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Synthesis of Peroxy-Containing Acetylenic Alcohols and Ethers Derived from γ-Amino Ketones

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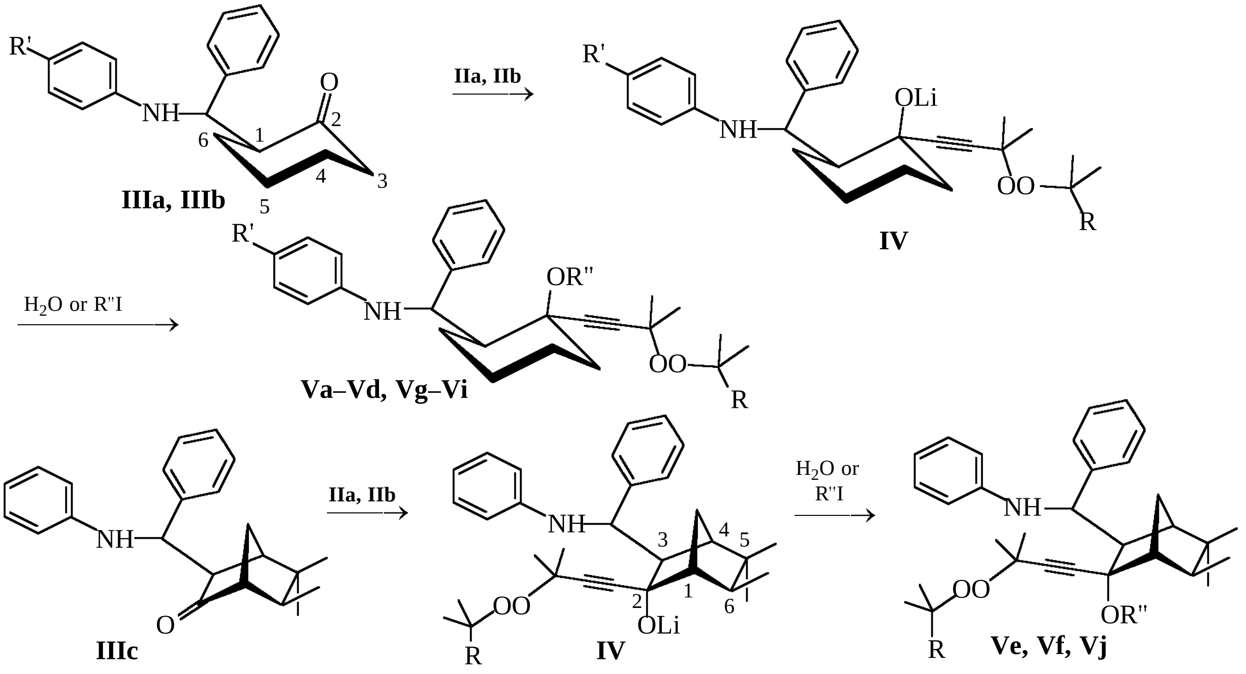
Abstract—A series of peroxy-containing tertiary alcohols were prepared by the reactions of lithium peroxy acetylenides with γ-amino ketones. The reactions of the intermediate lithium peroxy alcoholates with alkyl iodides in the presence of hexamethylphosphoramide yielded the corresponding peroxy ethers. The thermal stability of the compounds synthesized was evaluated by thermal analysis.

Previously [1, 2] we reported on the possibility of preparing acetylenic amino peroxy alcohols and their derivatives by the reactions of lithium peroxy acetylenides **IIa** and **IIb** with *p*-dimethylamino- or *p*-diethylaminobenzaldehydes and 2*e*-methyldecahydroquinol-4-one. Here we report on the synthesis of acetylenic peroxy-containing tertiary alcohols **Va**–**Vf** by the reactions of lithium peroxy acetylenides **IIa** and **IIb** with γ-amino ketones **IIIa**–**IIIc** which, in turn, are prepared by condensation of cyclohexanone and isocamphanone with benzalaniline and benzaltoluidine. The reaction occurred at 15–20°C; peroxy alcohols **Va**–**Vf** were isolated in 74–89% yields.

