SYNTHESIS AND MASS SPECTRA OF PIPERIDINE AND PIPERAZINE N-OXYL RADICALS

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It has been found that ultrasound could accelerate the synthesis of piperidine and piperazine N-oxyl radicals. These radicals were investigated for their utilization as spin probes for checking the properties of liquid crystals. Electron impact mass spectra of the N-oxyl radicals were recorded and their fundamental fragmentation pattern was proposed.

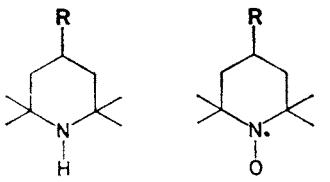
Oxidation of sterically hindered amines with hydrogen peroxide under catalysis of Na_2WO_4 was reported to proceed smoothly in the majority of experiments[1,2]. Difficulties with amines having a longer lipophilic chain were overcome by application of ultrasound[3]. The N-oxyl radicals of sterically hindered piperazine (C(15)-substituted 7,15-diazadispiro[5.1.5.3]hexadecanes) have so far not been prepared by oxidation of the respective starting amines by hydrogen peroxide and Na_2WO_4, or *m*-chloroperbenzoic acid[4]. Whereas the mass spectral fragmentation of piperidinyloxyls were already reported, these of piperazinyloxyls have not been studied.

This paper was aimed to verify the possibility to use ultrasound for acceleration of the synthesis of piperazine and some piperidinyloxyls, to measure and interprete their mass spectra, and to find suitable probes for investigation of kinematics of rotational and translational motions of molecules in liquid crystals and to measure the degree of their ordering.

The majority of piperidinyloxyls was obtained by oxidation of the appropriate sterically hindered amines with hydrogen peroxide under catalysis of Na_2WO_4 and application of ultrasound similarly as reported in our previous paper[3]. The same procedure was used to attempt the oxidation of 4-amino-2,2,6,6-tetramethylpiperidine; the reaction did not stop at the corresponding 1-oxyl, but at 4-hydroxyimino-2,2,6,6-tetramethylpiperidinyl-1-oxyl (*IIIa*).

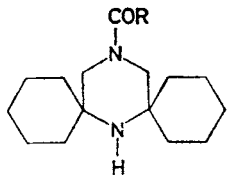
It was reported[4] that a direct oxidation of 15-substituted 7,15-diazadispiro[5.1.5.3]-hexadecanes did not occur. Our preliminary experiments brought evidence that this statement is only partially valid, since small amounts of *IVa*, *Va*, and *VIa* were

obtained upon standing of the respective piperazine derivative, a great excess of hydrogen peroxide, Na_2WO_4, and acetic acid for several weeks. Our previous experiments with acceleration of such oxidations with ultrasound prompted us to apply it also for preparation of sterically hindered piperazine nitroxyl derivatives. Neither this method proved successful for the synthesis of N-oxyls of 7,15-diazadispiro-[5.1.5.3]hexadecanes unsubstituted at the shielded nitrogen in position 15, but it worked with other derivatives, where the ultrasound promoted 20 h-oxidation afforded compounds *IVa*, *Va*, and *VIa* in 57–85% yields.

