JOURNAL OF PHYSICAL ORGANIC CHEMISTRY, VOL. 8, 761–773 (1995)

REVIEW COMMENTARY

CHIRAL POLYMETHINE DYES: A REMARKABLE BUT FORGOTTEN CONJUGATED π SYSTEM

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Chiral polymethine dyes constitute a particular class of conjugated π systems. Artificial chiral polymethine dyes were first synthesized by König and Langbein in 1928 in order to clarify the electronic structure of cyanine dyes; some natural dyes such as musca-aurin I (from the toadstool fly agaric) and betanin (from the vegetable red beets) are known to be chiral pentamethinium cyanine dyes, the chirality of which stems from L-α-amino acids as end-groups. The reasons why chiral polymethine dyes are not only of historical interest but once again the subject of research are explained.

INTRODUCTION

When a student of chemistry wishes to inform himself or herself on conjugated π systems by consulting a common modern textbook of organic chemistry, he or she will certainly find a wealth of information about *aromatic* π systems, presumably sufficient on *polyenic* π systems, but only sparse information about *polymethinic* π systems, if at all—and this in spite of the fact that polymethine dyes, particularly cyanine dyes, are of great theoretical and practical interest.[1] Polymethine dyes represent not only ideal π systems for the study of correlations between structure and colour, but are also important as spectral sensitizers in silver halide photography,[2] as active or mode-locking substances in dye lasers,[3] as possible material for non-linear optics (i.e. for frequency doubling caused by second harmonic generation),[4] as dyes in sensor chemistry,[5] in devices for optical data storage,[6] as optical probes in membranes or model membrane systems,[7] as initiators in photopolymerizations[8] and as fluorescent tags in DNA sequencing[9] and immunoassay[10] (i.e. covalent labelling of DNA molecules and proteins). Because of their preferential use outside the conventional textile colouration field, they belong to the class of so-called *functional dyes*.[11]

Polymethine dyes constitute an independent class of conjugated π systems as distinct from aromatics and polyenes.

According to Hückel's rule, ideal *aromatic* π *systems* are planar monocyclic ring systems of sp^2-hybridized carbon atoms possessing $(4n+2)$ π electrons delocalized over this ring. General characteristics of such aromatic π systems are high delocalization energies and high polarizabilities, equal π-bond orders and equal π-electron densities along the carbon chain and comparatively low chemical reactivities (substitution reactions are favoured over addition reactions).

Polyenic π *systems* are planar conjugated open-chain or ring systems of sp^2-hybridized carbon atoms with low delocalization energies and medium-sized polarizabilities, possessing unequal (alternating) π-bond orders and nearly equal π-electron densities along the carbon chain, as well as comparatively high chemical reactivities (addition reactions are favoured over substitution reactions). In principle, conjugated polyines with sp-hybridized carbon atoms belong also to this group of π-systems; they consist of two superimposed orthogonal polyenic π-systems.

Polymethinic π *systems* of the general formula **1** are planar conjugated open-chain (or sometimes ring) systems of sp^2-hybridized carbon atoms with medium-sized delocalization energies and high polarizabilities, possessing equal π-bond orders but unequal (alternating) π-electron densities along the carbon chain, as well as comparatively high chemical reactivities

CCC 0894–3230/95/120761–13
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Received 7 June 1995
Revised 15 August 1995

(substitution reactions are favoured over addition reactions).[12]

$$\overset{\cdots\cdots(n+3)\pi\cdots\cdots}{X{-}(CR)_n{-}X'}$$

1

$n = 1, 3, 5, 7, \ldots$; R = H or substituents
X, X′ = mostly atoms of the 5th or 6th main group of the Periodic System; e.g.

X = X′	:	**Polymethine dyes**
X = X′ = N	:	Cyanine dyes;
X = X′ = O	:	Oxonole dyes;
X ≠ X′	:	**Meropolymethine dyes**
X = N, X′ = O	:	Merocyanine dyes.

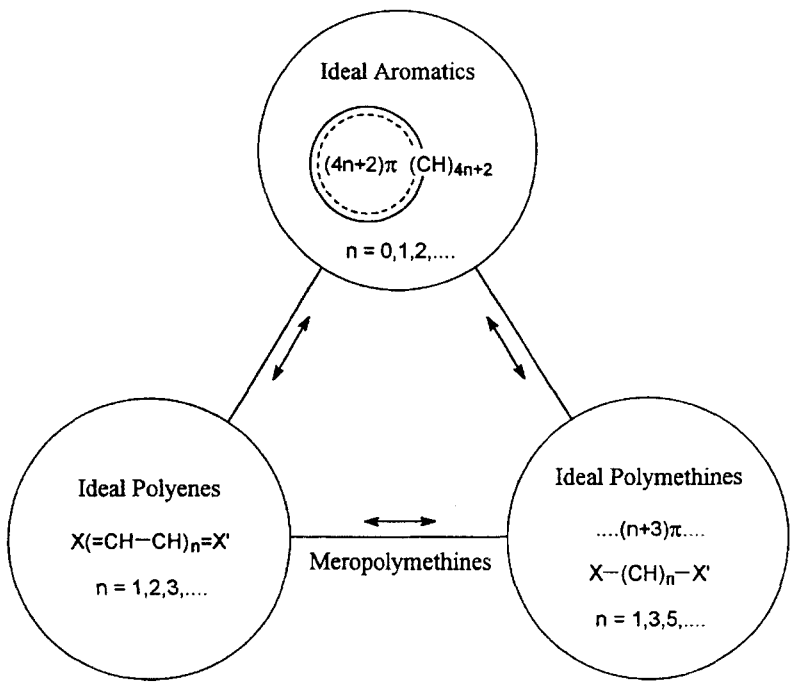
It is important to note that *cyanine dyes* (used by *Chemical Abstracts* as the main descriptor for this class of dyes) constitute only a particular, although important, subclass of polymethine dyes. According to the above-mentioned description, polymethine dyes have some properties in common with aromatics, e.g. large delocalization energies, equal π-bond orders and the preference for substitution reactions. However, in contrast to aromatics and polyenes with equal π-electron densities at each carbon atom, the pronounced alternation of π-electron densities along polymethine chains creates a striking difference to both other systems. This situation is best illustrated by Dähne's triad description of unsaturated, conjugated π systems, as shown in Scheme 1.[13]

Quantum chemical HMO calculations of polymethinic compounds by Fabian and Hartmann[14] have established the independent character of polymethinic π systems as compared with aromatics and polyenes. According to Scheme 1, depending on the nature of X and X′ there are also π systems known whose π-electronic structure lies somewhere between that of polymethines and that of polyenes (e.g. the meropolymethines), between that of polyenes and that of aromatics, and between that of polymethines and that of aromatics.

