REDUCTION OF PINACOLONE WITH 2-HEXYLMAGNESIUM CHLORIDE IN THE PRESENCE OF STRONG BASES

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The effect of the solvating capacity of a solvent on the reaction rate of organomagnesium compounds has been shown by a number of authors [1-8]. From these data it follows that displacement of the ligand (solvent) by the substrate and the formation of the organomagnesium compound – substrate complex are both determined by the relative basicity of the solvent and the substrate. Thus, the reaction rate of organomagnesium compounds with ketones and alkyl halides decreases when going to more strongly solvating solvents [7, 8]. It was also shown that the reaction rate of aliphatic organomagnesium compounds with aliphatic ketones in tertiary amines depends on the stability of the organomagnesium – amine complex and is determined by the compounds taking part in this complex [9]. It seemed interesting to us to study the effect of strong bases on the rate of the reaction for the reduction of pinacolone by 2-hexylmagnesium chloride. The reaction was studied in the presence of triethylamine, N-dimethylphenylethylamine (DMPEA) or hexamethylphosphamide (HMPA), in ether solution, or in the absence of ether. The reaction rate was judged by the yield of reaction products (isomeric hexenes) in a standard time (4 h).

From the results, given in Tables 1 and 2, it can be seen that when going from ether to tertiary amines, or to the mixed solvents: ether + amine and ether + HMPA, the total yield of reduction products in a standard time decreases with increase in the basicity of the solvent. Thus, when going from triethylamine to DMPEA the yield of reaction products decreases 3-fold. Important retardation of the reaction is also observed when it is run in mixed solvents. As can be seen from Table 2, when the reaction is run in ether containing DMPEA (ratio of RMgX : amine = 1 : 3) the yield of reaction products remains practically constant. When the same reaction is run in a mixture of ether and HMPA (ratio of RMgX : HMPA = 1 : 3) the yield of products changes by a factor of 10. This shows that HMPA is an even more powerful complexing agent than a tertiary amine. Based on the data given in [10], only the enolization process takes place when the reaction for the reduction of diisopropyl ketone with ethylmagnesium bromide is run in this solvent.

The yield of products also increases when a 5-fold dilution is made (cf. Tables 1 and 3). An increase in the reaction rate, observed when the ether solution is diluted, can apparently be explained by the relatively

TABLE 1. Yield of Reduction Products in Reaction of 2-$C_6H_{13}MgCl$ and $CH_3COC(CH_3)_3$

Products	Ether			Triethylamine			N-dimethylphenyl-ethylamine		
	yield, %	yield of blank experiment, %	true yield %	yield, %	yield of blank experiment, %	true yield, %	yield, %	yield of blank experiment, %	true yield, %
1-Hexene	4,62	1,05	3,57	3,56	1,50	2,06	8,10	7,85	0,25
trans-2-Hexene	5,80	0,35	5,45	2,54	0,57	1,97	6,28	5,15	1,13
cis-2-Hexene	1,00	0,11	0,89	0,47	0,06	0,41	3,37	2,75	0,62
Total amount of hexenes	11,42	1,51	9,91	6,57	2,13	4,44	17,75	15,75	2,00

Note: Concentration of 2-$C_6H_{13}MgCl$ = 1.5 M and of $CH_3CO(CH_3)_3$ = 0.92 M; temperature 40°C.

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TABLE 2. Yield of Reduction Products in Reaction of 2-$C_6H_{13}MgCl$ and $CH_3COC(CH_3)_3$ in Mixed Solvents

Products	Ether + N-dimethylphenyl-ethylamine RMgX: amine = 1:2.94			Ether + N-dimethylphenyl-ethylamine RMgX: amine = 1:8.15			Ether + N-dimethylphenyl-ethylamine RMgX: HMPA = 1:2.91			Ether + hexamethylphosphamide RMgX: HMPA = 1:2.91		
	yield, %	yield of blank experiment, %	true yield, %	yield, %	yield of blank experiment, %	true yield, %	yield, %	yield of blank experiment, %	true yield, %	yield, %	yield of blank experiment, %	true yield, %
1-Hexane	7.10	3.75	3.35	6.30	3.80	2.50	5.03	4.57	0.46	1.95	1.00	0.95
trans-2-Hexene	10.60	1.76	8.84	8.50	2.00	6.50	5.02	2.40	2.65	0.78	0.50	0.28
cis-2-Hexene	0.56	-	0.56	0.60	-	0.60	1.06	-	1.06	-	-	-
Total amount of hexenes	18.26	5.51	12.75	15.40	5.80	9.60	11.11	6.97	4.14	2.73	1.50	1.23

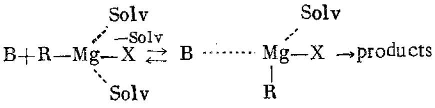
Note: Concentration of 2-$C_6H_{13}MgCl$ = 0.3 M; $CH_3COC(CH_3)_3$ = 0.184 M.

