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POLYMETINE DYES. PART III*. THE CATIONIC 1-H-INDOLO-3-DIMETHINE DYES

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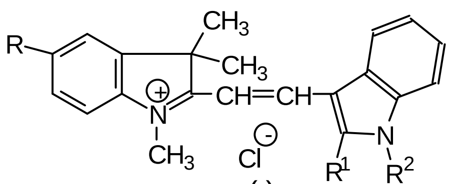
ABSTRACT. By means of elemental and spectral (I.R., UV-VIS and ^{1}H-NMR) analysis data, the structure of cationic 1-H-indolo-3-dimethine dyes (3) of the products resulted by condensation of unsubstituted 1-H-indolo-3-carbaldehyde (4) with different 2- or 4-methylcycloimmonium perchlorates (5) has been proved. The synthesised cationic 1-H-indolo-3-dimethine dyes (3) have an E (*trans*)- configuration relative to the C=C double bond in ethenylic bridge. The obtained compounds exhibit bacteriostatic activity against Grampositive bacteria and good applicability as dyes.

INTRODUCTION

The cationic 1-H-indolo-3-dimethine dye structure is present in some Astrazon dyes (**1**)[1-3]. In these Astrazon type cationic 1-H-indolo-3-dimethine dyes (**1**), the 1-H-indole moiety is substituted. Some drugs with cationic polymethine dye structure are known. Among these, there is one with the name pirvinium [4], a pyrolo-4-dimethine (**2**).

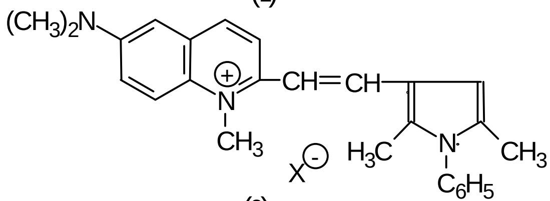


(1)

a: R=R^{1}=H; R^{2}=CH_3

b: R=H; R^{1}=CH_3; R^{2}=C_6H_5

c: R=OCH_3; R^{1}=CH_3; R^{2}=C_6H_5



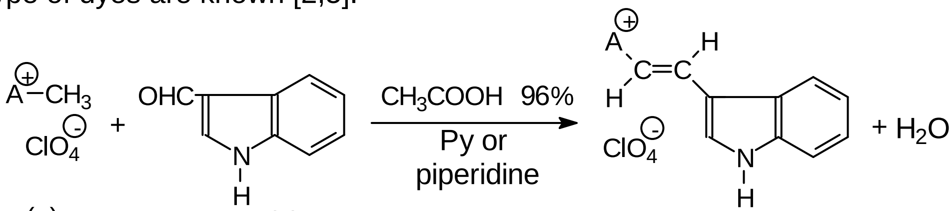
(2)

X^{-}: pamoate

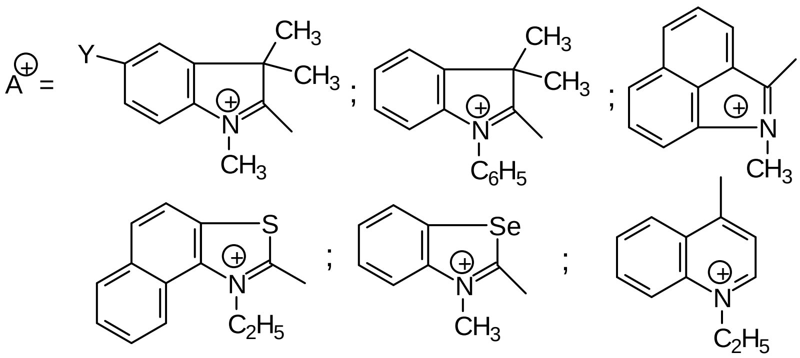
*) Part II, This Journal, this issue

Because 1-H-indolo-3-dimethines are analogues of benzologue at the pyrole ring in pirvinium, they are also expected to present biological activity.

