Notizen / Notes

Macrocyclic Pyridinophanetetraene

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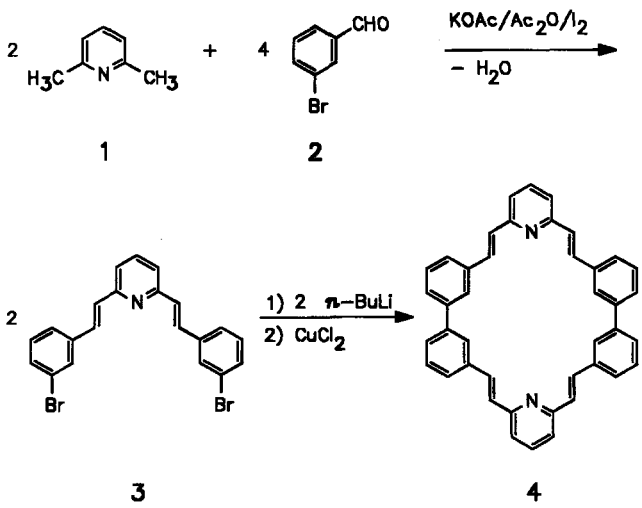
The new pyridinophanetetraene **4** has been prepared in a two-step synthesis by a modified Kharash coupling reaction of 2,6-bis[3-lithio-(*E*)-styryl]pyridine with copper(II) chloride. Starting from isomerically pure 2,6-bis[3-bromo-(*E*)-styryl]pyridine (**3**), the cyclization reaction takes place without rearrangement of the stilbazole double bonds. The electronic spectrum of **4** shows characteristic differences when compared to that of its open-chain analogue 2,6-bis[(*E*)-styryl]pyridine (**7**).

Cyclophane polyenes have been the object of a number of investigations[1]. Due to their non-rigid structure, they usually exhibit a variety of conformations, depending on their ring size, the substitution pattern of the aromatic rings, and the configuration of the double bonds.

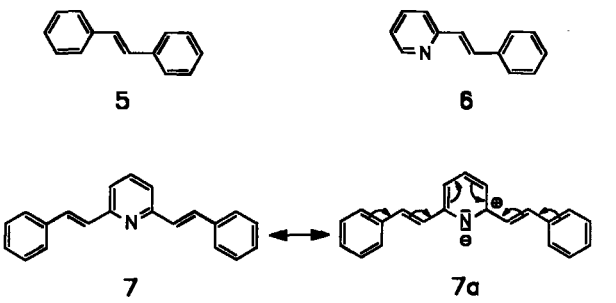
Hitherto the majority of cyclophane polyenes, which mostly contain (*Z*)-configurated double bonds, have been synthesized by a Wittig reaction, because it allows to control the stereochemistry to a certain extent[2]. Whereas most of these compounds are hydrocarbons, the incorporation of furan, thiophene, and ferrocene units has also been accomplished[3]. The synthesis of pyridinophane polyenes according to this route, however, seems to be more difficult as we conclude from the limited number of papers published in this domain[4]. For this reason and because of the *all*-(*E*) configuration of the macrocycle **4**, we decided to adopt a different synthetic strategy with the intention of opening a new and general access to phane-type polyenes.

From a thermodynamical viewpoint the (*E*) configuration of the stilbazole units is the most stable one, and there should be no problem of isomerization during a coupling reaction; thus, we decided to introduce the double bonds prior to cyclization. The latter should be accomplished by a double Kharash reaction, thus linking the benzene rings of **3** to form biphenyl units.



The synthesis of the dibromo-substituted distyrylpyridine precursor **3** was effected by an aldol- or Perkin-type condensation of 2,6-lutidine (**1**) with an excess of 3-bromobenzaldehyde (**2**)[5]. The reaction was performed in refluxing acetic anhydride using potassium acetate as a base and a catalytic amount of iodine. After separation from small amounts of 3-bromocinnamic acid formed as a byproduct, the only isomer to be isolated was the (*E*,*E*) stereoisomer of 2,6-bis[3-bromostyryl]pyridine (**3**). This isomer was subsequently dilithiated by *n*-butyllithium in THF and coupled by treatment with copper(II) chloride. The macrocycle **4** was formed in 8% yield, high-dilution techniques not being used. So far, only a few mg of the substance could be isolated in the form of pure colourless needles (high resolution MS, analytical HPLC). Its structure [*all*-(*E*)-**4**] could be ascertained by H-H-correlated ^{1}H-NMR and UV spectroscopy.

