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

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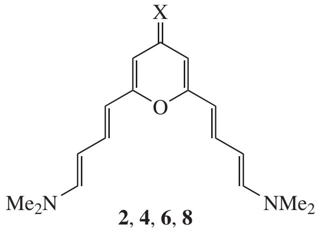
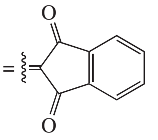
New non-linear cross-conjugated polyenes containing a central 4-ylidene-substituted pyran or *N*-methyldihydropyridine ring have been synthesized. Interaction of chromophores in these compounds occurs through the ylidene group linked to the heterocycles.

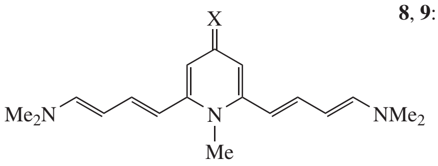
Previously, we performed the reaction of β-dimethylaminoacrolein aminal $Me_2NCH{=}CHCH(NMe_2)_2$ **1** with 2,6-dimethyl-4-pyrone or *N*-methyl-2,6-dimethylpyridin-4-one to give ketocyanine dyes **2** and **3** (cross-conjugated polyene ω,ω′-bisaminoketones with a central pyran or dihydropyridine moiety) containing two aminopolyene chromophores with equal lengths linked by a carbonyl group and a central bridge.[1,2]



2, **4**, **6**, **8**

2, **3**: X = O
4, **5**: X = $C(CN)_2$
6, **7**: X = $C(CN)C_6H_4NO_2$-*p*
8, **9**: X =



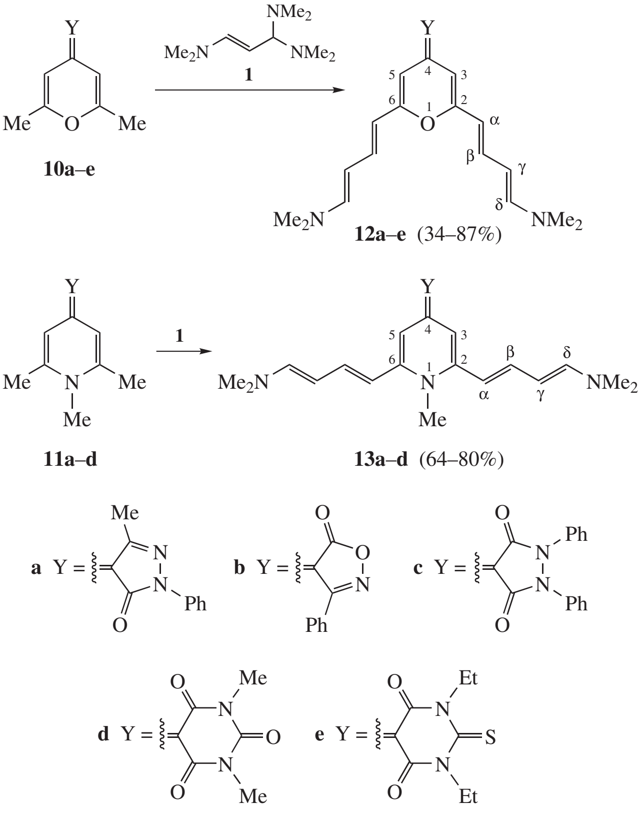


3, **5**, **7**, **9**

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*-methyldihydropyridine moiety. The aminopolyene chromophores in these compounds interact through 2,2-dicyano-, 2-cyano-2-(4-nitrophenyl)- or dioxoindan-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]



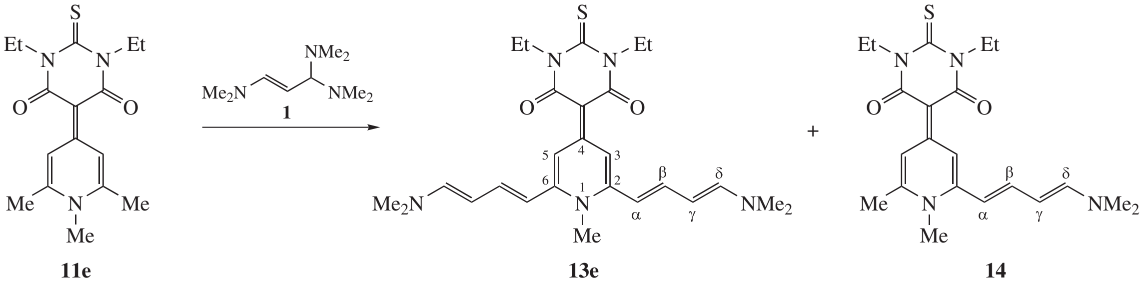
Scheme 1

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, ylidene derivatives of barbituric acids are promising not only as biologically active compounds[10] but also as potential dyes.[11]

