

Conversion of α -Amino Acids into Nitriles by Oxidative Decarboxylation with Trichloroisocyanuric Acid

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ABSTRACT

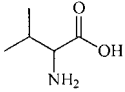

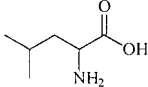
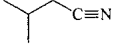
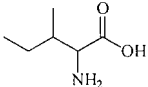
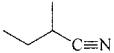
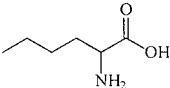
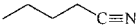
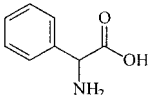
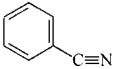
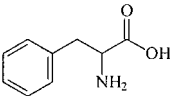
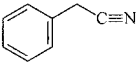
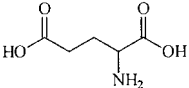
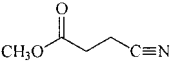
Trichloroisocyanuric acid oxidation of α -amino acids in water or methanol in the presence of pyridine produces nitriles with one less carbon in good yields and of high purity.

Key Words: α -Amino acids; Nitriles; Oxidative decarboxylation; Oxidation; Decarboxylation; Preparation; Synthesis; Trichloroisocyanuric acid.

Amino acid oxidations have been carried out with a variety of oxidizing agents to produce a variety of products. Silver oxide oxidation produces car-

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Table 1. Conversion of α -amino acids into nitriles.

Amino acid	Nitrile	Yield	Boiling point	GC purity
		58.4% ^a	102.7–103.0°C	99.1%
		79.3% ^a	128.0–128.5°C	97.9%
		88.0% ^a	124.0–125.0°C	97.4%
		84.2% ^a	139.5–140.0°C	98.9%
		66.1% ^a	190.0°C	99.3%
		77.0% ^b	— ^c	99.9%
		61.4% ^b	104.0–105.2°C (13.4–14.2 torr) ^d	96.5%

^aReaction run in water.

^bReaction run in methanol.

^cPurified by flash chromatography.

^dConverted to the methyl ester before isolation.

¹H FT-NMR spectra were recorded in CDCl₃ using an Anasazi-modified Varian EFT 90 MHz spectrometer. The FT-IR spectra were recorded using a Perkin Elmer 1650 spectrometer. GC analyses were carried out with a Hewlett-Packard 5890 Series II on a 6 ft × 1/8 in 10% Carbowax 20-M column. Optical rotations were recorded using a Rudolph Instruments Model 51 polarimeter equipped with a sodium vapor lamp.

Conversion of L-Isoleucine into (S)-(+)-2-Methylbutyronitrile

L-Isoleucine, 15.300 g (0.1166 mol), 120 mL water, 29.05 g (0.3673 mol) pyridine, and a magnet were placed in a 300-mL three-neck round bottom

flask fitted with a dry-ice condenser, a stopper, and a solid addition funnel containing 23.362 g (0.1000 mol, 0.3000 eq) TCICA. While stirring, TCICA was added over a period of 30 min. The reaction was exothermic. After 3 hr additional stirring at room temperature, solid NaHSO₃ was added in order to destroy excess TCICA until a negative test with iodide-starch paper was obtained. After filtration to remove the cyanuric acid that formed and washing the solid with ether, the mixture was acidified with HCl and the aqueous phase was saturated with NaCl. The mixture was extracted with ether (4 × 50 mL), dried over MgSO₄, and filtered. The ether was removed by distillation through a concentric tube column and the amine distilled to give several fractions of (S)-(+)-2-methylbutyronitrile, bp 124.0–125.0°C. Fractions 3–6, 8.532 g (88.0%), had a purity of 97.4% by GC. Fractions 4–6, 7.618 g (78.6%) had a purity of 99.2% by GC. Fraction 5, 4.904 g (50.6%), had a purity of 99.5% by GC: $[\alpha]_D^{20} + 37.46^\circ$ (neat). The FT-IR, ¹H FT-NMR, and GC retention time were identical to an authentic sample.

Conversion of L-Glutaric Acid into Methyl 3-Cyanopropanoic Acid

Glutaric acid, 15.655 g (0.1064 mol), 75 mL methanol, 17.67 g (0.2233 mol) pyridine, and a magnet were placed in a 300-mL three-neck round bottom flask fitted with a dry-ice condenser, a stopper, and a solid addition funnel containing 21.098 g (0.09077 mol, 0.2723 eq) TCICA. While stirring, TCICA was added over a period of 45 min. The reaction was exothermic. After 1 hr 50 min additional stirring at room temperature, solid NaHSO₃ was added in order to destroy excess TCICA until a negative test with iodide-starch paper was obtained. After filtration to remove the cyanuric acid that formed and washing the solid with methanol, 7 mL conc H₂SO₄ was added to the filtrate and the solution was refluxed for 3 hr in order to form the methyl ester. The methanol was removed using a rotary evaporator and 25 mL of water was added, and the mixture was extracted with ether (3 × 100 mL). The ether solution was dried over MgSO₄, and after filtration, the ether was removed using a rotary evaporator and the residue distilled using a concentric tube column to give 7.338 g (61.4%) [bp 104.0–105.2°C (13.4–14.2 torr)] methyl 3-cyanopropanoate with a purity by GC of 96.5% [reported bp 95–97°C (8 torr)];^[6] FT-IR (film) 2252 (CN), 1739 (CO), 1293, 1254, 1209, 1179, 1058, 1023, 1001, 981, 946, 878, 838, 784, 705 cm⁻¹ [reported (film) 2246, 1735, 1286, 1247, 1202, 1172, 1052, 1017, 996, 975, 940, 871, 833, 778, 697 cm⁻¹];^[7] ¹H FT-NMR (CDCl₃) δ 3.76 (s, 3, OCH₃), 2.70 (s, 4, CH₂CH₂).

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