CHEMISTRY LETTERS, pp. 1171-1172, 1982.

SYNTHESIS OF NEW 2-OXAZOLINONES FROM N-CARBOXY α-DEHYDROAMINO ACID ANHYDRIDES

Yasuchika YONEZAWA, Chung-gi SHIN,* Akira OHTSU, and Juji YOSHIMURA†
Laboratory of Organic Chemistry, Kanagawa University, Kanagawa-ku, Yokohama 221
†Laboratory of Chemistry for Natural Products, Tokyo Institute of Technology, Midori-ku, Yokohama 227

Addition of methanol to N-carboxy α-dehydroamino acid anhydride in the presence of NBS, followed by the treatment of the resulting product with base gave a new 2-oxazolinone-4-carboxylate.

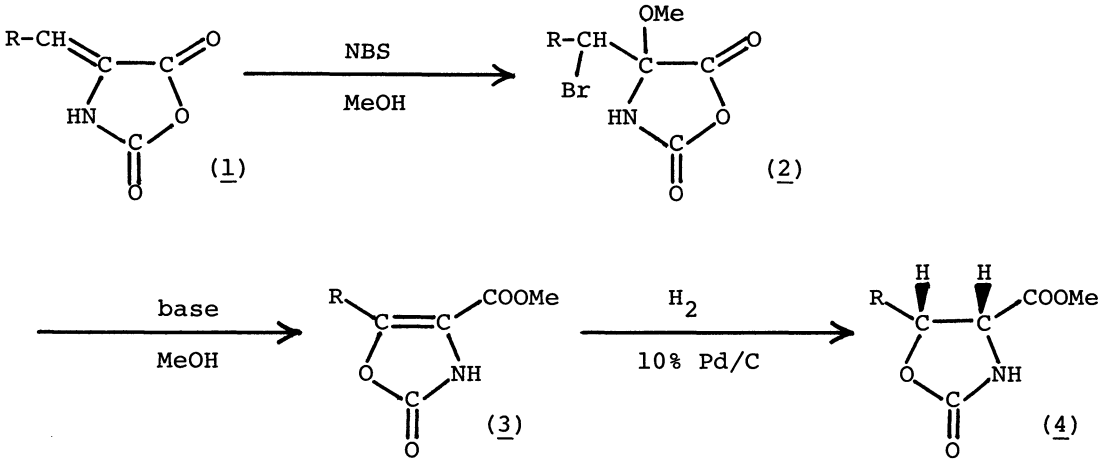
Recently, our attention has been directed to the utilization of N-carboxy α-dehydroamino acid anhydride (dehydro-NCA; 1), prepared by the cyclization of N-benzyloxycarbonyl-α-dehydroamino acid with $SOCl_2$.1) Of special interest are the addition reaction to 1 and the use of the adduct for the syntheses of peptides and heterocyclic compounds, which seem to be important to the new synthesis of various α-amino acids. Here, we will report the reaction of 1 with NBS in methanol, followed by the conversion of the resulting 4-methoxy-2,5-oxazolidione derivative into a new 2-oxazolinone-4-carboxylate.

Treatment of an equimolar 1 (2 mmol) with NBS in methanol (30 ml) under cooling for 40 minutes2) gave colorless crystals almost quantitatively, identified as 4-bromoalkyl-4-methoxy-2,5-oxazolidione (2). The subsequent treatment of 2 (1.5 mmol) with an organic or inorganic base (2 mmol), such as DBU and NaOH, in methanol (30 ml) at room temperature for 5 hr gave crude substance, which was purified on a silica gel column using a mixture of benzene and ethyl acetate (3 : 1 v/v) as the eluent to give colorless crystals.

Based on the spectroscopic data [IR: -O-CO- (1770-1755 cm^{-1}), -COOMe (1725-1715 cm^{-1}), C=C (1670-1630 cm^{-1}), NMR: δ 9.40-9.61 (NH)], satisfactory elemental analyses, and the conversion into the authentic samples, the compounds obtained above could be determined unambiguously as methyl 5-alkyl-2-oxazolinone-4-carboxylates (3). The formation of 3 from 2 would be explained by the ring cleavage of 2 with methoxide anion and recyclization of the resulting intermediate to 3, accompanied by the elimination of methanol prior to or after the cyclization.

Catalytic hydrogenation of 3a (0.1 mmol) with 10% Pd/C (0.8 g) in methanol (60 ml) at room temperature for 20 hr gave the expected methyl 5-methyl-2-oxazolidione-4-carboxylate [4a: mp 80-82 °C (lit.3) mp 83.5-84.5 °C), yield 75%. NMR ($CDCl_3$): δ 5.00 (double q, 1H, J=8.5, 6.5Hz, 5-H), 4.50 (d, 1H, J=8.5Hz, 4-H)]. From the vicinal coupling constant between ring protons,4) the compound 4a was suggested to be the erythro (cis)-isomer and this was confirmed by the comparison with the specimen derived from allo-threonine and phosgen in two steps.3)

The above results in conjunction with the previously reported conversions3,5) will be useful for the syntheses of both of erythro and threo-β-hydroxy-α-amino acids.



a; R=CH_3, b; R=C_2H_5, c; R=n-C_3H_7, d; R=i-C_3H_7, e; R=C_6H_5

Scheme 1

Table 1. The yields, melting points, and spectroscopic data of 2 and 3

Compd. No.	Yield %	Mp[a] °C	NMR, δ ($CDCl_3$) -CH-Br (J_{Hz})	Compd. No.	Yield[b] %	Mp[c] °C	IR[d] cm^{-1} C=C	NMR[e] δ NH
2a	98	93-94	4.44q (7.0)	3a	70	143-144	1670	9.43
2b	97	107-109	4.22dd (13.0, 2.5)	3b	62	111-112	1665	9.50
2c	98	86-87	4.26dd (13.0, 2.5)	3c	65	86.5-87.0	1660	9.50
2d	99	66-68	4.38d (12.0)	3c	63	90.5-91.5	1655	9.40
2e	95	140-141	5.24s	3e	75	165-166	1630	9.61

a) Colorless needles from n-hexane. b) Yield from 2 and DBU. c) Colorless needles from cyclohexane. d) Recorded in KBr. e) Measured in $CDCl_3$.

References

1) C. Shin, Y. Yonezawa, and J. Yoshimura, Chemistry Lett., 1981, 1635.
2) C. Shin, Y. Sato, H. Ohmatsu, and J. Yoshimura, Bull. Chem. Soc. Jpn., 54, 1134 (1981).
3) T. Kaneko and T. Inui, Nippon Kagaku Zasshi, 82, 1075 (1961).
4) S. Futagawa. T. Inui, and T. Shiba, Bull. Chem. Soc. Jpn., 46, 3308 (1973).
5) T. Inui, Nippon Kagaku Zasshi, 83, 493 (1962).

(Received April 30, 1982)