# PHENYL CYCLOPROPYL ETHER IN ELECTROPHILIC SUBSTITUTION REACTIONS

A. A. Petinskii, S. M. Shostakovskii,
and É. I. Kositsyna

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Compounds, containing a cyclopropane ring attached to a heteroatom (O, S, etc.), are of considerable practical interest [1-5]. The chemical transformations of these compounds have received only quite recent study. It is known [6, 7] that the reaction of gem-dichlorocyclopropyl alkyl ethers with alcohols in the presence of bases leads to an opening of the 3-membered ring and the formation of unsaturated acetals; the gem-dichlorocyclopropyl aryl ethers are reduced to the cyclopropyl aryl ethers [6, 8]; the ethylthio- and phenylthio-gem-dichlorocyclopropanes are oxidized to the corresponding sulfinyl and sulfonyl derivatives [9]; the gem-dichlorocyclopropyl phenyl ether [10] exhibits a high reactivity in electrophilic substitution reactions [11]. Some of the chemical transformations of the cyclopropyl [12], cyclopropyl vinyl [12-14] and β-chloroethyl cyclopropyl [14] ethers were studied, and also the esters of 1-alkoxy-2-cyclopropanecarboxylic acids [15].

Some electrophilic substitution reactions of cyclopropyl phenyl ether (I) were studied in the present paper, and also its reaction with dilute $HNO_3$ solution.

The bromination of (I) under mild conditions (−70°) leads to the formation of p-bromophenyl cyclopropyl ether (II) in high yield. Based on the data of GLC and the IR spectrum, the product is devoid of the o-isomer (III) and is identical to the (II) that is obtained by the methylenation of p-bromophenyl vinyl ether by the Simmons–Smith method [16]

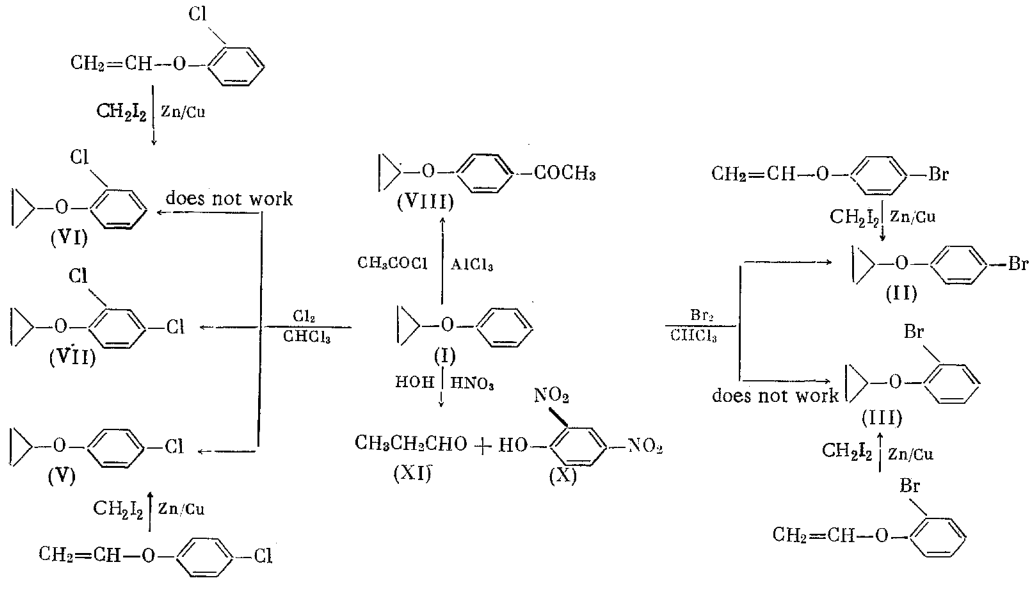

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TABLE 1. Properties of Synthesized Compounds

| Compound number | Bp, °C (p, mm of Hg) | $d_4^{20}$ | $n_D^{20}$ | MR |  | Yield, in % of theory | Found, % |  |  |  | Calc., % |  |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | found | calc. |  | C | H | Cl | Br | C | H | Cl | Br |
| II | 96 (3) | 1,4333 | 1,5625 | 48,22 | 48,07 | 93,4<br>17,3 * | 50,57 | 4,01 | — | 37,97 | 50,70 | 4,22 | — | 37,55 |
| III | 95 (3) | 1,4361 | 1,5683 | 48,54 | 48,07 | 0,7 * | 50,28 | 4,12 | — | 37,39 | 50,70 | 4,22 | — | 37,55 |
| IV | 71 (2) | 1,3660 | 1,5420 | 49,55 | 49,56 | 86 | 50,13 | 5,00 | — | 37,02 | 50,23 | 5,11 | — | 37,2 |
| V | 83 (3) | 1,2152 | 1,5400 | 45,53 | 45,18 | 79,4<br>9,4 * | 64,19 | 5,35 | 20,84 | — | 64,0 | 5,34 | 21,06 |  |
| VI | 57 (1) | 1,1531 | 1,5378 | 45,67 | 45,18 | 7 * | 63,95 | 5,12 | 20,77 | — | 64,0 | 5,34 | 21,06 | — |
| VII | 95 (3) | 1,1271 | 1,5505 | 50,42 | 50,04 | 13,3 | 53,38 | 4,00 | 35,30 | — | 53,20 | 3,94 | 34,94 | — |
| VIII | 42 † | — | — | — | — | 94,3 | 75,14 | 6,82 | — | — | 75,0 | 6,67 | — | — |

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* Obtained by the Simmons - Smith reaction [6].