Other theoretical treatments of the electronic structure of polymethine dyes, which also consider the polymethinic π system as a π system on its own, include the famous Elektronengasmodell (free-electron MO model) of Kuhn[15] and the method of Pariser, Parr and Pople (PPP MO method), used in its various versions, for example, by Griffiths[16] and Matsuoka.[17] Compilations of the various quantum chemical treatments of polymethine dyes can be found in Refs 1a, 1c, 1d, 14d and 16a.

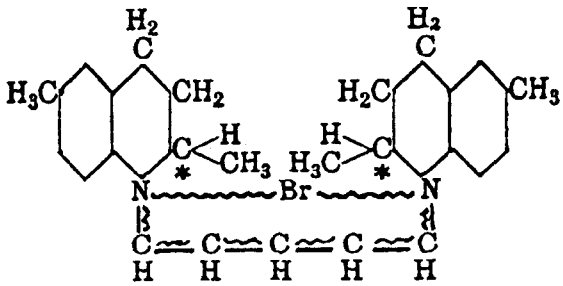
THE FIRST CHIRAL POLYMETHINE DYES

Although the first polymethine dyes were synthesized as early as 1856–57 by Williams in Glasgow, Scotland (e.g.



Scheme 1. Triad classification of organic compounds with conjugated π systems according to Dähne[13]

'Cyanine', from the Greek *kyanos* = dark blue, because of its brilliant blue solution colour)[18] and by von Babo in Freiburg, Germany (e.g. 'Irisine' from the Greek *iris* = rainbow, because of its rainbow colours),[19] the designation 'polymethine dye' and the first general description of their electronic structure was introduced more than 60 years later mainly by König,[20,21] one of the pioneers of the modern theory of dyestuffs, in Dresden, Germany (for a more detailed description of the development of the theory of dyestuffs, particularly polymethine dyes, see Ref. 22). At that time, i.e. before

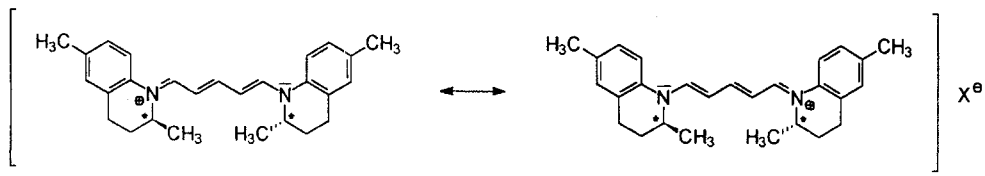


2

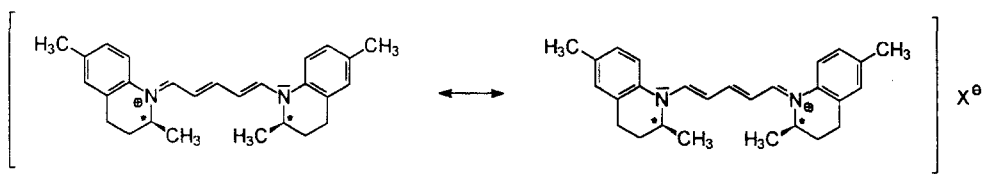
Scheme 2. Formula notation of a chiral pentamethinium cyanine dye (**2**) as used by König in 1928[24a]

the introduction of the concept of σ and π bonds[23] and that of π-electron delocalization (theory of resonance or mesomerism), it was very difficult to describe the structure of conjugated π systems such as polymethine dyes by means of passably correct formulae. Scheme 2 shows one of the polymethine dyes synthesized by König[24a] and Langbein[24b] in 1928 with a formula notation recommended by Gebhard in 1911,[25] using so-called Partialvalenzen (partial valences, i.e. the wavy lines in the formula in Scheme 2). A present-day notation of this polymethine dye **2** is given in Scheme 3.[26]

König's syntheses of trimethinium and pentamethinium cyanine dyes (such as **2**) in their monochiral and isochiral forms [the designation *monochiral* (one-handed), *isochiral* (equal-handed) and *anisochiral* (unequal-handed) in place of the ambiguous terms *homochiral, racemic* and *scalemic*, are used in this review, as recently recommended by Cornforth[27]] was a landmark in the development of a theory for the description of the π electronic ground state of polymethine dyes, which, according to König,[20,24] possess a particular 'Chromozustand' (chromo state) consisting of a so-called 'Mesochrome' and 'Perichromes'. The term 'Chromozustand' (chromo state) for a generalized description of the typical behaviour of unsaturated conjugated dyes was first proposed by Ismailsky,[28] who obtained his thesis with König in Dresden.[28b] In 1928, it was not by any means obvious that the two heterocyclic end-groups of



