REACTIONS OF AZINIUM CATIONS.

6.* $N_{(1)}$-ALKYL-1,2,4-TRIAZINIUM SALTS. REACTIONS WITH INDOLES — THE FIRST CASE OF THE DOUBLE ADDITION OF NUCLEOPHILES TO A TRIAZINE RING

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$N_{(1)}$-Alkyl-3-morpholino-1,2,4-triazinium salts and $N_{(1)}$-alkyl-3-pyrrolidino-1,2,4-triazinium salts were synthesized. The structures of these salts were established by ^{13}C NMR spectroscopy. 1,2,4-Triazinium cations add indoles at $C_{(5)}$ and $C_{(6)}$ thereby displaying properties characteristic for 1,4-diazinium salts.

The formation of diadducts due to the covalent addition of nucleophiles to both C=N bonds of the pyrazine ring is a characteristic feature of 1,4-diazines and 1,4-diazinium cations [2]. Since 1,2,4-triazines are aza analogs of pyrazines, their participation in double addition reactions at $C_{(5)}$ and $C_{(6)}$ is also likely. However, reactions leading to transformation of the triazine ring are more common in the chemistry of 1,2,4-triazines [3, 4] and reports of the reaction of 1,2,4-triazine cations with nucleophiles are limited to reactions with the hydroxyl anion [4-10].

In the present work, we synthesized $N_{(1)}$-alkyltriazinium salts not containing substituents at $C_{(5)}$ and $C_{(6)}$ and studied the possibility of the double addition of indoles by these salts; such addition is characteristic for 1,4-diazinium salts.

Quaternary 1,2,4-triazinium salts are obtained by ordinary methods by the action of alkylating agents on bases [4-9, 11] or using the condensation of N-substituted amidrazones and their derivatives [4, 12-14]. The latter method is used, as a rule, for the synthesis of condensed triazinium salts.

The quaternization site of 1,2,4-triazines may be any of the three ring nitrogen atoms. Triazines having bulky substituents at $C_{(5)}$ and $C_{(6)}$ or an aromatic system fused at the $C_{(5)}$—$C_{(6)}$ bond are quaternized at $N_{(2)}$ [5, 6]. On the other hand, bulky substituents at $C_{(3)}$ including an aromatic system fused at the $N_{(2)}$—$C_{(3)}$ bond direct the attack of the alkylating agent to $N_{(1)}$ [4, 5, 7-9, 11], although the possibility of obtaining $N_{(4)}$-alkyl quaternary salts is also not excluded [7].

In the present work, we studied the quaternization of 3-morpholino- (IIa) and 3-pyrrolidino-1,2,4-triazines (IIb) by triethyloxonium tetrafluoroboride or methyl iodide. Starting triazines IIa and IIb were synthesized by the nucleophilic substitution of the methylthio group in triazine I [15] by the corresponding amine (Table 1). The choice of the substituents at $C_{(3)}$ of triazines IIa and IIb was made in light of their electronic and steric effects. It was assumed that the mesomeric donor effect of cycloalkylamino groups would facilitate delocalization of the positive charge and thereby enhance the stability of the triazinium salts, while their steric effect should hinder the entry of the alkyl group at $C_{(2)}$ and $C_{(4)}$ and direct the quaternization exclusively toward $N_{(1)}$. Indeed, $N_{(1)}$-alkyltriazinium salts IIIa-c are obtained in high yield in the reactions of triazines IIa and IIb with methyl iodide and triethyloxonium tetrafluoroboride in methylene chloride at reflux (Table 1).

*For communication 5, see [1].

