CHEMISTRY LETTERS, pp. 621-622, 1987.

Optical Resolution by Preferential Crystallization of DL-Thiazolidine-4-carboxylic Acid

Tadashi SHIRAIWA,* Yujin SADO, Masamitsu KOMURE, and Hidemoto KUROKAWA
Faculty of Engineering, Kansai University, Suita, Osaka 564

It was found that DL-thiazolidine-4-carboxylic acid (DL-THC) is a conglomerate. A successive preferential crystallization in water gave D- and L-THC's with optical purity of 96-100%. D- and L-cysteines with 100% optical purity were obtained from the purified D- and L-THC's, respectively.

L-Cysteine (abbreviated as L-Cys) as a useful material of medicine, food additive, and cosmetic has been obtained from hair and D-Cys has been also noted as that of medicine.[1] It, however, is difficult to find D-Cys in natural products. Although a chemical synthesis is more favorable for obtaining a large quantity of Cys,[2] the optical resolution of DL-Cys is needed to obtain D- and L-Cys's. However, the optical resolution by preferential crystallization has not been reported, expect for that of DL-cysteine hydrochloride monohydrate.[1] This letter describes an attempt obtaining D- and L-Cys's by optical resolution by preferential crystallization.

DL-Thiazolidine-4-carboxylic acid (DL-THC) is easily obtained by reaction of DL-Cys with formaldehyde.[3] DL-THC shows identical infrared spectrum with that of L-THC and is more soluble than L-THC; solubility at 20 °C of DL-THC 5.977 g/(100 cm^3 water); that of L-THC 3.193 g/(100 cm^3 water). These results lead to the conclusion that DL-THC exists in a conglomerate at room temperature. The optical resolution by successive preferential crystallization was experimented at 20 °C in water. DL-THC (4.482 g) was dissolved in 50 cm^3 of water at 40 °C. After being cooled to 20 °C, the solution was seeded with 0.050 g of L-THC and stirred for 30 min. The precipitated L-THC was collected by filtration washed with a small amount of methanol, and dried. DL-THC (0.477 g) was dissolved in the filtrate. After being seeded with 0.050 g of D-THC at 20 °C, the mixture was treated similarly to the case of L-THC. The result of the optical resolution was

listed in Table 1. The degree of resolution of D- and L-THC's was calculated by

Degree of resolution / % =

[YOPM / g × 100] / [(Operation amount of D- or L-THC / g) - 1.494],

where YOPM is optically pure modification.[4] The successive preferential crystallization gave D- and L-THC's with 96-100% optical purity in degree of resolution of 59-77%; the optical resolution was also experimented in 6 times scale and D- and L-THC's with 80-100% optical purity were obtained in degree of resolution of 47-78%. The D- and L-THC's recrystallized from water were treated with hydroxylammonium hydrochloride to give optically pure Cys's in 82% yield.[5]

Table 1. Optical Resolution by Successive Preferential Crystallization of DL-Thiazolidine-4-carboxylic Acid [a]

Run	Added amount of DL-THC	Operation amount [b] / g		Resolution time	THC obtained			
					Yield	Optical purity	YOPM [c]	Degree of resolution
	g	L-THC	D-THC	min	g	%	g	%
1	4.482	2.241	2.241	30	0.527	L 96.3	0.458	61.3
2	0.477	2.011	2.469	20	0.624	D 100	0.574	58.9
3	0.574	2.298	2.182	30	0.685	L 97.2	0.619	77.0
4	0.635	1.988	2.491	30	0.668	D 98.8	0.610	61.2

a) Solvent: 50 cm^3 of water. Temperature: 20 °C. Seed crystals: 0.050 g of D- or L-THC. b) Operation amounts of D- and L-THC's in solution were calculated from analyses of the THC obtained in runs 1-3. c) YOPM: Yield of optically pure modification.

References

1) C. Inoue, Y. Kurima, and S. Moriguchi, Japan Patent, 70859 (1982); Chem. Abstr., 97, 163490 (1982).

2) J. Martens, H. Offermanns, and P. Scherberich, Angew. Chem., Int. Ed. Engl., 20, 668 (1981).

3) S. Ratner and H. T. Clarke, J. Am. Chem. Soc., 59, 200 (1937).

4) T. Shiraiwa, Y. Ohmichi, K. Iwafuji, K. Fujimoto, and H. Kurokawa, Nippon Kagaku Kaishi, 1983, 1070.

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

(Received January 16, 1987)