VINYL ETHER OF 2,2,6,6-TETRAMETHYL-4-HYDROXYPIPERIDINE-1-OXYL AND ITS OLIGOMERS

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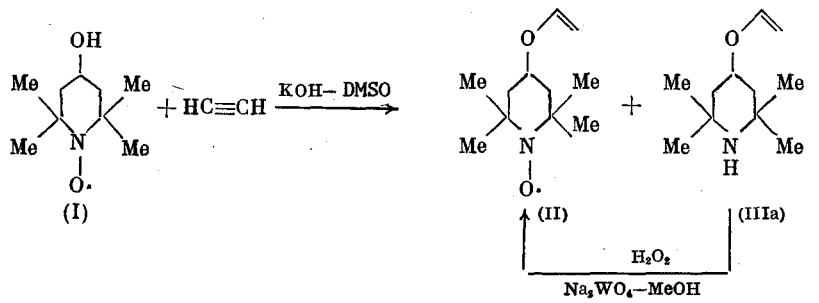
Stable nitroxyl radicals are convenient for studying the reactivity of different molecules and chemical bonds in relation to their character and structure [1]. It is of interest to study compounds which combine in one molecule a free-radical nitroxyl center and a group capable of polymerization, for example, a vinyl ether fragment.

The synthesis of the vinyl derivatives of 2,2,6,6-tetramethylpiperidine, their paramagnetic N-oxides [2], and spin-labeled polyvinylpyrrolidones based on them [3] have previously been reported. As a continuation of these works we have studied the possibility of obtaining the vinyl ethers of 2,2,6,6-tetramethyl-4-hydroxypiperidine, the corresponding N-oxide, and also their oligomers.

Recently a whole series of vinyl ethers previously difficult to prepare [4, 5] was obtained by reaction of functionally substituted alcohols with acetylene in superbasic media of type KOH–DMSO.

However, our experiments showed that when nitroxyl (I) is vinylated in a KOH–DMSO system, together with the expected 4-vinyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl (II) in the reaction mixture there is an accumulation of its reduction product, 4-vinyloxy-2,2,6,6-tetramethylpiperidine (IIIa), which according to [1] must be preceded by the corresponding hydroxylamine:



When DMSO is replaced by dioxane with other conditions being equal (90°C, 30 wt. % KOH, initial pressure of acetylene 12 atm), nitroxyl radical (I) is recovered unchanged. Reduction is observed at a higher temperature (150°C), the initial substance being reduced to 4-hydroxy-2,2,6,6-tetramethylpiperidine (IVa) with a yield of about 10%, and vinyl ethers (II) and (IIIa) are not formed at all. This fact is not trivial as special experiments [1] have shown that with a decrease in pH of the medium the rate of reduction of nitroxyls increases, while in neutral and alkaline media the process stops.

Under the conditions of vinylation the reducing agent may be MeCHO formed by hydration of acetylene according to the scheme:

$$ROH + KOH \rightleftarrows ROK + H_2O$$

$$H_2O + HC \equiv CH \rightarrow [CH_2{=}CHOH] \rightarrow MeCHO$$

In the system KOH–DMSO a hydrating trimerization of acetylene to 2-vinyloxy-1,3-butadiene occurs via the intermediate formation of MeCHO [4, 5], and superbasic systems of type t-BuOK–DMSO frequently have an active catalyzing effect on the different reduction processes [6].

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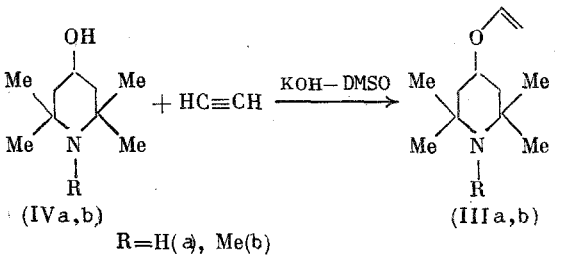
Since a general method for obtaining nitroxyl free radicals is the oxidation of secondary amines and hydroxylamines, it was possible to obtain vinyl ether (II) by reversing the order of the stages oxidation–vinylation. With this aim in mind 4-hydroxy-2,2,6,6-tetramethylpiperidine (IVa) underwent vinylation:



(IVa,b) (IIIa,b)

R=H(a), Me(b)

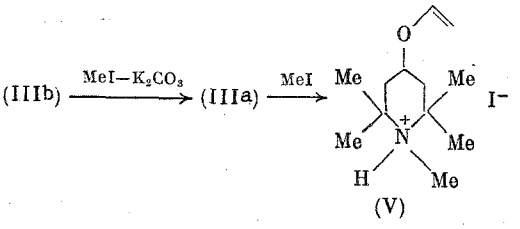
The following conditions turned out to be the best: a KOH–DMSO system, temperature 90°C, KOH concentration 20% based on the weight of (VIa), time 3-4 h. Acetylene was passed into an autoclave at an initial pressure of 10-14 atm until the solution was saturated. The yield of ether (IIIa) was 70%. According to the physical constants, IR and PMR spectra, the vinyl ether obtained was identical to the reduction product formed when nitroxyl (I) was vinylated.

An increase in the temperature of reaction (110°C) leads to a decrease in the purity of vinyl ether (IIIa) and the formation of tar, while the yield is reduced to 50-60%. An increase in the amount of alkali to 30 wt. % has no effect on the yield, whereas a decrease to 10 wt. % lowers the yield of the required product by a factor of 2–3 [calculated from the given alcohol (IVa) due to its incomplete conversion]. Changing the solvent to dioxane makes the vinylation reaction impossible even under more severe conditions (150°C, KOH concentration 30 wt. %, 5 h).

Vinylation of 4-hydroxy-1,2,2,6,6-pentamethylpiperidine (IVb) was carried out in a similar manner; the yield of vinyl ether (IIIb) was 60%.

Oxidation of vinyl ether (IIIa) was carried out using H_2O_2 in methanol in the presence of catalytic amounts of sodium tungstate. On oxidation, apart from the formation of vinyl ether radical (II) (~60%), formation of the alcohol radical – 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (~20%) – is also observed.

When vinyl ether (IIIa) is treated with MeI a salt is obtained – 4-vinyloxy-1,2,2,6,6-piperidinium iodide (V):



(V)

We did not succeed however in obtaining the corresponding N,N-dimethyl derivative, probably as a result of shielding of the N atom by methyl groups. Addition to the reaction mixture of K_2CO_3, capable of binding to the HI formed, leads to the formation of vinyl ether (IIIb). The rate of mixing and degree of dispersion of K_2CO_3 substantially influence the completeness of reaction.

Replacement of MeI by EtI has a strong effect on the rate of alkylation. The yield of 4-vinyloxy-2,2,6,6-tetramethyl-1-ethylpiperidine on boiling ether (IIIa) in EtI for 15 h was 38%, according to GLC. This confirms once again the low steric accessibility of the amino group in ether (IIIa).

The ability of the compounds obtained to polymerize when treated with $BF_3 \cdot OEt_2$ was studied on 4-vinyloxy-2,2,6,6-tetramethylpiperidine (IIIa) as a model. In this case the formation of a complex was observed between amine and BF_3, which was used in equimolar quantities. The complex was subsequently decomposed by the action of alkali in methanol:

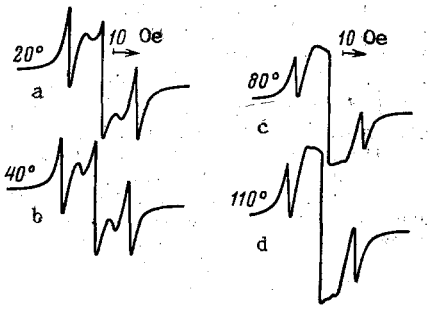
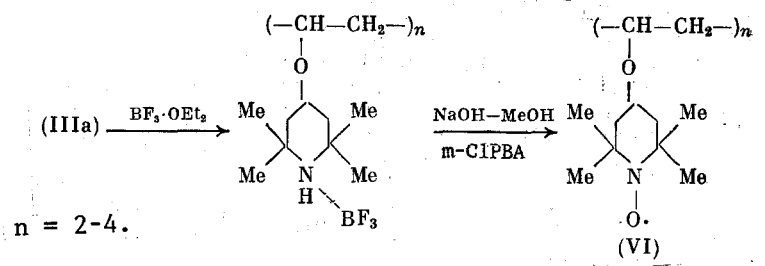


Fig. 1. EPR spectra of oligomer of 2,2,6,6-tetramethyl-4-hydroxy-piperidine-1-oxyl vinyl ether.