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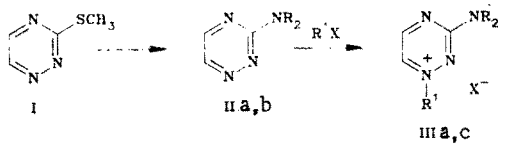
TABLE 1. Properties of Triazines II-IV

Compound	mp,* °C	UV spectrum (in ethanol), λ_{max}, nm (log ε)	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H	N		C	H	N	
IIa	86—88	247 (4,24), 349 (3,19)	50,6	6,2	34,0	$C_7H_{10}N_4O$	50,6	6,1	33,7	40
IIb	87—88	248 (4,25), 355 (3,27)	56,1	6,7	37,1	$C_7H_{10}N_4$	56,0	6,7	37,3	80
IIIa	170	220 (4,30), 259 (4,20), 307 (2,92), 392 (2,98)	31,2	4,3	17,9	$C_8H_{13}IN_4O$	31,2	4,3	18,2	71
IIIb	136—137	222 (4,22), 258 (4,07), 313 (2,90), 396 (2,90), 542 (2,16)	33,1	4,6	18,9	$C_8H_{13}IN_4$	32,9	4,5	19,2	81
IIIc	90	224 (3,81), 259 (4,21), 313 (2,88), 393 (2,94)	38,4	5,4	20,3	$C_9H_{15}BF_4N_4O$	38,3	5,4	19,9	88
IV a	280—282	221 (5,23), 282 (4,09), 290 (3,95), 421 (3,20)	52,9	5,2	15,7	$C_{24}H_{26}N_6O \cdot HI$	53,1	5,0	15,5	52
IVb	233—235	225 (4,95), 283 (4,16), 290 (4,04)	55,1	5,5	14,5	$C_{26}H_{30}N_6O \cdot HI$	54,7	5,5	14,7	52
IVc	216—218	222 (4,90), 282 (4,15), 290 (4,09)	57,7	5,6	16,0	$C_{25}H_{28}N_6O \cdot HBF_4$	58,2	5,6	16,3	45
IVd	240—241	225 (4,88), 285 (4,15), 290 (4,11)	59,5	6,1	15,3	$C_{27}H_{32}N_6O \cdot HBF_4$	59,6	6,1	15,4	58
IVe	200—220**	220 (4,92), 274 (5,02), 282 (5,04), 290 (5,00), 317 (2,76), 375 (2,65)	54,4	5,4	16,0	$C_{24}H_{28}N_6 \cdot HI$	54,6	5,5	15,9	46
IVf	207—212**	225 (4,96), 283 (5,13), 290 (5,08)	55,7	5,8	14,7	$C_{26}H_{32}N_6 \cdot HI$	56,1	6,0	15,1	49

*Crystallization solvents: IIa) butanol, IIIa,c) ethanol, IIIb) 1:4 ethanol—ether, IVa,b) 1:3 DMF—water, IVc,e,f) 1:4 ethanol—water, IVd) 1:4 ethanol—hexane; all these compounds except IIa, IIb, and IIIc melt with decomposition.
**No clear melting point.

The structures of the salts obtained were determined by ^1H and ^{13}C NMR spectroscopy, which permit the establishment of the quaternization site by a series of diagnostic criteria [16, 17].



I IIa,b IIIa,c

IIa, IIIa,c) NR_2 = morpholino, IIb, IIIb) NR_2 = pyrrolidino, IIIa,b) $R^1 = CH_3$, X = I, IIIc) $R^1 = C_2H_5$, X = BF_4

We should note that electron spectroscopy was used previously for the determination of the structure of triazinium salts [5] but this method does not permit the direct and unequivocal determination of the quaternization site.

Analysis of the ^1H NMR spectra of the reaction mixtures and products showed that quaternization gives only $N_{(1)}$-alkyl salts IIIa-c and the formation of $N_{(2)}$- and $N_{(4)}$-quaternary salts was not detected.

