SYNTHESIS AND PROPERTIES OF FURAN DERIVATIVES 2.* ROLE OF THE HALOGEN IN RMgX IN REACTIONS WITH ALKOXYTETRAHYDROFURANS

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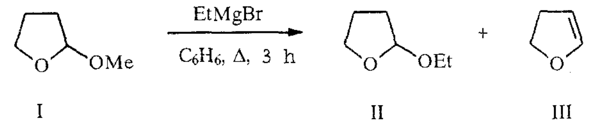
Heating 2-methoxytetrahydrofuran with ethylmagnesium bromide in benzene at reflux leads to the formation of 2-ethoxytetrahydrofuran and slight amounts of 4-methoxy-1-hexanol. Under analogous conditions, 2-ethoxytetrahydrofuran is quantitatively cleaved by methylmagnesium iodide to give 4-ethoxy-1-pentanol.

Cyclic ketals and acetals are cleaved by Grignard reagents upon heating in reflux in benzene to give alkoxyalcohols [2]. Dialkoxytetrahydropyrans behave analogously in this reaction [3]. Such behavior of oxygen heterocycles is related to the possibility of forming stable carbocations and carbanions upon the action of RMgX [4]. However, the effect of the halogen on this cleavage and the behavior of alkoxytetrahydrofurans in the presence of organomagnesium compounds have not been studied.

In the present work, we studied the reaction of 2-methoxy- (I) and 2-ethoxytetrahydrofurans (II) with methylmagnesium iodide and ethylmagnesium bromide. Alkoxytetrahydrofurans I and II are unreactive relative to RMgX in ethereal solution at room temperature. Heating I and EtMgBr in benzene at reflux gives II and traces of 2,3-dihydrofuran (III):



Since trans alkoxylation is observed for alkoxytetrahydrofurans in the presence of mineral acids and excess carbinol [5], the possibility of the formation of EtMgOBr was excluded (the reaction was carried out in degassed solvents in an inert gas atmosphere). In the presence of RMgX, which is a weak Lewis acid, EtMgOBr might analogously lead to transalkoxylation. In this case, nucleophilic substitution of the cryptobase of the Grignard reagent by the methyl group of the methoxy moiety in I probably takes place. The organomagnesium compound also displays basic properties leading, leading to the formation of III. Products of the heterolysis of the C—O σ-bond were not found. 4-Methoxyhexanol (IV) was found in trace amounts after prolonged heating at reflux.

Heating II in benzene at reflux in the presence of MeMgI leads to 4-ethoxy-1-pentanol (V) in quantitative yield. In this case, we find selective hydrolysis of a ring C—O bond. Since the nature of the halogen and structure of the cryptobase structure determine the electrophilicity of magnesium and nucleophilicity of the cryptobase, these properties of RMgX, in the final analysis, determine its structure in solution [6].

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[*] For Communication 1, see [1].

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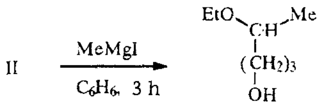
TABLE 1. Spectral Parameters for I-IV

Compound	Mass spectrum, m/z (I_{rel})	PMR spectrum, δ, ppm
I	102 (4) $[M]^{+\cdot}$, 101 (10) $[M-H]^+$, 72 (13) $[M-CH_2O]^{+\cdot}$, 71 (100) $[M-OCH_3]^+$, 61 (40), 43 (45), 42 (57), 41 (46), 39 (14), 31 (6)	1,82 (4H, m, $2CH_2$), 3,25 (3H, s, OCH_3), 3,85 (2H, t, OCH_2), 5,0 (1H, t, OCH)
II	116 (4) $[M]^{+\cdot}$, 115 (7) $[M-H]^+$, 87 (5) $[M-C_2H_5]^+$, 75 (10), 71 (100) $[M-OC_2H_5]^+$, 43 (45), 42 (57), 41 (46), 39 (14), 31 (6)	1,15 (3H, t, CH_3), 1,95 (4H, m, $2CH_2$), 3,55 (2H, m, CH_2), 3,95 (2H, m, OCH_2), 5,10 (1H, t, OCH)
III	70 (50) $[M]^{+\cdot}$, 55 (5), 41 (100), 40 (25), 39 (52)	
IV	117 (1) $[M-CH_3]^+$, 103 (18) $[M-C_2H_5]^+$, 85 (43) $[M-C_2H_5-H_2O]^+$, 73 (100), $[C_2H_5CH{=}O^+{-}CH_3]$, 71 (50), 71 (50), 45 (40), 43 (20), 41 (45), 31 (10) $[CH_2OH]^+$	0,95 (3H, t, CH_3), 1,52 (6H, $(CH_2)_3$), 2,8 (1H, s, OH), 3,2 (1H, m, CHO), 3,3 (3H, s, OCH_3), 3,6 (2H, t, CH_2OH)
V	117 (2) $[M-Me]^+$, 103 (5) $[M-Et]^+$, 85 (4) $[M-OEt]^+$, 73 (71) $[M-C_3H_7O]^+$, 45 (100) $[C_2H_5O]^+$, 43 (20), 41 (19), 45 (100) $[C_2H_5O]^+$, 43 (20), 41 (19), 31 (10) $[CH_2OH]^+$	0,95 (3H, d, CH_3), 1,25 (3H, d, CH_3), 1,52 (4H, $(CH_2)_2$), 2,8 (1H, s, OH), 3,52 (5H, m)



