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Intermolecular Dehydration of Alcohols by the Action of Copper Compounds Activated with Carbon Tetrabromide. Synthesis of Ethers

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Abstract—Copper compounds of the general formula CuX_n (X = Cl, Br, I, acac, OAc, $C_7H_4O_3$, $C_7H_5O_2$; $n = 1, 2$) activated by carbon tetrabromide catalyzed intermolecular dehydration of primary and secondary alcohols with formation of the corresponding ethers.

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Ethers are used as solvents, fuel additives, cosmetics, and detergents [1–3]. The commonest procedures for the preparation of ethers are based on the Williamson reaction, intermolecular dehydration of alcohols, and addition of alcohols to alkenes; the two latter reactions require acid catalysis [2, 4–9]. Synthesis of ethers via intermolecular dehydration in the presence of mineral acids or other acid catalysts is possible only from lower alcohols; higher alcohols undergo intramolecular dehydration with formation of olefins which polymerize under these conditions. Furthermore, the use of acid catalysts requires special corrosion-resistant equipment and considerably hinders the isolation procedure.

Reactions of alkenes with alcohols are characterized by low selectivity and are accompanied by side processes involving oligomerization and polymerization of alkenes. Insofar as Williamson reaction utilizes stoichiometric amounts of metallic sodium and sodium hydride as reagents, it is only of preparative value.

The goal of the present work was to find efficient catalysts for intermolecular dehydration of alcohols on the basis of copper compounds. Using copper(II) bromide as an example we found that intermolecular dehydration of alcohols in the presence of copper compounds is possible in principle. By heating cyclohexanol (**I**) in the presence of 1% of $CuBr_2$ (150°C, 8 h) we obtained 5% of dicyclohexyl ether (**II**). The reaction mixture also contained traces of cyclohexyl bromide (**III**). The yield of **II** reached 23% when the amount of $CuBr_2$ was raised to 5%. These findings prompted us to test a large number of copper(I) and copper(II) compounds for catalytic activity in intermolecular dehydration of alcohols. However, none of the following copper compounds displayed catalytic activity: CuCl, CuBr, CuI, $CuCl_2 \cdot 2H_2O$, $Cu(OAc)_2$, $Cu(acac)_2$, $Cu(C_7H_5O_2)_2 \cdot 2H_2O$, $Cu(C_7H_8O_6)_2$.

Taking into account importance of the problem concerning synthesis of ethers and accessibility of copper compounds, we tried to enhance catalytic activity of the above copper compounds in intermolecular dehydration of alcohols by selecting promoting dopes. As the latter we examined conventional activating ligands such as alkyl- and arylphosphines and nitrogen-containing compounds (amines, nitriles, pyridine and its derivatives). However, successful results were achieved with the use of halomethanes, the best of which was carbon tetrabromide; the most efficient catalytic system consisted of $Cu(acac)_2$ and CBr_4 at a molar ratio of 1:5. This catalytic system ensured 95% yield of dicyclohexyl ether (**II**) in 8 h at 150°C (Scheme 1). The activating effect of CBr_4 (which is converted into bromoform) was also observed toward

Scheme 1.

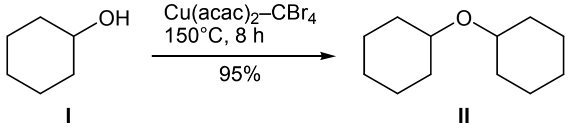


Table 1. Intermolecular dehydration of cyclohexanol (**I**) in the presence of different copper compounds and halomethanes[a]

