c**, respectively. The hexahydroquinine **3c** was separated into the corresponding diastereomers **3a** and **3b** by means of fractional crystallization of its salts with monochiral mandelic acid (Scheme 3).

Introduction

Amongst conjugated π-systems, in addition to aromatic and polyenic π-systems, polymethine dyes constitute a third independent type of π-systems which show their own specific intrinsic chemical and physical properties.[3][4] Whereas chiral aromatics (e.g. helicenes) and chiral polyenes (e.g. carotinoids) are well-known, chiral polymethines have hitherto received only scant attention.[5] This is despite the fact that, as functional dyes,[6] they should exhibit remarkable new chiroptical properties, e.g. they can be expected to show different sensitivities to circularly polarized light when used as sensitizers in photographic silver halide suspensions.

The first chiral polymethinium dyes were synthesized by König and Langbein[7] in 1928 and by Götze[8] in 1938. However, both reports were only rather short communications, and no experimental details were given in the first case.[7] The historical importance of König's work with regard to the determination of the electronic structure of polymethine dyes, which was almost overlooked, has recently been discussed in ref.[5] Some natural dyes, such as the orange-red fungus dye Musca-aurine I (from the toadstool fly agaric, *Amanita muscaria*)[9] and the red-violet betalain dye betanin (responsible for the colour of red beets, *Beta vulgaris*),[10] are known to be chiral pentamethinium cyanines with end groups stemming from monochiral[11] L-α-amino acids.

With the aid of modern techniques, we have recently repeated and significantly improved the work of König[1b,1d,7] and Götze.[1e,8] Moreover, we have also synthesized a variety of new chiral polymethinium dyes with stereogenic centers in the heterocyclic end groups or in the polymethine chain.[1a,1c,1f,1g] Further, more contemporary, work on intrinsically chiral polymethine dyes has been reported by Wolf et al.[12] and by Buß et al.,[13] while Dähne et al. have recently found that achiral trimethinium dyes bearing long *N*-alkyl groups spontaneously form chiral *J*-aggregates in solution, which exhibit optical activity.[14]

Most of the monochiral[11] polymethinium dyes synthesized by König[7] and by ourselves[1] contain 1,2,3,4-tetrahydroquinoline rings[15] with one stereogenic center at C-2[1b,1d] or C-3[1a] in each of the two heterocyclic quinoline end groups. For the syntheses of these monochiral polymethinium dyes, it was first necessary to prepare the 2- or 3-methyl-substituted 1,2,3,4-tetrahydroquinolines as enantiomerically pure starting materials. The separation into enantiomers has hitherto been performed by the classical but cumbersome method of repeated recrystallization of the corresponding diastereomeric salts (i.e. 3-bromocamphor-8-sulfonates).[1a,1d] In order to avoid this costly separation into enantiomers by forming diastereomeric salts, we have endeavoured to find *natural* monochiral compounds with known absolute configurations at their stereogenic centres, that contain 1,2,3,4-tetrahydroquinoline rings suitable for the synthesis of monochiral streptocyanines. Such compounds have been found among the cinchona alkaloids, isolated from the bark of various tropical *Cinchona* trees, which are now widely cultivated and the extracts of which are commercially available at reasonable prices.[16] Chemoselective reduction of the pyridine moiety of cinchona alkaloids such as quinine (**1a**) and quinidine (**4a**) or their 10,11-

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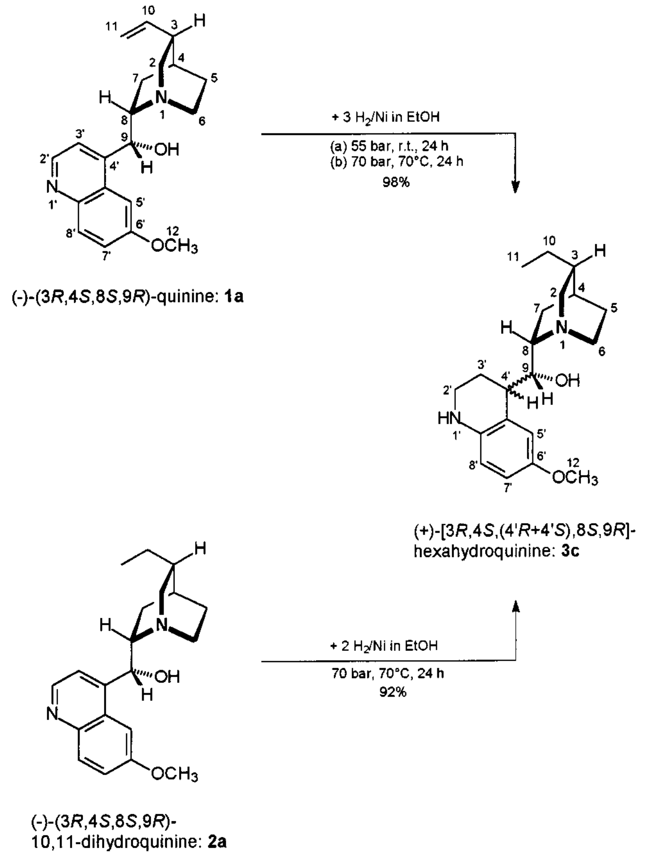


Scheme 1. Catalytic high-pressure hydrogenation of (−)-quinine **1a** and (−)-dihydroquinine **2a**

dihydro derivatives (**2a** and **5a**)[17] should lead to the corresponding 1′,2′,3′,4′,10,11-hexahydro derivatives (**3c** and **6c**), which, as secondary amines, should be suitable compounds for the preparation of new chiral polymethinium streptocyanine dyes (Scheme 1). In this paper, we describe for the first time the synthesis of new chiral, symmetrical pentamethinium streptocyanine dyes with two heterocyclic end groups stemming from hexahydroquinine and hexahydroquinidine moieties, with five stereogenic centres in each end group.

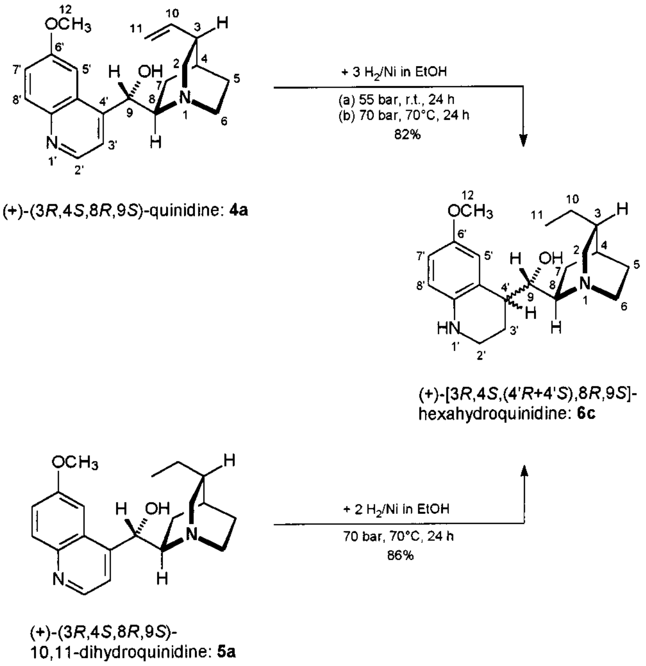
Results and Discussion

Catalytic Hydrogenation of Quinine and Quinidine and their 10,11-Dihydro Derivatives

The reduction of the quinoline moiety in quinine and in other cinchona alkaloids has been studied by many workers,[18−26] the earliest attempt being that by Zorn in 1873[18] (reduction of cinchonine with sodium amalgam and acetic acid). Partial reduction of the quinoline ring in various cinchona alkaloids has been attempted using sodium in ethanol or amyl alcohol,[19][20] electrolytically,[21][22] and by catalytic hydrogenation with various platinum and nickel catalysts.[23−26] However, the results obtained by the various research groups have often been rather inconclusive and sometimes even contradictory, e.g. concerning the sense of the optical rotation of the reduced products obtained.[23b] The precise structures of the hydrogenated products have also remained unsolved in many cases. That the catalytic hydrogenation of 10,11-dihydroquinine (**2a**) should lead to two diastereomers with opposite configurations at C-4′ was only established relatively recently.[26][27]

