REDUCTION OF HALOGENATED KETONES WITH MAGNESIUM HALOALKOXIDES*

I. I. Lapkin, E. V. Dormidontova,
Yu. P. Dormidontov, P. A. Sentebov,
and L. D. Parfenova

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547.284+547.288

The degree of thermal stability of magnesium haloalkoxycarbinolates containing thienyl groups and dichloro-, trichloro-, and trifluoromethyl groups was explained. The effect of substituents in the thienyl group on the stability of the magnesium haloalkoxycarbinolates was studied.

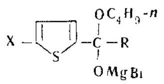
In one of our previous papers [2] it was assumed that the thermal stability of a magnesium haloalkoxycarbinolate formed by the reaction of an organomagnesium compound with a carboxylic acid ester would be associated with the dissociation constant of the acid. If the acid dissociation constant is equal to or higher than the first dissociation constant of oxalic acid ($K_{25} = 3.8 \cdot 10^{-2}$), reduced reaction products (secondary alcohols, esters of secondary α-hydroxyacids, etc.) are formed as a result of decomposition.

Dichloro-, trichloro-, and trifluoroacetic acids have dissociation constants of $5.6 \cdot 10^{-2}$, $2.2 \cdot 10^{-1}$, and $5.9 \cdot 10^{-1}$ [3], respectively, and their esters, as expected, form secondary alcohols instead of ketones in the Grignard reaction with organomagnesium compounds.

The different degree of electronegativity of the $CHCl_2$, CCl_3, and CF_3 groups, as well as the character of the α'-substituent of the thienyl group are also responsible for the different degree of stability of the corresponding carbinolates. The stabilities were studied by heating the reaction mass for 1.5 h in ether solution and by determination of the hydroxyl group in the hydrolysis products. The results are presented in Table 1.

The synthesis of the secondary alcohols is more conveniently carried out by the reaction of ketones with magnesium haloalkoxides rather than by the reaction of the acid esters with organomagnesium compounds and leads to the same carbinolate; the subsequent decomposition of the carbinolate leads to the formation of the carbinolate of the secondary alcohol.

TABLE 1. Stabilities of



X	R	Decomp., %
H	CF_3	100
Br	CF_3	80
H	CCl_3	75
Br	CCl_3	50
H	$CHCl_2$	60
C_2H_5	$CHCl_2$	50
Cl	$CHCl_2$	30
Br	$CHCl_2$	40
I	$CHCl_2$	50

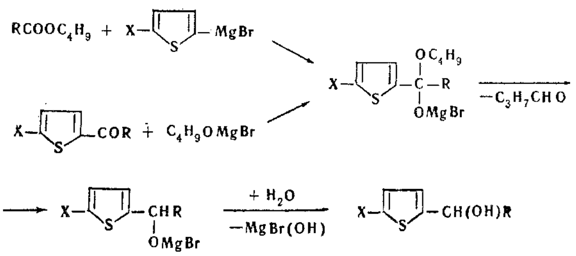


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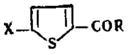
TABLE 2.



X	R	bp, °C (mm)	n_D^{20}	d_4^{20}	Empirical formula	Found		Calc.		Yield, %
						MR_D	S, %	MR_D	S, %	
H	$CHCl_2$	136—139 (13)	1,5685	1,1546	$C_6H_4Cl_2OS$	43,91	16,4	43,78	16,4	75
C_2H_5	$CHCl_2$	149—151 (5)	1,5860	1,4096	$C_8H_8Cl_2OS$	53,10	14,3	53,01	14,4	65
Cl	$CHCl_2$	140—143 (8)	1,5825	1,5383	$C_6H_3Cl_3OS$[a]	49,79	13,9	48,65	14,0	68
Br	$CHCl_2$	142—143 (3)[b]			$C_6H_3BrCl_2OS$		11,8		11,7	67
I	$CHCl_2$	mp 69—70[c]			$C_6H_3Cl_2IOS$		9,9		10,0	82
H	CCl_3	125—126 (4)[13]	1,5910	1,5524	$C_6H_3Cl_3OS$	49,96	13,9	48,65	14,0	66
Br	CCl_3	139—141 (3)[d]			$C_6H_2BrCl_3OS$		10,4		10,4	60
H	CF_3	70—71 (28)[14]	1,4350	1,3245	$C_6H_3F_3OS$[e]	35,49	17,7	33,74	17,8	52
Br	CF_3	100—102 (25)	1,4520	1,5886	$C_6H_2BrF_3OS$[f]	43,98	12,5	41,50	12,4	56