(-) - (*R*,*R*) : **2a**
(+) - (*S*,*S*) (as given by the formula) : **2b**



meso - (*S*,*R*) : **2d**

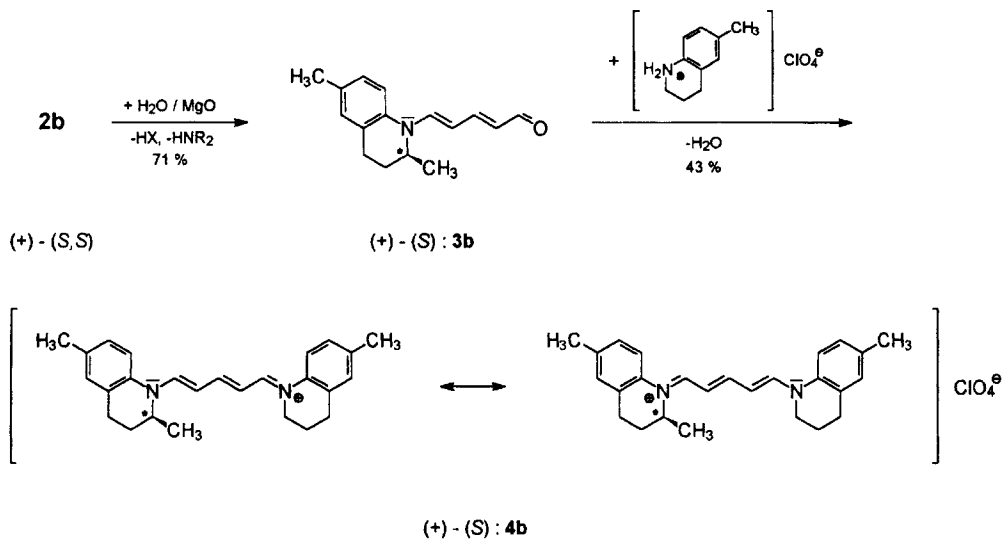
Scheme 3. Present-day notation of bis(1,2,3,4-tetrahydro-2,6-dimethylquinolin-1-yl)pentamethinium bromide (X = Br) in its monochiral (**2a**; **2b**) and *meso* forms (**2d**); the corresponding isochiral (racemic) dye has the formula number **2c**.[26] Throughout this paper, monochiral compounds are designated with the letter **a** (*R*) and **b** (*S*), isochiral (racemic) compounds with **c** [(*R*) + (*S*)] and *meso* compounds with **d** (*R*,*S*).

polymethine dyes such as **2** are chemically equivalent and that polymethine dyes with equal end groups have a symmetrical π electronic structure—as nowadays described by mesomeric or resonance forms with a double-headed arrow written between them, corresponding to some hybrid of these mesomeric structures (Scheme 3).

König and Langbein[24b] adduced evidence for the chemical equivalence of the two 1,2,3,4-tetrahydro-2,6-dimethylquinoline end-groups in pentamethinium cyanine dye **2** in the following brilliant way:[24] they not only synthesized the monochiral (+)-(*S*,*S*)-configured dye **2b** and the *meso*-(*S*,*R*)-configured dye **2d** (Scheme 3), both with two asymmetrically substituted carbon atoms within the respective end-groups, they also prepared according to the pathway shown in Scheme 4 the monochiral (+)-(*S*)-configured pentamethinium cyanine dye **4b** with only one chiral centre within the two-end groups. Partial hydrolysis of **2b** afforded the monochiral merocyanine dye **3b** as an intermediate, which was then allowed to react with an achiral 1,2,3,4-tetrahydro-6-methylquinolinium salt to give the unsymmetrical, monochiral, still (*S*)-configured pentamethinium dye **4b**.

Having now in hand the three pentamethinium dyes **2b**, **2d** and **4b**, the specific, $[\alpha]_D$, and molar optical rotation, $[\phi]_D$, of their diluted solutions in ethanol could be measured because the long-wavelength UV–visible absorption maxima of these dyes are with $\lambda_{max} = 492$ nm (**2b**, **2d**) and 497 nm (**4b**) sufficiently hypsochromically separated from the sodium D line emission at 589 nm. In contrast to the high optical rotations observed with the monochiral dye **2b**, the optical rotation of the corresponding *meso*-dye **2d** (with a symmetry plane through the central methine group) should be zero, provided the two heterocyclic end-groups are completely equivalent. Furthermore, if one compares the optical rotation of monochiral **2b** with that of monochiral **4b**, the optical rotation of dye **2b** with two stereocentres should be twice as large as that of dye **4b** with only one stereocentre, provided that the heterocyclic end-groups in **2b** are equivalent, and that the overall optical rotation of monochiral dyes with more than one stereocentre such as **2b** could be calculated simply by addition of the individual contributions, stemming from the two (or more), supposedly independent, end-groups with chiral centres. Both expectations were completely met by the experimental results given in Table 1. The average value of the molar optical rotation of **2a** and **2b** with $[\phi]_D = 11\,870$ is indeed nearly twice as large as the molar optical rotation of **4b** with $[\phi]_D = 6200$ ($6200 \times 2 = 12\,400$). The difference between the calculated and experimental molar optical rotations ($12\,400 - 11\,870 = 530$) is only 4·5 % of the experimental value. Within the accuracy of measurement, the experimental optical rotation of the *meso* dye **2d** is zero. Similar results have been obtained with the corresponding chiral trimethinium cyanine dyes.[24,26]

With this brilliantly designed experiment, König and Langbein made an important contribution to the elucidation of the electronic structure of polymethine dyes. Unfortunately, this work was only published as a short report of a lecture given by König[24a] on 1 June 1928, on the occasion of the '41. Hauptversammiung des Vereins



Scheme 4. Synthesis of the unsymmetrical chiral pentamethinium cyanine dye **4b** from the symmetrical cyanine dye **2b**, according to König[24,26]

Table 1. Specific, $[\alpha]_D$, and molar optical rotation, $[\phi]_D$, of the pentamethinium cyanine dyes **2a**, **2b**, **2d** and **4b**, measured in ethanol at room temperature[26]

Formula	Configuration	$[\alpha]_D$	$[\phi]_D$[a]	Average $[\phi]_D$
2a	(−)-(*R*,*R*)-	−2551	−11875	11870
2b	(+)-(*S*,*S*)-	+2549	+11866	
2d	*meso*-(*S*,*R*)-	0·00	0·00	
4b	(+)-(*S*)-	+1268	+6200	

[a] $[\phi]_D = ([\alpha]_D M_r)/100$.

