HOMONUCLEAR OVERHAUSER EFFECT STUDY
OF TRIMETHINIUM SALTS*

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^{1}H-NMR spectra of symmetrically substituted 1,3-bis-(dimethylamino)trimethinium perchlorates $[(CH_3)_2N—CR^1—CR^2—CR^1—N(CH_3)_2]ClO_4$ were measured and assigned. The results of proton-proton Overhauser effect measurements of the parent compound (all Rś hydrogen) confirmed the planar trans-trans conformation of the cation in which apparently the methyl group syn-periplanar to H^1 hydrogen atom is preferentially in the eclipsed conformation with the $N—C(H^1)$ bond and the anti-periplanar group is staggerred with this bond. The two methyl groups rotate by 120° jumps, the motion of the two methyl groups and that of the whole dimethylamino group is very likely to be of a gear type. Substitution of the parent compound by methyl or ethyl groups leads to small changes. Substitution by isopropyl or tert-butyl groups leads to changes which most likely affect the dihedral angles. These changes are larger for tert-butyl than for isopropyl derivative and are larger for 1,3-dialkyl than for 2-alkyl derivatives with the same substituent.

The most useful photosensitizers are polymethinium salts, especially cyanines[1]. In this connection, the polymethinium salts have received considerable attention both in synthetic and physico-chemical studies. Some characteristic properties of these compounds can be conveniently studied on simpler model compounds, namely, on trimethinium salts some of which have been prepared relatively recently. The purpose of the present work is to gain more information about the steric arrangements (especially about the relative interprotonic distances) in these model compounds by using the technique of (homo)nuclear Overhauser effect (NOE). It is of particular interest to determine what effects on the steric arrangement have the substituents of different steric requirements. In this respect, the NOE method is a good supplement to X-ray diffraction since it can yield relative interprotonic distances in solutions.

The compounds of the chosen model series of trimethinium salts have the structure $[(CH_3)_2N—CR^1—CR^2—CR^1—N(CH_3)_2]^+ClO_4^-$. The series includes, besides the

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parent unsubstituted salt I $(R^1 = R^2 = H)$, compounds with substituents on the middle (C-2) carbon $(R^1 = H, R^2 = CH_3$ for II, $R^2 = C_2H_5$ for III, $R^2 = $ iso-C_3H_7 for IV and $R^2 = $ tert-C_4H_9 for $V)$ and the compounds symmetrically disubstituted on 1,3-carbon atoms $(R^2 = H$, and $R^1 = CH_3$ for VI, $R^1 = C_2H_5$ for VII, and $R^1 = $ iso-C_3H_7 for $VIII)$.

RESULTS AND DISCUSSION

¹H-NMR *Spectra.*

NMR parameters (proton chemical shifts and proton-proton coupling constants) of compounds $I - VIII$ are given in Table I. The spectra were measured in the same samples as the NOE enhancements to be discussed latter. The assignment of the lines in the spectra on the basis of line intensities is straightforward, it is in an agreement with the published[2−4] assignments. The only exception being the assignment of the two methyl lines in compound I (in all the spectra of the other compounds only one line was observed for the protons of the dimethylamino group), which required NOE measurements in a different sample.

In the standard sample for the NOE measurement (see Experimental) saturation of one methyl proton line of the compound I leads to a complete disappearance of

TABLE I

¹H-NMR Chemical Shifts and ¹H-¹H Coupling Constants

Salt	Chemical shifts[a]			Coupling constants J[b]		
	R^1	R^2	$CH_3(a)N$; $CH_3(b)N$	$J(CH_3-N/R^1)$	$J(CH_3-N/R^2)$	$J(R^1/R^2)$
I	7·50	5·21	3·13; 3·33	[c]	[c]	1·8
II	7·15	2·20	3·33	0·3	0·1	0·3
III	7·11	3·08 (CH$_2$) 1·19 (CH$_3$)[d]	3·35	0·4 ± 0·2	[c]	[c]
IV	7·47	1·18 (CH$_3$)[e]	3·33	0·4 ± 0·2	[c]	[c]
V	7·80	1·27	3·08	0·4 ± 0·2	[c]	0·1
VI	2·36	5·04	3·26	0·4	0·1	0·1
VII	2·73 (CH$_2$) 1·28 (CH$_3$)[d]	4·89	3·26	[c]	0·1	[c]
$VIII$	1·26 (CH$_3$)[e]	4·93	3·09	0·4	0·2	[c]