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[a] The bis (2,4-dinitrophenylhydrazone) melted at 253-254°.

[b] mp 37-38° (from alcohol).

[c] From petroleum ether.

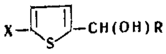
[d] mp 42-43° (from alcohol).

[e] The 2,4-dinitrophenylhydrazone melted at 151-152°.

[f] The 2,4-dinitrophenylhydrazone melted at 96-97°.

* Here and in Table 3, superscript numbers refer to literature citations.

TABLE 3.



X	R	bp, °C (mm)	n_D^{20}	d_4^{20}	Empirical formula	Found			Calc.			Yield, %
						MR_D	S, %	OH, %	MR_D	S, %	OH, %	
H	$CHCl_2$	151—153 (15)	1,5510	1,3800	$C_6H_6Cl_2OS$	45,57	16,2	8,6	45,29	16,3	8,6	95
C_2H_5	$CHCl_2$	139—140 (3)	1,5665	1,3430	$C_8H_{10}Cl_2OS$	54,72	14,3	7,5	54,53	14,2	7,5	95
Cl	$CHCl_2$	140—141 (5)	1,5630	1,4915	$C_6H_5Cl_3OS$	50,40	13,9	7,3	50,16	13,8	7,3	92
Br	$CHCl_2$	149—151 (3)	1,5685	1,6945	$C_6H_5BrCl_2OS$	53,32	11,7	6,1	53,06	11,6	6,1	87
I	$CHCl_2$	mp 61—62[a]			$C_6H_5Cl_2IOS$		9,8	5,2		9,9	5,3	83
H	CCl_3	130—133 (7)[15, 16] [b]			$C_6H_5Cl_3OS$		13,9	7,3		13,8	7,3	93
Br	CCl_3	156—158 (3)[c]			$C_6H_4BrCl_3OS$		10,2	5,5		10,3	5,5	88
H	CF_3	100—102 (30)	1,4230	1,2525	$C_6H_5F_3OS$	37,03	17,5	9,3	35,25	17,6	9,3	97
Br	CF_3	120—121 (30)	1,4405	1,5175	$C_6H_4BrF_3OS$	45,39	12,3	6,5	43,02	12,3	6,5	92

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[a] From petroleum ether.

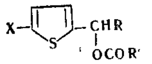
[b] mp 30-31° [16] (from petroleum ether).

[c] mp 43-44° (from petroleum ether).

EXPERIMENTAL

α-Chlorothiophene was obtained by the chlorination of thiophene in acetic acid [4]. The synthesis of α-bromo- and α,α'-dibromothiophenes was accomplished by the bromination of thiophene in CCl_4 [5]. The iodination of thiophene in benzene in the presence of HgO [6] was used to obtain α-iodothiophene. The dichloroacetylthiophenes were synthesized by the chlorination of the corresponding acetylthiophenes [7], which in turn were obtained by the method used to synthesize acetothienone [8]. The trichloromethyl α-thienyl ketones were synthesized by the reaction of α-thienylmagnesium bromide of α-(α'-bromothienyl)magnesium bromide with trichloroacetyl chloride [9]. The reaction of a Grignard reagent obtained from the appropriate bromothiophene with trifluoroacetic acid [10] was used in the synthesis of the trifluoromethyl thienyl ketones.

