Scientific and technical report

Financing contract

Project title: The synthesis of new hybrid [2.2]paracyclophane-flavonoids systems with potential antimicrobial activity

Project code: PN-III-P1-1.1-PD-2016-0962

Acronym: [2.2]PC-Flav

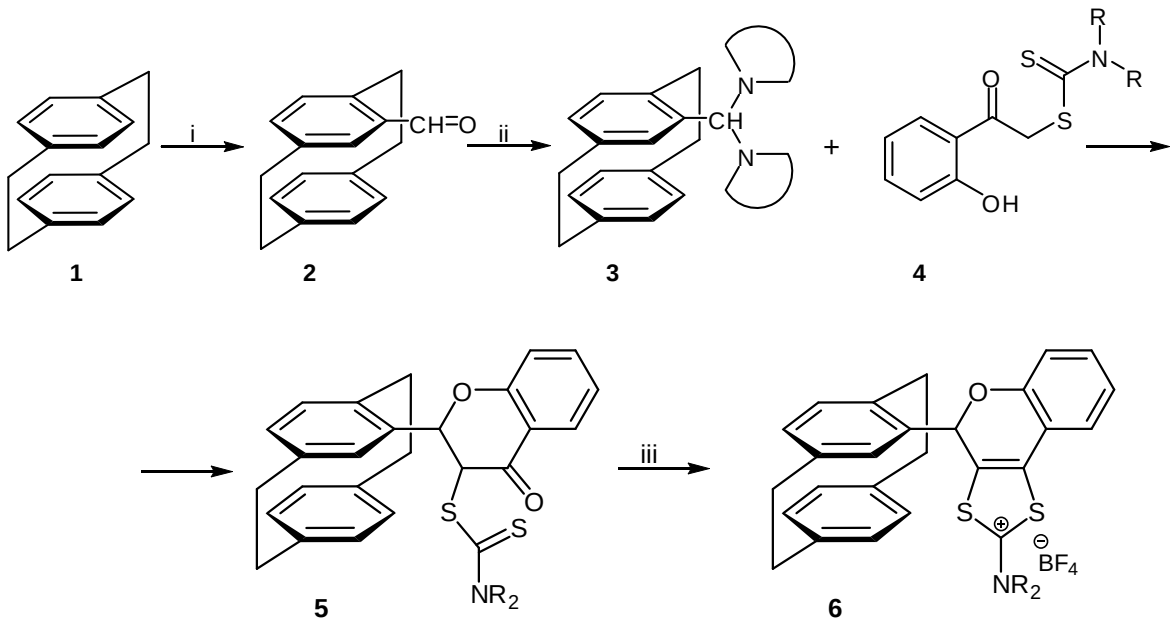
No. 48/2018

The structure-activity relationship regarding the antibacterial properties for the synthesized flavonoids

Stage 3 2020

Synthesis of tricyclic flavonoids with different substituents at position 2 of the 1,3-dithiolium ring

The synthetic path is described in Scheme 1 and involves the reaction of aminal **3** with various 2'-hydroxyphenacyl dithiocarbamates **4**. The benzopyranes **5** thus obtained are converted into tricyclic flavonoids **6** by heterocyclization in acid catalysis. The substituents found in position 2 of the 1,3-dithiolium ring are derived from dimethylamine, diethylamine, pyrrolidine, piperidine and morpholine.



i. Cl_2CHOCH_3 / $TiCl_4$; ii. NHR_2 ; iii. H_2SO_4 / AcOH 1:3 v/v, $NaBF_4$ aq **Scheme 1**

NR_2= NMe_2, NEt_2, pyrrolidine, piperidine, morpholine

Testing the activity of 1,3-dithiolium flavonoids on a wide spectrum of bacteria.

The inhibition zone diameter values determined for the five flavonoids tested against two bacterial strains (*Staphylococcus aureus* ATCC 25923 and *Escherichia coli* ATCC 25922) are presented in Table 1. Althoug the antimicrobial activity is important in both bacterial strains, it should be noted that the effect is much greater against the Gram positive bacteria tested. The tested flovonoids showed much more important antibacterial properties compared to other synthetic flavonoids: 2´,4´,3-trihydroxichalcone, 3-*O*-alkyl-(+)-catechine derivatives, 7-*O*-genisteine derivatives etc. Among the tested flavonoids, those substituted with diethylamino and dimethylamino proved to be the most active.

Table 1 – The inhibition zone diameter values for the investigated synthetic flavonoids[a, b]

Sample	**The diameter of inhibition zone (mm)**	
	Bacterial material	
	S. aureus	***E. coli***
	Concentration (mg/ml)	

	0,25	**0,5**	**1**	**0,25**	**0,5**	**1**
2-dimetylamino	**15 ± 1**	**17.33 ± 1,15**	**20.33 ± 0.57**	**8.33 ± 1.15**	**10.66 ± 1.15**	***11.66 ± 0.57***
2-dietylamino	**17.66 ± 1.15**	**18.66 ± 1**	***21.33 ± 0.57***	**9.66 ± 1.15**	**11.66 ± 1.15**	**12.66 ± 0.57**
2-pyrrolidinyl	**8.33 ± 0.57**	**14 ± 1**	**16.66 ± 0.57**	**7.66 ± 0.57**	**8.33 ± 0.57**	**9.33 ± 0.57**
2-piperidinyl	**7.66 ± 0.57**	**9.66 ± 0.57**	**13.66 ± 0.57**	**6.66 ± 0.57**	**7.33 ± 0.57**	**7.66 ± 0.57**
2-morphoolinyl	**7.33 ± 0.57**	**14.33 ± 1**	**16.33 ± 1**	**5.66 ± 0.57**	**6.33 ± 0.57**	**7.66 ± 0.57**
Gentamicine (10 µg/disc)	**18.33 ± 0.57**			**15.75 ± 1.7**		

[a] The diameter of the inhibition zones includes the disc (5 mm).

[b] Values are expressed in millimeters.

Project leader,

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