[a] Chemical shifts in δ-scale (ppm units, relative to internal TMS); error ±0·02 ppm. [b] Proton-proton coupling constants in Hz, error ±0·1 Hz. The coupled protons are indicated in the parentheses and separated by the slash. [c] Could not be estimated from the spectrum. [d] $J(CH_3/CH_2) = 7·6 ± 0·2$ Hz. [e] $J(CH_3/CH) = 6·8 ± 0·2$ Hz, the line of methine (CH) proton is overlapped by the CH_3N proton line.

the other methyl proton line. Such a magnetization transfer clearly indicates that the spin-lattice relaxation of the involved methyl protons is much slowlier than the rotation around the $C = N$ bond which makes the protons of the two methyl groups relaxationally equivalent[5] in this sample and, accordingly the rotation can be classified as fast, probably moderate fast[5]. If the two lines have to be assigned, the two types of protons had to be made relaxationally nonequivalent (either by slowing the rotation or by enhancing the relaxation or by both). This was achieved in a different sample by an addition of water and ethanol in concentrations of 0·8M and 0·2M, resp. These additives did not change the chemical shifts of the methyl protons but in their presence saturation of one methyl proton line had no effect on the intensity of the other methyl proton line, hence the rotation in the dopped sample was very slow[5]. Since in this dopped sample saturation of the high-field methyl proton line leads to approximately 30% enhancement of H^2 line (while that of H^1 proton is not affected) and, since in contrast the saturation of the low-field methyl proton line enhances the H^1 line by about 20% (and does not affect the H^2 line), the signal at $\delta = 3\cdot13$ must be assigned to the protons of the methyl group which is in an *anti* conformation relatively to the H^1 proton (methyl group *a* in Fig. 1) and the other line at $\delta = 3\cdot33$ to the other methyl group (methyl group *b* in Fig. 1) which is in a *syn* conformation to this proton. As the NOE enhancements observed in the
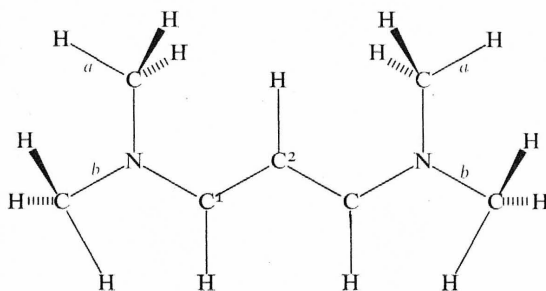

FIG. 1

The Structures of Trimethiniumcyanine Cation *I* as Projected into the N—C—C—C—N Plane

Structure	$(C)C—N^a$	$N—CH_3{}^a$	$(C)C—H^a$	$C{-}C^a$	$C{-}C{-}C^b$	$C{-}C{-}N^b$	$C{-}N{-}C^b$	$C^1{-}C^2{-}H^b$	$C^2{-}C^1{-}H^b$
A	$1\cdot35^c$	$1\cdot44^d$	$1\cdot08$	$1\cdot40^c$	$120\cdot0^c$	$120\cdot0$	$120\cdot0$	$120\cdot0$	$120\cdot0$
B	$1\cdot32^e$	$1\cdot47^f$	$1\cdot08$	$1\cdot38^a$	$117\cdot0^e$	$126\cdot5^e$	$120\cdot0^f$	$121\cdot5$	$116\cdot8$

[a] Bond length in Å. [b] Bond angles in degrees. [c] Taken from ref.[6]. [d] Taken from ref.[7]. [e] Taken from ref.[8]. [f] Taken from ref.[9].

dopped sample are essentially the same as those in the standard sample (Table II), the relaxational nonequivalence was apparently achieved by a slowing down the rotation around the $C{=}N$ bond and not by a decrease in the relaxation time.

Proton-Proton Overhauser Enhancements

The experimental values of NOE enhancements in trimethinium salts I−VIII are given in Table II. In this table as well as in the following discussion symbols and terms are used in the meaning defined previously[5]. Most notably, the steady-state NOE enhancements $f_D(S)$, which are observed on the protons of the class D when the protons of the class S are being saturated, are defined as

$$f_D(S) = (I_D(S) - I_D)/I_D \,,$$

where $I_D(S)$ and I_D are the integrated intensities of the line of protons D if the line of protons S is and is not saturated, resp. The indices indicate the specific classes of relaxationally equivalent nuclei in the molecule, the subscript the class of the observed nuclei, the parenthesized index the saturated nuclei.

