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A FACILE SYNTHESIS OF α,β-UNSATURATED α,β-DIAMINO ACIDS

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As the important component in the preparation of the several peptides containing 3-amino-dehydroalanine derivative such as griseoviridin,[1] tuberactinomycins[2] and the other similar substances,[3] the synthetic method for α,β-unsaturated α,β-diamino acid derivatives (5 and 12) has been pursued enthusiastically. Up to the present, no available method of synthesizing 5 and 12 has been reported, excepting the preparation of an analogue, ethyl 3-ureido-2-(N-benzylcarbonyl)dehydroalanine from ethyl benzylpenaldate and urea.[4]

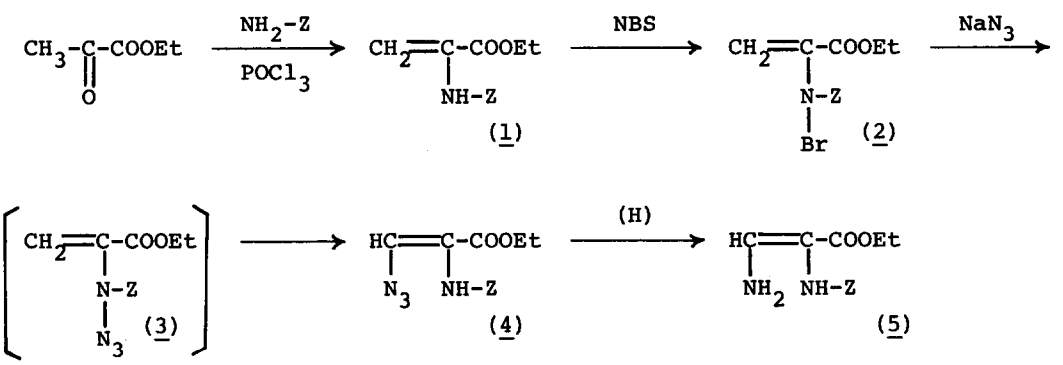
Recently, we have reported briefly that the reaction of t-butyl 2-(N-bromoacetyl)amino-2-alkenoate (7), obtained by the bromination of t-butyl 2-acetylamino-2-alkenoate (6) with N-bromosuccinimide (NBS), with sodium azide gave the expected N→C-3 azido migration product: t-butyl 3-azido-2-acetylamino-2-alkenoate (9) in a high yield.[5] It was believed that the olefin vicinally substituted with azido and amino groups was indispensable for the synthesis of the corresponding diamino olefin, since the selective reduction of azido olefins with aluminum-amalgam (Al-Hg) to amino olefins had been successful.[6] Therefore, compounds such as 9 seem to be very important starting material for 5 and 12.

In the present paper, we wish to communicate the available and facile synthesis of α,β-unsaturated α,β-diamino acids (5 and 12) by three steps from α-

dehydroamino acids (1 and 6) via β-azido-α-dehydroamino acids (4 and 9).

According to our useful preparative method for α-dehydroamino acid ester,[7] the direct condensation of ethyl pyruvate (0.10 mol) with benzyl carbamate (0.12 mol) in dry benzene (100 ml) in the presence of phosphoryl chloride (6 ml) was carried out under reflux for 5 hr to give the expected ethyl 2-(benzyloxycarbonyl)aminoacrylate (1) in a 75% yield. Subsequently, the bromination of 1 (0.10 mol) with NBS (0.11 mol) in carbon tetrachloride (150 ml) with stirring at room temperature for 1 hr gave ethyl 2-(N-bromobenzyloxycarbonyl)aminoacrylate (2) as crude syrup quantitatively, which was immediately subjected to the substitution reaction with sodium azide (0.12 mol) in dimethyl formamide (150 ml) to afford ethyl 3-azido-2-(benzyloxycarbonyl)aminoacrylate (4), via 1,3-shift of N-azido group in ethyl 2-(N-azidobenzyloxycarbonyl)aminoacrylate (3) formed as an unstable intermediate.

Although the reduction of 4 with Al-Hg did not proceed, that of 4 (7 mmol) with Raney nickel (ca. 2 ml) in ethanol (40 ml) at room temperature for 12 hr was successfully performed to give ethyl 3-amino-2-(benzyloxycarbonyl)aminoacrylate (5) in a 75% yield.

