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Synthesis and reactions of methylene bi-anthranilic acid

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تحضير وتفاعلات حامض ميثيلين ثنائي الأنثرانيلك

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Abstract:
Methylene bis anthranilic acid was synthesized by reacting anthranilic acid with formaldehyde in water at room temperature. The resulting compound was further treated with nitrous acid to form tetrazonium salts, which were then coupled with phenol and 2-naphthol to produce disazo derivatives. The structures of the synthesized compounds were confirmed using spectral analysis (e.g., IR, NMR), and the desired products were successfully obtained.

Keywords: Methylene bis-anthranilic acid, anthranilic acid, formaldehyde, tetrazonium salts, disazo dyes, azo coupling, phenol, 2-naphthol, spectral analysis, synthesis.

الملخص
تم تحضير حمض الميثيلين ثنائي الأنثرانيلك من خلال تفاعل حمض الأنثرانيلك مع الفورمالدهيد في الماء عند درجة حرارة الغرفة. ثم عُولج المركب الناتج بحمض النيتروز لتشكيل أملاح التترازونيوم، والتي تم بعد ذلك ربطها مع الفينول و2-نافثول لإنتاج مشتقات الداي آزو. تم تأكيد هياكل المركبات المحضرة باستخدام التحليل الطيفي (مثل الأشعة تحت الحمراء والرنين المغناطيسي النووي)، وتم الحصول بنجاح على المنتجات المرغوبة.

الكلمات المفتاحية: حمض الميثيلين ثنائي الأنثرانيلك، حمض الأنثرانيلك، فورمالدهيد، أملاح التترازونيوم، أصباغ الداي آزو، الاقتران الآزوي، فينول، 2- نافثول، التحليل الطيفي، تحضير.

Introduction

Reactive dyes represent the most advanced class of synthetic dyes, widely recognized for their ability to form covalent bonds with textile substrates, resulting in superior wash and light fastness properties [1]. Their water solubility, ease of application, and versatility in producing a broad spectrum of shades from vibrant to subdued tones have solidified their prominence in textile dyeing [2]. Initially developed for cellulose fibers, reactive dyes have since expanded in application to polyamide fibers, owing to their excellent wet fastness and extensive color range [3-4].

Recent advancements in reactive dye chemistry have further broadened their applicability, enabling high exhaustion and fixation rates on various fiber types [5]. Notably, monoazo and bisazo reactive dyes have gained significant attention for their ability to produce vivid hues on silk, wool, and cotton while maintaining exceptional fastness properties [1, 6]. Among these, triazine-based reactive dyes have demonstrated enhanced exhaustion, fixation, and durability, making them particularly suitable for high-value mercerized fabrics [2, 4].

Despite these advantages, challenges remain in optimizing dye-bath exhaustion and addressing environmental concerns associated with reactive dyeing processes. Recent research has focused on structural modifications to improve dye performance under varying application conditions. For instance, bisazo reactive dyes derived from 5,5'-methylene bis anthranilic acid have exhibited promising results, producing violet to yellow shades with excellent wash and rubbing fastness [7].

Building upon these developments, this study aims to synthesize and characterize novel reactive dyes, with a particular focus on bisazo derivatives, to evaluate their dyeing performance on both natural and synthetic fibers. The ultimate objective is to develop eco-friendly, high-performance dyes that meet the evolving demands of the textile industry while minimizing environmental impact.

Material and methods

Materials

All chemicals were purchased from Sigma-Aldrich (St. Louis, MO, USA) and used without further purification. Reaction progress was monitored by thin-layer chromatography (TLC) using ethyl acetate/petroleum ether as the mobile phase. Spectroscopic analyses of the synthesized compounds were performed at the Micro-Analytical Unit of the Faculty of Science Research Center, University of Cape Town. ^{1}H NMR spectra were recorded on a Bruker 300 MHz spectrometer (δ in ppm, tetramethylsilane [TMS] as internal standard, δ = 0) in DMSO-d_6. Signal multiplicities are denoted as follows: s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). ^{13}C NMR spectra were acquired on a Bruker 75 MHz spectrometer (TMS as reference, δ = 0). Fourier-transform infrared (FT-IR) spectra were obtained using a PerkinElmer Spectrum Two (Maltson 5000 FT-IR spectrometer, version 10.6.0), with absorption bands reported in wavenumbers (cm^{-1}). Melting points were determined in capillary tubes using a Stuart Scientific melting point apparatus and are uncorrected.

