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Substituted naphthoxy-phthalonitrile derivatives: Synthesis, substituent effects, DFT, TD-DFT Calculations, antimicrobial properties and DNA interaction studies

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ABSTRACT

Herein, substituted-naphthol derivatives **4a–e** were synthesized in two steps, namely the Diels Alder cycloaddition and Cu-catalyzed aromatization reactions, respectively. Then, pththalonitrile derivatives **7–12** have been prepared by a nucleophilic displacement reaction of 3-nitrophthalonitrile with the naphthol derivatives **4a-e, 5** and, obtained in excellent yields. Structural characterization of the compounds was identified by different spectroscopic techniques. Antimicrobial properties of the synthesized compounds were determined by the microdilution procedure against Gram-positive, Gram-negative bacteria, and yeast. Furthermore, the DNA interaction of the compounds were determined by gel electrophoresis. One of the most prominent findings is that compounds **9** and **10** have more inhibitory effects on Gram-positive bacteria than Gram-negative bacteria. These compounds especially exhibited the highest antibacterial potency against *S. aureus* (625 μg/mL) among Gram-positive bacteria. According to the plasmid DNA interaction results, the synthesized compounds caused changes in the structure and mobility of the plasmid DNA. Then, geometry optimizations and frequency calculations were conducted at B3LYP/6–311 G(d,p) level of DFT, and optimized structures were used for further analyses. The NBO results revealed that the π→π * and n→π * interactions were greatly contributed to lowering the stabilization energy of all compounds (**7–12**). FMO energy analyses showed that compound **9** has the biggest electrodonating power.

1. Introduction

Phthalonitriles (*o*-dicyanobenzenes) are a benzene derivative containing two adjacent nitrile groups with the formula $C_6H_4(CN)_2$ and are multifunctional molecules used as synthetic precursors for N4-macrocyclic scaffold (phthalocyanine dyes) and other pigments, fluorescent brighteners, and photographic sensitizers (Booysen et al., 2019; Nombona et al., 2010). The phthalonitriles due to their excellent processability and excellent high-temperature properties are key compounds used in polymeric materials with thermally stable, high-performance mechanical properties (Dominguez and Keller, 2007; Xu et al., 2016). In addition, they have attracted attention due to their potential use in material design for industrial use as well as their synthetic importance (Tunç et al., 2021). Especially for use in military or civilian areas where high-tech equipment is required, it has potential applications in electronics, machinery, automobile, aerospace, and marine fields (Xu et al., 2016; Tunç et al., 2021). Besides, they are used in liquid crystal displays (LCDs) due to their negative dielectric anisotropy values in liquid crystal forms (Okutan et al., 2007). On the other hand, substituted naphthalene derivatives are an important class of compounds with widespread applications in different fields such as materials science and medicine. The naphthalene ring is found in the main skeleton of many biologically and pharmacologically important molecules (Ponra et al., 2015). Especially, naphthalene-based molecules have been shown to have many medicinal properties, including anti-microbial, anti-inflammatory, antifungal, antiviral, antidiabetic, anticancer, antitubercular, antihypertensive, anti-psychotic, anti-neurodegenerative, antidepressant and anti-convulsant effects (Kelleyi et al., 2013; Kalariya et al., 2022; Patel and Patel, 2019; Makar et al., 2019). Fig. 1 shows FDA-approved some naphthalene-based molecules

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