SYNTHESIS AND REACTIONS OF HALOGEN-CONTAINING COMPOUNDS OF THE FURAN SERIES

I. Synthesis of α-Substituted Tetrahydrofurans

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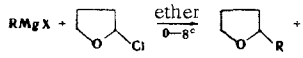
A study of the interaction of α-chlorotetrahydrofuran with Grignard reagents and with secondary amines.

The fundamental methods for obtaining tetrahydrofuran and its homologs are the hydrogenation of furan compounds [1–3] and the cyclization of 1,4-diols and of 1,4-halohydrins [4]. Not long ago Bel'skii and Shuikin [5] described a method for the catalytic synthesis of tetrahydrofuran homologs, which consisted of the hydrogenation of 1-furyl-3-alkanols in the vapor phase. In addition to these methods, α-substituted tetrahydrofurans may also be obtained by the interaction of α-chlorotetrahydrofuran (I) with nucleophilic reagents.

The aim of the present investigation was to study the interaction of I with alkyl(aryl)magnesium halides and secondary amines. The Grignard reagents were prepared by the usual method, and pentafluorophenylmagnesium chloride by the procedure described in the literature [6]. The reaction of I with Grignard reagents proceeded according to the usual pattern.



X = Br; Cl; R = propyl, butyl, amyl, hexyl, phenyl, o-tolyl, m-trifluoromethylphenylene, pentafluorophenyl.

The speed of the interaction of I with alkylmagnesium halides depends on the nucleophilicity of the reagent, and on the temperature and concentration of the reacting substances. Thus, I reacts very violently with propyl- and butylmagnesium bromides, and it is necessary to conduct the reaction with intensive stirring and good cooling. The reaction proceeds more smoothly when diluted ethereal solutions are employed. The interactions of amyl- and hyxylmagnesium bromides, and of arylmagnesium halides, with I proceed more smoothly and do not require intensive cooling.

The reaction mixtures were processed according to the usual methods. The separation of pure alkyltetrahydrofurans was accomplished by rectification under normal or reduced pressure, depending on the boiling point of the substance. The table summarizes the data on the yields of alkyl derivatives of tetrahydrofuran and their elementary analyses.

From the interaction of I with pyridine, a quaternary salt melting at 219°–220° C (decomp.) is obtained. With morpholine, I forms the corresponding amine with an 80% yield. With an excess of diethylamine, I reacts to form α-(N,N-diethyl)-aminotetrahydrofuran, but the yield is lower.

It is known from the literature [7,8] that α,β-dichlorotetrahydrofuran reacts with nucleophilic reagents, such as alcoholates, alkyl(aryl)magnesium-halides, and secondary amines, to form the corresponding α-substituted-β-chlorotetrahydrofurans with more than 80% yield. In this case, the side reaction leading to the separation of a molecule of hydrogen chloride is practically suppressed.

As may be seen from the table, the yield of α-substituted tetrahydrofurans, obtained by the interaction of I with alkyl(aryl)magnesium halides and secondary amines, is significantly lower. This is especially noticeable when the reaction is conducted with strong nucleophilic reagents. Evidently, this may be explained by the presence of competing reactions, such as the separation of a molecule of hydrogen chloride, which leads to the formation of 2,3-dihydrofuran.

EXPERIMENTAL

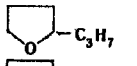
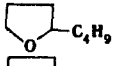
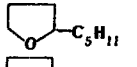
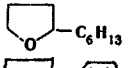
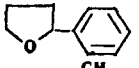
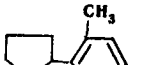
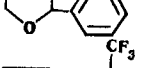
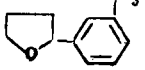
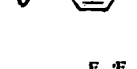
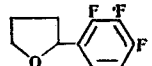
α-Propyltetrahydrofuran (II). 106.5 g (1 mole) of I in 250 ml absolute ether was added at 0°–2° C and under vigorous stirring in the course of 1–1 1/2 hr to a Grignard reagent prepared from 24 g (1 g-at) of Mg and 122 g (1.1 mole) of propyl bromide in 300 ml of absolute ether. After adding the total quantity of I, the reaction temperature was gradually raised to room conditions, and then the reaction mixture was boiled for 1/2–1 hr, thus eliminating 5% of HCl. Yield 66.7%.

α-Butyletrahydrofuran was obtained by an analogous method. Compounds IV–IX were synthesized under somewhat different conditions. After adding the ethereal solution of I to the Grignard reagent, the temperature was raised to boiling, most of the ether distilled off, and the reaction mixture maintained for 1 1/2–2 hr at 80°–90° C. This was followed by treatment in the usual way.

α-(N, N-Diethyl)aminotetrahydrofuran (X). 82 g (1.3 mole) of diethylamine in 160 ml of absolute ether was poured into a three-necked reaction vessel provided with a dropping funnel, a stirrer, and a reflux condenser. Through the dropping funnel and under vigorous stirring and cooling by ice-water, 60 g of I in 150 ml of absolute ether was added drop by drop in the course of 1 hr. The reaction mass was allowed to stand overnight. The precipitated crystals were filtered-off, washed twice with ether, and the ethereal solution distilled off. Yield 40%.

By an analogous procedure, α-(N-morpholyl) tetrahydrofuran (XI) is obtained with an 80% yield.

Yields and Properties of α-Substituted Tetrahydrofurans

No. of product	Compound	Bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	MR_D		Empirical formula	Found, %				Calculated, %				Yield, %
					Found	Calculated		C	H	N	F	C	H	N	F	
II		131—131.5 (757)	0.8628	1.4250	33.80	34.32	$C_{17}H_{14}O$	73.92	11.96	—	—	73.70	12.28	—	—	66.7
III		158—159 (754)	0.8626	1.4315	38.44	38.97	$C_8H_{16}O$	75.04	12.42	—	—	75.00	12.50	—	—	64.2
IV		62—63 (12)	0.8620	1.4360	43.08	43.62	$C_9H_{18}O$	76.19	12.60	—	—	76.05	12.07	—	—	58.0
V		73.5—74 (7)	0.8677	1.4385	47.24	47.27	$C_{10}H_{20}O$	76.92	12.80	—	—	76.91	12.56	—	—	72.4
VI		69.5—70 (3)	1.0310	1.5320	44.48	44.77	$C_{10}H_2O$	80.99	8.26	—	—	81.08	8.11	—	—	69.9
VII		82—83 (3)	1,0329	1,5362	48,91	49,22	$C_{11}H_{14}O$	81,58	8,77	—	—	81,42	8,64	—	—	72.6
VIII		96.5—97 (12)	1.2370	1.4676	48.49	48.71	$C_{11}H_{11}F_3O$	61.26	4.98	—	26.39	61.11	5.09	—	26.10	60.6
IX		90—91 (11)	1.4514	1.4508	44.12	43.59	$C_{10}H_7F_5O$	50.3	2.83	—	39.83	50.4	2.54	—	40.0	37.1
X		61—62 (12)	0.9394	1.4698	42.46	42.76	$C_8H_{17}NO$	67.05	11.73	9.60	—	67.13	11.89	9.79	—	40
XI		97—98 (12)	1.0428	1.4752	42.20	42.49	$C_8H_{15}NO_2$	60.5	9.30	8.79	—	61.15	9.55	8.92	—	80.5

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