

SYNTHESIS, IR AND $^1\text{H-NMR}$ SPECTRA OF N,N,N',N' -TETRAALKYL-1,6-HEXANEDIAMINE DIOXIDES

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The report describes preparation of N,N' -dimethyl-1,6-hexanediamine, N,N' -bis(alkylmethyl)-1,6-hexanediamines, N-alkyl-N,N' -dimethyl-1,6-hexanediamines, N,N' -bis(alkylmethyl)-1,6-hexanediamine dioxides, N-alkyl-N,N',N' -trimethyl-1,6-hexanediamines and N-alkyl-N,N',N' -trimethyl-1,6-hexanediamine dioxides. In the case of the dioxides IR and $^1\text{H-NMR}$ spectra are given. In all the cases the alkyl chain is linear and contains 4 to 16 carbon atoms.

Non-aromatic amine oxides containing at least one C_{10} or longer alkyl chain show marked surface active properties, which is utilized in many fields¹⁻⁶. Furthermore, they also exhibit marked antimicrobial activity⁷, their toxicity being substantially lower than that of analogous organic ammonium salts^{8,9}. The investigated substances have another advantage in being fully biodegradable and compatible with anion-active, cationactive and amphoteric detergents.

On the basis of our previous studies¹⁰ we have now followed the synthesis of amine oxides containing two N-O groups, since similar 1,6-hexanediamonium derivatives showed markedly higher antimicrobial activity than the monoammonium salts.

Synthesis of these substances started from 1,6-hexanediamine which was transformed into N,N' -dimethyl-1,6-hexanediamine by a procedure giving higher yields (by 30 to 70 per cent) than other preparations of this compound¹¹⁻¹³. Reaction of N,N' -dimethyl-1,6-hexanediamine with the corresponding 1-bromoalkane gives N,N' -bis(alkylmethyl)-1,6-hexanediamines (Table I, I-IX) and N-alkyl-N,N' -dimethyl-1,6-hexanediamines (Table I, X-XVII) which can be separated by fractionation. N-alkyl-N,N' -dimethyl-1,6-hexanediamines were methylated by modified Leuckart reductive alkylation¹⁴ (Table I, XVIII-XXV). The final amine oxides (Table II) were prepared by action of 30% aqueous hydrogen peroxide on the respective tertiary amines¹⁵. They are well soluble in polar solvents, being little soluble or insoluble in non-polar ones.

Interpretation of the IR spectra followed the procedure by Hummel¹⁶ which assigns the most intensive of the three bands in spectrum of dodecyltrimethylamine N-oxide to stretching vibration $\nu(\text{NO})$ in the region 1000 to 960 cm^{-1} . Similarly, Nakanishi¹⁷ gives the stretching vibration $\nu(\text{NO})$ for aliphatic amine oxides in the

