

Alkyl Cyanates. XVI. Reaction of Alkyl Cyanates with Grignard Reagents. Kinetic Studies

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A kinetic investigation of the reactions of alkyl cyanates with Grignard reagents* and dibutylmagnesium in diethyl ether has been carried out by means of thermographic measurements. In the presence of excess organomagnesium reagent first order plots are obtained for reaction of the cyanate, but the kinetic order in organomagnesium reagent is less than one and decreasing at high concentrations. In the presence of excess cyanate the same kinetics are observed, the order in organomagnesium reagent being one and the order in cyanate decreasing at high concentrations, which corresponds to a mechanism involving complex formation between the reactants. Addition of $MgBr_2$ to the organomagnesium reagent depresses the observed first-order rate constants. The depression is consistent with both R_2Mg and $RMgX$ contributing to the reactions.

The reactivity of aromatic Grignard reagents in reactions with alkyl cyanates is higher than the reactivity of dibutylmagnesium, which again is higher than the reactivities of aliphatic Grignard reagents. The Hammett ρ -value for the reactions of isobutyl cyanate with *p*-substituted "phenylmagnesium bromides" is found to be ca. -1.5 . On the basis of the kinetic data and the ρ -value the reactions are best described as involving a concerted four-center mechanism in the rate-determining step.

In another paper we have reported on the product formation in the reaction between alkyl or aryl cyanates and Grignard reagents,¹ and now we wish to report on a kinetic investigation of the reaction between alkyl cyanates and Grignard reagents.

The present work has been carried out with the aim of obtaining deeper insight into the

* The Grignard reagents are in the following symbolized as "RMgX".

reactions between alkyl cyanates and Grignard reagents which lead to the formation of alkoxy-magnesium halides and nitriles (I):



A thermographic method was used for the kinetic measurements.² This technique allowed reproducible rate measurements within $\pm 5\%$ when the limiting reagent was present in a concentration of 0.01 M. At lower concentrations the accuracy of measurements becomes unsatisfactory. At higher concentrations the error of the k_{obs} -values becomes too high due to the temperature dependence. All measurements were carried out with one of the reactants in excess.

Fig. 1 shows three examples of plots of $\ln(\Delta T_\infty - \Delta T_1)/(\Delta T_\infty - \Delta T)^*$ versus the reaction time, t , for the reaction of ethyl cyanate with "butylmagnesium bromide". From all kinetic experiments linear plots were obtained up to at least 70% reaction of the limiting reagent. The linearity of the plots means that the reaction order in ethyl cyanate is one. The pseudo first order rate constants (k_{obs}) are obtained from the slopes of the lines. In Fig. 2 is shown how the pseudo first order rate constants vary with the initial concentrations of "butylmagnesium

* $\ln a/(a-x) = \ln(\Delta T_\infty - \Delta T_1)/(\Delta T_\infty - \Delta T) = k_{obs} \times t$, where ΔT_∞ is the total rise in temperature, ΔT_1 is the rise in temperature after 2 ms and ΔT is the rise in temperature at the time t . ΔT_1 is a correction for heat evolved from reaction between traces of impurities (water) and the Grignard reagent and for heat of mixing.

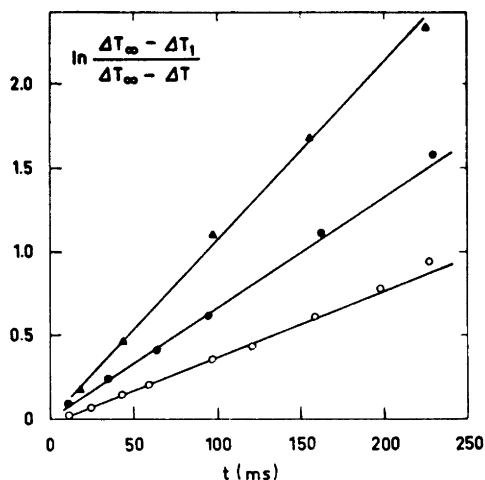


Fig. 1. Plots of $\ln(\Delta T_{\infty} - \Delta T_1)/(\Delta T_{\infty} - \Delta T)$ versus the reaction time, t , for the reaction of ethyl cyanate with excess "butylmagnesium bromide" in diethyl ether at 25 °C ($c^0_{\text{C}_4\text{H}_9\text{OCN}} = 0.010 \text{ M}$; $c^0_{\text{C}_4\text{H}_9\text{MgBr}} = 0.100 \text{ M}$ (O), 0.200 M (●) and 0.600 M (▲)).

