

Synthesis and conformations of cross-conjugated polyenes containing heterocyclic moieties with diverse structures

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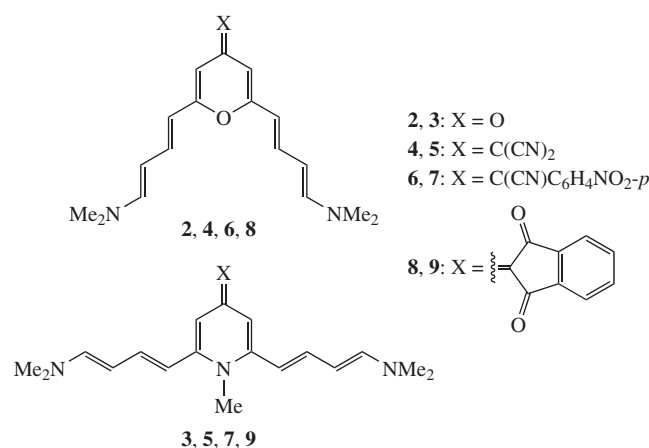
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New non-linear cross-conjugated polyenes containing a central 4-ylidene-substituted pyran or *N*-methyl-4-dihydropyridine ring have been synthesized. Interaction of chromophores in these compounds occurs through the ylide group linked to the heterocycles.

Previously, we performed the reaction of β -dimethylaminoacrolein aminal $\text{Me}_2\text{NCH}=\text{CHCH}(\text{NMe}_2)_2$ **1** with 2,6-dimethyl-4-pyrone or *N*-methyl-2,6-dimethylpyridin-4-one to give ketocyanine dyes **2** and **3** (cross-conjugated polyene ω,ω' -bisamino-ketones with a central pyran or dihydropyridine moiety) containing two aminopolyene chromophores with equal lengths linked by a carbonyl group and a central bridge.^{1,2}

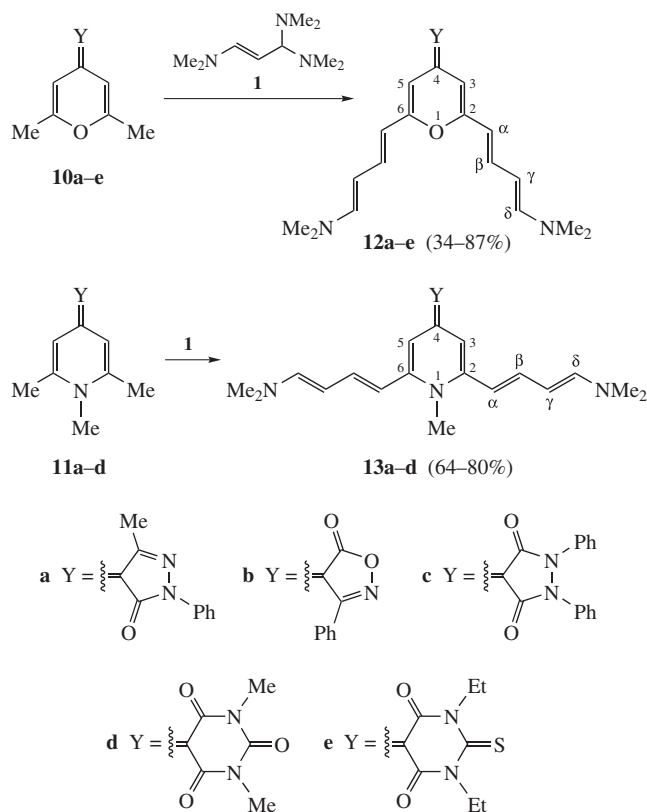


Replacement of the bridging O atom by an NMe group drastically changes the dye absorption spectrum, since in compound **2** the chromophores are arranged at a sharp angle to each other, whereas at an obtuse angle in compound **3**.^{3–5}

The same phenomenon occurred in the case of cross-conjugates ω,ω' -dimethylaminopolyenes **4–9** containing a central pyran or *N*-methyl-4-dihydropyridine moiety. The aminopolyene chromophores in these compounds interact through 2,2-dicyano-, 2-cyano-2-(4-nitrophenyl)- or dioxindan-2-ylidene groups located at 4-position of the heterocycle.⁶

