An Unusual β-Oxidation of *N*-Functionalized Alkyl Chains by 1*H*-Imidazole

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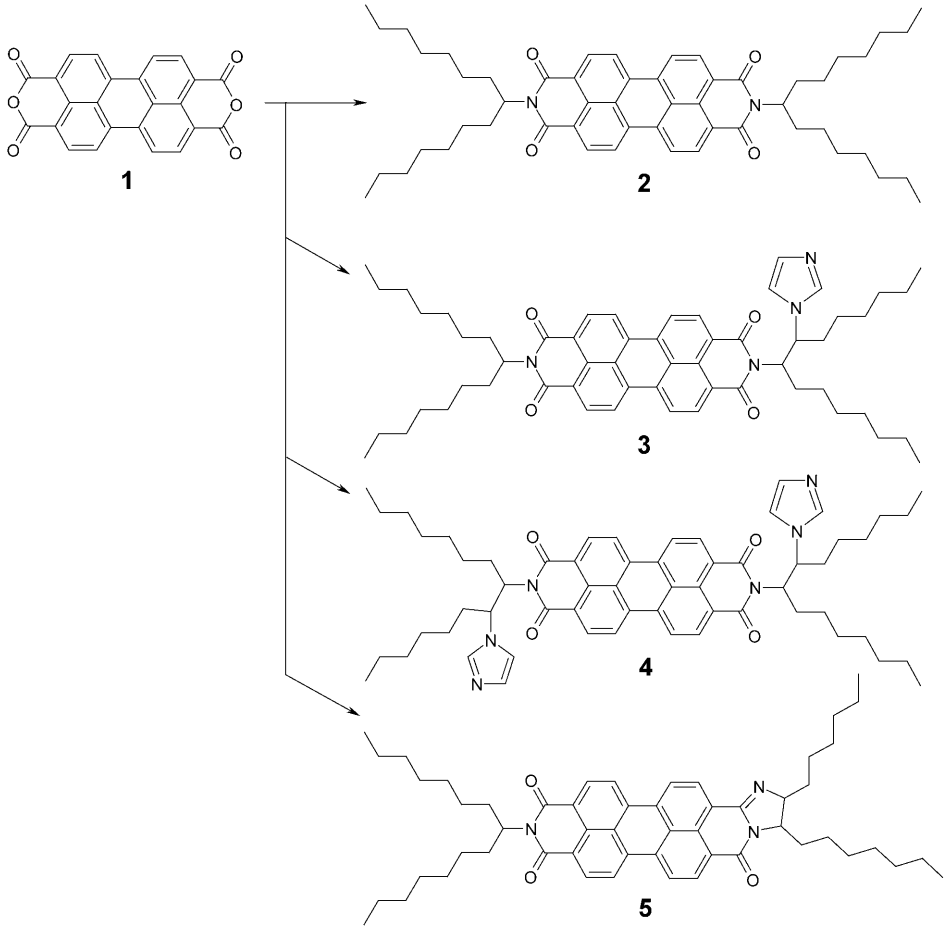
The 1*H*-imidazole-mediated condensation of primary aliphatic amines with perylene-3,4 : 9,10-tetracarboxylic bis-anhydride resulted in by-products where the aliphatic group was functionalized in the β-position by imidazole units.

The reaction of cyclic aromatic anhydrides such as **1** with primary amines to the carboxylic imides **2** [1] (see *Scheme*) is remarkably favored by the application [2][3] of 1*H*-imidazole [4] as the reaction medium. A temperature of some 200° (4 h reaction time) required for the condensation of aromatic amines with **1** in media such as quinoline can be lowered to 130° or even 100° in 1*H*-imidazole. Little is known about this remarkable effect of more than 18 $kJ \cdot mol^{-1}$ in free enthalpy. We examined the formation of by-products to get more information about the condensation reaction.

We carried out the well-established [2] condensation of **1** with (1-hexylheptyl)amine in larger-scale amounts and carefully separated by-products. However, the isolation of pure by-products proved to be difficult. Better results were obtained with the condensation of the bis-homologue (1-heptyloctyl)amine with **1** where an analogue pattern of products was obtained. The crude product mixture was separated by column chromatography (silica gel, $CHCl_3$) which gave a very small amount of a yellow forerun, the analytically pure main fraction **2** (85% isolated), a mixture of three by-products **3**–**5**, each in low yield, and some unchanged starting material (see *Scheme*). The yellow forerun is an efficient fluorescence quencher, especially for solid dyes; however, the yield was so low that its structure could not be established. The mixture of by-products **3**–**5** could not be resolved by column chromatography but successfully by the subsequent application of a chromatotron (rotary chromatograph) [5].