†Mp 0°C.

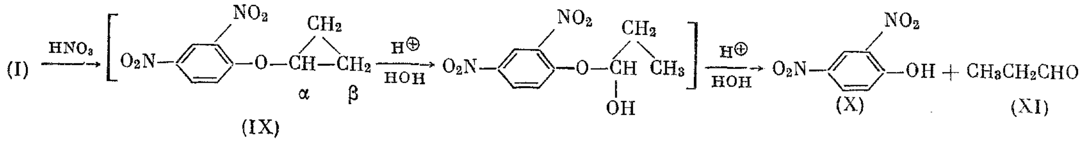
The bromination of phenyl isopropyl ether under these conditions also leads only to the formation of p-bromophenyl isopropyl ether (IV).

p-Chlorophenyl cyclopropyl ether (V) and 2,4-dichlorophenyl cyclopropyl ether (VII) are formed when (I) is chlorinated. The formation of the o-isomer (VI) is not observed. Based on the data of GLC and the IR spectrum, (V) is identical with the compound that is obtained from p-chlorophenyl vinyl ether [16]. The structure of (VII) was confirmed by the IR spectrum.

The Friedel–Crafts acylation of (I) leads to p-acetylphenyl cyclopropyl ether (VIII), the structure of which was confirmed by the IR spectrum. As a result, in electrophilic substitution reactions the cyclopropoxy group exhibits primarily a para-, and then (in the formation of the 2,4-disubstituted products) an ortho-orienting effect, which is found to be in agreement with the results of the quantum-mechanical calculation of the (I) molecule [17], carried out as a semiempirical variation of the MO LCAO method (Hofmann approximation).

The stability of the cyclopropane ring in (I) in the above-given reactions makes the direct halogenation of (I) a convenient method for the preparation of p-halophenyl cyclopropyl ethers. Here the yields of the end products are 80-90%, whereas the methylenation of the halophenyl vinyl ethers requires a longer reaction time, while the yields do not even reach 20%.

The nitration of (I) with dilute $HNO_3$ solution (d 1.06) apparently leads primarily to the formation of the cyclopropyl ether of 2,4-dinitrophenol (IX), which proves to be unstable under the reaction conditions. The presence of electron-acceptor nitro-groups in (IX) can promote the polarization of the $C^{\alpha}-C^{\beta}$ bond of the 3-membered ring, which should facilitate its cleavage, i.e., the formed (IX) is inclined to undergo hydrolysis, since (I) is quite stable in acid medium. For example, it fails to undergo hydrolysis when refluxed with 5% $H_2SO_4$ solution for 20 h. In summation, the reaction leads to the formation of 2,4-dinitrophenol (X) and propionaldehyde (XI) (which was isolated as the 2,4-DNPH), and it possibly proceeds via the intermediate step of the hemiacetal, as is the case when the 3-membered ring of ethers is cleaved under the conditions of the Levine reaction [12]



## EXPERIMENTAL METHOD

The GLC analysis was run by V. V. Keiko on a KhL-4 instrument (column 4 m × 6 mm, filled with didecyl sebacate deposited on Chromosorb W, 180°).

The IR spectra were taken as a film on a UR-10 instrument. In the case of compounds (II), (III) and (V)-(VIII), bands were observed at 1015-1030, 3015 and 3100 $cm^{-1}$, which characterize the presence of a cyclopropane ring [18]. The presence of bands in the 820-850 $cm^{-1}$ region in the case of (II), (IV), (V), and (VIII) indicates p-substitution, while the presence of bands in the 755-785 $cm^{-1}$ region in the case of (III) and (VI) indicates o-substitution in the benzene ring. The bands at 755, 825, and 865 $cm^{-1}$ characterize 1,2,4-substitution in the benzene ring of (VII).