Copper compound	Halomethane	Molar ratio catalyst–halomethane–alcohol	Conversion of **I**, %	Yield, %		
				II	**III**	**IV**
CuBr	–	5:0:100	0	0	0	0
CuBr	CBr_4	1:5:100	65	44	21	0
$CuBr_2$	–	1:0:100	6	5	1	0
$CuBr_2$	–	5:0:100	28	23	5	0
$CuBr_2$	CBr_4	1:5:100	58	44	14	0
$Cu(acac)_2$	–	1:0:100	0	0	0	0
$Cu(acac)_2$	CBr_4	1:1:100	15	12	1	2
$Cu(acac)_2$	CBr_4	1:5:100	100	95	3	2
$Cu(acac)_2$	CBr_4	1:20:100	67	38	22	7
$Cu(acac)_2$	CBr_4	1:30:100	100	20	30	50
$Cu(acac)_2$	$CHBr_3$	1:5:100	55	31	20	4
$Cu(acac)_2$	$CBrCl_3$	1:5:100	100	10	88	2
$Cu(acac)_2$	$CBrCl_3$	1:10:100	81	13	66	2
$Cu(acac)_2$	CCl_4	1:5:100	79	28	48	3
$Cu(acac)_2$	CCl_4	1:10:100	89	11	77	1
CuCl	CBr_4	1:5:100	64	44	20	0
$CuCl_2 \cdot 2H_2O$	CBr_4	1:5:100	65	39	26	0
CuI	CBr_4	1:5:100	64	39	15	0
$Cu(OAc)_2$	CBr_4	1:5:100	56	37	14	5
$Cu(C_7H_8O_6)_2$	CBr_4	1:5:100	51	46	5	0
$Cu(C_7H_5O_2)_2 \cdot 2H_2O$	CBr_4	1:5:100	53	42	11	0

[a] Temperature 150°C, reaction time 8 h.

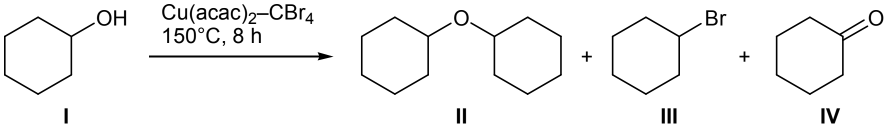
other copper compounds (Table 1). Replacement of CBr_4 by other halomethanes, such as $CHBr_3$, $CBrCl_3$, and CCl_4 resulted in lower selectivity and reduced yield of **II** (Table 1).

Using dehydration of cyclohexanol (**I**) as model reaction we determined the optimal concentrations of $Cu(acac)_2$, CBr_4, and substrate and optimal conditions. Higher concentration of CBr_4 [$Cu(acac)_2$–CBr_4–**I** 1:(10–100):100] favored side processes, in particular substitutive bromination and oxidation of cyclohexanol to cyclohexanone (**IV**) (Scheme 2). At an equimolar ratio of $Cu(acac)_2$ and CBr_4 the conversion of **I** was as low as 15%.

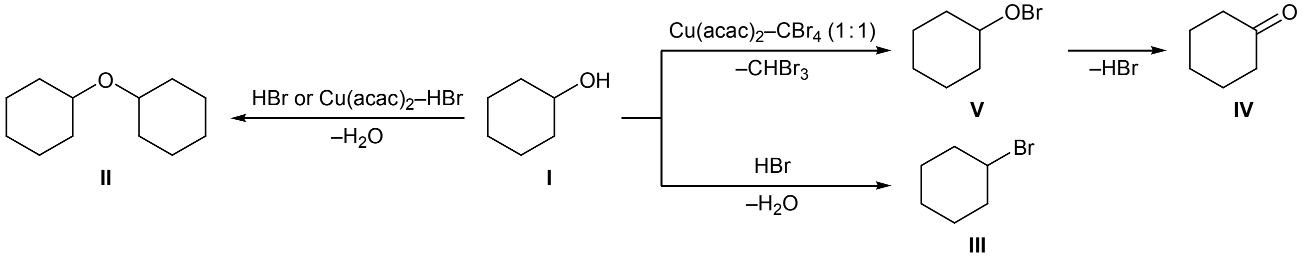
Taking into account the formation of bromoform, cyclohexyl bromide (**III**), and cyclohexanone (**IV**) as by-products, we presumed that the reaction follows Scheme 3. The process begins with catalytic reaction of CBr_4 with alcohol **I**, which leads to the formation of bromoform and cyclohexyl hypobromite (**V**) at a concentration of 1.5 mg/ml (according to the iodometric titration data). Unstable hypobromite **V** decomposes via elimination of HBr (20.34 mg/ml, mercurimetric titration) to give cyclohexanone **IV**. The liberated hydrogen bromide catalyzes [either alone or as the complex $Cu(acac)_2 \cdot HBr$] intermolecular dehydration of **I** with formation of ether **II**.