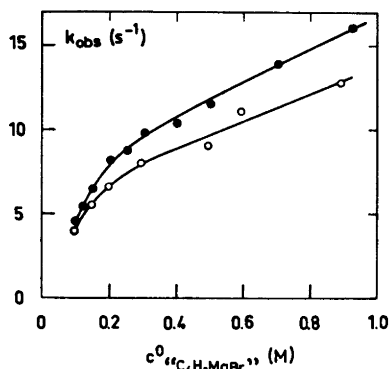


Fig. 2. Plots of the pseudo first order rate constants versus the initial concentrations of "butylmagnesium bromide" for reactions of this Grignard reagent with ethyl cyanate (O) and isobutyl cyanate (●) in diethyl ether at 25 °C ($c^0_{\text{ROCN}} = 0.010 \text{ M}$).

bromide" for the reactions of this Grignard reagent with ethyl and isobutyl cyanate. Because of the curvature of the plots shown it is concluded that the reaction order in Grignard reagent is less than one.

Kinetic experiments with excess isobutyl cyanate and 0.010 M "butylmagnesium bromide" likewise give linear pseudo first order

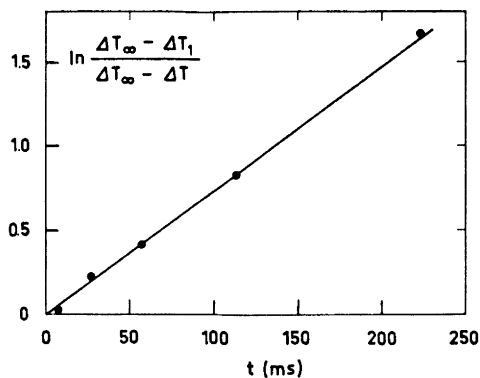


Fig. 3. Plot of $\ln(\Delta T_{\infty} - \Delta T_1)/(\Delta T_{\infty} - \Delta T)$ versus the reaction time, t , for the reaction of 0.138 M isobutyl cyanate with 0.010 M "butylmagnesium bromide" in diethyl ether at 25 °C.

plots (Fig. 3), and a plot of the pseudo first order rate constant versus the initial concentration of isobutyl cyanate is very similar to the plot obtained with excess "butylmagnesium bromide" (Fig. 4). The deviation appears roughly to be within the limits of the accuracy of measurements of this method.

Kinetic measurements on the reaction of isobutyl cyanate with dibutylmagnesium in diethyl ether have been carried out. The pseudo first order plot is linear up to 80 % reaction of isobutyl cyanate (Fig. 5). From the slope of the

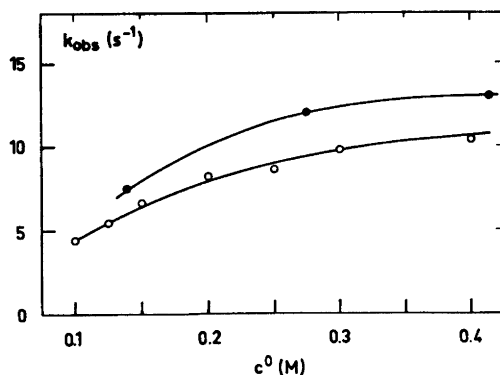


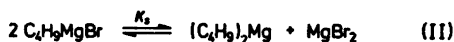
Fig. 4. Plots of the pseudo first order rate constant versus the initial concentrations of the reactant in excess for the reaction of isobutyl cyanate with "butylmagnesium bromide" in diethyl ether at 25 °C (O: 0.010 M $i\text{-C}_4\text{H}_9\text{OCN}$ and excess $\text{C}_4\text{H}_9\text{MgBr}$; ●: 0.010 M $\text{C}_4\text{H}_9\text{MgBr}$ and excess $i\text{-C}_4\text{H}_9\text{OCN}$).