TABLE II

NOE Enhancements[a]

Salt	$f_1(MN)$	$f_1(MC)$	$f_{MC}(MN)$	$f_2(MN)$	$f_2(MC)$	$f_{MN}(1)$
I	0.17 ± 0.01	—	—	0.35 ± 0.02	—	—
II[b]	0.17 ± 0.01	0.00 ± 0.01	0.03 ± 0.01	—	—	—
III	0.17 ± 0.02	0.00 ± 0.03^c	^{d}	—	—	—
IV[e]	0.28 ± 0.01^f	0.10 ± 0.01	0.01 ± 0.01^f	—	—	—
V	0.15 ± 0.02	0.13 ± 0.02	0.00 ± 0.03	—	—	—
VI	—	—	—	0.22 ± 0.01	^{d}	0.01 ± 0.01
VII	—	—	—	0.30 ± 0.01	0.00 ± 0.03	0.00 ± 0.01
VIII[g]	—	—	—	0.05 ± 0.02^h	0.30 ± 0.02	^{d}

[a] For the definition of $f_D(S)$ values and labeling of different proton classes see the text. [b] $f_{MN}(MC) = 0.00 \pm 0.01$. [c] Due to large separation of MC triplet lines the saturation was incomplete. [d] Not measured. [e] $f_{MC}(2) = 0.02 \pm 0.01$. [f] Saturation of MN line is accompanied by the saturation of the CH proton of the isopropylgroup. [g] $f_{MC}(1) = 0.00 \pm 0.01$. [h] Since the saturation of MN line leads also to the saturation of the overlapping CH(isopropyl) line, the true value of $f_2(MN)$ might be lower.

For the sake of brevity, the proton classes present in the salts $I - VIII$ are labelled as follows: index MN stands for the protons of the dimethylaminogroup (which have been shown above to be relaxationally equivalent), MC for the protons of the methyl groups bonded to a carbon atom (note that these are structurally different protons in different compounds *e.g.* in II and V), and 1 and 2 are the methine protons in place of substituents R^1 and R^2, resp.

Salt I. All the so far available evidence[2−4,6] indicates that the cation of salt I has the so-called *trans-trans* arrangement of the cyanine chain (N—C—C—C—N) with all these atoms in one plane. A recent X-ray study[8] found such a *trans-trans* arrangement in the closely related dipyrrolidyltrimethincyanine perchlorate.

In order to estimate the geometry around the nitrogen atoms, CNDO/2 calculations were performed for a model cation in which the methyl groups were substituted by hydrogen atoms. It was found that the total energy was smaller if the C—N—H bond angle was 120° while a minimum electronic energy corresponded to tetrahedral C—N—H angles. Therefore, in the real cation of I in which the bulkier methyl groups replace hydrogen atoms, steric interactions will favour the planar arrangement (120° bond angles) even more than in the model. On the basis of this reasoning and the available data[6−9], structures A and B of cation I were drawn as shown in Fig. 1. The idealized structure A is based on the data of Scheibe[6] while the structure B on the X-ray study of dipyrrolidyltrimethylcyanine perchlorate[8].

The results of the NOE measurements are in a qualitative agreement with the *trans-trans* structure of Fig. 1. In a molecule of this structure the two H^1 hydrogen atoms are close enough to have their total relaxation rate increased by their interaction. In addition, each of them has in its vicinity only one methyl group while the H^2 proton is surrounded by the protons of the two methyl groups in the *syn*-periplanar conformations and has no other protons in the molecule to provide an additional efficient relaxation mechanism. Hence larger enhancement of the H^2 than of the H^1 line is anticipated as observed.

According to NOE theory[5] the two determined values of NOE in compound I are not sufficient for a rigorrous quantitative evaluation of all relaxation rates R' but they can bring some usefull information. The following two equations can be derived