Surprisingly, in the by-products **3** and **4**, the saturated aliphatic side chain of dye **2** was substituted in β-position by a 1*H*-imidazol-1-yl substituent. The formation of the additional product **5** can be explained by a similar substitution. Since no other products could be detected, the substitution reaction of the aliphatic chain seems to occur regiospecifically at the β-position. The oxidation and functionalization of a saturated aliphatic chain is atypical for **2** and may be a consequence of a radical-type reaction during the condensation, because pure **2** is not affected by a mixture of 1*H*-imidazole and (1-heptyloctyl)amine under the reaction conditions. A photo-induced reaction by daylight is improbable for the formation of the by-products because their yield seems to be independent from illumination, and they are obtained even in very concentrated, nearly black mixtures. A carbonyl O-atom may be responsible for an initiating H-abstraction

Scheme. *Reaction Products of the Condensation of* **1** *with Long-Chain Primary Alkylamines in 1*H*-Imidazole*



because a favourable six-membered ring orientation can be formulated to explain the regiospecifity.

The novel oxidation reaction of saturated aliphatic side chains under the conditions of the condensation reaction is not a singular result but seems to be more general because the reported [6] aromatization of a perylene dihydroimidazole to an imidazole derivative proceeds only during the condensation and can be formally also described as a β-oxidation. A blocking of the β-position, such as present on condensation of neopentanediamine (=2,2-dimethylpropane-1,3-diamine) leads to oxidation products in the γ-position [7].

The novel functionalization of aliphatic side chains is not only of interest concerning information about details of the condensation but also because of the introduction of the basic 1*H*-imidazole heterocycle. Basic groups at similar positions in the side chains of perylene bis-imides are known [8][9] for the intercalation into DNA.

Dye **5** is highly fluorescent and exhibits a bathochromic shift in the UV/VIS spectra compared with **2** (see the *Figure*). The UV/VIS absorption is similar to a previously prepared dye with no side chains at the dihydropyrrole ring. The novel compound **5** exhibits a higher solubility because of the additional long-chain aliphatic groups.

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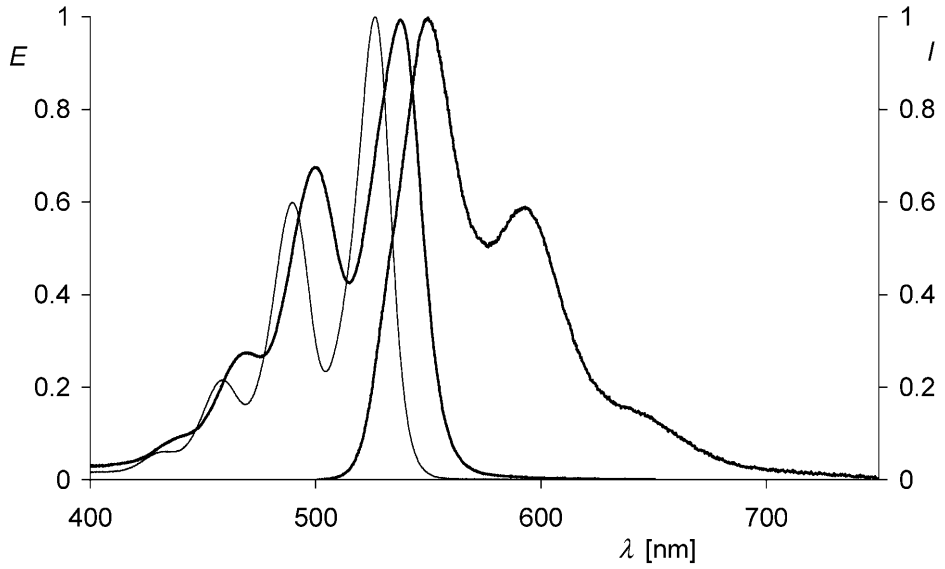

Figure. *UV/VIS absorption* (*E*) *and fluorescence* (*I*) *spectra of* **5** (bold lines left and right, resp.) *and absorption spectrum of* **2** (thin line).

