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A catalyst system for the formation of amides by reaction of carboxylic acids with blocked isocyanates

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Abstract—A catalyst for the reaction of blocked isocyanates (blocking agent diisopropylamine and dimethyl pyrazole) and carboxylic acids was identified. Magnesium and in some instances calcium salts proved to be highly active as catalyst. This reaction gives amides in quantitative yield and excellent selectivity and is suitable for coating and general chemical purposes.

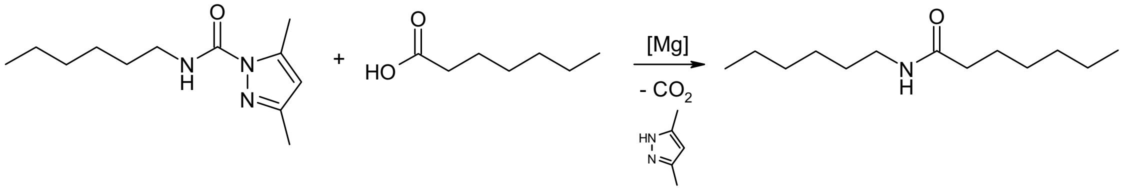
1. Introduction

When we were investigating the possibility of making polyamide coatings by the reaction of carboxylic acids with aliphatic isocyanates[1] we noticed that this particular reaction was dramatically accelerated by magnesium and calcium salts. The reaction of isocyanates with carboxylic acids is very fast and in most cases finished after one hour. To obtain systems that could be stored for a period of up to 6 months, for polymer applications we worked with blocked isocyanates that are commonly used in the industry (isocyanates, to which a suitable agent is attached that is released upon heating to liberate the original isocyanate).[3] However, this requires a catalyst for the reaction of blocked isocyanates with carboxylic acids. The result is the formation of amides from blocked isocyanates with carboxylic acids, and this methodology can be made use of apart from polymer applications.

The reaction of carboxylic acids with blocked isocyanates is known in principle, however it was used only once.[2] Described is a reaction of a primary carboxylic acid with an imidazole blocked isocyanate. This reaction gives the possibility of an N-activation (which is otherwise difficult to achieve) in peptide synthesis. The best yield reported was 70% for a reaction taking 8 h at 80 °C. In this study, we wish to report a catalytic version of this reaction (Scheme 1).

2. Catalyst screening

The reaction of blocked isocyanates with carboxylic acids to give polyamide coatings has not yet been used in the polymer case, but seemed us to be intriguing when it could be done at reasonable coating application conditions (140 °C, 30 min) with the help of a catalyst, since polycarboxylic acrylates and blocked isocyanates are



Scheme 1. Reaction of a dimethyl pyrazole blocked isocyanate with a carboxylic acid in the presence of magnesium ions.

Keywords: Blocked isocyanate; Amide; Magnesium salts; Catalyst screening.

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Table 1. Catalyst screening for the reaction of dimethyl pyrazole blocked hexyl isocyanate with heptanoic acid (conversion)

Catalyst	Turnover (%)	Anhydride (%)	Amide (%)
Magnesium triflate	100	0	100
Calcium triflate	79	62	17
Molybdenum(VI) dioxide bis(acetylacetonate)	53	47	6
Tin triflate	73	71	2
Zinc triflate	81	81	0
DBTL (dibutyltin dilaurate)	42	42	0
Zinc 2-ethylhexanoate	54	54	0
Lithium triflate	58	58	0
Ammonium molybdate	49	49	0
Without catalyst	49	49	0

Reaction conditions: Dimethylpyrazole blocked hexyl isocyanate and heptanoic acid were solved in chloroform (50% solid content). The reaction mixture was refluxed for 60 min. Magnesium triflate (1 wt %) was used; other catalysts were used in the same molar amount based on 1 wt % of magnesium triflate. Five gram scale, ratio carboxylic acid to blocked isocyanates is 1:1.

readily available. Therefore a small catalyst screening was performed. A model system consisting of dimethyl pyrazole (blocking agent for high quality polyurethane one component systems) blocked hexyl isocyanate and heptanoic acid was chosen. Yields were determined using ^{13}C NMR spectroscopy.

A number of catalysts accelerate the reaction of carboxylic acids with the blocked isocyanate (see Table 1). However, the reaction stops on the stage of the mixed anhydride (see Scheme 2). Only with calcium and especially with magnesium salts, the anhydride undergoes extrusion of carbon dioxide to form the amide. The reaction goes to completion within 20 min and is 100% selective (Table 2).