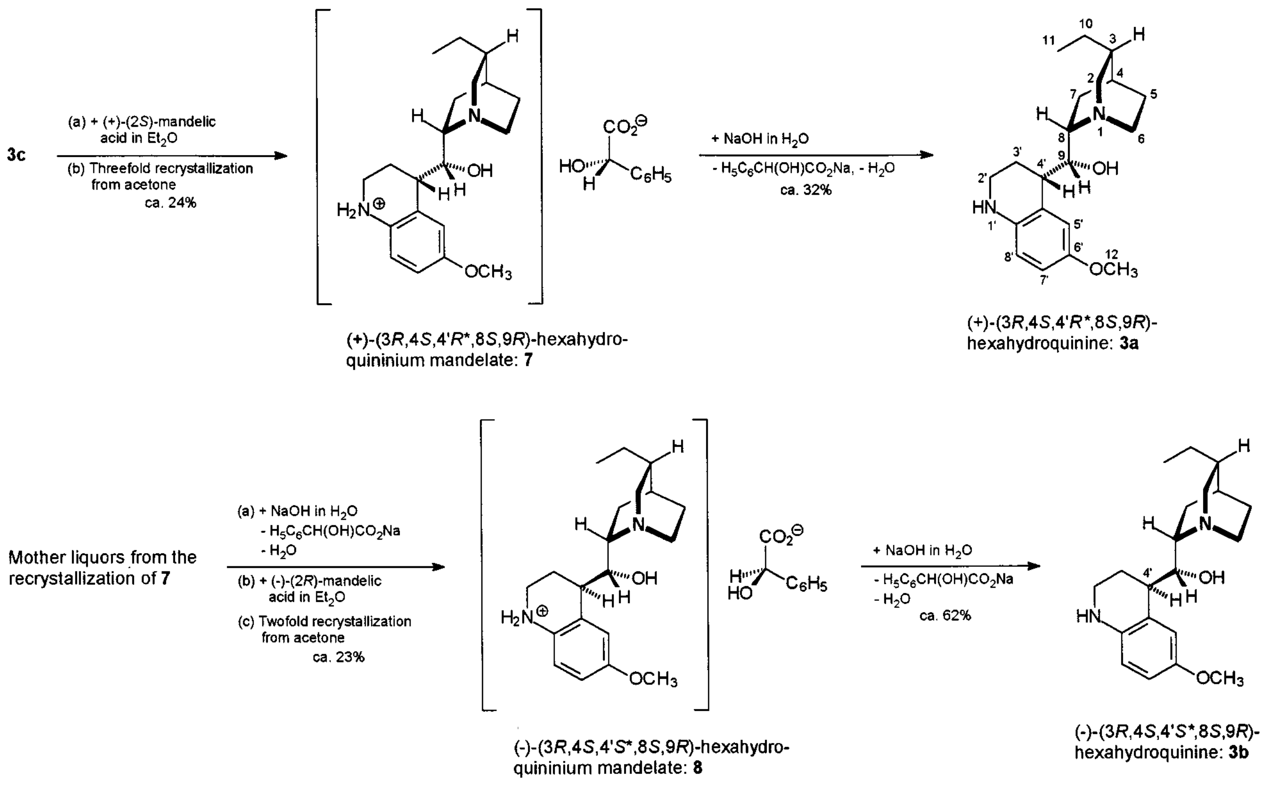
We have found that the catalytic hydrogenation of either commercially available (−)-quinine (**1a**)[17] or (−)-10,11-dihydroquinine (**2a**)[17] in ethanol, carried out in the presence of freshly prepared Raney nickel[28] at ca. 70 bar and ca. 70 °C in an autoclave equipped with a magnetic stirrer leads in both cases to good yields of (+)-hexahydroquinine (**3c**) as a colorless foamy solid (Scheme 1). The samples obtained had melting points of 56 °C and 54 °C and optical rotations of $[\alpha]_D^{27} = +28$ and $+27$ (measured in ethanol), respectively. The first step of the hydrogenation of (−)-quinine (**1a**), carried out at 55 bar and room temperature, corresponds to the addition of only one equiv. of dihydrogen, which is obviously first used for the reduction of the 10,11-double bond of **1a**.

Analogously, catalytic hydrogenations of commercially available (+)-quinidine (**4a**) and (+)-10,11-dihydroquinidine (**5a**) under the same reaction conditions led in both cases to good yields of (+)-hexahydroquinidine (**6c**) as a colorless foamy solid (Scheme 2). The samples obtained had melting points of 49−51 °C and 51 °C and optical rotations of $[\alpha]_D^{18} = +87.5$ and $+87.0$ (measured in ethanol), respectively.



Scheme 2. Catalytic high-pressure hydrogenation of (+)-quinidine **4a** and (+)-dihydroquinidine **5a**

The molecular structures of the two hexahydro compounds were confirmed by elemental analyses, mass spectrometry, and IR spectroscopy, and, as far as possible due to the high degree of complexity of the spectra, by ^1H and ^{13}C NMR spectroscopy (for details, see Experimental Sec-



Scheme 3. Separation of the (+)-hexahydroquinone **3c** into its diastereomers **3a** and **3b**; the classification of the configuration at C-4′ in **7** and **3a** as (*R**) and in **8** and **3b** as (*S**) is arbitrary; the absolute configuration at C-4′ is unknown

tion). Both hexahydro derivatives, **3c** and **6c**, consist of a mixture of two diastereomers with opposite configuration at C-4′, i.e. the new stereogenic center created by the hydrogenation of the pyridine ring, with the reasonable assumption that the hydrogenation does not affect the configuration of the other four stereogenic centers at C-3, C-4, C-8, and C-9. The structural difference between these pairs of diastereomers with opposite configuration only at C-4′ is so slight that the chances of separating the mixtures of diastereomers **3c** and **6c** directly would seem rather remote.

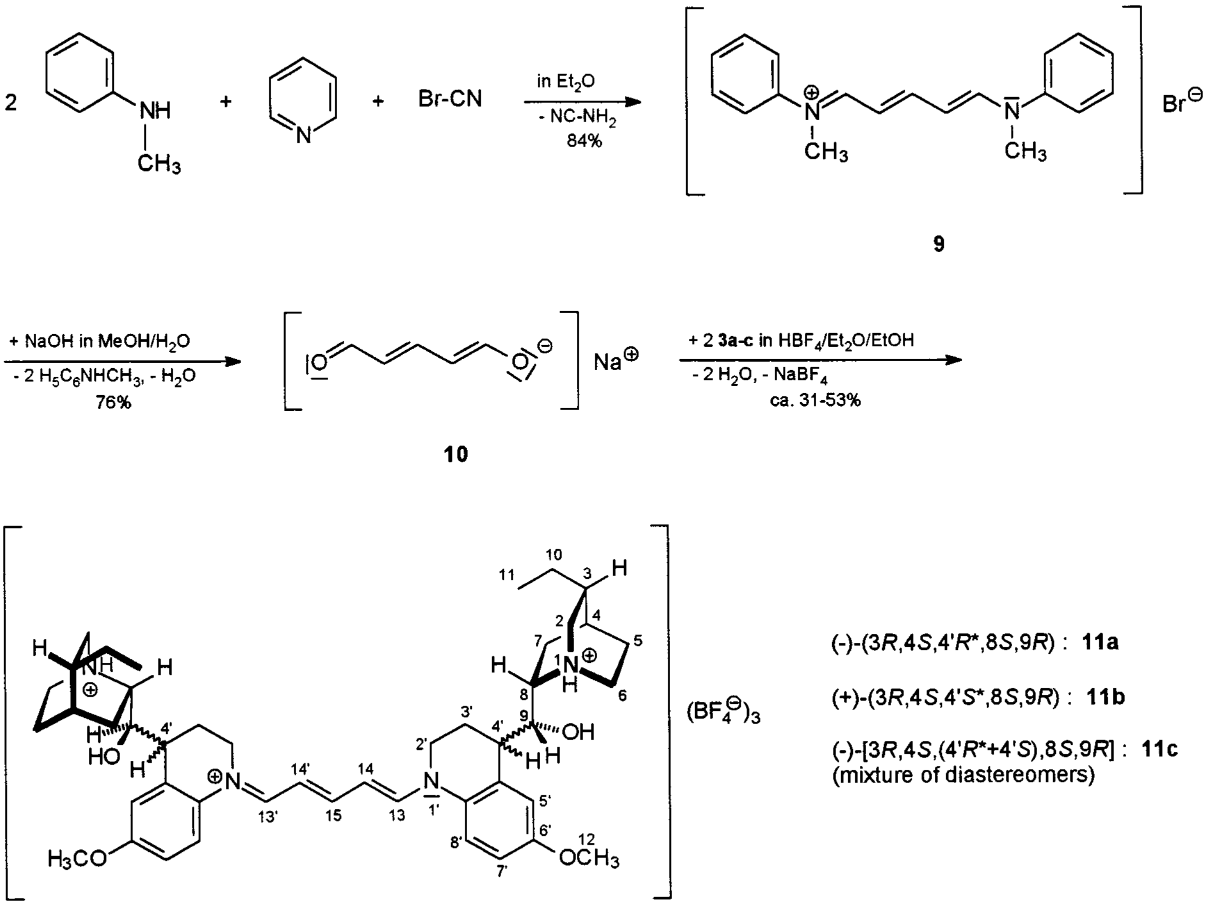
In the case of the hexahydroquinine **3c**, separation into the two diastereomers **3a** and **3b** could successfully be accomplished by the formation of salts with commercially available (+)-(2*S*)- and (−)-(2*R*)-mandelic acid,[29] according to the reaction sequence depicted in Scheme 3.

