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Asymmetric Transformation of N-Methyl-(RS)-2-phenylglycine

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The asymmetric transformation of N-methyl-(RS)-2-phenylglycine ((RS)-Mpg) via formation of the salt with (S)-camphor-10-sulfonic acid was achieved in butanoic acid without using a catalyst such as aldehydes or ketones. The salt purified by recrystallization was treated with triethylamine to give (R)-Mpg with approximately 100% optical purity in 71-77% yield.

N-Methyl-(S)-2-phenylglycine (abbreviated as (S)-Mpg) has been obtained by isolation from the hydrolysate of ethamycin.1) N-Acyl derivatives of synthetic (RS)-Mpg2) has been optically resolved by brucine2) and ephedrine3) as resolving agents. The optical resolution by using (S)-camphor-10-sulfonic acid ((S)-CS) gave a salt of (R)-Mpg with (S)-CS as its less soluble diastereomer. Although optically active amino acid is racemized in the presence of aldehydes or ketones in ethanoic acid,4,5) optically active Mpg is apt to racemize on heating in an acid solution without using such catalyst.2) The asymmetric transformation of (RS)-Mpg, therefore, was tried via formation of the salt with (S)-CS on heating in butanoic acid.

A mixture of 10.0 mmol of (RS)-Mpg and 9.50 mmol of (S)-CS in 10 cm^3 of butanoic acid was stirred for 4-8 h at 100 °C. After addition of 0.50 mmol of (S)-CS, the reaction mixture was stirred for 5 min at 50 °C and successively for 15 min in an ice bath. The salt of (R)-Mpg with (S)-CS was filtered off, washed with diethyl ether, and dried. The salt with 85-89% optical purity6) was obtained by reacting for 5-8 h in 93-96% yield, as listed in Table 1. To a suspension of the salt in ethanol (6 $cm^3\ g^{-1}$) was added equimolar triethylamine. After stirring the mixture for 0.5 h in an ice bath, (R)-Mpg was filtered off, washed with a small amount of cold methanol, and dried. (R)-Mpg with 82-88% optical purity was obtained in 84-92% yield. After refluxing a suspension of the salt with 85-89% optical purity in 1-propanol (5 $cm^3\ g^{-1}$) for 5 min and successively stirring for 10 min at 60 °C, the purified salt was rapidly filtered off and dried. Treatment of the salt with triethylamine gave (R)-Mpg with approximately 100% optical purity ($[\alpha]_D^{20}$ -169 - -168° (c 1.00, 1 mol dm^{-3} HCl)) in 71-77% yield based on the (RS)-Mpg, the starting material used, as shown in Table 1; lit. of (R)-Mpg,3) $[\alpha]_D^{34}$ -170.7° (c 0.571, 1 mol dm^{-3} HCl).

The asymmetric transformation of (RS)-Mpg is possible on heating in butanoic acid without using a catalyst such as aldehydes or ketones.

Table 1. Asymmetric Transformation of N-Methyl-(RS)-2-phenylglycine[a)]

Reaction period	Salt[b)]			(R)-Mpg	
	Yield	Specific rotation[d)]	Optical purity[e)]	Yield[f)]	Optical purity[g)]
h	g [%[c)]]	°	%	%	%
4	3.81 [96.0]	-30.5	59.1	89.4	55.9
5	3.72 [93.7]	-49.7	85.6	86.5	85.1
5	3.34 [84.1][h)]	-59.3	98.9	75.9	98.4
6	3.76 [94.7]	-50.5	86.7	91.9	82.0
6	3.35 [84.4][h)]	-58.5	97.8	71.1	98.4
7	3.76 [94.7]	-51.9	88.7	84.2	87.9
7	3.40 [85.6][h)]	-58.9	98.3	73.6	99.0
8	3.80 [95.7]	-50.9	87.3	89.2	84.4
8	3.39 [85.4][h)]	-59.5	99.2	77.0	98.4

a) N-Methyl-(RS)-2-phenylglycine ((RS)-Mpg) 10.0 mmol; (S)-camphor-10-sulfonic acid ((S)-CS) 10.0 mmol; butanoic acid 10 cm^3; temperature 100 °C. b) The salt is composed of (R)-Mpg and (S)-CS. c) The yield was calculated on the basis of 10 mmol (3.97 g) of the salt of Mpg with CS. d) $[\alpha]_D^{20}$ (c 1.00, 1 mol dm^{-3} HCl). e) See ref. 6. f) The yield was calculated on the basis of 10.0 mmol (1.65 g) of Mpg. g) The optical purity was determined on the basis of the specific rotation ($[\alpha]_D^{20}$ -170.7° (c 0.571, 1 mol dm^{-3} HCl)) of (R)-Mpg. h) The salt was purified by recrystallization.

References

1) J. C. Sheehan, H. G. Zachau, and W. B. Lawson, J. Am. Chem. Soc., 80, 3349 (1958).

2) T. Araga, T. Saito, and H. Kotake, Nippon Kagaku Zasshi, 86, 112 (1965).

3) H. Kinoshita, M. Shintani, T. Saito, and H. Kotake, Bull. Chem. Soc. Jpn., 44, 286 (1971).

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

5) T. Shiraiwa, K. Kataoka, S. Sakata, and H. Kurokawa, Bull. Chem. Soc. Jpn., 61, 4158 (1988).

6) The optical purity was determined on the basis of the specific rotation ($[\alpha]_D^{20}$ -60.1° (c 1.00, 1 mol dm^{-3} HCl)) of the salt of (R)-Mpg with (S)-CS and that ($[\alpha]_D^{20}$ +12.3° (c 1.00, 1 mol dm^{-3} HCl)) of the equimolar mixture of (RS)-Mpg and (S)-CS.

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