The arrangement of the signals in the ^1H NMR spectra of 1-methyl-3-morpholinotriazinium iodide (IIIa) for 5-H and 6-H depends on the nature of the solvent. In $CDCl_3$ solutions the signal for 6-H in the α-position to the N-methyl group is found downfield relative to the signal for the 5-H proton (H_β), while in DMSO-d_6 and CD_3OD, the signals for 6-H and 5-H are in reverse order (Table 2). The signals for 5-H and 6-H were assigned using the ^1H and ^{13}C NMR spectra of IIIa (see below) by selective decoupling of 5-H and 6-H. A feature of the ^1H NMR spectra of IIIa in $CDCl_3$, DMSO-d_6 and CD_3OD is additional splitting of the doublet components for the 6-H signal into quartets: $^3J_{5,6} = 2.6$ and $^4J_{6,NCH_3} \approx 0.8$ Hz. The existence of long-range coupling between the α-proton and the N-methyl group protons is in accord with quaternization at $N_{(1)}$ and excludes alkylation of $N_{(2)}$. The ^1H NMR spectra of salts IIIb and IIIc are quite similar to the spectrum for IIIa (Table 2).

TABLE 2. ^{1}H NMR Spectra of Triazines IIa, IIb, and IIIa-c

Compound	Solvent	Chemical shifts, δ, ppm				$^3J_{6,5'}$, Hz	Quaternization effect*	
		6-H	5-H, d	NR_2, m	NR^1		$\Delta\delta_6$	$\Delta\delta_5$
IIa	$CDCl_3$	8,54 d	8,14	3,85 (8H)		2,1		
	DMSO-d_6	8,65 d	8,33	~3,73 (8H)		2,4		
	CD_3OD	8,56 d	8,31	3,39 (8H)		2,3		
IIb	$CDCl_3$	8,52 d	8,14	1,8—2,2 (4H), 3,4—3,8 (4H)		2,2		
	DMSO-d_6	8,62 d	8,34	1,8—2,2 (4H), 3,3—3,8 (4H)		2,3		
	CD_3OD	8,49 d	8,27	1,9—2,3 (4H), 3,4—3,9 (4H)		2,3		
IIIa	$CDCl_3$	9,79**	9,40	3,87 (8H)	4,42 d (3H)	2,5	1,25	1,26
	DMSO-d_6	9,07**	9,34	3,78 (8H)	4,33 d (3H)	2,6	0,42	1,01
	CD_3OD	8,95**	9,24	3,90 (8H)	4,40 d (3H)	2,6	0,39	0,93
IIIb	$CDCl_3$	9,76**	9,39	1,8—2,3 (4H), 3,4—3,9 (4H)	4,49 d (3H)	2,6	1,24	1,25
	DMSO-d_6	9,10 br. d	9,36	1,8—2,2 (4H), 3,4—3,8 (4H)	4,34 s (3H)	2,6	0,48	1,02
	CD_3OD	8,86**	9,17	1,9—2,3 (4H), 3,4—4,0 (4H)	4,37 d (3H)	2,6	0,37	0,90
IIIc	$CDCl_3$	8,83 br. d	9,10	3,86 (8H)	1,68 t (3H), 4,61 q (2H)	2,6	0,29	0,96
	DMSO-d_6	9,08 br. d	9,31	3,78 (8H)	1,55 t (3H), 4,57 q (2H)	2,7	0,43	0,98
	CD_3OD	8,84 br. d	9,16	3,78 (8H)	1,66 t (3H), 4,61 q (2H)	2,8	0,28	0,85

*Quaternization effect $\delta_{H_i}(III) - \delta_{H_i}(II)$.
**Doublet of quartets with long-range coupling $^4J_{H(6),CH_3} \approx 0.8$ Hz.