Taking into account the two areas of interest concerning the compounds with a cationic 1-H-indolo-3-dimethine structure we were stimulated to undertake a study of such new dyes, unsubstituted at the 1-H-indolium moiety ***(3)***. It should be mentioned that only a few representatives of this last type of dyes are known [2,5].



(5) (4) (3)



Y= Cl, NO_2, CH_3O

This work aims to confirm the cationic 1-H-indolo-3-dimethine dyes structure ***3*** of the products obtained by condensation of 1-H-indolo-3-carbaldehyde ***(4)*** with different 2- or 4- methylcycloimmonium perchlorates ***(5)*** in glacial acetic acid as solvent, in the presence of catalytic amounts of pyridine or piperidine.

EXPERIMENTAL

The condensation product between 1-H-indolo-3-carbaldehyde ***(4)*** and different 2- or 4- methylcycloimmonium perchlorates ***(5)*** in glacial acetic acid as solvent were obtained and purified as previously described [7]. The elemental analysis has been performed at Raluca Ripan Institute of Chemistry in Cluj. I.R. spectra were registered by means of a Karl Zeiss Jena spectrophotometer, model UR-20, with solid powders in KBr pellets. The ^{1}H-NMR spectra were registered using a Varian Gemini 300 (300MHz) or a Tesla BS 487 (80 MHz) spectrometer. Hexadeuterodimethylsulfoxide has been used as solvent. Electronic spectra were recorded by means of a Karl Zeiss Jena UVVIS Specord spectrophotometer using methanol-water (64 %) solutions.

RESULTS AND DISCUSSION

The main method to synthesise dimethine cationic dyes is the condensation of cycloimmonium salts having an alkyl or alkylene active group [1,2,5,6] with heterocyclic aldehydes having the aldehyde group conjugated with the heteroatom of the cycle. 1-H-indolo-3 -carbaldehyde ***(4)*** fulfills this condition. Consequently, it was expected that its condensation with 2- or 4- methylcycloimmonium perchlorates ***(5)*** yields the desired cationic 1-H-indolo-3-dimethine dyes ***(3).***

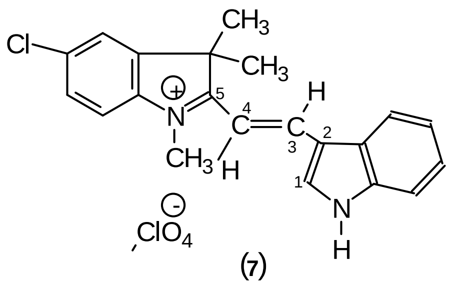
When condensation reaction has been performed in acetic acid (96%) in the presence of small amounts of pyridine or piperidine [7], some orange to blue coloured products were obtained from colourless starting materials. These products exhibit dyestuff properties. They easily dye polyacrylonitrile fibres, having a medium lightfastness [7]. It has been proved that the obtained dyes present bacteriostatic action, comparable to antibiotics used for therapy against Baccilus subtilis or Staphylococcus aureus (Oxford variant) [7]. The cationic 1-H-indolo-3-dimethine dyes structure ***(3)*** of the condensation products obtained has been confirmed by means of elemental analysis, as well as by spectral (UVVIS, IR, and ^{1}H-NMR) measurements.

The structure assignement is discussed in detail for the condensation product obtained between 1-H-indolo-3-carbaldehyde ***(4)*** and 5-chloro-1,2,3,3-tetramethyl-3-H-indolium perchlorate ***(6).*** The elemental analysis data, contained in table 1 are in agreement with the molar ratio 1:1 condensation product. This may be a dimolecular, crotonic type condensation yielding ***(7)*** or a polymolecular condensation product. The data in table 1 rule out a trimolecular condensation between an aldehyde molecule ***(4)*** and two perchlorate molecules ***(6).*** On the other hand, if a polycondensation product were obtained, it should have formed a polymethinic saturated chain, which is in contrast with the formation of a coloured product. Moreover, the UVVIS spectrum of the product exhibits an intense and quite narow peak in the visible range, as presented in table 2. This behaviour is characteristic to cyanine [8]. Hence, the electronic spectrum of examined condensation product is compatible only with the form of cationic dimethine ***(7)*** or of pentamethine dye [9].