Table 1. The influence of the magnesium bromide concentration on the pseudo first order rate constant for the reaction of isobutyl cyanate with "butylmagnesium bromide" in diethyl ether at 25 °C.

$c^0_{i-C_4H_9OCN}$ M	$c^0_{(C_4H_9)_2MgBr}$ M	$c^0_{MgBr_2}$ M	k_{obs} (s ⁻¹)
0.010	0.138	0.003	6.8
0.010	0.138	0.069	4.0
0.010	0.138	0.138	1.5

line a pseudo first order rate constant of 47 s⁻¹ is obtained for $c^0_{i-C_4H_9OCN} = 0.010$ M and $c^0_{(C_4H_9)_2Mg} = 0.100$ M.

When a large amount of magnesium bromide etherate is added to "butylmagnesium bromide" the pseudo first order rate constant is decreased, but the value of the rate constant is still considerable (Table 1). Therefore it is concluded that both butylmagnesium bromide and dibutylmagnesium present according to the Schlenk equilibrium ³ (II) react with the cyanate



when "butylmagnesium bromide" reacts with isobutyl cyanate. A decrease of k_{obs} on addition of magnesium bromide is expected because of a lowered content of the most reactive species, dibutylmagnesium. However, it cannot be excluded that magnesium bromide also forms a complex with the cyanate because the pseudo first order rate constant is decreased more than expected.* However, we have not been able to show the presence of a complex between a cyanate and magnesium bromide. The only products obtained when the reactants are mixed are magnesium cyanate and alkyl bromide. This result is due to nucleophilic attack of the halide ion on the cyanate, a wellknown proc-

* The contribution to the k_{obs} -value from the reaction between isobutyl cyanate and dibutylmagnesium present in 0.100 M "butylmagnesium bromide" can be calculated to be ca. 1.5 s⁻¹. The concentration of dibutylmagnesium in 0.100 M "butylmagnesium bromide" is ca. 0.0032 M for $K_s = 1 \times 10^{-3}$ (Ref. 4). The calculation of the contribution to the k_{obs} -value is made with the assumption that $k_{obs}(R_2Mg)$ is linearly dependent on the initial concentration of dibutylmagnesium in the interval 0–0.1 M; thus $k_{obs} = 47 \times 0.0032 / 0.100 = 1.5$ s⁻¹.

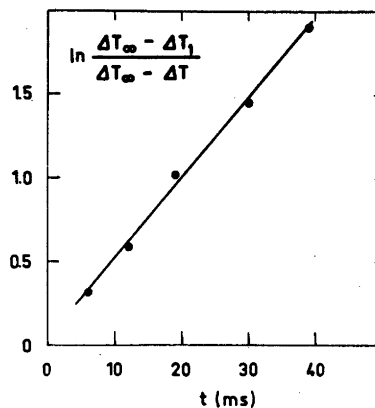


Fig. 5. Plot of $\ln (\Delta T_\infty - \Delta T_1) / (\Delta T_\infty - \Delta T)$ versus the reaction time, t , for the reaction of isobutyl cyanate with excess dibutylmagnesium in diethyl ether at 25 °C ($c^0_{i-C_4H_9OCN} = 0.010$ M and $c^0_{(C_4H_9)_2Mg} = 0.100$ M).

ess,^{5,6} but of course primary complex formation is still possible.

As shown above (Figs. 2 and 4) the pseudo first order rate constant is not linearly dependent on the initial concentration of the reactant in excess, regardless of whether it is the Grignard reagent or the alkyl cyanate. We therefore conclude that complexes between the cyanate