TABLE 4.



X	R	R′	bp, °C (mm)	n_D^{20}	d_4^{20}	Empirical formula	Found		Calc.	
							MR_D	S, %	MR_D	S, %
H	$CHCl_2$	CH_3	127—129 (3)	1,5550	1,3970	$C_8H_8Cl_2O_2S$	54,94	13,5	54,66	13,4
C_2H_5	$CHCl_2$	CH_3	134—135 (3)	1,5485	1,3240	$C_{10}H_{12}Cl_2O_2S$	64,13	11,9	63,89	12,0
Cl	$CHCl_2$	CH_3	150—152 (5)	1,5690	1,4990	$C_8H_7Cl_3O_2S$	59,79	11,7	59,52	11,7
Br	$CHCl_2$	CH_3	160—162 (4)	1,5820	1,6920	$C_8H_7BrCl_2O_2S$	62,72	10,0	62,42	10,1
H	CCl_3	CH_3	mp 64—65[a]			$C_8H_7Cl_3O_2S$		11,6		11,7
Br	CCl_3	CH_3	mp 103—104[a]			$C_8H_6BrCl_3O_2S$		8,9		9,1
H	CF_3	p-$C_6H_4NO_2$	mp 55—56[a]			$C_{13}H_8F_3NO_4S$[b]				

[a] From alcohol.

[b] Found %: N 4.2. Calculated %: N 4.3.

Trifluoromethyldi(α-thienyl)carbinol with bp 165-166° (28 mm) was isolated as a side product in the preparation of trifluoromethyl α-thienyl ketone. Found %: S 24.4; OH 6.3. $C_{10}H_7F_3OS_2$. Calculated %: S 24.3; OH 6.4. The p-nitrobenzoate melted at 170-171°. Found %: N 3.4. $C_{17}H_{10}F_3NO_4S_2$. Calculated %: N 3.4.

The 2,4-dinitrophenylhydrazones could be obtained for the fluorinated ketones, and the bis-2,4-dinitrophenylhydrazone was obtained for α′-chloro-α-dichloroacetylthiophene by known methods [11, 12]. The synthesized ketones are presented in Table 2.

Thienyl-Substituted Alcohols. Anhydrous butyl alcohol (0.2 mole) was added with stirring to 0.2 mole of ethylmagnesium bromide, the mixture was heated for 30 min on a water bath, and an ether solution of 0.1 mole of the ketone was added to it. The mass was heated for 2-5 h and then decomposed with water and 10% hydrochloric acid. The ether layer was washed with water, sodium bicarbonate solution, water again, and dried with anhydrous sodium sulfate. The solvent was removed by distillation, and the carbinol was vacuum distilled (Table 3). The acetates of some of the carbinols were obtained by heating the appropriate carbinol with acetyl chloride, and the p-nitrobenzoate of trifluoromethyl-α-thienylcarbinol was obtained by the Schotten–Baumann reaction (Table 4).

The thermal stability of the carbinolate obtained from magnesium bromobutoxide and trifluoromethyl β-(β′-bromothienyl) ketone [bp 96-98° (20 mm), n_D^{20} 1.4430, d_4^{20} 1.6083. Found %: S 12.2; MR_D 42.71. $C_6H_2BrF_3OS$. Calculated %: S 12.4; MR_D 41.50. Yield 45%. 2,4-Dinitrophenylhydrazone, mp 155-156°] proved to be lower than that of the carbinolate containing the α-(α′-bromothienyl) group. It was completely decomposed even on heating for 1 h in ether solution to form (after hydrolysis) trifluoromethyl-β-(β′-bromothienyl)carbinol [bp 87-89° (7 mm), n_D^{20} 1.4325, d_4^{20} 1.5345. Found %: S 12.2; OH 6.5; MR_D 44.16. $C_6H_4BrF_3OS$. Calculated %: S 12.3; OH 6.5; MR_D 43.02. Yield 94%].

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