Table 1

The composition of the condensation product between 1-H-indolo-3-carbaldehyde (**4**) and 5-chloro-1,2,3,3-tetramethyl-3-H-indolium perchlorate ***(6)***

Composition	% C	% H	%N
Calculated for 1:1molar ratio	58.0	4.6	6.4
Calculated for 1:2 molar ratio	53.3	4.7	5.65
Found experimentally	57.8	4.9	6.3



(7)

The formation of a polycondensation product is ruled out also by ^{1}H-NMR spectrum. The chemical shifts of hydrogen atom nuclei in methine group have values greater than 7 ppm, being in accord with an olefine structure of dimethine ***(7)*** [10] but in contrast to a saturated structure that should have δ smaller than 3 ppm [10]. Moreover the values obtained for chemical shifts of hydrogen nuclei in examined condensation product obey the alternation rule which is characteristic to cationic polymetine with delocalised charge [11]. In accordance with this rule, the chemical shifts of hydrogen atom nuclei in position 1 (δ = 8.68 ppm) and 3 (δ = 8.70 ppm) should be approximately the same and greater than that of hydrogen in position 4 (δ = 7.14 ppm). The experimental confirmation of this is presented in table 2.

A undoubted proof for the cationic dimethine structure ***(7)*** of the condensation product between ***(4)*** and ***(6)*** comes from the value of 15.65 Hz for the coupling constant of methine hydrogen nuclei, which is characteristic [10] to an ethenylic bridge having an E (*trans*) configuration. Such a configuration is also supported by the peak located at 950 cm^{-1} in IR spectrum, corresponding to an out of plane deformation of trans –HC=CH- group [12]

The involvement of 2-methyl group of cycloimmonium perchlorate ***(6)*** in the condensation process has been established on the base of ^{1}H-NMR spectra of the condensation product and those of starting materials, as presented in figure 1. NMR spectrum of the dye exhibits the signal characteristic to N-CH_3 and not for the gropup 2-CH_3.

The signal corresponding to the group $\diagdown\overset{\oplus}{N}{=}C{-}CH_3$ ($\delta < 3.3$ ppm for .C-CH_3) [13] is not found in ^{1}H-NMR spectrum of the condensation product while the signal corresponding to the quaternised $\overset{\oplus}{N}{-}CH_3$ group ($\delta \geq 3.9$ ppm for $\overset{\oplus}{N}{-}CH_3$)[14]. appears on this spectrum (see fig. 1 and table 2).

Table 2

Some properties of the condensation product between 1-H-indolo-3-carbaldehyde *(**4**)* and 5-chloro-1,2,3,3-tetramethyl-3-H-indolium perchlorate *(**6**)*

Property	Values
Melting point (^{o}C)	306-307 with decomposition
Visible range spectrum in MeOH :H_2O, λ_{max} (nm) ε_{max} ($M^{-1}cm^{-1}$)	485 55000
IR spectrum (KBr pellet) (cm^{-1}) for: CH=CH out of plane deformation ν Cl-O from ClO_4^- ν N-H	950 625,1000 3260
^{1}H-NMR spectrum in DMS-d_6 Chemical shift in ppm for $C(CH_3)_2$ + N-CH_3 C_4-H C_3-H C_1-H N-H Coupling constant J H_3-H_4 (Hz)	1.81(s)*; 6H** 3.97 (s) ;3H 7.14 (d);1H 8.70 (d);1H 8.68 (s);1H 12.85 (b);1H 15.65

*) multiplicity: (s)-singlet, (d)-doublet, (b) broad; **) number of hydrogen atoms.
Spectrarecorded with Varian Gemini 300 spectrometer.