Addition of an ethereal solution of (+)-(2*S*)-mandelic acid to a solution of **3c** in diethyl ether led to the colorless, very hygroscopic mandelate **7**. Threefold recrystallization of this compound from acetone led finally to a diastereomerically pure crystalline product in 24% yield, the purity of which was assessed by ^{1}H NMR spectrometry (see later). Treatment of recrystallized **7** with aqueous NaOH eventually yielded the diastereomerically pure hexahydroquinine **3a** as a colorless foamy solid with melting point 42 °C and an optical rotation of $[\alpha]_D^{24} = +76$.

The mother liquors from the recrystallizations of **7** were collected and treated with aqueous NaOH and the precipitate formed was extracted with diethyl ether. The ether was removed by distillation and the remaining oil was redissolved in diethyl ether. To this ethereal solution, a solution of (−)-(2*R*)-mandelic acid in diethyl ether was then added to afford the mandelate **8** as a light-yellow hygroscopic solid, which was found to be diastereomerically pure after a twofold recrystallization from acetone. Treatment of recrystallized **8** with aqueous NaOH eventually yielded the diastereomerically pure hexahydroquinine **3b** as a colorless foamy solid with melting point 55 °C and an optical rotation of $[\alpha]_D^{22} = -28$.

The classification of the configuration at C-4′ in **7** and **3a** as (*R*), and of that in **8** and **3b** as (*S*) is arbitrary and, therefore, the descriptors denoting the configuration at C-4′ are marked with an asterisk. The absolute configurations at C-4′ of **3a** and **3b** are not yet known. Unfortunately, it was not possible to obtain crystals of **3a** and **3b** suitable for an X-ray structure analysis.

It was not possible to follow the progress of purification during the recrystallization of **7** and **8** by means of their optical rotations because the $[\alpha]_D$ values of both diastereomeric salts, as measured in ethanol, were found to be unexpectedly strongly concentration dependent. For example, a solution of threefold recrystallized diastereomerically pure **7** in ethanol exhibits first a steady increase in the $[\alpha]_D$ value as the concentration of **7** increases from 20 to 60 mg/100 mL. Then, after reaching a maximum at $c(\mathbf{7}) =$ 60 mg/100 mL, the $[\alpha]_D$ value decreases asymptotically with a further concentration increase up to 160 mg/100 mL (for details, see ref.[21]). This concentration dependence of the optical rotation of **7** (and **8**) can presumably be attributed to



Scheme 4. Synthesis of the pentamethinium dyes **11a−c** with two hexahydroquinin-1-onium-1′-yl end groups

a concentration-dependent association equilibrium between cations and anions.

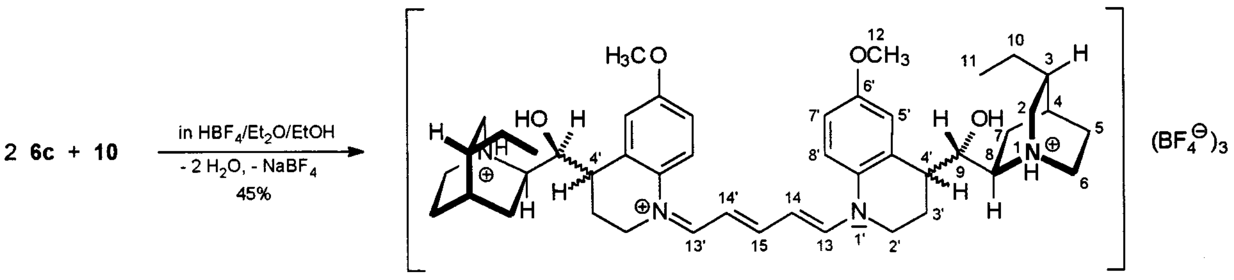
Fortunately, the purification of **7** and **8** could be followed by ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum of non-recrystallized **7**, recorded in $CDCl_3$ at 300 MHz, exhibits *two* close singlets at $\delta = 3.7$ for the methoxy group in the 6′-position and *two* multiplets at $\delta = 4.1$ and 4.3 for the diastereotopic 9-H proton; the latter signal is downfield-shifted due to the presence of the geminal OH group. Both groups of signals are well-separated from the other signals in the complex ^{1}H NMR spectrum and can easily be integrated. After just two recrystallizations from acetone, only *one* singlet (for the 12-H′s) and *one* multiplet (for 9-H) was observed, indicating the absence of the other diastereomeric hexahydroquininium mandelate (for details, see ref.[2]).

The diastereomeric purities of the hexahydroquinines **3a** and **3b** can also be proven by their ^{1}H NMR spectra, measured in $CDCl_3$ at 300 MHz, by comparison of the signal of the diastereotopic 9-H, which appears in the region $\delta = 2.0-4.5$. In principal, this signal should appear as a doublet of doublets due to vicinal coupling with 4′-H and 8-H, however, under the conditions of measurement, it is more likely to appear as a less well resolved multiplet. Whereas the ^{1}H NMR spectrum of **3c** (mixture of diastereomers) features two multiplets at $\delta = 3.57-3.67$ and $3.99-4.02$ for 9-H, the corresponding ^{1}H NMR spectrum of diastereomerically pure **3a** shows only one multiplet centered at $\delta = 3.60$ for this H-atom, while that of **3b** shows only one multiplet centered at $\delta = 4.07$. From the complete absence of the other 9-H signal, the diastereomeric ratio can be estimated to be in excess of 99:1 in both cases. Therefore, both hexahydroquinines **3a** and **3b**, prepared according to the sequence outlined in Scheme 3, are essentially diastereomerically pure.

Several attempts were made to separate the hexahydroquinidine **6c** into the corresponding pair of diastereomers using a procedure analogous to that shown in Scheme 3, but as yet these have not been successful.

Synthesis of Chiral Pentamethinium Streptocyanine Dyes

We first attempted to synthesize a symmetrical chiral trimethinium streptocyanine dye from the hexahydroquinine **3a** by condensation with 1,1,3,3-tetramethoxypropane or propargylaldehyde diethyl acetal in a mixture of diethyl ether and ethereal HBF_4 (54%). However, this strategy was not successful. With **3a** and the malonaldehyde bis(acetal), a yellow solid was obtained, which was found to contain some of the desired trimethinium dye on the basis of its ^{1}H NMR spectrum, but this could not be further purified.



(+)-[3*R*,4*S*,(4'*R*+4'*S*),8*R*,9*S*] : **12c** (mixture of diastereomers)

Scheme 5. Synthesis of the pentamethinium dye **12a** with two hexahydroquinidin-1-onium-1′-yl end groups

With **3a** and the propargylaldehyde acetal, only a brown oil was obtained.

First attempts to obtain the desired symmetrical chiral pentamethinium streptocyanine dyes by condensation of the hexahydroquinines **3a**,**b** or the hexahydroquinidine **6c** with cyanogen bromide and pyridine in ethanol, according to a method first described by König,[7][30] were likewise unsuccessful. For this reason, the glutaconaldehyde sodium salt **10**[31] was first prepared as a precursor by alkaline hydrolysis of the pentamethinium bromide **9**, which was obtained from *N*-methylaniline, cyanogen bromide, and pyridine according to König[30] (*cf.* Scheme 4).

Eventually, acid-catalyzed condensation of the hexahydroquinines **3a−c** with sodium pentadien-1-al-5-olate **10** in ethanol/diethyl ether/HBF_4 yielded the desired symmetrical chiral pentamethinium salts **11a−c** in modest yields of 31−53% as tris(tetrafluoroborates), with additional protonation at the two quinuclidine nitrogen atoms. Compounds **11a**,**b** were obtained as pure diastereomers (with unknown absolute configuration at C-4′), while **11c** was obtained as a mixture of two diastereomers (with opposite configurations at C-4′). Analogously, the pentamethinium salt **12c** was prepared from **10** and the hexahydroquinidine **6c** in 45% yield as a mixture of diastereomers with opposite configurations at C-4′ (*cf.* Scheme 5).

The structures of all the new dyes have been proven by elemental analysis, UV/vis and IR spectroscopy, mass spectrometry, and ^1H NMR and ^{13}C NMR spectroscopy (see Experimental Section). The monochiral compounds have also been characterized by their specific and molar optical rotations.

The NMR spectra of the new streptocyanine dyes are rather complicated and only a few signals could be assigned to the respective H and C atoms; see ref.[2] for the complete spectra. On the basis of the vicinal ^1H NMR coupling constants of the methine H atoms 13-H/14-H (^3J = 11.7 Hz) and 14-H/15-H (^3J = 12.6 Hz), the pentamethinium dye **11a** (and probably also **11b**,**c** and **12c**) adopts an all-(*E*) configuration along the methine chain in $[D_6]$DMSO solution.