Some of the properties of the synthesized compounds and the elemental analysis results are given in Table 1.

p-Bromophenyl Cyclopropyl Ether (II). a) From p-bromophenyl vinyl ether. To a suspension of a Zn–Cu couple, prepared from 42.5 g of Zn dust and 4.0 g of $CuSO_4$ [19] in 0.5 liter of absolute ether, was added a solution of 167 g of $CH_2I_2$ in 150 ml of absolute ether in 2.5 h. The mixture was stirred for another 0.5 h, after which a 1:1 ether solution of 70 g of the vinyl ether of p-bromophenol was added in 20 h. The reaction mixture was refluxed for 56 h, after which the ether was distilled off, while the residue was steam-distilled. The organic layer was washed with 30% NaOH solution, then with water, dried over $CaCl_2$, and vacuum-distilled. Repeated distillation in vacuo over Na gave 13 g of (II).

b) From cyclopropyl phenyl ether. With stirring, to 13.4 g of (I) [8, 20] in 100 ml of anhydrous $CHCl_3$ at −70° was added a solution of 19 g of bromine in 100 ml of $CHCl_3$. The mixture was stirred for 3 h at the same temperature, and then it was washed in succession with $Na_2SO_3$ solution, 10% $NaHCO_3$ solution, and water. The aqueous portion was additionally extracted with ether and then with $CHCl_3$. The combined organic extract was dried over $MgSO_4$. After distilling off the solvents the residue was vacuum-distilled. We isolated 19.9 g of (II).

o-Bromophenyl Cyclopropyl Ether (III). Obtained in the same manner as (II), starting with 295 g of $CH_2I_2$, Zn–Cu couple (from 72 g of Zn dust and 7.2 g of $CuSO_4$) and 199 g of the vinyl ether of o-bromophenol. We isolated 1.5 g of (III).

p-Bromophenyl Isopropyl Ether (IV). In the same manner as in the case of (II), from 13.1 g of isopropyl phenyl ether in 100 ml of $CHCl_3$ and 19 ml of bromine in 100 ml of $CHCl_3$ we obtained 18.8 g of (IV).

p-Chlorophenyl Cyclopropyl Ether (V). a) From p-chlorophenyl vinyl ether. Similar to (II), starting with 63 g of the vinyl ether of p-chlorophenol, Zn–Cu couple (from 38 g of Zn dust and 3.6 g of $CuSO_4$) and 150 g of $CH_2I_2$, we isolated 6.5 g of (V); see [21].

b) From cyclopropyl phenyl ether. With stirring, to 6.7 g of (I) in 50 ml of $CHCl_3$ at −70° was added a solution of 5.3 g of chlorine in 70 ml of $CHCl_3$. The mixture was stirred for 2 h, after which it was worked up in the same manner as in the case of (II), and then it was fractionally distilled in vacuo. Based on the GLC data, the product contains two principal components in a 5:1 ratio. Vacuum-distillation over Na gave 6.5 g of (V), which was identical (GLC, IR spectrum) with that obtained in the preceding experiment. We also isolated 1.4 g of 2,4-dichlorophenyl cyclopropyl ether (VII).

o-Chlorophenyl Cyclopropyl Ether (VI). In the same manner as in the case of (III), starting with 55 g of the vinyl ether of o-chlorophenol, 102 g of $CH_2I_2$ and Zn–Cu couple (from 25 g of Zn dust and 2.5 g of $CuSO_4$), we isolated 4 g of (VI).

p-Acetylphenyl Cyclopropyl Ether (VIII). With stirring, to a suspension of 26.6 g of $AlCl_3$ in 100 ml of $CHCl_3$ at 0-5° was added 15.7 g of $CH_3COCl$. The mixture was cooled down to −60 to −70° and then 6.7 g of (I) was added. After stirring for 2 h the mixture was decomposed at 0° with dilute HCl solution and then washed with 10% $NaHCO_3$ solution. The crystalline mass that was obtained after the usual workup was subjected to molecular sublimation. We isolated 8.3 g of (VIII), mp 42° (from alcohol); p-nitrophenylhydrazone, mp 206° (from toluene). Found: C 65.54; H 5.46; N 13.70%. $C_{17}H_{17}N_3O_3$. Calculated: C 65.59; H 5.46; N 13.50%.

Nitration of (I). a) A mixture of 9 g of (I) and 87 ml of dilute $HNO_3$ solution (d 1.06) was refluxed for 20 h. The obtained crystals were filtered and subjected to molecular sublimation. We isolated 6 g (34%) of 2,4-dinitrophenol (X), mp 112° (from alcohol). The mixed melting point with an authentic specimen was not depressed.

b) A mixture of 0.7 g of 2,4-DNPH, 2 g of (I) and 22 ml of dilute $HNO_3$ solution (d 1.06) in a sealed ampul was heated at 85-90° for 11 h. The obtained crystals were separated. When the crystals were chromatographed on an $Al_2O_3$ column (II activity) (elution with a 1:2 ethyl acetate–heptane mixture) we isolated the 2,4-DNPH of propionaldehyde, mp 154° (from alcohol). The mixed melting point with an authentic specimen was not depressed.

## CONCLUSIONS

1. The three-membered ring of cyclopropyl phenyl ether is stable in halogenation and acylation reactions, while the cyclopropoxy group exhibits a para-orienting effect.

2. The nitration of cyclopropyl phenyl ether with dilute $HNO_3$ solution is accompanied by a cleavage of the three-membered ring, with the formation of 2,4-dinitrophenol and propionaldehyde.

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