Decyclization of chlorocyclohexanone hydroperoxides under the action of ferrous salts

*E. K. Starostin, V. V. Gushchin, A. V. Ignatenko, A. V. Aleksandrov, and G. I. Nikishin**

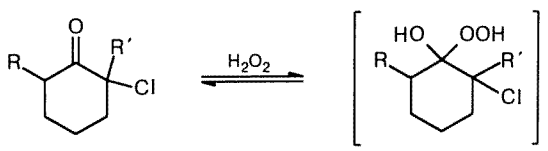
N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 117913 Moscow, Russian Federation. Fax: +7 (095) 135 5328

The decomposition of 2-chloro-, 2,2-dichloro-, and 2,6-dichloro-substituted cyclohexanone hydroperoxides on treatment with ferrous chloride and sulfate to give chloro-substituted aliphatic acids was investigated. A method for the synthesis of 2,6,6-trichlorohexanoic and 2,6,7,11-tetrachlorododecane-1,12-dioic acids was elaborated.

Key words: hydrogen peroxide, hydroperoxides, cyclohexanone, decyclization; chlorocarboxylic acids; ferrous salts.

Hydroperoxides of C_5—C_7 cycloalkanones are reduced by iron(II), copper(I), and titanium(III) salts with ring opening. The reaction occurs *via* cycloalkoxyl radicals, which undergo β-decomposition to give ω-carboxyalkyl radicals in nearly quantitative yields.[1—4] The decomposition of hydroperoxides containing substituents on the ring follows an analogous mechanism but with certain particular features. For example, 2-methyl- and 2-chlorocyclohexanone hydroperoxides react with Fe^{II} ions to give two isomeric 5-carboxypentyl radicals.[5] The effects of other substituents and their position on the cycloalkyl ring of cycloalkanone hydroperoxides on the cleavage mechanism and on the structure of the resulting carboxyalkyl radicals has practically not been studied.

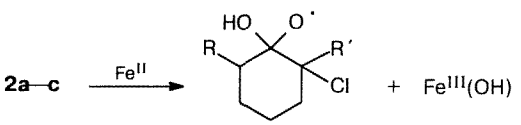
In the present work we synthesized 2-chloro-, 2,2-dichloro-, and 2,6-dichloro-substituted cyclohexanone hydroperoxides by treatment of chloro-substituted cycloalkanones **1a—c** with 30 % H_2O_2 in a neutral medium and studied the decomposition of compounds obtained (**2a—c**, respectively) in aqueous solutions of $FeSO_4$ and $FeCl_2$. The structure of compounds **2a—c** has not been really studied; however, it was assumed that α-hydroxy-α-hydroperoxycycloalkanes are formed under the conditions specified, as in the case of unsubstituted cycloalkanones.[6]



1a—c **2a—c**

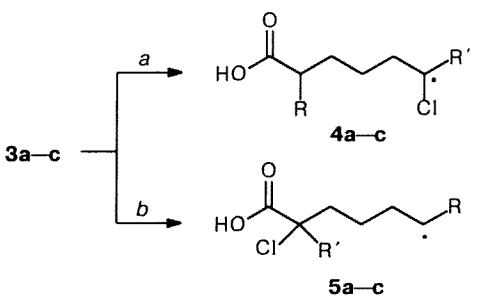
a: R = R′ = H
b: R = H, R′ = Cl
c: R = Cl, R′ = H

A stoichiometric amount of ferrous salts is required for complete decomposition of hydroperoxides **2a—c**.

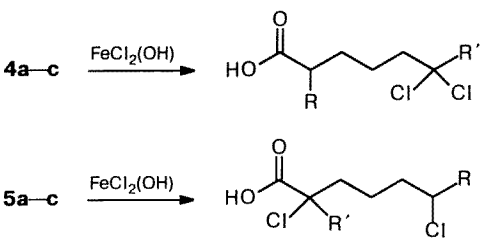


3a—c

The cycloalkoxyl radicals **3a—c** generated react by two pathways (*a* and *b*) to give chloro-substituted 5-carboxypentyl radicals **4** and **5**, respectively.



The subsequent transformations of radicals **4a—c** and **5a—c** are determined by the nature of the ligands coordinated to iron ions. They are oxidized by a ligand transfer mechanism under the action of iron(III) chloride to give the corresponding chloro-substituted monocarboxylic acids.



Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 1, pp. 143—146, January, 1996.

Table 1. Decomposition of hydroperoxides **2a—c** on treatment with $FeCl_2$

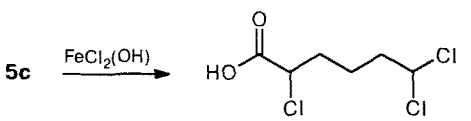
Hydroperoxide	Reaction products*	Yield (%)**
2a	$CHCl_2(CH_2)_4COOH$	68
	$CH_2Cl(CH_2)_3CHClCOOH$	28
2b	$CCl_3(CH_2)_4COOH$	70
	$CH_2Cl(CH_2)_3CCl_2COOH$	22
2c	$CHCl_2(CH_2)_3CHClCOOH$	95

* Analyzed by GLC as methyl esters. ** With respect to reacted chlorocyclohexanone (GLC data).

The composition of the products formed due to the decomposition of hydroperoxides **2a—c** (Table 1) suggests that β-decomposition (pathways *a* and *b*) tends toward the formation of C-centered radicals with Cl atoms at the radical center. For example, compound **3a** (R = R′ = H) gives 6,6-dichloro- and 2,6-dichlorohexanoic acids in 2.5 : 1.0 ratio. The preferential formation of 6,6-dichlorohexanoic acid is caused by the higher stability of radical **4a** in comparison with **5a**.

The effect of substituents on the direction of the β-decomposition is more pronounced in the decomposition of hydroperoxide **2b**. The ratio of the resulting isomeric radicals is **4b** : **5b** > 3 : 1, as indicated by the yields of the corresponding trichloro-substituted monocarboxylic acids. Such selectivity is conditioned by an even higher stability of radical **4b** compared to **5b**, since two Cl atoms are located at the radical center in this case.

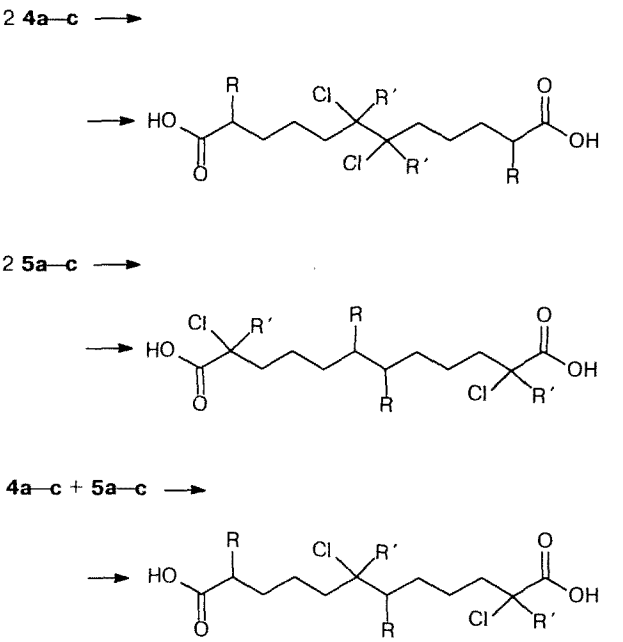
Unlike hydroperoxides **1a** and **1b**, the decomposition of compound **1c** (R = Cl, R′ = H) gives rise to radicals of only one type, *i.e.*, 2,5-dichlorocarboxypentyl radicals **5c**, because of the presence of two symmetrically arranged Cl atoms (pathways *a* and *b* are equivalent). 2,6,6-Trichlorohexanoic acid (**6**) is formed as the only reaction product in 95 % yield (with respect to the reacted ketone).



6

When ferrous sulfate is used to reduce hydroperoxides **2a—c**, the generated radicals **4a—c** and **5a—c** mostly undergo recombination to give the corresponding chloro-substituted dicarboxylic acids C_{12} (Table 2).

In addition, radicals **4a—c** and **5a—c** undergo disproportionation and elimination of H and Cl atoms, as suggested by the composition of the resulting monocarboxylic acids. It should be noted that the products of decomposition of hydroperoxides **2a—c** do not



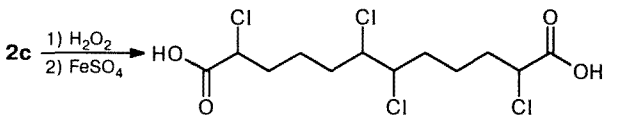
contain compounds formed due to rearrangements of radicals **4a—c** and **5a—c** with [1,5]-hydrogen shift, as has been observed previously in the decomposition of cyclohexanone hydroperoxide.[7,8] This is probably due to the presence of Cl atoms, which hinder this reaction, at positions 1 and 5 of radicals **4a—c** and **5a—c**.