The proposed mechanism was checked by carrying out experiments with specially added HBr to a concentration of 2%. This concentration is comparable with that of HBr generated *in situ* by reaction of **I** with CBr_4

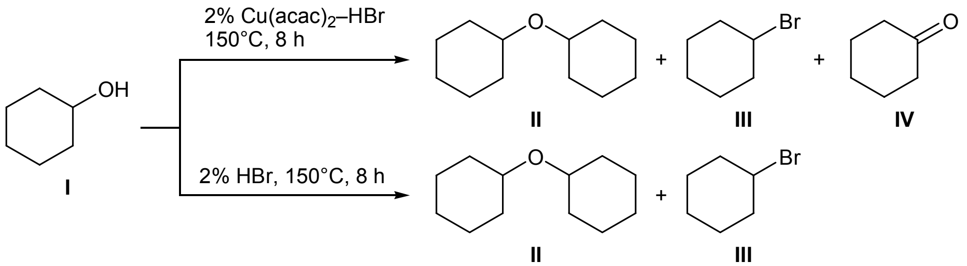
Scheme 2.



Scheme 3.



Scheme 4.



in the presence of Cu(acac)$_2$. In the reaction catalyzed by Cu(acac)$_2$–HBr the major product was dicyclohexyl ether (**II**). When only HBr was used as catalyst, the conversion of **I** decreased to 18%, and the yield of cyclohexyl bromide (**III**) appreciably increased (Scheme 4). Raising the concentration of hydrogen bromide (aqueous solution) to 8–20% resulted in the formation of cyclohexyl bromide (**III**) as the major product (Table 2).

Participation of Cu(acac)$_2$·HBr in the catalytic series was verified by experiments with that complex synthesized preliminarily. Heating of cyclohexanol (**I**) in the presence of Cu(acac)$_2$·HBr prepared by treatment of crystalline Cu(acac)$_2$ with gaseous HBr afforded 18% of **II**. The composition of the preliminarily synthesized Cu(acac)$_2$–HBr complex was estimated at 1:3. Found, %: C 17.66; H 2.82; O 10.20; Br 45.71. $C_{10}H_{17}O_4Br_3Cu$. Calculated, %: C 23.79; H 3.37; O 13.00; Br 47.52 (Table 3). We also tried to determine the composition of the catalyst isolated after the reaction was performed under standard conditions [150°C, 8 h, Cu(acac)$_2$–CBr$_4$–**I** 1:5:100]. Its elemental composition turned out to approach that of Cu(acac)$_2$·2.5HBr: Found, %: C 22.53; H 2.51; O 9.89; Br 43.61. $C_{10}H_{16.5}O_4Br_{2.5}Cu$. Calculated, %: C 25.08; H 3.06; O 13.08; Br 43.00. When gaseous hydrogen bromide was passed through a mixture containing cyclohexanol and Cu(acac)$_2$, the major product was cyclohexyl bromide (**III**) despite high conversion of cyclohexanol (75%). These findings led us to presume that the true catalyst in the system Cu(acac)$_2$–CBr$_4$–alcohol is the complex Cu(acac)$_2$·2.5HBr which is generated *in situ*; this complex is more active than Cu(acac)$_2$·3HBr prepared preliminarily from Cu(acac)$_2$ and HBr.