TABLE I
Diamines

Compound R	Formula (m.wt.)	B.p., °C/kPa n_D^{20}	Calculated/Found			Yield, % R_F
			% C	% H	% N	
<i>I</i> Butyl	C ₁₆ H ₃₆ N ₂ (256.5)	110—113/0.01 1.4451	74.64 74.75	14.09 14.00	10.88 11.03	44 0.72
<i>II</i> Hexyl	C ₂₀ H ₄₄ N ₂ (312.6)	165—167/0.05 1.4492	76.85 76.90	14.19 13.92	8.96 9.03	43 0.69
<i>III</i> Octyl	C ₂₄ H ₅₂ N ₂ (368.7)	214/0.01 1.4532	78.16 78.22	14.21 14.56	7.60 7.79	49 0.66
<i>IV</i> Nonyl	C ₂₆ H ₅₆ N ₂ (396.8)	204—206/0.04 1.4548	78.72 79.02	14.23 14.41	7.06 7.00	43 0.64
<i>V</i> Decyl	C ₂₈ H ₆₀ N ₂ (424.8)	237—239/0.13 1.4560	79.17 78.85	14.24 14.36	6.59 6.50	42 0.61
<i>VI</i> Undecyl	C ₃₀ H ₆₄ N ₂ (452.8)	235/0.07 1.4568	79.58 79.80	14.25 14.19	6.19 6.30	43 0.45
<i>VII</i> Dodecyl	C ₃₂ H ₆₈ N ₂ (480.9)	241/0.05 1.4591	79.92 79.74	14.25 14.16	5.83 5.87	44 0.41
<i>VIII</i> Tridecyl	C ₃₄ H ₇₂ N ₂ (509.0)	256—257/0.05 1.4594	80.24 79.99	14.26 14.06	5.50 5.70	46 0.30
<i>IX</i> Tetradecyl	C ₃₆ H ₇₆ N ₂ (537.0)	263—264/0.05 1.4601	80.52 80.57	14.26 14.14	5.22 5.09	48 0.18
<i>X</i> Nonyl	C ₁₇ H ₃₈ N ₂ (270.5)	142—145/0.007 1.4513	75.46 75.53	14.16 14.19	10.35 10.54	55 0.65
<i>XI</i> Decyl	C ₁₈ H ₄₀ N ₂ (284.5)	153—156/0.007 1.4521	75.99 75.74	14.17 14.01	9.85 9.64	54 0.62
<i>XII</i> Undecyl	C ₁₉ H ₄₂ N ₂ (298.6)	157/0.004 1.4536	76.43 76.59	14.18 14.11	9.38 9.40	56 0.59
<i>XIII</i> Dodecyl	C ₂₀ H ₄₄ N ₂ (312.6)	178—180/0.04 1.4545	76.84 76.77	14.19 14.30	8.96 9.08	55 0.54
<i>XIV</i> Tridecyl	C ₂₁ H ₄₆ N ₂ (326.6)	179—180/0.04 1.4550	77.22 77.19	14.20 14.21	8.58 8.41	53 0.50
<i>XV</i> Tetradecyl	C ₂₂ H ₄₈ N ₂ (340.7)	189—190/0.04 1.4566	77.57 77.70	14.20 14.28	8.22 8.31	51 0.45
<i>XVI</i> Pentadecyl	C ₂₃ H ₅₀ N ₂ (354.7)	183/0.02 1.4572	77.88 77.57	14.21 14.09	7.90 7.91	52 0.42
<i>XVII</i> Hexadecyl	C ₂₄ H ₅₂ N ₂ (368.7)	204—206/0.02 1.4610	78.18 77.98	14.21 14.30	7.60 7.84	54 0.38

TABLE I
(Continued)

Compound R	Formula (m.wt.)	B.p., °C/kPa n_D^{20}	Calculated/Found			Yield, % R_F
			% C	% H	% N	
<i>XVIII</i> Nonyl	C ₁₈ H ₄₀ N ₂ (284.5)	148/0.03 1.4483	75.99 76.03	14.17 13.96	9.85 9.99	76 0.59
<i>XIX</i> Decyl	C ₁₉ H ₄₂ N ₂ (298.6)	157/0.03 1.4499	76.43 76.21	14.18 14.06	9.38 9.29	84 0.55
<i>XX</i> Undecyl	C ₂₀ H ₄₄ N ₂ (312.6)	175/0.23 1.4507	76.84 76.67	14.19 14.01	8.96 9.12	71 0.53
<i>XXI</i> Dodecyl	C ₂₁ H ₄₆ N ₂ (326.6)	178—180/0.06 1.4522	77.22 77.50	14.20 14.14	8.58 8.30	75 0.50
<i>XXII</i> Tridecyl	C ₂₂ H ₄₈ N ₂ (340.7)	177—179/0.01 1.4529	77.57 77.40	14.20 14.47	8.22 8.15	81 0.47
<i>XXIII</i> Tetradecyl	C ₂₃ H ₅₀ N ₂ (354.7)	188—190/0.12 1.4536	77.88 77.73	14.21 14.12	7.90 7.98	76 0.41
<i>XXIV</i> Pentadecyl	C ₂₄ H ₅₂ N ₂ (368.7)	196/0.02 1.4551	78.18 78.05	14.21 14.37	7.60 7.54	78 0.35
<i>XXV</i> Hexadecyl	C ₂₅ H ₅₄ N ₂ (382.8)	202—204/0.03 1.4563	78.45 78.50	14.22 14.48	7.32 7.50	88 0.26

region 970 to 950 cm^{-1} . However, from ref.¹⁵ it can be presumed that the frequency lowering of the stretching vibration $\nu(\text{NO})$ of the prepared amine oxides (951 to 938 cm^{-1}) is due to the presence of crystal water. Table III gives also the values of mixed rocking vibrations $\rho(\text{CH}_2)$ which are characteristic for aliphatic chains having 4 or more carbon atoms^{18,19}.