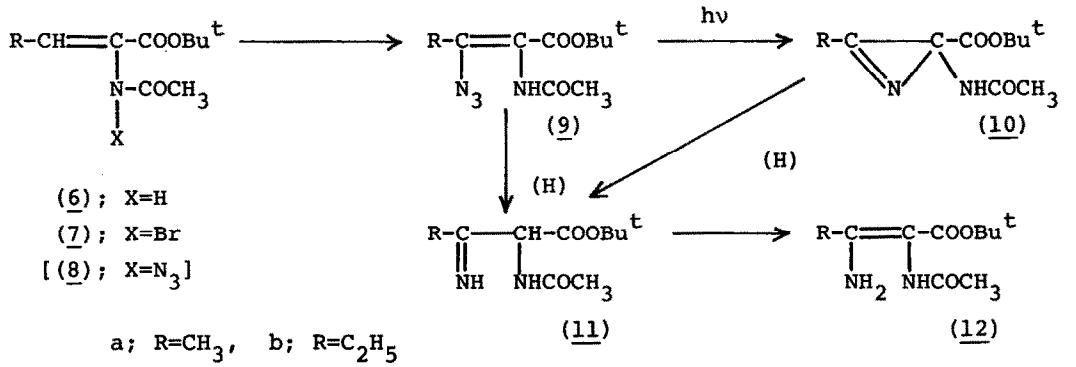


Scheme 1

In addition, similar conversions were extended to β-alkyl homologues (9: a; R=CH_3, b; R=C_2H_5)

The reduction of 9 (0.1 mol) with Al-Hg [made from Al (7 g) and $HgCl_2$ (7g)]

in ether (150 ml) at room temperature gave 12 in ca. 80% yield. In the Al-Hg reduction, surprisingly, the reaction intermediate, t-butyl 3-imino-2-acetylamino-2-pentanoate [11b; colorless syrup, IR: 3380, 3290 (NH), 1765, 1735 (C=O), 1675



Scheme 2

T A B L E 1

Yields, physical constants, and spectral data of 1, 4, 5, 10, and 12

Compound No.	Yield (%)	Mp °C (Bp °C/mmHg)	IR spectrum, cm^{-1} in KBr NH	N_3	COO	(C=N) C=C	NMR spectrum δ, in $CDCl_3$ NH	3-vinyl
1	75	33-35[a] (131-133/1)	3350	—	1740	1650	7.27s[h]	5.80s 6.22s
4	82	67-68[b]	3250	2120	1715	1650	6.16s	7.16s
5	75	104-104.5[c]	3350 -3200	—	1700	1660	6.06s 4.83s 4.77s	7.22s
10a	83	(60-63/1)	3270	—	1730	(1790)	6.94bs[i]	—
10b	82	(80-90/1)	3270	—	1740	(1785)	7.44bs	—
12a	91[d] 87[e] 67[f]	151[g]	3270 -3250	—	1675	1645	6.57s 6.28s	—
12b	91[d] 78[e] 58[f]	117-118[g]	3400 -3200	—	1675	1650	6.30s 6.17s	—

a) Colorless needles from hexane. b) Colorless needles from benzene-pet. ether. c) Colorless prisms from benzene. d) Yield from the reduction of 9 with Raney nickel. e) Yield from the reduction of 9 with Al-Hg. f) Yield from the reduction of 10 with Al-Hg. g) Colorless needles from ethanol. h) Singlet. i) Broad s.[h]

and 1520 (NHCO and C=N) cm^{-1}, NMR: δ 6.70 (1H, 2-NH, broad doublet), 5.14 (1H, 2-H, doublet, J=7.0 Hz)] was obtained purely in a 22% yield. It is unambiguous that the compound 11b was the important intermediate between 9b and 12b, since 11b was gradually isomerized at room temperature to afford 12b. However, the isolation of 11a failed.

On the other hand, interestingly, the photochemical reaction of 9 (0.01 mol) in benzene (70 ml) by means of high-pressure mercury lamp at room temperature gave 1-t-butoxycarbonyl-1-acetylamino-2-azirine (10) in a fairly good yield as a colorless syrup and its subsequent reduction with Raney nickel gave 12 in a high yield as shown in Scheme 2.

The structure of all the new compounds were characterized spectroscopically as listed in Table 1 and gave satisfactory results in elemental analysis.

Further work including the analogous study and the configurational assignment of the olefins (4, 5, 9, and 12) are now in progress.

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