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Novel Synthesis of a New Class of Strongly Fluorescent Phenanthridine Analogues[†]

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A novel synthesis of strongly fluorescent phenanthridine and phenanthrene analogues as a possible new class of laser dyes utilizing the reactions of tetralin-1-ylidenecyanothioacetamide or tetralin-1-ylidenemalononitrile with β -(2-furyl)- and β -(2-thienyl)-acrylonitriles is reported.

Continuing our interest in the development of efficient and simple procedures for the synthesis of antimetabolites,¹⁻³ we have recently reported successful syntheses of sulfanyl purine and 3-deazapyrimidine nucleosides and of folic acid analogues.⁴⁻⁶ Here we report novel syntheses of phenanthridine analogues and their condensed derivatives as a possible new class of laser dye. It was found that tetralin-1-ylidenecyano-thioacetamide **1b** reacted with β -(2-furyl)- and β -(2-thienyl)-methylidenemalononitriles **2a**, **b** in refluxing ethanol contain-



Scheme 1



*To receive any correspondence.

[†]This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1997, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*. ing catalytic amounts of piperidine for 3 h to give the unexpected phenanthridine analogues **4** (Scheme 1).

The formation of 4 from 1b and 2a, b is assumed to proceed via addition of the active methylene group of 1b to the double bond of 2a,b to give Michael intermediates which then cyclize via malononitrile elimination and oxidation under the reaction conditions to yield 4. The unexpected course of the reaction between the β -(2-furyl)- and β -(2-thienyl)-methylidenemalononitriles 2a,b and 1b prompted us to investigate the reaction between the tetralin-1-ylidenemalononitrile 1a and β -(2-furyl)- and β -(2-thienyl)-methylidenecyanothioacetamides 2c,d under the same reaction conditions. The products 4 obtained were shown to be the same as those obtained from the reaction of 1b with 2a,b by TLC, melting point and spectral data. The mechanism of the reaction of 1a and 2c,d is assumed to proceed through the exchange reaction between the cycloalkylidene group of 1a and the arylmethylidene group of 2c,d, followed by Michael addition which leads to the intermediate 3 and hence to the final product 4 as produced by the reaction of 1b with 2a,b.

We studied the reaction of β -(2-furyl)- and β -(2-thienyl)-1-tetralone **5** with cyanothioacetamide **6**. It was found that **5** reacts with **6** in boiling ethanol containing a catalytic amount of piperidine to give two products (TLC), of which the first was formulated as the phenanthridine analogues **4** and the second as the carbocyclic nitriles **9** (Scheme 2).

The products 4 obtained from this reaction were shown to be the same as those obtained from the reaction of 1 and 2 by TLC, melting point and spectral data. The mechanism for the formation of 4 from reaction of 5 and 6 is assumed to proceed through the formation of the initial adducts 7, which cyclized and oxidized under the reaction conditions to yield 4. The mechanism for the formation of 9 from the reaction of 5 and 6 is assumed to proceed *via* addition of the active methylene group of 6 to the double bond of 5 to give intermediate 8. This Michael adduct then cyclizes *via* water elimination to form a 1,4-dihydrothiopyran species, which undergoes ring contraction and elimination of ammonia followed by oxidation to give the phenanthrene analogues 9.

Table 1 The absorption and emission maxima together with the $\phi_{\rm f}$ values in ethanol^a

Compound	Absorption maxima/nm	Emission maxima/nm	$\phi_{ m f}$
9a	381.5, 275.5, 227.0	425	0.35
9b	374.5, 274.0, 227.0	420	0.29
10a	373.0, 282.0, 241.0	410	0.04
10b	366.0, 280.5, 233.0	410	0.03
11a	370.5, 281.0, 243.0	400	0.04
11b	373.5, 272.0, 228.0	420	0.11
12a	369.5, 263.0, 222.5	410	0.99
12b	369.5, 278.5	435	0.98
12c	367.0, 271.0, 224.5	410	0.99
12d	373.0, 283.0, 229.0	460	0.99

^aExcitation wavelengths corresponding to the lowest energy absorption maxima were used.

