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Synthesis of novel tripodal-benzimidazole from 2,4,6-tris(p-formylphenoxy)-1,3,5-triazine: Structural, electrochemical and antimicrobial studies

Ziya Erdem Koc[a,*], Haluk Bingol[a], Ahmet O. Saf[a], Emrah Torlak[b], Ahmet Coskun[a]

[a] *Department of Chemistry, Faculty of Science, Selcuk University, 42031 Konya, Turkey*
[b] *Provincial Control Laboratory, Konya, Turkey*

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ABSTRACT

Four new tripodal-benzimidazole derivatives were synthesized by Schiff base reaction between 2,4,6-tris(p-formylphenoxy)-1,3,5-triazine (TRIPOD) and different diamine derivatives. The structures of the obtained compounds were identified by FT-IR, ^{1}H NMR, ^{13}C NMR and UV–vis spectral data, thermal analysis and elemental analysis. Electrochemical behaviors of the compounds were studied by cyclic voltammetry in DMF including 0.1 M [NBu$_4$] [PF$_6$]. The voltammograms showed peaks having similar characteristics except tripodal-benzimidazole including –NO$_2$ derivative. In addition, their antimicrobial activities were evaluated by using the standard disk diffusion method in dimethylformamide media. The activities were determined against 4 bacteria cultures by comparing to those of gentamycin.

1. Introduction

An important class of compounds consisting of substituted s-triazine derivatives has biological activities such as anticancer [1], antiviral [2], estrogen receptor modulators [3] and antimalarials [4–10]. In addition, many of the compounds containing imidazole structure have exhibited the antibacterial activities [11–13]. The compounds have also been used in the treatment of depression and hence gained a considerable importance [14]. Considering information above, the design and synthesis of potent antimicrobials have been an important area of immense significance for medicinal chemists [15,16]. Much afford has been devoted to the synthesis of s-triazine derivatives by different groups in the recent years due to their attractive characteristics [17–22].

The reaction of trimeric cyanuric chloride ($C_3N_3Cl_3$) with 3 equiv. of 4-hydroxybenzaldehyde in benzene yielded the desired trialdehyde in a single step, 2,4,6-tris(p-formylphenoxy)-1,3,5-triazine, coded as TRIPOD [23,24]. In this paper, we aimed to make four new benzimidazole derivatives by using TRIPOD and different diamines (o-phenylenediamine, 4-methyl-o-phenylenediamine, 4-chloro-o-phenylenediamine and 4-nitro-o-phenylenediamine). We called them as “tripodal-benzimidazole”. The structure characterizations, electrochemical properties and antibacterial activities of the obtained compounds were reported.

2. Experimental

2.1. Materials and methods

All solvents, o-phenylenediamine, 4-methyl-o-phenylenediamine, 4-chloro-o-phenylenediamine and 4-nitro-o-phenylenediamine used for the synthesis were of reagent grade and used without further purification. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer. The FT-IR spectra were recorded using KBr discs (4000–440 cm^{-1}) on a Perkin Elmer 1600 series FT-IR spectrophotometer. Melting points were measured using a Buchi SMP-20 melting point apparatus. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 MHz in d$_6$–DMSO. The thermal analyses were performed on Shimadzu DTA 50 and TG 50 H models using 10 mg samples. DTA and TG curves were obtained at a heating rate of 10 °C min^{-1}. In all cases the 22–750 °C temperatures range was studied under a dry nitrogen atmosphere. UV–vis absorption spectra were obtained by using a Shimadzu UV-1800 double beam spectrophotometer.

Electrochemical measurements were performed with an EG&G Princeton Applied Research PAR 263/A2 potentiostat/galvanostat with a positive feedback. Cyclic voltammetry studies of the compounds were carried out in dimethylformamide (DMF) solution containing 0.1 M [NBu$_4$] [PF$_6$] as supporting electrolytes, using platinum wires of 0.2 cm diameter as a working and counter electrodes. In all cases, the reference electrode was the Ag/Ag$^+$ (0.1 mol L^{-1}) in DMF with a vycor glass interfacing the working electrode compartment. Ferrocene redox couple was used as an external standard

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* Corresponding author. Tel.: +90 536 226 33 03.
E-mail address: zerdemkoc@gmail.com (Z.E. Koc).

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($E_{1/2}$ = 0.400 V, ΔE_p = 63–69 mV at 100 mV s^{-1}) under the experimental conditions [25]. Cyclic voltammograms were performed in a potential range of +1.50 to −1.80 at scan rates (ν) between 50 and 400 mV s^{-1}. All solutions were purged with nitrogen steam for 30 min before measurement and the working electrode was polished before each experiment with different alumina powders. The procedure was performed at room temperature and a nitrogen atmosphere was maintained over the solution during the measurements.

