Synthesis of Glycidamide from Acrylonitrile Using Basic Hydrotalcite Catalyst in the Presence of Aqueous Hydrogen Peroxide and Unsaturated Amide

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Glycidamide (GA) can be synthesized from acrylonitrile (AN) by using hydrotalcite as a solid base catalyst and 25% aqueous H_2O_2 as an oxidant, in the presence of acrylamide (AA) as a cocatalyst in methanol solvent at 313 K for 18 h. The GA yield and H_2O_2 utilization efficiency reached 74% and 60%, respectively. The hydrotalcite catalyst could be easily separated from the reaction mixture and reused at least once.

Glycidamide (GA) has epoxide and amide moieties (Scheme 1) and has the possibility for use as an industrial starting material for resins, adhesive agents, and dyes.¹ GA has been synthesized from acrylonitrile (AN) by using NaOH and aqueous (aq.) hydrogen peroxide (H_2O_2) via epoxidation of the double bond to give glycidonitrile (GN) and subsequent hydration of the nitrile moiety (Scheme 1, Route A).^{1a} Because of its high reactivity, however, it has not been industrialized till now.

The use of a heterogeneous catalyst generally makes the chemical process clean and simple because of the easy separation of the catalyst after the reaction. Here, we aim at the development of a heterogeneous catalytic system for GA synthesis from AN using aq. H₂O₂ as a clean oxidant.² We found that the basic hydrotalcite, a layered Mg–Al double hydroxide,³ exhibited high catalytic activity for GA formation when using aq. H₂O₂. The hydrotalcite is known to be a unique base catalyst that can function in aqueous media.^{3k,4} It was also found that α,β -unsaturated amides specifically facilitated the synthesis of GA from AN via Route A, as outlined in Scheme 1.

Hydrotalcites (HTs) with Mg/Al = 3.0 and 5.3 or 5.4 were supplied from Tomita Phamaceutical Co., Ltd. as AD500 (Lot. S31064) and AD500PF (Lot. R20101 or R30104), respectively. The HT with Mg/Al = 3.0 (HT-3.0) has 0.21 mmol g⁻¹ basic sites, which convert the color of brilliant cresyl blue ($pK_a = 11$) to a basic color.⁵ High-purity MgO (1000A) was purchased from Ube Industries Ltd. Further, aq. H₂O₂ and CaO (99.9%) were supplied from Wako Pure Chem. Co., Ltd. The Catalyst Society of Japan supplied γ -Al₂O₃ as JRC-ALO-8. SrO (99.9%), and Amberlyst A26 OH were purchased from Sigma Aldrich Co.,



Scheme 1. Synthetic routes for glycidamide (GA) from acrylonitrile (AN).

Ltd. Amberlyst A26 OH has 0.20 mmol g^{-1} basic sites, which could change the color of 2,4-dinitroaniline (p $K_a = 15$), indicating that the base strength of Amberlyst A26 OH is stronger than that of the HT.⁵ The reaction was performed in a 35-mL cylindrical pressure glass-tube reactor. Methanol (Kanto Chem. Co., Inc.) was used as the solvent. Products were analyzed by using a GC (GC-2014, Shimadzu) equipped with a polar DB-FFAP column (Agilent Technol. Inc.). 2-Butanol was used as an internal standard. The actual concentration of H₂O₂, determined by the iodometric titration method,⁶ was found to be 25.4%.

The reaction of AN generally gave both GA and AA (Scheme 1) when using the catalysts listed in Table 1, with methanol solvent. Table 1 shows the effect of various catalysts on the AN conversion, GA yield, and selectivity. Basic catalysts⁴ such as HT, MgO, Amberlyst A26 OH, CaO, and SrO could convert AN into AA and GA in methanol solvent. Among them, HT-5.3 exhibited the highest GA yield and selectivity (Entry 1). The moderate basicity of the HTs seems to be preferential for the GA synthesis. The use of other alcoholic solvents such as ethanol and 2-propanol also gave GA comparatively as with that using methanol.⁷

The reactions of AA as a substrate using the same HT catalyst under identical conditions at 313 and 373 K never give GA; AA remains silent during the experiment. This reaction system, therefore, cannot epoxidize AA to GA. In the present case, GA is formed via Route A in Scheme 1, via the epoxidation of AN to GN and subsequent hydration to GA (vide infra).⁸ The basic sites of the HTs convert H_2O_2 to HOO^- to promote the first epoxidation of AN.^{3f,3j}

Accordingly, we tried to optimize the reaction conditions as follows. Increasing the amount of aq. H_2O_2 over 0.75 mL resulted in a drastic decrease in the GA yield. Increases in the reaction temperature (373 K) also decreased the GA yield, due to the decomposition of H_2O_2 . The tentative maximum GA yield was only 28% with 56% selectivity (HT-5.3 0.15 g, AN 2 mmol, aq. H_2O_2 0.75 mL, methanol 3 mL, 313 K, and 13 h).⁹

Table 1. Effect of catalyst on formation of GA from AN^a

Entry	Catalyst	AN conv./%	Yield/%		Selectivity
			AA	GA	for GA/ $\%$
1	HT (Mg/Al = 5.3)	43	11	15	35
2	HT $(Mg/Al = 3.0)$	34	17	11	32
3	MgO	44	21	6	14
4	Amberlyst A26 OH	59	5	7	12
5	CaO	49	12	2	4
6	SrO	99	14	3	3
7	γ -Al ₂ O ₃	<1	0	0	0
8	_	0	0	0	0

^aReaction conditions: catalyst 0.15 g, AN 2 mmol, methanol 3 mL, 25.4% H₂O₂(aq.) 0.75 mL, 313 K, and 5 h.