Compounds 4 bearing latent functional substituents were found useful for the synthesis of fused pyridines. It was found that 4 reacted with methyl iodide in sodium ethoxide to afford the corresponding S-alkyl derivatives 10 (Scheme 3). When salts of 4 were treated with phenacyl bromide as an alkylating agent, the S-alkylated derivatives were not isolated, but instead gave the cyclized thieno[3,4-b]isoquinoline derivative 11. Table 1 summarizes some spectral and $\phi_{\rm f}$ data for compounds 9-12. Relatively high values are obtained only in the case of 9a,b, yet the values are much lower than the phenyl analogues 12, the latter showing very high fluorescence efficiencies (ϕ_f values as high as 0.99 were obtained for X = OMe, Me and Cl). This suggests that these derivatives may be potential candidates for laser dyes, solar harvesting dyes, fluorogenic dyes, etc. For compounds 9-11, the presence of a heteroatom plays a role in fluorescence quenching. Molecular flexibility in 11a,b also reduces the fluorescence efficiency by enhancing internal conversion to the ground state.



Experimental

Melting points are uncorrected. For TLC aluminium sheets [silica-gel 60 F₂₅₄ (Merck)] were used. Detection was effected by viewing under a short-wavelength UV lamp. IR spectra were obtained (KBr discs) on a Pye Unicam Spectra-1000. ¹H NMR were measured on a Wilmad 270 MHz or on a Varian 400 MHz spectrometer for solutions in (CD₃)₂SO using SiMe₄ as internal standard. Mass spectra were recorded on a Varian MAT 112 spectrometer. Analytical data were obtained from the Microanalytical Data Center at Cairo University. Emission and excitation spectra, together with fluorescence quantum yields (ϕ_t) were measured using a Shimadzu RF 510 spectrofluorophotometer connected to an ultrathermostat (Julabo F 10) of temperature precision ± 0.1 °C. $\phi_{\rm f}$ was measured relative to 9,10-diphenylanthracene as a reference standard⁷ applying low concentrations to avoid reabsorption. The following relation was applied to calculate the fluorescence quantum yields $\phi_{\rm f}(s)$ relative to the fluorescence quantum yield of 9,10-diphenylanthracene, $\phi_{\rm f}(r)$:

$$\phi_{\rm f}(s) = \phi_{\rm f}(r) \frac{\int I_{\rm s}(v) \mathrm{d}v}{\int I_{\rm r}(v) \mathrm{d}v} \frac{A_{\rm r}}{A_{\rm s}} \frac{n_{\rm s}^2}{n_{\rm r}^2}$$

where the integrals represent the corrected fluorescence peak areas. *A* and *n* are the absorbance at the excitation wavelengths and the refractive index of the applied solvents respectively. UV–VIS absorption spectra were measured using a Shimadzu UV-160 A spectrophotometer. We have previously described compounds $12.^{8}$

5,6-Dihydrobenzo[f]isoquinoline-2(3H)-thiones 4. —To a mixture of **1b** and **2a,b** or **1a** and **2c,d** (0.01 mol) in ethanol (50 ml), piperidine (0.3 ml) was added. The reaction mixture was heated under reflux for 3 h and then left to stand overnight. The resultant precipitate was filtered off and crystallized from dioxane to afford yellow crystals. **4a**: mp 200 °C, yield 24%; v_{max}/cm^{-1} (KBr) 3280 (NH), 2216 (CN); $\delta_{\rm H}$ ([²H₆]Me₂SO) 2.51 (s, 2 H, CH₂), 2.82 (s, 2 H, CH₂), 6.82 (d, 1 H, furan 4-H), 7.34 (m, 4 H, Ar-H), 7.94 (d, 1 H, furan 3-H), 8.06 (s, 1 H, furan 5-H), 13.92 (brs, 1 H, NH); m/z 304 (Found: C, 71.2; H, 4.1; N, 9.0.C₁₈H₁₂N₂OS requires C, 71.1; H, 3.9; N, 9.2%). **4b**: mp 276 °C, yield 20%; v_{max}/cm^{-1} (KBr) 3300 (NH), 2215 (CN); m/z 320 (Found: C, 67.2; H, 4.0; N, 9.1. C₁₈N₁₂N₂S₂ requires C, 67.5; H, 3.8; N, 8.8%).

