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QUATERNARY SALTS OF AZAAROMATICS AS BIOLOGICAL AGENTS AND AS COMPONENTS OF SUPRAMOLECULAR SYSTEMS

Abstract: In the paper selected examples of quaternary salts of azaaromatics are presented showing them as biological agents and as components of supramolecular systems.

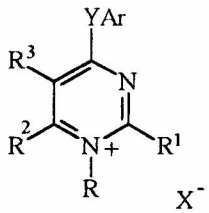
Introduction

Quaternary salts of azaaromatics are intensively studied [1-6] in view of their reactivity [7-9], physicochemical [10,11] and biological [12,13] properties, as well as due to their interesting application possibilities [14,15], *e.g.* as dyes, catalysts, modified polymers and materials for optoelectronic devices.

In the first part of the present paper biological activities of quaternary azaaromatics are described, and in the second one the supramolecular systems built with quaternary azaaromatics are characterized.

1. Quaternary salts of azaaromatics as biological agents

Quaternary salts of azaaromatics often show biological activities, *e.g.* compounds **1** serve as herbicides [16].



Y = O, S, SO, SO_2, NH

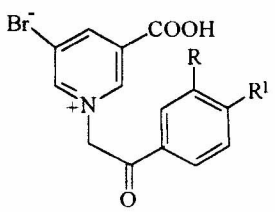
R = alkyl, nitroalkyl

R^1, R^2, R^3 = H, OH, NO_2, alkyl, alkenyl, alkynyl

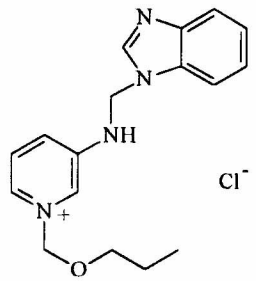
X^- = organic or inorganic anion

1

Quaternary salts **2** [17] and **3** [18] have antibacterial properties.

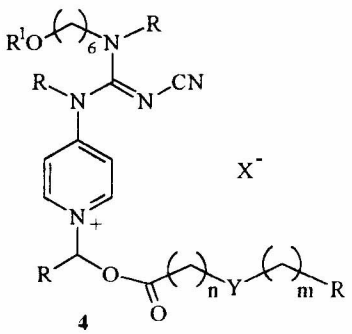


		R	R^1	X
2	**a**	OH	H	Cl
	b	H	Br	Br



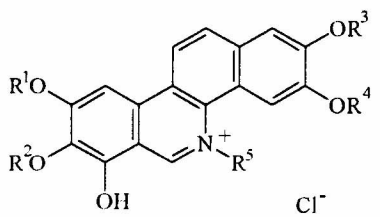
3

Antitumor activity has been observed in N-cyano-N-pyridinium-guanidine derivatives **4** [12] and in benzo[c]phenanthridinium quaternary salts **5** showing intercalating properties [19].



4

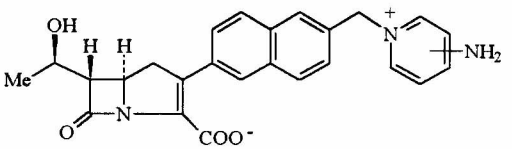
R = H, alkyl
R^1 = aryl, heteroaryl
Y = O, NH
n, m = 0-4
X = Cl, Br, NO_3



5

R^1, R^2, R^3, R^4, R^5 = C_1- C_5 alkyl

Syntheses of antibiotics - naphthylcarbapenems **6** [20] as well as those of cephalosporins **7** [21] and **8** [13] have been reported.