The new pyridinophanetetraene **4** exhibits a strong violet fluorescence and – in the context of our concept of modifying classical chromophores by incorporation into macrocyclic structures[6] – we have compared its electronic absorption and emission spectra to those of its open-chain analogues **3**, **6**, and **7**.



Compared to the macrocyclic diarylhexatrienes[6] the pyridinophane **4** has a less rigid structure. It may adopt several conformations by rotation around the formal single bonds. Strictly speaking, it does not belong to the class of polyene hydrocarbons, but nevertheless shows significant similarities to stilbene-type compounds because of its styrylpyridine units.

While the UV spectrum of stilbene (**5**) shows only one single band above 250 nm (294 nm, ethanol[7]), 2-styrylpyridine (**6**) exhibits two absorptions in this region: one at shorter wavelength (ca. 280

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nm, ethanol[7]) and a more intense one at longer wavelength (310 nm, ethanol[7]). Two bands are also present in the spectra of 2,6-distyrylpyridine (7) [290 nm (42700), 335 (25100); ethanol[7] resp. 293 (40000), 345 (25000); DMF[8]], of 2,6-bis[3-bromostyryl]pyridine (3) [293 nm (40000), 341 (22000); 1,4-dioxane], and of the macrocycle 4 [275 nm (81000), 341 (35000); 1,4-dioxane]. In these cases however, the band on the shorter wavelength side is the more intense one.

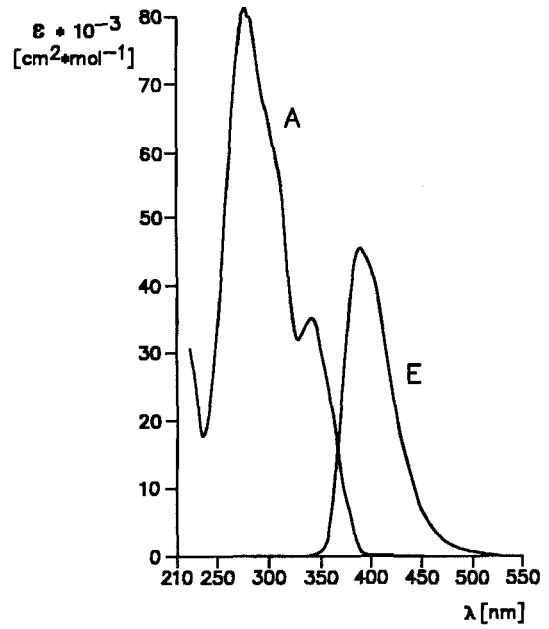

Figure 1. Absorption (A) and (qualitative) emission (E) spectra of pyridinophane 4 (1,4-dioxane, T = 293 K, λ_{ex} = 350 nm)

Earlier investigations have shown that the connection of two chromophores by a *m*-disubstituted benzene ring does not induce a bathochromic shift to the electronic absorption. The chromophores have to be considered as isolated, and only a hyperchromic effect proportional to their number can be observed, e.g. in *m*-distyrylbenzene[9]. This relation is well verified by the short-wavelength-band extinction coefficient of cyclophane 4 which is nearly twice as large as that of the 2,6-distyrylpyridines 3 and 7. The long-wavelength-band extinction coefficient, however, is smaller than expected, so that the ratio of the band intensities is not the same in the macrocycle (4) as in the open-chain analogues (3 and 7).

