Specific Isotopic Hydrogen Labelling of (-)-Inositol by Catalytic Self-Activation on Platinum Oxide

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The two most widely used general one-step methods for tritium labelling of organics are the Wilzbach gas irradiation technique [1] with T_2 and catalytic exchange with T_2O [2]. In (-)-inositol (I), tritium labelling by the former procedure is non-specific and non-uniform [3] whereas using catalytic exchange with isotopic water on pre-reduced platinum, predominant isotope incorporation occurs at C1 and C6 [4].

Recently, a new type of catalytic exchange procedure has been developed involving *in situ* reduction of platinum oxide ($PtO_2.2H_2O$) by organic compounds [5]. The important aspect of this "self-activation" process is that it provides a convenient tritiation procedure for a large range of compounds without the necessity for hydrogen pre-activation of the catalyst. In general, it is found [5] that aromatic compounds are more reactive than aliphatics in self-activation and exchange although hydroxyl groups in an aliphatic molecule may exert an activating influence. Recent experiments have shown that self-activated catalysts possess certain specificity [6] when compared with conventionally prepared catalysts. In the present studies the applicability of the technique to compounds of biological interest was studied using the labelling of (-)-inositol with tritium by self-activation on platinum oxide and the results compared with previous methods.

(-)-Inositol (1 g) dissolved in 4 ml of tritiated water (0.5 c/ml) was added to platinum oxide (0.011 g), the reaction vessel was vacuum sealed and heated at 130° C for 48 hrs without shaking. At the end of this time, the tube was opened, T_2O removed under vacuum and the crude material chromatographed to radiochemical purity (3.39 c/mole).

(-)-Inositol because of its twofold axis of symmetry (AB, Fig. 1), has three pairs of equivalent positions (1 and 6, 2 and 5, 3 and 4) [7]; hence the tritium content needs to be determined in three positions only. The (-)-inositol (specific activity 3.39 c/mole) was converted into its di-isopropylidene acetal [8] (II) which was cleaved by lead tetra-acetate to give the dialdehyde (III, spec. act. 3.36 c/mole) where all the carbonbound hydrogen atoms are still present. Oxidation of the aldehydic groups to carboxyl groups causes loss of H3 and H4, hence the reduction of the specific activity in this step is the measure of the tritium in these positions. Oxidation of (III) by bromine yielded the dicar-

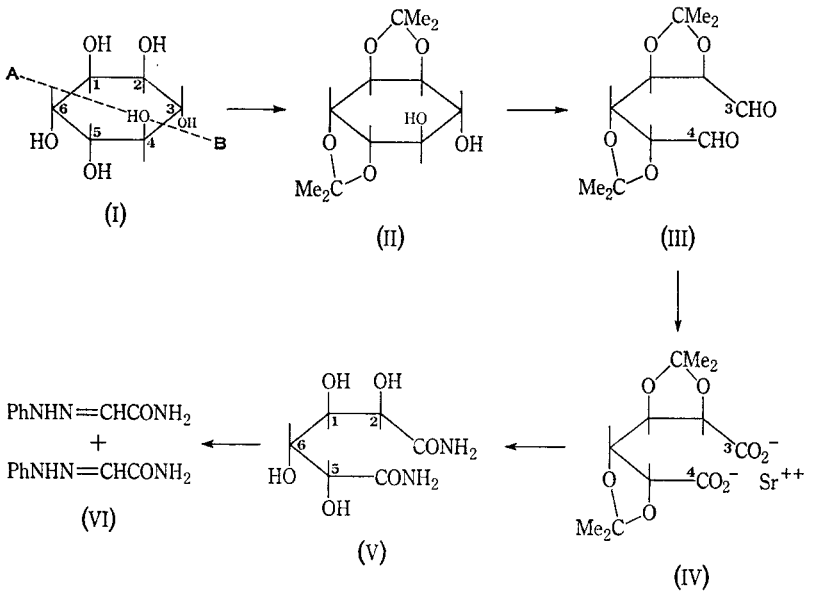

Fig. 1. Degradation of (—)-inositol. The numbers on the carbon atoms throughout the reaction sequence refer to the original numbering of the inositol (I).

boxylic acid (IV, 2,3 : 4,5- di-*O*-isopropylidene - *D*-mannaric acid), isolated as its strontium salt (spec. act. 3.23 c/mole). The acid was converted through its dilactone to *D*-mannaramide (V) which was cleaved by sodium periodate to glyoxylamide, isolated as its phenylhydrazone (VI, spec. act. 0.13 c/mole). Glyoxylamide contains only H2 and H5 of the original hydrogen atoms of the inositol and its specific activity measures the tritium in these positions. The difference in the activity between IV and VI is a measure of the amount of tritium on C1 and C6.

The results show that most of the tritium (92.5%) is at C1 and C6, thus indicating that it is possible to obtain specifically labelled (-)-inositol by the catalytic self-activation exchange process. This principle of specificity may also be possible in other members of the inositol series and related compounds.

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