Experimental Part

1. *General.* UV Spectra: λ_{max} (E_{rel}) in nm. Fluorescence: λ_{max} (I_{rel}) in nm. Fluorescence quantum yield: reference 2,9-bis(1-hexylheptyl)anthra[2,19]-*def*:6,5,10-*d′e′f′*]diisoquinoline-1,3,8,10-tetrone with $\phi = 100\%$. IR Spectra: in cm^{-1}. ^{1}H-NMR Spectra: δ in ppm. MS: in *m*/*z* (rel. %).

2. *Reaction of Perylene-3,4:9,10-tetracarboxylic Bis-anhydride* (**1**) *with 1-(Heptyloctyl)amine and* 1*H-Imidazole.* According to [2], (1-heptyloctyl)amine (7.00 g, 30.8 mmol), **1** (5.14 g, 13.1 mmol), and 1*H*-imidazole (20 g) were allowed to react for 4 h at 160° under Ar: 10.2 g (*ca.* 96%) of dye material. Column chromatography (silica gel, $CHCl_3$) gave a yellow forerun, *2,9-bis(1-heptyloctyl)-anthra[2,1,9*-def:*6,5,10*-d′e′f′*]diisoquinoline-1,3,8,10-tetrone* (**2**) [10] (9.00 g, 85%; anal. pure) and 200 mg of a dye mixture. The latter was separated by means of a chromatotron [5] (rotatory chromatograph, silica gel, CH_2Cl_2/acetone 20:1). Some material was firmly adsorbed, a forerun was discarded, and three fractions, **3**–**5**, were collected.

*2-[(1-Heptyl-2-(1*H*-imidazol-1-yl)octyl]-9-(1-heptyloctyl)anthra[2,1,9*-def:*6,5,10*-d′e′f′*]diisoquinoline-1,3,8,10-tetrone* (**3**): 67 mg (0.5%). M.p. 287–291°. R_f (silica gel, $CHCl_3$) 0.09. R_f (silica gel, $CHCl_3$/EtOH 10:1) 0.33. R_f (silica gel, CH_2Cl_2/acetone 10:1) 0.77. UV ($CHCl_3$): 528 (1.00), 491 (0.590), 460 (0.206), 435 (0.051), 370 (0.034). Fluorescence ($CHCl_3$): 536 (1.00), 579 (0.517), 627 (0.118) 685 (0.016). Fluorescence quantum yield ($\lambda_{exc.}$ 490 nm, $E_{528} = 0.0593$/l cm in $CHCl_3$): 95%. IR (KBr): 2925*s*, 2854*m*, 1700*s*, 1655*m*, 1595*m*, 1508*w*, 1458*w*, 1403*w*, 1344*m*, 1264*m*, 1175*w*, 1112*w*, 854*w*, 810*m*, 741*w*. ^{1}H-NMR ($CDCl_3$): 0.84 (*t*, 4 Me); 1.23–1.35 (*m*, 38 H, CH_2); 1.05–2.52 (*m*, 8 H, CH_2); 4.90–5.15 (*m*, 3 H, CH); 6.77 (*s*, 1 H im.); 6.87 (*s*, 1 H, im.); 7.33 (*s*, 1 H, im.); 8.53–8.68 (*m*, 8 H, perylene). MS (70 eV): 879 (11), 878 (37), 877 (60, M^+), 713 (9), 712 (18), 699 (12),

698 (25), 669 (9), 668 (18), 667 (18), 614 (10), 602 (13), 601 (48), 600 (77), 403 (15), 392 (24), 391 (81), 390 (100), 373 (12), 179 (15), 83 (27). HR-MS: 875.5540 ($C_{57}H_{71}N_4O_4^+$; calc. 875.5475). Anal. calc. for $C_{57}H_{72}N_4O_4$ (877.2): C 78.04, H 8.27, N 6.39; found C 77.31, H 7.69, N 6.81.

*2,9-Bis[1-heptyl-2-(1*H*-imidazol-1-yl)octyl]anthra[2,1,9*-def:*6,5,10*-d′e′f′*]diisoquinoline-1,3,8,10-tetrone* (**4**): 13 mg (0.1%). R_f (silica gel, $CHCl_3$/EtOH 10 : 1) 0.04. UV ($CHCl_3$): 528.5 (1.00), 491 (0.649), 461.5 (0.288), 436.5 (0.122). Fluorescence ($CHCl_3$): 536 (1.00), 578 (0.587), 626 (0.174), 689 (0.029). Fluorescence quantum yield ($\lambda_{exc.}$ 490 nm, $E_{528.5}=0.0482$/l cm in $CHCl_3$): 85%. MS (70 eV): 943 (3, M^+), 942 (7), 874 (6), 858 (12), 778 (10), 777 (16), 764 (11), 763 (18), 679 (12), 668 (13), 667 (15), 600 (7), 487 (7), 455 (19), 454 (14), 404 (13), 403 (24), 392 (28), 391 (100), 390 (88), 373 (15), 276 (12), 179 (26), 165 (20), 128 (12), 95 (13), 69 (22), 68 (57), 55 (13).