In evaluation of the ¹H-NMR spectra we followed refs^{15,21}. By this method we investigated the effect of N-oxidation of the tertiary nitrogen atom on chemical shifts of methyl and methylene protons. It was found that the prepared N-oxides show, in all the cases, a marked shift of both methyl and α -methylene proton signals towards lower values of magnetic field due to increased electronegativity of nitrogen. The shift observed in the both cases was 77.6 Hz. Furthermore, the spectra of amine oxides (in contrast to those of tert-amines) showed further signals due to β -methylene protons. In case of the compounds *XXVI*–*XXXIV* (Table IV) the δ values are shifted to higher field by 10.4 Hz (for α -CH₂ protons) and 11.2 Hz (γ -CH₂), which is probably connected with steric arrangement of the alkyl chain¹⁵. The analogous shifts of the compounds *XXXV*–*XLII* (Table V) were not so marked.

TABLE II
Diamine Dioxides

Compound R	Formula (m.wt.)	M.p., °C	Calculated/Found			Yield, % R_F
			% C	% H	% N	
<i>XXVI</i> Butyl	$C_{16}H_{36}N_2O_2^a$ (288.5)	99—102	66.61 59.32	12.58 12.52	9.71 8.53	95 0.63
<i>XXVII</i> Hexyl	$C_{20}H_{44}N_2O_2^a$ (344.6)	124—126	69.71 63.19	12.87 12.61	8.13 7.58	98 0.66
<i>XXVIII</i> Oktyl	$C_{24}H_{52}N_2O_2^a$ (400.8)	127—128	71.93 66.32	13.08 12.90	6.99 6.69	96 0.68
<i>XXIX</i> Nonyl	$C_{26}H_{56}N_2O_2^a$ (428.8)	134—135	72.83 67.08	13.16 12.97	6.53 6.13	95 0.69
<i>XXX</i> Decyl	$C_{28}H_{60}N_2O_2^a$ (456.9)	123.5	73.61 68.00	13.24 13.14	6.13 5.42	97 0.70
<i>XXXI</i> Undecyl	$C_{30}H_{64}N_2O_2^a$ (484.9)	127—128	74.30 69.27	13.30 13.20	5.78 5.40	98 0.71
<i>XXXII</i> Dodecyl	$C_{32}H_{68}N_2O_2^a$ (513.0)	129—131	74.94 70.09	13.36 13.18	5.46 5.00	98 0.72
<i>XXXIII</i> Tridecyl	$C_{34}H_{72}N_2O_2^a$ (541.0)	127—130	75.49 70.49	13.42 12.99	5.18 4.85	97 0.74
<i>XXXIV</i> Tetradecyl	$C_{36}H_{76}N_2O_2^a$ (569.1)	131—131.5	73.87 71.41	13.46 13.28	4.92 4.65	98 0.77
<i>XXXV</i> Nonyl	$C_{18}H_{40}N_2O_2^b$ (316.5)	148—149.5	68.30 64.51	12.74 12.47	8.85 8.37	95 0.73
<i>XXXVI</i> Decyl	$C_{19}H_{42}N_2O_2^b$ (330.6)	147.5—148	69.03 66.00	12.81 12.83	8.47 8.06	93 0.70
<i>XXXVII</i> Undecyl	$C_{20}H_{44}N_2O_2^b$ (344.6)	154	69.71 66.42	12.87 12.81	8.13 7.51	95 0.65
<i>XXXVIII</i> Dodecyl	$C_{21}H_{46}N_2O_2^b$ (358.6)	143	70.33 66.87	12.93 12.80	7.81 7.34	97 0.61
<i>XXXIX</i> Tridecyl	$C_{22}H_{48}N_2O_2^b$ (372.7)	156	70.91 67.52	12.98 12.85	7.52 7.15	99 0.56
<i>XL</i> Tetradecyl	$C_{23}H_{50}N_2O_2^b$ (386.7)	141	71.44 68.43	13.04 12.70	7.24 6.76	97 0.50
<i>XLI</i> Pentadecyl	$C_{24}H_{52}N_2O_2^b$ (400.7)	152—152	71.93 69.03	13.08 12.86	6.99 6.60	98 0.43
<i>XLII</i> Hexadecyl	$C_{25}H_{54}N_2O_2^b$ (414.8)	137—138	72.40 69.28	13.14 13.26	6.75 6.34	96 0.35

^a Dihydrate; ^b monohydrate.

