# Multivalent Metal Salts as Versatile Catalysts for the Amidation of Long-Chain Aliphatic Acids with Aliphatic Amines

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**Abstract:** Multivalent metal salts, such as ferric chloride and sulfate, are active and versatile catalysts for the amidation of aliphatic fatty acids with long-chain aliphatic amines.

**Key words:** multivalent metal salts, FeCl<sub>3</sub>·6H<sub>2</sub>O, amidation, longchain aliphatic acid, aliphatic amine

*N*-Alkyl fatty acid amides, such as *N*-decylhexadecanamide, are important chemical substances for photographic materials, polyolefin foaming materials, polymer stabilizers, photocurable developers and pigments.<sup>1</sup> *N*-alkylcarboamides have been prepared by many classical methods,<sup>2–5</sup> such as the reaction of carboxylic acid esters with amines, acid chlorides or anhydrides with amines, and the direct reactions of acids with amines. In most of the methods, a large excess of either the carboxylic acid or the amine is essential in order to achieve high yields of amides, and tedious work-up procedures are required to obtain the reaction products. Since it is not practical to use large amounts of condensing reagents in larger scale productions, there is a need to develop new methods for environmentally friendly amidation processes.

Recently, Ishihara and Yamamoto have developed new catalysts, such as *N*-alkyl-4-(borono)pyridinium salts, 3,5-bis(perfluorodecyl)phenylboronic acid, and 4,5,6,7-tetrachlorobenzo[d][1,3,2]dioxaborol-2-ol, for the preparation of amides from equimolar mixtures of carboxylic acids and amines.<sup>6,7</sup> Some of these catalysts are highly active and recyclable in fluorinated solvent.<sup>7</sup> Catalysts derived from boric acid, arylboronic acid and borane have also been developed for the amidation of N-substituted carboamides.<sup>8</sup>

We previously described the use of some highly catalytically active multivalent metal salts, such as zirconyl and ferric salts, for the esterification of long-chain fatty acids with long-chain aliphatic alcohols.<sup>8</sup> Here, we describe their application to the amidation of long-chain fatty acids with long-chain aliphatic amines, and propose that a number of them, particularly ferric salts, are highly active and versatile catalysts for amidation even when equimolar amounts of acid and amine are present. Figure 1 shows the performance of a range of metal chloride catalysts in the amidation of palmitic acid with decylamine in refluxing mesitylene. The yield of palmitic acid in the absence of catalyst was approximately 20% after 6 and 24 hours. All the multivalent metal salts examined were active for the amidation, with the catalytic activity over 6 hours decreasing in the order: FeCl<sub>3</sub>·6H<sub>2</sub>O > ZnCl<sub>2</sub> > NiCl<sub>2</sub>·6H<sub>2</sub>O  $\approx$  MnCl<sub>3</sub>·6H<sub>2</sub>O > CoCl<sub>2</sub>·6H<sub>2</sub>O > ZrCl<sub>3</sub> · CrCl<sub>3</sub>·6H<sub>2</sub>O > ZrOCl<sub>2</sub>·8H<sub>2</sub>O > CuCl<sub>2</sub>·4H<sub>2</sub>O > InCl<sub>3</sub> > AlCl<sub>3</sub>·6H<sub>2</sub>O >> none. FeCl<sub>3</sub>·6H<sub>2</sub>O was thus found to be the most active among the multivalent metal chlorides.



**Figure 1** The amidation of palmitic acid with decylamine catalyzed by multivalent metal chlorides. *Reaction conditions*: metal salt (0.12 mmol), palmitic acid (6.0 mmol), decylamine (6.0 mmol), mesitylene (40 mL), reflux.

Table 1 summarizes the influence of a range of aromatic hydrocarbon solvents on the amidation of palmitic acid with decylamine catalyzed by  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  under reflux. The conversions of palmitic acid were less than 20% even in mesitylene under reflux. The catalytic activity was found to be dependent on the solvent: the reaction was enhanced with increasing reaction temperature in the order: benzene << toluene < m-xylene << mesitylene.

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Table 1	Influence of	Solvent on	the Amida	ation of P	almitic A	Acid
with Decy	lamine Catal	yzed by Fe	Cl <sub>3</sub> ·6H <sub>2</sub> O <sup>a</sup>			

		Yield (	%)		
		No catalyst		FeCl <sub>3</sub> ·6H <sub>2</sub> O	
Solvent	Bp (°C)	6 h	24 h	6 h	24 h
Benzene	80	0.0	0.5	7.0	24
Toluene	110	0.7	3.2	48	78
<i>m</i> -Xylene	140	18	20	60	90
Mesitylene	160	23	24	81	94

<sup>a</sup> Reaction conditions: metal salt (0.12 mmol), palmitic acid (6.0 mmol), decylamine (6.0 mmol), solvent (40 mL), 6 h, reflux.