Table 2. Decomposition of hydroperoxides **2a—c** on treatment with $FeSO_4$

Hydro-peroxide	Reaction products*	Yield** (%)
2a	$CH_3(CH_2)_3CHClCOOH$	11
	$CHCl{=}CH(CH_2)_3COOH$	12
	$CH_2Cl(CH_2)_4COOH$	15
	$CHCl_2(CH_2)_4COOH$	5
	$CH_2Cl(CH_2)_3CHClCOOH$	2
	$HOOCCHCl(CH_2)_4CHCl(CH_2)_4COOH$	6
	$HOOCCHCl(CH_2)_8CHClCOOH$	Traces
	$HOOC(CH_2)_4CHClCHCl(CH_2)_4COOH$	38
2b	$CH_2{=}CH(CH_2)_2CCl_2COOH$	2
	$CH_3(CH_2)_3CCl_2COOH$	2
	$CCl_2{=}CH(CH_2)_3COOH$	23
	$CHCl_2(CH_2)_4COOH$	28
	$HOOC(CH_2)_4CCl_2CCl_2(CH_2)_4COOH$	36
2c	$CHCl{=}CH(CH_2)_2CHClCOOH$	5
	$CH_2Cl(CH_2)_3CHClCOOH$	18
	$CHCl_2(CH_2)_3CHClCOOH$	18
	$HOOCCH(CH_2)_3CHCH(CH_2)_3CHCOOH$ (Cl, Cl, Cl, Cl)	50

* Analyzed by GLC as methyl esters. ** With respect to reacted chlorocyclohexanone (GLC data).

The synthesis of 2,6,7,11-tetrachlorododecane-1,12-dioic acid (**7**) can easily be performed by decomposing hydroperoxide **2c** with $FeSO_4$.



7

Acid **7** (yield 50 %, see Table 2) can readily be isolated from the reaction mixture (in an almost pure form) after extraction of monocarboxylic acids with *n*-hexane.

Experimental

^{1}H NMR spectra were obtained on a Bruker WM-250 spectrometer in $CDCl_3$. IR spectra were obtained on a UR-20 spectrophotometer. GLC analyses were performed on an LKhM-80 chromatograph (flame ionization detector, 2000×3 mm column, 10 % XE-60 fixed phase on Chromosorb W (60—80 mesh)).

Methyl esters were separated on a preparative gas-liquid chromatograph (katharometer as detector, 2000×10 mm column, 15 % fixed phase on Chromaton N-AW (0.35—0.40 mm), He as the carrier gas) at 180—200 °C. The yields of the reaction products were determined using an internal standard.

2-Chloro-, 2,2-dichloro-, and 2,6-dichlorocyclohexanones were obtained by direct chlorination of an aqueous emulsion of cyclohexanone.[9] Individual products were isolated from the reaction mixture by distillation.

(±)-2-Chlorocyclohexanone (1a). M.p. 23 °C (Ref. 10: m.p. 22—23 °C), b.p. 82—83 °C (10 Torr). ^{1}H NMR, δ: (4.27 ddd, 1 H, CHCl, J = 9.3 Hz, J = 5.2 Hz, J = 1.3 Hz); 2.55 (m, 1 H, CHHCO); 2.23 (m, 2 H, CHHCO, CHHCHCl); 1.55—1.95 (m, 5 H, $CH_2CH_2CHHCHCl$). Found (%): C, 54.06; H, 6.64; Cl, 26.58. C_6H_9ClO. Calculated (%): C, 54.34; H, 6.79; Cl, 26.79.

2,2-Dichlorocyclohexanone (1b). M.p. 17 °C, b.p. 90—91 °C (10 Torr) (Ref. 11: b.p. 118 °C (19 Torr)). ^{1}H NMR, δ: 2.82 (t, 2 H, CH_2CCl_2, J = 6.5 Hz); 2.65 (t, 2 H, CH_2CO, J = 5.5 Hz); 1.92 (m, 4 H, CH_2CH_2). Found (%): C, 42.98; H, 4.69; Cl, 42.77. $C_6H_8Cl_2O$. Calculated (%): C, 43.11; H, 4.75; Cl, 42.52.