*10-Heptyl-2-(1-heptyloctyl)-11-hexyl-10,11-dihydroimidazo[2,1-*a*]anthra[2,1,9*-def:*6,5,10*-d′e′f′*]diisoquinoline-1,3,8(2*H*)-trione* (**5**): 3 mg (0.03%). R_f (silica gel, $CHCl_3$) 0.09. R_f (silica gel, $CHCl_3$/EtOH 10 : 1) 0.95. R_f (silica gel, CH_2Cl_2/acetone 20 : 1) 0.77. UV ($CHCl_3$): 538 (1.00), 500 (0.683), 469.5 (0.281), 439 (0.099). Fluorescence ($CHCl_3$): 550 (1.00), 593 (0.590), 642 (sh, 0.151). Fluorescence quantum yield ($\lambda_{exc.}$ 490 nm, $E_{538}=0.0516$/l cm in $CHCl_3$): 87%. IR (KBr): 2956*m*, 2924*s*, 2855*m*, 1697*s*, 1657*s*, 1620*w*, 1595*w*, 1462*w*, 1344*m*, 808*w*, 744*w*. ^{1}H-NMR ($CDCl_3$): 0.80–0.86 (*m*, 4 Me); 1.19–1.35 (*m*, 38 H, CH_2); 1.40–1.70 (*m*, 2 H, CH_2); 1.70–1.90 (*m*, 1 H, CH_2); 1.90–2.10 (*m*, 2 H, CH_2); 2.10–2.30 (*m*, 3 H, CH_2); 4.05–4.20 (*m*, 1 H, CH); 4.30–4.50 (*m*, 1 H, CH); 5.12–5.30 (*m*, 1 H, CH); 8.53–8.64 (*m*, 8 H, perylene). MS (70 eV): 809 (12), 808 (22, M^+), 807 (10), 806 (12), 725 (11), 724 (46), 723 (96), 711 (11), 710 (52), 709 (100), 625 (5), 604 (14), 603 (6), 602 (17), 512 (10), 498 (10), 414 (13), 338 (6), 337 (20), 335 (25), 210 (13), 111 (9), 98 (6), 97 (22), 85 (6), 84 (11), 83 (28), 82 (7), 71 (11), 70 (19), 69 (32), 67 (10), 57 (23), 56 (21), 55 (34), 44 (94), 43 (24), 41 (22). HR-MS: 807.5319 ($C_{54}H_{69}N_3O_3^+$; calc. 807.5338).

Reaction of **1** *with 1-(Hexylheptyl)amine and 1*H*-Imidazole.* According to [2], 1-(hexylheptyl)amine (24.7, 124 mmol), **1** (20.7 g, 52.8 mmol), and 1*H*-imidazole (30 g) were allowed to react for 4 h at 160° under Ar: 39.3 g (*ca.* 98%) of dye material. Column chromatography (silica gel, $CHCl_3$) gave a yellow forerun, *2,9-bis(1-hexylheptyl)anthra[2,1,9*-def:*6,5,10*-d′e′f′*]diisoquinoline-1,3,8,10-tetrone* [11] (32.7 g, 82%; anal. pure), and 740 mg of a dye mixture. The latter was separated by means of a chromatotron [5] (rotatory chromatograph, silica gel, CH_2Cl_2/acetone 20 :1). Some material was firmly adsorbed, a forerun was discarded, and the two following fractions were collected.