Table 2 summarizes the influence of metal salts on the amidation of palmitic acid with decylamine. Metal sulfates, nitrates and acetates were active for the reaction as well as chlorides, although the yields of the amides varied with the salt used. These results show that the active center for the amidation is on the metal cation and that the anionic part did not significantly influence the catalysis.

	Yield (%)				
Metal salt	Cl-	SO4 <sup>2-</sup>	$NO_3^-$	AcO <sup>-</sup>	
Fe <sup>3+</sup>	81	77	68	80	
Al <sup>3+</sup>	27	42	33	40	
In <sup>3+</sup>	37	51	52	_	
ZrO <sup>2+</sup>	51	62	67	79	
Co <sup>2+</sup>	65	52	62	71	
Ni <sup>2+</sup>	75	75	72	50	
Zn <sup>2+</sup>	76	73	55	79	

<sup>a</sup> Reaction conditions: metal salt (0.12 mmol), palmitic acid (6.0 mmol), decylamine (6.0 mmol), mesitylene (40 mL), 6 h, reflux.

The influence of chain lengths of the acid and amine are summarized in Table 3. The increase in chain length enhances the yield of the corresponding amide. Hexadecanamides from C8, C10, C12 and C14 amines were formed in about 80% yield, however, those from C16 and C18 amines were obtained in lower yields. On the other hand, decanamides from C8, C10 and C12 acids were obtained in high yields of over 90%, whereas the yields obtained from C16 and C18 acids were around 70–80%. These results indicate that FeCl<sub>3</sub>·6H<sub>2</sub>O is a versatile catalyst for the amidation of long-chain aliphatic acids and amines.

The reactions were carried out under reflux using a Dean– Stark trap to remove water as azeotropic mixtures. It is thus difficult to apply this method to lower molecular weight acids and amines due to their lower boiling points.

Table 3	Influence of Chain Length of Acid and Amine in the Ami-
dation Ca	talyzed by FeCl <sub>3</sub> ·6H <sub>2</sub> O <sup>a</sup>

Acid	Amine	Yield (%)
Palmitic acid	Octylamine	84
Palmitic acid	Decylamine	81
Palmitic acid	Dodecylamine	81
Palmitic acid	Tetradecylamine	77
Palmitic acid	Hexadecylamine	62
Palmitic acid	Octadecylamine	47
Octanoic acid	Decylamine	93
Decanoic acid	Decylamine	92
Dodecanoic acid	Decylamine	90
Myristic acid	Decylamine	92
Palmitic acid	Decylamine	81
Stearic acid	Decylamine	71

<sup>a</sup> Reaction conditions: FeCl<sub>3</sub>·6H<sub>2</sub>O (0.12 mmol), acid (6.0 mmol), amine (6.0 mmol), mesitylene (40 mL), 6 h, reflux.

When the amidation was conducted in an autoclave at 160 °C under autogeneous pressure without removing water, the yield of *N*-decylhexadecanamide from palmitic acid and decylamine (63%) was slightly lower than that observed using above method under atmospheric pressure (81%). This means that the amidation occurs smoothly in the presence of the small amounts of water formed by the reaction. The addition of 3 Å molecular sieves enhanced the amidation by removing water formed by the reaction (yields were improved from 63% to 75%). Thus, the amidation of palmitic acid with hexylamine and butylamine in the presence of molecular sieves gave yields of 86% and 81%, respectively, at 160 °C after 6 hours under autogeneous pressure.

The presence of carboxyl groups is essential for the amidation because the reaction did not occur between methyl palmitate and decylamine. These results indicate that cooperation between the carboxylic groups and the multivalent salt is related to the extent of the amidation.

The reaction mixture was yellow colored after the reaction when FeCl<sub>3</sub>· $6H_2O$  was used as catalyst. This suggests that the catalyst species are dispersed and stabilized as cationic clusters or their agglomerated colloides formed by the hydrolysis of FeCl<sub>3</sub>· $6H_2O$ , although Tyndall phenomena were not observed.<sup>10</sup> Further investigation is necessary in order to clarify the role of the catalytically active species and the mechanism of the amidation.

