

Table of Contents

1	INTRODUCTION.....	1
1.1	CANCER	1
1.1.1	<i>Treatment</i>	2
1.2	APOPTOSIS	3
1.3	AIMS AND SCOPES	5
2	SYNTHESIS OF BENZAMIDE RIBOSIDE DERIVATIVES WITH ANTITUMOR ACTIVITY.....	7
2.1	INTRODUCTION	7
2.2	MECHANISM OF ACTION OF BENZAMIDE RIBOSIDE	8
2.3	SYNTHESIS OF BENZAMIDE RIBOSIDE	8
2.3.1	<i>Synthesis of C-glycosides</i>	8
2.3.2	<i>Preparation of 2,3,5-tri-O-benzyl-γ-ribonolactone (2-7).....</i>	9
2.3.3	<i>Coupling of 1,4-Ribonolactone (2-7) with organometallic reagent 2-11</i>	11
2.3.4	<i>Cleavage of the oxazoline group and transformation to benzamide riboside (2-2)</i>	12
2.4	SYNTHESIS OF BENZAMIDE RIBOSIDE ANALOGUES	14
2.4.1	<i>Preparation of 3-deoxy sugar derivative (2-32).....</i>	14
2.4.2	<i>Preparation of derivatives with different substituents on the aromatic ring.....</i>	17
2.5	INVESTIGATION TOWARDS THE SYNTHESIS OF 2-DEOXY- AND 2,3-DIDEOXY-BENZAMIDE RIBOSIDE ..	20
2.5.1	<i>Preparation of 2,3-dideoxy-5-benzyl-ribonolactone (2-46)</i>	20
2.5.2	<i>Preparation of 2-deoxy-3,5-dibenzyl-ribonolactone (2-52)</i>	22
2.5.3	<i>Investigation on the coupling of deoxy-lactones 2-46 and 2-52 with lithiated oxazoline 2-11</i>	23
2.6	BIOLOGICAL TEST RESULTS.....	24
3	SYNTHESIS OF BENZAMIDE RIBOSIDE ADENINE DINUCLEOTIDE.....	26
3.1	INTRODUCTION	26
3.2	SYNTHESIS OF BENZAMIDE RIBOSIDE ADENINE DINUCLEOTIDE (3-5)	27
3.3	ENZY-M-SUBSTRATE COMPLEX STUDIES	28
4	SYNTHESIS AND STRUCTURE-ACTIVITY RELATIONSHIP OF ANTIFUNGAL CONIOTHYRIOMYCIN ANALOGUES.....	29
4.1	INTRODUCTION	29
4.2	DEVELOPING A NEW METHOD FOR THE SYNTHESIS OF MIXED IMIDES.....	30
4.3	SYNTHESIS OF CONIOTHYRIOMYCIN ANALOGUES – VARIATION OF THE SUBSTITUTION PATTERN OF THE BENZYL-RING	31
4.4	SYNTHESIS OF CONIOTHYRIOMYCIN ANALOGUES – CHANGING THE DEGREE OF SATURATION, AND HYDROPHOBICITY IN THE FUMARIC ESTER SIDE-CHAIN	32
4.5	SYNTHESIS OF CONIOTHYRIOMYCIN ANALOGUES - REPLACEMENT OF CARBON BY NITROGEN, OXYGEN OR SULFUR IN THE MIDDLE PART OF THE MOLECULE	33
4.6	BIOLOGICAL STUDIES	34

5	STRUCTURE-ACTIVITY RELATIONSHIPS IN ALLERGIC CONTACT DERMATITIS ..	36
5.1	INTRODUCTION	36
5.1.1	<i>The investigated phenanthrene-quinones</i>	38
5.2	SENSITIZATION	40
5.3	SENSITIZATION TEST RESULTS.....	41
5.4	QUANTUM MECHANICAL CALCULATIONS.....	44
6	DETERMINATION OF THE ABSOLUTE CONFIGURATION BY QUANTUM CHEMICAL CALCULATION OF CD SPECTRA.....	47
6.1	INTRODUCTION	47
6.2	THEORETICAL PRINCIPLES - CALCULATION OF CD SPECTRA.....	48
6.3	DETERMINATION OF THE ABSOLUTE CONFIGURATION OF AN ERGOCHROME	51
6.3.1	<i>Atropismерism</i>	54
6.3.2	<i>Determination of rotation barrier of ergochrome (6-1)</i>	55
6.4	CALCULATION OF THE ABSOLUTE CONFIGURATION OF EPIEUDESMIN (6-4).....	58
6.5	DETERMINATION OF THE ABSOLUTE CONFIGURATION OF A XYLOKETAL (6-5)	60
6.6	DETERMINATION OF THE ABSOLUTE CONFIGURATION OF ASCOCHIN (6-6)	62
6.7	DETERMINATION OF THE ABSOLUTE CONFIGURATION OF A METABOLIC PRODUCT OF <i>PHOMOPSIS OBLONGA</i> (6-8) USING UV-CORRECTION.....	66
6.8	DETERMINATION OF ABSOLUTE CONFIGURATION OF PLUMERICINE (6-9) AND PLUMENOSIDE (6-10) ..	69
7	SUMMARY	72
8	EXPERIMENTAL PART	74
8.1	INSTRUMENTATION	74
8.2	EXPERIMENTAL PART TO CHAPTER 2	75
8.3	EXPERIMENTAL PART TO CHAPTER 3	100
8.4	EXPERIMENTAL PART TO CHAPTER 4	103
9	ABBREVIATIONS	118
10	LITERATURE	119