The signals for the quaternary carbon atoms $C_{(3)}$ in the ^{13}C NMR spectra of triazines IIa, IIIa, and IIIc were identified on the basis of coupling between a single bond $^1J_{(C-H)}$ in proton-coupled ^{13}C NMR spectra. The signal for $C_{(3)}$ in going from base IIa to quaternary salts IIIa and IIIc is shifted only very slightly downfield by 0.71 ppm for IIIa and only by 0.15 ppm for IIIc (Table 3). According to our previous work [16, 17], in which we established that quaternization of the nitrogen atom leads to a shift of the signals for the α-carbons upfield by 7-10 ppm, and our data, we may conclude that the alkylation of triazine IIa proceeds at $N_{(1)}$ and not at $N_{(2)}$ or $N_{(4)}$. Analysis of the chemical shifts and the signs for the shifts of the two remaining signals for the methine carbon atoms in the ^{13}C NMR spectra of triazines of IIa, IIIa, and IIIc permits their assignment to $C_{(5)}$ and $C_{(6)}$ (Table 3, Fig. 1). The signals for $C_{(6)}$ in the α-position to the quaternary nitrogen atom are shifted downfield in the spectra of cations IIIa and IIIc by 6.63 and 8.40 ppm relative to base IIa (Table 3), which is in complete accord with the previously established effect of the quaternization of azines on the chemical shifts of carbon atoms [16, 17]. This assignment of the signals for $C_{(5)}$ and $C_{(6)}$ for IIa is in good accord with the data of Radel et al. [18] for 3-dimethylamino-1,2,4-triazine IIc (Table 3).

Quaternization of $N_{(1)}$ in 3-morpholino-1,2,4-triazine IIa is also indicated by other criteria in the ^{13}C and ^{1}H NMR spectra of cations IIIa and IIIc. Thus, the ^{13}C NMR spectra of salts IIIa and IIIc show an increase of the $^1J_{(C-H)}$ coupling constant for $C_{(5)}$ and $C_{(6)}$ in the β and α positions to the quaternization site relative to starting base IIa by 15-18 Hz and a decrease in the absolute coupling constants of β-carbons $C_{(5)}$ with the 6-H protons in the α position by 4.4 and 4.7 Hz, respectively (Table 3). The presence of the alkyl substituent at $N_{(1)}$ in IIIa and IIIc is also indicated by the additional splitting doublet—

TABLE 3. ^{13}C NMR Data for Triazines II and III in $CDCl_3$

Compound	δ, ppm								^1J, Hz							^2J, Hz		$^3J^*$, Hz
	$C_{(3)}$	$C_{(5)}$ (β)	$C_{(6)}$ (α)	$N-CH_2$	$O-CH_2$	NCH_2CH_3	CH_3CH_2	$N-CH_3$	$C_{(5)}, H_{(5)}$	$C_{(6)}, H_{(6)}$	NCH_2	OCH_2	NCH_2CH_3	CH_3CH_2	NCH_3	$C_{(5)}, H_{(6)}$	$C_{(6)}, H_{(5)}$	$C_{(3)}, H_{(5)}$
IIa	161,11	148,55	140,13	43,65	66,40				183,3	188,5	139,9	144,3				10,6	9,6	~10—11
IIc*	160	148	138					36										
IIIa	161,26	160,51	133,50	44,62	65,99			53,43	199,7	~206	141,9	145,6			145,9	5,9		~11
IIIc	161,82	160,22	131,73	44,41	65,73	61,69	13,96		200,1	203,4	142,3	145,3	147,5	130,5		6,2	12,2	~13
(IIIa—IIa)	0,15	11,96	−6,63	0,97	−0,41				16,4	~17,5	2,0	1,3				−4,7		~0—1
(IIIc—IIa)	0,71	11,67	−8,40	0,76	−0,67				16,8	14,9	2,4	1,0				−4,4	2,6	~2—3

*For IIa, $J_{C_{(6)},NCH_3}$ = 3.0, for IIIc, $J_{C_{(6)},NCH_2}$ = 3.2 Hz.
**3-Dimethylamino-1,2,4-triazine [18].

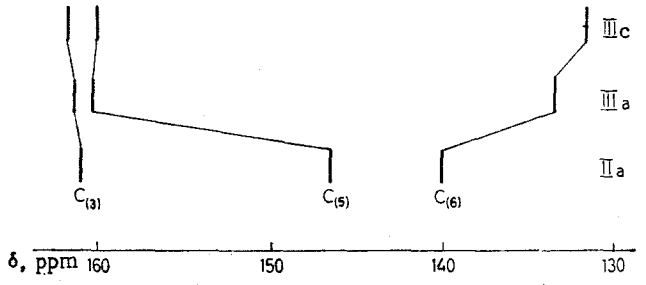


Fig. 1. Diagram of changes in the ^{13}C NMR shifts in going from 3-morpholine-1,2,4-1,2,4-triazine (IIa) to quaternary salts IIIa and IIIc.

doublet components of the signal for $C_{(6)}$ which is found at highest field of the triazine ring carbon atoms due to coupling with the protons of the N—CH_3 and N—CH_2 groups with ^3J = 3.0 and 3.2 Hz, respectively (Table 3).