*9-(1-Hexylheptyl)-2-[1-hexyl-2-(1*H*-imidazol-1-yl)heptyl]anthra[2,1,9*-def:*6,5,10*-d′e′f′*]diisoquinoline-1,3,8,10-tetrone:* 300 mg (0.7%). M.p. 275–278°. R_f (silica gel, toluene/acetone 4 : 1) 0.15. R_f (silica gel, $CHCl_3$/EtOH 10 : 1) 0.36. R_f (silica gel, $CHCl_3$/AcOH 10 : 1) 0.14. R_f (silica gel, CH_2Cl_2/acetone 20 : 1) 0.27. UV ($CHCl_3$): 528 (83200), 491 (48600), 459 (16500), 434 (3600). Fluorescence ($CHCl_3$): 536, 576. Solid-state fluorescence: 626. IR (KBr): 2955*m*, 2927*s*, 2857*m*, 1698*s*, 1658*s*, 1594*s*, 1578*w*, 1495*w*, 1458*w*, 1435*w*, 1405*m*, 1339*s*, 1258*w*, 1174*w*, 1126*w*, 1107*w*, 854*w*, 810*w*, 748*w*. ^{1}H-NMR ($CDCl_3$): 0.81 (*t*, 4 Me); 1.21–1.32 (*m*, 30 H, CH_2); 1.70–1.95 (*m*, 4 H, α-CH_2); 1.95–2.10 (*m*, 1 H, α-CH_2); 2.10–2.29 (*m*, 2 H, α-CH_2); 2.30–2.48 (*m*, 1 H, α-CH_2); 4.98–5.09 (*m*, 1 H, CH); 5.09–5.19 (*m*, 1 H, CH); 5.38–5.50 (*m*, 1 H, CH); 6.75 (*s*, 1 H, im.); 6.88 (*s*, 1 H, im.); 7.32 (*s*, 1 H, im.); 8.50–8.67 (*m*, 8 H, perylene). ^{13}C-NMR ($CDCl_3$): 14.5 (*q*); 22.9 (*t*); 23.0 (*t*); 26.4 (*t*); 26.8 (*t*); 27.1 (*t*); 27.3 (*t*); 29.3 (*t*); 29.6 (*t*); 32.0 (*t*); 32.2 (*t*); 32.8 (*t*); 33.9 (*t*); 55.2 (*d*); 57.8 (*d*); 59.4 (*d*); 117.1, 122.4, 123.1, 123.3, 123.6, 126.8, 129.3, 129.8, 131.8, 132.5, 134.6, 135.3, 137.7 (13 *s*); 164.2 (*s*, C=O); 164.6 (*s*, C=O). MS (70 eV): 822 (10), 821 (36, $[M+H]^+$), 820 (61, M^+), 752 (5, $[M-\text{imidazole}]^+$), 749 (3, $[M-C_5H_{11}]^+$), 735 (2, $[M-C_6H_{13}]^+$), 670 (6), 669 (13), 656 (12), 655 (24), 640 (8), 639 (17), 638 (5, $[M-C_{13}H_{26}]^+$), 586 (6), 585 (15), 574 (12), 573 (42), 572 (67, $[M^+-C_{13}H_{26}-\text{imidazole}]^+$), 473 (5), 404 (11), 403 (24), 393 (6), 392 (29), 391 (98), 390 (100), 374 (8), 373 (27), 346 (8), 345 (15), 248 (8), 166 (5), 165 (19), 151 (11), 109 (9), 95 (11), 85 (9), 83 (13), 69 (11), 55 (17). ESI-MS: 2463 (2, [3 $(M+H)]^+$), 1713 (20), 1712 (31), 1711 (23), 1643 (13), 1642 (42, [2 $(M+H)]^+$), 822 (70, $[M+2\ H]^+$), 821 (100, $[M+H]^+$), 753 (13). HR-MS: 820.4955 ($C_{53}H_{64}N_4O_4^+$; calc. 820.4927).

*2,9-Bis[1-hexyl-2-(1*H*-imidazol-1-yl)heptyl]anthra[2,1,9*-def:*6,5,10*-d′e′f′*]diisoquinoline-1,3,8,10-tetrone:* 34 mg (0.07 %). R_f (silica gel, $CHCl_3$/EtOH 10 : 1) 0.09. MS (70 eV): 886 (1, M^+), 822 (7), 821 (22), 820 (39, $[M-C_3H_2N_2]^+$), 753(6), 752 (7, $[M-C_3H_2N_2-\text{imidazole}]^+$), 670 (8), 669 (15), 656 (7), 655 (13), 640 (6), 639 (12), 585 (10), 574 (10), 573 (33), 572 (51, $[M-C_{13}H_{26}-2\ C_3H_2N_2]^+$), 404 (9), 403 (17), 393 (5), 392 (24), 391 (84), 390 (100), 374 (6), 373 (19), 346 (7), 345 (11), 248 (7), 165 (8), 151 (8), 69 (5), 55 (7).

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