Synthesis and Antimicrobial Activity of some Disperse Dyes derived from Pyridones

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Abstract: Pyridone derivatives 4a,b are prepared by reacting N-alkyl-2-cyanoacetamide 1a,b with methyl propionylacetate. Compounds 4a,b are coupled with aromatic diazonium salts to produce the corresponding new azo disperse dyes 6a,b. The antimicrobial activity of the synthesized azo disperse dyes are evaluated.

Keywords: pyridones; azo dyes; disperse dyes; antimicrobial activity.

1. Introduction

Azo dyes are the principal class of synthesized dyes. They have been extensively used in different purposes, like textile dyeing or printing and non-textile applications [1-5]. Pyridone disperse dyes are moderately recent heterocyclic intermediates for the preparation of azo dyes because azo pyridone dyes generate bright hues. Pyridone as coupling components have been shown to be significant colorants for different dyes in industrial applications. Furthermore, \( N \)-substituted pyridone azo disperse dyes shows good color strength and excellent light fastness [6-11]. In a continuation of our strategy aims to synthesize novel azo disperse dyes and elucidate their structures, the present study focuses on the synthesis of new azo disperse dyes derived from pyridones and evaluate their antimicrobial activities.

2. Materials and Methods

2.1. General

Melting points were recorded on a Gallenkamp apparatus. IR spectra were recorded using KBr pellets on a JASCO FTIR-6300 FT-IR spectrophotometer. \(^1\)H- and \(^{13}\)C-NMR spectra were recorded on AvanceII 600 MHz super-conducting NMR spectrometers with proton spectra measured at 600 MHz and carbon spectra at 150 MHz, respectively. Mass spectra were measured on a high resolution GC/MS DFS-Thermo. Microanalyses were performed on Elemental-Vario Micro cube Analyzer.
2. General procedure for the preparation of compounds (4a,b).

A mixture of N-ethyl-2-cyanoacetamide or N-butyl-2-cyanoacetamide (10 mmol) and methyl propionylacetate (1.30 g, 10 mmol) was refluxed for six hours. The solution is diluted with water and acidified with hydrochloric acid to give white crystals of compounds 4a [12] or 4b [13].

2.3 General procedure for the synthesis of disperse dyes (6a,b).

A cold solution of aryldiazonium salt (10 mmol) [prepared by adding sodium nitrite (1.00 g in 10 mL H2O) to a cold solution of aryl amine hydrochloride or aryl amine nitrate (10 mmol) with stirring as described earlier] [14]. The resulting solution of the aryldiazonium was then added to a cold solution of compound 4a,b (10 mmol) in ethanol (20 mL) containing sodium acetate (2.00 g). The mixture was stirred at room temperature for one h and the solid product so formed was collected by filtration and recrystallized from ethanol to give compounds 6a,b.

1,4-Diethyl-2,6-dioxo-5-(o-toly1-hydrazono)-1,2,5,6-tetrahydro-pyridine-3-carbonitrile (6a): Orange crystals (Scheme 1). Yield: 61%, M.p.: 202-204 °C, FT-IR (KBr cm-1): 3439 (NH), 2224 (CN), 1669, 1631 (2CO), λmax in DMF = 445 (nm). 1H NMR (600 MHz, CDCl3, δ, ppm): 1.77 (t, 3H, CH3, J = 7.2 Hz), 1.38 (t, 3H, CH3, J = 7.2 Hz), 2.51 (s, 3H, CH3), 3.08 (q, 2H, CH2, J = 7.2 Hz), 4.07 (q, 2H, CH2, J = 7.2 Hz), 2.73 (t, 1H, J = 7.2 Hz, o-tolyl-H), 7.28 (t, 1H, J = 7.2 Hz, o-tolyl-H), 7.36 (t, 1H, J = 7.8 Hz, o-tolyl-H), 7.76 (d, 1H, J = 8.4 Hz, o-tolyl-H), 15.29 (s, 1H, NH). 13C NMR (150 MHz, CDCl3, δ, ppm): 13.95 (CH2), 14.57 (CH2), 17.28 (CH3), 24.35 (CH3), 35.43 (CH2), 100.78, 114.48, 115.10, 122.44, 127.08, 127.51, 128.10, 131.63, 139.37, 160.34, 162.10, 164.26. MS (m/z, (%)): 310 (M+, 100), Anal. calcd. for C17H18N4O2: C, 65.79; H, 5.85; N, 18.05. Found: C, 65.78; H, 6.49; N, 18.65. HRMS: m/z (EI) for C17H18N4O2: calcd. 310.1424; found: 310.1424.