EXPERIMENTAL

The $^1\text{H-NMR}$ spectra were measured with a Tesla BS 487A apparatus at 80 MHz in 10% solutions in CDCl_3 at 30°C using tetramethylsilane as internal standard. Accuracy of the frequency readings was ± 0.5 Hz. Content of crystal water in the amine oxides was determined by thermogravimetry using a Derivatograph MOM 102 (Mom, Budapest). Purity of the prepared amines and amine oxides was checked by elemental analysis and TLC using Silufol and acetone-1M-HCl (1 : 1) and detection with Dragendorff reagent in the Munier modification²⁰. All the amine oxides were dried (before elemental analyses and the measurements) in a vacuum desiccator over P_4O_{10} at 13 Pa for 48 h. The melting points were determined with a Boetius apparatus. All given temperature data are not corrected.

TABLE III

IR Spectral Characteristics of the Prepared Diamine Dioxides (wave numbers in cm^{-1})

The IR spectra were measured with a Perkin-Elmer 377 apparatus (*XXVI-XXXIV*) in NaCl cells or with a UR-20 spectrometer (Zeiss, Jena) (*XXXV-XLII*) in KBr cell in paraffine oil suspension. The spectrometers were calibrated with a polystyrene foil, the accuracy of the wave number readings being $\pm 1 \text{ cm}^{-1}$.

Compound	$\nu(\text{NO}^a)$		$\rho(\text{CH}_2)$	Compound	$\nu(\text{NO}^a)$		$\rho(\text{CH}_2)^b$
<i>XXVI</i>	938	920	727	<i>XXXV</i>	945	923	729
		965				969	742
<i>XXVII</i>	939	920	723	<i>XXXVI</i>	945	922	726
		968				968	742
<i>XXVIII</i>	948	926	722	<i>XXXVII</i>	946	921	728
		967				970	740
<i>XXIX</i>	950	930	722	<i>XXXVIII</i>	945	920	725
		968				969	741
<i>XXX</i>	948	930	721	<i>XXXIX</i>	946	922	725
		975				972	742
<i>XXXI</i>	948	930	721	<i>XL</i>	946	924	725
		974				971	743
<i>XXXII</i>	948	930	721	<i>XLI</i>	946	920	729
		975				970	742
<i>XXXIII</i>	948	929	721	<i>XLII</i>	946	920	728
		975				970	742
<i>XXXIV</i>	951	930	721				
		975					

^a Triplet of sharp peaks, the central peak having the maximum intensity; ^b doublet of sharp peaks, the first one being the more intensive.

N,N'-Dimethyl-1,6-hexanediamine

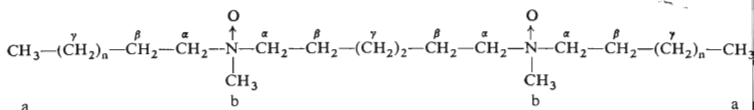
Benzaldehyde (1.2 mol) was added to solution of 0.5 mol 1,6-hexanediamine in 200 ml benzene at room temperature. The mixture was refluxed 30 min, whereupon benzene and the water formed in the reaction were distilled off in vacuum. The evaporation residue was treated with 1.2 mol dimethyl sulphate in 400 ml benzene at room temperature. After the exothermic reaction had ceased, the mixture was refluxed 1 h, the non-reacted dimethyl sulphate and benzene were vacuum distilled off, and the residue was treated with 400 ml water and 1 mol 98% H₂SO₄. After 1 h boiling benzaldehyde was steam distilled. The residue was cooled, and solid NaOH was added with stirring and cooling until separation of the amine. The amine was extracted with ether, the extracts were dried with solid NaOH whereupon the solvent was distilled off under atmospheric pressure. The product was distilled in vacuum. B.p. 92°C/1.60 kPa; n_{D}^{20} 1.4469; R_F 0.57; yield 86%. IR spectrum: $\nu(\text{NH})$ 3280 cm⁻¹; $\delta(\text{NH})$ broad intensive band with the maximum at 740 cm⁻¹; $\nu(\text{N}-\text{CH}_2)$ 2690 cm⁻¹; $\nu(\text{C}-\text{N})$ doublet 1125 and 1150 cm⁻¹. ¹H-NMR spectrum: chemical shifts δ in ppm: CH₃ 2.29 d; NH 1.33 s; N-CH₂- 2.44 m; (CH₂)₄ 1.22 m. ³J_{HC-NH} = 0.92 Hz.