$$-12R'_{MN2} + 2R'_{12}f_1(MN) + 2R'_2f_2(MN) = 0 \tag{1}$$

$$-12R'_{MN1} + R_{12}f_2(MN) + 2R'_1f_1(MN) = 0, \tag{2}$$

where

$$R'_2 = 2R'_{12} + 12R'_{2MN} + G^*_2 \quad \text{and}$$

$$R'_1 = R'_{12} + (3/2)R'_{11} + 12R'_{1MN} + G^*_1.$$

If we adopt the usually made assumption of equal independent relaxation rates G_1^* and G_2^* an important conclusion about the methyl group conformations can be derived from these equations for each of the structures A and B as follows. The relaxation rates of trimethinium protons due to their mutual interactions R_{12}' and R_{11}' can be calculated according to the established formulas[5,10] from the geometrical parameters of the cyanine chain; the calculated values are given for both structures in Table III. Now, the remaining relaxation rates occuring in Eqs (*1*) and (*2*) can be calculated for various models of rotation of the methyl groups (and their different conformations). The results of the calculations which are based on models and mathematical formulas described in detail earlier[5] are also summarized in Table III for the two structures. It is readily apparent from the results in Table III that the condition of equal rates of independent relaxation is satisfied only for methyl group a jumping from one staggered conformation (relatively to N=C bond) into another and methyl group b jumping between eclipsed conformations (with the N=C bond). The rate of jumping motion is for either structure in the fast[5] region, the idealized structure is compatibile with both limits of fast motion (moderate and superfast) while the structure B requires low frequency limit of the fast region *i.e.* moderate fast rate of jumping motion. Recalling that the rotation around C=N bond is probably moderate fast, the combination of motion of methyl groups with the motion of the whole dimethylamino group relatively to the trimethinium chain appears as a gear (or cogwheel) motion. The rotation of the dimethylamino group by which the methyl group a (*anti* periplanar) becomes b (*syn* periplanar) and *vice versa* is accompanied by a rotation of these methyl groups in which the eclipsed methyl group changes into the staggerred methyl group (and *vice versa*). (One should bear in mind, however, that these conclussions are based on the condition of equal independent relaxation rates which condition, though it seems to be very likely and is employed by various authors, has not been proofed).

Alkylsubstituted Trimethinium Salts II—VIII

Substitution of a hydrogen atom of the *trans-trans* 1,3-bis(dimethylamino)trimethinium chain by an alkyl group leads to a steric interaction the magnitude of which depends on the size of the substituent. In the case of 2-alkylsubstituted trimethinium salts, it is especially the interaction between the alkyl substituent and the methyl (a) group which is on the nitrogen atom in *syn*- δ arrangement to the C-2 carbon atom, while in 1,3-dialkylsubstituted compounds the dominant interaction is that between the two alkyl substituents.

Salt II. Calculations show that if an unperturbed methyl group (tetrahedral bond angles, standard bond lengths) is substituted for H^2 hydrogen atom of the parent salt I without perturbing the structures A or B, the hydrogen atoms of MC and MN

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TABLE III

Relaxation Rates Calculated for Different Rotation Models and Methyl Group Conformations of Salt I^a

Model[b]	Conformation[c]		Structure A[d]				Structure B[e]			
	$CH_3(a)N$	$CH_3(b)N$	R'_{1MN}	R'_{2MN}	G^*_1	G^*_2	R'_{1MN}	R'_{2MN}	G^*_1	G^*_2
F-M	—	—	0·76	7·7	8 ± 1	37 ± 8	0·87	3·6	4 ± 1	15 ± 4
F-S	—	—	0·47	3·3	1 ± 1	14 ± 3	0·52	1·8	-4 ± 1	6 ± 2
J-M	ecl	ecl	0·92	14	12 ± 1	69 ± 14	1·07	5·8	9 ± 2	27 ± 6
	ecl	stag	0·61	14	5 ± 1	69 ± 14	0·69	5·8	0 ± 1	27 ± 6
	stag	ecl	0·92	3·2	12 ± 1	14 ± 3	1·07	1·9	9 ± 2	7 ± 2
	stag	stag	0·61	3·2	5 ± 1	14 ± 3	0·69	1·9	0 ± 1	7 ± 2
J-S	ecl	ecl	0·56	6·4	4 ± 1	30 ± 6	0·63	2·9	-2 ± 1	12 ± 3
	ecl	stag	0·40	6·4	0 ± 1	30 ± 6	0·44	2·9	-6 ± 1	12 ± 3
	stag	ecl	0·56	1·6	4 ± 1	5 ± 2	0·63	1·1	-2 ± 1	3 ± 1
	stag	stag	0·40	1·6	0 ± 1	5 ± 2	0·44	1·1	-6 ± 1	3 ± 1