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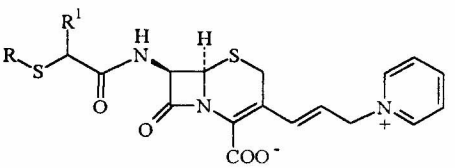
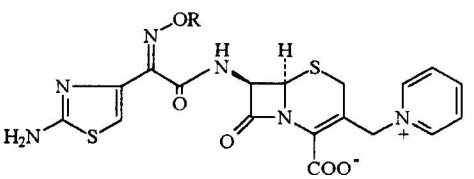


7 R = alkyl, aryl
R^1 = H, alkyl, Ph

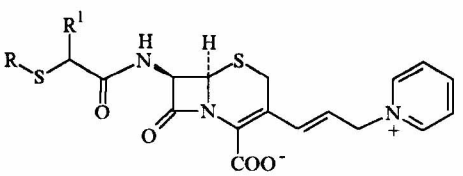


8

R = $C(R^1)(R^2)COOH$

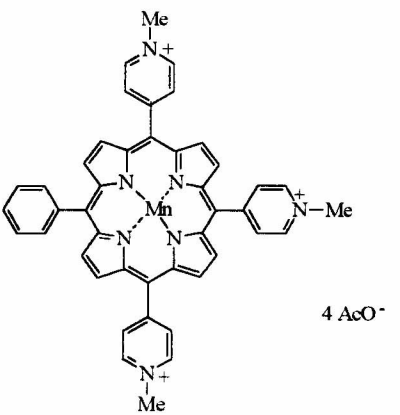
R^1, R^2 = H, alkyl, cycloalkyl

It was established that quaternary salt **9** acts as inhibitor of the bacterial NAD synthetase [22] and porphyrin **10** is a synthetic nuclease which may decompose DNA [23-25].



