The Amidation of Carboxylic Acid with Amine over Hydrous Zirconium(IV) Oxide

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Synopsis. The reaction of a carboxylic acid or an ester with an amine to give the corresponding amide was carried out efficiently over hydrous zirconium(IV) oxide, whether in the vapor phase or in the liquid phase.

Hydrous zirconium(IV) oxide is a colorless, translucent, amorphous, and hard solid. It is insoluble in organic solvents and stable at room temperature in air. In previous papers,[1–3] we reported that the reduction of aldehydes and ketones with 2-propanol proceeded efficiently over hydrous zirconium(IV) oxide. During our studies to clarify the scope and the limitations of the reaction and to characterize the hydrous zirconium(IV) oxide, it was found that the oxide could also catalyze the amidation of carboxylic acid with amine. A homogeneous catalyst such as phosphoric acid or alkoxide[4] of titanium or zirconium was ordinarily used in the amidation, but the isolation of the products involves tedious work-up procedures. On the other hand, alumina,[5–7] silica gel,[8,9] and silica-alumina have also been reported as heterogeneous catalysts of the amidation, and they had such advantages as the easy isolation of products. In order to compare the catalytic activity, amidations were carried out using hydrous zirconium(IV) oxide and other catalysts.

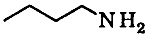
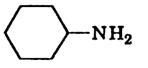
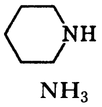
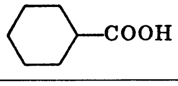
Experimental

Materials. The hydrous zirconium(IV) oxide was prepared in the manner reported earlier.[1–3] Commercial reagents were used for the amidation without further purification.

Vapor-Phase Reaction Procedure. The catalytic amidation was carried out in a glass-flow reactor (6.5 mm or 7.0 mm in diameter) with a fixed-bed catalyst: flow rate of nitrogen gas=30—60 $cm^3 min^{-1}$, catalyst=2.0 g, reaction temperature=150—200 °C. A mixture of carboxylic acid or ester, amine or aqueous ammonia (28%), and dodecane or tridecane as an internal standard was fed, by means of a microfeeder, into the reactor (5 $cm^3 h^{-1}$). In the case of the reaction with ammonia gas, a benzene solution of carboxylic acid or ester was fed an excess amount of ammonia gas. The products were then analyzed by means of gas chromatography (a capillary column; PEG 20M 30 m).

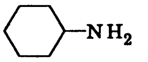
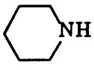
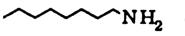
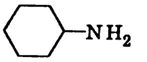
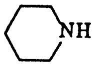
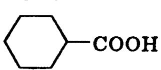
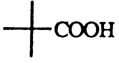
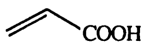
Liquid-Phase Reaction Procedure. In a 25 cm^3 round-bottomed flask equipped with a reflux condenser were placed the catalyst (2.0 g), a carboxylic acid or ester, an amine, and a hydrocarbon as an internal standard. The contents were heated under a gentle reflux. In the reaction with ammonia, excess ammonia was supplied to the reaction solution of benzene before heating. In some reactions, xylene or toluene was added to the solution in order to raise the reaction temperature. The reaction mixture was col-

Table 1. Vapor-Phase Amidations over Hydrous Zirconium(IV) Oxide[a)]

Entry	Reactant		Conditions[b)]	Temp/°C	Yield/%
1	CH_3COOH		A	200	100
2	$CH_3COOC_2H_5$		B	200	100
3	$CH_3COOC_2H_5$		B	200	100
4	$CH_3COOC_2H_5$		B	200	96
5	CH_3COOH	NH_3	C	150	97
6	C_2H_5COOH	NH_3	C	150	88
7	CH_3COOH	NH_3	C	100	—
8	CH_3COOH	NH_3	C	200	Tr[c)]
9		NH_3	C	150	—[d)]
10	C_2H_5COOH	aq. NH_3	D	150	33
11	C_2H_5COOH	aq. NH_3	D	200	53
12	CH_3COOH	aq. NH_3	E	200	58
13		aq. NH_3	E	200	57

a) Catalyst: 2.0g, N_2: 30—60 $cm^3 min^{-1}$, sample feed: 5 $cm^3 h^{-1}$. b) Conditions A: CH_3COOH: n-$C_4H_9NH_2$=1 : 5; Conditions B: $CH_3COOC_2H_5$: amine=10 : 1; Conditions C: acid: 0.20 mol dm^{-3} in benzne; Conditions D: acid: 0.20 mol dm^{-3} in aq NH_3 (28%); Conditions E: acid: 0.10 mol dm^{-3} in aq NH_3 (28%). c) Acetonitrile was mainly produced. d) Polymerization.