***cis,trans*-2,6-Dichlorocyclohexanone (1c).** B.p. 106—107 °C (10 Torr). ^{1}H NMR, δ: 4.69 (dd, 2 H, 2 CHCl, J = 7.6 Hz, J = 5.1 Hz); 2.15—2.3 (m, 2 H, CHHCH$_2$CHH); 1.85—2.05 (m, 4 H, CHHCH$_2$CHH). Found (%): C, 43.05; H, 4.74; Cl, 42.76. $C_6H_8Cl_2O$. Calculated (%): C, 43.11; H, 4.75; Cl, 42.52.

Synthesis of hydroperoxides 2a—c. A 30 % aqueous solution of H_2O_2 (11 mL, 0.1 mol) was added with vigorous stirring to a solution of chlorocyclohexanone (0.1 mol) in methanol (10 mL). The reaction mixture was stirred for 15—20 min at ~20 °C until homogenization was attained.

Decomposition of hydroperoxides 2a—c. A previously prepared solution of a hydroperoxide was added dropwise to a solution of $FeSO_4 \cdot 7H_2O$ (or $FeCl_2 \cdot 4H_2O$) (0.12 mol) in water (100 mL). The temperature of the reaction mixture was kept at 15—20 °C by cooling in an ice bath. After the whole hydroperoxide solution was added, the reaction mixture was stirred for an additional 1 h and acidified with 2 N H_2SO_4 to pH ~2. The reaction products were extracted with ether (3 × 100 mL). The ethereal extracts were treated with aqueous Na_2CO_3; the resulting aqueous solutions of sodium salts were acidified with 2 N H_2SO_4 to pH ~2, and the acids that formed were extracted with ether and methylated with diazomethane.[12] Individual products were isolated by preparative GLC. The *erythro*- and *threo*-isomers of chloro-substituted dicarboxylic acids were identified as mixtures of dimethyl esters without isolating the isomers.

(±)-$CH_3(CH_2)_3CHClCOOCH_3$. ^{1}H NMR, δ: 4.27 (dd, 1 H, CHCl, J = 7.9 Hz, J = 6.1 Hz); 3.78 (s, 3 H, OCH_3); 1.95 (m, 2 H, β-CH_2); 1.35 (m, 4 H, γ-, δ-CH_2); 0.91 (t, 3 H, CH_3, J = 7.2 Hz).

$CH_2Cl(CH_2)_4COOCH_3$. ^{1}H NMR, δ: 3.66 (s, 3 H, OCH_3); 3.52 (t, 2 H, CH_2Cl, J = 6.5 Hz); 2.32 (t, 2 H, α-CH_2, J = 7.4 Hz); 1.78 (m, 2 H, β-CH_2); 1.65 (m, 2 H, CH_2); 1.47 (m, 2 H, CH_2).

$CHCl_2(CH_2)_4COOCH_3$. ^{1}H NMR, δ: 5.74 (t, 1 H, $CHCl_2$, J = 5.9 Hz); 3.67 (s, 3 H, OCH_3); 2.34 (t, 2 H, α-CH_2, J = 7.2 Hz); 2.20 (dt, 2 H, β-CH_2, J = 6 Hz); 1.63 (m, 4 H, β-, γ-CH_2).

(±)-$CH_2Cl(CH_2)_3CHClCOOCH_3$. ^{1}H NMR, δ: 4.29 (dd, 1 H, CHCl, J = 7.8 Hz, J = 5.9 Hz); 3.78 (s, 3 H, OCH_3); 3.54 (t, 2 H, CH_2Cl, J = 6.4 Hz); 2.0 (m, 2 H, β-CH_2); 1.8 (m, 2 H, δ-CH_2); 1.6 (m, 2 H, γ-CH_2).

***cis*-$CHCl=CH(CH_2)_3COOCH_3$.** ^{1}H NMR, δ: 6.07 (dt, 1 H, HClC=, J = 7 Hz, J = 1.5 Hz); 5.75 (q, 1 H, =CH, J = 7 Hz); 3.68 (s, 3 H, OCH_3); 2.35 (t, 2 H, α-CH_2, J = 7.3 Hz); 2.28 (dq, 2 H, γ-CH_2, J = 7.3 Hz, J = 1.5 Hz); 1.76 (m, 2 H, β-CH_2).