[a] All the relaxation rates should be multiplied by the factor 10^{57} if they are to be in m^{-6} units. [b] The rotation models F-M (free rotation, moderate fast), F-S (free rotation, superfast), J-M (120° random jumps, moderate fast), and J-S (120° random jumps, superfast) are defined in ref.[5]. [c] Conformations (ecl — eclipsed and stag — staggerred) of the methyl groups a and b on the nitrogen atom relatively to the C-N bond of the cyanine chain. [d] $R'_{11} = 4·9 \cdot 10^{57}\ m^{-6}$, $R'_{12} = 1·1 \cdot 10^{57}\ m^{-6}$. [e] $R'_{11} = 9·4 \cdot 10^{57}\ m^{-6}$, $R'_{12} = 1·2 \cdot 10^{57}\ m^{-6}$.

clases would be 1·3 Å apart only. Obviously the real structure deviates from such „unperturbed" one. The NOE results only indicate the direction of perturbation without giving exact values of geometry changes. The observed NOE values in *II* (as compared with those in *I*) can be consistently interpreted by a limited deviation of the dihedral angles in the trimethinium chain from the values in *I* rather than by a change in bond angles. Since, according to model calculations, the NOE enhancement observed on methyl protons should be larger than 0·05 if the saturated proton is closer to a methyl proton than 2·1 Å even if the independent relaxation rate is in the range of $15 . 10^{57}$ m^{-6}, the very small NOE enhancements observed on both methyl proton lines (MC and MN) indicate rather large distance between protons of the methyl groups of the two types. Though the required distance can be achieved by combination of bond length and angle and dihedral angle changes (relatively to those in salt *I*), changes in the dihedral angles seem to be the most probable explanation. These changes cannot be, however, too large since the H^1 proton is remote enough from the methyl (MC) protons as nill f_1(MC) enhancement was observed.

Salt III. Judging from the observed NOE values, which are in *III* the same as in *II*, the replacement of the MC methyl group in *II* by an ethyl group in *III* has very little (if any) effect on the structure of the trimethinium cyanine chain.

Salts IV *and* V. Further increase of the size of the C-2 substituent leads to a marked increase in f_1(MC) value. This trend indicates that the larger the substituent, the more the dihedral angles are changed; approximately equal values of f_1(MN) and f_1(MC) in salt *V* suggest approximately equal distances from the methyl groups of the two types.

Salts VI — VIII. Similarly to 2-substituted compounds, 1,3-disubstitution by methyl or ethyl groups leads only to small changes in the trimethinium skeleton as judged from small variations in NOE values. The substitution by the isopropyl group, however, brings about dramatic changes in NOE values. It follows from the small value of f_2(MN) and large value of f_2(MC) that the H^2 hydrogen atom on the middle carbon is practically surrounded by isopropyl protons only. Obviously, the all *trans-trans* arrangement of the cyanine chain is most distorted in cation *VIII*.

The observation that the ethyl substituted compounds (either 1,3- or 2-derivatives) do not differ appreciably in their NOE values from the methyl substituted compounds in contrast to the large changes by isopropyl or tert-butyl groups is easy to understand. In ethyl derivatives the steric interactions can be relieved by conformational changes while for the isopropyl and tert-butyl there are no conformations without the interactions and consequently the structure is altered in the described way.

EXPERIMENTAL

Compounds *I* and *II* were prepared according to a described procedure[11], the preparation
of compounds *III* and *V— VIII* was described elsewhere[12] similarly as the preparation[13] com-
pound *IV*.

The NMR spectrometer employed in the spectral and NOE measurements as well as the mea-
suring techniques were described earlier[5].

The standard samples for NOE measurements were $0\cdot3-0\cdot4$M solutions in sulphur dioxide
containing also tetramethylsilane (TMS) in concentrations $0\cdot4-0\cdot8$M. This relatively high TMS
concentration had no effect on the observed NOE enhancements since intermolecular NOE
enhancement of H^2 proton line in *VI* was $0\cdot009 \pm 0\cdot020$. The samples were degassed by the
repeated freeze-pump-thaw cycles using a vacuum better than 10^{-3} Torr.

The CNDO/2 calculations[14] were performed using the standard programme[15] and bond
lengths and angles of the idealized structure *A* as given in Fig. 1 except that the methyl groups
were replaced by hydrogen atoms with N—H bond length $1\cdot02$ Å. The bond angles C—N—H
and H—N—H were varied from $109\cdot5°$ to $120°$ gradually with $2°$ increments. Equality H—N—H
and C—N—H angles was always supposed.

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