Tetrahedron Letters No. 8, pp 525-527, 1963. Pergamon Press Ltd.
Printed in Great Britain.

THE RELATIVE CONFIGURATIONS OF THE DIASTEREOMERS OF THE DL-3-AMINO-2-METHYLBUTYRIC ACID; A CONVENIENT METHOD FOR THEIR PREPARATION VIA THE HOFMANN REARRANGEMENT

Ivan G. Pojarlieff and Bogdan I. Kurtev
Institute of Organic Chemistry, Bulgarian Academy of Sciences
Sofia 13, Bulgaria

(Received 2 January 1963)

IN a previous paper[1] the synthesis of 3-amino-2-methylbutyric acid by the Rodionow reaction[2] from acetaldehyde-ammonia and methylmalonic acid was reported. Two diastereomers with m.p. 227-229° dec. and 213-214° dec. were isolated and several of their derivatives obtained. In order to establish the relative configurations of the two asymmetric carbon atoms of the two amino acid diastereomers we used the Hofmann rearrangement which has been proved[3] to proceed with retention of the configuration of the carbon atom attached to the amide group. For this purpose we prepared the imide of DL-2,3-dimethylsuccinic acid (I) and the monoamide of meso-2,3-dimethylsuccinic acid (II). The configuration of these compounds has been carefully

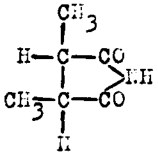
---

[1] B.I. Kurtev and I. Pojarlieff, *Comptes rendus, Acad. bulg. sc.* 16, No1, 65, (1963).

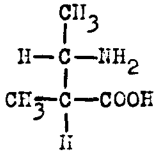
[2] V.M. Rodionow and E.F. Malevinskaya, *Chem. Ber.* 59, 2952 (1926); V.M. Rodionow and N.N. Besinger, *Izv. Akad. Nauk SSSR, OKhN*, No4, 962 (1952).

[3] S. Archer, *J. Amer. Chem. Soc.* 62, 1872 (1940); C.L. Arcus and J. Kenyon, *J. Chem. Soc.* 916 (1939).

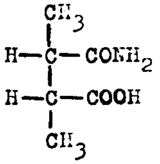
examined by hydrolysis experiments by R.P. Linstead[4] and W. Hückel[5] who have also given sure methods for their preparation. Treatment of I (0,1 mol) with an alkaline solution of KOCl (0,1 mol active chlorine and 0,52 mol free potassium hydroxide) for 75 min at 60° after acidification, extracting the residue left after evaporation in vacuo with boiling absolute ethanol and passing the extract in aqueous solution through a strongly acidic cation exchanger in H-form gave, after eluation with an 1N ammonia solution, an amino acid (III) with m.p. 232-233° (from ethanol) identical with the amino acid obtained by the Rodionow reaction with m.p. 227-229°. Similar treatment of II (0,42 mol free potassium hydroxide, 45 min, 60°) gave an amino acid (IV) with m.p. 213-214° (from ethanol) identical with that obtained by the Rodionow reaction with m.p. 213-214°.



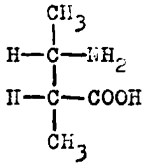
I



III



II



IV

---

[4] R.P. Linstead and M. Whalley, J. Chem. Soc. 3722 (1954).

[5] W. Hückel and H. Müller, Chem. Ber. 64, 1989 (1931).

In order to obtain compounds with more reliable melting points the reaction mixture, after the rearrangement, was treated with benzoyl chloride. From I we obtained an N-benzoyl derivative with m.p. 160-161° (from water-methanol) and from II - an N-benzoyl derivative with m.p. 128-129° (from water-methanol) which were identified with the ones obtained previously[1]. Thus the amino acid (III) with m.p. 232-233° should have threo configuration and IV - erythro configuration.

The yields of the amino acids are 65-80 % for the pure diastereomers and no isomerization was observed under the conditions of the reaction. We suppose that similar good results will also be obtained in applying this method to the preparation of other 3-amino-2,3-dialkylpropionic acids.

K. Balenović[6] reports the synthesis of two optically active diastereomers of the 3-amino-2-methylbutyric acid from L-alanin and diazoethan by his method for preparing optically active β-amino acids. Resolution of the diastereomers obtained by us and comparison with those prepared by Balenović will establish the absolute configurations of all four possible optically active isomers.

---

[6] K. Balenović, Ciba Foundation Symposium on Amino Acids, Peptides and Antimetabolytic Activity, 5, London, 1958.