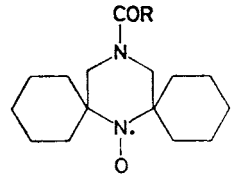


I

Ia, *IIa*, *VIIa*, *VIIIa*



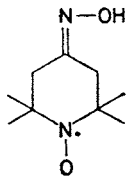
IV, *V*, *VI*



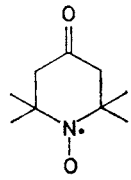
IVa, *Va*, *VIa*

I, *Ia*, R = $OCO(CH_2)_{16}CH_3$
IIa, R = $OCOC_6H_4OC_8H_{17}$-*p*
VIIa, R = $NHCOC_6H_4OC_8H_{17}$-*p*
VIIIa, R = OH

IV, *IVa*, R = *p*-$C_6H_4OC_8H_{17}$
V, *Va*, R = $(CH_2)_{16}CH_3$
VI, *VIa*, R = C_5H_{11}



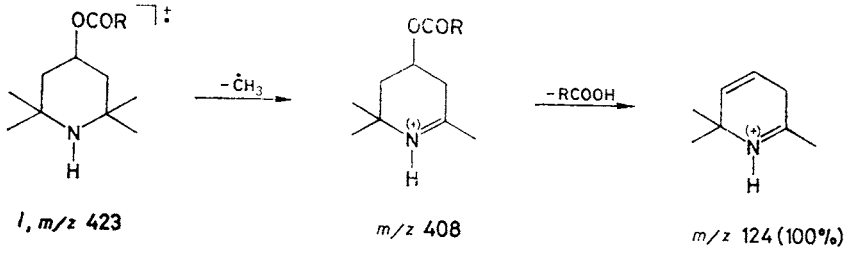
IIIa



IXa

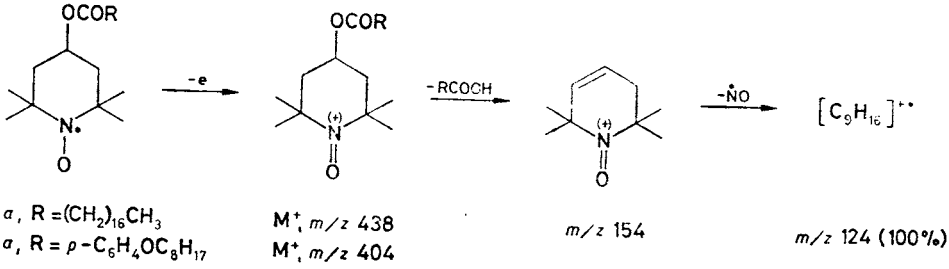
The EPR spectra of N-oxyl radicals obtained showed the unshared electron to be predominantly located at nitrogen. The spin-probe properties of N-oxyl radicals *Ia*, *IVa*, and *Va*–*IXa* were examined, and as shown[5], the most suitable for investigation of kinematics of rotational and translational motions of liquid crystal molecules were found to be *IVa* and *VIIa*. As it follows, the long lipophilic chain of *e.g.* compounds *Ia* and *Va* was not sufficient for monitoring the motion of molecules, which requires the probe to be structurally similar to the liquid crystals. This condition was to some extent met with the 4-octylbenzoyl group, especially if it was bound to the subunit of the probe through an amide function, which makes the rotation about the N—CO bond more difficult and consequently, ensures a greater linearity of the whole probe.

The mass spectral fragmentation pattern of N-oxyl radicals was contrasted with the known data[6-12]. The mass spectra of compounds *VIIIa*, *IXa*, *VIII*, and *IX*, which were chosen for models, were in agreement with refs[6,8,10,12]. To establish the influence of nitroxyl group on the fragmentation process of piperidine and piperazine skeletons also spectra of starting amines related to 2,2,6,6-tetramethyl-4--stearoyloxypiperidine (*I*), 15-(4-octyloxy)benzoyl-7,15-diazadispiro[5.1.5.3]hexadecane (*IV*), and 15-stearoyl-7,15-diazadispiro[5.1.5.3]hexadecane (*V*) were recorded. The mass spectral data of *Ia* – *VIa*, *I*, *IV*, and *V* are listed in Table I. The base peak of *I* at *m/z* 124 originates by a subsequent elimination of $^{\bullet}CH_3$ and RCOOH from the molecular ion (Scheme 1), this being in line with[12], recently reporting the fragmentation of 2,2,6,6-tetramethyl-4-benzoyloxypiperidine (*cf.* Scheme 1).



SCHEME 1

The mass spectra of *Ia* and *IIa* revealed an $(M + 1)^{+\bullet}$ radical-ion resulting from addition of hydrogen in the ion source; this hydrogen can predominantly stem from water present in the ion source[6]. We observed that the relative intensity of this ion is approximately 1–4 *per* the isotopic ion $(M + 1)^+$ excepting compound *IIIa*, where this value was found to be 15, depending on experimental conditions of the measurement. The relative intensity of these ions and also that of M^+ was quite low (about 1%). The base peak corresponds to the $(C_9H_{16})^{+\bullet}$ species with *m/z* 124 and its formation took a different route from that of *I*. (Scheme 2).