$$RMe_2COOCMe_2C\equiv CH \xrightarrow{BuLi} RMe_2COOCMe_2C\equiv CLi$$

Ia, Ib **IIa, IIb**



I, II, R = Me (**a**), Et (**b**); **III**, R' = H (**a**), Me (**b**); **V**, R = Me, R' = R" = H (**a**); R = Et, R' = R" = H (**b**); R = R' = Me, R" = H (**c**); R = Et, R' = Me, R" = H (**d**); R = Me, R" = H (**e**); R = Et, R" = H (**f**); R = R' = R" = Me (**g**); R = Et, R' = R" = Me (**h**); R = R' = Me, R" = Et (**i**); R = R" = Me (**j**).

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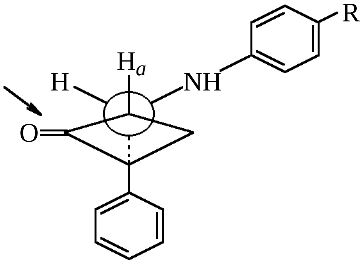
The starting amino ketones **IIIa** and **IIIb** contain a cyclohexanone ring in the *chair* conformation with an α-substituent (relative to the carbonyl group) in the equatorial position. Amino ketone **IIIc** contains a bicyclo[2.2.1]heptane fragment with the methyl group at C^5 and a substituent at C^3 in the *exo* position.

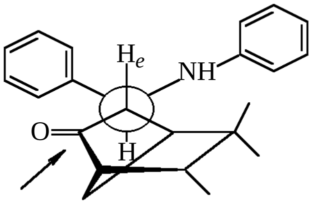
The structure of **IIIa**–**IIIc** was determined by ^1H NMR spectroscopy. In the spectra of *N*-phenyl-1-(2'-oxocyclohexyl)-1-phenylmethylamine **IIIa** and *N*-*p*-tolyl-1-(2'-oxocyclohexyl)-1-phenylmethylamine **IIIb**, we identified the signals of aromatic protons at 6.39–7.36 ppm and of the cyclohexane ring protons at 1.80–2.90 ppm. In addition, the spectrum of **IIIb** contains a CH_3–Ar singlet at 2.18 ppm.

The NH proton gives a broadened singlet at 4.7 ppm, and the proton at the C^1 atom in α-position relative to N, a doublet at 4.6 ppm (^3J 8 Hz). The doublets at 2.30 and 2.35 ppm (*J* 12 Hz) belong to the geminal protons of the $C^{3'}$ atom in the cyclohexane ring. A doublet of doublets (^3J 8, ^3J 3 Hz) at 2.78 ppm belongs to the $C^{1'}H$ proton.

Consideration of the Dreiding models for **IIIa** and **IIIb**, taking also into account the vicinal coupling constant of protons at C^1 and $C^{1'}$ (8 Hz) [3], shows that the proton at $C^{1'}$ in the cyclohexane ring of amino ketones **IIIa** and **IIIb** is in the axial position, and the dihedral angle between the C–H bonds C^1–H and $C^{1'}$–H is about 40° in the Newman projection along the C^1–$C^{1'}$ bond.

Apparently, phenyl-containing substituents at the C^1 atom of amino ketones hinder attack by lithium peroxy acetylenides of the keto group of amino ketones **IIIa** and **IIIb** from the axial side of the molecule. Therefore, we suggest that the ethynyl substituent adds to amino ketones **IIIa** and **IIIb** from the equatorial side, yielding axial isomers of alcohols **Va**–**Vd**.