Deutscher Chemiker' in Dresden, Germany. Therefore, it was largely overlooked by his contemporaries and also not appreciated later. The reasons why König did not publish these results in a full paper are presumably that the absolute configurations of all synthesized chiral polymethine cyanine dyes and their optical purity were not known at that time.[24b]

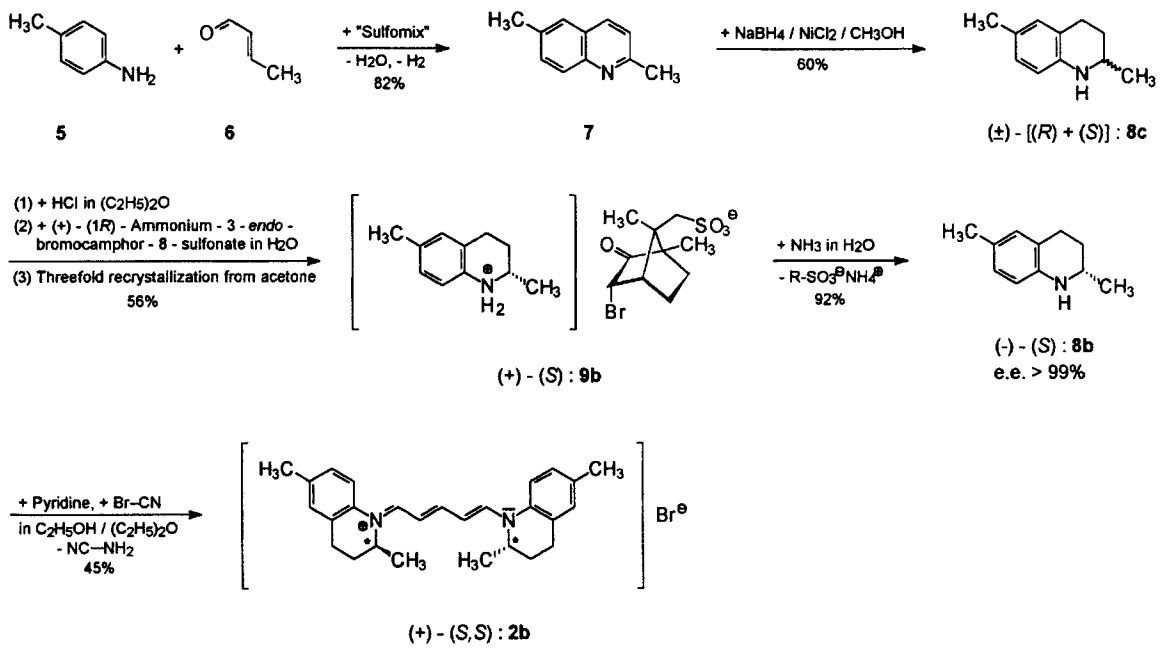
NEW SYNTHESES OF CHIRAL POLYMETHINE DYES

Because of the historical importance, the sometimes insufficient elaboration of the synthetic procedures, the mostly unknown enantiomeric purity and absolute configuration and their possible applications, and also in continuation of our recent work on chiral polymethine dyes,[29–32] we have recently repeated and significantly improved some of König's work.[26] The absolute configurations of dyes **2a**, **2b** and **4b** (as given in Schemes 3 and 4) and their molar optical rotations (as given in Table 1) are taken from this more recent work.[26]

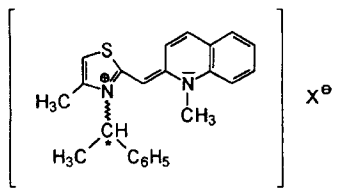
Following the work of König[24a] and Langbein,[24b] the pentamethinium cyanine dye **2b** was synthesized as follows (Scheme 5): 2,6-dimethylquinoline (**7**) was prepared from 4-methylaniline (**5**) and crotonaldehyde (**6**) according to Doebner and Miller's variation of Skraup's quinoline synthesis. Reduction of **7** with $NaBH_4$–$NiCl_2$ led to isochiral (racemic)[27] 1,2,3,4-tetrahydro–2,6-dimethylquinoline (**8c**). The separation of **8c** into its enantiomers was carried out with the nowadays commercially available ammonium (+)-(1*R*)-3-*endo*-bromocamphor-8-sulphonate. The diastereomeric sulphonate salt of **8c** was recrystallized three times from acetone to give the homochiral (+)-(*S*)-sulphonate **9b**. Addition of aqueous ammonia afforded the monochiral quinoline **8b** with high enantiomeric purity (*e.e.* >99%). From the remaining mother liquor of the crystallization of **9b** the other enantiomer of **8b** (i.e. **8a**) was isolated.

The absolute configuration of **8b** was determined by means of a single-crystal x-ray structure analysis of its perchlorate: the stereocentre at C-2 has the (*S*)-configuration. With this result, the absolute configuration of all polymethine dyes derived from **8b** is established.

Eventually, reaction of monochiral **8b** with cyanogen bromide and pyridine afforded the pentamethinium dye



Scheme 5. Synthesis of the symmetrical chiral pentamethinium cyanine dye **2b**, according to König[24,26]



(-) - (*R*) : **10a** $[\alpha]_D$ = -1750 (EtOH)

(+) - (*S*) : **10b** $[\alpha]_D$ = +1750 (EtOH)

Scheme 6. An unsymmetrical chiral monomethinium cyanine dye, **10a** and **b**, first synthesized by Götze in 1938[31,33]

2b as brilliant red plates; its structure was also confirmed by a single-crystal x-ray analysis. The chiroptical properties of **2b** (and of the other chiral polymethine dyes) were in satisfactory agreement with the corresponding values measured by König[24a] and Langbein.[24b] Details of this synthesis and the structure determinations can be found in Ref 26.

Apart from the work of König[24a] and Langbein,[24b] there is only one another report on chiral polymethine dyes in the old literature: Götze, at the Otto Perutz film factory in Munich, Germany, published in 1938 a short communication on the syntheses of unsymmetrical, chiral monomethinium cyanine dyes with thiazolyl and quinolyl end-groups, using 1-phenylethylamine as a monochiral starting material, one example of which (**10a** and **b**) is shown in Scheme 6.[33] The paper did not mention the pioneering work of König and ended with the remark that the work would be continued. However, to the best of the author's knowledge, further work in this field has not subsequently been published. We have also recently repeated and significantly improved this work of Götze.[31]

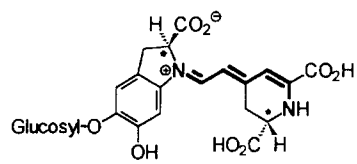
NATURAL CHIRAL POLYMETHINE DYES

In the 1960s and 1970s, it was surprisingly found that some well known natural dyes such as the red–violet betalain dye betanin (responsible for the colour of red beets, *Beta vulgaris*)[34] and the orange–red fungus dye musca-aurin I (from the toadstool fly agaric, *Amanita muscaria*)[35] are indeed chiral polymethine dyes (Scheme 7). Both dyes contain a pentamethinium cyanine chromophore with two chiral end groups stemming from L-α-amino acids. Another natural chiral pentamethinium cyanine dye, indicaxanthin (with a structure similar to that of betanin), belongs to the betaxanthins and causes the yellow colour of the fruit of the cactus *Opuntia ficus-indicans*. Betalains are found in many plant families usually classified in the order *Centrospermae*.[34b]