To perform this task, we studied the reaction of aminal **1** with substituted 2,6-dimethyl-4*H*-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-4*H*-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% $MeNH_2$ aqueous solution or 15% $MeNH_2$ 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 aminal **1** involves both methyl groups to afford polyenes containing two polyene chromophores. The reaction of dihydropyridine **11e** with aminal **1** in dry benzene without heating gave a mixture of polyene **13e** and tetraene **14** in 2:3 ratio (Scheme 2).[‡]

Fractional crystallization of this mixture provided pure tetraene **14**. Heating of the mixture of compounds **13e** and **14** with excess aminal **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 ^{1}H and

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[†] *4-{2,6-Bis[(1*E*,3*E*)-4-dimethylaminobuta-1,3-dienyl]-4*H*-pyran-4-ylidene}-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one* **12a**. Aminal **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 Et$_2$O was added to the residue; the precipitate that formed was filtered off and washed with Et$_2$O to give 0.12 g (76%) of polyene **12a** as dark violet crystals, mp 230–233 °C. UV [$\lambda_{\max}$/nm (ε)]: 380 (44 850), 520 (67 600), 580 (sh., 39 000) (EtOH); 360 (26 000), 540 (46 800) (CHCl$_3$). ^{1}H NMR (DMSO-d_6, 80 °C) δ: 5.87 (d, 2H, H$^\alpha$, *J* 14.7 Hz), 7.29–7.33 (m, 2H, H$^\beta$), 5.31 (t, 2H, H$^\gamma$, *J* 12.0 Hz), 7.12 (d, 2H, H$^\delta$, *J* 12.7 Hz), 8.04 (d, 2H, *o*-H$_{\text{Ph}}$, *J* 8.0 Hz), 7.29–7.33 (m, 2H, *m*-H$_{\text{Ph}}$), 7.04 (t, 1H, *p*-H$_{\text{Ph}}$, *J* 7.3 Hz), 2.95 (s, 12H, NMe$_2$), 7.33 (s, 1H, H^3), 6.50 (s, 1H, H^5), 2.39 (s, 3H, Me). ^{13}C NMR (DMSO-d_6, 80 °C) δ: 107.58 (C$^\alpha$), 140.29 (C$^\beta$), 97.66 (C$^\gamma$), 151.28 (C$^\delta$), 117.38 (*o*-C$_{\text{Ph}}$), 127.74 (*m*-C$_{\text{Ph}}$), 122.04 (*p*-C$_{\text{Ph}}$), 39.49 (NMe$_2$), 162.76 (C^2, C^6), 108.28 (C^3, C^5), 17.59 (Me). MS (ESI), *m*/*z*: 443.2433 [M + H]$^+$ (calc. for C$_{27}$H$_{30}$N$_4$O$_2$, *m*/*z*: 443.2442).

*4-{2,6-Bis[(1*E*,3*E*)-4-dimethylaminobuta-1,3-dienyl]-4*H*-pyran-4-ylidene}-3-phenylisoxazol-5(4*H*)-one* **12b**. Aminal **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 Et$_2$O 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 [$\lambda_{\max}$/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) (CHCl$_3$). ^{1}H NMR (DMSO-d_6, 80 °C) δ: 5.55 (d, 2H, H$^\alpha$, *J* 12.0 Hz), 7.21 (t, 2H, H$^\beta$, *J* 12.0 Hz), 5.31 (t, 2H, H$^\gamma$, *J* 12.1 Hz), 6.71 (d, 2H, H$^\delta$, *J* 12.1 Hz), 7.44–7.55 (m, 5H, Ph), 7.37 (s, 2H, H^3, H^5), 2.91 (s, 12H, NMe$_2$). ^{13}C NMR (DMSO-d_6, 80 °C) δ: 109.39 (C$^\alpha$), 140.30 (C$^\beta$), 98.39 (C$^\gamma$), 150.32 (C$^\delta$), 129.00, 128.47, 132.74 (Ph), 162.71 (C^2, C^6), 104.19 (C^3, C^5), 46.37 (NMe$_2$), 149.82 (C^8), 97.69 (C^7), 105.61 (C^4). MS (ESI), *m*/*z*: 430.2136 [M + H]$^+$ (calc. for C$_{26}$H$_{27}$N$_3$O$_3$, *m*/*z*: 430.2125).