Table 2. Effect of HBr concentration (aqueous solution) on the yield of dicyclohexyl ether (**II**)[a]

Catalyst	Concentration of HBr, %	Conversion of cyclohexanol (**I**), %	Yield, %		
			II	**III**	**IV**
–	2	18	13	5	0
Cu(acac)$_2$	2	33	25	4	4
–	8	68	16	52	0
Cu(acac)$_2$	8	66	22	40	4
–	20	77	8	69	0
Cu(acac)$_2$	20	83	9	73	1

[a] Temperature 150°C, reaction time 8 h.

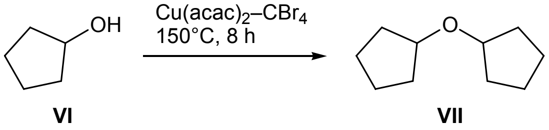
Table 3. Effect of $Cu(acac)_2 \cdot nHBr$ complexes on the yield of dicyclohexyl ether (**II**)[a]

Catalytic system	Catalyst composition[b]	Conversion of cyclohexanol (**I**), %	Yield, %		
			II	**III**	**IV**
$Cu(acac)_2 \cdot nHBr$[c] + cyclohexanol	$Cu(acac)_2 \cdot 3HBr$[c]	22	18	2	2
$Cu(acac)_2–CBr_4$ + cyclohexanol	$Cu(acac)_2 \cdot 2.5HBr$[d]	100	95	3	2

[a] 150°C, 8 h.
[b] According to elemental analysis data.
[c] Preliminarily prepared complex.
[d] Complex generated *in situ* and isolated after reaction completion.

Another cyclic alcohol, cyclopentanol (**VI**) at 150°C in 8 h was converted into dicyclopentyl ether (**VII**) in 95% yield (Scheme 5).

Scheme 5.



Primary aliphatic alcohols underwent catalytic dehydration in the presence of $Cu(acac)_2–CBr_4$ under more severe conditions (175–200°C, 8–16 h; Scheme 6). The conversion of the alcohol and the yield of the corresponding ether strongly depended on the length of the hydrocarbon chain: the yield decreased from 92 to 33% as the length of the alkyl radical increased in going from butan-1-ol to undecan-1-ol. Favorable conditions for the synthesis of ethers from primary alcohols were temperature 200°C and reaction time 10 h. Reduction of the temperature to 175°C required twice as long reaction time to attain a high yield of ether. Such long-chain alcohols as tridecan-1-ol and hexadecan-1-ol were not converted into ethers under the above conditions (200°C, 10 h), whereas raising the temperature to 250°C resulted in their intramolecular dehydration to give the corresponding alkenes.

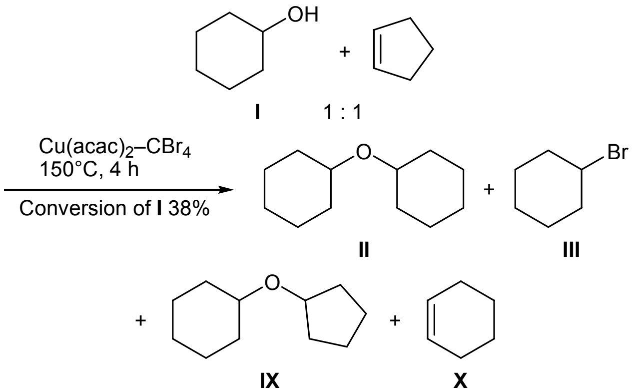
Scheme 6.

$$\text{ROH} \xrightarrow[200°\text{C, 10 h}]{Cu(acac)_2–CBr_4} \underset{\textbf{VIIIa–VIIIf}}{\text{ROR}}$$

R = C_4H_9 (**a**), C_5H_{11} (**b**), C_6H_{13} (**c**), C_7H_{15} (**d**), C_8H_{17} (**e**), $C_{11}H_{23}$ (**f**).