Table 2. Liquid-Phase Amidations with Hydrous Zirconium(IV) Oxide[a]

Entry	Reactant (mmol)				Yield/%
1	CH_3COOH	(10)		(50)	100
2[b]	CH_3COOH	(10)		(15)	60
3[c]	CH_3COOH	(10)		(15)	75
4	$CH_3COOC_2H_5$	(50)		(5)	79
5	$CH_3COOC_2H_5$	(50)		(5)	10
6	$C_2H_5COOC_2H_5$	(50)		(5)	80
7	$CH_3COOC_2H_5$	(50)		(5)	60
8[b]	C_2H_5COOH	(10)	NH_3[d]		31
9[c]	C_2H_5COOH	(10)	NH_3[d]		27
10[c]	C_2H_5COOH	(10)	NH_3[d]		51[e]
11[c]		(10)	NH_3[d]		34[e]
12[c]		(10)	NH_3[d]		44[e]
13[b]		(10)	NH_3[d]		—[f]

a) Catalyst: 2.0 g, reflux for 5 h. b) Toluene: 8 cm^3. c) Xylene: 8 cm^3. d) NH_3 was saturated in the solvent. e) NH_3 was added during the reaction. f) Polymerization.

lected after 5 hours' reflux, and the products were analyzed by means of gas chromatography. The products was identified by a comparison of their retention times with those of authentic samples.

Results and Discusion

Vapor-Phase Reaction. The results of the vapor-phase amidation of some carboxylic acids or esters with amine, ammonia, and aqueous ammonia over hydrous zirconium(IV) oxide are listed in Table 1. The amidation of acetic acid or ethyl acetate with amine gave a corresponding amide in high yields at 200 °C (Entries 1—4). The amidation of acetic acid with ammonia at 150 °C gave acetamide in a high yield (Entry 5). At 100 °C, the amidation did not proceed (Entry 7). At 200 °C, acetonitrile was mainly obtained by the subsequent dehydration of the product (Entry 8). These results suggest that the selectivity of the reaction is strongly affected by the reaction temperature. The reaction of acrylic acid with ammonia caused undesirable polymerization (Entry 9). The amidation of carboxylic acid with aqueous ammonia at 200 °C gave the corresponding amides (Entries 10—13), though in lower yields.

Liquid-Phase Reaction. The results of the liquid-phase amidation of carboxylic acid or ester with amine or ammonia over hydrous zirconium(IV) oxide are shown in Table 2. The hydrous zirconium(IV) oxide also catalyzed the amidation of carboxylic acid with ammonia in the liquid phase. Since ammonia gas was liberated under the reflux conditions, an additional supply of ammonia during the reaction could improve the yield, as is shown in the case of the amidation of propionic acid (Entry 10).

Table 3. Catalytic Activities of Several Catalysts

Catalyst	Yield/%	
	A	B
Hydrous zirconium(IV) oxide	100	100
Hydrous titanum(IV) oxide	92	63
Hydrous tin(IV) oxide	90	3
Hydrous cerium(IV) oxide	—	39
Hydrous aluminum(III) oxide	14	1
Hydrous iron(III) oxide	29	8
Hydrous niobium(V) oxide	75	24
Silica gel	87	2
Zeolite, A-4	25	8
Al_2O_3	1	2
ZrO_2	1	2
Al_2O_3-SiO_2	91	2

Catalyst: 2.0 g. A Vapor-phase: 200 °C, N_2; 60 $cm^3\ min^{-1}$, CH_3COOH: n-$C_4H_9NH_2$=1:5, sample feed; 5 $cm^3 h^{-1}$. B Liquid-phase: reflux 5 h, CH_3COOH; 10 mmol, n-$C_4H_9NH_2$; 50 mmol.

Comparison of Catalytic Activity among Several Catalysts. The liquid-phase and vapor-phase amidations of acetic acid with butylamine were carried out by using different heterogeneous catalysts. The results are shown in Table 3. In the case of vapor-phase amidation, hydrous zirconium(IV) oxide, hydrous titanium(IV) oxide, hydrous tin(IV) oxide, silica gel, and silica-alumina worked efficiently. However, only hydrous zirconium(IV) oxide acted as an efficient catalyst for the liquid-phase amidation. It was concluded that the hydrous zirconium(IV) oxide is the most active catalyst in these types of amidations.

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