SCHEME 2

TABLE I

Mass spectral data of compounds *I*—*VIa*

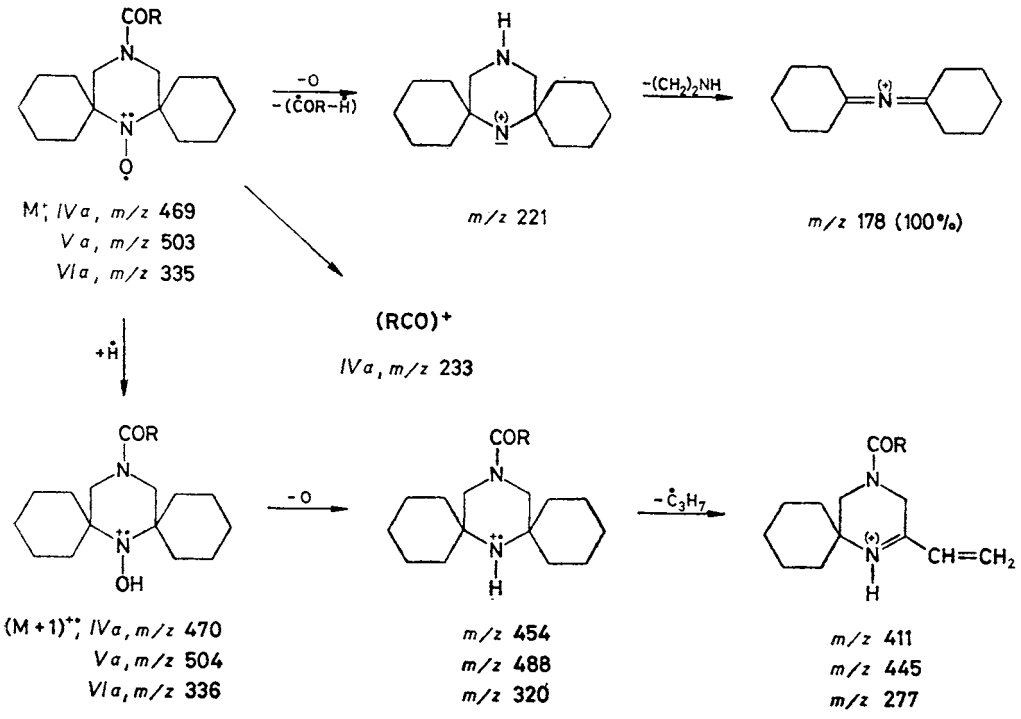
Compound	m/z[a]
I	423 $M^{+\cdot}$ (0·6), 408 (5), 140 (19), 125 (8), 124 (100), 83 (4), 58 (21), 57 (6), 55 (7), 44 (4), 43 (7), 42 (5), 41 (8)
Ia	439 $(M + 1)^{+\cdot}$ (0·8), 438 M^+ (1·1), 408 (4), 156 (4), 155 (4), 154 (7), 140 (29), 125 (9), 124 (100), 109 (5), 83 (4), 82 (4), 74 (4), 69 (5), 58 (19), 57 (8), 56 (5), 55 (9), 44 (5), 43 (10), 42 (4), 41 (9)
IIa	405 $(M + 1)^{+\cdot}$ (0·3), 404 M^+ (0·3), 390 (0·3), 389 (0·2), 140 (7), 125 (8), 124 (100), 121 (6), 58 (13), 57 (4), 55 (6), 44 (6), 43 (6), 42 (5), 41 (8)
IIIa	186 $(M + 1)^{+\cdot}$ (14), 185 M^+ (7), 171 (37), 170 (8), 155 (13), 154 (5), 153 (8), 140 (12), 139 (15), 138 (5), 137 (9), 136 (6), 127 (9), 124 (8), 123 (5), 122 (12), 113 (22), 112 (4), 111 (62), 99 (14), 98 (30), 97 (25), 96 (25), 95 (8), 94 (10), 88 (4), 84 (6), 83 (10), 82 (45), 81 (14), 80 (7), 79 (6), 74 (42), 73 (4), 72 (5), 70 (8), 69 (6), 68 (5), 67 (8), 59 (27), 58 (43), 57 (24), 56 (100), 55 (63), 54 (10), 53 (9), 44 (9), 43 (9), 42 (65), 41 (68)
IV	454 $M^{+\cdot}$ (50), 411 (8), 233 (22), 222 (5), 221 (33), 191 (4), 179 (17), 178 (100), 149 (5), 124 (6), 123 (5), 122 (7), 121 (46), 111 (4), 110 (8), 109 (4), 98 (28), 97 (6), 96 (4), 95 (12), 94 (6), 93 (8), 91 (4), 85 (4), 83 (7), 82 (5), 81 (13), 79 (5), 77 (5), 71 (8), 70 (5), 69 (8), 67 (10), 65 (4), 57 (21), 56 (8), 55 (22), 54 (4), 44 (21), 43 (25), 42 (9), 41 (30)
