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STEREOSELECTIVE FORMATION OF α,α-DIAMINO ACID RESIDUE BY THE ADDITION OF L-α-AMINO ACID TO α-IMINO ACID

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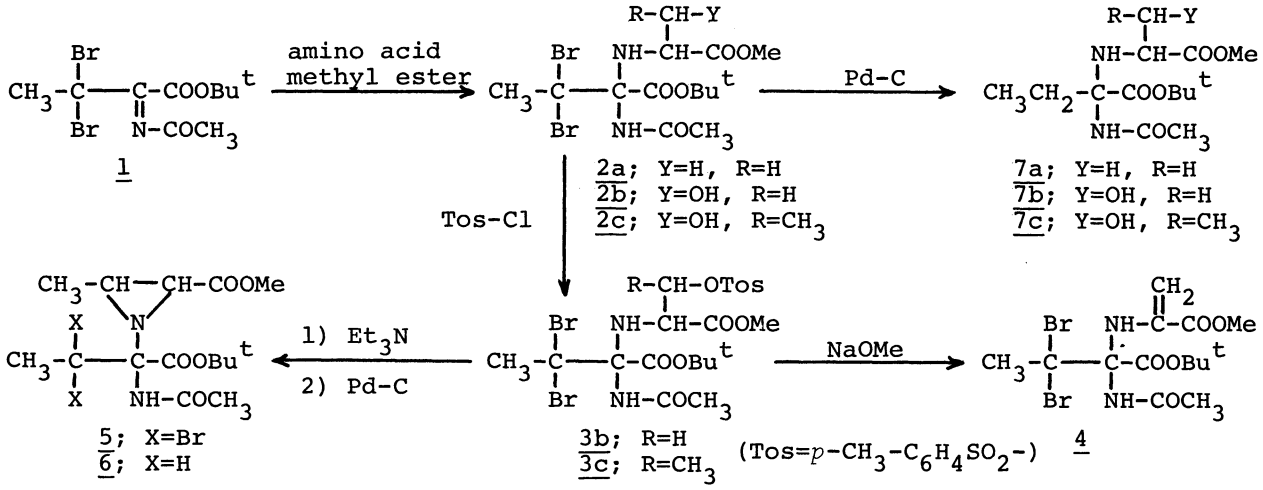
An addition of L-α-amino acids to β,β-dibromo-α-imino acids proceeded to give the corresponding optically active α,α-diamino acid derivatives. A several conversions of the products are also described.

Recently, we reported the addition of protic reagents, such as alcohols and amines, to t-butyl β,β-dibromo-α-(acetylimino)alkanoate (1).[1-3] Although a few reports on the addition of chiral reagent to the C=N bond of achiral substrate appeared, no report has been published on the direct addition of L-α-amino acid ester to α-imino acid ester giving an optically active α,α-diamino acid derivative.

In the present paper, we wish to communicate on the facile synthesis of structurally interesting as well as optically active protected α,α-diamino acid derivative linked to an α-dehydroamino acid (DHA) or containing aziridino acid moiety at α-position.

It was found that the reaction of 1 with L-α-amino acid methyl ester readily proceeded in $CHCl_3$ below 5° C to give the adduct of α-amino acid ester (2) quantitatively. From the NMR spectral data of 2, the presence of the two stereoisomers was recognized and the diastereomeric excess yield (d. e., %) could be easily calculated (Table 1). Interestingly, when the recrystallization of 2 was repeated two times, only one chemical species, of which rotational value was listed in Table 1, was isolated purely. Subsequently, in order to convert the α-amino acid moiety into DHA residue, compound 2 containing Ser or Thr residue was subjected to the O-tosylation, followed by the base-catalyzed β-elimination by the usual method. The O-tosylated 2 (3b) thus obtained was then treated with NaOMe to give a colorless syrup, identified as t-butyl 3,3-dibromo-2-(1-methoxycarbonyl)vinylamino-2-(acetylamino)butanoate (4). As a result, it was found that compound 4 showed still a large optical rotation ($[\alpha]_D^{25}$ = +32.7°, c=2.91), even after the chirality of Ser residue was extinguished. On the other hand, another O-tosylated compound (3c) gave the unexpected but an interesting α,α-diamino acid derivative (5) containing aziridine acid ester moiety by the treatment with Et_3N.

The structural assignment of 4 and 5 has been established on the basis of the spectral data and satisfactory results in elemental analysis. In the NMR spectrum of 4, the signals at δ 5.14 and δ 4.65 appearing as two singlets are



attributable to the vinyl protons, while the signal at comparatively higher field (δ 4.05) in the spectrum of 5 exhibit a doublet (J=5.0Hz), which has been assigned as aziridine ring proton.

Furthermore, the two bromo groups at β-position of 2 and 5 thus obtained were readily reduced by the catalytic hydrogenation with 10% Pd-C in the presence of Et_3N to give t-butyl 2-(1-methoxycarbonyl)alkylamino-2-(acetylamino)butanoate (7) and the corresponding 2-aziridino-butanoate derivative (6) respectively as a colorless syrup in good yields.

Table 1. The yields, physical constants, and NMR spectral data of 2-7

Compd. No.	Yield[a] (%)	d. e.[a] (%)	NMR spectrum, δ in $CDCl_3$[a] NH	(OH)	α-H[b] (vinyl-H) (J_{Hz})	Mp[c] (°C)	$[\alpha]_D^{25}$ in EtOH[c] (c)
2a	97	33.8	6.38, 6.36,		3.90m	93-94	-21.03 (2.03)
2b	96	33.9	6.56, 6.54,	(3.44),	3.86m	125-126	-9.82 (2.05)
2c	94	85.3	6.44,	(3.65),	3.80m	74-76	-45.44 (2.02)
3b	96		6.61, 6.49,		4.09m	107-108	+14.03 (2.01)
3c	76		6.55,		4.40m	111-112	-5.58 (1.15)
4	94		6.75, 6.25,		(5.18s, 4.65s)	121.5-122	+32.70 (2.91)
5	89		6.28,		4.30m, 4.05d[d]	149-149.5	-32.50 (2.14)
6	91		6.61,		2.42m, 2.63d[e]	syrup	-49.15 (1.88)
7a	62		6.91,		3.31q (7.0)	syrup	-22.65 (0.19)
7b	78		6.67,	(2.88),	3.55t (5.0)	syrup	-37.47 (0.92)
7c	90		7.11,	(3.70),	3.49d (8.0)	syrup	-38.51 (3.37)

a) Listed are the yield, d. e., and the NMR spectral data of the initial products. b) α-Position in α-amino acid residue. c) Values of pure one chemical species obtained as colorless needles after repeated recrystallization. d) Ring proton (J=5.0Hz). e) Ring proton (J=7.0Hz).

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