An efficient route to the synthesis of novel zwitterionic pyridinium-cyanopropenides with 3-heteroaryl-substituted trimethinium salts†

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In this study, eight new zwitterionic derivatives were synthesized using a simple design method from the reaction of various 2-substituted 1,3-bis(dimethylamino)-trimethinium salts with malononitrile or ethyl 2-cyanoacetate in excellent yields in the presence of triethylamine in ethanol at reflux. The molecular structures of the new compounds were confirmed by IR, UV/vis, mass, \( ^1H \) and \( ^{13}C \) NMR spectra as well as by elemental analyses.

Introduction

Polymethine dyes constitute an independent class of conjugated \( \pi \) systems different from polyenes and aromatics. Polymethinic \( \pi \) systems are conjugated planar open-chain or ring compounds of the general formula 1 with high polarizabilities and medium-sized delocalization energies, with equal \( \pi \)-bond orders but unequal (alternating) \( \pi \)-electron densities along the carbon chain as well as relatively high chemical reactivity, preferring substitution over addition reactions.\(^1,2\) Polymethine dyes have unique inherent properties include conjugated structure, relatively good stability, medium fluorescence intensities, high molar absorption coefficients (about \( 10^5 \text{ dm}^{-3} \text{ mol}^{-1} \text{ cm}^{-1} \)), and narrow bandwidths invisible region.\(^3,4\)

Cyanine dyes are compounds that have a wide range of applications in many fields of science, pharmacology, medicine, and technology engineering. Such as bactericidal and fungicidal, anti-cancer, acid-base indicators, laser technology, organic solar cells, dyes for polymers, and spectral sensitizers for silver halide emulsion, etc.\(^5\)–\(^14\)

According to formula 1, cyanine dyes are a conjugate chain of carbon atoms located between two nitrogen centers, which this polymethine bridge links an electron donor group at one end and an electron acceptor group at the other. Conjugation between electron donor and acceptor group leads to delocalization of \( \pi \) electrons and hence positive charge over the two nitrogen atoms. The dye with 3 methine groups (\( n = 1 \) in formula 1) is classified as carboxycyanine dyes or trimethine cyanine dyes. The wavelength of the cyanine dye absorption/emission depends on the nature of the end groups and the length of the polymethine chain. Monomethine and trimethine dyes are usually absorbed in the visible region (500–600 nm) of the electronic spectrum, and with each added methine unit (CH=CH) cause a bathochromic shift of about 100 nm in the

Scheme 1  Representative condensation reactions towards cyanine dyes synthesis.
Results and discussion

The synthetic pathway for the synthesis of these new compounds is consisting of two steps. First, trimethinium salts 1 were prepared similar to the previous studies. Second, for the synthesis of novel zwitterionic pyridinium-cyanopropenides, trimethinium salts were isolated as perchlorate salts and reacted directly without additional purification were reacted with malononitrile derivatives in the presence of triethylamine in ethanol as a green solvent at reflux. Then, In order to optimize the reaction conditions for the synthesis of zwitterionic pyridinium-cyanopropenides derivatives, the model reaction between 1,3-indandione (Scheme 1B). Mazières isolated trimethinium benzothiazole cyanine dyes using the orthoester approach (Scheme 1C).

In continuation of our interest in the development of trimethinium salts in organic synthesis, herein we report a simple and highly efficient synthetic procedure for the preparation of new zwitterionic pyridinium-cyanopropenides from the reaction of trimethinium salts and malononitrile derivatives in the presence of triethylamine in ethanol as a green solvent in excellent yields without any by-products (Scheme 1D).

Experimental

All chemicals were purchased from Merck or Fluka chemical companies. The $^1$H NMR (300 MHz) and $^{13}$C NMR spectra (75 MHz) were run on a Bruker Avance 400. Tetramethyldisilane (TMS) was used as the internal standard for the NMR analysis. IR spectra were recorded using an FTIR apparatus. Melting points were recorded on a Stuart Scientific Apparatus SMP3 (UK) in open capillary tubes. Elemental C, H and N analyses, were performed using a Costech CHNS-O elemental analyzer. UV/vis absorption spectra were recorded at room temperature in DMSO using a PerkinElmer Lambda 25 spectrophotometer.