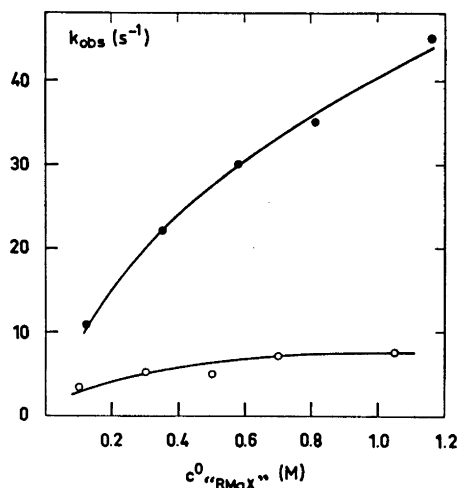


Fig. 6. Plot of the pseudo 1st order rate constant versus the initial concentration of the Grignard reagent for the reactions of isobutyl cyanate with "methylmagnesium bromide" (○) and "ethylmagnesium bromide" (●) in diethyl ether at 25 °C ($c^0_{i-C_4H_9OCN} = 0.010$ M).

Table 2. Pseudo first order rate constants for the reaction of 0.010 M isobutyl cyanate with Grignard reagents and dibutylmagnesium in diethyl ether at 25°C ($c^0_{\text{RMgX}} = c^0_{\text{R}_2\text{Mg}} = 0.100$ M).

"RMgX" or R ₂ Mg	k _{obs} (s ⁻¹)
" <i>p</i> -CH ₃ C ₆ H ₄ MgBr"	619
"C ₆ H ₅ MgBr"	244
" <i>p</i> -ClC ₆ H ₄ MgBr"	85
(C ₄ H ₉) ₂ Mg	47
"C ₂ H ₅ MgBr"	10
"C ₂ H ₅ MgBr"	4.4
"CH ₃ MgBr"	3.5
" <i>t</i> -C ₄ H ₉ MgCl"	< 3.5

and the magnesium species in the Grignard reagent have been formed.

In Fig. 6 are shown plots of the pseudo first order rate constant *versus* the initial concentration of the Grignard reagent for the reactions of isobutyl cyanate with "methylmagnesium bromide" and "ethylmagnesium bromide". The pseudo first order rate constant is not linearly dependent on the initial concentration of the Grignard reagent in these cases either. Therefore the mechanism of the reactions of isobutyl cyanate with these Grignard reagents is assumed to be the same as for the reaction with "butylmagnesium bromide".

Alkyl cyanates are found to react faster with aromatic Grignard reagents than with dibutylmagnesium and with aliphatic Grignard reagents (Table 2). An electron-donating substituent (CH₃) in the *p*-position of a "phenylmagnesium bromide" increases the reactivity, and on *p*-substitution with an electron-attracting group (Cl) the reactivity decreases (Table 2). From the k_{obs} -values and the Hammett *sigma* values a reaction constant of *ca.* -1.5 is

calculated signifying electron deficiency at the magnesium carbon atom in the transition state. This effect of substitution is only slightly more pronounced than what we have found in reactions of phenyl cyanate with *p*-substituted "phenylmagnesium bromides". In this case the constant is *ca.* -0.8.⁷

A free radical mechanism for the reaction between alkyl cyanates and Grignard reagents can be excluded for the same reasons discussed in another paper⁷ concerning the reaction between aryl cyanates and Grignard reagents.

Since complex formation takes place in these reactions two alternatives are possible which are kinetically indistinguishable. 1. A complex is formed in equilibrium with the starting materials. Rate-determining decomposition of the complex leads to products. 2. The complex formed is in equilibrium with the reactants but it does not lead to products but represents a "blind alley".

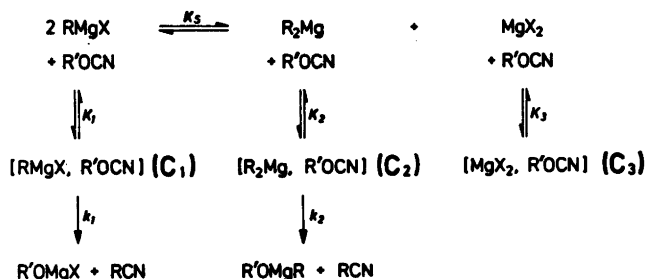
From the rate expression $v_{\text{obs}} = k_{\text{obs}} \times [\text{R}'\text{OCN}]_{\text{total}} = k_{\text{obs}}([\text{R}'\text{OCN}] + [\text{C}_1] + [\text{C}_2] + [\text{C}_3])$ together with $v = k_1[\text{C}_1] + k_2[\text{C}_2]$ and $v = k_1 \times [\text{RMgX}][\text{R}'\text{OCN}] + k_2[\text{R}_2\text{Mg}][\text{R}'\text{OCN}]$, respectively, for Scheme 1 and 2 the following equation is derived:

$$\frac{1}{k_{\text{obs}}} = \frac{1}{k'} \times \frac{1}{[\text{RMgX}]} + \frac{k''}{k'} \quad (1)$$