When diisopropylamine is used as a blocking agent, no formation of the anhydride is observed. In the case of the DIPA blocked polyisocyanates, good results are achieved using both calcium and magnesium catalysts, however overall yields are only half of dimethyl pyrazole, which is due to the basic character of the amine.

This methodology can be used for the formation of a series of amines starting from blocked isocyanates (Table 3).

Table 2. Results of the reaction of diisopropylamine blocked hexyl isocyanate with heptanoic acid

Catalyst	Yield (%)
Magnesium triflate	45
Calcium triflate	40
Zinc triflate	5
Molybdenum(VI) dioxide bis(acetylacetonate)	5
Tin triflate	0
DBTL (dibutyltin dilaurate)	0
Zinc-2-ethylhexanoate	0
Ammonium molybdate	0
Lithium triflate	0
Without catalyst	0

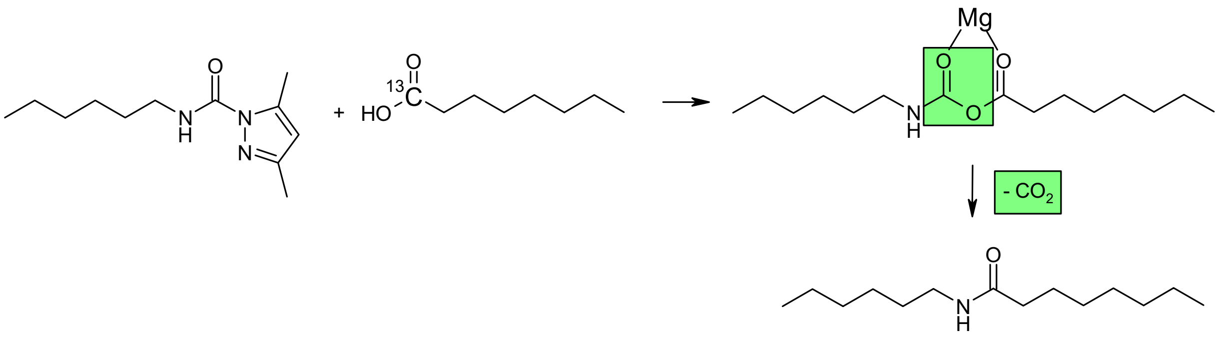
Reaction conditions: Diisopropylamine blocked hexyl isocyanate and heptanoic acid were solved in butyl acetate (50% solid content). The reaction mixture was heated for 60 min to 90 °C. Magnesium triflate (1 wt %) was used; other catalysts were used in the same molar amount based on 1 wt % of magnesium triflate. Five gram scale, ratio carboxylic acid to blocked isocyanates is 1:1.

In the case of the dimethyl pyrazole blocked phenyl isocyanate little or no reaction occurred in reactions with propiolic acid due to polymerisation, acrylic acid, trimellit acid anhydride, most probably due to insufficient nucleophilicity, however good reaction was observed with cinnamic acid (yield 75%).

In the case of the dimethyl pyrazole blocked hexyl isocyanate little or no reaction was observed with hydroxypivalic acid and pyrrole 2-carboxylic acid.

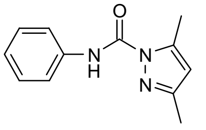
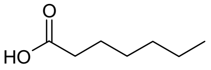
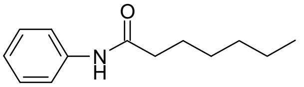
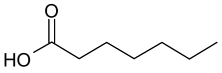
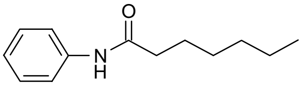
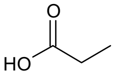
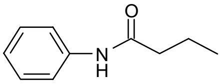
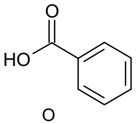
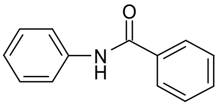
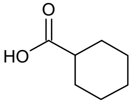
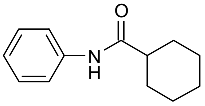
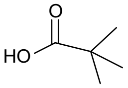
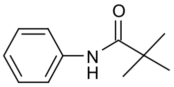
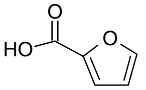
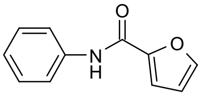
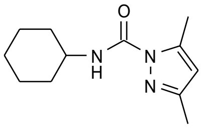
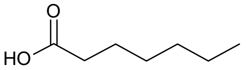
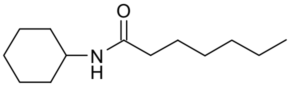
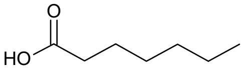
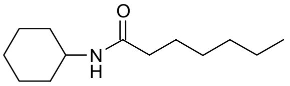
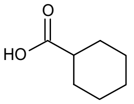
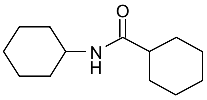
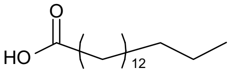
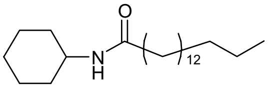
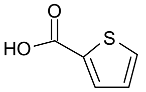
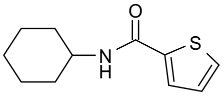
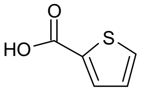
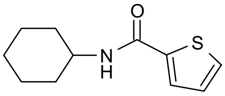
When ^{13}C marked octanoic acid (1-^{13}C-octanoic acid) is used as a acid in the reaction with a blocked isocyanate it can be ascertained that after the reaction, which means after the extrusion of carbon dioxide from the intermediate, the ^{13}C labelling remained in the product. Thus the carbon dioxide stems from the blocked isocyanate.

