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Enantioselective Extraction of Dinitrophenyl Amino Acids Mediated by Lipophilic Deoxyguanosine Derivatives: Chiral Discrimination by Self-Assembly**

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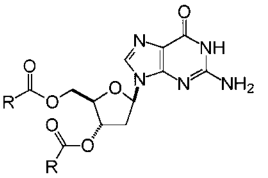
The lipophilic deoxyguanosine derivatives **1** are versatile molecules which, depending on to the experimental conditions, undergo different self-assembly patterns.[1] In the presence of K^+ ions, octamers or columnar oligomers are formed based on the G-quartet structure. In these aggregates the quartets constitute the inner part of the structure, whereas the sugars with their lipophilic pendants are on the outside and in contact with the organic solvent. Alkali metal ions act like cement to keep the quartets **Q** together: If the K^+:**1** molar ratio is 1:8 or lower, the octamer **O** is the most abundant species observed, while for higher ratios oligomeric or polymeric columnar aggregates **P** are progressively observed.[2, 3] Lipophilic guanosines and isoguanosines[4] are able to transfer alkali metal ions from water to organic solvents and act as self-assembled ionophores. Apparently the anion is also dragged into the organic phase, and, considering that the cation is inside a chiral cage, it was thought that the anion could be in contact with the chiral surface of the octamer or of the columnar oligomer. Chiral anions could possibly be discriminated by the chiral surface formed by the substituted deoxyribose moieties.



1a, R = C_9H_{19}
1b, R = p-$(C_{12}H_{25}O)C_6H_4$

The potassium salts of the *N*-2,4-dinitrophenyl (DNP) derivatives of amino acids tryptophan (K(DNP-Trp), **2**), phenylalanine (K(DNP-Phe), **3**), alanine (K(DNP-Ala), **4**), isoleucine (K(DNP-Ile), **5**), and proline (K(DNP-Pro), **6**) were chosen to test the validity of this hypothesis: They are

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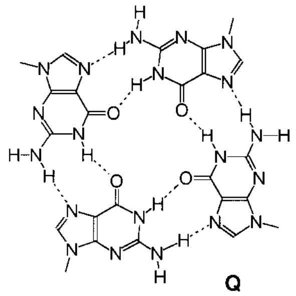
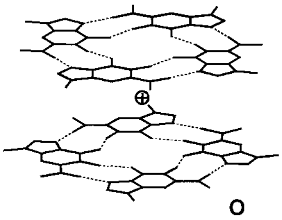
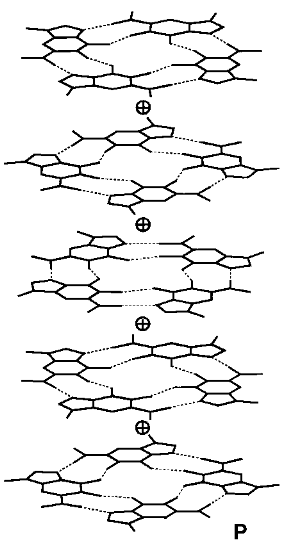


Q



O



P

readily available and absorb in the visible region, facilitating the determination of the extraction yield by absorption spectroscopy; furthermore, the enantiomeric excess can be measured by HPLC. The results obtained by a single extraction of the solutions of racemic **2**–**6** in water with solutions of **1a** and **1b** in chloroform, with different amino acid:nucleoside molar ratios corresponding to the prevailing formation of **O** or **P** assembled species,[5] are reported in Table 1.

While data obtained with **1a** are not promising, the use of **1b**, which has more rigid aromatic pendants on the sugar moiety, proved to be more fruitful. The selectivities observed as measured by the enantiomer distribution constant (EDC),[7] although not optimized, are in some cases very encouraging.[8] Surprisingly, the results obtained with the two molar ratios of 1:8 and 1:2 are very different, and indicate that in the region between the two extreme conditions (prevailing formation of octamer **O** or polymer **P**) there is a gradual change of the enantiomer that is preferentially extracted. This is evident for **2** and **3**, where the D enantiomer is better extracted by the octamer and the L enantiomer by the polymer. This seems to be connected to different interactions of the dinitrophenyl amino acid anions with the **O** and **P** aggregates.