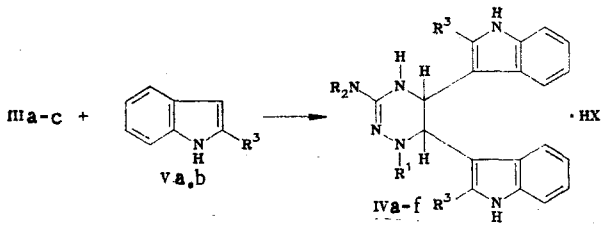
The structure of 1-methyl-3-pyrrolidino-1,2,4-triazinium iodide (IIIb) was established by comparison of its UV and ^1H NMR spectra with those corresponding to quaternization [16, 17] (Table 2).

The ^1H NMR spectra of IIIa-c show some increase in the vicinal coupling constants between 5-H and 6-H, which is also one of the diagnostic criteria for determination of the quaternization site [16, 17] (Table 2).

The reactions of 1,2,4-triazines with nucleophiles proceed, as a rule, through a step involving their addition to one of the carbon atoms of the triazine ring. Depending on the nature of the substituents, the nucleophilic attack may be directed toward $C_{(3)}$ [4, 15, 19-23], $C_{(5)}$ [4, 10, 15, 19-27], or $C_{(6)}$ [5, 8, 20, 21, 28]. Carbon atoms $C_{(5)}$ and $C_{(3)}$ are most frequently the most active sites of 1,2,4-triazines [4, 10, 15, 19-27]. On the other hand, quaternization of $N_{(1)}$ strongly activates the α-carbon atom, $C_{(6)}$, in $N_{(1)}$-alkyl-1,2,4-triazinium salts and directs the attack of the hydroxyl anion predominantly to $C_{(6)}$ [5, 8]. In light of the steric hindrance of $C_{(3)}$ in 1,2,4-triazinium salts IIIa-c and the activation of triazine ring by existence of charge, both carbon atoms $C_{(5)}$ and $C_{(6)}$ may be considered as probable sites for the addition of nucleophiles to cations IIIa-c.

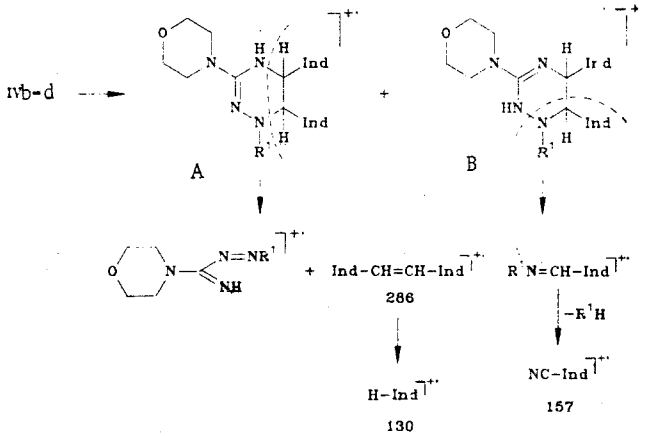
A study of the reactions of triazinium salts IIIa-c with indole and 2-methylindole established that they lead to the products of the double addition of indoles at $C_{(5)}$ and $C_{(6)}$, IVa-f.

The composition and structure of diadducts IVa-f were indicated by elemental analysis and their ^1H NMR and mass spectra (Tables 1 and 4).