***trans*-$CHCl=CH(CH_2)_3COOCH_3$.** ^{1}H NMR, δ: 5.98 (dt, 1 H, HClC=, J = 12.8 Hz, J = 1 Hz); 5.87 (dt, 1 H, =CH, J = 12.8 Hz, J = 7 Hz); 3.68 (s, 3 H, OCH_3); 2.33 (t, 2 H, α-CH_2, J = 7.3 Hz); 2.11 (dq, 2 H, γ-CH_2, J = 7.3 Hz, J = 1 Hz); 1.74 (m, 2 H, β-CH_2).

***erythro,threo*-$CH_3OOCCHCl(CH_2)_4CHCl(CH_2)_4$—$COOCH_3$.** B.p. 138—140 °C (0.08 Torr). ^{1}H NMR, δ: 4.28 (dd, 1 H, α-CHCl, J = 8 Hz, J = 6.4 Hz); 3.85 (m, 1 H, ε-CHCl); 3.77 (s, 3 H, OCH_3); 3.65 (s, 3 H, OCH_3); 2.31 (t, 2 H, α-CH_2, J = 7.4 Hz); 1.35—2.05 (m, 14 H, 7 CH_2).

***erythro,threo*-$CH_3OOCCHCl(CH_2)_8CHClCOOCH_3$.** ^{1}H NMR, δ: 4.31 (dd, 2 H, 2 CHCl, J = 8 Hz, J = 6.4 Hz); 3.81 (s, 6 H, 2 OCH_3); 1.4—2.1 (m, 16 H, 8 CH_2).

***erythro,threo*-$CH_3OOC(CH_2)_4CHClCHCl(CH_2)_4$—$COOCH_3$.** ^{1}H NMR, δ: 4.01 and 3.94 (both m, 2 H, 2 CHCl, *threo*-/*erythro*-isomers); 3.65 (s, 6 H, 2 OCH_3); 2.32 (t, 4 H, 2 α-CH_2, J = 7.4 Hz); 1.35—2.05 (m, 12 H, 6 CH_2).

$CCl_3(CH_2)_4COOCH_3$. ^{1}H NMR, δ: 3.69 (s, 3 H, OCH_3); 2.70 (t, 2 H, β-CH_2, J = 7.4 Hz); 2.38 (t, 2 H, α-CH_2, J = 7.1 Hz); 1.7—1.9 (m, 4 H, β-, γ-CH_2).

$CH_2Cl(CH_2)_3CCl_2COOCH_3$. ^{1}H NMR, δ: 3.91 (s, 3 H, OCH_3); 2.57 (t, 2 H, CH_2Cl, J = 5.9 Hz); 2.46 (t, 2 H, β-CH_2, J = 7.9 Hz); 1.7—1.9 (m, 4 H, γ-, δ-CH_2).

$CH_2=CH(CH_2)_2CCl_2COOCH_3$. ^{1}H NMR, δ: 5.85 (m, 1 H, =CH); 5.10 (m, 2 H, CH_2=); 3.92 (s, 3 H, OCH_3); 2.55 (m, 2 H, γ-CH_2); 2.45 (t, 2 H, β-CH_2, J = 8 Hz).

$CH_3(CH_2)_3CCl_2COOCH_3$. ^{1}H NMR, δ: 3.92 (s, 3 H, OCH_3); 2.45 (t, 2 H, β-CH_2, J = 8 Hz); 1.3—1.7 (m, 4 H, γ-, δ-CH_2); 0.97 (t, 3 H, CH_3, J = 7 Hz).

$CH_3OOC(CH_2)_4(CCl_2)_2(CH_2)_4COOCH_3$. ^{1}H NMR, δ: 3.69 (s, 6 H, 2 OCH_3); 2.61 (br.m, 4 H, 2 δ-CH_2); 2.41 (t, 4 H, 2 α-CH_2, J = 7.4 Hz); 1.7—1.95 (m, 8 H, 2 β-, 2 γ-CH_2).

