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Asymmetric Transformation of DL-4-Thiazolidinecarboxylic Acid

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A mixture of DL-4-thiazolidinecarboxylic acid (DL-THC), (+)- or (-)-tartaric acid ((+)- or (-)-TA), and salicylaldehyde in acetic acid was stirred at 80 °C to give a salt composed of equimolar amounts of L-THC and (-)-TA or that of D-THC and (+)-TA. D- and L-THC with optical purity of 97-99% were obtained from these salts in 68-78% yield.

DL-4-Thiazolidinecarboxylic acid (abbreviated as DL-THC) has been optically resolved by preferential crystallization to obtain D- and L-cysteine (D- and L-Cys),[1] as a useful material for medicines, food additives, and cosmetics. An aqueous solution containing DL-THC and (+)-tartaric acid ((+)-TA) gave selectively a salt composed of equimolar amounts of D-THC and (+)-TA.[2] It has been reported that free amino acids are racemized easily in the presence of aldehydes in acetic acid.[3] On the basis of these facts, the asymmetric transformation of DL-THC was attempted by combination of crystallization of less soluble diastereomeric salt and epimerization of more soluble salt.

A mixture of 0.010 mol (1.332 g) of DL-THC, 0.010 mol (1.501 g) of (+)- or (-)-TA, and 0.005 mol of salicylaldehyde in 20 cm^3 of acetic acid was stirred for 0.5-4 h at 80 °C. The mixture was cooled to 15 °C. The formed salt was collected by filtration, washed with a small amount of diethyl ether, and dried. After adding the salt to 200 cm^3 of methanol and stirring the mixture for 1 h at room temperature, THC was filtered, washed with methanol, and dried. The result of asymmetric transformation is listed in Table 1. The salt of D-THC with (+)-TA or that of L-THC with (-)-TA was obtained in 73-85% yield and the optical purity[4] showed 97-99%. These salts gave D- and L-THC in 68-78% yield. L-THC was also transformed using (+)-TA into D-THC with 99.3% optical purity[5] in 70.9% yield. The obtained D- and L-THC gave D- and L-Cys in 83% yield by treatment with hydroxylamine hydrochloride,[1,6] respectively.

Table 1. Asymmetric Transformation of DL-4-Thiazolidinecarboxylic Acid [a]

Configuration		Reaction period	Salt obtained			THC obtained		
THC	TA	h	Yield g[%[b]]	Specific rotation[c] °	Optical purity %	Configuration	Yield g[%[d]]	Optical putity %
DL	(-)	0.5	2.076[73.3]	-73.3	98.9	L	0.905[67.9]	99.3
DL	(+)	1.0	2.235[78.9]	+73.1	98.6	D	0.936[70.3]	97.2
DL	(+)	1.5	2.344[82.7]	+73.0	98.5	D	0.962[72.2]	98.8
DL	(+)	2.0	2.403[84.8]	+72.2	97.2	D	1.035[77.7]	97.9
DL	(-)	2.5	2.390[84.4]	-73.3	98.9	L	1.023[76.8]	99.3
DL	(+)	3.5	2.283[80.6]	+72.4	97.5	D	1.004[75.4]	98.4
DL	(+)	4.0	2.290[80.8]	+72.6	97.8	D	0.988[74.2]	97.2
L	(+)	3.0	2.148[75.8]	+73.6	99.4	D	0.945[70.9]	99.3

a) DL- or L-THC (0.010 mol), 0.010 mol of (+)- or (-)-TA, and 0.005 mol of salycilaldehyde were consumed. b) Yield / % = [Yield x 100 / g] / 2.833. c) $[\alpha]_D^{20}$ (c 1.00, water). d) Yield / % = [Yield x 100 / g] / 1.332.

References

1) T. Shiraiwa, Y. Sado, M. Komure, and H. Kurokawa, Chem. Lett., 1987, 621.

2) Salt of D-THC with (+)-TA: Found: C, 33.80; H, 4.54; N, 4.81% (Calcd for $C_6H_{13}NO_8S$: C, 33.92; H, 4.63; N, 4.95%); mp 171-172 °C (decomp); $[\alpha]_D^{20}$ +74.0° (c 1.00, water).

3) S. Yamada, C. Hongo, R. Yoshioka, and I. Chibata, J. Org. Chem., 48, 843 (1983).

4) The optical purities were determined on the basis of the specific rotation of the salt of D-THC with (+)-TA and that of equimolar mixture of L-THC and (+)-TA ($[\alpha]_D^{20}$ +9.03° (c 1.00, water)).

5) Specific rotation of D-THC: $[\alpha]_D^{20}$ +141° (c 1.00, water).

6) H. Bethge, K. Drauz, A. Kleemann, J. Martens, and H. Weigel, German Patent, 3202295 (1983); Chem. Abstr., 99, 105700 (1983).

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