IVa-d) NR_2 = morpholino, e,f) NR_2 = pyrrolidino, a,b,e,f) R^1 = CH_3, X = I, c,d) R^1 = C_2H_5, X = BF_4, a,c,e) R^3 = H, b,d,f) R^3 = CH_3, Va) R^3 = H, b) R^3 = CH_3.

Organic salts under mass spectral conditions do not give molecular ion peaks M^+ [29]. Thus, strong peak ions for $[M - HX]^+$ with m/z 442 and 456 were found in the mass spectra of IVb and IVd, respectively (see Experimental). The pseudomolecular ions $[M - HX]^+$ may exist in two tautomeric forms A and B and, as shown by analysis of the mass spectral data, their retro-Diels—Alder fragmentation indeed proceeds by two pathways:



Ind = 2-methylindol-3-yl

^{13}C NMR spectra were also obtained for IVa and IVd in DMSO-d_6, in which all the molecular fragments appear: two nonequivalent indole residues, signals for the methine carbon atoms $C_{(5)}$ and $C_{(6)}$ of the triazine ring at 47.8-62.5 ppm, signal for $C_{(3)}$ at 152.9 and 154.0 ppm as well as signals for the morpholine and N-alkyl groups in the corresponding spectral regions (see Experimental).

The ^1H NMR spectra of diadducts IVa-f show 5-H and 6-H of the triazine ring as two doublets at 4.1-5.7 ppm with vicinal coupling constant $^3J_{5,6}$ = 9.7-11.0 Hz (Table 4), indicating considerable similarity with the spectral data for the products of the double addition of indoles to pyrido[2,3-b]pyrazinium cations [30]. The finding of two indole NH signals in the ^1H NMR spectra of IVa-f at 10.8-11.1 ppm, the protons of two benzene rings at 6.8-7.8 ppm, and signals for the protons of the cycloalkylamino groups in the corresponding region (Table 4) is in complete accord with the structure of the diadducts. The lack of signals for the indole β-protons at 6.2-6.4 ppm [31] indicates the addition of indoles at $C_{(3)}$.

In conclusion, we note that these indole double addition reactions are the first case of the formation of diadducts in the 1,2,4-triazine series.

TABLE 4. Characteristics of ^1H NMR Spectra of Compounds IVa-f in DMSO-d_6

Compound	Chemical shifts, δ, ppm, and SSCC, Hz							
	5-H, d	6-H, d	$^3J_{5,6}$	N—R¹	NR_2,m	$N_{(4)}H$, s	NH, s	Indole residue protons
IVa	4,82	5,66	10,8	2,07, s (3H)	3,2—3,9 (8H)	9,05	10,22	6,9—7,8 (10H, m, arom.), 10,82 (2H, br.s, NH)
IVb	4,17	5,25	10,2	2,55, s (3H)	3,2—3,9 (8H)	9,12	9,68	6,9—7,5 (8H, m, arom.), 1,51 (3H, s, CH_3), 1,61 (3H, s, CH_3), 10,82, 10,85 (2NH)
IVc	4,91	5,64	10,8	1,13, t (3H), 2,82, q (2H)	3,2 -3,9 (8H)	9,07	10,08	6,8—7,7 (10H, m, arom.), 11,00 (2H, br.s NH)
IVd	4,30	5,27	10,2	1,09, t (3H), 2,90, q (2H)	3,3—3,9 (8H)	9,20	9,42	6,8—7,5 (8H, m, arom.), 1,51 (3H, s, CH_3), 1,61 (3H, s, CH_3), 10,82, 10,85 (2NH)
IVe	4,85	5,68	11,0	2,51, s (3H)	1,8—2,2 (4H), 3,1—3,7 (4H)	8,52	9,89	6,9—7,8 (10H, m, arom.), 11,07 (2H, br.s NH)
IVf	4,19	5,26	9,7	2,56, s (3H)	1,8—2,2 (4H) 3,1—3,7 (4H)	8,66	9,30	6,8—7,8 (8H, m. arom.), 1,54 (3H, s, CH_3), 1,62 (3H, s, CH_3), 10,87 (2H, br.s NH)