1-*Thioxo*-1H-*cyclopenta*[a]*naphthalene-2-carbonitriles* **9**.—A solution of β-(2-furyl)- and β-(2-thienyl)-methylidene-1-tetralone **5** (0.01 mol) and cyanothioacetamide **6** (0.01 mol) in ethanol (30 ml) and a few drops of piperidine was refluxed for 3 h, cooled, and the precipitate was filtered off and crystallized from the appropriate solvent. The first fraction comprised compounds **4**. Water (2 ml) was then added to the filtrate and the formed solid was filtered off and recrystallized from aqueous ethanol to yield compounds **9**. **9a**: mp 152 °C, yield 18%; v_{max}/cm^{-1} (KBr) 2218 (CN); $\delta_{\rm H}$ ([²H₆]Me₂SO) 6.76 (d, 1 H, furan 4-H), 6.81 (s, 2 H, C₆H₂), 6.95–7.40 (m, 4 H, C₆H₄), 7.97 (d, 1 H, furan 3-H), 8.16 (d, 1 H, furan 5-H); *m/z*287 (Found: C, 75.5; H, 3.3; N, 5.1. C₁₈H₉NOS requires C, 75.3; H, 3.1; N, 4.9%). **9b**: mp 189 °C, yield 21%; v_{max}/cm^{-1} (KBr) 2216 (CN); *m/z* 303 (Found: C, 71.0; H, 3.4; N, 4.5. C₁₈H₉NS₂ requires C, 71.3; H, 3.0; N, 4.6%).

5,6-Dihydro-2-(methylsulfanyl)benzo[f]isoquinoline 10.—5,6-Dihydrobenzo[f]isoquinoline-2(3H)-thione 4 (0.0017 mol) was suspended in a solution of sodium ethoxide (from 0.0051 mol of sodium) in ethanol (25 ml). An excess of methyl iodide (0.0028 mol) was added dropwise to the resulting mixture. The precipitate obtained after 2 h stirring at room temperature was filtered off and recrystallized from ethanol to afford yellow crystals. 10a: mp 153 °C, yield 63%; v_{max}/cm^{-1} (KBr) 2215 (CN); $\lambda_{max}/mm 285$, 298, 316 and 346; m/z 318 (Found: C, 71.5; H, 4.6; N, 9.0. C₁₉H₁₄N₂OS requires C, 71.7; H, 4.4; N, 8.8%). 10b: mp 171 °C, yield 60%; v_{max}/cm^{-1} (KBr) 2218 (CN); m/z 334 (Found: C, 68.1; H, 4.5; N, 8.3. C₁₉H₁₄N₂S₂ requires C, 68.3; H, 4.2; N, 8.4%).

6,7-*Dihydrobenzo*[f]*thieno*[3,4-b]*isoquinoline* 11.—A mixture of 4 (0.01 mol), sodium ethoxide (0.01 mol) and phenacyl bromide (0.01 mol) in dry ethanol (50 ml) was refluxed for 3 h and then allowed to cool to room temperature and acidified with cold dilute hydrochloric acid. The resulting solid product was collected by filtration and recrystallized from ethanol to afford yellow crystals. 11a: mp 193 °C, yield 57%; v_{max} (cm⁻¹ (KBr) 3400, 3280 (NH₂), 1700 (CO); $\delta_{\rm H}$ ([²H₆]Me₂SO) $\delta_{\rm H}$ 2.76 (s, 2 H, CH₂), 2.88 (t, 2 H, CH₂), 6.41 (s, 2 H, NH₂), 6.88 (m, 1 H, furan 4-H), 7.22–7.94 (m, 9 H, C₆H₅ and C₆H₄), 8.20 (d, 1 H, furan 3-H), 8.28 (d, 1 H, furan 5-H); *m/z* 422 (Found: C, 73.6; H, 4.0; N, 6.8. C₂₆H₁₈N₂O₂S requires C, 73.9; H, 4.3; N, 6.6%). 11b: mp 180 °C, yield 56%; v_{max} /cm⁻¹ (KBr) 3450, 3285 (NH₂), 1690 (CO); $\delta_{\rm H}$ ([²H₆]Me₂SO) $\delta_{\rm H}$ 2.62 (t, 2 H, CH₂), 2.69 (t, 2 H, CH₂), 6.83 (s, 2 H, NH₂), 7.24 (m, 10 H, C₆H₅, C₆H₄ and furan 4-H), 7.78 (d, 1 H, furan 3-H), 8.17 (d, 1 H, furan 5-H); *m/z* 438 (Found: C, 71.4; H, 4.3; N, 6.6. C₂₆H₁₈N₂OS₂ requires C, 71.2; H, 4.1; N, 6.4%).

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