IV

Thus, the nature of the halogen in the organomagnesium compound determines the pathway for the reaction examined.

EXPERIMENTAL

The PMR spectra were taken on a Bruker 80 spectrometer in $CDCl_3$ with TMS as the internal standard. The mass spectra were taken on a Finnigan MAT-112 GC/MS at 70 eV using a 25-m capillary column packed with SE-52. The chromatographic analysis was carried out on a Chrom 5 gas-liquid chromatograph with a flame ionization detector using a 5 mm × 1 m column packed with 5% SE-52 on Chromaton N-AW-DM.

The starting methoxytetrahydrofuran and ethoxytetrahydrofuran were obtained according to Normant [7]. All the experiments were carried out in an inert gas atmosphere and absolute solvents.

The elemental analysis data for IV and V for C and H corresponded to the calculated values.

Reaction of 2-alkoxytetrahydrofurans with MeMgI and EtMgBr in Ether. A three-fold excess of ethereal EtMgBr (or MeMgI) was added to an ethereal solution of alkoxytetrahydrofuran and stirred for 3 h. The reaction mixture was decomposed by adding saturated aqueous ammonium chloride and extracted with ether. The organic layer was dried over $CaCl_2$. The solvent was distilled off. Starting alkoxytetrahydrofurans I and II in the residue were identified using GC/MS and gas-liquid chromatography and authentic samples.

Reaction of 2-alkoxytetrahydrofurans with MeMgI and EtMgBr in an Ether-Benzene Mixture. A three-fold excess of Grignard reagent was added to a solution of 2-alkoxytetrahydrofuran in absolute benzene, heated at reflux for 3 h, decomposed by the addition of saturated aqueous sodium chloride, and extracted with ether. The organic layer was dried over $CaCl_2$ and the solvent was distilled off. The residue was distilled at atmospheric pressure. The composition of the reaction mixture was determined using GC/MS and gas-liquid chromatography and authentic samples.

2-Methoxytetrahydrofuran (I). bp 105°C.

2-Ethoxytetrahydrofuran (II). bp 115°C. The yield upon heating I with EtMgBr at reflux was 13% according to GC/MS data.

4-Methoxy-1-hexanol (IV, $C_7H_{16}O_2$). bp 152-153°C. The yield in the reaction of I with EtMgBr was 3% according to GC/MS data.

4-Ethoxy-1-pentanol (V, $C_7H_{16}O_2$). bp 151-153°C. The yield in the reaction of II with MeMgI was 91% according to GC/MS data.

LITERATURE CITED

1. R. A. Karakhanov, E. S. Bogacheva, I. Romero, and V. I. Kelarev, Khim. Geterotsikl. Soedin., No. 4, 449 (1991).
2. G. Westera, C. Blomberg, and F. Bickelhaupt, J. Org. Chem., **144**, 285 (1978).
3. L. N. Kralina, R. I. Kruglikova, and T. I. Tarulina, Khim. Geterotsikl. Soedin., No. 3, 311 (1970).
4. Yu. N. Polivin, R. A. Karakhanov, and V. N. Postnov, Usp. Khim., No. 3, 403 (1990).
5. R. A. Karakhanov and R. M. Gafarov, Proceedings of the Fourth All-Union Symposium on Heterogeneous Catalysis of Heterocyclic Compounds [in Russian], Riga (1987), p. 127.
6. E. C. Ashby, Pure Appl. Chem., **52**, 545 (1980).
7. H. Normant, Comptes Rendus, **43**, 3816a (1949).