# NOTE

## ONE POT SYNTHESIS OF SODIUM $^{14}$C-FORMATE*

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### SUMMARY

A one pot synthesis of sodium $^{14}$C-formate by reduction of $^{14}CO_2$ with $NaBH(OMe)_3$ in THF solution is described. This process is suitable for large scale, high specific activity preparations.

Key Words: Sodium $^{14}$C-formate, one pot reaction.

### INTRODUCTION

Sodium $^{14}$C-formate, 1, is an important labelled reagent used most conspicuously for the synthesis of $^{14}$C-labelled purines and other heterocyclic compounds[1,2].

Older preparations of 1 involved hydrolysis of $K^{14}CN$ or catalytic reduction of $NaH^{14}CO_3$.[3] Both methods afford the product in 95% yield. However, there is considerable inconvenience and risk involved since these reactions require high pressure and/or temperature.

Reduction of $CO_2$ with solid $NaBH(OMe)_3$ to give unlabelled 1 was described by Brown in 1953.[4] This process was adapted by Nystrom[5] to the labelled

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synthesis. The product 1, was acidified and $^{14}$C-formic acid was isolated by steam distillation. Yields ranged between 80-90%. Although this was more convenient than the previous methods, we felt that the isolation of large quantities of labelled product by steam distillation was a serious drawback. In order to avoid this isolation problem and make the synthesis more practical, a one pot vacuum line process, based on the Brown/Nystrom method was developed.

## RESULTS AND DISCUSSION

Reaction conditions are more easily controlled in solution than in heterogenous systems. Since $NaBH(OMe)_3$ is readily soluble in THF, homogenous reaction conditions seemed feasible. Furthermore, the desired product, 1, is non-volatile while the other reaction product, $B(OMe)_3$, boils at 68°. Sodium $^{14}$C-formate could, therefore, be isolated directly in the reaction flask as a residue following evaporation of all volatile materials. A large scale reduction of $^{14}CO_2$ was implemented to demonstrate this approach.

$NaBH(OMe)_3$ contained in a side-arm reaction flask and connected to a vacuum line was dissolved in THF. $Ba^{14}CO_3$ (224 mCi, 7.34 mmol) was acidified and the liberated $^{14}CO_2$ was vacuum transferred into the cooled reaction flask. After stirring at ambient temperature for several days excess reducing agent was quenched with acetone and all volatile materials were removed on the vacuum line into a liquid nitrogen cooled receiver. The residue of $NaO_2{}^{14}CH$ was obtained in 96.4% radiochemical yield and this product was radiochemically pure by tlc.

Reaction conditions were not optimized with respect to time. Secondly, a two fold excess of reducing agent was employed to ensure complete utilization of $^{14}CO_2$. The acetone quench of the excess reducing agent generated NaOPr-i as a nonvolatile by-product. This did not interfere with subsequent reaction in our case.

Although 1 may be dissolved and transferred into another reaction flask, it is not necessary to do so. Subsequent reactions may be performed directly in the original reaction flask thereby avoiding the hazards associated with the transfer of large quantities of radioactive materials. We have, in fact, achieved excellent yields of 8-$^{14}$C-labelled purines in this manner (manuscript in preparation).

The availability of pure product directly in a one pot reaction under mild conditions makes this process safe, convenient, and useful for the preparation of any desired quantity of $NaO_2{}^{14}CH$.

## EXPERIMENTAL

Barium $^{14}$C-carbonate was obtained from Amersham Corp. and used without dilution. Sodium trimethoxyborohydride was purchased from Alfa Products Inc. Radiochemical purity was determined using a Bethold Model 2760 Radiochromatography Scanner. Radioassays were obtained using a Packard Tri-Carb Model 574 liquid scintillation counter.

### Sodium $^{14}$C-Formate

A side-arm septum flask containing $NaBH(OMe)_3$ (1.94 g, 15.1 mmol) was connected to a vacuum line and evacuated. After cooling to -78°, approximately 15 ml of THF was distilled over from $LiAlH_4$.

$H_2SO_4$ was injected into a second evacuated side-arm septum flask containing $Ba^{14}CO_3$ (1.45 g, 7.34 mmol, 224 mCi, 30.5 mCi/mmol). The liberated $^{14}CO_2$ was vacuum transferred into the cooled reaction flask. Following this transfer, the stopcock to the reaction flask was closed and the cooling bath removed. The homogenous reaction was stirred at ambient temperature for seven days. Acetone was injected to destroy any remaining reducing agent and volatiles were vacuum transferred into a liquid nitrogen cooled receiver. Two additional evaporations from methanol ensured complete removal of volatile materials. The solid white residue of sodium $^{14}$C-formate, 216 mCi, was obtained in 96.4% radiochemical yield. The chromatographic mobility of the product was identical to standard.

Radiochromatography: $SiO_2$; MeOH-i-PrOH-$NH_4OH$-$H_2O$ (9:6:3:2).
Visualized with bromphenol blue spray.

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