NOTE

SYNTHESIS OF 4-(3-t-BUTYLAMINO-2-HYDROXYPROPOXY)-BENZIMIDAZOL-2(^{11}C)-ONE (CGP 12177)

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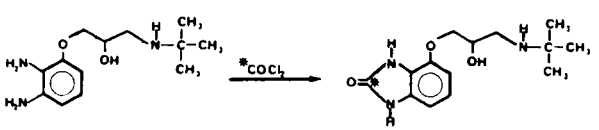
SUMMARY

4-(3-t-butylamino-2-hydroxypropoxy)-benzimidazol-2 (^{11}C)-one (CGP 12177) was synthetized in a short time (30 min) and with a specific activity of 130 mCi/μMol for β receptor studies by the positron emission tomography. The radioactive reagent was ^{11}C-phosgene and the starting material 1-(3-t-butylamino-2-hydroxypropoxy)-2,3-diamino benzene.

Key words : ^{11}C, CGP 12177, 4-(3-t-butylamino-2- hydroxypropoxy) benzimidazol-2-one, Positron, β receptor.

INTRODUCTION

4-(3-t-butylamino-2-hydroxypropoxy)-benzimidazol-2-one (CGP 12177) is a new ligand which binds to β adrenergic receptors (1). This compound has high affinity for those receptors and shows low-capacity for non-specific binding. It has been labelled with carbone-11 for in vivo studies by positron emission tomography technic and was synthetized by reaction of ^{11}C- phosgene on the diamino precursor 1, 1-(3-t-butylamino-2-hydroxypropoxy)-2,3-diamino benzene (Fig.1).



1 CGP 12177

Fig. 1 Schema of the synthesis

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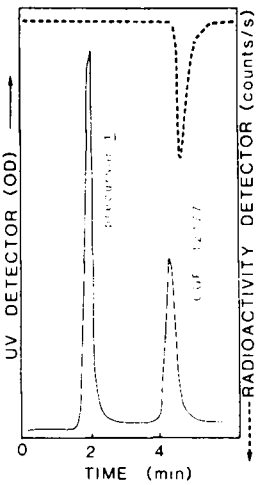

Fig. 2 Separation of ^{11}C-CGP 12177 by HPLC

Experimental and results :

All synthetic operations were carried out semi automatically in a well shielded cell (2). The synthesis of ^{11}C-$COCl_2$ has been described previously (3).

The labelled phosgene ^{11}C-$COCl_2$ is transfered after its synthesis under a helium stream at a flow rate of 10 mL/min into the reactional mixture containing 0.2 mg (0.79 µMol) of diamino precursor 1 previously dissolved in 30-40 µL of CH_2Cl_2 then diluted by 400 µL of toluene. After trapping ^{11}C-$COCl_2$, the reaction mixture is evaporated to dryness using a heating bath at 130° C under a helium stream, then cooled in a water bath. The radioactive residue is dissolved in 1 mL of a mixture of a physiological saline solution-ethanol 8:2 containing phosphate buffer (1 M) at 4.10^{-3} M. used as chromatography eluent and injected in the chromatographic system. The products are separated with a divinylbenzene columm (PRP1 ; length : 30.5 cm, internal diameter 7 mm ; Hamilton) at a flow rate of 4 mL/min and their mass detected by a UV detector at 254 nm and their radioactivities by an ionisation chamber. The retention times are 4.50 min for CGP 12177 and 2.10 min for the precursor 1. The radioactive fraction, containing the labelled product, is collected,

ethanol is evaporated under a nitrogen stream at 80-90°C, then the solution is sterilised by passage through a Millipore filter and introduced into a seringe.

The synthesis of ^{11}C-CGP 12177 has been optimised by previous experiments using non radioactive products. The melting point and the mass spectra of the obtained product are similar to those of authentic samples. The time for the synthesis of the ^{11}C-CGP 12177 solution ready for injection, after the end of the bombardment is 30 min. After 30 min. of irradiation of the nitrogen target by 20 MeV protons (30 μA), we obtain 180-250mCi of ^{11}C-CGP 12177 and a specific activity of 130 mCi/μ Mol.

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BIBLIOGRAPHY

1. Staehelin M., Simon P., Jaeggi K., Wigger N. ; J. Biol. Chem. 358, 3496 (1983).

2. Berger G., Maziere M., Knipper R., Comar D. ; Int. J. Appl. Radiat. Isot. 30, 393 (1979).

3. Crouzel C., Roeda D.,Berridge M., Knipper R., Comar D. ; Int. J. Appl. Radiat. Isot. 34,11 (1983).