The structure of betanin was elucidated by Dreiding and co-workers,[36] followed by several successful attempts to synthesize such betalain dyes,[37,38] which are of interest as food colourants. The structure determination of the group of musca-aurins I–VII, isolated from the white-spotted, orange–red skin of the head of fly agaric, was performed by Musso and co-workers,[39] in part at the University of Marburg, Germany. I remember that the co-workers of Professor Musso very often had to spend their weekends collecting fly agarics in the forests surrounding Marburg!

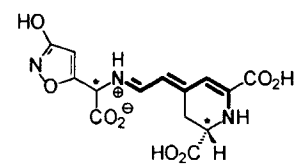
RECENT STUDIES ON CHIRAL POLYMETHINE DYES

Our first study of chiral polymethine dyes was accidentally inspired in 1990 when we attempted to analyse the ^{1}H NMR spectrum of a trimethinium cyanine dye (**12**) which we believed to have been obtained by condensation of the heterocyclic quaternary iminium salt **11** with triethyl orthoformate in pyridine (Scheme 8).[29] The reason for attempts to synthesize an α,α′-dimethyl chain-substituted trimethinium cyanine dye such as **12** was to distort the usually all-*trans*- or (*E*,*E*,*E*,*E*)-configured trimethine chain of **12** to such an extent that its configuration would change to a mono-*cis* or even di-*cis*-configuration. (Diastereomers of polymethine dyes created by rotation around C—C bonds of the methine chain can be considered to be conformational or



Betanin

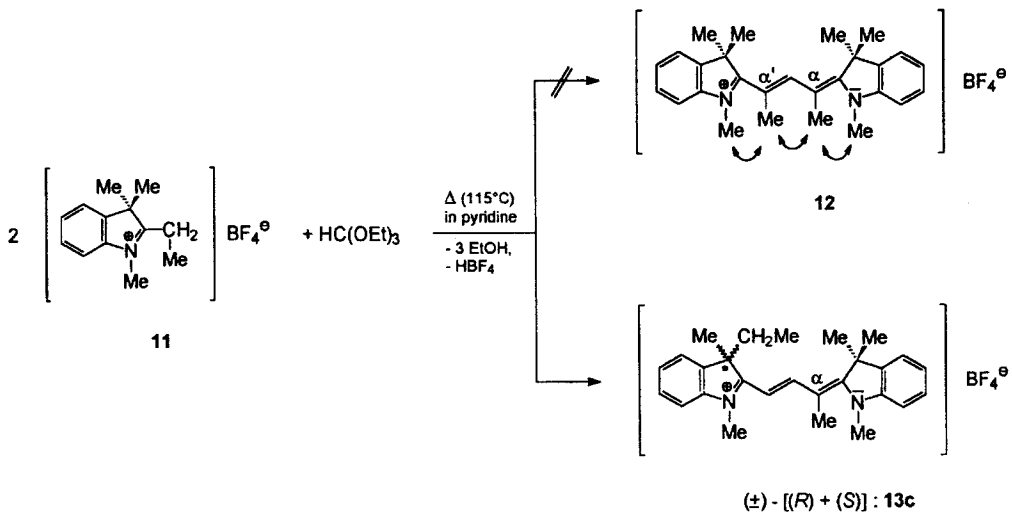
λ_{max} = 537 nm (red - violet)
from vegetable *Red Beet*
(*Beta Vulgaris*)



Musca - aurin I

λ_{max} = 475 nm (orange - red)
from toadstool *Fly Agaric*
(*Amanita muscaria*)

Scheme 7. Two natural chiral polymethine dyes, both with a pentamethinium cyanine chromophore[34,35]

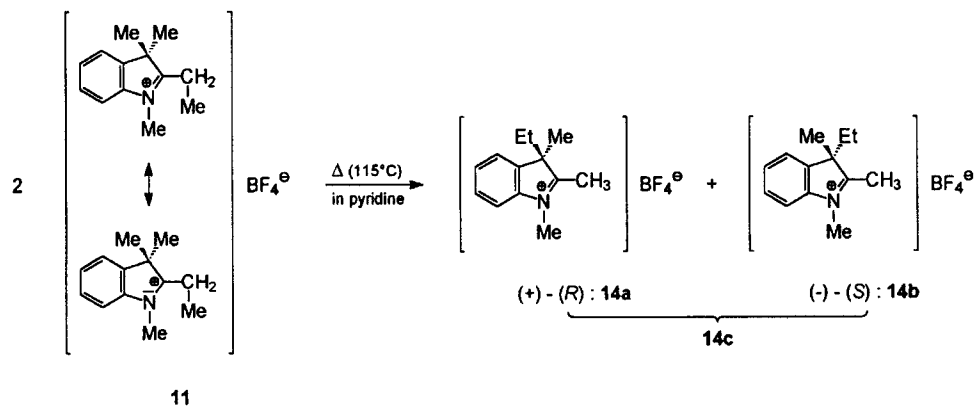


Scheme 8. The surprising result of the condensation reaction of **11** with triethyl orthoformate to yield isochiral **13c** instead of achiral **12**[29]

configurational isomers; for stereoisomers obtained by rotation around C—C bonds of the formal bond order 1·5 (as in polymethine dyes), there is so far no uniform notation.[40]) However, under these reaction conditions, we obtained isochiral **13c** instead of **12**, as shown by the careful analysis of the ^{1}H NMR spectrum and a single-crystal x-ray analysis of the product.[29] It seems that one of the two α,α'-methyl groups in **12** migrated from the α'-position to one of the methyl groups in the 3-position of the indoline ring to give **13c**, which now has, with the indoline C-3, an asymmetrically substituted carbon atom. This at first sight strange result can be easily explained by the reaction sequence given in Scheme 9.