The conclusion of the above presented data is that the condensation product between 1-H-indolo-3-carbaldehyde and 5-chloro-1,2,3,3-tetramethyl-3-H- indolium prechlorate has a cationic dimethine dye structure, namely that of 5-chloro-1,3,3-trimethyl-2-[2-(1-H-indol-3-yl)ethenyl]-3-H-indolium perchlorate *(**7**).* As convincing evidence to assign the cationic dimethine day structure for *(**7**)* we used ^{1}H-NMR data (especially the vicinal coupling constant $J_{1,3}$ = 16 Hz, characteristic to a *trans* configuration ethenylic group). We have used such parameters to assign the structure *(**3**)* with an E (*trans*) configuration relative to ethenylic bridge to several other dyes obtained. The results are presented in table 3.

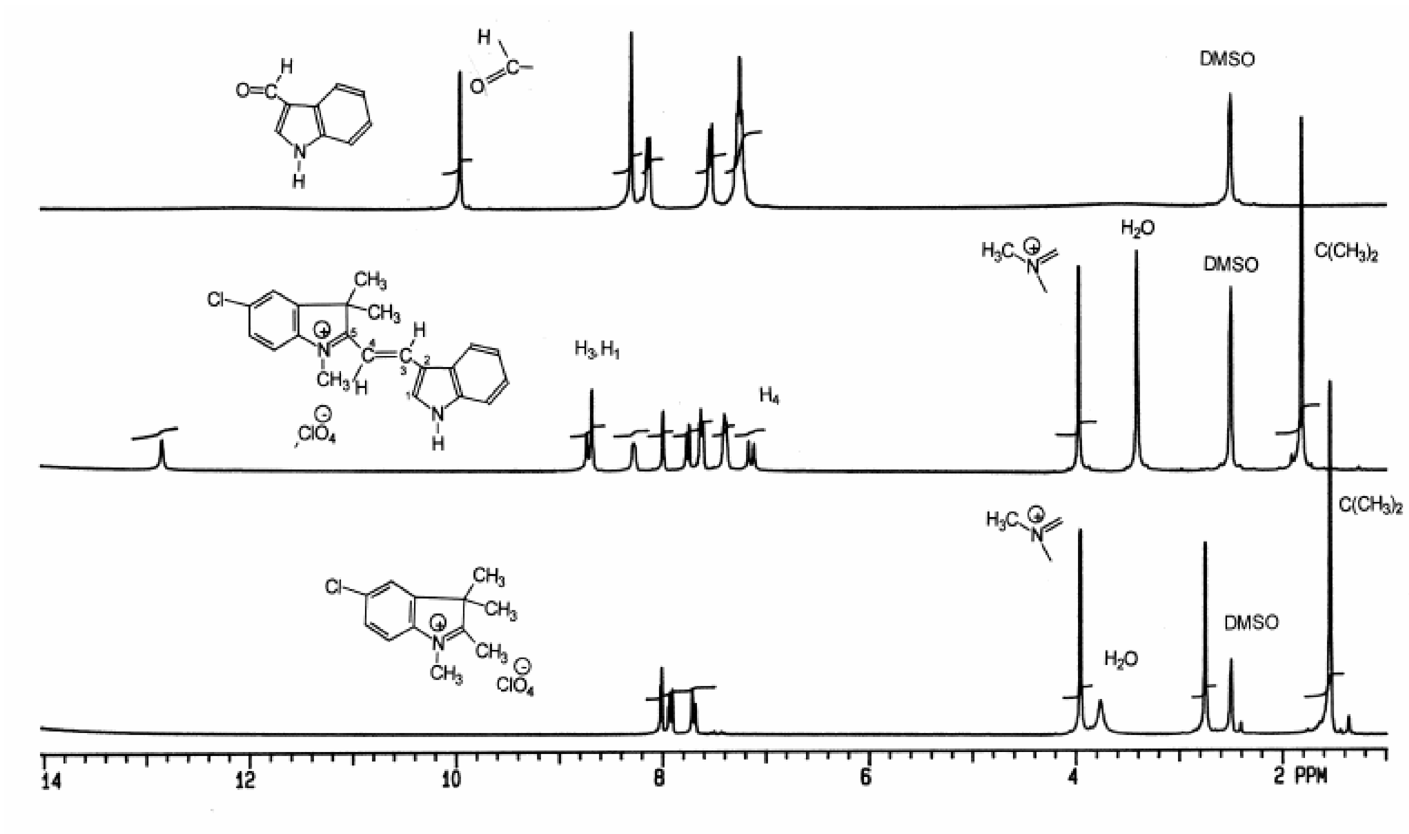
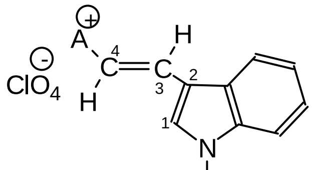