The antibacterial screenings were evaluated against selected two gram-positive organisms, *Bacillus subtilis* (ATCC 6633) and *Staphylococcus aureus* (ATCC 6538P), and two gram-negative organisms, *Salmonella typhimurium* (NRRL B 4420) and *E. coli* (ATCC 25922), by using "the standard disk diffusion technique" [26] by comparing with gentamycin (Genta).

2.2. Synthesis of compounds

*2.2.1. Synthesis of 2,4,6-tris(p-formylphenoxy)-1,3,5-triazine (**1**)*

2,4,6-Tris(p-formylphenoxy)-1,3,5-triazine (TRIPOD) was prepared by the reaction of cyanuric chloride and 4-hydroxybenzaldehyde according to previous literatures [23,24].

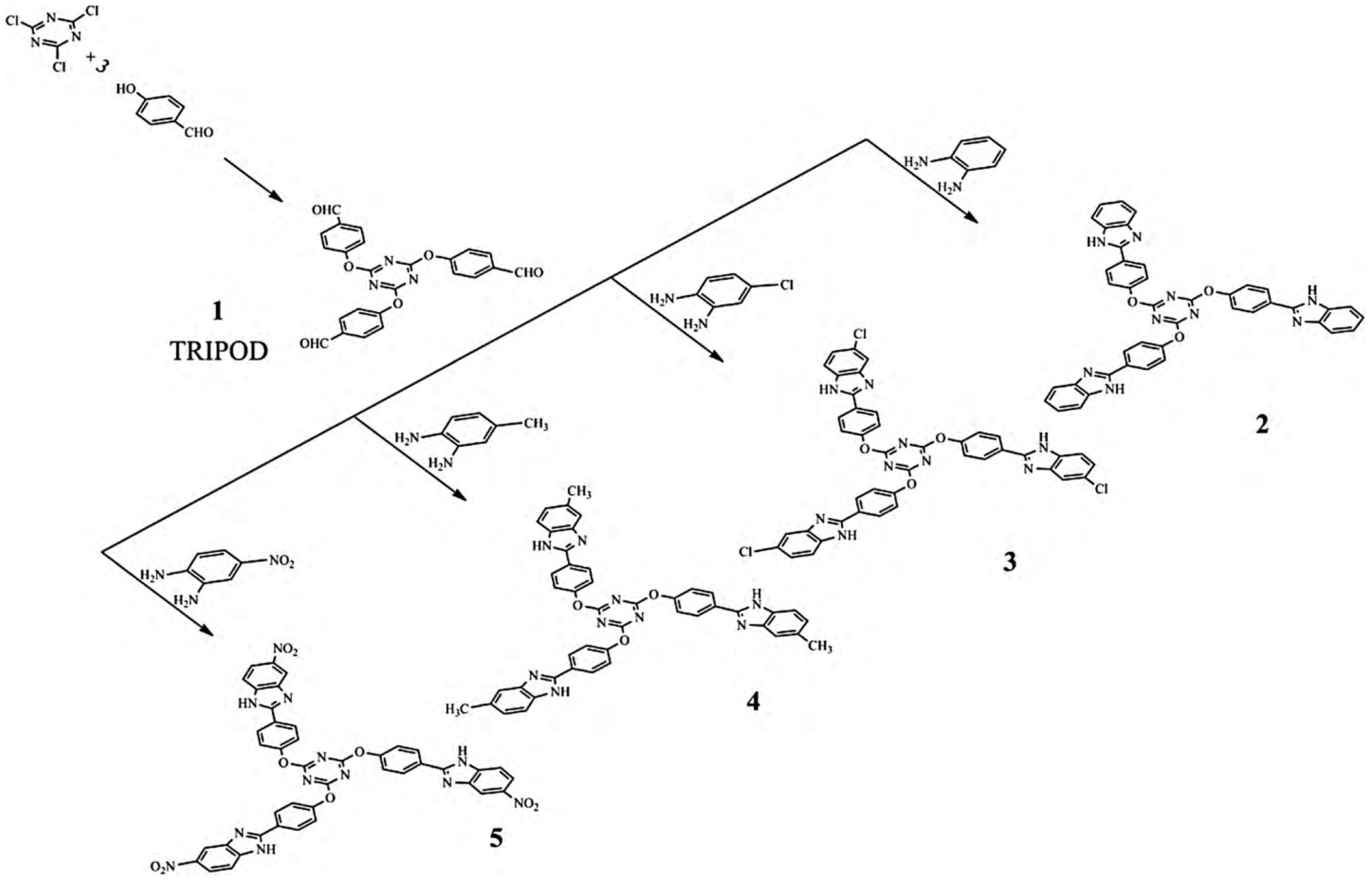
*2.2.2. The synthesis of tripodal-benzimidazoles from TRIPOD (**2**–**5**)*