9

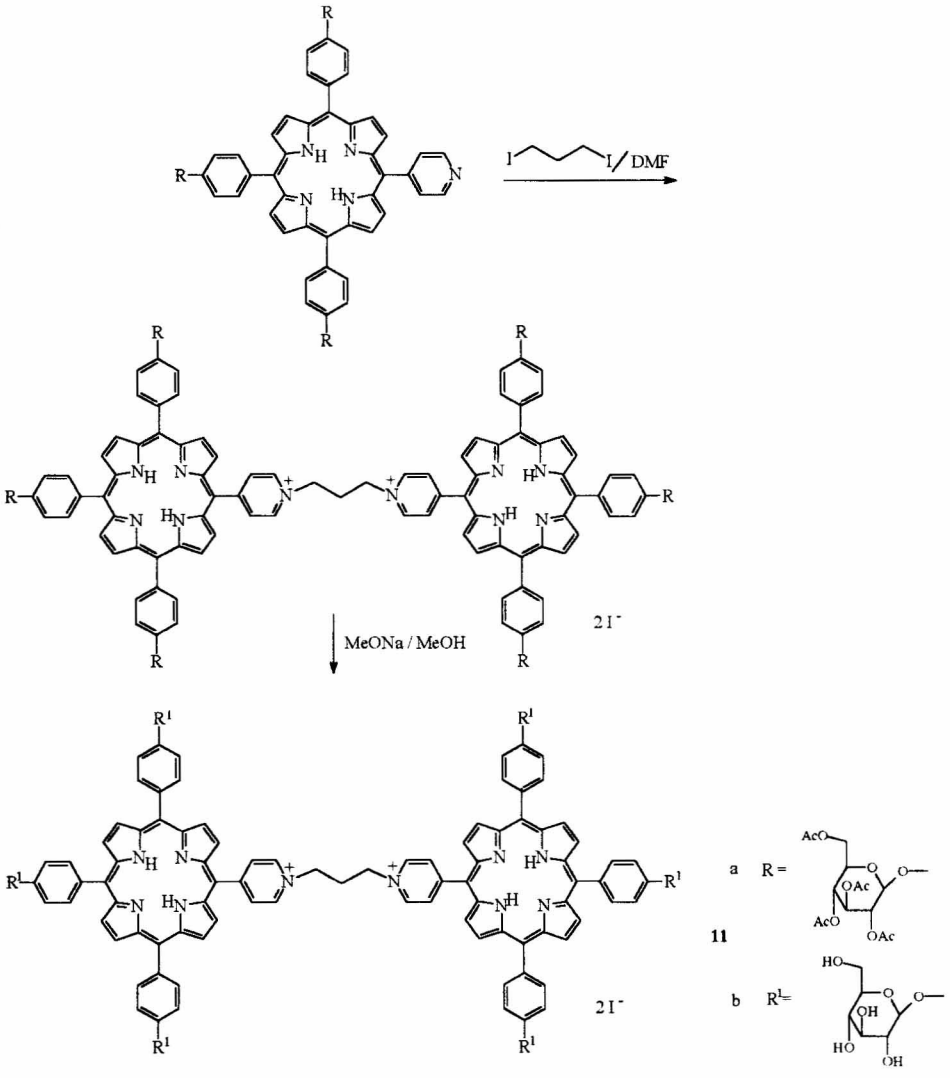
R = alkyl, aryl
R^1 = H, alkyl, Ph



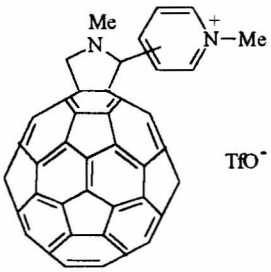
4 AcO^-

10

The dimeric porphyrin **11b** bearing glucose moieties shows antitumor activity [26]. The synthesis of **11b** proceeds as follows:

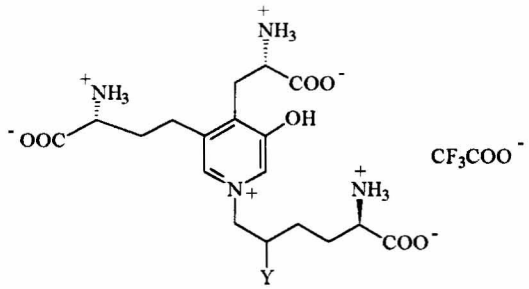


In the study of fullerenes functionalized with N-methylpyridinium group it was observed that the water soluble **12** is able to decompose DNA under photolytic conditions [27].



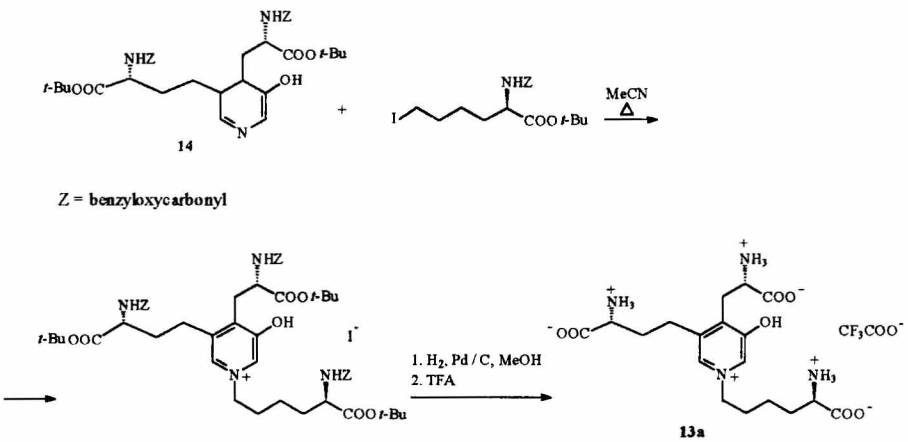
12

Quaternary salts **13a,b** may be used as biochemical labels in bone diseases, *e.g.* in osteoporosis [28-30].