The methyl groups at $C^{5'}$ in the starting *N*-phenyl-1-(5',5',6'-trimethyl-2'-oxobicyclo[2.2.1]hept-3'-yl)-1-phenylmethylamine **IIIc** give singlets at 0.81 and 0.87 ppm, and the methyl group at $C^{6'}$, a doublet at 0.90 ppm (^3J 7.5 Hz). The bridge geminal protons (*anti* and *syn*) give a doublet at 1.58 ppm and a multiplet at 2.0 ppm (^2J 10 Hz), respectively. A broadened singlet at 2.21 ppm and a multiplet at 2.0 ppm were assigned to the bridgehead protons at $C^{1'}$ and $C^{4'}$, respectively. The *endo*-$C^{6'}H$ proton gives a quartet at 1.58 ppm, and the proton in the amino group at C^1, a broadened singlet at 5.55 ppm. The doublet of doublets at 2.45 ppm (^3J 2.5, ^3J 12) belongs to the $C^{3'}H$ proton. The C^1H proton in the α-position relative to the amino group gives a doublet at 4.19 ppm (^3J 12 Hz), which corresponds to the dihedral angle between the C^1–H and $C^{3'}$–H bonds of 180°. The multiplets at 7.32 (5H), 7.0 (2H), and 6.53 ppm (3H) belong to the aromatic protons.

Analysis of the ^1H NMR spectrum of amino ketone **IIIc** in comparison with the spectra of the model compounds [4] shows that the substituent at the $C^{3'}$ atom of the isocamphane skeleton is in the *exo* position, as indicated by the vicinal coupling constant of the $C^{3'}H$ and $C^{4'}H$ protons, equal to 2.5 Hz. It is evident from consideration of the Dreiding model and the Newman projection along the $C^{3'}$–$C^{1'}$ bond in **IIIc** that the steric arrangement of the phenyl-containing substituents prevents attack of the carbonyl group from the *endo* side. Therefore, in the reactions with lithium peroxy acetylenides **IIa** and **IIb**, the bulkiest acetylene-containing substituent adds to the $C^{2'}$ atom from the *exo* side, yielding the *endo* isomers of alcohols **Ve** and **Vf**.

Reactions of the intermediate lithium peroxy alcoholates **IV** with alkyl iodides in the presence of hexamethylphosphoramide gave the corresponding peroxy ethers **Vg**–**Vj** in 59–66% yields.

In contrast to acetylenic peroxy-containing hydroxydecahydroquinolines [2], peroxy-containing acetylenic alcohols and ethers **Va**–**Vj** derived from γ-amino ketones do not react with carboxylic acids and methyl iodide to give the corresponding salts.

Compounds **Va**–**Vj** are viscous slightly colored liquids readily soluble in common organic solvents and stable in prolonged storage at 0–5°C without air access in the dark. The yields and analytical data are given in Table 1; the ^1H NMR data, in Table 2; and the IR and UV data, in Table 3.

The thermal stability of **Va**–**Vj** was evaluated by thermal analysis. The results for the first decomposition step are listed in Table 4. It is seen that the thermal stability of peroxides **Va**–**Vj** is relatively high.

Table 1. Properties of peroxides **Va**–**Vj**

Comp. no.	Yield, %	Found, %			Formula	Calculated, %			*M*	
		C	H	N		C	H	N	found	calculated
Va	77	77.54	8.61	3.10	$C_{28}H_{37}NO_3$	77.20	8.56	3.22	412.8	435.6
Vb	74	77.69	8.83	3.04	$C_{29}H_{39}NO_3$	77.47	8.74	3.12	435.8	449.6
Vc	87	77.64	8.81	3.04	$C_{29}H_{39}NO_3$	77.47	8.74	3.12	421.0	449.6
Vd	89	77.99	9.03	2.90	$C_{30}H_{41}NO_3$	77.71	8.91	3.02	440.9	463.7
Ve	82	79.03	8.74	2.60	$C_{32}H_{43}NO_3$	78.49	8.85	2.86	470.3	489.7
Vf	87	79.12	8.91	2.33	$C_{33}H_{45}NO_3$	78.69	9.00	2.78	480.6	503.7
Vg	63	77.98	8.93	2.60	$C_{30}H_{41}NO_3$	77.71	8.91	3.02	420.3	463.7
Vh	59	78.11	9.13	2.80	$C_{31}H_{43}NO_3$	77.95	9.07	2.93	451.8	477.7
Vi	66	78.18	9.22	2.64	$C_{31}H_{43}NO_3$	77.95	9.07	2.93	448.0	477.7
Vj	61	79.44	8.83	2.50	$C_{33}H_{45}NO_3$	78.69	9.00	2.78	488.3	503.7