The compounds **2**–**5** were firstly synthesized by using the procedure described in the literature [27]. To a stirring solution of TRIPOD (441 mg, 1 mmol) in ethanol (25 mL), $NaHSO_3$ (381 mg, 3 mmol) in ethanol (25 mL) was added at room temperature. The reaction mixture was treated with o-phenylenediamine (324 mg, 3 mmol), 4-chloro-o-phenylenediamine (426 mg, 3 mmol), 4-methyl-o-phenylenediamine (366 mg, 3 mmol), and 4-nitro-o-phenylenediamine (459 mg, 3 mmol) in dimethylformamide (20 mL) and boiled under reflux. After 3 h the contents were poured into iced-water (60 mL) and filtered. The precipitate was crystallized from ethanol.

Data for (**2**). Yield: 74%; m.p.: 220 °C; Elemental analysis (Found: C, 71.42; H, 3.83; N, 17.78%). Calc. for $C_{42}H_{27}N_9O_3$: C, 71.48; H, 3.86; N, 17.86%. IR (KBr) ν_{max}/cm^{-1}: 3420 (N–H), 2927 (C–H_{Ar}), 1571 (C=N), 1561 (C=$N_{triazine}$), 1213 (C–N), 1367 (C_{Ar}–O–C). ^{1}H NMR (400 MHz, DMSO–d_6, 25 °C) (δ: ppm): 7.72 (d, 6H, Ar–H, *J* 8.7 Hz), 7.33 (d, 6H, Ar–H, *J* 7.2 Hz), 7.28 (d, 6H, Ar–H, *J* 8.7 Hz), 6.80 (d, 6H, Ar–H, *J* 7.2 Hz), 12.15 (s, 3H, N–H). ^{13}C NMR (100 MHz, DMSO–d_6, 25 °C) (δ: ppm): 181.84, 154.35, 141.58, 137.93, 132.42, 128.07, 122.93, 121.66, 115.41.

Data for (**3**). Yield: 69%; m.p.: 235 °C; Elemental analysis (Found: C, 62.32; H, 2.96; N, 15.52%). Calc. for $C_{42}H_{24}Cl_3N_9O_3$: C, 62.35; H, 2.99; N, 15.58%. IR (KBr) ν_{max}/cm^{-1}: 3421 (N–H), 2922 (C–H_{Ar}), 1573 (C=N), 1564 (C=$N_{triazine}$), 1214 (C–N), 1364 (C_{Ar}–O–C), 840 (C–Cl). ^{1}H NMR (400 MHz, DMSO–d_6, 25 °C) (δ: ppm): 7.73 (s, 3H, Ar–H), 7.67 (d, 3H, Ar–H, *J* 8.5 Hz), 7.33 (d, 6H, Ar–H, *J* 7.4 Hz), 7.28 (d, 3H, Ar–H, *J* 8.5 Hz), 6.78 (d, 6H, Ar–H, *J* 7.4 Hz), 12.33 (s, 3H, N–H). ^{13}C NMR (100 MHz, DMSO–d_6, 25 °C) (δ: ppm): 181.87, 154.41, 141.62, 139.39, 136.05, 132.47, 128.24, 123.36, 121.69, 116.82, 115.83.

Data for (**4**). Yield: 72%; m.p.: 240 °C; Elemental analysis (Found: C, 72.23; H, 4.39; N, 16.79%). Calc. for $C_{45}H_{33}N_9O_3$: C, 72.28; H, 4.45; N, 16.86%. IR (KBr) ν_{max}/cm^{-1}: 3430 (N–H), 2962 and 2926 (C–H), 1572 (C=N), 1490 (C=$N_{triazine}$), 1215 (C–N), 1364 (C_{Ar}–O–C). ^{1}H NMR (400 MHz, DMSO–d_6, 25 °C) (δ: ppm): 7.59 (d, 3H, Ar–H, *J* 8.3 Hz), 7.51 (s, 3H, Ar–H), 7.32 (d, 6H, Ar–H, *J* 7.3 Hz), 7.07 (d, 3H, Ar–H, *J* 8.3 Hz), 6.77 (d, 6H, Ar–H, *J* 7.3 Hz), 11.93 (s, 3H, N–H). ^{13}C NMR (100 MHz, DMSO–d_6, 25 °C) (δ: ppm): 181.83, 154.34, 141.52,



Scheme 1. The synthesis of the tripodal-benzimidazoles.