1-Butyl-4-ethyl-2,6-dioxo-5-(phenyl-hydrazono)-1,2,5,6-tetrahydro-pyridine-3-carbonitrile (6b): Dark Yellow crystals (Scheme 1). Yield: 62%, M.p.: 168-170 °C, FT-IR (KBr cm-1): 3445 (NH), 2218 (CN), 1678, 1630 (2CO). λmax in DMF = 435 (nm). 1H NMR (600 MHz, CDCl3, δ, ppm): 0.97 (t, 3H, CH3, J = 7.2 Hz), 1.38 (t, 3H, CH3, J = 7.8 Hz), 1.31-1.41 (m, 2H, CH2), 1.66-1.61 (m, 2H, CH2), 3.06 (q, 2H, CH2, J = 7.8 Hz), 3.97 (t, 2H, CH2, J = 7.2 Hz), 7.33-7.27 (m, 1H, phenyl-H), 7.50-7.47 (m, 4H, phenyl-H), 15.09 (s, 1H, NH). 13C NMR (150 MHz, CDCl3, δ, ppm): 13.95 (CH2), 14.57 (CH2), 20.46 (CH3), 24.34 (CH2), 30.01 (CH3), 40.09 (CH2), 101.01, 114.40, 117.25, 121.87, 127.68, 130.22, 141.04, 160.47, 161.16, 164.20. MS (m/z, (%)): 324 (M+, 100), Anal. calcd. for C19H19N4O2: C, 66.65; H, 6.21; N, 17.27. Found: C, 66.06; H, 7.01; N, 16.21. HRMS: m/z (EI) for C19H19N4O2: calcd. 324.1581; found: 324.1580.

2.4 Antimicrobial Activity Test

The antimicrobial activities of disperse dyes 6a,b were tested using the agar-well diffusion technique [15] against ten different microbial cultures obtained from the Regional Center for Mycology and Biotechnology, Al-Azhar University (Cairo, Egypt). Pure cultures of Bacillus cereus RCMB 027 (1), Bacillus subtilis RCMB 015 (1) NRRL B-543, Staphylococcus aureus (RCMB 010010) and Streptococcus mutans RCMB 017 (1) ATCC 25175 (Gram positive bacterium), Enterobacter cloacae RCMB 001 (1) ATCC 23355, Klebsiella pneumonia RCMB 003 (1) ATCC 13883, Escherichia coli RCMB 010052 ATCC 25955 and Proteus vulgaris RCMB 004 (1) ATCC 13315 (Gram negative bacterium), Candida albicans RCMB 005003 (1) ATCC 10231 and Aspergillus flavus (RCMB 002002) (fungi) were used in the test. An aliquot of 0.1 mL of each bacterial strain was inoculated and spread on nutrient agar (NA) while 0.1 mL of each fungus were spread on potato dextrose agar (PDA). The inoculated plates were supplied with 100 μL of each of the tested dyes with a final total concentration of 100 mg mL-1. The dyes were included in 4 mm wells produced by sterile cork borer. The NA plates were incubated at 37 °C for 24 h while PDA plates were incubated at 25 °C for 24–48 h.

3. Results and Discussion

3.1. Chemistry and characterizations

Our primary strategy is to synthesize pyridone derivative 4a and convert it into a new monoazo disperse dyes that were used in dyeing polyester fabrics by utilizing different dyeing methods [12,14]. In order to complete this strategy, novel monoazo disperse dyes arylhydrazono-1,4-diethyl-2,6-dioxo-
tetrahydropyridine-3-carbonitrile and arylhydrazono-1-butyl-4-ethyl-2,6-dioxo-tetrahydropyridine-3-carbonitrile 6a,b were synthesized in a simple and efficient route (Scheme 1).