Previously, interesting data were reported that new chromophores based on pyranone and functionalised conjugated aldehydes containing bridging moieties demonstrated nonlinear optical properties,⁷ whereas pyran dyes with push-pull structures incorporating a CN group were found to be promising for solar energy cells.⁸ Furthermore, a D- π -A- π -D dye containing a central acceptor core A similar to the core of polyene **3** and heterocyclic donor groups D was recently synthesized.⁹

In view of this, we decided to synthesize new cross-conjugated polyenes containing a pyran or dihydropyridine ring and a methylidene acceptor linked to carbonyl-containing polynitrogen or nitrogen-oxygen heterocycles with various structures. Of these,



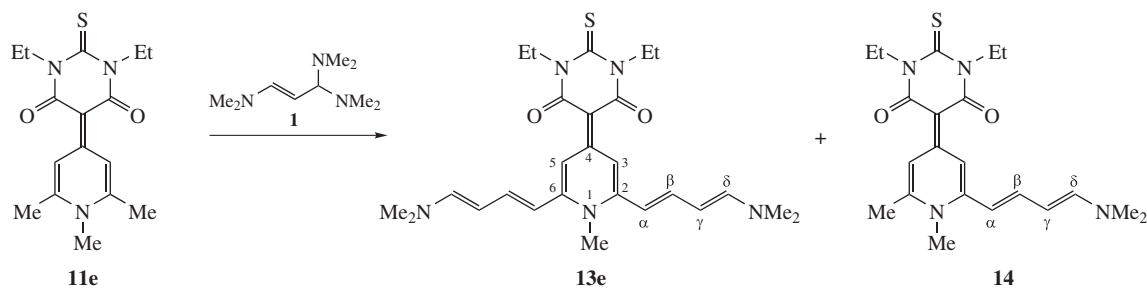
Scheme 1

ylidene derivatives of barbituric acids are promising not only as biologically active compounds¹⁰ but also as potential dyes.¹¹

To perform this task, we studied the reaction of aminal **1** with substituted 2,6-dimethyl-4H-pyrans **10a–e** and 1,2,6-trimethyl-1,4-dihydropyridines **11a–e** containing the corresponding heterocycles at 4-position (Schemes 1 and 2).

Compounds **10a–e** were obtained by heating 2,6-dimethyl-4H-pyran-4-one with heterocyclic compounds containing a reactive methylene group (the residue of the latter is denoted as Y in Scheme 1) in acetic anhydride. Substituted 1,2,6-trimethyl-1,4-dihydropyridines **11a–e** were synthesized from the corresponding pyrans **10a–e** by treatment with 40% MeNH₂ aqueous solution or 15% MeNH₂ solution in EtOH (see Online Supplementary Materials).

Dyes **12a–e** and **13a–d** were prepared by condensation of pyrans **10a–e** or dihydropyridines **11a–d** with excess aminal **1** (reactant ratio of 1:3) in the absence of a solvent, except for



Scheme 2

polyenes **12b,e** which were obtained in dry benzene.[†] Note that, though the reaction conditions vary, in all cases (except for dihydropyridine **11e**), the reaction of amination **1** involves both methyl groups to afford polyenes containing two polyene chromophores. The reaction of dihydropyridine **11e** with amination **1** in dry benzene without heating gave a mixture of polyene **13e** and tetraene **14** in 2:3 ratio (Scheme 2).[‡]

[†] 4-{2,6-Bis[(1E,3E)-4-dimethylaminobuta-1,3-dienyl]-4H-pyran-4-ylidene}-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one **12a**. Amination **1** (0.18 g, 1.08 mmol) was added to substituted pyran **10a** (0.1 g, 0.36 mmol). The reaction mixture was heated for 15 min at 65 °C, then evaporated *in vacuo*. Dry Et₂O was added to the residue; the precipitate that formed was filtered off and washed with Et₂O to give 0.12 g (76%) of polyene **12a** as dark violet crystals, mp 230–233 °C. UV [$\lambda_{\max}/\text{nm}$ (ϵ): 380 (44 850), 520 (67 600), 580 (sh., 39 000) (EtOH); 360 (26 000), 540 (46 800) (CHCl₃). ¹H NMR (DMSO-*d*₆, 80 °C) δ : 5.87 (d, 2H, H^a, *J* 14.7 Hz), 7.29–7.33 (m, 2H, H^b), 5.31 (t, 2H, H^c, *J* 12.0 Hz), 7.12 (d, 2H, H^d, *J* 12.7 Hz), 8.04 (d, 2H, *o*-H_{Ph}, *J* 8.0 Hz), 7.29–7.33 (m, 2H, *m*-H_{Ph}), 7.04 (t, 1H, *p*-H_{Ph}, *J* 7.3 Hz), 2.95 (s, 12H, NMe₂), 7.33 (s, 1H, H^e), 6.50 (s, 1H, H^f), 2.39 (s, 3H, Me). ¹³C NMR (DMSO-*d*₆, 80 °C) δ : 107.58 (C^a), 140.29 (C^b), 97.66 (C^c), 151.28 (C^d), 117.38 (*o*-C_{Ph}), 127.74 (*m*-C_{Ph}), 122.04 (*p*-C_{Ph}), 39.49 (NMe₂), 162.76 (C^e, C^f), 108.28 (C^g, C^h), 17.59 (Me). MS (ESI), *m/z*: 443.2433 [M+H]⁺ (calc. for C₂₇H₃₀N₄O₂, *m/z*: 443.2442).