All four pentamethinium salts were obtained as red crystals, ethanolic solutions of which exhibit intense long-wavelength UV/vis π-π* absorption maxima at λ_{max} = 511 (**11a**), 506 (**11b**), 510 (**11c**), and 508 nm (**12c**) with molar extinction coefficients of ca. 7000−9000 $L{\cdot}mol^{-1}{\cdot}cm^{-1}$. The positions and intensities of these visible absorption bands are in the expected region for pentamethinium streptocyanine dyes;[4][32] *cf.* dye **9** with λ_{max} = 449 nm.[34] In comparison with the recently prepared monochiral pentamethinium streptocyanine dyes bearing two 1,2,3,4-tetrahydro-2,6-dimethylquinolin-1-yl end groups (λ_{max} = 491 nm)[1b,1d] and those with two 1,2,3,4-tetrahydro-3,6-dimethylquinolin-1-yl end groups (λ_{max} = 500 nm),[1a,1b] the long-wavelength absorption bands of **11a−c** and **12c** are bathochromically shifted by $\Delta\lambda$ = 15−20 nm and $\Delta\lambda$ = 6−11 nm, respectively. These small bathochromic shifts can be attributed to the presence of two electron-donating (+*M*) methoxy groups (instead of two methyl groups) in the *para*-positions of the two *N*-phenyl rings of **11a−c** and **12c**, which can further delocalize the positive charge and thus enlarge the chromophoric π-system.

The long-wavelength visible absorption maxima of the chiral dyes **11a−c** and **12c** are sufficiently hypsochromically separated from the sodium D line emission at 589 nm to permit polarimetric measurement of their specific optical rotations (Table 1).

For the dyes **11a**,**b**, the optical rotations are rather high and lie in the range observed for chiral aromatic π-systems such as the helicenes.[5] The optical rotation of the mixture of two diastereomeric dyes **11c** should correspond to the difference between the optical rotations of the diastereomerically pure dyes **11a** and **11b**. This is indeed almost the case: the experimental value of −455 for **11c** shows a deviation of ca. 10% from [(−1545) − (+1135)] = −410. The rather high optical rotations of **11a**,**b** cannot only be attributed to the presence of ten stereogenic centers in this tris-cation, but are probably also the result of some helical twist of the chromophoric pentamethine chain, caused by the sterically demanding end groups. The relatively small optical rotation of **12c** compared to that of **11c** may thus stem from the fact that the two sterically demanding quinuclidinyl groups are more remote from each other in **12c** than in **11c**.

In conclusion, chiral pentamethinium streptocyanine dyes have, for the first time, been obtained using monochiral starting compounds of natural origin such as (−)-quinine and (+)-quinidine as well as their 10,11-dihydro derivatives as sources of the stereogenic centers in the dyes (Schemes 4 and 5). A Raney nickel catalyzed hydrogenation

Table 1. Long-wavelength visible π-π* absorption maxima, λ_{max}, specific $[\alpha]_D$, and molar optical rotations, $[\Phi]_D$, of the pentamethinium streptocyanine dyes **11a−c** and **12c**, measured in ethanol at room temperature

Formula number	Configuration	λ_{max}/nm	$[\alpha]_D^{18}$[a]	$[\Phi]_D^{18}$[b]
11a	(3*R*,4*S*,4′*R**,8*S*,9*R*)	511	−1545	−15210
11b	(3*R*,4*S*,4′*S**,8*S*,9*R*)	506	+1135	+11990
11c	[3*R*,4*S*,(4′*R*+4′*S*),8*S*,9*R*]	510	−455[c]	−4480
12c	[3*R*,4*S*(4′*R*+4′*S*),8*R*,9*S*]	508	+73[c]	+719

[a] Units: $10^{-1}\cdot deg\cdot cm^2\cdot g^{-1}$. − [b] $[\Phi]_D = ([\alpha]_D\cdot M_r)/100$, where M_r = relative molar mass. − [c] Measured in acetone.

procedure for the preparation of the corresponding hexahydro derivatives (Schemes 1 and 2) as well as a procedure for the separation of (+)-hexahydroquinine into its diastereomers employing mandelic acid have been devised (Scheme 3)

Experimental Section

General: Melting points (not corrected): Kofler-Mikroheiztisch (Reichert, Wien). − Elemental analyses: Analytik-Servicelabor, Marburg, CHN Automat Vario EL (Elementar, Hanau). − UV/vis: U-3410 spectrophotometer (Hitachi, Tokyo) with 1.00 cm quartz cells at room temperature. − IR: IFS-88 spectrometer (Bruker, Rheinstetten); films between NaCl plates for liquids and KBr pellets for solids. − ^{1}H and ^{13}C NMR: AC-200, AC-300, and AM 400 instruments (Bruker, Rheinstetten), with tetramethylsilane as internal standard. Assignments of the signals according to the formula numbering are given in the reaction schemes. − MS: MAT CH-7 mass spectrometer with electron impact (EI), MAT 711 with field desorption (FD) (Varian, Darmstadt), and Hewlett-Packard 5989 B with electrospray technique. − Optical rotation: Polarimeter 241 (Perkin−Elmer, Überlingen) with 10 cm quartz cell at λ = 589 nm (sodium D-line) at ambient temperature; concentration *c* expressed in g of substance in 100 mL of solution. − Analytical TLC: Micro cards 60F-245 with silica gel and fluorescence indicator on aluminium foil (Merck, Darmstadt). − Flash chromatography: Silica gel 60 (Merck, Darmstadt), particle size 0.040−0.063 mm, with mixtures of petroleum ether (b.p. 40−60°C) (PE) and diethyl ether (DE) as eluents; carried out according to Still et al.[33]

(+)-[3*R*,4*S*,(4′*R*+4′*S*),8*S*,9*R*]-1′,2′,3′,4′,10,11-Hexahydroquinine (3c):

(a) Preparation of the Raney Nickel:[28] To a stirred suspension of aluminium/nickel alloy (16.00 g, Al:Ni = 1:1; Merck, Darmstadt), in water (200 mL) was added portionwise sodium hydroxide (26.00 g) in such a way that the mixture did not foam up violently. The mixture was then heated to 70°C for 30 min. After cooling to room temp., the solution was decanted off from the black nickel residue. The sediment was thoroughly washed by twofold decantation with water and threefold decantation with ethanol. The Raney nickel thus obtained was stored under 100 mL of dry ethanol prior to use.

(b) By Reduction of (−)-(3*R*,4*S*,8*S*,9*R*)-Quinine (1a): To a solution of anhydrous (−)-quinine (**1a**) [10.00 g, 30.82 mmol; Fluka, Buchs; purity >99%, m.p. 172−175°C, $[\alpha]_D^{20} = -131 \pm 1$ (*c* = 1 in chloroform)] in 100 mL of ethanol, placed in a 500 mL autoclave equipped with an externally driven stirrer, was added Raney nickel in 100 mL of ethanol prepared as described above. The autoclave was then closed, the air was flushed out with nitrogen, and the hydrogenation was carried out by introducing H_2 at a pressure of 55 bar and stirring for 24 h at room temp. During this time, ca. 40 mmol of H_2 were absorbed, corresponding to the hydrogenation of only one C=C double bond. Therefore, the hydrogenation was continued for a further 24 h with stirring at 70 bar and 70°C. After cooling to room temp., the autoclave was opened, and the suspension was vacuum filtered through a kieselguhr mat in a filter crucible with a sintered glass bottom. The kieselguhr mat was washed with 200 mL of ethanol and the filtrate and washings were combined. The solvent was then removed on a rotary evaporator. To the yellow oily residue was added 10 mL of anhydrous diethyl ether and the solvent was again removed, to leave **3c** (9.99 g, 98%) as a colorless foamy solid (m.p. 56°C). − $[\alpha]_D^{27} = +28$ (*c* = 0.043 in ethanol). − IR (KBr): $\tilde{\nu}$ = 3398 cm^{-1} (O−H), 2929, 2860 (C−H), 1607, 1585, 1507, 1463 (C=C). − ^{1}H NMR (mixture of diastereomers; 300 MHz; CDCl$_3$): δ = 0.78−0.85 (m, 6 H, 11-H), 1.25−1.36 (m, 12 H), 1.52−1.55 (m, 2 H), 1.67−1.70 (m, 2 H), 1.81−1.96 (m, 4 H), 2.35 (m, 2 H), 2.55−2.62 (m, 4 H), 2.88−2.90 (m, 2 H), 3.05−3.34 (m, 7 H), 3.47−3.57 (m, 6 H), 3.67 (s, 6 H, 12-H), 3.99 (dd, ^3J = 9.2 and 2.6 Hz, 1 H, 9-H), 6.37−6.41 (m, 2 H, 5′-H), 6.52−6.57 (m, 2 H, 7′-H), 6.66 (m, 2 H, 8′-H). − ^{13}C NMR (75 MHz; CDCl$_3$): The spectrum features a total of 35 signals, of which only those at δ = 12.1 (C-11) and 80.1 (C-9) could be assigned. − MS (FD): *m*/*z* (%) = 331 (26) [M$^+$ + H], 330 (100) [M$^+$]. − $C_{20}H_{30}N_2O_2$ (330.5): calcd. C 72.69, H 9.15, N 8.48; found C 72.63, H 9.20, N 8.37.