TABLE 3. Yield of Reduction Products in Reaction of 2-$C_6H_{13}MgCl$ and $CH_3COC(CH_3)_3$

Products	Ether			Triethylamine			N-Dimethylphenylethylamine		
	yield, %	yield of blank experiment %	true yield, %	yield, %	yield of blank experiment, %	true yield, %	yield, %	yield of blank experiment, %	true yield, %
1-Hexene	6,92	2,06	4,86	3,40	1,74	1,66	6,10	4,43	1,67
trans-2-Hexene	8,56	0,67	7,89	2,13	0,65	1,48	4,53	3,33	1,20
cis-2-Hexene	0,87	0,20	0,67	0,24	0,17	0,07	2,94	2,77	0,17
Total amount of hexenes	16,36	2,93	13,43	5,77	2,56	3,21	13,57	10,53	3,04

Note: Concentration of 2-$C_6H_{13}MgCl$ = 0.3 M and of $CH_3COC(CH_3)_3$ = 0.184 M; temperature 40°.

higher concentration of the reactive monomeric particles in a dilute solution [1,8] when compared with a concentrated solution. In the case of triethylamine and DMPEA the yield of reaction products remains almost constant. In these solvents the Grignard reagent exists as the monomer $(RMgX)_1$ at the higher concentrations [11]. The obtained result corroborates our previously expressed opinion that the effect of the solvent on the reaction of organomagnesium compounds consists in changing the position of the equilibrium for the formation of the intermediate complex.



$$\mathrm{B} + \mathrm{R{-}}\overset{\mathrm{Solv}}{\underset{\mathrm{Solv}}{\mathrm{Mg}}}\mathrm{(-Solv){-}X} \rightleftarrows \mathrm{B}\cdots\cdots\overset{\mathrm{Solv}}{\underset{\mathrm{R}}{\mathrm{Mg}}}\mathrm{{-}X} \rightarrow \text{products}$$

EXPERIMENTAL

Starting compounds: 2-chlorohexane was obtained and analyzed by the method given in [7]; pinacolone was obtained as described in [8]. The ether was purified in the usual manner and was distilled over $LiAlH_4$ [12]. Hexamethylphosphamide was made absolute by distillation with $CHCl_3$. The triethylamine was dried over NaOH for several days and then distilled in a dry N_2 stream (bp 89.4°). N-Dimethylphenylethylamine was obtained from acetophenone and formamide in the presence of HCOOH [13]. The obtained α-phenylethylamine was distilled in a dry N_2 stream [bp 81-82° (15 mm)] and then was methylated with formaldehyde and HCOOH [14]. The end product, N-dimethylphenylethylamine, was distilled in a dry N_2 stream [bp 78.0-78.5° (15 ml)].

The reduction reaction was run in a dry N_2 atmosphere. To the obtained Grignard reagent, prepared from magnesium turnings, activated with iodine, and the alkyl halide (magnesium : alkyl halide ratio = 1.5 : 1), was added the calculated amount of pinacolone in the appropriate solvent. The flask was placed in a thermostat at 40°, and, after the lapse of the standard length of time (4 h), the flask contents were decomposed. The obtained products were extracted with ether, while the ether extracts were washed with dilute

HCl solution to separate the amine, then in succession with water, 10% $Na_2S_2O_3$ solution and 10% K_2CO_3 solution, and dried over K_2CO_3.

The obtained products were analyzed by the capillary gas chromatography method [8].

CONCLUSIONS

1. The reduction rate of pinacolone with 2-hexylmagnesium chloride decreases in the order: ether, triethylamine, N-dimethylphenylethylamine.

2. The addition of strong bases to an ether solution of the Grignard reagent leads to a substantial slowing up of the rate of the reduction reaction.

3. The effect of dilution on the rate of the reduction reaction in the presence of strong bases was examined.

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