In summary, multivalent metal halides, typically  $FeCl_3 \cdot 6H_2O$ , are versatile catalysts for the amidation of long-chain aliphatic acids and amides under mild conditions. Further aspects of the amidation catalyzed by mul-

tivalent metal salt hydrates will be discussed in the near future.

Metal salts and all acids and amines used in this study were obtained commercially and used without further purification. The product yields were analyzed by gas chromatography using a Shimadzu Gas Chromatograph 14A, Ultra-1 ( $25 \text{ m} \times 0.3 \text{ mm}$ ; 0.33 mm thick layer) capillary column equipped with an FID. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded at 500 and 125 MHz, respectively, on a JEOL ECA-500 NMR spectrometer. IR spectra were recorded on a Nexus 470 (Thermo Nicolet) FT-IR spectrometer using KBr discs. Elemental analyses of all amides were performed at the Center for Organic Elemental Microanalysis, Kyoto University.

# Amidation of Long-Chain Carboxylic Acids with Amines; General Procedure

The amidation was carried out in a single-neck, round-bottom flask (100 mL) equipped with a Teflon-coated magnetic stirring bar and a Dean–Stark apparatus. Equimolar amounts of the substrates (long-chain primary acid and amine; 6 mmol each) and FeCl<sub>3</sub>·6H<sub>2</sub>O (0.12 mmol) in solvent (benzene, toluene, *m*-xylene, mesitylene; 40 mL) were charged into the flask and the mixture was heated to reflux temperature with continuous removal of H<sub>2</sub>O generated from the reaction. After 6 h or 24 h, the resulting reaction mixture was cooled to r.t. and an aliquot of the reaction mixture was subjected to analysis by GC in order to determine the conversion and product yield (biphenyl as a standard). The solvent was removed in vacuo from the reaction mixture and the amide product was extracted with CHCl<sub>3</sub>. The amides were purified by column chromatography using silica gel (0.063–0.2 mm; CHCl<sub>3</sub>–EtOAc, 10:1) to give the pure product.

## *N*-Octylhexadecanamide

Mp 78-79 °C.

IR (KBr): 3318, 1637 cm<sup>-1</sup>.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.9 (6 H, br t), 1.2 (34 H, br t), 1.5–1.6 (4 H, m), 2.1 (2 H, t, *J* = 7.4 Hz), 3.2 (2 H, dd, *J* = 6.9, 7.5 Hz), 5.4 (1 H, br s).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 14.0, 22.8, 26.0, 27.0, 29.4, 29.5, 29.6, 29.6, 29.7, 29.7, 29.8, 174.7.

Anal. Calcd for  $C_{28}H_{57}NO$ : C, 78.40; H, 13.43; N, 3.81. Found: C, 78.22; H, 13.29; N, 3.74.

#### N-Decylhexadecanamide

Mp 82–83 °C.

IR (KBr): 3318, 1637 cm<sup>-1</sup>.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.9 (6 H, br t), 1.3 (38 H, br t), 1.5–1.6 (4 H, m), 2.2 (2 H, t, *J* = 7.6 Hz), 3.2 (2 H, dd, *J* = 7.5, 7.6 Hz), 5.4 (1 H, br s).

 $^{13}\text{C}$  NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.2, 22.8, 26.0, 27.0, 29.4, 29.5, 29.6, 29.6, 29.7, 29.7, 29.8, 32.0, 32.0, 37.1, 40.0, 173.1.

Anal. Calcd for  $\rm C_{26}H_{53}NO:$  C, 78.92; H, 13.50; N, 3.54. Found: C, 78.97; H, 13.59; N, 3.52.

### N-Dodecylhexadecanamide

Mp 86-87 °C.

#### IR (KBr): 3315, 1637 cm<sup>-1</sup>.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.9 (6 H, br t), 1.3 (42 H, br t), 1.5–1.6 (4 H, m), 2.1 (2 H, t, *J* = 7.5, 8.3 Hz), 3.2 (2 H, dd, *J* = 6.9 Hz), 5.4 (1 H, br s).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 14.2, 22.7, 22.8, 26.0, 27.0, 29.3, 29.3, 29.4, 29.5, 29.5, 29.6, 29.7, 29.8, 29.9, 31.9, 32.0, 37.1, 39.6, 173.1.

Anal. Calcd for  $C_{24}H_{49}NO$ : C, 79.36; H, 13.56; N, 3.31. Found: C, 79.36; H, 13.6; N, 3.31.

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