(c) By Reduction of (−)-(3*R*,4*S*,8*S*,9*R*)-10,11-Dihydroquinine (2a): Raney nickel catalyzed reduction of anhydrous (−)-dihydroquinine (**2a**) [10.00 g, 30.63 mmol; Fluka, Buchs, purity >98%, m.p. 168−170°C, $[\alpha]_D^{20} = -137 \pm 2$ (*c* = 1 in ethanol)] in 100 mL of ethanol, with stirring for 24 h at 70°C under a H_2 pressure of 70 bar followed by work-up analogous to the procedure described above for the reduction of **1a**, gave **3c** (9.33 g, 92%) as a colorless foamy solid (m.p. 54°C). − $[\alpha]_D^{27} = +27$ (*c* = 0.068 in ethanol). − All spectroscopic data for this product were identical to those of the product obtained by reduction of **1a**.

(+)-[3*R*,4*S*,(4′*R*+4′*S*),8*R*,9*S*]-1′,2′,3′,4′,10,11-Hexahydroquinidine (6c):

(a) By Reduction of (+)-(3*R*,4*S*,8*R*,9*S*)-Quinidine (4a): To a solution of (+)-quinidine (**4a**) [10.00 g, 30.82 mmol; Fluka, Buchs; purity >90%, water content 4−6%, m.p. 169−172°C, $[\alpha]_D^{20} = +245 \pm 5$ (*c* = 0.8 in ethanol)] in 400 mL of ethanol, placed in a 1 L autoclave, was added a batch of Raney nickel in 100 mL of ethanol, prepared as described above. In analogy with the hydrogenation of **1a**, the hydrogenation of **4a** was carried out first at a H_2 pressure of 55 bar with stirring for 24 h at room temp., then at 70 bar with stirring for a further 24 h at 70°C. After work-up in the same manner as described for the reduction of **1a**, compound **6c** (8.32 g, 82%) was isolated as a colorless foamy solid (m.p. 49−51°C). − $[\alpha]_D^{18}$ = +87.5 (*c* = 0.220 in ethanol). − IR (KBr): $\tilde{\nu}$ = 3398 cm^{-1} (O−H), 2932 (C−H), 1606, 1585, 1507, 1462 (C=C). − ^{1}H NMR (mixture of diastereomers; 300 MHz; CDCl$_3$): δ = 0.78−0.85 (m, 6 H, 11-

H), 1.29−1.65 (m, 16 H), 1.80−1.95 (m, 6 H), 2.37−2.39 (m, 1 H), 2.48−2.51 (m, 1 H), 2.78−2.89 (m, 6 H), 3.09−3.58 (m, 11 H), 3.68 and 3.69 (2 s, each 3 H, 12-H), 4.01−4.04 (m, 1 H, 9-H), 6.34−6.44 (m, 2 H, 5′-H), 6.53−6.61 (m, 2 H, 7′-H), 6.66−6.67 (m, 2 H, 8′-H). − ^{13}C NMR (75 MHz; CDCl$_3$): The spectrum features a total of 35 signals, of which only those at δ = 12.0 (C-11) and 79.7 (C-9) could be assigned. − MS (EI, 70 eV): *m/z* (%) = 331 (6) [M$^+$], 330 (21) [M$^+$ − H], 300 (10) [M$^+$ − CH$_2$O], 299 (9) [M$^+$ − CH$_3$O], 169 (20) [M$^+$ − C$_{11}$H$_{15}$N], 168 (100) [M$^+$ − H − C$_{11}$H$_{15}$N]. − $C_{20}H_{30}N_2O_2$ (330.5): calcd. C 72.69, H 9.15, N 8.48; found C 71.97, H 9.16, N 8.35.

(b) By Reduction of (+)-(3*R*,4*S*,8*R*,9*S*)-10,11-Dihydroquinidine (5a): Raney nickel catalyzed reduction of anhydrous (+)-dihydroquinidine (**5a**) [10.00 g, 30.63 mmol; Fluka, Buchs; purity >95%; m.p. 169−170 °C; $[\alpha]_D^{20}$ = +226 ± 2 (*c* = 2 in ethanol)] in 100 mL of ethanol, with stirring for 24 h at 70 °C under a H$_2$ pressure of 70 bar, followed by work-up analogous to the procedure described above for the reduction of **1a**, gave **6c** (8.70 g, 86%) as a colorless foamy solid (m.p. 51 °C). − $[\alpha]_D^{18}$ = +87.0 (*c* = 0.140 in ethanol). − All spectroscopic data for this product were identical to those of the product obtained by reduction of **4a**.

Separation of (+)-Hexahydroquinine 3c into its Diastereomers 3a and 3b:

(a) (+)-(3*R*,4*S*,4′*R,8*S*,9*R*)-1′,2′,3′,4′,10,11-Hexahydroquininium (2S)-Mandelate (7):** To a solution of (+)-hexahydroquinine **3c** (4.00 g, 12.10 mmol) in anhydrous diethyl ether (50 mL) was added dropwise a solution of (+)-(2S)-mandelic acid [3.68 g, 24.20 mmol; Merck, Darmstadt; purity > 99%; m.p. 131−134 °C; $[\alpha]_D^{20}$ = +153 to +157 (*c* = 2 in water)] in anhydrous diethyl ether (50 mL) with stirring at 0 °C. After stirring for a further 30 min. at 0 °C, the resulting microcrystalline precipitate was filtered off and washed with anhydrous diethyl ether. After drying the very hygroscopic solid in vacuo, the crude **7** obtained (6.30 g) was recrystallized three times from anhydrous acetone. Thus, crude **7** (6.30 g) was dissolved in 20 mL of acetone. After stirring for a few minutes at room temp., a colorless precipitate was formed, which was recrystallized from the same mother liquor by heating and then cooling to −17 °C. The precipitate formed was filtered off and dried in vacuo to give **7** (3.61 g, 62%, based on the starting material **3c**) as colorless needles {m.p. 168 °C; $[\alpha]_D^{24}$ = +50 (*c* = 0.039 in ethanol)}. This optical rotation was found to be strongly concentration-dependent and was therefore not suitable for monitoring the progress of the purification process. Instead, the purification was monitored by ^{1}H NMR spectroscopy (300 MHz, CDCl$_3$) by focusing on the two close singlets at δ = 3.7 due to the methoxy groups and the two multiplets at δ = 4.1 and 4.3 due to the diastereotopic 9-H atom. A third recrystallization of **7** (3.55 g, 7.36 mmol) from anhydrous acetone, in which the solution was left for 24 h at −17 °C, the precipitate collected by filtration and the product dried in vacuo, yielded pure **7** (1.41 g, 24% based on **3c**) as colorless needles (m.p. 170 °C). The ^{1}H NMR spectrum of the recrystallized material exhibited only one singlet for the 12-H atoms and only one multiplet for 9-H. (All mother liquors and filtrates from these recrystallizations were collected and used for the preparation of **8**). − $[\alpha]_D^{25}$ = +52 (*c* = 0.039 in ethanol). − IR (KBr): ṽ = 3392 cm^{-1}, 3256 (O−H), 3064, 3032 (aromatic C−H), 2955, 2924, 2883, 2868 (aliphatic C−H), 1606, 1513, 1480 (aromatic C=C), 1332, 1254 (OH). − ^{1}H NMR (300 MHz, CD$_3$OD): δ = 0.92−0.98 (m, 3 H, 11-H), 1.54 (m, 2 H), 1.52−2.17 (several m, 9 H), 2.79−3.24 (several m, 5 H), 3.32−3.53 (m, 2 H), 3.74 (s, 3 H, 12-H), 3.92 (m, 1 H, mandelate C−H), 4.15 (m, 1 H, 9-H), 6.57−6.74 (m, 3 H, 5′-, 7′-, and 8′-H), 7.24−7.33 (m, 3 H, mandelate *m*- and *p*-H), 7.48 (m, 2 H, mandelate *o*-H). − ^{13}C NMR (75 MHz, CD$_3$OD): δ = 11.7 (C-11), 18.1 (C-10), 23.8 (C-3′), 24.8 (C-7), 24.9 (C-5), 27.0 (C-4), 35.7 (C-4′), 38.0 (C-6), 39.6 (C-3), 42.9 (C-2′), 55.8 (C-12), 57.8 (C-2), 71.7 (C-8), 74.2 (C-9), 114.5, 115.7, 116.4, 119.6, 126.4, 126.7, 127.8 (C-5′, C-7′, C-8′, C-4a′, and phenyl-C of mandelate ion), 139.1 (C-8a′), 142.6 (C-2 of mandelate ion), 151.2 (C-6′), 178.4 (carboxyl C of mandelate ion). − MS (FD): m/z (%) = 331 (33) [M$^+$ − mandelate ion], 330 (100) [M$^+$ − H − mandelate ion]. − $C_{28}H_{38}N_2O_5$ (482.6): calcd. C 69.68, H 7.94, N 5.80; found C 69.48, H 7.96, N 6.08.

