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LETTERS TO THE EDITOR

Synthesis of 2-Substituted Benzoxazoles and Benzimidazoles from 3-Phenoxyphenyl-Containing Acrylonitriles

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Diphenyl oxide derivatives are promising active compounds that exhibit a number of pharmacological properties. In particular, Nimesulide [4-(4-nitro-2-phenoxyphenyl)methanesulfonamide] provides antiinflammatory, analgesic, antipyretic, and antiplatelet effects [1].

Some 2-aryl-substituted benzoxazoles have been used as herbicides [2] and drugs [3]. Some benzimidazole derivatives have shown fungicidal activity [4].

It was of interest to prepare previously never described 2-substituted benzimidazoles and benzoxazoles based on 3-phenoxyphenyl derived acrylonitriles.

The starting 1-phenyl-2-(3-phenoxyphenyl)acrylonitrile **II** and 1,2-bis-(3-phenoxyphenyl)acrylonitrile **III** were prepared via reaction of 3-phenoxyphenylacetonitrile **I** [5] with the corresponding aldehydes.

The synthesis was carried out via stirring the reactants in ethanol in the presence of sodium hydroxide at room temperature (20–25°C) during 1 h (3-phenoxyphenylacetonitrile:aldehyde = 1 : 1.2 mol/mol). Yields of nitriles **II** and **III** were of 84–90% (Scheme 1).

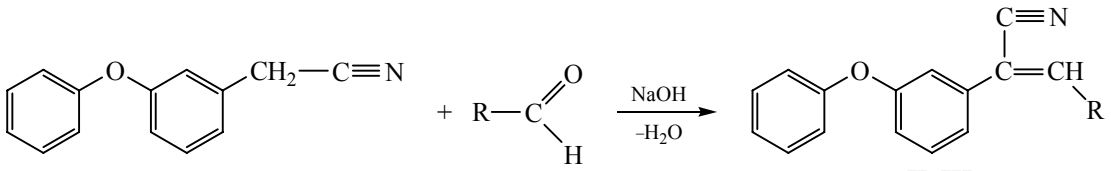
When selecting the optimal reaction temperature, we took into account that at $T > 30$°C a competitive Cannizzaro reaction and disproportionation of the starting aldehyde could occur. On top of that, at 20–30°C the formed 3-phenoxyphenyl acrylonitriles readily crystallized and precipitated, thus greatly facilitating the product isolation.

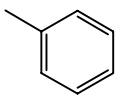
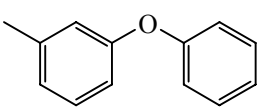
Interaction of the synthesized 3-phenoxyphenyl-derived acrylonitriles **II** and **III** with *o*-phenylenediamine hydrochloride or *o*-aminophenol hydrochloride resulted in formation of 2-(3-phenoxyphenyl)benzoxazoles and benzimidazoles **IV**–**VII** (Scheme 2).

The reactions were carried out at room temperature in sealed tubes.

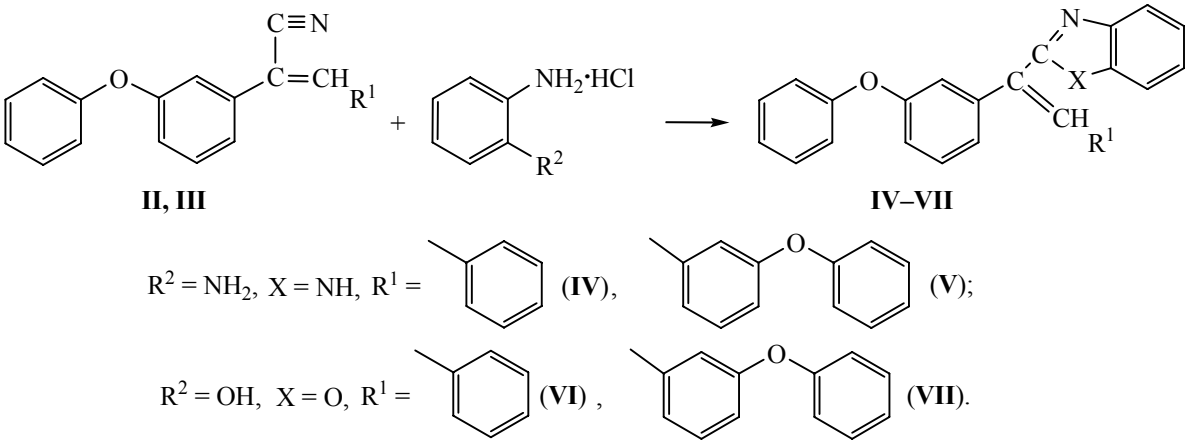
The structure and composition of the obtained 2-(3-phenoxyphenyl)benzimidazoles and benzoxazoles **IV**–**VII** were confirmed by IR and ^{1}H NMR spectroscopy as well as gas chromatography–mass spectrometry.

Scheme 1.



R =  (**II**),  (**III**).

Scheme 2.