*4-{2,6-Bis[(1*E*,3*E*)-4-dimethylaminobuta-1,3-dienyl]-1-methylpyridin-4(1*H*)-ylidene}-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one* **13a**. Aminal **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*. Et$_2$O 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 [$\lambda_{\max}$/nm (ε)]: 485 (62 840) (EtOH); 465 (54 170) (CHCl$_3$). ^{1}H NMR (DMSO-d_6) δ: 3.62 (s, 3H, NMe), 8.12 (s, 2H, H^3, H^5), 2.41 (s, 3H, Me), 6.07 (d, 2H, H$^\alpha$, *J* 14.5 Hz), 7.05 (dd, 2H, H$^\beta$, *J* 14.5 Hz, *J* 11.1 Hz), 5.28 (t, 2H, H$^\gamma$, *J* 11.1 Hz, *J* 11.9 Hz), 7.00 (d, 2H, *J* 11.9 Hz), 8.15 (d, 2H, *o*-H$_{\text{Ph}}$, *J* 7.6 Hz), 7.30 (t, 2H, *m*-H$_{\text{Ph}}$, *J* 7.9 Hz), 6.98 (t, 1H, *p*-H$_{\text{Ph}}$, *J* 3.4 Hz), 2.88 (s, 12H, NMe$_2$). ^{13}C NMR (DMSO-d_6) δ: 38.11 (NMe), 105.22 (C^3, C^5), 18.02 (Me), 108.08 (C$^\alpha$), 141.05 (C$^\beta$), 98.15 (C$^\gamma$), 150.08 (C$^\delta$), 118.15 (*o*-C$_{\text{Ph}}$), 128.08 (*m*-C$_{\text{Ph}}$), 122.02 (*p*-C$_{\text{Ph}}$), 40.08 (NMe$_2$), 161.22 (C^2, C^6). MS (ESI), *m*/*z*: 456.2744 [M + H]$^+$ (calc. for C$_{28}$H$_{33}$N$_5$O, *m*/*z*: 456.2758).

*4-{2,6-Bis[(1*E*,3*E*)-4-dimethylaminobuta-1,3-dienyl]-1-methylpyridin-4(1*H*)-ylidene}-3-phenylisoxazol-5(4*H*)-one* **13b**. Aminal **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 Et$_2$O 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 [$\lambda_{\max}$/nm (ε)]: 360 (22 100), 430 (sh., 35 360), 490 (61 880) (EtOH); 470 (47 883) (CHCl$_3$). ^{1}H NMR (DMSO-d_6) δ: 5.97 (d, 2H, H$^\alpha$, *J* 14.5 Hz), 6.54 (dd, 2H, H$^\beta$, *J* 13.5 Hz, *J* 12 Hz), 5.22 (t, 2H, H$^\gamma$, *J* 12 Hz), 6.76 (d, 2H, H$^\delta$, *J* 12.7 Hz), 7.45 (m, 2H, *m*-H$_{\text{Ph}}$, *J* 7.7 Hz), 7.59 (m, 3H, *p*-H$_{\text{Ph}}$, *o*-H$_{\text{Ph}}$, *J* 7.04 Hz), 7.28 (s, 2H, H^3, H^5), 2.89 (s, 12H, NMe$_2$), 3.56 (s, 3H, NMe). MS (ESI), *m*/*z*: 443.2403 [M + H]$^+$ (calc. for C$_{27}$H$_{30}$N$_4$O$_2$, *m*/*z*: 443.2442).