	Y
13 **a**	H
b	OH

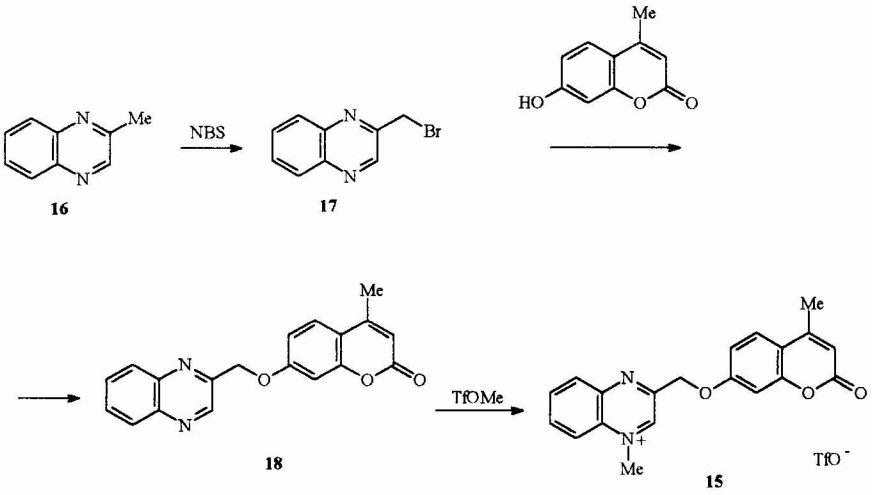
Synthesis of **13a** involves the quaternization of the pyridine **14**, followed by deprotection of amino groups.



13a

The quaternary quinoxalinium salt **15** serves for the determination of the NAD(P)H level in cells [31,32], since its reduction with NADH results in the elimination of intensively fluorescent 4-methylumbelliferone [33].

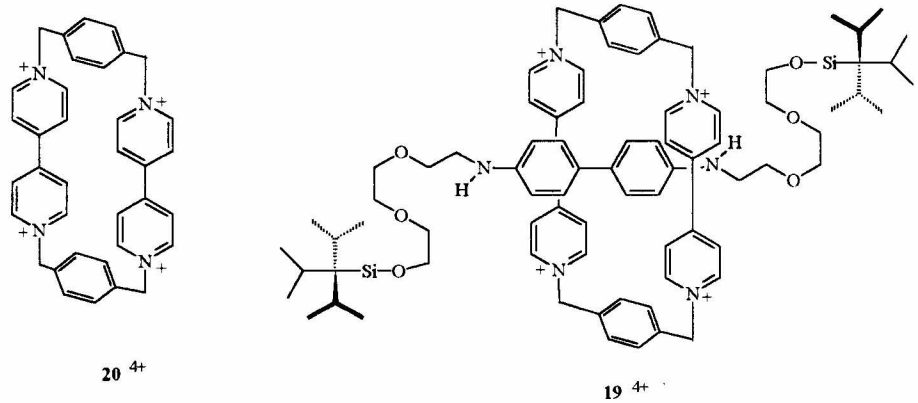
The synthesis of **15** begins with the bromination of 2-methylquinoxaline **16** with NBS. The formed **17** reacts with 4-methylumbelliferone affording **18** which was quaternized to give **15**.



2. Quaternary salts of azaaromatics as components of supramolecular systems

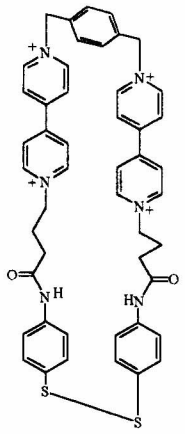
Supramolecular systems bearing quaternary azaaromatics - rotaxanes and catenanes deserve a special attention due to their promising application possibilities [34-39]. Among receptors in host-guest systems, calixarenes [40,41] and cyclodextrins [42-45] should be mentioned.

An example of rotaxanes is **19**$^{4+}$ [46] in which the cyclophane **20**$^{4+}$ [47] serves as a ring.