***cis*-CHCl=CH(CH$_2$)$_2$CHClCOOCH$_3$.** ^{1}H NMR, δ: 6.08 (dt, 1 H, HClC=, J = 7 Hz, J = 1.5 Hz); 5.72 (q, 1 H, =CH, J = 12.8 Hz, J = 7 Hz); 4.27 (d, 1 H, CHCl, J = 8 Hz, J = 5.8 Hz); 3.77 (s, 3 H, OCH$_3$); 2.38 (dq, 2 H, γ-CH$_2$, J = 7 Hz, J = 1.5 Hz); 2.06 (m, 2 H, β-CH$_2$).

***trans*-CHCl=CH(CH$_2$)$_2$CHClCOOCH$_3$.** ^{1}H NMR, δ: 6.04 (dd, 1 H, HClC=, J = 12.8 Hz, J = 1 Hz); 5.85 (dt, 1 H, =CH, J = 12.8 Hz, J = 7 Hz); 4.28 (dd, 1 H, CHCl, J = 8 Hz, J = 5.1 Hz); 3.79 (s, 3 H, OCH$_3$); 2.26 (m, 2 H, γ-CH$_2$); 2.07 (m, 2 H, β-CH$_2$).

(±)-CHCl$_2$(CH$_2$)$_3$CHClCOOCH$_3$. B.p. 136—138 °C (13 Torr). IR, ν/cm^{-1}: 750, 765 (C—Cl); 1745 (C=O). ^{1}H NMR, δ: 5.76 (t, 1 H, CHCl$_2$, J = 5.7 Hz); 4.29 (dd, 1 H, CHCl, J = 8 Hz, J = 5.6 Hz); 3.78 (s, 3 H, OCH$_3$); 2.22 (dt, 2 H, δ-CH$_2$, J = 8 Hz, J = 5.6 Hz); 2.05 (m, 2 H, β-CH$_2$); 1.7 (m, 2 H, γ-CH$_2$).

(±)-CHCl$_2$(CH$_2$)$_3$CHClCOOH. B.p. 139—140 °C (0.2 Torr), n_D^{20} 1.4950.

***erythro,threo*-HOOCCHCl(CH$_2$)$_3$CHClCHCl(CH$_2$)$_3$—CHClCOOH.** ^{1}H NMR, δ: 4.34 (dd, 2 H, 2 α-CHCl, J = 7 Hz, J = 5.6 Hz); 4.15—4.0 (m, 2 H, 2 ε-CHCl, *threo-/erythro*-isomers); 1.4—2.1 (m, 12 H, 6 CH$_2$).

This study was financially supported by the Russian Foundation for Basic Research (Project No. 94-03-09189) and the International Science Foundation (Grant No. NGS 000).

References

1. M. S. Kharash and G. Sosnovsky, *J. Org. Chem.*, 1958, **23**, 1322.
2. A. Citterio and E. Vismara, *Synthesis*, 1980, 751.
3. G. I. Nikishin, A. V. Aleksandrov, A. V. Ignatenko, and E. K. Starostin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1984, 2628 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1984, **33**, 2407 (Engl. Transl.)].
4. F. Minisci and V. Pallini, *Gazz. Chim. Ital.*, 1959, **89**, 2438.
5. H. E. De La Mare, J. K. Kochi, and F. F. Rust, *J. Am. Chem. Soc.*, 1963, **85**, 1437.
6. V. L. Antonovskii, in *Organicheskie perekisnye initsiatory* [*Organic Peroxide Initiators*], Khimiya, Moscow, 1972, 135 (in Russian).
7. D. C. Nonhebel and J. C. Walton, *Free-Radical Chemistry*, Cambridge University Press, Cambridge, 1974.
8. R. Kh. Freidlina, A. B. Terent'ev, M. Ya. Khorlina, and S. Ya. Aminov, *Zh. Vses. Khim. Obshch. im D. I. Mendeleeva* [*J. of D. I. Mendeleev All-Union Chem. Soc.*], 1966, **11**, 211 (in Russian).
9. *Organic Syntheses*, J. Wiley—Chapman and Hall, New York—London, 1949.
10. *Org. Synth. Col.*, J. Wiley, New York, 1963, **3**, 188.
11. E. I. Corey and H. J. Burke. *J. Am. Chem. Soc.*, 1955, **77**, 5148.
12. K. Weygand and G. Hilgetag, *Organisch-Chemische Experimentierkunst*, J. A. Barth Verlag, Leipzig, 1964.

Received March 21, 1995