Whereas a *m*-disubstituted benzene ring does not cause an extension of a chromophore, the situation is different for 2,6-disubstituted pyridines. In these compounds, conjugation is not entirely suppressed, as it is demonstrated by the dipolar structure **7a**[7]. Thus, when passing from 2-styrylpyridine (6) to the 2,6-distyrylpyridines 3 and 7 as well as to phane 4, a red shift of the longest wavelength band is noticed, which is nearly equal for all three polyenes. The short wavelength absorption of pyridinophane 4, however, is blue-shifted by 17 nm when compared to the open-chain analogues 3 and 7.

All styrylpyridine compounds discussed here exhibit another absorption between 220 and 230 nm, whose maximum lies below 220 nm only for the phane 4.

When irradiated at 366 nm, 4 exhibits an intense violet fluorescence. In contrast to the broad emission maximum of 2,6-distyrylpyridine (7) (387, 404 nm, DMF[8]; 412–428 nm, benzene[5a]), the fluorescence spectrum of 4 shows a sharp unstructured maximum at 390 nm (1,4-dioxane, excitation maximum at λ = 350 nm). Thus, if solvent effects are neglected, 4 absorbs at nearly the same but emits at a shorter wavelength than its open-chain analogue 2,6-distyrylpyridine (7).

Whereas the poorly structured UV spectrum of the new macrocyclic tetraene 4 shows similarities in its general shape to that of the reference substances 2-styrylpyridine (6), 2,6-distyrylpyridine (7), and 2,6-bis[3-bromostyryl]pyridine (3), it exhibits marked differences in the exact location and extinction coefficients of the bands. Conformational effects as well as reciprocal influences of the pyridine dipoles may contribute to the observed spectroscopic properties. The macrocycle 4 is subdivided into two chromophores, not by the 2,6-disubstituted pyridine units, but by the *m*-disubstituted benzene rings.

The synthetic approach described in this note should render accessible a variety of carbo- and heterocyclic phane polyenes. The latter (e.g. 4) – containing donor atoms at a fixed distance and relative orientation – may be particularly interesting with respect to their ability of including guest molecules with acidic protons by hydrogen bonding.

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Experimental

Melting points are uncorrected. – MS: MS-50 (AEI). – ^{1}H NMR: WH-400 (400 MHz) (Bruker Physik AG). – IR: Unicam SP-1100 IR spectrometer (Pye Unicam). – UV: CARY-219 spectrophotometer (Varian Associates). – Fluorecence spectra: 204-A fluorescence spectrometer (Perkin-Elmer). – Elemental analyses: Mikroanalytisches Laboratorium, Institut für Organische Chemie und Biochemie, Universität Bonn.

(E,E)-2,6-Bis[3-bromostyryl]pyridine (3): 5.36 g (50 mmol) of 2,6-lutidine, 27.8 g (150 mmol) of 3-bromobenzaldehyde, 4.9 g (50 mmol) of potassium acetate, and a catalytic amount of iodine are refluxed for 48 h in 15.3 g (150 mmol) of acetic anhydride. After cooling to room temp., the reaction mixture is poured on 40% ice/sodium hydroxide. The resulting precipitate is ground and extracted for 1 h. After filtration, it is washed thoroughly with water and dried in vacuo. The crude product is purified by flash chromatography (silica gel, dichloromethane) and subsequent crystallization from ethanol to yield 9.7 g (44%) of isomerically pure (*E,E*)-3, m.p. 127–128°C. – MS (70 eV): *m/z* (%) = 441 [M^+, $^{79}Br_2$, $^{81}Br_2$], 440 [M^+ – H, $^{79}Br_2$, $^{81}Br_2$] (100). – ^{1}H NMR (400 MHz, $CDCl_3$, δ = 7.25): δ = 7.16 (d, ^3J = 16 Hz, 2H; olefinic CH attached to pyridine), 7.23 (d, ^3J = 7.7 Hz, 2H; pyridine H), 7.24 (dd, ^3J = 7.8, ^3J = 7.9 Hz, 2H; aromatic H), 7.41 (ddd, ^3J = 7.9, ^4J = 2, ^4J = 1 Hz, 2H; aromatic H), 7.50 (dddd, ^3J = 7.8, ^4J = 1.6, ^4J = 1, ^4J = 0.6 Hz, 2H; atomatic H), 7.63 (t, ^3J = 7.7 Hz, 1H; pyridine H), 7.64 (d, ^3J = 16 Hz, 2H; olefinic CH attached to benzene), 7.75 (m, 2H; aromatic H). – ^{13}C NMR (50.27 MHz, $CDCl_3$): δ = 121.25 (CH), 122.94 (CBr), 125.87 (CH), 129.43 (CH), 129.88 (CH), 130.26 (CH), 131.13 (CH), 131.40 (CH), 137.19 (CH), 138.96 (C), 154.84 (C). – IR (KBr): $\tilde{\nu}$ = 690 cm^{-1} (s), 740 (s), 805 (s), 985 (s), 1455 (s), 1480 (s), 1570, 1585, 1600 (m, s). – UV (dioxane) [nm]: λ_{max} (ε) = 236 (25000), 293 (40000), 341 (22000).