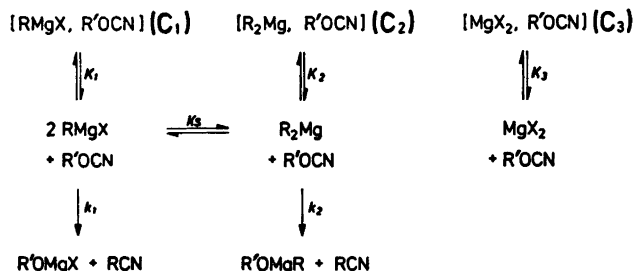
In case 1, $k' = k_1K_1 + k_2K_2K_3^{\frac{1}{2}}$ and $k'' = K_1 + (K_2 + K_3)K_3^{\frac{1}{2}}$. In case 2, $k' = k_1 + k_2K_3^{\frac{1}{2}}$ and $k'' = K_1 + (K_2 + K_3)K_3^{\frac{1}{2}}$.

As seen from Fig. 7 good agreement with eqn. (1) is obtained when $1/k_{\text{obs}}$ is plotted against $1/[\text{RMgX}]$, supporting the assumption of reversible complex formation.

The reactions between alkyl cyanates and Grignard reagents leading to nitriles and alco-

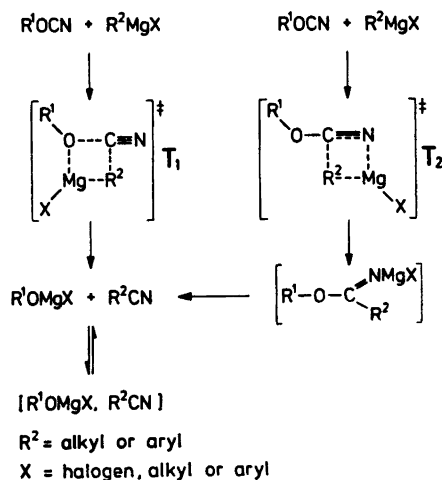


Scheme 1.



Scheme 2.

holates are strongly exothermic whereas complex formation between MgX_2 and cyanate does not give rise to any noticeable evolution of heat. According to the Hammond principle⁸ the transition states leading to products should therefore be more similar to the reactants than to the products and likewise more similar to the complexes. Two transition states T_1 and T_2 in accordance with this formulation leading to the observed products have been visualized in Scheme 3. It is clearly not possible to distinguish between those two alternatives from the kinetics or from the final products. However, the presence of an intermediate such as the imido-ester salt shown in Scheme 3 certainly would point to the likelihood of T_2 . Despite numerous



Scheme 3.

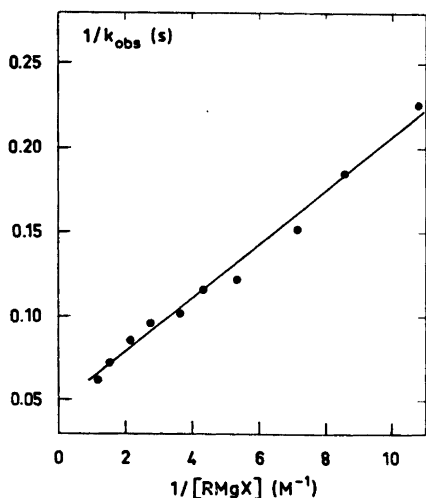


Fig. 7. Plot of $1/k_{\text{obs}}$ versus $1/[\text{RMgX}]$ for the reaction of isobutyl cyanate with excess "butylmagnesium bromide" in diethyl ether at 25 °C ($c_{\text{I-C}_4\text{H}_9\text{OCN}} = 0.010 \text{ M}$).

attempts¹ it has, however, not been possible to obtain any evidence for this substance and no distinction between T_1 and T_2 can thus be made.