4-{2,6-Bis[(1E,3E)-4-dimethylaminobuta-1,3-dienyl]-4H-pyran-4-ylidene}-3-phenylisoxazol-5(4H)-one **12b**. Amination **1** (0.33 g, 2 mmol) was added dropwise with stirring to a suspension of substituted pyran **10b** (0.2 g, 0.75 mmol) in 2 ml of dry benzene. The reaction mixture was stirred for 45 min at 20 °C and then concentrated *in vacuo*. The residue (a black viscous substance) was repeatedly triturated with anhydrous Et₂O which then was poured off. EtOH (1 ml) was added to the residue; the mixture was triturated and mixed with water (30 ml). After 1.5 h, the resulting extra-fine precipitate was filtered off and washed with water and diethyl ether to give 0.11 g (34%) of polyene **12b** as dark green crystals, mp 250 °C. UV [$\lambda_{\max}/\text{nm}$ (ϵ): 363 (26 658), 400 (25 177), 495 (54 798), 595 (26 658) (EtOH); 370 (31 100), 518 (53 317), 546 (sh., 44 430) (CHCl₃). ¹H NMR (DMSO-*d*₆, 80 °C) δ : 5.55 (d, 2H, H^a, *J* 12.0 Hz), 7.21 (t, 2H, H^b, *J* 12.0 Hz), 5.31 (t, 2H, H^c, *J* 12.1 Hz), 6.71 (d, 2H, H^d, *J* 12.1 Hz), 7.44–7.55 (m, 5H, Ph), 7.37 (s, 2H, H^e, H^f), 2.91 (s, 12H, NMe₂). ¹³C NMR (DMSO-*d*₆, 80 °C) δ : 109.39 (C^a), 140.30 (C^b), 98.39 (C^c), 150.32 (C^d), 129.00, 128.47, 132.74 (Ph), 162.71 (C^e, C^f), 104.19 (C^g, C^h), 46.37 (NMe₂), 149.82 (Cⁱ), 97.69 (C^j), 105.61 (C^k). MS (ESI), *m/z*: 430.2136 [M+H]⁺ (calc. for C₂₆H₂₇N₃O₃, *m/z*: 430.2125).

4-{2,6-Bis[(1E,3E)-4-dimethylaminobuta-1,3-dienyl]-1-methylpyridin-4(1H)-ylidene}-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one **13a**. Amination **1** (0.17 g, 1.02 mmol) was added to substituted dihydropyran **11a** (0.1 g, 0.34 mmol). The reaction mixture was stirred for 1 h at 60 °C and then concentrated *in vacuo*. Et₂O was added to the residue. The precipitate was separated and washed with diethyl ether to give 0.12 g (77%) of polyene **13a** as bright orange crystals, mp 227–229 °C. UV [$\lambda_{\max}/\text{nm}$ (ϵ): 485 (62 840) (EtOH); 465 (54 170) (CHCl₃). ¹H NMR (DMSO-*d*₆) δ : 3.62 (s, 3H, NMe), 8.12 (s, 2H, H³, H⁵), 2.41 (s, 3H, Me), 6.07 (d, 2H, H^a, *J* 14.5 Hz), 7.05 (dd, 2H, H^b, *J* 14.5 Hz, *J* 11.1 Hz), 5.28 (t, 2H, H^c, *J* 11.1 Hz, *J* 11.9 Hz), 7.00 (d, 2H, *J* 11.9 Hz), 8.15 (d, 2H, *o*-H_{Ph}, *J* 7.6 Hz), 7.30 (t, 2H, *m*-H_{Ph}, *J* 7.9 Hz), 6.98 (t, 1H, *p*-H_{Ph}, *J* 3.4 Hz), 2.88 (s, 12H, NMe₂). ¹³C NMR (DMSO-*d*₆) δ : 38.11 (NMe), 105.22 (C³, C⁵), 18.02 (Me), 108.08 (C^a), 141.05 (C^b), 98.15 (C^c), 150.08 (C^d), 118.15 (*o*-C_{Ph}), 128.08 (*m*-C_{Ph}), 122.02 (*p*-C_{Ph}), 40.08 (NMe₂), 161.22 (C^e, C^f). MS (ESI), *m/z*: 456.2744 [M+H]⁺ (calc. for C₂₈H₃₃N₅O, *m/z*: 456.2758).