General procedure for the synthesis of pyridinium-cyanopropenides 4a–h

A solution of a 2-heteroraryl-substituted trimethinium salt 3a–d (1 mmol), malononitrile (2 mmol) or ethyl cyanoacetate (2 mmol) and triethylamine (1 mmol) in ethanol (10 mL) was heated under reflux for 5 h. Then, after cooling to room temperature, the precipitate formed was filtered off, washed with 2-propanol (3 x 3 mL), and dried under vacuum at 80 °C, to yield the desired betaine product 4a–h in excellent yields.
Table 2  Synthesis of product 4 via the reaction of 2-substituted trimethinium salts 3 with malononitrile and ethyl cyanoacetate in the presence of Et₃N in ethanol at reflux

| Entry | Trimethinium salts | X     | Product 3   | Yield\(^\text{a}\) (%) |
|-------|--------------------|-------|-------------|------------------------|
| 1     | ![3a](image)       | CN    | ![4a](image) | 95                     |
| 2     | ![3a](image)       | CO₂Et | ![4b](image) | 90                     |
| 3     | ![3b](image)       | CN    | ![4c](image) | 94                     |
| 4     | ![3b](image)       | CO₂Et | ![4d](image) | 95                     |
| 5     | ![3c](image)       | CN    | ![4e](image) | 98                     |
| 6     | ![3c](image)       | CO₂Et | ![4f](image) | 92                     |
| 7     | ![3d](image)       | CN    | ![4g](image) | 90                     |
### Table 2 (Contd.)

| Entry | Trimethinium salts | X | Product 3 | Yield\(^a\) (%) |
|-------|--------------------|---|-----------|-----------------|
| 8     | CO\(_2\)Et         |   | 3d        | 95              |

\(^a\) Isolated yield.

### Entry 8

**1,1,5,5-Tetracyano-3-(pyridinium-1-yl) penta-propenides (4a)**

Red powder, mp. > 260 °C, \(^1\)H NMR (DMSO-\(d_6\), 300 MHz), \(\delta\) (ppm): 7.76 (s, 2H), 8.36 (t, \(J = 6.6\) Hz, 2H), 8.81 (t, \(J = 7.6\) Hz, 1H), 9.19 (d, \(J = 5.1\) Hz, 2H). \(^{13}\)C NMR (DMSO-\(d_6\), 75 MHz) \(\delta\) (ppm): 14.8, 60.7, 76.5, 116.7, 119.0, 129.2, 148.0, 153.1, 154.0, 165.5. Anal. calcd for C\(_{14}\)H\(_7\)N\(_5\): C, 68.57; H, 2.88; N, 28.56%. Found: C, 68.55; H, 2.85; N, 28.57%. \(\lambda_{\text{max}}\) (DMSO) = 457 nm.

**Scheme 2** Proposed reaction mechanism for the synthesis of 4a–h.

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**2,6-Dicyano-1,7-diethoxy-1,7-dioxo-4-(pyridinium-1-yl) penta-propenides (4b)**

Orange powder, mp. > 260 °C, \(^1\)H NMR (DMSO-\(d_6\), 300 MHz), \(\delta\) (ppm): 1.20 (t, \(J = 6.9\) Hz, 6H), 4.13 (q, \(J = 6.9\) Hz, 4H), 8.01 (s, 2H), 8.30 (t, \(J = 6.6\) Hz, 2H), 8.75 (t, \(J = 7.5\) Hz, 1H), 9.12 (d, \(J = 5.4\) Hz, 2H). \(^{13}\)C NMR (DMSO-\(d_6\), 75 MHz) \(\delta\) (ppm): 14.8, 60.7, 76.5, 116.7, 119.0, 129.2, 148.0, 153.1, 154.0, 165.5. Anal. calcd for C\(_{14}\)H\(_7\)N\(_5\): C, 68.57; H, 2.88; N, 28.56%. Found: C, 68.55; H, 2.85; N, 28.57%. \(\lambda_{\text{max}}\) (DMSO) = 457 nm.