1,2-Bis(3-phenoxyphenyl)acrylonitrile (III). 5 mL of a 40% alcoholic solution of sodium hydroxide was added dropwise upon stirring to a mixture of 17.46 g (0.09 mol) of freshly distilled 3-phenoxybenzaldehyde, 19.7 g (0.09 mol) of 3-phenoxyphenylacetonitrile, and 10 mL of 95% ethanol The reaction was exothermic. After cooling, the precipitate was filtered off and sequentially washed with distilled water and 95% ethanol. Alcoholic filtrates were combined, evaporated, and the residue was recrystallized from 95% ethanol. Yield 84% (32.6 g), mp 98–100°C. IR spectrum, ν, cm^{-1}: 2254 (C≡N), 1620 (C=C). ^{1}H NMR spectrum, δ, ppm: 6.77–7.37 m (9H, $C_6H_5OC_6H_4$), 6.40 s (H, CH). Mass spectrum, *m*/*z* (I_{rel}, %): 389 (100), 77 (15), 51 (16). $C_{27}H_{19}O_2N$. *M* 389.

1-Phenyl-2-(3-phenoxyphenyl)acrylonitrile (II) was prepared similarly. Yield 90% (29 g), mp 87–89°C. IR spectrum, ν, cm^{-1}: 2246 (C≡N), 1607 (C=C). ^{1}H NMR spectrum, δ, ppm: 6.70–7.21 m (14H, $C_6H_5OC_6H_4$, C_6H_5), 6.51 s (H, CH). Mass spectrum, *m*/*z* (I_{rel}, %): 297 (100) [M^+], 77 (25), 51 (14). $C_{21}H_{15}ON$. *M* 297.

2-[1-Phenyl-2-(3-phenoxyphenyl)vinyl]benzimidazole (IV). A mixture of 3.47 g (0.024 mol) of *o*-phenylenediamine hydrochloride and 6 g (0.02 mol) of 1-phenyl-2-(3-phenoxyphenyl)acrylonitrile was heated at 220–250°C in a sealed glass tube during 10 h. Then the reaction mixture was triturated and heated (90–95°C) with 5% hydrochloric acid during 1 h. The mixture was filtered, and aqueous ammonia was added to the filtrate. The solution color changed from blue to purple, and precipitation occurred. The precipitate was filtered off, dried, and recrystallized from anhydrous ethanol. Yield 52% (4.0 g), mp 234–235°C. IR spectrum, ν, cm^{-1}: 1632 (C=N), 1650 (C=C), 3405(NH). ^{1}H NMR spectrum, δ, ppm: 6.83–7.75 m (18H, $C_6H_5OC_6H_4$, C_6H_5, C_6H_4), 6.65 s (1H,CH).

2-[1,2-Bis(3-phenoxyphenyl)vinyl]benzimidazole (V) was prepared similarly. Yield 35% (3.4 g), mp 256–258°C. IR spectrum, ν, cm^{-1}: 1625 (C=N), 1670 (C=C), 3400 (NH). ^{1}H NMR spectrum, δ, ppm: 6.70–7.53 m (22H, $2C_6H_5OC_6H_4$, C_6H_4), 6.61 s (1H, CH).

2-[1-Phenyl-2-(3-phenoxyphenyl)vinyl]benzoxazole (VI). A mixture of 3.5 g (0.024 mol) of *o*-aminophenol hydrochloride and 6 g (0.02 mol) of 1-phenyl-2-(3-phenoxyphenyl)acrylonitrile was heated at 220–250°C in a sealed glass tube during 10 h. Then, the reaction mixture was triturated with diethyl ether and washed with 4 mol/L solution of NaOH. The resulting precipitate was filtered off, washed with warm water and diethyl ether, and dried. Yield 36% (3 g), mp 165–168°C. ^{1}H NMR spectrum, δ, ppm: 7.17–7.74 m (18H, $C_6H_5OC_6H_4$, C_6H_5, C_6H_4), 6.96 s (1H, Ar-CH), 5.62–5.67 d (1H, CHCN). Mass spectrum, *m*/*z* (I_{rel}, %): 389 (24) [M^+], 388 (100), 207 (48), 77 (19).

2-[1,2-Bis(3-phenoxyphenyl)vinyl]benzoxazole (VII) was prepared similarly. Yield 25% (2.4 g), mp 180–182°C. ^{1}H NMR spectrum, δ, ppm: 7.14–7.74 m (22H, $C_6H_5OC_6H_4$, C_6H_4), 6.99 s (1H, Ar-CH). Mass spectrum, *m*/*z* (I_{rel}, %): 481 (14) [M^+], 480 (100), 352 (51), 281 (17), 207 (28), 77 (29), 51 (18).

IR spectra were recorded using a Specord M 82 spectrometer (KBr, paraffin oil). ^{1}H NMR spectra of the solutions in DMSO-d_6 were recorded with a Varian Mercury 300 instrument (300 MHz). Gas chromatography–mass spectra were obtained with a Varian MAT-11 spectrometer at 70 eV (EI).

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