Table 2. Effect of amide on formation of GA from AN^a

Entry	Additive AN	AN conv./%	Yiel	d/%	Selectivity
2			AA	GA	tor GA/%
1	_	56	10	14	25
2	NH ₂ isobutyramide	58	10	15	26
3	benzamide	57	11	15	26
4	crotonamide	67	17	51	76
5 6 ^b	acrylamide (A	71 89		56 74	79 83

^aReaction conditions: HT (Mg/Al = 5.4) 0.15 g, AN 2 mmol, amide 2 mmol, methanol 3 mL, 25.4% $H_2O_2(aq.)$ 0.75 mL, 313 K, and 5 h. ^b18 h, AA 4 mmol.

It has been reported that amide compounds such as isobutyramide promote the epoxidation of 1-octene in the presence of sodium dodecyl sulfate.^{3f,10} Hence, various amides were examined as additives in the present reaction system. The results are shown in Table 2. We found that isobutyramide (Entry 2) and benzamide (Entry 3) did not affect the GA yield and selectivity at all. Surprisingly, the addition of an equimolar α , β -unsaturated amide such as crotonamide and acrylamide could increase the GA yield and selectivity (Entries 4 and 5). Prolonging the reaction time (18 h) and increasing AA amount (4 mmol) afforded GA in 74% yield with 83% selectivity (Entry 6).¹¹

The amount of AA after the reaction was measured to ensure the role of the additive amide in this reaction. Interestingly, we found that AA was not consumed at all during the reaction.¹² It is, therefore, suggested that the unsaturated amide acts as a cocatalyst in the GA formation. The double bond of the unsaturated amide might accept the nucleophilic HOO⁻ species to release oxygen into AN, affording a GN intermediate (Route A, Scheme 1).⁸ The reaction of cyclooctene and 1octene under the standard conditions (HT-5.4 0.15 g, aq. H₂O₂ 0.75 mL, methanol 3 mL, AA 2 mmol, 313 K, and 5 h) did not produce the corresponding epoxides.¹³ Hydration of GN into GA might proceed spontaneously when using aq. H₂O₂ solution.

It was found that 4.65 mmol H_2O_2 was consumed during the reaction with 6.16 mmol H_2O_2 for 18 h, while the amount of GA formed was 1.42 mmol. The reaction of AN in the absence of H_2O_2 (HT-5.4 0.15 g, AN 2 mmol, H_2O 0.75 mL, methanol 3 mL, AA 2 mmol, 313 K, and 5 h) did not give GA at all. This implies that aq. H_2O_2 is necessary for both epoxidation and hydration (Scheme 1). According to previous reports, ^{1a,3h} hydration of the nitrile moiety proceeded via a peroxycarbox-imidic acid intermediate, formed by the reaction of the nitrile with H_2O_2 under basic conditions. Thus, the H_2O_2 utilization

efficiency was calculated to be 60%, assuming that two $\rm H_2O_2$ molecules were consumed to produce one GA molecule from one AN molecule. 14

In conclusion, acrylonitrile can be transformed into glycidamide by using layered hydrotalcite as a heterogeneous base catalyst and aqueous H₂O₂ as an oxidant, in the presence of α , β unsaturated amide as a cocatalyst in methanol solvent at 313 K. The maximum GA yield was 74% and the H₂O₂ utilization efficiency was 60%. The hydrotalcite catalyst could be easily separated from the reaction mixture and reused at least once.¹⁵

References and Notes

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- 6 Determination of Hydrogen Peroxide Concentration, Technical Date Sheet, Solvay Chemicals, Inc. USA, 2004.
- 7 The GA yields in alcohol solvent were 28% (methanol), 23% (ethanol), and 12% (propanol), respectively. Names in parentheses show solvent used. Note that the reaction time was 13 h.
- 8 We could not observe GN during the reaction checked by GC-MS.
- 9 With HT-5.3 catalyst, we found that addition of hexadodecyltrimethylammonium bromide (0.1 mmol) made worse in both GA yield and selectivity, while addition of TritonX-100 (0.16 mmol) improved GA selectivity to 68% keeping the similar GA yield. The TritinX-100 inhibites the side

reactions. At this time, however, we are not able to verify the side reactions.

- 10 A combination use of more than 10 equiv of formamide and 15 equiv of H₂O₂ could produce epoxide without catalyst. See: Y. Chen, J.-L. Reymond, *Tetrahedron Lett.* 1995, *36*, 4015.
- 11 Increase of AA amount from 2 to 4 mmol slightly improved the GA yield from 56 to 58% (The reaction time 5 h), whereas increase of reaction time from 5 to 18 h drastically improved the GA yield from 56 to 71% (AA 2 mmol).
- 12 The amount of AA, after the reaction using 6.14 mmol AA under the standard conditions, was 6.18 mmol with 64% GA yield.

- 13 The electron-withdrawal nature of CN moiety of AN may play an important role in the GN formation.
- 14 (mole of formed GA)/[(mole of consumed H_2O_2)/2] × 100.
- 15 The GA yield for fresh catalyst was 56% under the standard condition. The used HT catalyst was separated from the reaction mixture, and washed with water and acetone, followed by drying at room temperature under a vacuum overnight. The GA yields after the first and second recycles were 54% and 32%, respectively. However, the GA selectivities in the fresh and recyle experiments were almost the same (ca. 80%). The deactivation might be caused by an irreversible adsorption of the amide compound on basic sites of the hydrotalcite.