Facile Synthesis of ε-Caprolactam by Cyclodehydration of 6-Aminocaproic Acid on Adsorbents

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ε-Caprolactam is readily synthesized by refluxing a suspension of 6-aminocaproic acid adsorbed on zeolite, silica gel, or alumina in toluene.

The application of solid adsorbents such as alumina and silica gel as solid supports in organic synthesis affords a new procedure for selective reactions[1] involving oxidation,[2] alkylation,[3] condensation[4] and acetylation.[5] Such media are advantageous for milder reaction conditions, simpler work-up and often higher selectivity. We have previously reported the selective monomethyl esterification of dicarboxylic acids,[6] and of long chain acids in the presence of acids with shorter carbon chains.[7] Adsorbents such as alumina and silica gel have been used deliberately as the reaction medium as the substrate can be orientated and translational movement is suppressed. We report here the facile synthesis of ε-caprolactam (ε-CL), which is the source material of 6-nylon, from 6-aminocaproic acid (6-ACA).

Cyclodehydration of 6-ACA adsorbed on solid adsorbents was carried out by the following method (adsorption method): 6-ACA was adsorbed on zeolite (F-9, Wako Chemicals; faujasite type, pore size *ca.* 1.0 nm), silica gel (C-200, Wako Chemicals), and alumina (neutral aluminium oxide 90, Merck) as follows: adsorbent (10 g) was added to a dimethylformamide (DMF) solution of a certain amount of 6-ACA; then DMF was eliminated under reduced pressure. The solid obtained (adsorption sample) was added to toluene (50–100 ml) and heated under flux for 20 h using a Dean-Stark trap to collect the water formed in the reaction. The reaction period of 20 h was sufficient for the reaction to reach the end point with each solid. After the reaction the mixture was filtered and the solid was thoroughly washed with distilled water. The combined washings and filtrate were evaporated to low volume (*in vacuo*, to dryness) and the product analysed by GLC and/or HPLC by the use of β-naphthol as an internal standard.

The results of cyclodehydration of 6-ACA to ε-CL are shown in Table 1. According to the adsorption method the product ε-CL was readily obtained in *ca.* 99% yield with zeolite and in a 90% yield with silica gel, while ε-CL was obtained in lower yields according to the mixing method. The smaller the amount of 6-ACA contained in the adsorption

Table 1 Selective cyclodehydration of 6-ACA to ε-CL[a]

Adsorbent	Method	Amount of 6-ACA/ 10^{-4} mol	Intact 6-ACA (%)	Yield (%)	Selectivity (%)[b]
None	Homogeneous[c]	1.3	35.2	22.8	35.2
SiO_2	Adsorption[d]	4.6	10.2	89.6	99.8
SiO_2	Adsorption[d]	38	0.0	74.9	74.9
SiO_2	Adsorption[d]	260	28.2	3.1	4.3
SiO_2	Mixing[e]	0.97	3.1	44.7	46.1
Al_2O_3	Adsorption[d]	4.8	0.0	78.9	78.9
Al_2O_3	Mixing[e]	1.2	3.1	5.9	6.1
Zeolite	Adsorption[d]	0.79	0.0	99.1	99.1
Zeolite	Mixing[e]	1.6	0.0	6.4	6.4

[a] Each experiment was carried out under reflux for 20 h. [b] The value of [yield/(100 − intact 6-ACA)] × 100. [c] In a DMF solution (120 ml) of 6-ACA in the absence of adsorbent. [d] Conditions as in the main text. [e] In a DMF solution. (120 ml) of 6-ACA in the presence of adsorbents (10 g).

Table 2 Dependence of water addition into the adsorption sample on the yield of ε-CL[a]

Amount of water/% m/m	Intact 6-ACA (%)	Yield (%)	Selectivity (%)[b]
0.0	10.2	89.6	99.8
30.0	26.0	68.3	92.3
50.0	32.1	57.4	84.5
80.0	5.2	38.9	41.0

[a] Water was added into the adsorption sample of silica gel (4.6×10^{-5} mol g^{-1}). Other conditions as in the main text. [b] The value of [yield/(100 − intact 6-ACA)] × 100.

sample of silica gel, the higher the yield and selectivity become.

Water was added into the adsorption sample of 6-ACA on silica gel (4.6×10^{-5} mol g^{-1}), and the sample was introduced to the reaction system; the results are shown in Table 2. The higher the amount of water added the lower yield and selectivity. However, even on addition of 30% m/m water, ε-CL is obtained in a 68% yield and in 92% selectivity. Thus, this adsorption method is moderately insensitive to water, and ε-CL is readily and easily obtained.

The IR absorption of 6-ACA contained in the adsorption sample of silica gel was measured. At fairly high loadings (1.7×10^{-4} mol g^{-1}), the spectrum of the adsorption sample was similar to that of neat 6-ACA in the solid state, *i.e.* both of the spectra exhibited the characteristic bands at 2700–2500 cm^{-1} due to $\nu(NH_3^+)$ and at 1560 cm^{-1} due to $\nu_{as}(CO_2^-)$. On decreasing the amount of 6-ACA on silica gel (1.2×10^{-5} mol g^{-1}), changes in the IR spectra were observed, *i.e.* new bands appeared at 1655 cm^{-1} due to $\nu(C{=}O)$ from the hydrogen bonding among carboxy groups and at 3460–3296 cm^{-1} due to $\nu(NH_2)$ or $\nu(NH)$. The amount required for complete surface coverage could be estimated at 1.6×10^{-3} mol g^{-1} on the basis of the cross sectional area of 6-ACA (*ca.* 0.39 nm^2 molecule^{-1} by molecular modelling) and the specific surface area of silica gel (371 m^2 g^{-1}) by BET measurement. These data imply that a decrease in the amount of 6-ACA on silica gel allows easier dispersion of the acid on the surface of silica gel to become easy, thus suppressing intermolecular interactions between acid molecules. Acid sites on silica gel would promote the reaction. Hence, the selective cyclodehydration to ε-CL could be achieved with the aid of intramolecular interactions of the acid. Silica gel is considered to play a dual role as a catalyst for the cyclodehydration and a reaction medium like an organic solvent.

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