Methods

1. Preparation of 5,5'-methylene-bis-anthranilic acid (I)

Anthranilic acid (0.1 mol, 13.7 g) was dissolved in a mixture of water (125 mL) and 36.5% hydrochloric acid (25 mL) at 50°C. The reaction mixture was then treated with a 3% aqueous formaldehyde solution (25 mL) at 60°C under stirring for 1 hour. After completion of the reaction, the mixture was neutralized with 10% sodium hydroxide, resulting in the formation of a yellow precipitate. The precipitate was collected by filtration, washed with hot water, and dried. Purification was achieved by recrystallization from ethanol upon heating, yielding compound (I).

Preparation of tetrazolium salt

5,5-'methylene-bis-anthranilic acid (0.01 mol, 2.86 g) was dissolved in water (60 mL), and hydrochloric acid (10 mL) was added dropwise to the well-stirred suspension. The mixture was gradually heated to above 70°C until a clear solution was obtained. The solution was then cooled to 0–5°C in an ice bath. Subsequently, a solution of sodium nitrite ($NaNO_2$, 0.02 mol, 1.3 g) in water (8 mL) was added at 0°C over a period of 5 minutes with continuous stirring. Stirring was maintained for an additional hour while keeping the temperature below 5°C. The resulting clear tetrazotized solution (II) at 0–5°C was obtained and used directly in the subsequent coupling reaction.

2. Synthesis of Azo-Coupling Adducts (II) and (III) (general method)

A cold solution of phenol and 2-naphthol (0.02 mol) dissolved in 10% NaOH (10 mL) was treated with tetrazonium solution (0.01 mol) at 0–5 °C, leading to the formation of the coupling adducts :

5,5′-Methylenebis(2-(4-hydroxyphenyl) diazenyl) benzoic acid (II)

5,5′-Methylenebis(2-(2-hydroxynaphthalen-1-yl) diazenyl) benzoic acid (III)

Results and discussion

Results

5-'5 ,methylene-bis-anthranilic acid (I)

%64 yield p.m. 226.3-228.7°C (lit. 233-235°C) IR (3473.99 cm-1–3372.07 cm-1 (NH2), 2922.91 cm-1– 2586.72 cm-1 (OH), 1659.31cm-1 (CO). 1H-NMR (DMSO-d6) 3.5 (s, 2H, CH2), 6.6 (d, 2H, Ar H), 7.0 (dd, 2H, Ar-H), 7.45 (d, 2H, Ar-H), 8.3 (broad, 2H, OH). 13C-NMR (DMSO-d6) 42.38 (t, 1C), 110.73 (s, 2C), 118 (d, 2C), 129.3 (s, 2C), 131.8 (d, 2C), 135.7 (d, 2C), 151.2 (s, 2C), 171.8 (s, 2C).

5-`5 ,methylene bis (2-(-(2-hydroxynaphthalen-1-yl) diazenyl) benzoic acid) (II)

Yield (76%) p.m. 155-160.5°C.

IR (1602 cm-1 N=N, 1692 cm-1 C=O).

5-`5 ,methylenebis (2-(-(4 hydroxyphenyl) diazenyl) benzoic acid) (III)