Oxidation of the amine groups in the oligomer to the corresponding nitroxyl radical groups was achieved by the action of m-chloroperbenzoic acid (m-ClPBA). According to the data of mass spectrometric analysis the paramagnetic oligomer obtained, which does not have any free NH groups, is a mixture of dimer, trimer, and tetramer. The EPR spectrum of (VI) at 20°C (Fig. 1a) displays a quintuplet. At 40°C (see Fig. 1b) an increase in the second and fourth components of the spectrum is observed, which indicates the conformational nature of the interaction of the paramagnetic centers [7]. At 80°C and higher (see Fig. 1c and d) the quintuplet changes to a poorly resolved multiplet, which is related to an intramolecular interaction of the three or four paramagnetic centers of the oligomer.

An attempt to repeat the vinylation on a piperidine diol with tertiary hydroxyl groups — 1,4-bis(4-hydroxy-2,2,6,6-tetramethyl-4-piperidinyl)butane — proved unsuccessful. Under the conditions described above it does not react with acetylene nor undergo any other changes.

EXPERIMENTAL

EPR spectra were recorded on a Varian E-104 radiospectrometer with an oligomer concentration of 10^{-4} M in toluene; samples were degasified under a vacuum of $2.5 \cdot 10^{-4}$ mm Hg at the temperature of liquid nitrogen. Molecular weights were determined on a LKB-900 chromatograph-mass spectrometer (Sweden). IR spectra of the materials were recorded on a UR-20 instrument in a microlayer for liquid samples, and in KBr pellets for solid samples. PMR spectra were obtained on a Tesla BS-567A spectrometer (100 MHz) for 10% solutions in $CDCl_3$ and CD_3OD (internal standard was HMDS). UV spectra of the compounds in EtOH were obtained on a Specord UV-VIS spectrophotometer.

4-Vinyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl (II). A 5-g (0.029 mole) portion of nitroxyl (I), 1.5 g of KOH, and 50 ml of DMSO were added to an autoclave, acetylene (pressure 12 atm) was passed in and when the mixture was saturated it was heated for 4 h at 90°C. The reaction mass was diluted with three times its volume of water and extracted with 6 × 50 ml of ether. The extract was washed with water, dried with potash, the ether was distilled off and the residue underwent vacuum distillation. The fraction with bp 92-125°C (30 mm) (2.3 g) consisted of vinyl ethers (II) (33%) and (IIIa) (67%). Separation was carried out by means of preparative chromatography on Chromaton N-AW-DMCS, liquid phase was silicone DS-550, 5%. Ether (II) was a red liquid, yield 0.78 g (13%). Found: C 66.48; H 10.18; N 7.01%. $C_{11}H_{20}NO_2$. C 66.63; H 10.17; N 7.06%. EPR spectrum: triplet a_N = 15.2 Oe (in benzene). IR spectrum (ν, cm^{-1}): 825, 965, 1195, 1320, 1605, 1625, 3105 (CH_2=CHO). Absorption in the region 3300-3600 cm^{-1} (OH) was absent.

4-Vinyloxy-2,2,6,6-tetramethylpiperidine (IIIa). Acetylene at a pressure of 12 atm (12 liters in all) was passed into a mixture of 5 g (0.03 mole) of alcohol (IVa), 1.0 g of KOH, and 50 ml of DMSO until it was saturated; the mixture was heated in a rotating steel autoclave at 90°C for 3 h. The reaction mixture was treated with water and extracted with ether.