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra of 6-12% solutions of the compounds studied in $CDCl_3$, DMSO-d_6, and CD_3OD were recorded at 40°C using a Bruker WH-90 pulse spectrometer (manufactured in West Germany) at 90 MHz for the ^1H NMR spectra and at 22.62 MHz for the ^{13}C NMR spectra. The chemical shifts in the ^1H NMR spectra were measured relative to TMS as the internal standard (δ, 0.00 ppm), while the chemical shifts in the ^{13}C NMR spectra were measured relative to the solvent signal (δ_{CDCl_3} 76.90 and $\delta_{DMSO\text{-}d_6}$ 39.60 ppm). The error in the determination of the chemical shifts and coupling constants was 0.01 ppm and 0.2 Hz for the ^{13}C NMR spectra and 0.15 Hz for the ^1H NMR spectra. The experiments with selective decoupling of the proton–carbon interaction were carried out at reduced decoupler power $\gamma H_2/2\pi$ = 500 Hz.

The UV spectra were taken on a Specord UV-VIS spectrometer. The mass spectra were taken on a Varian MAT spectrometer with direct sample inlet into the ion source. The accelerating voltage was 3.6 kV. The ionizing electron energy was 30 eV. The cathode emission current was 1.5 mA. The injector temperature was 250°C.

The characteristics of the compounds synthesized are given in Tables 1-4.

3-Morpholino-1,2,4-triazine (IIa). A sample of 20.6 ml (236 mmoles) morpholine was added to a solution of 20 g (157 mmoles) 3-methylthio-1,2,4-triazine (I) [15] in 10 ml ethanol. The mixture obtained was heated at reflux for 30 h, cooled to –20°C and the precipitate formed was filtered off, washed with 100 ml hexane and 20 ml butanol, and crystallized from butanol to give 10.4 g (40%) IIa, which sublimes at 80°C (1 mm Hg).

3-Pyrrolidino-1,2,4-triazine (IIb). A mixture of 10 g (78.6 mmoles) I and 8.5 ml (102.2 mmoles) pyrrolidine in 5 ml ethanol was heated at reflux for 25 h and then cooled. The reaction mass was treated with 150 ml hexane. The brown precipitate was filtered off and purified by sublimation at 80°C (1 mm Hg) to give 9.41 g (80%) IIb as yellow crystals.

1-Methyl-3-morpholino-1,2,4-triazinium Iodide (IIIa). A sample of 2.91 ml (36.1 mmoles) methyl iodide was added dropwise to a solution of 5 g (30.0 mmoles) triazine IIa in 10 ml methylene chloride. The reaction mixture was heated at reflux for 4 h and cooled. The precipitate was filtered off and recrystallized from ethanol to give 6.53 g (71%) IIIa.

1-Methyl-3-pyrrolidino-1,2,4-triazinium Iodide (IIIb). A sample of 3.25 ml (40.0 mmoles) methyl iodide was added to a solution of 5 g (33.3 mmoles) triazine IIb in 15 ml methylene chloride. The mixture was heated at reflux for 4 h and then evaporated to dryness in vacuum. The residue was dissolved in 15 ml ethanol at reflux. The mixture obtained was filtered and cooled. Then, 60 ml ether was added to give 7.08 g (81%) IIIb.

3-Morpholino-1-ethyl-1,2,4-triazinium Tetrafluoroboride (IIIc). A sample of 5.7 g (30.0 mmoles) triethyloxonium tetrafluoroboride was added to a solution of 5 g (30.0 mmoles) triazine IIa in 10 ml methylene chloride. The mixture was heated at reflux for 4 h and then evaporated to dryness in vacuum. The residue was recrystallized from ethanol to give 7.46 g (88%) IIIc.