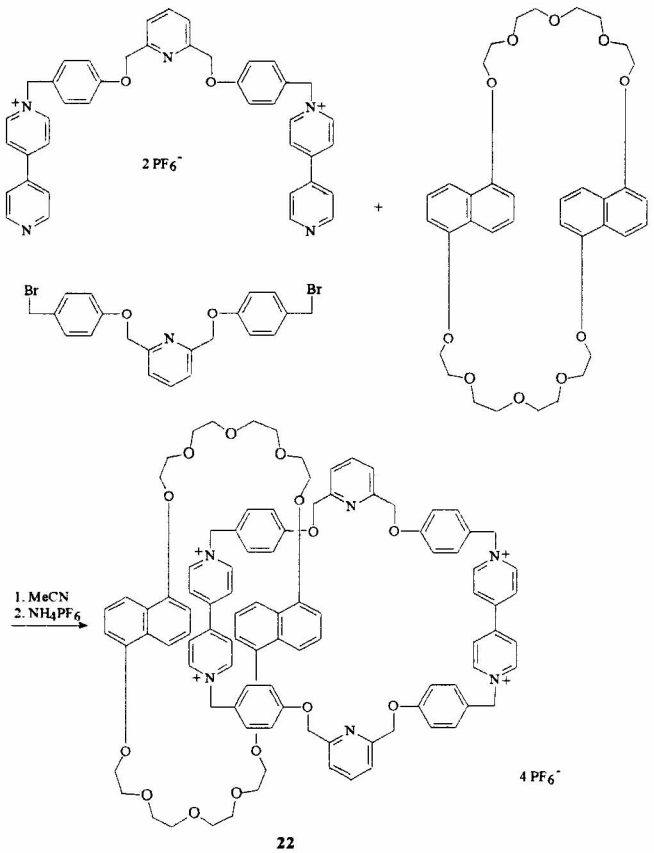
20 $^{4+}$ **19** $^{4+}$

Compound 21^{4+} may also play the role of a ring in rotaxanes [46].



21^{4+}

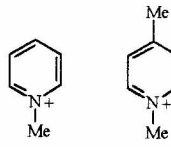
An example of catenanes is [2]catenane **22**, obtained as follows [48,49]:



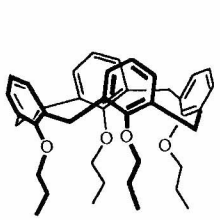
22

Catenanes built with more rings are known, *e.g.* [3]catenane in which one among three rings contains quaternary salt moiety [50].

Calixarenes may serve as host molecules for quaternary azaaromatic ions. For example, **23 - 26** are guest molecules of biscalixarene **27**; the inclusion into calixarene **28** however is possible only for **23** and **24**, larger molecules **25** and **26** cannot incorporate into cavity of **28** for steric reasons [51].



23 **24** **25** **26**



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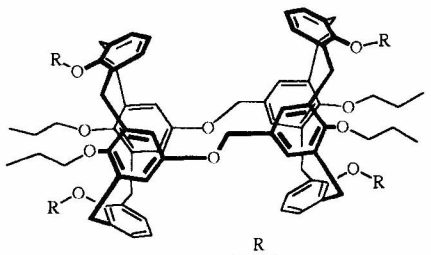
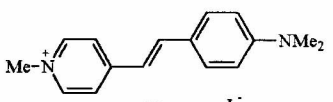


	R
a	H
b	*n*-Pr

27

In the investigation of inclusion properties of **27a** and **27b** for **23** it was found that the association constant for **27a** is higher than that for **27b**, due to the presence of phenol units increasing π-basicity as compared with the propoxybenzene units [52].

Stilbazolium dyes **29 - 31** are guest molecules of water soluble calixarenes **32a-c** [53].



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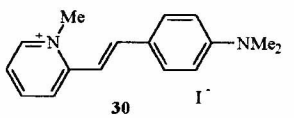

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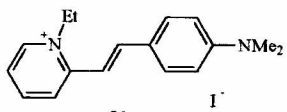

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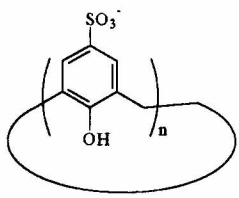

	n
a	4
b	6
c	8

32

Concluding remarks

In the paper only selected examples of quaternary salts of azaaromatics showing biological activities and those serving as components of supramolecular systems have been presented. A large amount of quaternary azaaromatics of various structures enables their interesting applications, this fact finding reflection in numerous reports concerning this topic [54-60].

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Czwartorzędowe sole związków azaaromatycznych jako środki biologicznie czynne i jako składniki układów supramolekularnych

Streszczenie: W artykule opisano czwartorzędowe sole związków azaaromatycznych ze szczególnym uwzględnieniem ich aktywności biologicznej oraz możliwości tworzenia układów supramolekularnych.