IVa	470 $(M + 1)^{+\cdot}$ (5), 469 M^+ (8), 455 (16), 454 (50), 411 (8), 356 (4), 343 (8), 254 (4), 234 (14), 233 (77), 231 (4), 222 (6), 221 (29), 191 (13), 179 (16), 178 (100), 177 (4), 150 (5), 149 (6), 148 (5), 134 (4), 133 (8), 125 (4), 124 (14), 123 (8), 122 (12), 121 (85), 120 (4), 112 (4), 111 (7), 110 (16), 109 (5), 108 (5), 107 (6), 105 (6), 104 (4), 103 (25), 99 (4), 98 (32), 97 (9), 96 (24), 95 (23), 94 (12), 93 (16), 91 (6), 86 (4), 85 (4), 84 (4), 83 (9), 82 (8), 81 (20), 80 (5), 79 (12), 78 (23), 77 (12), 74 (10), 73 (5), 72 (12), 71 (12), 70 (9), 69 (19), 68 (7), 67 (21), 65 (9), 61 (8), 60 (5), 58 (4), 57 (38), 56 (22), 55 (36), 54 (10), 53 (8), 52 (5), 51 (8), 50 (6), 44 (35), 43 (92), 42 (69), 41 (81)
V	488 $M^{+\cdot}$ (68), 445 (7), 222 (10), 221 (15), 179 (15), 178 (100), 124 (5), 112 (6), 111 (5), 110 (10), 109 (4), 98 (18), 97 (7), 96 (5), 95 (12), 93 (4), 85 (6), 83 (8), 82 (5), 81 (11), 79 (5), 71 (8), 70 (5), 69 (9), 68 (4), 67 (10), 57 (16), 56 (7), 55 (15), 54 (4), 44 (19), 43 (18), 42 (7), 41 (18)
Va	504 $(M + 1)^{+\cdot}$ (3), 503 M^+ (4), 489 (26), 488 (69), 445 (6), 262 (4), 222 (10), 221 (24), 206 (4), 180 (4), 179 (15), 178 (100), 167 (4), 153 (4), 125 (4), 124 (16), 112 (9), 111 (15), 110 (12), 98 (26), 97 (6), 96 (12), 95 (16), 94 (5), 93 (4), 85 (4), 83 (6), 82 (5), 81 (11), 79 (5), 71 (6), 69 (9), 68 (4), 67 (10), 57 (13), 56 (6), 55 (14), 54 (4), 44 (7), 43 (17), 42 (7), 41 (15)
VIa	336 $(M + 1)^{+\cdot}$ (24), 335 M^+ (21), 321 (13), 320 (59), 319 (13), 305 (9), 277 (20), 263 (8), 262 (38), 249 (7), 234 (4), 224 (6), 223 (10), 222 (13), 221 (69), 219 (5), 210 (18), 209 (38), 206 (4), 194 (25), 192 (5), 191 (5), 190 (6), 181 (5), 180 (18),

TABLE I
(*Continued*)