An anionotropic Wagner–Meerwein 1,2-alkyl rearrangement of the iminium salt **11** leads partly to an isochiral (racemic)[27] mixture of the new iminium salts **14a** and **14b**. Thus, during the condensation reaction between **11** and triethyl orthoformate (Scheme 8), one part of the iminium salt **11** reacts conventionally with the orthoformate to give an intermediate merocyanine dye, which then reacts with the rearranged isochiral iminium salt **14a** and **b** to give eventually isochiral **13c**. Such Wagner–Meerwein 1,2-alkyl shifts with 1,2,3,3-tetraalkylindoleninium salts were first described by Plancher in 1898–90,[41] who found that during the determination of the melting points of such iminium salts, rearrangement to isomers with higher melting points took place.[41] For details on this rearrangement, and the formation of **13c**, see Ref. 29.

The relevance of this Wagner-Meerwein rearrange-



Scheme 9. Wagner–Meerwein rearrangement of 2-ethyl-1,3,3-trimethylindoleninium tetrafluoroborate (**11**) to give an equimolar mixture of **14a** and **14b** (=**14c**)[29,41]

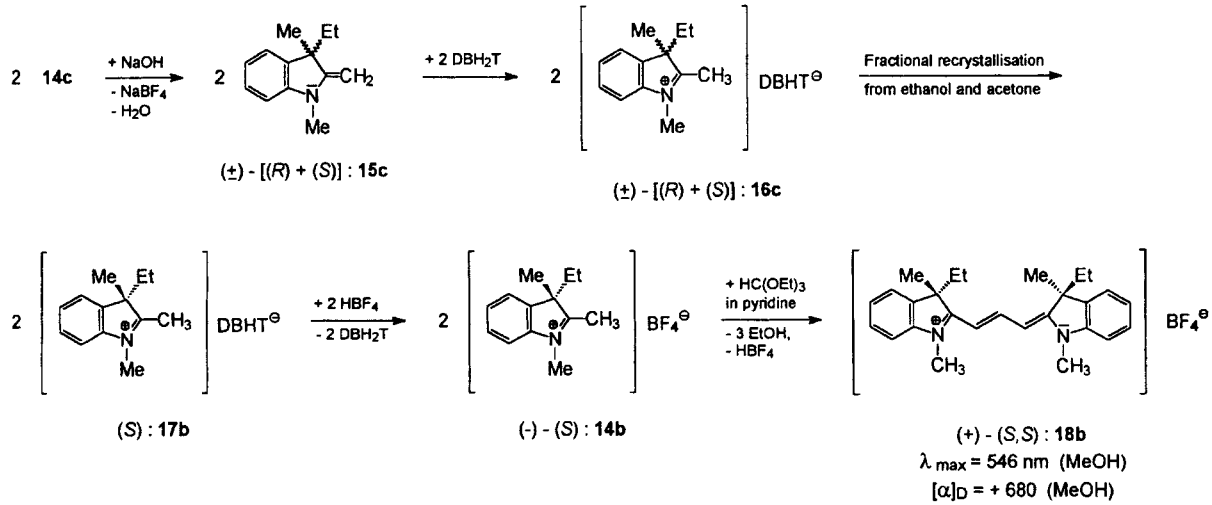
ment within the scope of this review is the formation of a new stereocentre at C-3 of the indoleninium ring of **14** (Scheme 9). However, in order to obtain chiral polymethine dyes using this rearrangement, a laborious (and badly reproducible) separation into enantiomers by fractional crystallization of the corresponding diastereomeric salts (such as **16c** in Scheme 10) is necessary,[29] in the same manner as König obtained the first chiral polymethine dyes by separation of **8c** into enantiomers (Scheme 5).[24,26] Fractional crystallization of the di-*O*-benzoylhydrogentartrate **16c** (prepared from isochiral **14c** via isochiral **15c**) led to monochiral (*S*)-configured **17b**. After the conversion of **17b** in its tetrafluoroborate **14b**, reaction with triethyl orthoformate in pyridine afforded the new monochiral trimethinium cyanine dye **18b** with a high optical rotation.[29]

A more elegant and simpler synthetic route to chiral polymethine dyes would be the use of monochiral natural compounds (from the chiral pool of nature) as educts, in the same manner as Götze obtained some chiral polymethine dyes by first using (+)-(*R*)- and (−)-(*S*)-1-phenylethylamine as monochiral starting material (cf. Scheme 6).[31,33]