Fractional crystallization of this mixture provided pure tetraene **14**. Heating of the mixture of compounds **13e** and **14** with excess amination **1** finally led to polyene **13e**.

The structures and conformations of the obtained compounds **12a–e**, **13a–e** and **14** were proved from 1D and 2D ¹H and

4-{2,6-Bis[(1E,3E)-4-dimethylaminobuta-1,3-dienyl]-1-methylpyridin-4(1H)-ylidene}-3-phenylisoxazol-5(4H)-one **13b**. Amination **1** (0.13 g, 0.76 mmol) was added to substituted dihydropyridine **11b** (0.07 g, 0.2 mmol) and the mixture was stirred for 35 min at 70–75 °C. The reaction mixture containing a cherry-coloured precipitate was concentrated *in vacuo*, then Et₂O was added. The precipitate was filtered off and washed with a small amount of EtOH to give 0.08 g (73%) of polyene **13b** as brick-red crystals, mp > 240 °C. UV [$\lambda_{\max}/\text{nm}$ (ϵ): 360 (22 100), 430 (sh., 35 360), 490 (61 880) (EtOH); 470 (47 883) (CHCl₃). ¹H NMR (DMSO-*d*₆) δ : 5.97 (d, 2H, H^a, *J* 14.5 Hz), 6.54 (dd, 2H, H^b, *J* 13.5 Hz, *J* 12 Hz), 5.22 (t, 2H, H^c, *J* 12 Hz), 6.76 (d, 2H, H^d, *J* 12.7 Hz), 7.45 (m, 2H, *m*-H_{Ph}, *J* 7.7 Hz), 7.59 (m, 3H, *p*-H_{Ph}, *o*-H_{Ph}, *J* 7.04 Hz), 7.28 (s, 2H, H^e, H^f), 2.89 (s, 12H, NMe₂), 3.56 (s, 3H, NMe). MS (ESI), *m/z*: 443.2403 [M+H]⁺ (calc. for C₂₇H₃₀N₄O₂, *m/z*: 443.2442).

For synthesis and characteristics of compounds **12c–e** and **13c,d**, see Online Supplementary Materials.

[‡] 5-{2,6-Bis[(1E,3E)-4-dimethylaminobuta-1,3-dienyl]-1-methylpyridin-4(1H)-ylidene}-1,3-diethyl-2-thioxodihydropyrimidine-4,6(1H,5H)-dione **13e** and 1,3-diethyl-5-{2-[(1E,3E)-4-dimethylaminobuta-1,3-dienyl]-1,6-dimethylpyridin-4(1H)-ylidene}-2-thioxodihydropyrimidine-4,6(1H,5H)-dione **14**. Procedure A. Amination **1** (0.32 g, 1.88 mmol) was added dropwise to a suspension of dihydropyrimidine **11e** (0.2 g, 0.63 mmol) in 1.2 ml of dry benzene. The reaction mixture was stirred at 20–22 °C. After 2.5 h, a fine carrot-coloured precipitate formed. Stirring was continued for more 2 h, the precipitate was separated and washed with dry Et₂O to give a mixture of polyene **13e** and tetraene **14** in 2:3 ratio (according to ¹H NMR data in DMSO-*d*₆). After double recrystallization of the mixture of compounds **13e** and **14** from EtOH, the mother liquor was cooled to give tetraene **14** as bright-orange crystals, mp 175–178 °C. UV [$\lambda_{\max}/\text{nm}$ (ϵ): 285 (60 149), 380 (46 992), 440 (sh., 39 473), 490 (54 510) (EtOH); 325 (12 530), 390 (26 315), 480 (43 232) (CHCl₃). ¹H NMR (DMSO-*d*₆) δ : 6.20 (d, 1H, H^a, *J* 14.4 Hz), 7.18 (dd, 1H, H^b, *J* 11.8 Hz, *J* 14.2 Hz), 5.38 (t, 1H, H^c, *J* 12.0 Hz), 7.16 (d, 1H, H^d, *J* 12.0 Hz), 2.95 (s, 6H, NMe₂), 3.75 (s, 3H, NMe), 2.54 (s, 3H, Me), 8.42 (s, 1H, H^e), 8.98 (s, 1H, H^f), 1.15 (t, 6H, NCH₂Me, *J* 6.8 Hz), 4.48 (q, 4H, NCH₂Me, *J* 6.8 Hz). ¹³C NMR (DMSO-*d*₆) δ : 106.53 (C^a), 143.25 (C^b), 98.08 (C^c), 151.59 (C^d), 160.35 (C=O), 39.63 (NMe₂), 37.40 (NMe), 21.37 (Me), 119.08 (C^e), 115.19 (C^f), 175.45 (C=S), 12.56 (NCH₂Me), 41.86 (NCH₂Me). MS (ESI), *m/z*: 401.2009 [M+H]⁺ (calc. for C₂₁H₂₈N₄O₂S, *m/z*: 401.2006).

