Tetrahedron Letters,Vol.29,No.47,pp 6183-6184,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

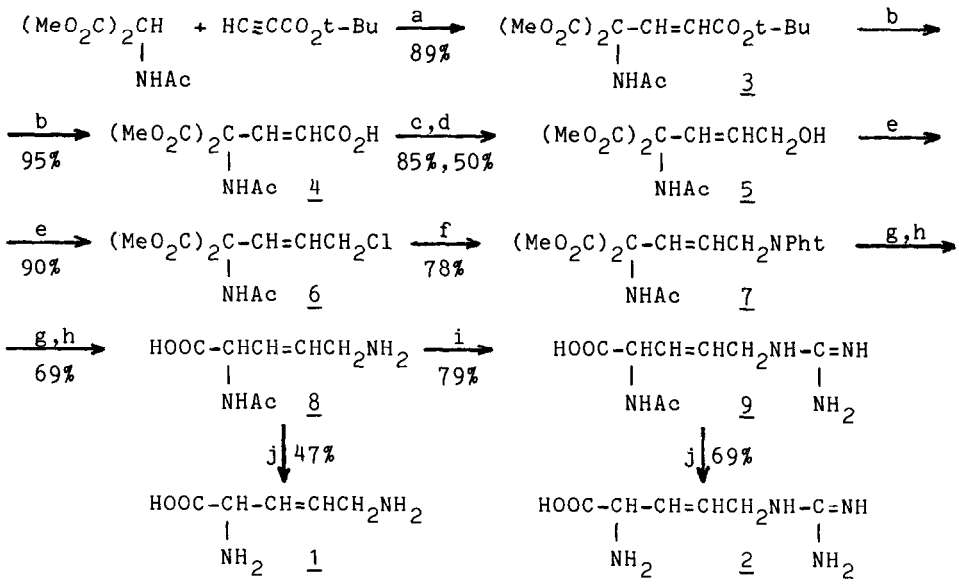
UNSATURATED AMINO ACIDS: SYNTHESIS OF TRANS-3,4-DIDEHYDRO ANALOGUES OF L-ORNITHINE AND L-ARGININE

V. Tolman *[a] and P. Sedmera [b]
a) Institute of Nuclear Biology and Radiochemistry
b) Institute of Microbiology
Czechoslovak Academy of Sciences, 142 20 Prague, Czechoslovakia

Summary: A multistep synthesis of trans-3,4-didehydro-L-ornithine and trans-3,4-didehydro-L-arginine is described.

Unsaturated analogues of naturally occuring α-amino acids are enzyme inhibitors [1], antimetabolites for certain microorganisms [2,3], antibiotics [3], chiral synthetic intermediates [4], and potential precursors for the preparation of ^{2}H- or ^{3}H-labelled amino acids. This communication describes the synthesis of L-2,5-diamino-trans-3-pentenoic acid 1 and L-2-amino-5-guanidino--trans-3-pentenoic acid 2. Racemic 1 was already mentioned by Rando [5] but no details of its preparation were given.

Our synthesis is depicted in the following Scheme. According to NMR of 3 the first step proceeds exclusively in the trans-manner. All intermediates were characterized [6] and gave satisfactory both NMR spectra and elemental analyses. The structure of target compounds was confirmed by ^{1}H and ^{13}C NMR spectra [7].



Reaction conditions:
a) KF/18-crown-6, MeCN, 25° (ref. [8]); b) CF_3CO_2H, 25°, 20 min; c) $SOCl_2$, 25°, 3 h; d) $Li(t\text{-}BuO)_3AlH$, THF, -30°, 1 h; e) $SOCl_2$, 25°, 2 h; f) potassium phthalimide/NaI, DMF, 60°, 4 h; g) NaOH, H_2O/THF, 20°; h) diluted HCl, 50°, 2 h; i) S-methylisothiourea, NaOH, 20°, 70 h; j) acylase I (Merck), pH 7.2, 37°, separation on Dowex 50 column.

References and Notes

1) a) Rando R.R.: Biochemistry **13**, 3859 (1974);
b) Chrystal E., Bey P., Rando R.R.: J. Neurochem. **32**, 1501 (1979);
c) Cooper A.J.L., Fitzpatrick S.M., Kaufman C., Dowd P.: J. Am. Chem. Soc. **104**, 332 (1982);
d) Cooper A.J.L., Fitzpatrick S.M., Ginos J.Z., Kaufman C., Dowd P.: Biochem. Pharmacol. **32**, 679 (1983).

2) Robertson A.V., Witkop B.: J. Am. Chem. Soc. **84**, 1697 (1962).

3) a) Scannell J.P., Preuss D.L., Demney T.C., Sello L.H., Williams T., Stempel A.: J. Antibiot. **25**, 122 (1972);
b) Sahm U., Knobloch G., Wagner F.: J. Antibiot. **26**, 389 (1973);
c) Preuss D.L. et al.: J. Antibiot. **27**, 229 (1974);
d) Kuroda Y., Okuhara M., Goto T., Kohsaka M., Aoki H.: J. Antibiot. **33**, 132 (1980).

4) a) Hagedorn A.A., Miller B.J., Nagy J.O.: Tetrahedron Lett. **21**, 229 (1980)
b) Uyeo S., Ona H.: Chem. Pharm. Bull. **28**, 1563 (1980).

5) Rando R.R.: Biochem. Biophys. Res. Commun. **67**, 392 (1975).

6) Melting points 3: 144-5°; 4: 149-150°; 5: 100-1°; 6: 86-7°; 7: 171-3°; 8: 183° decompn.; 9: 205-8° decompn.; L-1.HCl: 206.5° decompn., $[\alpha]_D^{20}$ +74.4° (c 0.18, 5N HCl); L-2.HCl: 174-5° decompn., $[\alpha]_D^{20}$ +85.6° (c 0.20, 5N HCl).

7) NMR spectra (Varian VXR-400, D_2O, 25°, 400 MHz for ^1H, 100 MHz for ^{13}C):
L-1.HCl - ^1H NMR: 3.583 (2H, ddd, $J_{2,5}$=1.0, $J_{3,5}$=1.0, $J_{4,5}$=4.6, H-5), 4.498 (1H, ddt, $J_{2,3}$=6.5, $J_{2,4}$=1.0, H-2), 6.153 (1H, ddt, $J_{3,4}$=15.6, H-3), 6.210 (1H, dtd, H-4); ^{13}C NMR: 41.13 (t, C-5), 56.76 (d, C-2), 129.18 (d, C-4), 129.81 (d, C-3), 172.77 (s, C-1).
L-2.HCl - ^1H NMR: 4.070 (2H, ddd, $J_{4,5}$=4.7, $J_{3,5}$=1.8, $J_{2,5}$=0.8, H-5), 4.464 (1H, ddt, $J_{2,3}$=8.0, $J_{2,4}$=1.0, H-2), 5.943 (1H, ddt, $J_{3,4}$=15.7, H-3), 6.319 (1H, dtd, H-4); ^{13}C NMR: 42.72 (t, C-5), 56.88 (d, C-2), 124.84 (d, C-3), 132.87 (d, C-4), 157.84 (s, C-6), 173.38 (s, C-1).

8) Belsky I.: J. Chem. Soc., Chem. Commun. **1977**, 237.

(Received in UK 20 September 1988)