Insofar as the reaction under study occurs at elevated temperature (150–200°C) which favors dehydration of alcohols to olefins, our further experiments were aimed at estimating the relative contributions of intermolecular dehydration and intramolecular dehydration followed by addition of alcohol to the resulting olefin to the formation of ether. For this purpose, cyclohexanol (**I**) was brought into reaction with cyclopentene in the presence of $Cu(acac)_2–CBr_4$ [150°C, 4 h, $Cu(acac)_2–CBr_4$–cyclohexanol–cyclopentene 1:5:50: 50]. The reaction gave a mixture of 7% of dicyclohexyl ether (**II**), 8%, of cyclohexyl cyclopentyl ether (**IX**), 8% of cyclohexyl bromide (**III**), and 15% of cyclohexene (**X**) (Scheme 7).

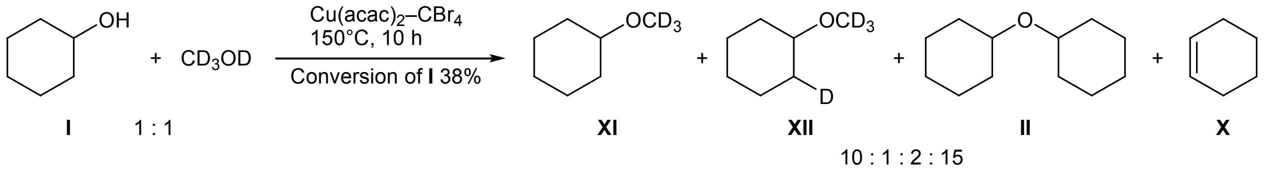
Scheme 7.



The product structure (specifically, the formation of ethers **II** and **IX**) indicated that both reaction paths are operative. Cyclohexene is formed during the process via dehydration of cyclohexanol. Despite the presence of unreacted cyclohexanol in the reaction mixture, the addition of **I** to cyclopentene was not complete.

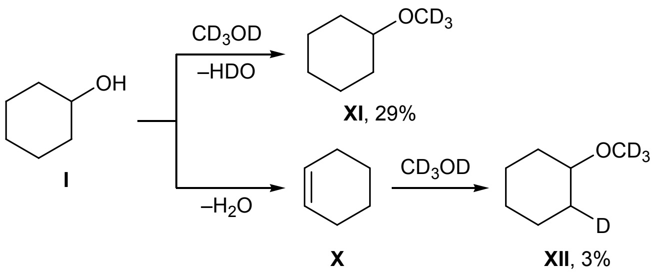
Additional information on the reaction mechanism was obtained by studying the reaction of cyclohexanol (**I**) with methanol-d_4 (CD_3OD) [150°C, 10 h, $Cu(acac)_2–CBr_4$–cyclohexanol–CD_3OD 1:5:100:100; Scheme 8]. According to the GC–MS data, the reaction mixture contained cyclohexyl methyl ether molecules with different concentrations of deuterium, D_3-**XI** (*m*/*z* 117 $[M]^+$, yield 29%) and D_4-**XII** (*m*/*z* 118 $[M]^+$, yield 3% on the reacted cyclohexanol). The conversion of cyclohexanol was not complete (82%). In addition, 45% of cyclohexene was detected in the reaction mix-

Scheme 8.



ture. Scheme 9 illustrates the mechanism of formation of isotopic congeners **XI** and **XII**. Neither CD_3OH nor $C_6H_{11}OD$ H–D exchange product was detected by GC–MS in a 1 : 1 mixture of cyclohexanol with methanol-*d*$_4$ kept over a period 4 days at room temperature or at 60°C. These findings indicated that ethers **XI** and **XII**, as well as **II** and **IX**, are formed according to both reaction paths, but the contribution of the second path is smaller.

Scheme 9.