Compound	m/z[a]
	179 (22), 178 (100), 177 (5), 167 (24), 166 (8), 165 (7), 154 (4), 153 (19), 150 (4), 149 (14), 148 (5), 137 (4), 136 (4), 135 (4), 134 (4), 128 (7), 126 (7), 125 (19), 124 (96), 123 (7), 122 (7), 116 (6), 114 (10), 113 (4), 112 (34), 111 (95), 110 (42), 109 (7), 108 (7), 99 (15), 98 (42), 97 (16), 96 (71), 95 (64), 94 (29), 93 (19), 91 (7), 85 (4), 84 (5), 83 (15), 82 (18), 81 (41), 80 (8), 79 (25), 78 (38), 77 (18), 72 (7), 71 (19), 70 (10), 69 (23), 68 (19), 67 (47), 65 (4), 60 (5), 58 (5), 57 (20), 56 (23), 55 (5), 54 (20), 53 (15), 52 (6), 51 (6), 50 (5), 44 (20), 43 (89), 42 (53), 41 (69)

[a] Relative intensities ≧4% excepting those of M^+ and $(M + 1)^{+\cdot}$ are given in parentheses.

The loss of 30 mass units from the molecular radical-ions of *Ia* and *IIa* (*m/z* 408, 374), in line with[6], could be rationalized either by a subsequent double elimination



SCHEME 3

of $^{\bullet}CH_3$ and cleavage of $^{\bullet}NO$ radical, or a neutral CH_2O species. The loss of $^{\bullet}CH_3$ from $(M + 1)^{+\bullet}$ led to unconventional $(M - 14)^+$ ions, which could eliminate RCOOH to furnish the fragment at m/z 140.

The N-oxyl radicals of sterically hindered piperazines *IVa*, *Va*, and *VIa* also afforded the $(M + 1)^{+\bullet}$ radical-ions as a result of addition of hydrogen in the ion source (Scheme 3). Cleavage of oxygen from the $(M + 1)^{+\bullet}$ species led to the corresponding starting amines. This and other fragmentations presented in Scheme 3

TABLE II
Characteristic data of compounds *I*—*VIIa*

Compound (Yield, %)	Formula (M_r)	M.p., °C	Calculated/found		
			% C	% H	% N
I	$C_{27}H_{53}NO_2$	43·5—45·5	76·51	12·63	3·30
(15)	(423·7)		76·10	13·41	3·30
Ia	$C_{27}H_{52}NO_3$	49—52	76·70	12·39	3·40
(84)	(438·7)		76·80	12·45	3·31
IIa	$C_{24}H_{38}NO_4$	83·5—86	71·22	9·49	3·49
(38)	(404·6)		71·05	9·71	3·47
IIIa	$C_9H_{17}N_2O_2$	165—168	58·37	9·18	15·13
(9)	(185·2)		58·43	10·02	15·19
IV	$C_{29}H_{46}N_2O_2$	74—79	76·65	10·13	6·17
(50)	(454·7)		76·88	10·82	6·13
IVa	$C_{29}H_{45}N_2O_3$	91·5—93	74·15	9·68	5·97
(58)	(469·7)		74·14	10·06	5·79
V	$C_{32}H_{60}N_2O$	64—66	78·60	12·39	5·52
(55)	(488·8)		78·49	13·05	5·68
Va	$C_{32}H_{59}N_2O_2$	70—71	76·27	11·83	5·56
(86)	(503·8)		76·27	12·30	5·52
VI	$C_{20}H_{36}N_2O$	oil	74·93	11·34	8·74
(46)	(320·5)		74·80	11·85	8·62
VIa	$C_{20}H_{35}N_2O_2$	95·5—96·5	71·58	10·53	8·35
(63)	(335·5)		71·54	11·09	8·32
VII	$C_{24}H_{40}N_2O_2$	85·5—87·5	74·17	10·40	7·21
(33)	(388·6)		74·33	10·66	7·21
VIIa	$C_{24}H_{39}N_2O_3$	83—86	71·41	9·76	6·94
(64)	(403·6)		71·74	10·31	7·01

were corroborated by the presence of metastable transitions in the first field free region. The elemental composition of ions was evidenced *via* high resolution measurement. Scheme 3 presents only frgmentations important for structures of these compounds, since it was proved that *e.g.* the ion with m/z 233 of our substance *IVa* could originate from up to eight precursors.