N,N'-Bis(alkylmethyl)-1,6-hexanediamines and N-Alkyl-N,N'-dimethyl-1,6-hexanediamines (Table I, I-IX and X-XVII, resp.)

N,N'-Dimethyl-1,6-hexanediamine (0.3 mol) was dissolved in 300 ml benzene and heated to boiling whereupon 0.1 mol 1-bromoalkane was added within 1 h. After 6 h refluxing and cooling the precipitated N,N'-dimethyl-1,6-hexanediamonium dibromide was filtered off and washed with

TABLE IV

¹H-NMR Spectral Characteristics of N,N'-Bis(alkylmethyl)-1,6-hexanediamine Dioxides (chemical shift δ given in ppm)



Compound	<i>n</i>	<i>a</i> <i>t</i>	<i>b</i> <i>s</i>	α <i>t</i>	β <i>m</i> *	γ <i>m</i>
XXVI	1	0.86	2.98	3.11	1.75	1.29
XXVII	3	0.79	2.96	3.09	1.76	1.23
XXVIII	5	0.76	2.95	3.07	1.75	1.19
XXIX	6	0.77	2.96	3.05	1.75	1.18
XXX	7	0.76	2.99	3.04	1.75	1.16
XXXI	8	0.77	2.99	3.04	1.76	1.16
XXXII	9	0.77	2.98	3.01	1.73	1.15
XXXIII	10	0.77	2.99	3.00	1.71	1.15
XXXIV	11	0.76	2.96	2.98	1.73	1.15

benzene. The benzene solution was treated with 0.6 mol 37% HCl and, after shaking, the benzene layer was separated and extracted with 100 ml water. Solid NaOH was added to the combined aqueous extracts until separation of amine layer which was extracted with ether. The ether extracts were dried with Na_2SO_4 , the solvent was distilled off, and the product was fractionated in vacuum. The products are oils.

N-Alkyl-N,N',N'-trimethyl-1,6-hexanediamines (Table I, *XXVIII—XXV*)

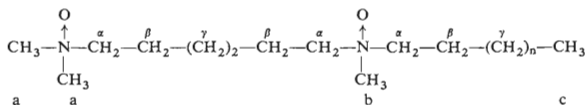
The compounds were prepared according to ref.¹⁴, the only difference being in that methylation mixture consisting of 0.44 mol 36% formaldehyde and 0.74 mol 98% formic acid was added to 0.1 mol secondary amine heated at 70°C within 1 h.

N,N'-Bis(alkylmethyl)-1,6-hexanediamine Dioxides and N-Alkyl-N,N',N'-trimethyl-1,6-hexanediamine Dioxides (Table II, *XXVI—XXXIV* and *XXXV—XLII*, respectively)

The compounds were prepared according to ref.¹⁵ and crystallized from acetone.

TABLE V

¹H-NMR Spectral Characteristics of N-Alkyl-N,N',N'-trimethyl-1,6-hexanediamine Dioxides (chemical shift δ given in ppm)



compound ^a	n	a s	b s	c t	α t	β m*	γ m
<i>XXXV</i>	6	3.05	2.95	0.75	3.15	1.84	1.16
<i>XXXVI</i>	7	3.07	2.95	0.76	3.15	1.81	1.15
<i>XXXVII</i>	8	3.08	2.95	0.76	3.14	1.79	1.15
<i>XXXVIII</i>	9	3.09	2.95	0.76	3.15	1.78	1.15
<i>XXXIX</i>	10	3.08	2.95	0.76	3.15	1.78	1.15
<i>XL</i>	11	3.09	2.96	0.76	3.16	1.75	1.15
<i>XLI</i>	12	3.10	2.95	0.76	3.16	1.76	1.14
<i>XLII</i>	13	3.10	2.96	0.75	3.16	1.75	1.14

^a The coupling constant $^3J_{\text{HC-CH}}$ in CH_3-CH_2- was within 7.1 to 7.3 Hz in all the cases. The coupling constant $^3J_{\text{HC-CH}}$ in $-\text{CH}_2-\text{CH}_2-\text{N}\rightarrow\text{O}$ was within 7.5 to 7.7 Hz in all the cases. t triplet; s singlet; m multiplet; m* multiplet, the maximum of the broad band being given.

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