(b) (+)-(3*R*,4*S*,4′*R,8*S*,9*R*)-1′,2′,3′,4′,10,11-Hexahydroquinine (3a):** To a suspension of **7** (3.40 g, 7.04 mmol) in 15 mL of water, was added dropwise 50 mL of a 2 N aqueous NaOH solution with stirring at room temp. The sticky precipitate formed was then extracted with 100 mL of diethyl ether, the ethereal solution was dried over MgSO$_4$, and the desiccant was filtered off. Evaporation of the solvent left a colorless oily residue which, after drying in vacuo, gave **3a** (0.75 g, 32%) as a colorless foamy solid (m.p. 42 °C). − $[\alpha]_D^{24}$ = +76 (*c* = 0.057 in ethanol). − IR (KBr): ṽ = 3355 cm^{-1} (N−H), 3053 (aromatic C−H), 2926, 2858 (aliphatic C−H), 1605, 1582, 1506, 1463 (aromatic C=C), 1254 (O−H). − ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.82 (t, ^3J = 7.2 Hz, 3 H, 11-H), 1.25−1.34 (m, 6 H), 1.51−1.54 (m, 1 H), 1.68−1.76 (m, 2 H), 1.86−1.99 (m, 2 H), 2.37−2.41 (m, 1 H), 2.56−2.65 (m, 2 H), 2.91 (m, 1 H), 3.06−3.20 (m, 3 H), 3.45−3.53 (m, 2 H), 3.60 (dd, ^3J = 8.3 and 2.5 Hz, 1 H, 9-H), 3.68 (s, 3 H, 12-H), 6.39−6.41 (m, 1 H, 5′-H), 6.55−6.97 (m, 2 H, 7′-, 8′-H). − ^{13}C NMR (75 MHz, CDCl$_3$): δ = 12.0 (C-11), 25.0 (C-5), 25.4 (C-3′), 27.2 (C-7), 27.5 (C-10), 28.4 (C-3), 37.2 (C-4), 37.4 (C-4′), 39.4 (C-12), 42.4 (C-2′), 55.7 (C-6), 57.7 (C-2), 58.3 (C-8), 79.9 (C-9), 114.4 (C-8′), 115.3 (C-5′), 116.0 (C-6′), 120.1 (C-4a′), 139.8 (C-8a′), 151.4 (C-7′). − MS (FD): *m/z* (%) = 661 (28) [2M$^+$ + H], 660 (14) [2M$^+$], 331 (27) [M$^+$ + H], 330 (100) [M$^+$]. − $C_{20}H_{30}N_2O_2$ (330.5): calcd. C 72.69, H 9.15, N 8.48; found C 72.57, H 9.15, N 8.42.

(c) (−)-(3*R*,4*S*,4′*S,8*S*,9*R*)-1′,2′,3′,4′,10,11-Hexahydroquininium (2*R*)-Mandelate (8):** To the collected mother liquors and filtrates from the recrystallizations of the (2*S*)-mandelate **7**, was added dropwise 50 mL of a 2 N aqueous NaOH solution with stirring at room temp. until pH 11 was attained. The sticky precipitate formed was extracted from the aqueous suspension with diethyl ether, and the ethereal solution was washed with water and dried over MgSO$_4$. The desiccant was filtered off and the solvent was evaporated from the filtrate to leave crude **3b** (2.74 g, 8.29 mmol) as a light-brown oil. To a solution of this oil in 50 mL of anhydrous diethyl ether, was added dropwise a solution of (−)-(2*R*)-mandelic acid [2.52 g, 16.58 mmol; Merck, Darmstadt, purity > 99%, m.p. 131−134 °C; $[\alpha]_D^{20}$ = −153 to −157 (*c* = 2 in water)] in 50 mL of anhydrous diethyl ether with stirring at 0 °C. The resulting light-yellow precipitate was filtered off, the hygroscopic residue was washed with anhydrous diethyl ether, and dried in vacuo, to give crude diastereomerically enriched **8** (4.12 g) as a light-yellow solid {m.p. 110 °C; $[\alpha]_D^{22}$ = −60 (*c* = 0.025 in ethanol)}. After a twofold recrystallization from anhydrous acetone, in analogy to the preparation of **7**, diastereomerically pure **8** (0.92 g, 23%) was obtained as colorless needles (m.p. 117−119 °C). The ^{1}H NMR spectrum of the recrystallized product featured only one singlet due to the 12-H atoms and only one multiplet due to 9-H. − $[\alpha]_D^{22}$ = −84 (*c* = 0.076 in ethanol). − IR (KBr): ṽ = 3390 cm^{-1} (O−H), 3089, 3064, 3032 (aromatic C−H), 2955, 2924, 2883 (aliphatic C−H), 1605, 1512, 1480 (aromatic C=C). − ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.84 (t, ^3J = 7.3 Hz, 3 H, 11-H), 1.25−1.43 (m, 2 H), 1.52−1.60 (m, 2 H), 1.71 (m, 1 H), 1.90−2.22 (m, 5 H), 2.51−2.55 (m, 1 H), 2.67−2.79 (m, 2 H), 2.99−3.16 (m, 4 H), 3.66 (s, 3 H, 12-H), 4.02

(m, 1-H, mandelate C−H), 4.34 (br. d, 1 H, 9-H), 4.93 (s, 2 H, 1′-H), 5.97 (br. s, 1 H, OH), 6.40−6.64 (m, 2 H, 5′-, 7′-H), 6.60−6.64 (m, 1 H, 8′-H), 7.20−7.37 (m, 5 H, mandelate phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.6 (C-11), 19.3 (C-10), 21.5 (C-3′), 24.3 (C-7), 24.7 (C-5), 27.0 (C-4), 35.7 (C-4′), 37.8 (C-6), 39.5 (C-3), 43.0 (C-2′), 55.6 (C-12), 55.7 (C-2), 69.6 (C-8), 73.5 (C-9), 113.9, 114.1, 116.3, 121.8, 126.5, 127.5, 128.1 (C-5′, C-7′, C-8′, C-4a′, and phenyl C of mandelate ion), 137.5 (C-8a′), 140.3 (C-2 of mandelate ion), 151.9 (C-6′), 177.6 (carboxyl C of mandelate ion). − MS (EI, 70 eV): *m/z* (%) = 331 (5) [M^+ − mandelate ion], 330 (26) [M^+ − H − mandelate ion], 169 (20) [M^+ − 2H − mandelate ion − $C_{11}H_{15}N$], 168 (100) [M^+ − H − mandelate ion − $C_{11}H_{15}N$]. − $C_{28}H_{38}N_2O_5$ (482.6): calcd. C 69.68, H 7.94, N 5.80; found C 69.48, H 7.80, N 5.71.

(d) (−)-(3*R*,4*S*,4′*S,8*S*,9*R*)-1′,2′,3′,4′,10,11-Hexahydroquinine (3b):** To a suspension of **8** (0.92 g, 1.91 mmol) in 10 mL of water, was added dropwise 50 mL of a 2 N aqueous NaOH solution with stirring at room temp. The sticky precipitate formed was extracted with diethyl ether, the ethereal solution was dried over $MgSO_4$, and the desiccant was filtered off. Evaporation of the solvent from the filtrate left a colorless oil which, after drying in vacuo, gave **3a** (0.39 g, 62%) as a foamy solid (m.p. 55°C). − $[\alpha]_D^{22}$ = −28 (*c* = 0.055 in ethanol). − IR (KBr): ṽ = 3350 cm^{-1} (O−H), 3022 (aliphatic C−H), 2929, 2856 (aliphatic C−H), 1606, 1585, 1506, 1463 (aromatic C=C). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, ^3J = 6.9 Hz, 3 H, 11-H), 1.27−1.41 (m, 5 H), 1.57−1.62 (m, 2 H), 1.74−2.00 (m, 5 H), 2.15−2.36 (m, 1 H), 2.64−2.78 (m, 2 H), 2.94 (m, 1 H), 3.09−3.18 (m, 1 H), 3.58 (s, 1 H), 3.74 (s, 3 H, 12-H), 4.05−4.09 (m, 1 H, 9-H), 6.47−6.51 (m, 1 H, 5′-H), 6.60−6.66 (m, 1 H, 7′-H), 6.71−6.73 (m, 1 H, 8′-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0 (C-11), 21.6 (C-5), 25.2 (C-3′), 26.7 (C-7), 27.5 (C-10), 28.6 (C-3), 37.4 (C-4), 38.0 (C-4′), 41.2 (C-12), 42.2 (C-2′), 55.8 (C-6), 56.3 (C-2), 57.9 (C-8), 77.6 (C-9), 112.5 (C-8′), 113.5 (C-5′), 115.9 (C-6′), 124.0 (C-4a′), 141.1 (C-8a′), 152.7 (C-7′). − MS (FD): *m/z* (%) = 331 (6) [M^+ + H], 330 (32) [M^+], 169 (26) [M^+ − $C_{11}H_{15}N$], 168 (100) [M^+ − H − $C_{11}H_{15}N$]. − $C_{20}H_{30}N_2O_2$ (330.5): calcd. C 72.69, H 9.15, N 8.48; found C 72.73, H 9.04, N 8.39.

