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Cp_2TiCl_2-CATALYZED REACTION OF GRIGNARD REAGENTS WITH ISOCYANATES, FORMATION OF REDUCTION-COUPLING PRODUCT OF ISOCYANATES[*]

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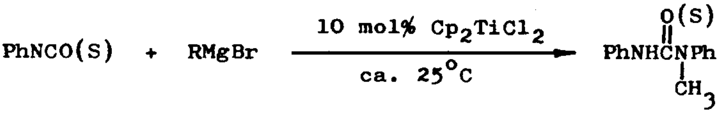
Abstract: Phenylisocyanate and phenylthioisocyanate react with Grignard reagents in the presence of a small amount of Cp_2TiCl_2 at room temperature to afford reduction-coupling products, N-methyl-N,N'-diphenylurea and N-methyl-N,N'-diphenylthiourea.

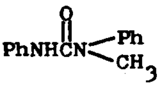
In previous paper[1] we have shown that at ca. -15°C - -5°C isocyanates react with α-methylalkylmagnesium bromides in the presence of a small amount of Cp_2TiCl_2 to form amides with rearranged carbonskeleton. Now we found that the completely different products are obtained when this reaction is carried out at room temperature. In this paper we present the formation of N-methyl-N,N'-diphenylurea and N-methyl-N,N'-diphenylthiourea in the Cp_2TiCl_2-catalyzed reaction of Grignard reagents with isocyanates.



$$\text{PhNCO(S)} + \text{RMgBr} \xrightarrow[\text{ca. } 25^\circ\text{C}]{10\text{ mol\% } Cp_2TiCl_2} \text{PhNH}\overset{\text{O(S)}}{\overset{\|}{\text{C}}}\underset{\text{CH}_3}{\underset{|}{\text{N}}}\text{Ph}$$

The following example represents a typical experiment procedure: The reaction was performed under nitrogen. An ether solution of isobutylmagnesium bromide (24.2 mmol) and Cp_2TiCl_2 (2.4 mmol) was stirred at 0°C for 5 min and then at 25°C for 10 min. To it phenylisocyanate (15.1 mmol) was added dropwise over about 2 hr., then stirred about 1 hr. at the same temperature. After normal work-up, N-methyl-N,N'-diphenylurea was obtained in 82% yield.

Table I Catalytic Reduction-coupling of Isocyanates

No	Substrates	R in RMgBr	Reduction-coupling Product [b]	Yield (%) [a]	Addition Product Yield (%)
I	PhNCO	$(CH_3)_2CHCH_2$-	 $\text{PhNH}\overset{\text{O}}{\overset{\|}{\text{C}}}\underset{\text{CH}_3}{\underset{|}{\text{N}}}\text{Ph}$	82	0
II		$(CH_3)_2CH$-		68	0
III		$CH_3CH_2(CH_3)CH$-		78	0
IV		$CH_3CH_2CH_2CH_2$-		63[c]	31[c]
V		$CH_3CH_2CH_2$-		50[c]	25[c]
VI	PhNCS	$(CH_3)_2CHCH_2$-	 $\text{PhNH}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{N}\begin{matrix}\text{Ph}\\ \text{CH}_3\end{matrix}$	95	0
VII		$(CH_3)_2CH$-		88	0

a. isolated yield; b. satisfied M.P., IR, 'H NMR and element analysis are obtained; c. determined by 'H NMR.

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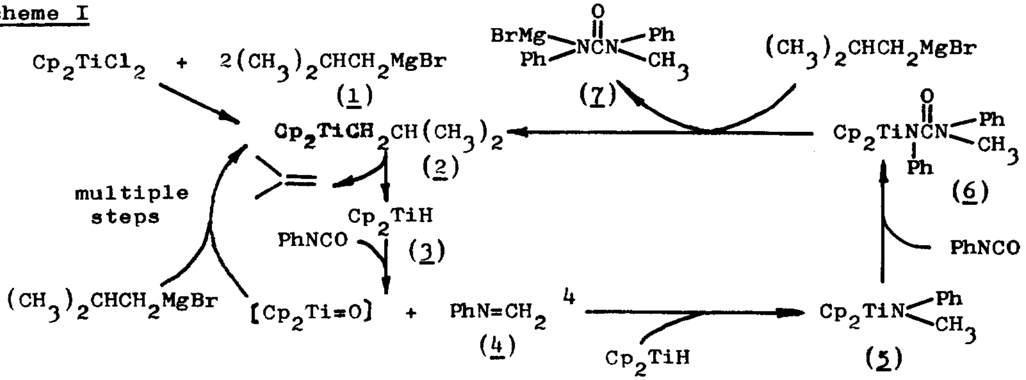
By analogy with the mechanism suggested for Cp_2TiCl_2-catalyzed reduction of carbonyl compounds[2], and deoxygenation of CO_2[3] and PhNCO[4] with $Cp_2Zr(H)Cl$, we suggest that the principal intermediate of this catalytic reduction-coupling reaction to be Cp_2TiH. The possible explanation is as follows:

Scheme I



As shown in Scheme I, there are two active intermediates, Cp_2TiR and Cp_2TiH, in the catalytic cycle. Cp_2TiR(2) can exist only at low temperature and is the species of addition to PhNCO[1]. While at room temperature, if R has active β-hydrogen, Cp_2TiR is not stable and can easily be decomposed to Cp_2TiH that reacts with PhNCO to form reduction-coupling product, N-methyl-N,N'-diphenylurea. Support for above reaction cycle is that the products obtained and the yield of reduction-coupling product are depended on R group in Cp_2TiR and the reaction temperature. For example, when reaction was carried out even at -5°C for $(CH_3)_2CHCH_2MgBr$ in which β-hydrogen can be eliminated more easily than that in the others[2], only reduction-coupling product was formed, but for $CH_3(CH_2)_3MgBr$ and $CH_3(CH_2)_2MgBr$ the reaction formed only addition product at -5°C and produced a mixture of reduction-coupling product and addition product even at ca. 25°C(Run IV and V). By the way it is also found that the ratio of reduction-coupling product and alkyl-rearranged addition product for $(CH_3)_2CHMgBr$ and $CH_3CH_2(CH_3)CHMgBr$ depended on the reaction temperature between -5°C - 10°C and that for CH_3MgBr and CH_3CH_2MgBr only direct addition products were found because there is no β-hydrogen or the β-hydrogen is not easily eliminated.

This reaction may be of importance for studying the mechanism of organometallic complex-catalyzed organic reaction, and also provide a method to synthesize N-methyl-N,N'-diphenylurea and N-methyl-N,N'-diphenylthiourea[5].

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