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Synthesis and Antimicrobial Activity of 5-(2-Aminoethylamino)-2-(2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[*de*]isoquinoline-1,3-diones

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GOAL OF THE STUDY

This article presents a method for the synthesis of novel 5-(2-aminoethylamino)-2-(2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[de]isoquinoline-1,3-diones, based on the reaction of various 5-bromo-2-(2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[de]isoquinoline-1,3-diones with ethane-1,2-diamine. The resulting naphthalimide derivatives were characterized using physicochemical methods, IR, 1H NMR, and 13C NMR spectroscopy. Furthermore, their antimicrobial activity was evaluated against both Gram-positive and Gram-negative bacteria, as well as yeasts, and molds.

METHODOLOGY OF THE INVESTIGATION

All chemicals used were obtained from Merck and Sigma-Aldrich. Melting points were measured using an SMP-10 digital melting point apparatus. The IR spectra were recorded on a Perkin-Elmer FTIR-1600 spectrometer using KBr disks. The NMR spectra were obtained with a Bruker Avance III HD spectrometer (operating at 500.13 MHz for ^{1}H and 125 MHz for ^{13}C) in DMSO-d_6 solutions. The chemical shifts were referenced to tetramethylsilane (TMS). The purity of the compounds was checked by thin layer chromatography on Kieselgel 60 F_{254}, 0.2 mm Merck plates, eluent system (vol. ratio): ethyl acetate : petroleum ether = 1 : 2.

MAIN RESULTS FROM THE STUDY

5-Bromo-1*H*,3*H*-naphtho[1,8-*cd*]pyran-1,3-dione was synthesized *via* a modified procedure, followed by condensation with 3-aminospirohydantoins. An attempt was made to obtain a Schiff base of compound Vd with 4-methoxybenzaldehyde according to Fig. 1.

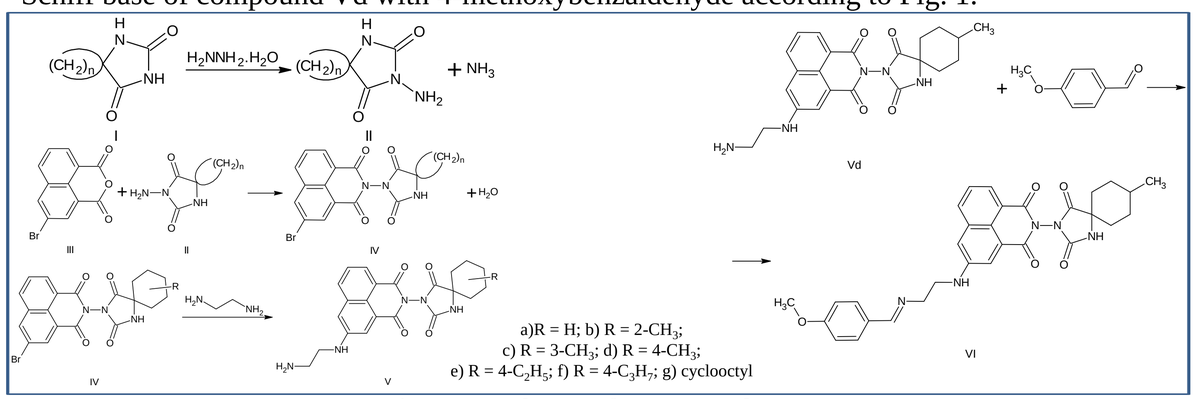

Fig. 1. Synthesis of compound VI

The physicochemical characteristics of products Va–g and VI are presented in Table 1. It should be noted that the melting points of compounds Va–g are approximately 100°C lower than those of IVa–g.

Table 1. Physicochemical parameters of compounds Va-g and VI

№	Systematic name	Yield, %	M. p., °C	R_f
Va	5-(2-aminoethylamino)-2-(2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[de]isoquinoline-1,3-dione	94	156-157	0.45
Vb	5-(2-aminoethylamino)-2-(6-methyl-2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[de]isoquinoline-1,3-dione	98	167-168	0.42
Vc	5-(2-aminoethylamino)-2-(7-methyl-2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[de]isoquinoline-1,3-dione	94	136-137	0.46
Vd	5-(2-aminoethylamino)-2-(8-methyl-2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[de]isoquinoline-1,3-dione	91	160-161	0.40
Ve	5-(2-aminoethylamino)-2-(8-ethyl-2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[de]isoquinoline-1,3-dione	88	138-139	0.35
Vf	5-(2-aminoethylamino)-2-(2,4-dioxo-8-propyl-1,3-diazaspiro[4.5]decan-3-yl)benzo[de]isoquinoline-1,3-dione	72	177-178	0.39
Vg	5-(2-aminoethylamino)-2-(2,4-dioxo-1,3-diazaspiro[4.7]dodecan-3-yl)benzo[de]isoquinoline-1,3-dione	95	143-144	0.32
VI	5-[2-[(E)-(4-methoxyphenyl)methyleneamino]ethylamino]-2-(8-methyl-2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[de]isoquinoline-1,3-dione	86	195-196	0.34

In the IR spectra, absorption bands corresponding to NH_2 group vibrations, absent in IVa–g, are observed.

The spectral data unambiguously confirm the proposed structures of the synthesized compounds.

The antimicrobial activity of products Va–g was evaluated and found to be significantly higher than that of IVa–g.

The results indicate that compounds Va–g exhibit moderate activity against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus subtilis*, *Bacillus cereus*, *Escherichia coli*, *Salmonella abony*, and *Candida albicans*, and strong activity against *Pseudomonas aeruginosa*.

Compound VI was inactive against the tested microorganisms.

CONCLUSIONS

A series of 5-(2-aminoethylamino)-2-(2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[*de*]isoquinoline-1,3-diones (Va–g), as well as the Schiff base 5-[2-[(*E*)-(4-methoxyphenyl)methyleneamino]ethylamino]-2-(8-methyl-2,4-dioxo-1,3-diazaspiro[4.5]decan-3-yl)benzo[*de*]isoquinoline-1,3-dione (VI), were synthesized and structurally characterized.

Antimicrobial studies demonstrated that, unlike compound VI, compounds Va–g exhibit activity against the tested Gram-positive and Gram-negative bacteria, yeasts, and molds. It was found that compounds Va–g are most active against the Gram-negative bacterium *Pseudomonas aeruginosa*.

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