Table 2. ^{1}H NMR spectra of peroxides **Va–Vj**

Comp. no.	^{1}H NMR spectrum, δ, ppm
Va	1.25 s (9H, Me$_3$COO), 1.35–2.80 m [10H, CH, OH, and (CH$_2$)$_4$], 1.53 s (6H, Me$_2$C), 4.68 d (1H, C*H*NH, *J* 7.1 Hz), 6.45–7.50 m (10H, 2Ph)
Vb	0.90 t (3H, Me), 1.22 s (6H, Me$_2$COO), 1.30–2.20 m [12H, CH, OH, CH$_2$, and (CH$_2$)$_4$], 1.55 s (6H, Me$_2$C), 4.70 d (1H, C*H*NH, *J* 7.1 Hz), 6.50–7.50 m (10H, 2Ph)
Vc	1.21 s (9H, Me$_3$COO), 1.35–2.40 m [10H, CH, OH, and (CH$_2$)$_4$], 1.52 s (6H, Me$_2$C), 2.21 s (3H, *p*-*Me*C$_6$H$_4$), 4.91 d (1H, C*H*NH, *J* 7.1 Hz), 6.55–7.55 m (9H, *p*-C$_6$H$_4$ and Ph)
Vd	0.89 t (3H, *Me*CH$_2$), 1.20 s (6H, Me$_2$COO), 1.30–2.40 m [12H, CH, OH, CH$_2$, and (CH$_2$)$_4$], 1.50 s (6H, Me$_2$C), 2.21 s (3H, *p*-*Me*C$_6$H$_4$), 4.92 d (1H, C*H*NH, *J* 7.1 Hz), 6.55–7.55 m (9H, *p*-C$_6$H$_4$ and Ph)
Ve	0.80 d (3H, C^{6}Me, *J* 7.0 Hz), 0.91 s (3H, C^{5}Me *endo*), 1.05 s (3H, C^{5}Me *exo*), 1.25 s (9H, Me$_3$C), 1.55 s (6H, Me$_2$C), 1.55–2.60 m (7H, OH, 4CH, and CH$_2$), 4.40 d (1H, C*H*NH, *J* 8.3 Hz), 6.45–7.45 m (10 H, 2Ph)
Vf	0.65–1.05 m (12H, C^{5}Me$_2$, C^{6}Me, and *Me*CH$_2$), 1.20 s (6H, Me$_2$COO), 1.52 s (6H, Me$_2$C), 1.45–2.60 m (9H, OH, 4CH and 2CH$_2$), 4.40 d (1H, C*H*NH, *J* 8.3 Hz), 6.45–7.50 m (10H, 2Ph)
Vg	1.22 s (9H, Me$_3$COO), 1.30–2.30 m [9H, CH, and (CH$_2$)$_4$], 1.35 s (6H, Me$_2$C), 2.22 s (3H, *p*-*Me*C$_6$H$_4$), 3.32 s (3H, MeO), 4.72 d (1H, C*H*NH, *J* 4.5 Hz), 6.20–7.50 m (9H, *p*-C$_6$H$_4$ and Ph)
Vh	0.89 t (3H, *Me*CH$_2$), 1.15 s (6H, Me$_2$COO), 1.32 s (6H, Me$_2$C), 1.30–2.30 m [11H, CH, CH$_2$, and (CH$_2$)$_4$], 2.22 s (3H, *p*-*Me*C$_6$H$_4$), 3.32 s (3H, MeO), 4.73 d (1H, C*H*NH, *J* 4.5 Hz), 6.20–7.50 m (9H, *p*-C$_6$H$_4$, and Ph)
Vi	1.19 t (3H, *Me*CH$_2$), 1.20 s (9H, Me$_3$COO), 1.40 s (6H, Me$_2$C), 1.30–2.30 m [9H, CH, and (CH$_2$)$_4$], 2.22 s (3H, *p*-*Me*C$_6$H$_4$), 3.25–3.88 m (2H, Me*CH$_2$*), 4.81 d (1H, C*H*NH, *J* 4.5 Hz), 6.25–7.50 m (9H, *p*-C$_6$H$_4$, and Ph)
Vj	0.82 d (3H, C^{6}Me, *J* 7.0 Hz), 0.90 s (3H, C^{5}Me *endo*), 1.00 s (3H, C^{5}Me *exo*), 1.21 s (9H, Me$_3$COO), 1.50 s (6H, Me$_2$C), 1.45–2.50 m (6H, 4CH, and CH$_2$), 3.36 s (3H, MeO), 4.54 d (1H, C*H*NH, *J* 8.0 Hz), 6.40–7.50 m (10H, 2Ph)

