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ASYMMETRIC SYNTHESIS OF N-SUBSTITUTED DIMETHYL AZIRIDINE-2,3-DICARBOXYLATE AND THE FORMATION OF OPTICALLY ACTIVE ASPARTIC ACID[1)]

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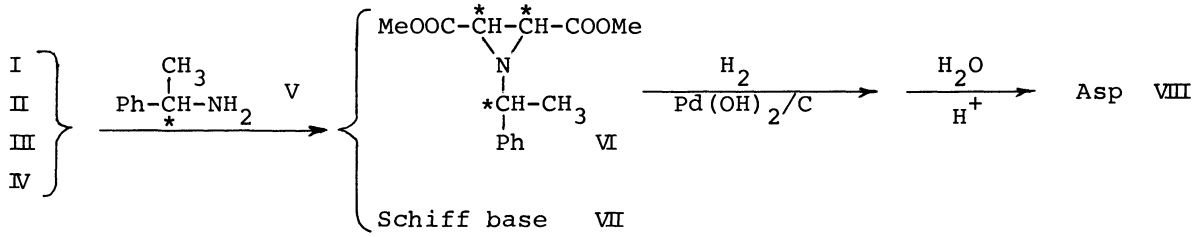
Optically active dimethyl aziridine-2,3-dicarboxylate(VI) was asymmetrically synthesized from dimethyl meso- and racemic dibromosuccinate(I and II), dimethyl bromofumarate(III) and dimethyl bromomaleate(IV) by treating with optically active α-methylbenzylamine. The optically active aziridine(VI) was hydrogenolyzed and hydrolyzed to form optically active aspartic acid(VIII). The optical purity of VIII reached up to 37%.

Stereochemical studies on the reaction of dialkyl meso and racemic α,β-dibromosuccinate(I and II), dialkyl α-bromofumarate(III) and dialkyl α-bromomaleate(IV) with ammonia have been reported.[2)] Recently, We have investigated the reaction of dimethyl meso and racemic dibromosuccinate, (I) and (II), with optically active α-methylbenzylamine(V).[3)] It was found that each of these reactions gave two same products, trans-aziridine(VI) and Schiff base(VII). The isomeric enamine was not found in the reaction mixture under the conditions used in this reaction. The Schiff base(VII) was catalytically hydrogenated to convert optically active aspartic acid.[3)]

In this communication, asymmetric synthesis of dimethyl aziridine-2,3-dicarboxylate(VI) from I, II, III and IV with optically active (S)- or (R)-α-methylbenzylamine (V) was described. If optically active VI is synthesized, the aziridine could be converted to optically active aspartic acid(VIII).[4,5)] It was found that each of these reactions gave trans-aziridine(VI). Therefore, it could be assumed that the reactions of V with I, II, III and IV passed through a same intermediate in the formation of trans-VI. The schematic route of the reactions is shown in Scheme 1. A typical reaction is as follows: Diethyl α,β-dibromosuccinate(I)(0.021 mol)(or equivalent amount of each, II, III and IV) in ethanol(50 ml) was mixed with a solution



Scheme 1

of racemic, (R)- or (S)-α-methylbenzylamine(V) at room temperature(~20 °C) or at lower temperatures(-20~-25 °C). In each reaction, two same compounds, VI and VII, were obtained. These were separated by silica gel column chromatography by eluting with a solvent composed of benzene and ethyl acetate(6 : 1). The yields of VI and VII are in the range of 26~35% and 51~60%, respectively. The structure of VI was confirmed by the chemical properties, IR and NMR analyses.[6] The VI was hydrogenolyzed[7] with palladium hydroxide on charcoal and then the product was hydrolyzed to optically active aspartic acid(VIII). The VIII was isolated by the use of Dowex 50 column(H^+ form) by eluting with aqueous ammonia. A part of VIII was treated with 1-fluoro-2,4-dinitrobenzene and the resulting DNP-aspartic acid was purified by celite column chromatography.[8] The summerized results of yields, optical purities(O.P.) and configurations are shown in Table 1.

Table 1 Asymmetric synthesis of N-substituted aziridine 2,3-dicarboxylate and the formation of aspartic acid

Starting material	Config[a] of amine V	Reaction time (hr)	Reaction temp (°C)	Synthetic[b] yield % VI (VII)	Synthetic[c] yield % VIII	Config VIII	$[\alpha]_D^{25}$ DNP-Asp	O.P. %[d] DNP-Asp
I	±	24	r.t.	33(54)	56	±	-	-
I	R	24	r.t.	31(55)	57	S	+11.9,(c 1.97)	13
II	±	24	r.t.	35(51)	57	±	-	-
II	S	24	r.t.	34(56)	55	R	-13.8,(c 1.26)	15
III	R	24	r.t.	31(57)	58	S	+15.6,(c 1.15)	17
IV	S	24	r.t.	32(55)	57	R	-13.8,(c 1.72)	15
III	R	48	-20~-25	28(59)	56	S	+31.8,(c 1.27)	34
IV	S	48	-20~-25	26(60)	57	R	-34.0,(c 1.76)	37

I: meso-α,β-dibromosuccinate, II: racemic α,β-dibromosuccinate, III: α-bromofumalate, IV: α-bromomaleate

a) R: R(+)-α-methylbenzylamine, $[\alpha]_D^{25}$ + 39.0° neat; S: S(-)-α-methylbenzylamine, $[\alpha]_D^{25}$ - 39.0° neat.
b) based on the starting material.
c) based on VI.
d) based on the maximum of rotation of DNP-aspartic acid, ± 92.0° (1 N NaOH soln).

References and Notes

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4) H. Naganawa, N. Usui, T. Takita, M. Hamada, H. Umezawa, J. Antibiotics, 28, 828 (1975).
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6) NMR of VI: δ($CDCl_3$) 1.50(3H, d, J = 6.6 Hz, -CH-C$\underline{H}_3$), 2.50(2H, ABq, δA = 2.44, δB = 2.56, J = 6.2 Hz, ring proton), 2.77(1H, q, J = 7.2 Hz, -C$\underline{H}$-CH_3), 3.65(3H, s, -$CO_2C\underline{H}_3$), 3.73(3H, s, -$CO_2C\underline{H}_3$), 7.12-7.50(5H, m, Ar$\underline{H}$).
7) The VI was hydrogenolyzed easily to form VIII, however, free aziridine dicarboxylic acid, which was obtained by alkaline hydrolysis, was not hydrogenolyzed under the same condition.
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