**1,1,5,5-Tetracyano-3-(3,5-dimethylpyridinium-1-yl) penta-propenides (4c)**

Violet powder, mp. > 260 °C, \(^1\)H NMR (DMSO-\(d_6\), 300 MHz), \(\delta\) (ppm): 2.51 (s, 6H), 7.74 (s, 2H), 8.53 (s, 1H), 8.93 (s, 2H). \(^{13}\)C NMR (DMSO-\(d_6\), 75 MHz), \(\delta\) (ppm): 18.2, 53.8, 114.5, 118.2, 120.9, 139.1, 146.3, 147.7, 148.2, 149.1, 149.9. Anal. calcd for C\(_{16}\)H\(_{11}\)N\(_5\): C, 70.32; H, 4.06; N, 25.63%. Found: C, 70.33; H, 4.08; N, 25.62%. \(\lambda_{\text{max}}\) (DMSO) = 455 nm.

**2,6-Dicyano-1,7-diethoxy-1,7-dioxo-4-(3,5-dimethylpyridinium-1-yl)-penta-propenides (4d)**

Red powder, mp. > 260 °C, \(^1\)H NMR (DMSO-\(d_6\), 300 MHz), \(\delta\) (ppm): 1.20 (t, \(J = 3.4\) Hz, 6H), 2.51 (s, 6H), 4.11–4.16 (m, 4H), 7.99 (d, \(J = 3.6\) Hz, 2H), 8.46 (s, 1H), 8.85 (s, 2H). \(^{13}\)C NMR (DMSO-\(d_6\), 75 MHz), \(\delta\) (ppm): 12.2, 53.8, 116.7, 119.0, 120.9, 139.1, 146.3, 147.7, 148.2, 165.5. Anal. calcd for C\(_{20}\)H\(_{21}\)N\(_3\)O\(_4\): C, 65.38; H, 5.76; N, 11.44%. Found: C, 65.75; H, 5.77; N, 11.43%. \(\lambda_{\text{max}}\) (DMSO) = 453 nm.

**1-(1,1,5,5-Tetracyano-3-(quinolinium-1-yl)-penta-propenides) (4e)**

Red powder, mp. > 260 °C, \(^1\)H NMR (DMSO-\(d_6\), 300 MHz), \(\delta\) (ppm): 7.97 (s, 2H), 8.12 (t, \(J = 6.9\) Hz, 4H), 8.01 (s, 2H), 8.30 (t, \(J = 6.6\) Hz, 2H), 8.75 (t, \(J = 7.5\) Hz, 1H), 9.12 (d, \(J = 5.4\) Hz, 2H). \(^{13}\)C NMR (DMSO-\(d_6\), 75 MHz) \(\delta\) (ppm): 14.8, 60.7, 76.5, 116.7, 119.0, 129.2, 148.0, 153.1, 154.0, 165.5. Anal. calcd for C\(_{18}\)H\(_{17}\)N\(_3\)O\(_4\): C, 68.71; H, 5.05; N, 12.38%. Found: C, 68.70; H, 5.05; N, 12.37%. \(\lambda_{\text{max}}\) (DMSO) = 452 nm.
1H, 8.32–8.40 (m, 2H), 8.60 (d, J = 7.8 Hz, 1H), 9.54 (d, J = 8.1 Hz, 1H), 9.65 (dd, J = 1.2, 5.7 Hz, 1H). 13C NMR (DMSO-d6, 75 MHz), δ (ppm): 53.9, 114.7, 118.3, 121.1, 127.4, 127.8, 128.3, 131.4, 131.7, 138.1, 138.5, 140.1, 148.2, 154.9, 165.5. Anal. calcld for C12H18N3O4: C, 67.86; H, 4.92; N, 10.79%. Found: C, 67.85; H, 4.90; N, 10.80%.

Conclusions

In conclusion, we report on a highly efficient, one-pot method for the synthesis of new zwitterionic pyridinium-cyanopropenides by reaction of 2-heteroaryl-substituted trime-thinimium salts with malononitrile or ethyl cyanoacetate in DMSO-

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