We can conclude that catalytic systems based on copper compounds are more advantageous than mineral acids due to their universal character and high selectivity for ethers which is achieved as a result of almost complete suppression of intramolecular dehydration of alcohols with formation of olefins.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were measured on a Bruker Avance-400 spectrometer at 400.13 and 100.62 MHz, respectively, from solutions in $CDCl_3$ using tetramethylsilane as reference. The mass spectra were run on a Shimadzu GCMS-QP2010Plus instrument (SPB-5 capillary column, 30 m × 0.25 mm; carrier gas helium; oven temperature programming from 40 to 300°C at a rate of 8 deg/min; injector temperature 280°C, ion source temperature 200°C; electron impact, 70 eV). GLC analyses were run on Shimadzu GC-9A and GC-2014 instruments (2 m × 3-mm column packed with 5% of SE-30 on Chromaton N-AW-HMDS; oven temperature programming from 50 to 270°C at a rate of 8 deg/min; carrier gas helium, flow rate 47 ml/min). The elemental compositions were determined on a Carlo Erba 1106 analyzer.

Commercially available methanol, ethanol, propan-1-ol, propan-2-ol, butan-1-ol, pentan-1-ol, cyclopentanol, hexan-1-ol, cyclohexanol, heptan-1-ol, octan-1-ol, phenylmethanol, undecan-1-ol, tridecan-1-ol, hexadecan-1-ol, cyclopentene, carbon tetrachloride, bromoform, chloroform, and carbon tetrabromide were distilled or recrystallized prior to use. Copper(I) chloride, copper(I) bromide, copper(I) iodide, copper(II) bromide, copper(II) acetylacetonate $Cu(acac)_2$, copper(II) acetate $Cu(OAc)_2$, copper(II) salicylate $Cu(C_7H_8O_6)_2$, copper(II) chloride dihydrate $CuCl_2 \cdot 2H_2O$, and copper(II) benzoate dihydrate $Cu(C_7H_5O_2)_2 \cdot 2H_2O$ (Acros Organics) were preliminarily dried in a vacuum desiccator. Gaseous hydrogen bromide was prepared according to the procedure described in [11]. Hydrobromic acid (39.3%) was distilled prior to use.

All reactions were carried out in a 10-ml glass ampule placed into a 17-ml stainless steel high-pressure microreactor under controlled heating and steering.

General procedure for the synthesis of ethers from alcohols II–VIIIa. An ampule was charged under argon with 0.0052 g (1 mmol) of $Cu(acac)_2$, 0.03 g (5 mmol) of CBr_4, and 0.2 ml (100 mmol) of the corresponding alcohol. The ampule was sealed and placed into a high-pressure reactor which was hermetically closed and heated at 150–250°C for 4–20 h under continuous stirring. When the reaction was complete, the reactor was cooled to 20°C, the ampule was opened, the mixture was neutralized with 10% aqueous sodium carbonate under stirring for 0.5–1 h on a magnetic stirrer, the organic phase was separated, the aqueous phase was extracted with chloroform, and the extract was passed through a layer of silica gel (2 g) using hexane as eluent. The solvent was distilled off, and the residue was distilled under reduced pressure or recrystallized from benzene–hexane.

The structure of the isolated compounds was proved by spectral data and by comparing with authentic samples and reference data: dicyclohexyl ether (**II**, yield 95%), dicyclopentyl ether (**VII**, 95%) [9, 11], dibutyl ether (**VIIIa**, 92%), dipentyl ether (**VIIIb**, 90%) [12], dihexyl ether (**VIIIc**, 84%), diheptyl ether (**VIIId**, 82%), dioctyl ether (**VIIIe**, 80%) [2].

Cyclohexyl cyclopentyl ether (IX). Yield 8%, bp 100–101°C (9 mm). ^{1}H NMR spectrum, δ, ppm: 1.05–2.05 m (18H, CH_2), 3.20–3.35 m (1H, CH in cyclohexyl), 3.80–4.10 m (1H, CH in cyclopentyl). ^{13}C NMR spectrum, δ_C, ppm: 80.27 ($C^{1'}$), 76.69 (C^1), 33.36 (C^2, C^6), 32.67 ($C^{2'}$, $C^{5'}$), 25.84 (C^4), 24.58 (C^3, C^5), 23.34 ($C^{3'}$, $C^{4'}$). Mass spectrum, *m*/*z* (I_{rel}, %): 168.27 (14) $[M]^+$, 18 (14), 28 (100), 32 (43), 41 (25), 55 (43), 57 (27), 62 (25), 82 (55), 83 (27), 100 (48). Found, %: C 78.56; H 12.00; O 9.44. $C_{11}H_{20}O$. Calculated, %: C 78.51; H 11.98; O 9.51. *M* 168.27.

