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# $Cp_2TiCl_2$-CATALYZED REACTION OF GRIGNARD REAGENTS WITH ISOCYANATES, FORMATION OF CARBOXAMIDE WITH REARRANGED CARBONSKELETON

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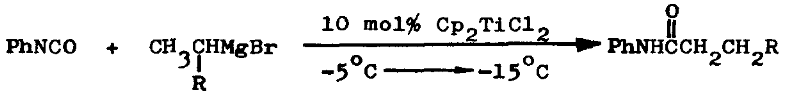
Summary: Isocyanates react with isopropyl or sec-butylmagnesium bromide in the presence of a small amount of $Cp_2TiCl_2$ to afford amides with normal alkyl group. A possibl mechanism for this reaction is proposed.

$Cp_2TiCl_2$ has recently received more and more attention in organic synthesis. Sato and his co-workers have reported $Cp_2TiCl_2$-catalyzed reaction of Grignard reagents with several kinds of organic substrates[1]. Recently we also described $Cp_2TiCl_2$-catalyzed reduction of imines to amines with isopropylmagnesium bromide[2]. Now we wish to report a novel reaction of $\alpha$-methylalkylmagnesium bromides with phenylisocyanate in the presence of a small amount of $Cp_2TiCl_2$ to give only normal carboxanilides of the rearranged carbonskeleton, with no trace of anilides with the original alkyl group.



$$\text{PhNCO} + CH_3\underset{R}{\underset{|}{C}}HMgBr \xrightarrow[-5^{\circ}C \longrightarrow -15^{\circ}C]{10\ mol\%\ Cp_2TiCl_2} PhNH\overset{O}{\overset{\|}{C}}CH_2CH_2R \qquad (1)$$

General procedures are as follows: The reaction was performed under nitrogen. To an ether solution of isopropylmagnesiun bromide (22 mmol) and $Cp_2TiCl_2$ (2.2 mmol) phenylisocyanate (14 mmol) in ether was added dropwise at ca. $-10^{\circ}C$ over about 40 min, then stirred for 30 min at the same temprature. After normal work-up, n-butylanilide was obtained in 68% yield. The results of reactions of phenylisocyanate and thioisocyanates with some alkylmagnesium bromides are summarized in Table I.

By analogy with the mechanism suggested for $Cp_2TiCl_2$-catalyzed olefine isomerization[3], we suggest that the catalytic reaction involves an equilibrium between two forms of $Cp_2TiR$ and proceeds through the mechanism shown in Scheme I. In the first step, isopropylmagnesium bromide reacts with $Cp_2TiCl_2$ to form the isopropyltitanium compound (1), Which establishes an equilibrium with the n-propyltitanium compound (3) via the $\pi$-complex 2. In the next step, phenylisocyanate inserts into 3 to form aminotitanium compound (4), and then, in the last step, metal-exchange of 4 with isopropylmagnesium bromide gives the aminomagnesium compound (5) with reproduction of 1 (Path A). Another possible insertion of isocyanate into 1 (Path B) is decelerated presumably because of the steric hindrance around the titanium in 1[4]. Under the same conditions, the exclusive formation of normal carboxanilide in the reaction of normal alkylmagnesium bromides with phenylisocyanate (Run III and IV in Table I) may support the view.

When the reactant was the thioisocyanates (Run VI and VII in Table I), both normal and rearranged products were obtained. This result is explained by as-

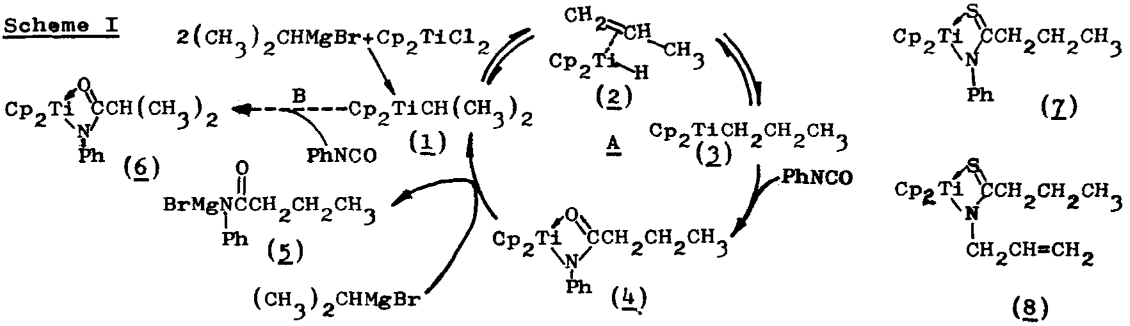
TABLE I $RNCO(S) + R^1MgBr \xrightarrow{10\ mol\%\ Cp_2TiCl_2} RNH\overset{O}{\overset{\|}{C}}R^2$ [a]

| No. | Substrates | $R^1$ | $R^2$ in rearranged product | $R^2$ in normal product | total yield (%)[b] | ratio of rearranged and normal product[d] |
|---|---|---|---|---|---|---|
| I | PhNCO | $(CH_3)_2CH$- | $CH_3CH_2CH_2$- | ——— | 68 | 100:0 |
| II | PhNCO | $CH_3CH_2CH(CH_3)$- | $CH_3(CH_2)_2CH_2$- | ——— | 59[c] | 100:0 |
| III | PhNCO | $CH_3CH_2CH_2$- | ——— | $CH_3CH_2CH_2$- | 71 | 0:100 |
| IV | PhNCO | $CH_3(CH_2)_2CH_2$- | ——— | $CH_3(CH_2)_2CH_2$- | 64[c] | 0:100 |
| V[e] | PhNCO | $(CH_3)_2CH$- | $CH_3CH_2CH_2$- | ——— | 85 | 100:0 |
| VI | PhNCS | $(CH_3)_2CH$- | $CH_3CH_2CH_2$- | $(CH_3)_2CH$- | 66[c] | 55:45 |
| VII | $CH_2$=$CHCH_2NCS$ | $(CH_3)_2CH$- | $CH_3CH_2CH_2$- | $(CH_3)_2CH$- | 67[c] | 56:44 |

a. reaction II and IV run at -10°C ⟶ -15°C, others run at -5°C ⟶ -10°C; b. isolated yield; c. determined on distilled product; d. determined by ¹H NMR; e. ratio of $Cp_2TiCl_2/R^1MgBr$ is 1:2.

suming that the thioaminotitanium compounds (7 and 8) are more stable than the corresponding oxygen compound (4), and their exchanges with isopropylmagnesium bromide are not as easy as that of 4 to release the catalytic species, $Cp_2TiCH(CH_3)_2$. Therefore some of the thioisocyanates in the reaction have to react directly with isopropylmagnesium bromide, and the carboxanilides with unrearranged carbonskeleton are formed. Support for this direct reaction of thioisocyanates with isopropylmagnesium bromide, but not through Path B, is provided by the observation that no normal addition products were found when the amount of $Cp_2TiCl_2$ is increased to 50 mol%.

Scheme I



Transition metal catalyzed rearrangement of Grignard reagents has seldom been found[5]. This reaction may be of importance for studying the mechanism of organometallic complex-catalyzed reaction.

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