Journal of Labelled Compounds and Radiopharmaceuticals—Vol. XXIV, No. 5

SYNTHESIS OF METHANOL TRITIATED IN THE METHYL GROUP ONLY

Desmond V. Dass, Victor J. Dempsey, R.Wayne Martin
and Allan L. Odell
Urey Radiochemical Laboratory, University of
Auckland, Private Bag, Auckland, New Zealand.
Received on

SUMMARY

Methanol has been labelled with tritium in the methyl group, and the position of the label confirmed using Tritium N.M.R. spectrometry. The methanol was prepared by reacting tritium, hydrogen and carbon dioxide over a copper/zinc/chromium catalyst at a total pressure of 500 psi. Water was removed by micro-distillation followed by preparative G.L.C. These procedures also removed tritium from the hydroxyl group of the methanol.

Key Words: Tritiated Methanol, Tritium N.M.R., Specific Labelling

INTRODUCTION

As part of our programme of study on mechanistic aspects of the conversion of methanol to gasoline over the zeolite catalyst ZSM-5, we had need of a sample of methanol labelled with tritium in the methyl group but free from tritium in the hydroxyl group. This latter condition was regarded as important as we wished to avoid having labile tritium in the test system which could become incorporated in reaction products not involved in the reactions of the methyl group.

Most synthetic methods for the production of ^{3}H-methanol have utilised either tritiated water[1] or lithium tritide[2] as the isotope source. In order to develop a method capable of producing a high specific activity product we chose tritium gas to provide the isotopic label. A route was developed based on the method used by Ott et al.[3] to produce fully deuterated methanol. This involved reacting carbon dioxide, tritium and hydrogen gas over a copper/zinc/chromium catalyst. As this method produces labelling of both carbon-bound and oxygen-bound hydrogens, it becomes necessary to remove oxygen-bound tritium and to do this quantitatively. A method of demonstrating that the -OH group is finally

0362-4803/87/050517-04$05.00

Received June 19, 1986
Revised October 7 1986

completely free from tritium is necessary.

EXPERIMENTAL

(a) Preparation of catalyst:

The catalyst, containing copper, zinc, and chromium in a ratio 7:2:1 was prepared[3] by the following procedure. Hydroxides of the three metals were precipitated from an aqueous solution of the mixed nitrates by adding sodium carbonate and the precipitate was filtered, washed and extruded into cylindrical pellets 2 mm long by 1 mm wide. These pellets were dried in air and slowly heated to 250 °C and then reduced in a stream of hydrogen at 400 p.s.i. at 240 °C in the methanol synthesis apparatus, described in the next section.

(b) Apparatus

The high pressure synthesis apparatus consisted of two stainless steel cylinders, connected by stainless steel tubes in a similar design to that described by Ott[3], and named "Small Scale Apparatus". The total volume of this apparatus was 496 ml. Three Curies of tritium gas, in a glass break-seal ampoule, were inserted in a rubber tube in line from the hydrogen tank to the reactor inlet. The tube was evacuated to 0.3 Torr, the ampoule broken, and tritium swept into the reactor by a stream of hydrogen gas to a pressure of 20 p.s.i. Carbon dioxide was added to give a total pressure of 120 p.s.i. followed by hydrogen gas to give a final pressure of 500 p.s.i. The catalyst bed was heated to 225 °C and the condenser maintained at room temperature both to encourage convection of the reacting gases and also to condense the product and so displace the equilibrium towards methanol. After 3 days the pressure had fallen to 180 p.s.i. and the product was drained off into a chilled vial, 3.2 ml being obtained, and sealed in glass. A total of 3.2 ml of liquid was obtained giving a methanol yield of 28 %.

(c) Removal of water by micro-distillation

3.2 ml of tritiated methanol/water mixture was diluted with 5 ml of unlabelled water and distilled in a micro pyrex still using a column 75 mm long and having I.D. 10 mm, filled with stainless steel Dixon rings (2.5 mm x 2.5 mm, 100 mesh). Below a dripping point at the bottom of the condensor a glass cup of capacity 50 µl was suspended to collect the reflux but allow the overflow to return down the column packing. A 200 mm long hypodermic needle mounted on a syringe was inserted down the condensor and used to withdraw the contents of the cup from time to time without interrupting the distillation. The tritiated water by-product was diluted and stored.

The undecoupled Tritium NMR spectrum of the product showed a sharp singlet arising from tritium in the hydroxyl position and a triplet confirming the presence of tritium in the methyl group.

Addition of 5 ml of water and a repeat of the distillation procedure lowered the abundance of hydroxyl tritium as revealed by N.M.R. studies, but not to zero even after a second repeat. This result suggests that exchange of the hydroxyl hydrogen in methanol with solvent water may not be rapid.

A procedure using exchange with sorbitol was therefore adopted as follows.

(d) Final removal of tritium from hydroxyl group.

The product was passed through a semi-preparative GLC column packed with Sorbitol on Gas Chrom.Q under the following conditions: Column 1.5 m x 10 mm I.D., Packing 25 % Sorbitol on Gas Chrom.Q., Detector T.C.D., Carrier dry nitrogen 30 ml min^{-1}, Collector 3-turn radiator trap (100 mm O.D. pyrex tubing) cooled in dry ice/acetone. With injection of 250 µl of methanol collection efficiencies of 85-95 % were obtained. Between injections of tritiated methanol, 10 to 12 samples of unlabelled water, aggregating to 2 or 3 ml in all, were injected to flush out exchangeable tritium from the stationary phase.

(e) The product

Tritium NMR study showed strong signals for methyl tritium but no detectable activity for tritium in the hydroxyl position. From a consideration of the amplitude of the noise, we estimate that any tritium remaining in this position must be less than 2 % of the total. Dry methanol (1.1 ml) of specific activity 150 mCi ml^{-1} was obtained. Higher specific activity products should be readily attainable using this method.

ACKNOWLEDGEMENTS

We wish to thank Mr A.A.T. Bailey, Mr A. Wernham and Mr D. Newton for design and construction of apparatus and the N.Z. Energy Research and Development Committee for a salary grant (for D.V.D.).

REFERENCES

(1) W.G. Verly, J.R. Rachele, V. Du Vigneaud, M.L. Eidinoff and J.E. Knoll; J. Amer. Chem. Soc. 74: 5941 (1952).

(2) M. Zielinski; Nukleonika, 7: 789 (1962).

(3) D.G. Ott, V.N. Kerr, T.W. Whaley, T. Benziger and R.K. Rohwer; J. Label. Cmpds. 10: 315 (1974).