1,5-Bis(*N*-methyl-*N*-phenylamino)pentamethinium Bromide (9):[30] To a stirred solution of freshly distilled *N*-methylaniline (22.50 g, 0.21 mol) and anhydrous pyridine (8.40 g, 0.11 mol) in 75 mL of anhydrous diethyl ether, was added a solution of cyanogen bromide (10.59 g, 0.10 mol) in 20 mL of dry diethyl ether at room temp. Stirring was continued for 1 h, then the red precipitate formed was filtered off, washed with diethyl ether, and dried in vacuo. Recrystallization from ca. 450 mL of water and drying in vacuo over P_4O_{10} yielded **9** (30.00 g, 84%) as red-blue needles (m.p. 140°C; ref.[30] 139°C). − UV/vis (ethanol): λ_{max} = 449 nm [ref.[43a] 449 nm; ref.[34b] 450 nm (lg ε = 4.96)]. − IR (KBr): ṽ = 3429 cm^{-1} (O−H), 3047 (aliphatic C−H), 1601, 1527, 1493 (aromatic C=C), 1368, 1340 (O−H). − ^{1}H NMR (300 MHz, $CDCl_3$): According to the ^{1}H NMR spectrum, in solution **9** exists as a mixture of three (*E*)/(*Z*)-isomers **A**, **B**, and **C** in the ratio 2:1:1. δ = 3.36 (s, 3 H, *N*−CH_3 of **C**), 3.56 (s, 3 H, *N*−CH_3 of **A**), 3.76 (s, 3 H, *N*−CH_3 of **B**), 5.53−5.70 (2 m, 4 H, ß-methine-H of **B** and **C**), 6.34 (dd, ^3J = 12.3 and 12.4 Hz, 2 H, ß-methine-H of **A**), 7.19−7.47 (m, 36 H, all phenyl-H), 7.90 (d, ^3J = 11.9 Hz, 2 H, α-methine-H of **B**), 8.33−8.37 (d, superimposed by two t, 4 H, α-methine-H of **A**, γ-methine-H of **B** and **C**), 8.61 (t, ^3J = 12.6 Hz, 1 H, γ-methine-H of **A**), 9.25 (d, ^3J = 11.4 Hz, 2 H, ß-methine-H of **C**). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.6 (*N*−CH_3), 108.9 (ß-methine-C), 121.1, 121.4, 125.0, 127.6, 130.0, 130.4 (all phenyl-C), 159.9 (α-methine-C), 168.3 (γ-methine-C). − MS (FD): *m/z* (%) = 278 (19) [M^+ + H − Br], 277 (100) [M^+ − Br]. − $C_{19}H_{21}BrN_2\cdot1.5H_2O$ (357.3 + 27.0 = 384.3): calcd. C 59.38, H 6.29, N 72.8; found C 59.07, H 6.37, N 7.36. The water of crystallization could be removed by drying over P_4O_{10} in vacuo at high temperature.

Sodium Penta-2,4-dien-1-al-5-olate ("Glutaconaldehyde Sodium Salt") (10):[31] To a stirred suspension of anhydrous **9** (6.00 g, 16.80 mmol) in 150 mL of methanol, was added dropwise a solution of NaOH (7.50 g, 187.50 mmol) in 40 mL of water at room temp. The reaction mixture was heated to reflux for 5 min., then allowed to cool to room temp., and was allowed to stand for 24 h at +5°C. The resulting precipitate was filtered off, washed with diethyl ether, and dried in vacuo, to give **10** (1.54 g, 76%) as yellow needles (m.p. >350°C). − IR (KBr): ṽ = 3379 cm^{-1} (O−H), 1593, 1548 (C=C), 1374 (O−H). − ^{1}H NMR (300 MHz, CD_3OD): δ = 5.49−5.57 (m, 2 H, 2- and 4-H), 7.37 (t, ^3J = 13.0 Hz, 1 H, 3-H), 8.48 (d, ^3J = 9.6 Hz, 2 H, 1- and 5-H). − ^{13}C NMR (75 MHz, CD_3OD): δ = 110.6 (C-2 and C-4), 165.2 (C-1 and C-5), 187.7 (C-3). − MS (EI, 70 eV): *m/z* (%) = 44 (100) [$C_2H_4^+$]. − $C_5H_5NaO_2\cdot1.5H_2O$ (120.1 + 27.0 = 147.1): calcd. C 40.83, H 5.48; found C 40.70, H 5.65. The water of crystallization could be removed by drying over P_4O_{10} in vacuo at high temperature.

(−)-(3*R*,4*S*,4′*R,8*S*,9*R*)-1,5-Bis(1′,2′,3′,4′,10,11-hexahydroquinin-1-onium-1′-yl)pentamethinium Tris(tetrafluoroborate) (11a):** To a stirred solution of **3a** (0.50 g, 1.51 mmol) in 5 mL of anhydrous ethanol, was added dropwise a solution of anhydrous **10** (0.091 g, 0.76 mmol) in 15 mL of dry ethanol at room temp. After the addition of ethereal HBF_4 (0.34 mL, 54% in diethyl ether; Merck, Darmstadt) stirring was continued for 30 min. The solvents were then evaporated and the shiny oily residue was redissolved in 100 mL of dichloromethane. This solution was washed with water (3 × 100 mL) and then dried over $MgSO_4$. The desiccant was filtered off and the solvent was removed from the filtrate in a rotary evaporator. The residue was dissolved in 10 mL of acetone and to this solution 500 mL of dry diethyl ether was added dropwise with stirring at room temp. The resulting suspension was allowed to stand for 24 h at ca. −18°C. The red precipitate formed was filtered off and dried in vacuo at 50°C to give **11a** (0.40 g, 53%) as red crystals [m.p. 164°C (dec.)]. − $[\alpha]_D^{18}$ = −1545 (*c* = 0.011 in ethanol). − UV/vis (ethanol): λ_{max} (lg ε) = 511 nm (4.93), 279 (3.97). − IR (KBr): ṽ = 3414 cm^{-1} (O−H), 2957, 2836 (aliphatic C−H), 1609, 1571, 1529, 1495, 1467 (aromatic C=C), 1124, 1083 (BF_4), 1038 (N−H). − ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 0.86 (t, ^3J = 7.2 Hz, 6 H, 11-H), 1.42−1.49 (m, 4 H), 1.63 (m, 2 H), 1.84−2.05 (m, 12 H), 2.20−2.24 (m, 2 H), 2.83−3.00 (m, 5 H), 3.30−3.56 (m, 9 H), 3.76 (s, 6 H, 12-H), 3.86−4.00 (m, 6 H), 5.40 (br. d, 2 H, OH), 6.31 (dd, appearing as t, 2 H, 14-H and 14′-H), 6.88 (d, ^4J = 2.8 Hz, 2 H, 5′-H), 6.90 (dd, ^3J = 9.0 and ^4J = 2.8 Hz, 2 H, 7′-H), 7.50 (d, ^3J = 9.1 Hz, 2 H, 8′-H), 7.96 (t, ^3J = 12.6 Hz, 1 H, 15-H), 8.38 (d, ^3J = 11.7 Hz, 2 H, 13-H and 13′-H), 9.25 (br. s, 2 H, 1-H = N−H). − ^{13}C NMR (125 MHz, [D_6]DMSO): δ = 11.6 (C-11), 23.8 (C-5), 24.1 (C-4), 24.1 (C-7 or C-10), 24.5 (C-10 or C-7), 34.9 (C-3′), 39.0 (C-3), 40.0 (C-4′), 40.1 (C-12), 42.5 (C-2′), 44.5 (C-2), 55.2 (C-6), 55.5 (C-8), 57.8 (C-9), 108.4 (C-14 and C-14′), 113.8, 116.0, 120.0 (C-5′, C-7′, C-8′), 131.6 (C-4a′), 132.5 (C-8a′), 154.9 (C-6′), 157.0 (C-13, C-13′), 164.0 (C-15). − MS (electrospray): *m/z* = 898 [M^+ − HBF_4]. − $C_{45}H_{65}B_3F_{12}N_4O_4$ (986.4): calcd. C 54.79, H 6.64, N 5.68; found C 54.66, H 6.73, N 5.60.

