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A FACILE SYNTHESIS OF α,β-UNSATURATED β-BROMO-N-ACYL-α-AMINO ACIDS

Chung-gi Shin, Katsumi Nanjo, and Juji Yoshimura*
Laboratory of Organic Chemistry, Kanagawa University, Kanagawa-ku, Yokohama 221
*Laboratory of Chemistry for Natural Products, Tokyo Institute of Technology,
Meguro-ku, Tokyo 152

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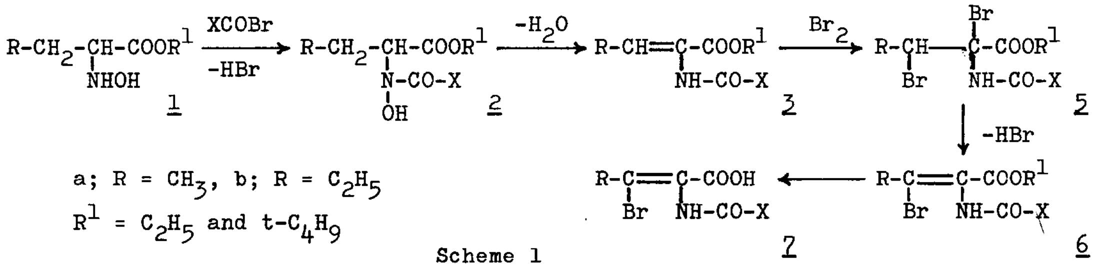
In previous papers,[1-3] we reported the synthesis of α,β-unsaturated N-acyl-α-amino acid ester (3) by the condensation of ethyl α-oxocarboxylate with amide or by the treatment of N-acetoxy-N-acyl-α-amino acid ester with Et_3N. Up to date, however, the available synthetic method of the title compounds 6 and 7 has never been reported except the preparation of β-halo-sec- and tert-enamines.[4-6] Owing to the synthetic utility of 6 and 7, a facile synthetic method was pursued here.

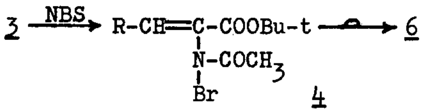
Attempts on addition of Br_2 to 3 (R^1=Et) in $CHCl_3$ and subsequent elimination of HBr was unsuccessful except the direct conversion of 3a (R^1=t-Bu) into 7a (X=CH_3; yield 59%. mp 150°C: X=OEt; yield 60%. mp 154-156°C: X=phthaloyl; yield 38%. mp 188°C). Furthermore, it was found that the treatment of ethyl α-hydroxyaminopropanoate (1a) with bromoacetyl bromide in benzene in the absence of pyridine[7] gave directly the expected ethyl N-bromoacetyl-α-amino-β-bromo-α-pentenoate (6a; X=CH_2Br, mp 118-119°C), though the yield was 6.7%. It was deduced thatthe formation of 3 viathe corresponding hydroxamic acid ester (2)[2] was successively followed by addition of Br_2 formed oxidatively from HBr, and by elimination of HBr to



Scheme 1

afford the compound 6.

On the other hand, the treatment of 3 with N-bromosuccinimide in CCl_4 gave unstable oily product; tert-butyl N-acetyl-N-bromo-α-alkenoate (4a; ν_{max} 1740, 1720, 1680 cm^{-1}: 4b; ν_{max} 1740, 1725, 1680 cm^{-1}), in quantitative yields, which gradually rearranged at room temperature for two days to give 6 as crystals in good yields. Compound 6 was composed of E- and Z-isomers, which were separated chromatography on silica-gel column using benzene-ethyl acetate (5 : 1) as effluent (Table 1). All of the new compounds and their structures have been chracterized spectroscopically and gave satisfactory elementry analysis.



$$\underline{3} \xrightarrow{NBS} R\text{-}CH{=}\underset{\underset{Br}{|}}{\underset{N\text{-}COCH_3}{\underset{|}{C}}}\text{-}COOBu\text{-}t \xrightarrow{\Delta} \underline{6}$$

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Scheme 2

Table 1. tert-Butyl N-Acetyl-α-amino-β-bromo-α-alkenoate (6)

Compound		Mp °C a)	Yield (%)	IR Spectrum, cm^{-1} in KBr	NMR Spectrum, in $CDCl_3$, NH
6a	E	138-139	54	3340,1715,1680,1645	7.06
	Z	101.5-102.5	36	3340,1715,1685,1640	7.94
6b	E	84-87	45	3270,1725,1670,1635	7.16
	Z	syrup	18	3270,1730,1680	8.35

a) Recrystallization from dibutyl ether gave colorless needles.

References and Note

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7) This reaction performing in the presence of pyridine, the corresponding hydroxamic acid esters were obtained in good yield (reference 2).