When transferring these results to the polymer case it was found that the catalysis of this reaction is possible only in the presence of a magnesium salt. Other metal salts proved not to be suitable as catalysts. When a carboxylic acid functional polyacrylate is used as a binder, a film can be obtained from the reaction of a dimethyl pyrazole blocked hexamethylene diisocyanate trimer (Desmodur N3300), which is resistant against chemicals and shows a considerable 'slip' on its surface as it is typical for



Scheme 2. Reaction of a carboxylic acid with blocked isocyanates.

Table 3. Formation of amides starting from blocked isocyanates and carboxylic acids[4]

Entry	Blocked isocyanate	Carboxylic acid	Product	Yield (%)	Cat. (%)	Temperature (°C)
1				93	1.0	110 °C/16 h
2				40 (GC)	w/o cat.	110 °C/16 h
3				86	1.0	110 °C/12 h
4				80	1.0	110 °C/12 h
5				80	1.0	110 °C/12 h
6				54	1.0	110 °C/12 h
7				62	1.0	110 °C/16 h
8				80	1.0	110 °C/16 h
9				7	w/o cat.	110 °C/12 h
10				75	1.0	110 °C/24 h
11				91	1.0	110 °C/24 h
12				55	1.0	110 °C/15 h
13				6 (GC)	w/o cat.	110 °C/15 h

polyamide films. Even at a curing temperature of 140 °C, very little thermal yellowing is observed. Surprisingly even at a film thickness of 120 μm (wet, as obtainable by use of a coating knife) no bubbles of CO_2 were found in the film. This reaction also works with butanone oxime blocked isocyanates (e.g., Desmodur BL 3175), however the coating systems tend to yellow upon curing.

3. Conclusion

Magnesium salts were identified as highly active catalysts for the reaction of blocked isocyanates (blocking agent diisopropylamine and dimethyl pyrazole) with carboxylic acids. This reaction gives amides in quantitative yield and excellent selectivity and can be used for coating purposes for low temperature curing polyamide coatings.

Acknowledgement

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References and notes

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2. Gante, J. *Angew. Chem.* **1966**, *78*, 334.
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4. Experimentals: solvent: toluene, ratio blocked isocyanate: carboxylic acid 1:1, 10 g scale. Workup method (A): Remove toluene, recrystallise from stated solvent, filter off precipitate/product. Workup method (B): Remove toluene, precipitate dimethyl pyrazole in suitable solvent (0–7 °C), filtration and removal of solvent. Entry **1**: (B), 0.04 mol recrystallised from 50 g *n*-hexane. Compound **3**: (A), 0.02 mol dissolved in 15 ml *tert*-butyl methylether (TBME) and 5 ml methyl-cyclohexane. Compound **4**: (A 2×), 0.017 mol dissolved in 15 ml TBME and 5 ml methyl-cyclohexane. Compound **5**: (A 2×), 0.017 mol dissolved in 15 ml TBME and 5 ml methyl cyclohexane. Compound **6**: (A 2×), 0.02 mol dissolved in 15 ml TBME and 5 ml methyl cyclohexane. Compound **7**: (A), 0.043 mol dissolved in 30 g cyclohexane and 2 g TBME. Compound **8**: (B), 0.042 mol product dissolved in 100 g *n*-hexane, precipitation. Compound **10**: (A), 0.03 mol product dissolved in 100 g methyl cylohexane and 2 g TBME. Compound **11**: (A), 0.028 mol dissolved in 100 g methyl cylohexane and 2 g TBME. Compound **12**: (B), 0.041 mol dissolved in 30 g *n*-hexane, precipitate at 5 °C contains 76.5% product. Yield given are isolated yields.