Table 1. The results of the extraction of amino acid derivatives **2**–**6** (AA) with nucleosides **1** (N) at two different AA:N molar ratios. X is the stereochemical descriptor of the most abundant enantiomer in the aqueous layer, and ee_{aq} its enantiomeric excess; EY is the extraction yield,[a] EDC the enantiomer distribution constant,[b] and DS the discrimination factor.[c]

N	AA	A:N	ee_{aq} [%]	X	EY [%]	EDC	DS × 10^3
1a	**2**	1:8	1	L	82	1.02	0.19
1a	**2**	1:2	<1	L	28	1.03	1.3
1b	**2**	1:8	18	L	98	1.44	0.49
1b	**2**	1:2	25	D	46	3.03	71.3
1b	**3**	1:8	21	L	>99	1.54	0.076
1b	**3**	1:2	29	D	50	2.63	67.5
1b	**4**	1:8	8	L	75	1.23	2.4
1b	**4**	1:2	5	L	38	1.28	15.0
1b	**5**	1:8	14	L	98	1.34	0.44
1b	**5**	1:2	12	L	45	1.05	3.4
1b	**6**	1:8	4	L	73	1.12	1.46
1b	**6**	1:2	2	L	32	1.15	7.6

[a] In the case of AA:N = 1:2 (and assuming the existence of the **P** aggregate with a stoichiometry of 1:4), the maximum theoretical value for the EY is 50. [b] EDC is the ratio between the distribution constants of the more extracted and the less extracted enantiomer.[7] [c] DS = ([D-AA] – [L-AA])/[N] represents the molar enantiomeric enrichment of AA per mole of N. It gives a picture of the efficiency of the discrimination when the overall extraction is high (e.g. for **5**, AA:N = 1:8). The maximum theoretical value for DS × 10^3 is 250 in the case of total enantioselectivity of the extraction, and AA:N = 1:2.

We have measured the induced CD spectra of the complex between **1b** and the achiral potassium *N*-(2,4-dinitrophenyl)-glycinate (**7**) as a function of the molar ratio (Figure 1). The CDs induced in the achiral dinitrophenyl chromophore for the two molar ratios are different, and there is a smooth passage from one extreme to the other for intermediate ratios corresponding to the presence of both **O** and **P**, confirming the different interactions of the amino acid with the octamer and the polymer. Furthermore, the intensity of the CD is relatively high, considering that we are dealing with optical activity induced in an achiral molecule;[9] this suggests a tight packing of the anion with the chiral aggregate. The NMR relaxation times for the protons of the complexed derivatives **7** are short with respect to those of the (uncomplexed) methyl ester derivative of **7**, indicating that no independent motion of the dinitrophenylglycinate anion occurs.

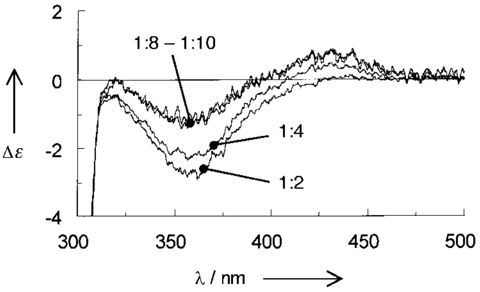


Figure 1. CD spectra of the organic phase obtained after extraction of a solution of **7** in water with a solution of **1b** in chloroform at different **7**:**1b** molar ratios.