EXPERIMENTAL

All Grignard reagents were prepared in diethyl ether distilled from lithium aluminium hydride directly into the glass apparatus. This solvent was used in all experiments. The magnesium used (monosublimed, Dow Chemical Corp.) was washed with anhydrous diethyl ether. Every precaution was taken against oxygen and moisture. The halides used in the preparation of the Grignard reagents were distilled or recrystallized and their purity checked gas-chromatographically. Grignard reagents were always prepared with an excess of magnesium. The molarity of the Grignard reagents was determined by titration with standard acid and the content of halogen by titration with standard silver nitrate. The content of halogen was never more than 4 % higher than the content of Grignard reagent.

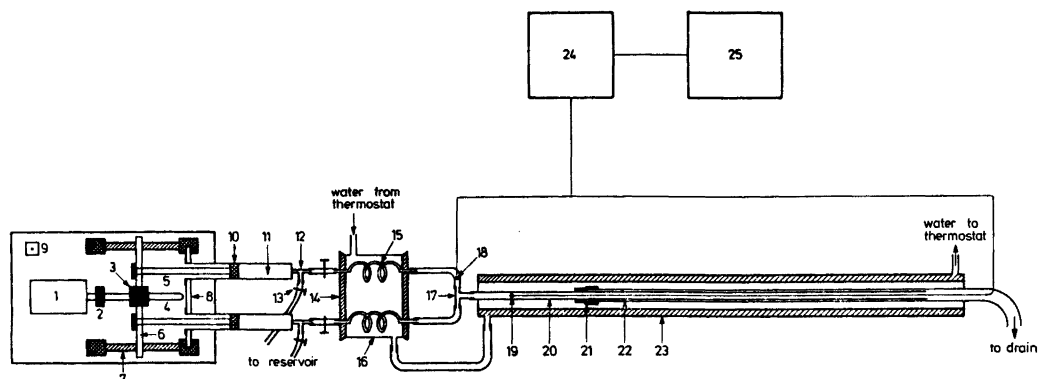


Fig. 8. Schematic drawing of the apparatus used for the kinetic measurements.

The different concentrations were obtained by dilution of *ca.* 2 M standard solutions.

The alkyl cyanates were prepared from 5-alkoxy-1,2,3,4-thiazotriazoles.^{9,10} The purity of the cyanates was checked by infrared and nuclear magnetic resonance spectroscopy and elemental analysis.

Dibutylmagnesium was prepared from "butylmagnesium chloride" and butyllithium.¹¹ Magnesium bromide etherate was prepared from 1,2-dibromoethane and magnesium.¹²

Explanation of Fig. 8: 1. Berger synchronous motor, type RSM 65 NG, 220 V, geared down to 60 rpm; 2. Ball bearing; 3. Brass bushing with 14 mm thread, 1 mm pitch; 4. Shaft with 14 mm thread, 1 mm pitch; 5. Piston rod; 6. Crossbar driving the pistons back and forth; 7. Guide rod; 8. Stand for piston cylinders; 9. Switch; 10. Teflon piston; 11. Metrohm piston cylinder; 12. Stainless steel T-tube, diameter 0.6 mm; 13. Clamp; 14. Rubber stopper; 15. Stainless steel tubing, diameter 0.6 mm, length 1.5 m; 16. Glass cylinder with circulating water from a thermostat; 17. Stainless steel T-tube, diameter 0.6 mm; 18. Reference thermocouple of copper-constantan; 19. Measuring thermocouple of copper-constantan; 20. Reaction tube, diameter 0.75 mm (Polystan polyethylene tubing); 21. Rubber tubing for fastening the outlet tubing to which the measuring thermocouple is fastened; 22. Outlet tubing; 23. Thermostated glass cylinder (air bath); 24. Philips DC-microvoltmeter PM 2436; 25. Philips recorder PM 8100. The thermocouples were soldered with tin. With 50 ml Metrohm piston cylinders a flow rate of 2788 mm/s is obtained; with 20 ml cylinders, the rate is 1152 mm/s.

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