Peroxy alcohols **Va**–**Vd** with the cyclohexane fragment (axial isomers) start to decompose at a noticeable rate with a pronounced exothermic effect only at 130–135°C. Peroxy alcohols **Ve** and **Vf** with the isocamphane fragments (*endo* isomers) exhibit somewhat lower thermal stability and decompose at 124–125°C. Peroxy ethers **Vg**–**Vj** derived from peroxy alcohols **Vc**–**Ve** by replacement of the hydroxy group by methoxy and ethoxy groups show noticeably higher thermal stability. They start to decompose at 140–145°C, i.e., at temperatures 8–24°C higher than those of thermolysis of peroxy alcohols **Vc**–**Ve**.

EXPERIMENTAL

The IR spectra were recorded on a Specord IR-75 spectrophotometer (thin films). The ^{1}H NMR spectra were taken on a Tesla BS-567A spectrometer in CDCl$_3$, internal reference TMS. The UV spectra were recorded on a Specord UV-Vis spectrophotometer

Table 3. IR and UV spectra of peroxides **Va**–**Vj**

Comp. no.	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm ($\varepsilon \times 10^{-3}$, $l\ mol^{-1}\ cm^{-1}$)
Va	3630–3250 s (OH); 3415 v.s (NH); 3090 m, 3060 m, 3040 m (CH_{Ar}); 2990 v.s, 2940 v.s, 2870 v.s (CH_{Alk}); 1610 v.s, 1510 v.s (skeleton vibrations of Ar); 755 v.s, 710 v.s (CH_{Ar})	207 (28), 248 (14), 292 (5)
Vb	3630–3200 s (OH); 3415 v.s (NH); 3090 m, 3060 m, 3030 m (CH_{Ar}); 2985 v.s, 2930 v.s, 2875 v.s, 2860 v.s (CH_{Alk}); 1510 v.s (skeleton vibrations of Ar); 760 v.s, 710 v.s (CH_{Ar})	205 (28), 248 (14), 295 (5)
Vc	3625–3150 s (OH); 3400 v.s (NH); 3080 w, 3055 m, 3025 m (CH_{Ar}); 2980 v.s, 2940 v.s, 2860 v.s (CH_{Alk}); 1610 v.s, 1590 v.s, 1520 v.s (skeleton vibrations of Ar); 760 v.s, 710 v.s (CH_{Ar})	208 (45), 245 (18), 290 (4)
Vd	3635–3160 s (OH); 3405 v.s (NH); 3085 w, 3060 m, 3030 m (CH_{Ar}); 2980 v.s, 2940 v.s, 2880 v.s, 2860 v.s (CH_{Alk}); 1610 v.s, 1595 v.s, 1520 v.s (skeleton vibrations of Ar); 755 v.s, 710 v.s (CH_{Ar})	208 (44), 244 (18), 290 (4)
Ve	3620–3150 s (OH); 3405 v.s (NH); 3090 w, 3060 m, 3025 m (CH_{Ar}); 2975 v.s, 2930 v.s, 2870 s (CH_{Alk}); 1600 v.s, 1500 v.s (skeleton vibrations of Ar); 745 v.s, 700 v.s, 690 v.s (CH_{Ar})	206 (30), 246 (15)
Vf	3620–3225 s (OH); 3400 v.s (NH); 3085 w, 3055 m, 3025 m (CH_{Ar}); 2975 v.s, 2940 v.s, 2870 s (CH_{Alk}); 1595 v.s, 1495 v.s (skeleton vibrations of Ar); 755 m, 745 v.s, 695 v.s, 685 v.s (CH_{Ar})	205 (29), 249 (14)