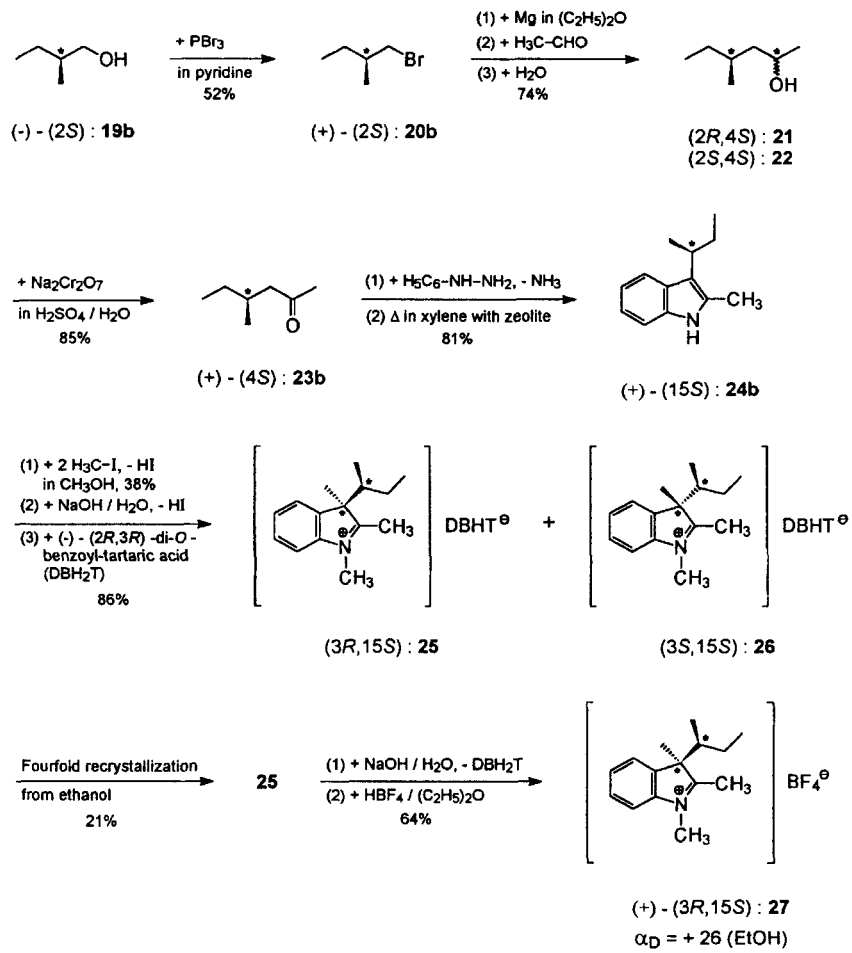
A common, cheap, commercially available starting material is the optically active amyl alcohol **19b** [(−)-(*S*)-2-methylbutan-1-ol], the asymmetrically substituted carbon of which originated from (+)-(*S*)-leucine during the process of alcoholic fermentation. According to Scheme 11, the monochiral quaternary iminium salt **27** was prepared in a multi-step reaction sequence with monochiral **19b** as educt, using a specially designed Fischer indole synthesis of monochiral 2-methyl-3-(1-methylpropyl)indole (**24b**) as key step; treatment of the ketone **23b** with phenylhydrazine in boiling xylene in the presence of an activated zeolite catalyst yielded the desired indole regioisomer **24b** with retention of the (*S*)-configuration at the stereogenic centre of the *sec*-butyl group. Alkylation of the enamine **24b** with iodomethane and conversion of the intermediate iminium iodide into the diastereomeric di-*O*-benzoylhydrogentartrates **25** and **26**, followed by fractional crystallization, allowed the isolation of the (3*R*,15*S*)-diastereomeric salt **25**, which was eventually converted into the monochiral tetrafluoroborate **27**.[32]

With the monochiral (3*R*,15*S*)-configured quaternary iminium salt **27**, a versatile starting material for the synthesis of various new monochiral polymethinium dyes with promising chiroptical properties is now available. Only two examples, taken from Ref. 32, are given in Scheme 12.

Reaction of salt **27** with 1,1,3,3-tetramethoxypropane in pyridin furnished the monochiral dinuclear pentamethinium cyanine dye **28**, whereas reaction of **27** with triformylmethane in acetic anhydride–sodium acetate yielded the monochiral trinuclear [2.2.2]heptamethinediium dye **29**. Trinuclear polymethine dyes such as **29** are methinylogous guanidinium ions, which constitute a new class of Y-conjugated polymethine dyes.[42] [The *methinylogy principle* implies that the electronic donor–acceptor interaction between electron-pair donor (D) and electron-pair acceptor (A) substituents in organic π systems such as D—[CH]$_n$—A (with $n = 1,2,3,\ldots$ sp^2-hybridized methine groups) is not interrupted by the methine groups. With even n, methinylogous compounds are also vinylogous or phenylogous compounds. The methinylogy principle was first formulated by us in Ref. 42a. For the *vinylogy principle*, see Ref. 43.) The absolute configuration at the indoline carbon C-3 in **27**–**29** has been determined by means of a single-



Scheme 10. Synthesis of the symmetrical chiral trimethinium cyanine dye **18b**, according to Reichardt *et al.*[29]

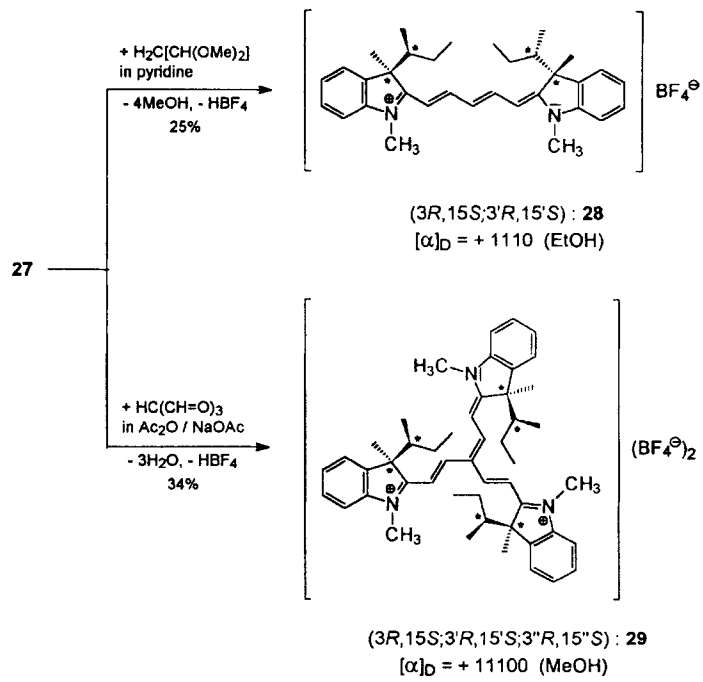


Scheme 11. Synthesis of the monochiral (+)-(3*R*,15*S*)-1,2,3-trimethyl-3-(1-methylpropyl)indoleninium tetrafluoroborate (**27**) from monochiral (−)-(*S*)-2-methylbutan-1-ol, according to Reichardt *et al.*[32]

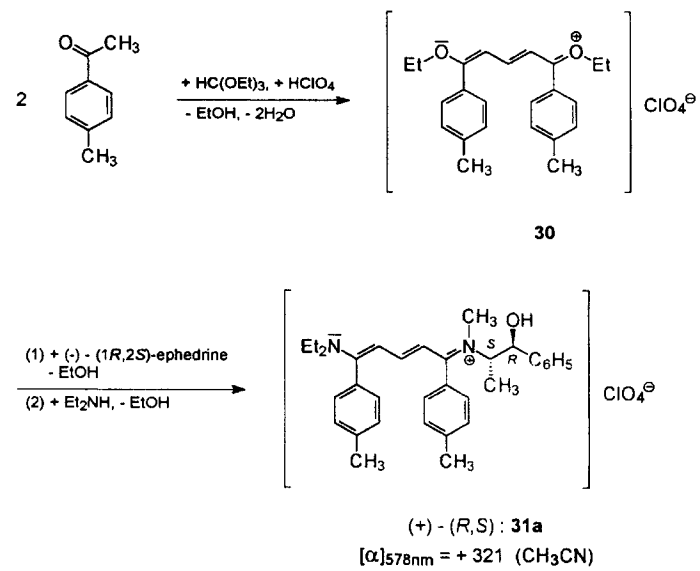
crystal x-ray analysis of **28**: the newly introduced stereocentre at C-3 is (*R*)-configured, whereas the stereocentre at C-15, introduced with the starting compound **19b**, is (*S*)-configured as expected.[32] In spite of the fact that the four and six stereocentres in **28** and **29** respectively, are not directly part of the light-absorbing π system, both dyes exhibit large specific rotations.