EXPERIMENTAL

The starting 2,2,6,6-tetramethyl-4-piperidinol was synthesized according to ref.[13] and 7,15--diazadispiro[5.1.5.3]hexadecane was obtained by reduction of 7,15-diazadispiro[5.1.5.3]hexadecane-14,16-dione[14] with $LiAlH_4$. The amines *I*, *IV*– *VI* were prepared from 2,2,6,6-tetramethyl-4-piperidinol, 7,15-diazadispiro[5.1.5.3]hexadecane, and 4-amino-2,2,6,6-tetramethylpiperidine, respectively, and the corresponding acid chlorides in pyridine. Compound *IIa* was obtained from 4-hydroxy-2,2,6,6-tetramethylpiperidinyl-1-oxyl and 4-octyloxybenzoyl chloride in pyridine, and *VIIa* by oxidation of *VII* according to ref.[1]. Preparation of *Ia*, *VIIIa*, and *IXa* by oxidation with hydrogen peroxide catalyzed with Na_2WO_4 and action of ultrasound was already described in ref.[3]. Physical constants of compounds *VIIIa* and *IXa* are in accordance with those reported in refs[1,15].

The EPR spectra of benzene solutions ($1 . 10^{-3}$ mol dm^{-3}) were measured at room temperature. The electron impact mass spectra were recorded with an AET-MS 902 S (AEI-Kratos) spectrometer at 70 eV electron energy, 100 μA trap current and 40—135°C ion source temperature. The high resolution measurement (resolution 15 000, 10% valey) was contrasted with heptacosafluorotributylamine as internal reference. The ultrasound source was the cleaning vessel UC 002 BM 1 (20 kHz, 160 W).

Physical constants and yields of compounds prepared are listed in Table II

4-Hydroxyimino-2,2,6,6-tetramethylpiperidinyl-1-oxyl (*IIIa*)

A mixture of 4-amino-2,2,6,6-tetramethylpiperidine (0·3 g; 2 mmol), $Na_2WO_4.2\,H_2O$ (0·05 g; 0·15 mmol), Chelaton 3 (0·05 g; 0·15 mmol), H_2O_2 (30%; 1 ml) and ethanol (20 ml) was exposed to ultrasound for 3 h, the solvent was evaporated to dryness and the content of N-oxyl radicals in the residue was determined by EPR. The pure compound was obtained by column chromatography on silica gel (elution with benzene–ethyl acetate 10 : 1) followed by recrystallization from benzene–hexane 1 : 5.

15-(4-Octyloxy)benzoyl-7,15-diazadispiro[5.1.5.3]hexadecyl-7-oxyl (*IVa*)

The same procedure was employed starting from *IV* (0·3 g; 0·7 mmol), $Na_2WO_4.2\,H_2O$ (0·02 g; 0·06 mmol), Chelaton 3 (0·02 g; 0·06 mmol), and H_2O_2 (1 ml) in ethanol (20 ml). The ultrasound was applied for 20 h, the product was purified by chromatography on silica gel (eluent benzene) and recrystallized from benzene–hexane 1 : 5.

15-Stearoyl-7,15-diazadispiro[5.1.5.3]hexadecyl-7-oxyl (*Va*)

The title product was obtained by reaction of *V* (1 g; 2 mmol), $Na_2WO_4.2\,H_2O$ (0·04 g; 0·1 mmol), Chelaton 3 (0·04 g; 0·1 mmol), H_2O_2 (2 ml) in ethanol (20 ml) applying the procedure specified for *IVa*.

15-Hexanoyl-7,15-diazadispiro[5.1.5.3]hexadecyl-7-oxyl (*VIa*)

From *VI* (0·5 g; 1·5 mmol), $Na_2WO_4.2\,H_2O$ (0·02 g; 0·06 mmol), Chelaton 3 (0·02 g; 0·06 mmol), H_2O_2 (1 ml) in ethanol (20 ml), the *VIa* was prepared by the same procedure as described for *IVa*.

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