PREPARATION OF SOME CARBOXYLIC ACIDS-$^{14}C(U)$ FROM AMINO ACIDS-$^{14}C(U)$

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SUMMARY

A procedure for the facile preparation of labelled carboxylic acids from labelled α-amino acids has been described. The reaction is attractive for the small scale synthesis of such compounds.

Keywords: Hydroxylamine O-sulfonic acid, amino acids-$^{14}C(U)$, carboxylic acids-$^{14}C(U)$

During our investigations[1] on the use of labelled amino acids for the preparation of other useful labelled compounds by one step reactions, we observed that amino acids are very convenient precursors for carboxylic acid synthesis. The reduction of amino groups in amino acids was initially attempted by refluxing or heating them in a sealed tube in presence of hydrogen iodide and a slight amount of red phosphorus. However, the yields were poor, ranging between 5 and 15%.[2] In a recent paper [3] the use of hydroxylamine O-sulfonic acid(HAOS) for reduction of amino group has been reported to give better yields(40-70%).

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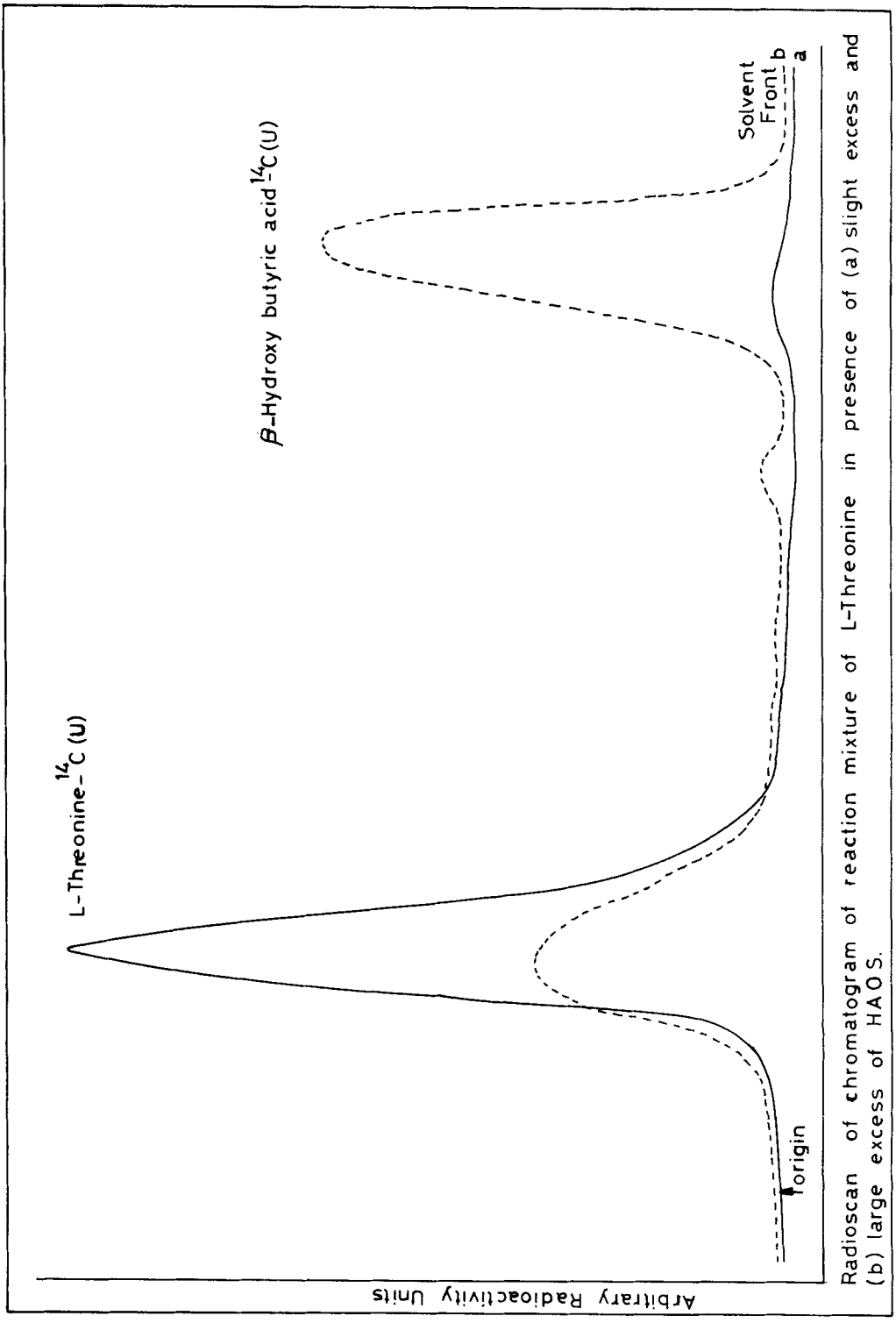
The reaction can be represented as:

$$RNH_2 + H_2NOSO_3H \xrightarrow[OH^-]{0^\circ C} RNHNH_2 \longrightarrow RN{=}NH \longrightarrow RH$$

Both amino acids and amines have been reported to give the corresponding deaminated compounds. In view of mild conditions, good yields and wide applicability of the reaction, we studied the synthesis of some carboxylic acids from amino acids- $^{14}C(U)$. Since amino acids and products have widely different properties, isolation of products was also expected to be easy. The initial tracer experiments showed that taking HAOS and the amino acid in a ratio of 2 or 3 to 1, was not sufficient to give the product in yields more than about 5%(Fig.1). Use of large amounts of HAOS was therefore resorted to. A ratio of 20:1 was found satisfactory and good yields (60-85%) without much side products could be obtained. The great advantage of the method was that the reaction could be performed at very low concentrations such as 50 micromoles of amino acids and it was very easy to carry out. The products were identified by standard paper chromatography and TLC techniques using authentic compounds for comparison. Glutaric acid-$^{14}C(U)$ and succinic acid-$^{14}C(U)$ were isolated by ether extraction of the acidified reaction mixtures. In case of β-hydroxy butyric acid-$^{14}C(U)$ and isovaleric acid-$^{14}C(U)$ further purification of the ether extracts was found to be necessary.



Radioscan of chromatogram of reaction mixture of L-Threonine in presence of (a) slight excess and (b) large excess of HAOS.

Following were the full results:

No.	Amino acid	Quantity taken (μCi)	(μM)	Product	Yield (%)
1.	L-Threonine-^{14}C(U)	100	50	β-Hydroxy butyric acid-^{14}C(U)	55
2.	L-Glutamic acid-^{14}C(U)	100	50	Glutaric acid-^{14}C(U)	70
3.	L-Aspartic acid-^{14}C(U)	100	50	Succinic acid-^{14}C(U)	89
4.	L-Valine-^{14}C(U)	250	100	Isovaleric acid-^{14}C(U)	65

EXPERIMENTAL

Succinic acid-^{14}C(U)

To an ice-cold solution of L-aspartic acid-^{14}C(U) (50 micromoles, 100 microcuries) in 1 ml of 2.5 N NaOH, 2 millimoles of hydroxylamine O-sulfonic acid (225 mg) was added and the reaction mixture stirred at 0°C for 4 hours. The reaction mixture was periodically analysed by paper chromatography followed by radioactivity scanning. When most of the aspartic acid had changed to succinic acid, the mixture was acidified with dilute sulphuric acid, concentrated to a small volume and extracted with ether in a liquid-liquid extractor for 6 hours. The ether extract was rotary evaporated to dryness, the residue, namely succinic acid-^{14}C(U) was dissolved in water and counted (89 microcuries, yield 89%). An aliquot of the succinic acid-^{14}C(U) was analysed by paper chromatography in butanol: acetic acid:water (4:1:5) solvent system and was found to be radiochemically pure (99%). The same procedure was used for the preparation of glutaric acid-^{14}C(U) from L-glutamic acid-^{14}C(U).

In the case of the preparation of isovaleric acid-^{14}C(U) and β-hydroxy butyric acid-^{14}C(U) the product in the ether extract was found to contain some other labelled impurities. Therefore after evaporation of the ether, the residue was taken up in 2ml of water and loaded an a column(110 cm x 1 cm) of Dowex 50 x 8(200 mesh) resin and eluted with water. The fraction coming out in the eluent from 72 to 85 ml was found to contain the product in a radiochemically pure form.

CONCLUSION

The specific reduction of amino groups in amino aicds by means of hydroxylamine O-sulfonic acid can be used for preparative uses in labelled compounds synthesis. This method may be of considerable value for reduction of β-hydroxy amino acids to prepare β-hydroxy acids which are difficult to prepare by other methods.

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