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

[‡] *5-{2,6-Bis[(1*E*,3*E*)-4-dimethylaminobuta-1,3-dienyl]-1-methylpyridin-4(1*H*)-ylidene}-1,3-diethyl-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione* **13e** and *1,3-diethyl-5-{2-[(1*E*,3*E*)-4-dimethylaminobuta-1,3-dienyl]-1,6-dimethylpyridin-4(1*H*)-ylidene}-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione* **14**. *Procedure A*. Aminal **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 Et$_2$O to give a mixture of polyene **13e** and tetraene **14** in 2:3 ratio (according to ^{1}H 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 [$\lambda_{\max}$/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) (CHCl$_3$). ^{1}H NMR (DMSO-d_6) δ: 6.20 (d, 1H, H$^\alpha$, *J* 14.4 Hz), 7.18 (dd, 1H, H$^\beta$, *J* 11.8 Hz, *J* 14.2 Hz), 5.38 (t, 1H, H$^\gamma$, *J* 12.0 Hz), 7.16 (d, 1H, H$^\delta$, *J* 12.0 Hz), 2.95 (s, 6H, NMe$_2$), 3.75 (s, 3H, NMe), 2.54 (s, 3H, Me), 8.42 (s, 1H, H^3), 8.98 (s, 1H, H^5), 1.15 (t, 6H, NCH$_2$*Me*, *J* 6.8 Hz), 4.48 (q, 4H, NC*H*$_2$Me, *J* 6.8 Hz). ^{13}C NMR (DMSO-d_6) δ: 106.53 (C$^\alpha$), 143.25 (C$^\beta$), 98.08 (C$^\gamma$), 151.59 (C$^\delta$), 160.35 (C=O), 39.63 (NMe$_2$), 37.40 (NMe), 21.37 (Me), 119.08 (C^3), 115.19 (C^5), 175.45 (C=S), 12.56 (NCH$_2$*Me*), 41.86 (NC*H*$_2$Me). MS (ESI), *m*/*z*: 401.2009 [M + H]$^+$ (calc. for C$_{21}$H$_{28}$N$_4$O$_2$S, *m*/*z*: 401.2006).

Procedure B. Aminal **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 Et$_2$O and boiled with EtOH to give 0.03 g of polyene **13e** as red crystals, mp > 240 °C. UV [$\lambda_{\max}$/nm (ε)]: 285 (21 690), 430 (15 424), 500 (22 172) (EtOH); 325 (7680), 370 (7680), 440 (plateau, 14 880), 490 (19 280). ^{1}H NMR (DMSO-d_6) δ: 6.11 (d, 2H, H$^\alpha$, *J* 14.4 Hz), 7.05 (dd, 2H, H$^\beta$, *J* 11.8 Hz, *J* 14.2 Hz), 5.30 (t, 2H, H$^\gamma$, *J* 12.0 Hz), 7.04 (d, 2H, H$^\delta$, *J* 12.0 Hz), 3.7 (s, 3H, NMe), 2.90 (s, 12H, NMe$_2$), 8.67 (s, 2H, H^3, H^5), 1.15 (t, 6H, NCH$_2$*Me*, *J* 6.8 Hz), 4.48 (q, 4H, NC*H*$_2$Me, *J* 6.8 Hz). ^{13}C NMR (DMSO-d_6) δ: 107.89 (C$^\alpha$), 141.67 (C$^\beta$), 97.86 (C$^\gamma$), 150.52 (C$^\delta$), 37.90 (NMe), 39.77 (NMe$_2$), 114.19 (C^3, C^5), 160.34 (C=O), 175.26 (C=S), 12.61 (NCH$_2$*Me*), 41.83 (NC*H*$_2$Me). MS (ESI), *m*/*z*: 482.2582 [M + H]$^+$ (calc. for C$_{26}$H$_{35}$N$_5$O$_2$S, *m*/*z*: 482.2584).

^{13}C NMR, UV and micrOTOF mass spectra. Assignment of signals in the ^{1}H 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$^\alpha$ protons but no correlation between the H^3/H^5 and H$^\beta$ 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$^\alpha$ protons but not with H$^\beta$ protons, which give correlation with the H^3/H^5 protons; there is no correlation between the H$^\alpha$ 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 C$^\alpha$=C$^\beta$ and C$^\gamma$=C$^\delta$ double bonds are *trans*-arranged, while the diene moieties in polymethine chains C$^\alpha$=C$^\beta$ and C$^\gamma$=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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