Vg	3400 v.s (NH); 3080 w, 3060 m, 3025 s (CH_{Ar}); 2980 v.s, 2930 v.s, 2855 v.s, 825 s (CH_{Alk}); 1600 v.s, 1580 v.s, 1515 v.s (skeleton vibrations of Ar); 745 v.s, 705 m, 700 v.s (CH_{Ar})	208 (45), 248 (18), 295 (4)
Vh	3405 v.s (NH); 3080 w, 3060 m, 3025 s (CH_{Ar}); 2980 v.s, 2930 v.s, 2875 s, 2855 s, 2820 m (CH_{Alk}); 1600 v.s, 1580 v.s, 1515 v.s (skeleton vibrations of Ar); 745 v.s, 705 m, 700 v.s (CH_{Ar})	209 (45), 248 (18), 295 (3)
Vi	3395 v.s (NH); 3090 w, 3060 m, 3030 m (CH_{Ar}); 2980 v.s, 2940 v.s, 2865 v.s (CH_{Alk}); 1605 v.s, 1585 v.s, 1510 v.s (skeleton vibrations of Ar); 755 v.s, 725 m, 705 v.s (CH_{Ar})	205 (43), 246 (18), 295 (4)
Vj	3405 v.s (NH); 3090 w, 3060 m, 3030 m (CH_{Ar}); 2980 v.s, 2940 v.s, 2875 s, 2825 s (CH_{Alk}); 1600 v.s, 1505 v.s (skeleton vibrations of Ar); 770 v.s, 750 v.s, 705 v.s, 695 s (CH_{Ar})	206 (28), 249 (12)

(1×10^{-4} M methanolic solutions). The thermal behavior of the compounds was studied on a Paulik–Paulik–Erdey derivatograph under argon at a linear heating rate of 7 deg min^{-1} (sample weight 100 mg, DTA 1/10, DTG 1/10). The purity of the compounds was checked by thin-layer chromatography on 20-cm-high Silufol plates, eluent hexane–diethyl ether (3 : 1), developer *N*,*N*-dimethyl-*p*-phenylenediamine hydrochloride. Column chromatography was performed on Al_2O_3 L 40/250 μm, neutral, Brockmann grade II, and on silica gel L 100/160 μm. Determination of the content of available oxygen by iodometric titration using concentrated HCl [6] gave overestimated results, probably due to the presence of the C≡C bond. The molecular weights were determined cryoscopically in benzene.

The starting peroxy alkynes **Ia** and **Ib** [7] and butyllithium [8] were prepared by published procedures.

γ-Amino ketones IIIa–**IIIc.** A 0.1-mol portion of appropriate azomethine (benzalaniline or benzaltoluidine) was dissolved in 20 ml of ethanol and heated to 60°C; 0.1 mol of appropriate ketone (cyclohexanone or isocamphanone) and a drop of concentrated HCl were added, and the mixture was heated for an additional 5 min. After cooling, the crystalline precipitate of γ-amino ketone was washed with 10% ammonia and water, dried, and recrystallized from methanol. **IIIa**, mp 140–141°C, yield 92% (published data [9]: mp 139–140°C, yield 90% [9]); **IIIb**, mp 127–129°C, yield 95% (published data [9]: mp 116–118°C, yield 97% [9]); **IIIc**, mp 156–157°C, yield 90%.