The extract was dried with calcined K_2CO_3 and the ether was evaporated. After vacuum distillation 4.2 g (70%) of ether (IIIa) was obtained, with bp 66-67°C (5 mm), n_D^{20} 1.4650, d_4^{20} 0.9019. Found: C 72.52; H 10.93; N 7.15%. MR 56.15. $C_{11}H_{21}NO$. Calculated: C 72.06; H 11.55; N 7.65%. MR 56.036. LD_{50} = 80 mg/kg. PMR spectrum ($CDCl_3$, δ, ppm): 6.33 q (=CHO), 4.25 q, 3.98 q (CH_2=, J_{cis} = 8.5, J_{trans} = 17.0, J_{gem} = 1.9 Hz), 4.10 m (CH), 1.92 q and 1.00 q (CH_2, ^2J = 12.68, ^3J = 3.78 Hz), 1.19 s and 1.14 s (CH_3). UV spectrum [λ_{max}, nm (log ε)]: 200.2 (4.05). IR spectrum (ν, cm^{-1}): 820, 950, 1200, 1325, 1610, 1635, 3020 (CH_2=CHO). Absorption in the region 3300-3600 cm^{-1} (OH) was absent.

4-Vinyloxy-1,2,2,6,6-pentamethylpiperidine (IIIb). a) Under the conditions for the synthesis of ether (IIIa), from 6 g (0.035 mole) of alcohol (IVb), 1.8 g of KOH, and 100 ml of DMSO was obtained 4.15 g (60%) of ether (IIIb), bp 68-69°C (4 mm), n_D^{20} 1.4745. b) 1.6 g (0.0087 mole) of ether (IIIa), 1.38 g (0.01 mole) of carefully ground K_2CO_3, and 10 ml of CH_3I were agitated at about 20°C for 5 h. The precipitate, which was a mixture of unreacted potash, KI, and small quantities of salt (V) (0.3 g), was filtered off, and excess CH_3I was distilled off. After vacuum distillation 0.89 g (52%) of ether (IIIb) was obtained, with bp 78-79°C (5 mm), n_D^{20} 1.4755, d_6^{20} 0.9269. Found: C 73.43; H 11.72; N 6.98%. MR 60.048. $C_{12}H_{23}NO$. Calculated: C 73.04; H 11.75; N 7.10%. MR 60.876.

The samples obtained by methods a) and b) were shown to be identical by spectroscopy (PMR, UV, IR) and chromatography [LKhM-8MD (III), 5% silicone DS-550 on Chromaton N-AW-DMCS]. PMR spectrum ($CDCl_3$, δ, ppm): 6.35 q (=CHO), 4.29 q, 4.00 q (CH_2=, J_{cis} = 6.8, J_{trans} = 13.6, J_{gem} = 2.0 Hz), 4.10 m (CH), 2.24 s (NCH_3), 1.91 q and 1.40 t (CH_2, ^2J = 11.73, ^3J = 4.22 Hz), 1.17 s and 1.06 s (CH_3). UV spectrum (λ_{max}, nm (log ε)]: 201.0 (4.25). IR spectrum (ν, cm^{-1}): 840, 970, 1186, 1310, 1640, 1650, 3133 (CH_2=CHO), 2805 (NCH_3).

Oxidation of 4-Vinyloxy-2,2,6,6-tetramethylpiperidine. 100 mg ($0.56 \cdot 10^{-3}$ mole) of (IIIa) was dissolved in 20 ml of MeOH, and 100 mg of sodium tungstate with 0.5 ml of a 30% solution of H_2O_2 were added; the mixture was allowed to stand for 3 days, the color of the reaction mixture changing from colorless to red. The methanol was distilled off and the residue was dissolved in 5 ml of chloroform and dried over $MgSO_4$. The chloroform was removed under vacuum and the residue chromatographed on silica gel (eluant was chloroform and chloroform–ethyl acetate, 7:3). 4-Vinyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl was obtained as a red liquid with yield 20 mg (21%), R_f 0.45 (chloroform) was identical to the R_f of nitroxyl (II) isolated by vinylation reaction of nitroxyl (I). EPR spectrum: triplet a_N = 15.2 Oe (in benzene). Found: C 66.01; H 9.92; N 7.11%. $C_{11}H_{20}NO_2$. Calculated: C 66.63; H 10.17; N 7.06%. 4-Hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl was also isolated; it was identified by chromatography from a comparison with a known sample.