Diundecyl ether (VIIIf). Yield 33%, bp 135–137°C (0.2 mm). ^{1}H NMR spectrum, δ, ppm: 0.88 t (6H, CH_3), 1.05–1.75 m (36H, CH_2), 3.38 t (4H, CH_2). ^{13}C NMR spectrum, δ_C, ppm: 13.87 (C^{11}, $C^{11'}$), 22.90 (C^{10}, $^{10'}$), 27.55 (C^9, $C^{9'}$), 27.65 (C^8, $C^{8'}$), 27.99 (C^7, $C^{7'}$), 28.08 (C^6, $C^{6'}$), 28.32 (C^5, $C^{5'}$), 28.92 (C^4, $C^{4'}$), 29.23 (C^3, $C^{3'}$), 31.53 (C^2, $C^{2'}$), 70.83 (C^1, $C^{1'}$). Mass spectrum: *m*/*z* 326.60 $[M]^+$. Found, %: C 80.95; H 14.10; O 4.95. $C_{22}H_{46}O$. Calculated, %: C 80.90; H 14.20; O 4.90. *M* 326.60.

REFERENCES

1. Fujii, Y., Furugaki, H., Kita, K., Uno, M., Tamura, E., and Matsumoto, H., US Patent no. 5914430, 1999; *Ref. Zh., Khim.*, 2000, no. 19N34P.
2. Olah, G.A., Shamma, T., and Prakash, G.K.S., *Catal. Lett.*, 1997, vol. 46, p. 1.
3. Olah, G.A., US Patent no. 5520710, 1996; *Chem. Abstr.*, 1996, vol. 125, no. 9103.
4. Makarova, M.A., Paukshtis, E.A., Thomas, J.M., Williams, C., and Zamaraev, K.I., *J. Catal.*, 1994, vol. 149, p. 36.
5. Habenicht, C., Kam, L.C., Wilschut, M.J., and Antal, M.J., Jr., *Ind. Eng. Chem. Res.*, 1995, vol. 34, p. 3784.
6. Dueno, E.E., Chu, F., Kim, S., and Jung, K.W., *Tetrahedron Lett.*, 1999, vol. 40, p. 1843.
7. Ballantine, J.A., Davies, M., Patel, I., Purnell, J.H., Rayanakorn, M., Williams, K.J., and Thomas, J.M., *J. Mol. Catal.*, 1984, vol. 26, p. 37.
8. Kim, S., Chung, K.N., and Yang, S., *J. Org. Chem.*, 1987, vol. 52, p. 3917.
9. Chatterjee, D., Mody, H.M., and Bhatt, K.N., *J. Mol. Catal. A: Chem.*, 1995, vol. 104, p. L115.
10. Sassaman, M.B., Kotian, K.D., Prakash, G.K.S., and Olah, G.A., *J. Org. Chem.*, 1987, vol. 52, p. 4314.
11. Nemkova, O.G., Burova, E.I., Vorob'eva, O.I., Ippolitova, E.A., and Lapitskii, A.V., *Praktikum po neorganicheskoi khimii* (Laboratory Works on Inorganic Chemistry), Spitsin, V., Ed., Moscow: Mosk. Gos. Univ., 1965, p. 318.
12. *Spravochnik khimika* (Chemist's Handbook), Nikol'skii, B.P. and Zonis, S.A., Eds., Leningrad: Khimiya, 1971, vol. 2.