Procedure B. Amination **1** (0.035 g) was added to 0.04 g of the mixture of polyene **13e** and tetraene **14** obtained as described above and the mixture was stirred for 75 min at 60–70 °C. The crystalline mixture was concentrated *in vacuo*. The residue was repeatedly washed with dry Et₂O and boiled with EtOH to give 0.03 g of polyene **13e** as red crystals, mp > 240 °C. UV [$\lambda_{\max}/\text{nm}$ (ϵ): 285 (21 690), 430 (15 424), 500 (22 172) (EtOH); 325 (7680), 370 (7680), 440 (plateau, 14 880), 490 (19 280). ¹H NMR (DMSO-*d*₆) δ : 6.11 (d, 2H, H^a, *J* 14.4 Hz), 7.05 (dd, 2H, H^b, *J* 11.8 Hz, *J* 14.2 Hz), 5.30 (t, 2H, H^c, *J* 12.0 Hz), 7.04 (d, 2H, H^d, *J* 12.0 Hz), 3.7 (s, 3H, NMe), 2.90 (s, 12H, NMe₂), 8.67 (s, 2H, H^e, H^f), 1.15 (t, 6H, NCH₂Me, *J* 6.8 Hz), 4.48 (q, 4H, NCH₂Me, *J* 6.8 Hz). ¹³C NMR (DMSO-*d*₆) δ : 107.89 (C^a), 141.67 (C^b), 97.86 (C^c), 150.52 (C^d), 37.90 (NMe), 39.77 (NMe₂), 114.19 (C^e, C^f), 160.34 (C=O), 175.26 (C=S), 12.61 (NCH₂Me), 41.83 (NCH₂Me). MS (ESI), *m/z*: 482.2582 [M+H]⁺ (calc. for C₂₆H₃₅N₅O₂S, *m/z*: 482.2584).

^{13}C NMR, UV and microTOF mass spectra. Assignment of signals in the ^1H and ^{13}C NMR spectra was based on COSY, NOESY, HSQC and HMBC 2D experiments. Dyes **12a–e** possess a conformation with a sharp angle between the chromophores since the NOESY and ROESY spectra demonstrate correlation between the H^3/H^5 and H^α protons but no correlation between the H^3/H^5 and H^β protons, whereas dyes **13a–e** and **14** have a conformation with an obtuse angle between the chromophores since the protons of the NMe group show coupling with H^α protons but not with H^β protons, which give correlation with the H^3/H^5 protons; there is no correlation between the H^α and H^3 protons.

The configuration of double bonds in all the dyes was determined from NOESY and ROESY NMR spectra and the vicinal coupling constants of methine protons (J 11.1–14.5 Hz). It follows from these data that the protons at the $\text{C}^\alpha=\text{C}^\beta$ and $\text{C}^\gamma=\text{C}^\delta$ double bonds are *trans*-arranged, while the diene moieties in polymethine chains $\text{C}^\alpha=\text{C}^\beta$ and $\text{C}^\gamma=\text{C}^\delta$ exist predominantly in the *S-trans*-conformation.

The spectrofluorescent and photochemical properties of cross-conjugated polyenes **12a–e**, **13a–e** and **14** will be described in detail in a subsequent paper.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2014.11.024.

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