The separation of enantiomers by preferential extraction of one enantiomer from water into an immiscible solvent containing a chiral selector has been reviewed recently.[8] However, all examples reported are based on discrimination mechanisms, ranging from the recognition of chiral ammonium salts by chiral crown ethers[10] to the direct interaction between analyte and selector based on hydrogen bonds and π charge–tranfer interactions,[11] and these mechanisms are different from the one described here. The work most similar to the present one is that of the selective transport of sodium mandelate across a membrane, mediated by a chiral crown ether which acts on Na^+ ions but chirally discriminates between the mandelate anions.[12] In none of the cases reported is the selector a self-assembled species:[13] We therefore think that our discrimination mechanism is new and, given the nonoptimized single extraction results obtained for aromatic amino acids, if used in connection with "resolving machines"[8, 11] could lead to very high enantiomeric excesses.

We are presently investigating the binding site of the anion and extending the extraction experiments to different substrates.

Experimental Section

The synthesis of **1a** has been described;[1] **1b** was synthesized according to the same procedure. Solutions of enantiopure **1a** or **1b** in $CHCl_3$ (7×10^{-3} molL^{-1}) were shaken at 20°C with an equivalent volume of solutions of **2**–**6** in water. The layers were separated, and the amount of guest in each layer was determined spectrophotometrically. The HPLC analysis of the enantiomeric excess was carried out on an analytical HSA column.

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Functionalizable Alkylidenes: Tungsten Complexes of Phosphanyl-, Amino-, Alkynyl-, and Tinalkylidenes and Their Dimetallic Derivatization**

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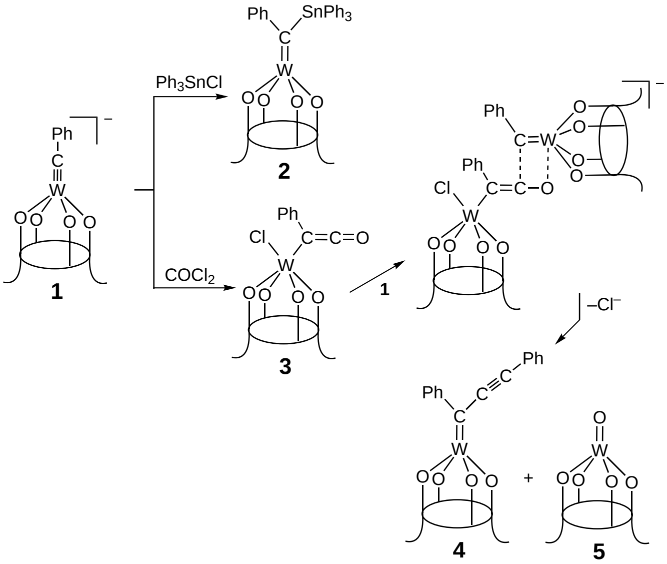
The presence of a heteroatom at the alkylidene carbon atom moves the properties of metal–alkylidene complexes to the borderline of Fischer carbene chemistry.[1] The changes in the M=C bond polarization caused by the heteroatom and the introduction of functional groups increases the possible use of the metal–alkylidene[2] synthon both in organic and organometallic synthesis.[3] Anionic tungsten–alkylidyne derivatives, exemplified by [(cal)W≡CPh] (**1**,[4] H_4cal = *p-t*Bu-calix[4]arene; Scheme 1), are the appropriate starting materials for entering the area of functionalized metal–alkylidenes.[5–7] Two major complementary synthetic routes have been devised to this purpose. The first is the reaction of **1** with a variety of electrophiles, such as Ph_3SnCl (Scheme 1). The tin derivative **2** may be particularly useful in transmetalation reactions with transition metal derivatives. The reaction with $COCl_2$, when carried out with two equivalents of **1**, proceeded straight to an equimolar mixture of **4** and **5**. The difference in



Scheme 1. Synthetic pathways to functionalized alkylidenes. The counterion M^+ of the anionic complexes is $Mg_{0.5} \cdot 6THF$.

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