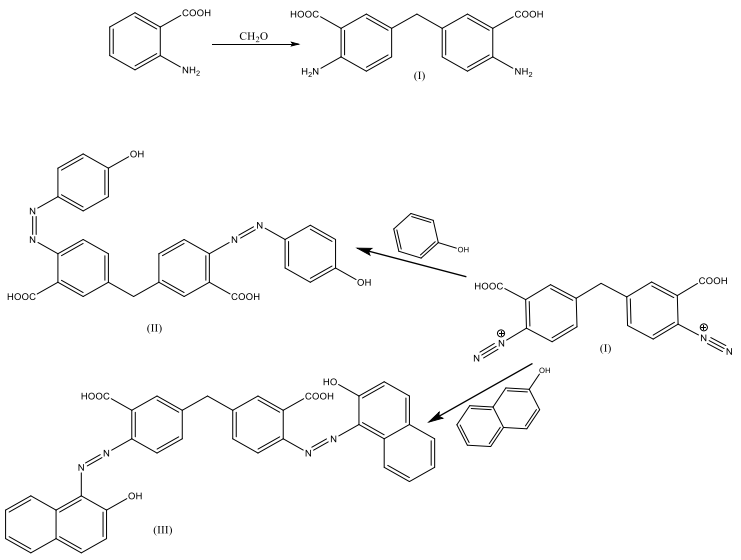
Yield (69%) p.m. dec.

IR (1603 cm-1 N=N, 1673 cm-1 C=O).

Discussion

The electrophilic substitution behavior of anthranilic acid is governed by its ortho-positioned functional groups (-NH_2 and -COOH), which direct incoming electrophiles to the 4-position, being para to the amino group and meta to the carboxylic acid. In this study, formaldehyde served as an effective electrophile under acidic conditions, selectively attacking the 4-position to yield 5,5′-methylene-bis-anthranilic acid (I) with good efficiency. Comprehensive spectroscopic analysis confirmed the structure of compound (I), with IR spectroscopy revealing characteristic NH_2 stretching vibrations at 3473.99 cm^{-1} and 3372.07 cm^{-1}, along with a broad absorption band at 2922.91-2586.72 cm^{-1} corresponding to the methylene bridge. The carbonyl stretch appeared at 1659.31 cm^{-1}, while the absence of a carboxylic acid proton signal indicated zwitterion formation through proton exchange between the carboxylic acid and amino groups. Nuclear magnetic resonance studies provided further structural confirmation, with ^1H NMR showing a distinctive methylene singlet at 3.5 ppm and aromatic protons between 6.6-7.45 ppm, while ^{13}C NMR/APT analysis clearly identified the methylene carbon at 42.38 ppm and the carbonyl carbon at 171.8 ppm among seven aromatic carbons.

Subsequent conversion of compound (I) to its tetrazonium salt enabled successful coupling reactions with phenol and β-naphthol, producing the corresponding disazo derivatives (II) and (III) respectively as shown in scheme 1.



Scheme 1 Synthesis and reactions of methylene bi-anthranilic acid

The transformation was evidenced by the disappearance of NH_2 stretching vibrations (3400-3300 cm^{-1}) and emergence of characteristic N=N stretches at 1602-1603 cm^{-1} in the IR spectra. These coupling reactions proceeded efficiently under mild conditions, yielding the target compounds in 70-76% yield. The synthetic pathway demonstrates the versatility of anthranilic acid derivatives, employing sequential nucleophilic (amine diazotization) and electrophilic (azo-coupling) transformations to construct complex molecular architectures. The high yields and straightforward reaction conditions underscore the practical utility of this methodology for preparing functionally diverse azo compounds with potential applications in various fields of chemistry.

Conclusion

In this study, 5,5′-methylene-bis-anthranilic acid (I) was successfully synthesized through the electrophilic substitution of anthranilic acid with formaldehyde under acidic conditions. The structure of the product was confirmed by spectroscopic techniques, including IR and NMR, which revealed characteristic functional group vibrations and proton/carbon environments consistent with the proposed structure. Subsequent diazotization of (I) and coupling with phenol and β-naphthol afforded the corresponding disazo derivatives (II) and (III) in good yields (70–76%). The formation of the azo linkage was verified by the disappearance of NH_2 stretches and the appearance of N=N vibrations in the IR spectra. This work demonstrates an efficient and practical synthetic route for preparing methylene-bridged bis-azo compounds from anthranilic acid derivatives. The mild reaction conditions, high yields, and straightforward purification make this method attractive for potential applications in medicinal chemistry and materials science. Future studies could explore the biological activity of these compounds or their utility as dyes and functional materials. Overall, this synthetic approach provides a valuable addition to the toolbox for constructing structurally diverse azo-based architectures.

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Conflict of interest: All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report.

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