4-Vinyloxy-1,2,2,6,6-pentamethylpiperidinium Iodide (V). 5 g (0.027 mole) of ether (IIIa) (IIIa) and 30 ml of freshly distilled CH_3I were agitated at 35-40°C for 5 h. The white crystals of precipitate (6.8 g, yield 79%) were filtered off and recrystallized from ethanol, mp 177-179°C (with decomp.). Found: C 44.68; H 7.21; I 39.30; N 4.28%. $C_{12}H_{24}NOI$. Calculated: C 44.32; H 7.44; I 39.02; N 4.31%. PMR spectrum (CD_3OD, δ, ppm): 6.42 q (=CHO), 4.35 q, 4.07 q (CH_2=, J_{cis} = 6.8, J_{trans} = 13.6, J_{gem} = 1.2 Hz), 4.40 m (CH), 2.85 s (NCH_3), 2.32 q and 1.75 m (CH_2), 1.54 s and 1.50 s (CH_3). UV spectrum [λ_{max}, nm (log ε)]: 196.3 (4.23), 218.9 (4.17).

Oligomer of 4-Vinyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl. To a solution of 1 g ($0.56 \cdot 10^{-2}$ mole) of 4-vinyloxy-2,2,6,6-tetramethylpiperidine (IIIa) in 10 ml of hexane, cooled to 0°C, was added dropwise in a stream of Ar and with agitation a solution of 1.2 g ($0.76 \cdot 10^{-2}$ mole) of $BF_3 \cdot OEt_2$ in 10 ml of hexane. The mixture was kept at 0°C for 1 h and then at 40-50°C for 3 h. The precipitate obtained was treated with a saturated solution of NaOH in MeOH, extracted with 300 ml of chloroform, and the extract was dried over $MgSO_4$, cooled to 0°C, and a solution of 20 ml of m-ClPBA in 20 ml of chloroform was added dropwise with agitation. The mixture was left at 0°C for 20 h; it was then chromatographed on a Sephadex LH-20 column (in chloroform). 400 mg of a product was isolated, with EPR spectrum giving a quintuplet (in toluene). The mixture of polynitroxyls obtained, including those with free NH groups, was chromatographed on Al_2O_3 (eluent was methanol–chloroform, 1:1), and 300 mg of oligomer (VI) was obtained as a dense yellow oil, gradually solidifying in air. According to the data of potentiometric titration, the oligomer contained virtually no free NH groups, mp 65-70°C. EPR spectrum at 20°C gave a quintuplet (in toluene) (see Fig. 1).

CONCLUSION

1. Vinylation of 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl in the superbasic system KOH—DMSO gives 4-vinyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl and is accompanied by partial reduction of the nitroxyl group to an amine. In the system KOH—dioxane, instead of vinylation partial reduction of nitroxyl to the corresponding amine occurs.

2. The vinyl ether of 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl is obtained independently by oxidation of 4-vinyloxy-2,2,6,6-tetramethylpiperidine.

3. A low-molecular oligomer of the vinyl ether of 2,2,6,6-tetramethyl-4-hydroxypiperidine-1-oxyl has been obtained.

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SYNTHESIS, ISOLATION, AND EPR SPECTRA OF THE STABLE RADICAL 1-HYDROXY-2,4,6,8-TETRAKIS(TERT-BUTYL)-10-PHENOXAZINYL

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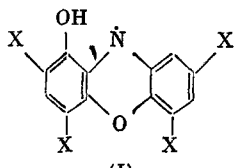
It was reported earlier [1, 2] that upon oxidation of 2-amino-4,6-di-tert-butylphenol by atmospheric oxygen in boiling pyridine 2,4,6,8-tetrakis(tert-butyl)phenoxazine-1-oxyl radical is formed as shown by EPR of the solution. The final product of the reaction is 1H-1-oxo-2,4,6,8-tetrakis(tert-butyl)phenoxazine.

In this work the reaction of 2-amino-4,6-di-tert-butylphenol with 3,5-di-tert-butyl-o-quinone in ethanol in the presence of a small amount of pyridine was studied. Upon dilution of the reaction mixture with water a precipitate was obtained which when chromatographed on SiO_2 gave two products. Upon elution with hexane a blue paramagnetic substance was obtained after removal of solvent, to which the above-mentioned phenoxazine-1-oxyl radical structure was initially assigned. However, on the basis of EPR and IR spectra (see below) this compound is known to be the radical 1-hydroxy-2,4,6,8-tetrakis(tert-butyl)-10-phenoxazinyl (I)



(I)
X = *t*-Bu

(1)

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