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NITROUS ACID DEAMINATION OF (R)-β-AMINOADIPIC ACID

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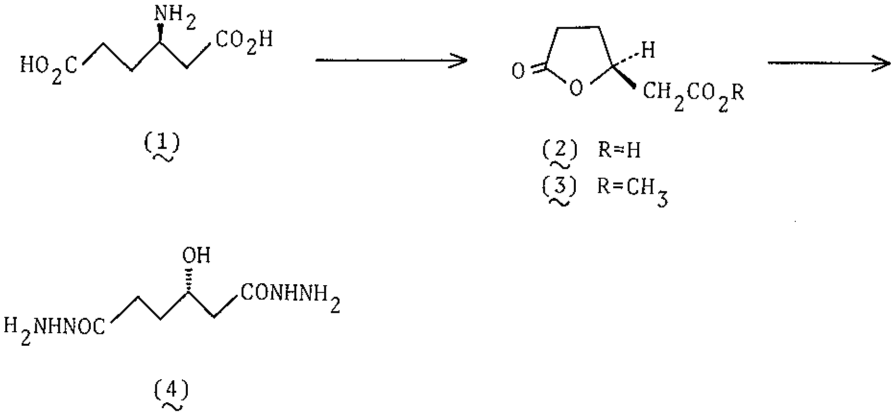
Intramolecular participation by carboxyl group in diazotization processes has received much attention. The deamination of (R)-β-aminoadipic acid in aqueous nitrous acid affords (S)-carboxymethylbutanolide (2) with 69% net inversion.

In connection with diazotization of L-glutamic acid which affords (S)-γ-carboxy-γ-butyrolactone with retention of configuration[1], we have first attempted to investigate which of the β-carboxylate and the γ-one would participate more in nitrous acid deamination of (R)-β-aminoadipic acid (1) which has the both carboxylates in one molecule.

(R)-(-)-β-aminoadipic acid (1) was obtained by the asymmetric synthesis according to our described procedure[2]. Treatment of the hydrochloride of (R)-(-)-β-aminoadipic acid [$[\alpha]_D^{23}$ -18.6° (C=1.0, H_2O), e.e. 94%] with $NaNO_2$ (1.5 equiv. mole) in 3N-HCl at -4°C for 1.5 hr and then at 24°C for 4 hr followed by evaporation in vacuo to dryness and extraction of the residue with ethyl acetate gave crude γ-carboxymethylbutanolide (**2**). Esterification with diazomethane and purification of the product by silica gel chromatography afforded (*S*)-γ-methoxycarbonylmethylbutanolide (**3**) (11%), $[\alpha]_D^{22}$+28.8° (C=0.4, EtOH). Treatment of the (*S*)-lactone (**3**) with hydrazine hydrate in methanol followed by Tlc purification (SiO_2, benzene-AcOEt 1:1) gave (*S*)-β-hydroxyadipic acid dihydrazide (**4**) (30.3%), m.p. 153-155°, $[\alpha]_D^{25}$+17.2° (C=1.0, 1N-HCl). *S*-configuration and 65% optical purity of the (*S*)-dihydrazide (**4**) were determined by comparing its optical rotation value with that for optically pure (*S*)-(+)-β-hydroxyadipic acid dihydrazide (**4**), $[\alpha]_D^{20}$+26.4° (C=1.06, 1N-HCl), derived from natural agrimonolide[3b]. This result corresponds to 69% net inversion in diazotization of (*R*)-(-)-β-aminoadipic acid (**1**) based on 94% optical purity of the starting material (**1**). This diazotization process also constitutes a first asymmetric synthesis of (*S*)-γ-carboxymethylbutanolide (**2**).

Scheme 1



(**1**)

(**2**) R=H
(**3**) R=CH_3

(**4**)

No β-lactone was found in the above diazotization of (*R*)-(-)-β-aminoadipic acid (**1**).

Intramolecular substitution of the diazonium group by the β-carboxylate in the deamination of (**1**) may lead to a β-lactone or (*R*)-γ-carboxymethylbutanolide with retention of configuration which is formed through two consecutive reactions analogous to those proposed in diazotization of α-amino acid, eg. L-phenylalanine[4]; (1) β-lactone opening by water in a back-side attack, (2) relactonization of (*R*)-β-hydroxyadipic acid. However this is not the case. In conclusion the participation of the γ-carboxyl group is remarkably preferred than that of the β-carboxylate in the deamination of (*R*)-β-aminoadipic acid (**1**), yielding (**2**) with 69% net inversion of configuration.

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REFERENCES

1. A. T. Austin and J. Howard, *J. Chem. Soc.* 3278, 3284, (1961).
2. T. Wakabayashi, Y. Kato and K. Watanabe, *Chemistry Letters*, 1283 (1976).
3. (a) Y. Kato and T. Wakabayashi, *Synth. Comm.*, in press.
   (b) H. Arakawa, N. Torimoto and Y. Masui, *Tetrahedron Letters*, 4115 (1968).
4. K. Koga, C. C. Wu and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **20**, 1282 (1972).

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