(+)-(3*R*,4*S*,4′*S,8*S*,9*R*)-1,5-Bis(1′,2′,3′,4′,10,11-hexahydroquinin-1-onium-1′-yl)pentamethinium Tris(tetrafluoroborate) (11b):** In analogy to the preparation of **11a**, from **3b** (0.50 g, 1.51 mmol) in 5 mL of ethanol, anhydrous **10** (0.091 g, 0.76 mmol) in 15 mL of ethanol, and 0.34 mL of ethereal HBF_4 (54%), was obtained **11b** (0.24 g, 32%) as red crystals [m.p. 186−190°C (dec.)]. − $[\alpha]_D^{18}$ = +1135 (*c* = 0.015 in ethanol). − UV/vis (ethanol): λ_{max} (lg ε) = 506 nm (4.96), 277 (4.10). − IR (KBr): $\tilde{\nu}$ = 3440 cm^{-1} (O−H), 3210 (N−H), 2961 (aliphatic C−H), 1610, 1573, 1529, 1494 (aromatic C=C), 1182, 1124 (BF_4), 1084 (N−H). − ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 0.79 (t, ^3J = 7.2 Hz, 6 H, 11-H), 1.29−1.34 (m, 4 H), 1.59 (m, 2 H), 1.76−1.99 (m, 11 H), 2.22 (m, 2 H), 2.64−2.68 (m, 2 H), 2.82 (m, 2 H), 2.95 (m, 2 H), 3.12 (m, 2 H), 3.24−3.65 (m, 5 H), 3.71 (s, 6 H, 12-H), 3.81 (m, 4 H), 3.94 (m, 2 H), 5.76 (m, 2 H, OH), 6.31−6.34 (m, 2 H, 14-H, 14′-H), 6.84 (d, ^4J = 2.6 Hz, 5′-H), 6.91 (dd, ^3J = 8.9 Hz, ^4J = 2.6 Hz, 2 H, 7′-H), 7.44 (d, ^3J = 9.1 Hz, 2 H, 8′-H), 8.26 (m, 1 H, 15-H), 8.27 (d, ^3J = 11.6 Hz, 2 H, 13-H and 13′-H), 8.99 (br. s, 2 H, 1-H = N−H). − ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 11.5 (C-11), 18.9 (C-5), 22.0 (C-4), 23.7 (C-7 or C-10), 24.1 (C-10 or C-7), 26.0 (C-3′), 30.6 (C-3), 34.6 (C-4′), 42.5 (C-12), 44.6 (C-2′), 55.0 (C-2), 55.6 (C-6), 58.3 (C-8), 69.5 (C-9), 108.5 (C-14 and C-14′), 114.0 and 114.2 (C-5′ and C-7′), 120.5 (C-8′), 131.8 (C-4a′), 132.4 (C-8a′), 154.9 (C-6′), 157.6 (C-13 and C-13′), 164.3 (C-15). − MS (FD): *m*/*z* (%) = 821 (12) [M$^+$ − 165], 820 (45) [M$^+$ − 166], 819 (100) [M$^+$ − 167], 818 (47) [M$^+$ − 168], 789 (38) [M$^+$ − 197], 788 (11) [M$^+$ − 198]. − $C_{45}H_{65}B_3F_{12}N_4O_4 \cdot 4H_2O$ (986.4 + 72.1 = 1058.5): calcd. C 51.06, H 6.95, N 5.29; found C 51.33, H 6.78, N 5.25.

(−)-[3*R*,4*S*,(4′*R*+4′*S*),8*S*,9*R*]-1,5-Bis(1′,2′,3′,4′,10,11-hexahydroquinin-1-onium-1′-yl)pentamethinium Tris(tetrafluoroborate) (11c; mixture of diastereomers): In analogy to the preparation of **11a**, from **3c** (0.50 g, 1.51 mmol) in 5 mL of ethanol, anhydrous **10** (0.091 g, 0.76 mmol) in 15 mL of ethanol, and 0.34 mL of ethereal HBF_4 (54%), was obtained **11c** (0.21 g, 31%) as red crystals [m.p. 156−160°C (dec.)]. − $[\alpha]_D^{18}$ = −455 (*c* = 0.007 in acetone). − UV/vis (ethanol): λ_{max} (lg ε) = 510 nm (4.85), 305 (3.97), 284 (4.12). − IR (KBr): $\tilde{\nu}$ = 3450 cm^{-1} (O−H), 3203 (N−H), 2959 (aliphatic C−H), 1610, 1573, 1530, 1466 (aromatic C=C), 1184, 1126 (BF_4), 1037 (O−H). − ^{1}H NMR (300 MHz, CD_3CN): δ = 0.81−0.90 (m, 6 H, 11-H), 1.02−3.97 (several m, 42 H), 6.30 (m, 2 H, 14-H and 14′-H), 6.76 (m, 2 H, 5′-H), 6.91 (m, 2 H, 7′-H), 7.30 (d, ^3J = 8.4 Hz, 2 H, 8′-H), 7.81−7.90 (m, 1 H, 15-H), 8.05−8.11 (m, 2 H, 13-H and 13′-H); the broad signals for the OH and NH protons are beneath the other signals. − ^{13}C NMR (125 MHz, [D$_6$]DMSO): The NMR spectrum is essentially identical to that of **11a**. − MS (FD): *m*/*z* (%) = 900 (29) [M$^+$ − 86], 899 (47) [M$^+$ − 87], 821 (13) [M$^+$ − 165], 820 (100) [M$^+$ − 166], 819 (97) [M$^+$ − 167], 818 (47) [M$^+$ − 168], 817 (19) [M$^+$ − 169]. − $C_{45}H_{65}B_3F_{12}N_4O_4$ (986.4): calcd. C 54.79, H 6.65, N 5.68; found C 54.90, H 6.91, N 5.48.

(+)-[3*R*,4*S*,(4′*R*+4′*S*),8*R*,9*S*]-1,5-Bis(1′,2′,3′,4′,10,11-hexahydroquinidine-1-onium-1′-yl)pentamethinium Tris(tetrafluoroborate) (12c; mixture of diastereomers): In analogy to the preparation **11a**, from **6c** (0.50 g, 1.51 mmol) in 5 mL of ethanol, anhydrous **10** (0.091 g, 0.76 mmol) in 15 mL of ethanol, and 0.34 mL of ethereal HBF_4 (54%), was obtained **12c** (0.34 g, 45%) as red crystals [m.p. 177°C (dec.)]. − $[\alpha]_D^{18}$ = +73 (*c* = 0.012 in acetone). − UV/vis (ethanol): λ_{max} (lg ε) = 508 nm (4.93), 250 (4.08). − IR (KBr): $\tilde{\nu}$ = 2957 cm^{-1} (aliphatic C−H), 1609, 1573, 1529, 1495 (aromatic C=C), 1183, 1126, 1084 (BF_4), 1057 (N−H). − ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 0.78 (m, 6 H, 11-H), 1.38 (m, 4 H), 1.73−2.17 (several m, 13 H), 2.79 (m, 2 H), 2.89 (m, 2 H), 3.07−3.36 (several m, 11 H), 3.73 and 3.75 (2 s, 6 H, 12-H), 3.83 and 3.95 (2 m, 6 H), 5.34 (m, 1 H, OH), 5.73 (m, 1 H, OH), 6.25−6.39 (m, 2 H, 14-H and 14′-H), 6.85−6.93 (m, 4 H, 5′-H and 7′-H), 7.42−7.49 (m, 2 H, 8′-H), 7.92−7.97 (m, 1 H, 15-H), 8.29−8.33 (m, 2 H, 13-H and 13′-H), 9.01 (br. m, 2 H, 1-H = N−H). − ^{13}C NMR (125 MHz, [D$_6$]DMSO): This spectrum featured a total of 36 signals, the assignment of which was not possible. − MS (FD): *m*/*z* (%) = 822 (6) [M$^+$ − 164], 821 (13) [M$^+$ − 165], 820 (17) [M$^+$ −166], 819 (100) [M$^+$ − 167], 818 (68) [M$^+$ − 168], 817 (4) [M$^+$ − 169]. − $C_{45}H_{65}B_3F_{12}N_4O_4$ (986.4): calcd. C 54.79, H 6.64, N 5.68; found C 54.94, H 6.86, N 5.53.

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