Scheme 1. Synthesis of disperse dyes 6a, b.

1-Alkyl-4-ethyl-2,6-dioxo-1,2,5,6-tetrahydro-pyridine-3-carbonitrile 4a,b were prepared via reaction of N-ethyl-2-cyanoacetamide 1a or N-butyl-2-cyanoacetamide 1b with methyl propionylacetate 5. Coupling of compounds 4a,b with aromatic diazonium salts afforded the corresponding pyridone azo disperse dyes 6a,b in a good yields. Structural elucidations of these disperse dyes were confirmed by mass spectroscopy, FTIR, elemental analysis, and NMR spectroscopic data.
3.2. Antimicrobial activity

The obtained results listed in Table 1 showed that the prepared disperse dyes have given adequate and promising results that can be utilized for medical and pharmaceutical objectives. Firstly, disperse dyes 6a,b showed moderate antibacterial activities against *Streptococcus mutants*. In contrast dyes 6a,b showed no antibacterial activities against *Bacillus cereus, Bacillus subtilis* and *Staphylococcus aureus* as Gram positive bacteria. Secondly, the same phenomena repeated with disperse dyes 6a,b showed no anti-fungi activities against of *Aspergillus flavous* while disperse dye 6b showed good anti-fungi activities against of *Candida albicans*. Thirdly, disperse dyes 6a,b showed moderate antibacterial activities against *Enterobacter cloacae* whilst the both dyes showed no antibacterial activities against *Klebsiella pneumonia*. Furthermore, disperse dye 6a showed good antibacterial activities against both *Escherichia coli* and *Proteus vulgaris* whereas disperse dye 6b showed no activities for the same microorganisms as Gram negative bacteria.

Evaluations of different dyeing methods either at temperatures in the region of 130 °C or at lower temperatures in the presence of an accelerating agent (carriers) and estimation of dyeing performance for these azo disperse dyes are under investigations.

Table 1. Antimicrobial results of the synthetic disperse dyes 6a,b.

| Microorganisms | Dye numbers | Control |
|----------------|-------------|---------|
| *Candida albicans* (RCMB 005003 (1) ATCC 10231) | 6a NA, 6b 8 | Ketoconazole 20 |
| *Aspergillus flavous* (RCMB 002002) | NA NA | 16 |
| Gram Positive Bacteria | | Gentamycin |
| *Bacillus cereus* (RCMB 027 (1)) | NA NA | 25 |
| *Bacillus subtilis* (RCMB 015 (1) NRRL B-543) | NA NA | 26 |
| *Staphylococcus aureus* (RCMB 010010) | NA NA | 24 |
| *Streptococcus mutants* (RCMB 017 (1) ATCC 25175) | 6a 12, 6b 10 | 20 |
| Gram Negative Bacteria | | Gentamycin |
| *Enterobacter cloacae* (RCMB 001 (1) ATCC 23355) | 6a 11, 6b 9 | 27 |
| *Klebsiella pneumonia* (RCMB 003 (1) ATCC 13883) | 6a NA, 6b NA | 21 |
| *Escherichia coli* (RCMB 010052 ATCC 25955) | 6a 8, 6b NA | 30 |
| *Proteus vulgaris* (RCMB 004 (1) ATCC 13315) | 6a 10, 6b NA | 25 |

RCMB: Regional Center for Mycology and Biotechnology, NA: No activity

4. Conclusions

New disperse dyes arylhydrazono-1,4-diethyl-2,6-dioxo-tetrahydropyridine-3-carbonitrile and arylhydrazono-1-butyl-4-ethyl-2,6-dioxo-tetrahydropyridine -3-carbonitrile 6a,b were synthesized in a simple and efficient route with a good yields by reacting pyridones with aromatic diazonium salts. These dyes showed satisfactory antimicrobial activity against Gram positive bacteria, Gram negative bacteria and fungi.

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Conflicts of Interest:

“The author declares no conflict of interest.”

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