Fig. 1. NMR spectra of 1-H-indolo-3-carbaldehyde, 5-chloro-1,2,3,3-tetrametthyl-3-H-indolium perchlorate ***(6)*** and of 5-chloro-1,3,3-trimethyl-2-[2-(1-H-indol-3-yl)ethenyl]-3-H-indolium perchlorate in Hexadeutero-dimethylsulfoxide, registered with Varian Gemini 300 spectrometer.

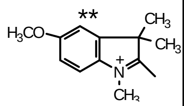
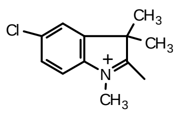
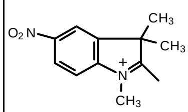
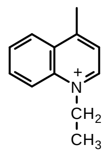
Table 3

^{1}H-NMR data (chemical shift δ in ppm, multiplicity*, number of hydrogen atoms and coupling constant J in Hz) for some condensation products of 1-H-indolo-3-carbaldehyde *(**4**)* with 2- or 4-methyl-cycloimmonium perchlorate *(**5**)*.

Assigned structure:



(3)

Compound **3** A^+ =					
Hydrogen atoms of the group	$C(CH_3)_2$	1.95 (s) 6H	1.98 (s) 6H	2.02 (s) 6H	
	$+NCH_2R$	δ NCH_3 4.12 (s) 3H	δ NCH_3 4.12 (s) 3H	δ NCH_3 4.12 (s) 3H	δ NCH_2- 4.05 (q) 2H 7 Hz δ NCH_2-CH_3 1.75 (t) 3H 7 Hz
	CH aromatic	7.2-8.5 (m) 7H	7.45-8.5 (m) 7H	7.4-8.9 (m) 7H	7.3-9.3 (m) 10H
	C_4-H	7.07 (d) 1H 16 Hz	7.27 (d) 1H 16 Hz	7.27 (d) 1H 16 Hz	8.1 (d) 1H 16 Hz
	C_3-H	8.73 (d) 1H 16 Hz	8.83 (d) 1H 16 Hz	8.95 (d) 1H 16 Hz	8.70 (d) 1H 16 Hz
	C_2-H	8.70 (s) 1H	8.80 (s) 1H	8.90 (s) 1H	8.60 (s) 1H
	N-H	12.84 (b) 1H	13.00 (b) 1H	14.29 (b) 1H	13.20 (b) 1H

*) multiplicity: (s)-singlet, (d)-doublet, (t)-triplet, (q)-quartet, (b)-broad, (m)-complex multiplet
**) δ O-CH_3 = 4.0(s), 3H. Spectra recorded with Tesla BS 487 spectrometer.

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