Acetylenic peroxy-containing tertiary alcohols Va–**Vf.** A solution of 0.025 mol of butyllithium in

Table 4. Characteristics of the first step of thermolysis of **Va**–**Vj** (thermal analysis data)

Comp. no.	T_{dec}, °C			Weight loss, %
	onset	end	maximum	
Va	133	198	170	23
Vb	131	202	173	24
Vc	135	200	176	22
Vd	130	195	175	23
Ve	125	190	165	19
Vf	124	208	164	22
Vg	143	216	180	23
Vh	140	200	175	22
Vi	151	215	175	21
Vj	149	212	174	23

hexane was added in an argon flow over a period of 0.5 h to a vigorously stirred solution of 0.03 mol of peroxy alkynes **Ia** and **Ib** in 50 ml of absolute ether, cooled to –40 to –20°C. The mixture was stirred for an additional 1 h, after which 0.02 mol of γ-amino ketones **IIIa**–**IIIc** was added, and the mixture was warmed to 20–23°C over a period of 1–2 h, stirred for an additional 3–4 h, and allowed to stand for 18 h at room temperature. Then 100 ml of hexane was added, and the organic layer was washed with water and dried over $MgSO_4$. The solvent was removed. Peroxides **Va**–**Vf** were purified by column chromatography on silica gel, eluent hexane or hexane–diethyl ether, 3 : 1.

Acetylenic peroxy ethers Vg–**Vj.** A 0.012-mol portion of methyl or ethyl iodide and 3 ml of hexamethylphosphoramide were added to a solution containing 0.01 mol of lithium peroxy alcoholates **IV** formed as intermediates in syntheses of peroxy alcohols **Va**–**Vf**. The reaction was complete in 18 h at 20–23°C. Then 100 ml of hexane was added, and the organic layer was washed with water and 30% NaOH and dried over $CaCl_2$. The solvent was removed. Compounds **Vg**–**Vj** were purified by column chromatography on Al_2O_3, eluent hexane.

REFERENCES

1. Dikusar, E.A., Yuvchenko, A.P., Murashko, V.L., Makhnach, S.A., and Moiseichuk, K.L., *Zh. Obshch. Khim.*, 2000, vol. 70, no. 5, p. 791.
2. Dikusar, E.A., Kozlov, N.G., and Moiseichuk, K.L., *Zh. Obshch. Khim.*, 2001, vol. 71, no. 6, p. 981.
3. Gordon, A.J. and Ford, R.A., *The Chemist's Companion. A Handbook of Practical Data, Techniques, and References*, New York: Wiley, 1972. Translated under the title *Sputnik khimika*, Moscow: Mir, 1976, p. 297.
4. Kozlov, N.G., Popova, L.A., Biba, V.I., Potkina, T.N., and Korshuk, V.K., *Zh. Obshch. Khim.*, 1988, vol. 58, no. 11, p. 2593.
5. Wendlandt, W.Wm., *Thermal Methods of Analysis*, New York: Interscience, 1964.
6. Mair, R.D. and Graupner, A.J., *Anal. Chem.*, 1964, vol. 36, no. 1, p. 194.
7. Yuvchenko, A.P., Moiseichuk, K.L., Dikusar, E.A., and Ol'dekop, Yu.A., *Vestsi Akad. Navuk Bel. SSR, Ser. Khim. Navuk*, 1985, no. 2, p. 65.
8. Talalaeva, T.V. and Kocheshkov, K.A., *Metody elementoorganicheskoi khimii. Litii, natrii, kalii, rubidii, tsezii* (Methods of Organometallic Chemistry. Lithium, Sodium, Potassium, Rubidium, and Cesium), Moscow: Nauka, 1971, book 1, pp. 99, 554.
9. Kozlov, N.G., Vorob'eva, G.V., and Stremok, I.P., *Vestsi Akad. Navuk Bel. SSR, Ser. Khim. Navuk*, 1969, no. 2, p. 89.