Hydroiodide Salt of 5,6-bis(Indol-3-yl)-1-methyl-3-morpholino-1,4,5,6-tetrahydro-1,2,4-triazine (IVa). A sample of 0.76 g (6.50 mmoles) indole in 3 ml dry chloroform was added to a solution of 1 g (3.25 mmoles) salt IIIa in 5 ml dry chloroform. The solution obtained was left at room temperature for 48 h. The solution was decanted and the oily residue was triturated with ether at from 0 to –20°C. The precipitate was filtered off (1.64 g) and dissolved in a mixture of 1:3 DMF–H_2O at reflux. The mixture was filtered and the solution was left to crystallize for two weeks. The precipitate was filtered off to give 0.92 g (52%) IVa. ^{13}C NMR spectrum in DMSO-d_6, δ: 38.0 (CH_3), 46.1 (CH_2NCH_2), 47.7 and 59.8 ($C_{(5)}$ and $C_{(6)}$), 65.4 (CH_2OCH_2), 108.8, 111.4, 112.0, 118.4, 119.0, 121.2, 121.4, 124.5, 124.8, 125.2, 125.4, 126.9, 136.0, 136.2 (indole residue signals), 152.9 ppm ($C_{(3)}$).

Hydroiodide Salt of 5,6-bis(2-Methylindol-3-yl)-1-methyl-3-morpholino-1,4,5,6-tetrahydro-1,2,4-triazine (IVb). This salt was obtained by analogy from salt IIIa and methyl iodide in 52% yield (0.97 g). Mass spectrum, m/z (J ≥ 20%): 57 (52), 61 (20), 70 (23), 97 (20), 128 (20), 130 (30), 157 (21), 173 (44), 271 (24), 286 (100), 287 (24), 442 (48).

Hydrotetrafluoroboride Salt of 5,6-bis(Indol-3-yl)-3-morpholino-1-ethyl-1,4,5,6-tetrahydro-1,2,4-triazine (IVc). This salt was obtained by analogy from triazine IIIc and indole with the exception that the reaction was carried out in methylene chloride and bisadduct IVc

was dissolved in the purification step in ethanol at reflux. Activated charcoal was added and and filtered off. The solution obtained was diluted with four volumes of water. The precipitate was filtered off after one week to give 0.86 g IVc (45%).

Hydrotetrafluoroboride Salt of 5,6-bis(2-Methylindol-3-yl)-3-morpholino-1-ethyl-1,4,5,6-tetrahydro-1,2,4-triazine (IVd). The salt was obtained by anaolgy to IVc from salt IIIc and methyl iodide. For purification, bisadduct IVd was dissolved in ethanol at reflux and filtered. Then, four volumes of hexane were added. The precipitate was filtered after 48 h to give 1.12 g IVd (58%). ^{13}C NMR spectrum in DMSO-d_6 at 100°C, δ: 10.5, 10.7, 11.5 (signals for the three CH_3 groups), 46.5 (NCH_2CH_3 and CH_2NCH_2), 53.5 and 62.5 ($C_{(5)}$ and $C_{(6)}$), 65.7 (CH_2OCH_2), 104.7, 106.4, 111.0, 111.2, 117.3, 118.3, 119.1, 120.6, 120.7, 126.1, 126.6, 134.6, 135.4, 135.5, 135.7 (indole residue signals), 154.0 ppm ($C_{(3)}$). Mass spectrum, m/z (J ≥ 20%): 130 (60), 131 (38), 154 (22), 157 (22), 187 (29), 286 (100), 287 (24), 456 (35).

Hydroiodide Salt of 5,6-bis(Indol-3-yl)-1 methyl-3-pyrrolidino-1,4,5,6-tetrahydro-1,2,4-triazine (IVe). The salt was obtained by analogy to IVc from salt IIIb and indole. The bisadduct was recrystallized from 1:4 ethanol—water to give 0.84 g IVe (46%).

Hydroiodide Salt of 5,6-bis(2-Methylindol-3-yl)-1-methyl-3-pyrrolidino-1,4,5,6-tetrahydro-1,2,4-triazine (IVf). This salt was obtained by analogy to IVe from salt IIIb and methylindole. The yield was 0.94 g IVf (49%).

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