$C_{21}H_{15}Br_2N$ (441.2) Calcd. C 57.15 H 3.43 N 3.17
Found C 57.34 H 3.50 N 3.38

all-(E)-[2](2,6)Pyridino[2](3,3')biphenylo[2](2,6)pyridino[2](3,3')biphenylophane-1,15,23,37-tetraene (4): 6.62 g (15 mmol) of 3 is dissolved in 350 ml of absol. THF under argon. After cooling to –78°C, 23.5 ml (37 mmol) of a solution of *n*-butyllithium (1.6 M in hexane) is added dropwise. After stirring for 15 min, 6.05 g (45

mmol) of copper(II) chloride (dried in vacuo at 120°C for 3 h) is added in one portion. The reaction mixture is slowly heated to room temp. and then refluxed for 2 h. It is then hydrolyzed at 20°C by addition of 100 ml of 2 N H_2SO_4 and stirred for 1 h. The organic layer is separated and the aqueous one extracted several times with THF. The combined organic layers are washed with concentrated aqueous ammonia until it remains colourless. The extracts are dried with magnesium sulfate, and the solvent is removed in vacuo. The total yield of the poorly soluble phane is evaluated from the HPLC chromatogram of the partially purified product to be 0.34 g (8%). However, so far only a few mg of pure **4** could be isolated by chromatography of the crude brown oil (silica gel, dichloromethane/cyclohexane 2:1, v/v). Purity is verified by HPLC chromatography: HPLC pump M-305, Holochrome detector (λ = 360 nm), Gilson-Abimed; LiChrosorb RP-18, toluene, 2.5 ml/min, 10 bar, R_t = 23.75 min. – **4**: m.p. >250°C (dec.). – MS (70 eV): *m/z* (%) = 562.2413 [M^+, calcd. 562.2409], 561 [M^+ – H] (100), 281 [M^{2+}], 280.5, 280. – ^{1}H NMR (400 MHz, [D_8] THF): δ = 7.30 (d, ^3J = 8 Hz, 4H; pyridine H), 7.42 (d, ^3J = 16 Hz, 4H; olefinic CH attached to pyridine), 7.48 (t, ^3J = 7.8 Hz, 4H; aromatic H), 7.70 (t, ^3J = 8 Hz, 2H; pyridine H), 7.68 (d, ^3J = 7.5 Hz, 4H; atomatic H), 7.79 (d, ^3J = 7.5 Hz, 4H; aromatic H), 8.07 (d, ^3J = 16 Hz, 4H; olefinic CH attached to benzene), 8.13 (m, 4H; aromatic H). – IR (KBr): $\tilde{\nu}$ = 570 cm^{-1} (w), 705 (s), 740 (m), 810 (vs), 990, 1000 (d,s), 1180, 1200 (d,w), 1460 (s), 1590 (m), 2980 (w), 3100 (w). – UV (dioxane) [nm]: λ_{max} (ε) = 275 (81000), 341 (35000).

CAS Registry Numbers

1: 108-48-5 / **2**: 3132-99-8 / **3**: 129812-49-3 / **4**: 129812-50-6

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