Another simple way to obtain chiral polymethine dyes using monochiral educts from the chiral pool of nature is shown in Scheme 13. Reaction of the pentamethinium oxonole dye **30** (obtained from 4-methylacetophenone and triethyl orthoformate) with (−)-(1*R*,2*S*)-ephedrine yielded the monochiral pentamethinium cyanine dye **31a**.[44] The naturally occurring alkaloid (−)-L-ephedrine can be isolated from tropical bushes and the Chinese drug *ma-huang* (e.g. *Ephedra vulgaris, Ephedra equisetina*). The specific rotation of **31a** is also high, in spite of the fact that the two stereocentres are not part of the light-absorbing 8π system.[44]

When monochiral dyes are dissolved in enantiomeric pairs of monochiral solvents, diastereomorphic solvates with slightly different UV–visible absorption maxima should be formed. The possibly resulting hypso- or bathochromic shift of the long-wavelength absorption band of the dissolved monochiral solute, as compared with its band position in the corresponding isochiral solvent, has been called *chiro-solvatochromism*.[45] Monochiral polymethine dyes such as **2a** and **b** have been dissolved in pairs of monochiral solvents such as (−)-(*R*)- and (+)-(*S*)-propane-1,2-diol, (−)-(*R*,*R*)- and (+)-(*S*,*S*)-butane-2,3-diol, and (−)-(*R*)- and (+)-(*S*)-butan-2-ol, and the position of the long-wavelength π–π^* absorption band has been



Scheme 12. Synthesis of a monochiral dinuclear pentamethinium cyanine dye (**28**) and a monochiral trinuclear [2.2.2]heptamethinediium dye (**29**), according to Reichardt *et al.*[32]



Scheme 13. Synthesis of the unsymmetrical chiral pentamethinium cyanine dye **31a**, according to Wolf and co-workers.[44]

carefully determined. Disappointingly, the absorption band of **2a** and **b** at $\lambda_{max} = 492$ nm does not exhibit any chiro-solvatochromism.[26]

First studies of the circular dichroism (CD) spectra of a monochiral pentamethinium cyanine dye at low temperatures indicated the formation of a chiral dimer with a twisted sandwich-like structure.[46]

CONCLUSIONS

It has been emphasized that polymethine dyes constitute a separate class of π systems with inherently new physical and chemical properties, in addition to the well known aromatic and polyenic π systems. The first syntheses of chiral polymethine dyes by König *et al.*[24a] in 1928 was a landmark in the development of a theory for the description of the π electronic ground state of polymethine dyes, which have been largely overlooked and forgotten for many years. More recent attempts at the syntheses of monochiral polymethine dyes have not only confirmed the basic results obtained by König[24a,26] and Götze,[31,33] but have also opened up new pathways for the preparation of such chiral polymethine dyes.[29–32,44]

The syntheses of chiral polymethine dyes satisfy a long-felt need in the study of the relationships between structure and chiroptical properties of π systems. Such relationships are well established for chiral aromatic and chiral polyenic π systems, but not for chiral polymethinic π systems, the study of which is just beginning.[46]

Among *chiral aromatic* systems, the group of *helicenes* offers particularly interesting chiroptical properties, characterized by large specific rotations,[47] e.g. $[\alpha]_D = +3640$ ($CHCl_3$) for (+)-(*P*)-hexahelicene.[47b]

Chiral polyenic π systems are found within the group of *carotenoids*. According to a list from 1976,[48] more than half of the *ca* 400 naturally occurring carotenoids of known structure possess chiral end groups, the absolute configurations of which have been established for about 60 of them.[49] Such chiral carotenoids are responsible for many of the brilliant colours in fruits, vegetables, fish, crustacea, eggs and plants. For example, (+)-(6′*R*)-α-carotene with $[\alpha]_D = +538$ (benzene) is found in carrots (*Daucus carota*) and in red palm oil, and (−)-(3*R*,3′*R*) 3,3′-dihydroxy-β-carotene (zeaxanthin) with $[\alpha]_{Hg,\ C\text{-line}} = -40$ ($CHCl_3$) is the xanthophyll pigment of yellow maize (*Zea mays*) and egg yolk.[49]

The chiral polymethine dyes mentioned in this review are the first representatives of *chiral polymethinic* π systems according to Scheme 1, the study of which seems to be not only of theoretical but also of practical interest. With respect to the manifold applications of achiral polymethine dyes in various fields as mentioned in the Introduction, chiral polymethine dyes will certainly also be useful materials because of their particular chiroptical properties. Since achiral polymethine dyes are used as spectral sensitizers in silver halide photography,[2] what would happen with chiral polymethine dyes as sensitizers? Would they exhibit different sensitivities for right and left circularly polarized light? This is only one of the questions which have to be answered in the near future.

ACKNOWLEDGEMENTS

Our research on chiral polymethine dyes has been kindly supported by the Deutsche Forschungsgemeinschaft, Bonn, and the Fonds der Chemischen Industrie, Frankfurt am Main. The outstanding efforts of my coworkers U. Budnik, H.-D. Engel, M. Kinzel, G. Schäfer and J. Stein are gratefully acknowledged. Professor Dr S. Dähne, Berlin, Professor Dr W. Liebscher, Berlin, and Professor Dr R. Maier, Dresden, are sincerely thanked for bringing some references to my attention. For the determination and discussion of the CD spectra of some chiral polymethine cyanine dyes I cordially thank Professor Dr V. Buss, Duisburg.

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