

## A CONVENIENT PREPARATION OF $^{18}\text{O}$ -DIMETHYLFORMAMIDE

R. Rao Koganty and George A. Digenis\*

College of Pharmacy, University of Kentucky,  
Lexington, Kentucky 40506, U.S.A.

Received on March 26, 1974.

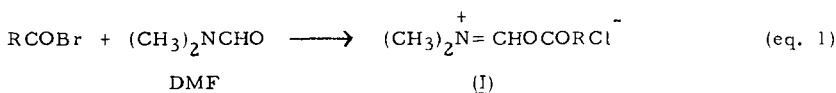
### SUMMARY

*A method is described by which  $^{18}\text{O}$ -DMF can be prepared conveniently and in very high yields (~90%) by reacting at room temperature an equimolar quantity of benzoyl chloride, DMF and  $^{18}\text{O}$ -labelled water.*

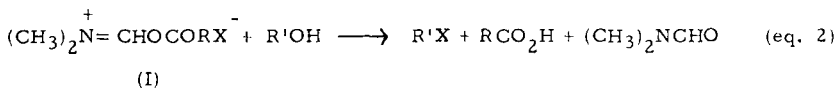
### INTRODUCTION

A number of studies are known that illustrate the chemical reactivity of the carbonyl oxygen in N,N-dimethylformamide (DMF).<sup>1-6</sup> Stephens et al.<sup>7</sup> have described a reaction of sulfonyl chlorides with primary amides which probably involves O-acylation. Haszeldine<sup>8</sup> found that Lewis acids also react with DMF at the oxygen atom. Hall<sup>5</sup> noticed that when either acyl or benzoyl bromides were mixed with DMF in equimolar proportions, 1:1 crystalline salts were formed (eq. 1). These were assigned formula I on the basis of their reactions with aniline and water. Thus, the salt from benzoyl bromide gave benzanilide in 84.8% yield with aniline and benzoic acid in 79.3% yield in water.<sup>5</sup>

\*To whom correspondence should be addressed.

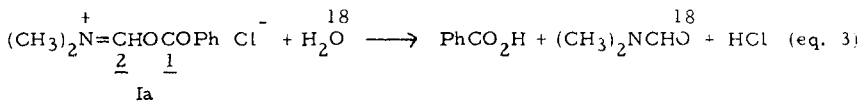


We have recently reported<sup>9</sup> that when DMF-acyl halide intermediates (I) were treated with aliphatic alcohols at room temperature, alkyl halides were produced in quantitative yields (eq. 2).



In the course of investigating the mechanism of the above reaction (eq. 2) it became necessary to synthesize <sup>18</sup>O-dimethylformamide (<sup>18</sup>O-DMF).

We wish to report here that <sup>18</sup>O-DMF can be prepared conveniently and in very high yields by reacting at room temperature an equimolar quantity of benzoyl chloride, DMF and <sup>18</sup>O-labelled water (eq. 3).



## EXPERIMENTAL

### Preparation of <sup>18</sup>O-Dimethylformamide

7.3 g (0.1 m) of dimethylformamide (dried over pulverized KOH and distilled) and 14.0 g (0.1 m) of benzoyl chloride were placed in an erlenmeyer flask equipped with a magnetic stirrer and a calcium chloride drying tube. The contents were cooled to 0-5° in an ice bath for about 10 min. 1.85 g (0.1 m) of <sup>18</sup>O-labelled water (20% mole of <sup>18</sup>O isotope) was then introduced slowly while stirring. In about 5 min after addition of isotope labelled water the contents were solidified due to the precipitation of benzoic acid. [At this stage a sample of the reaction examined mass spectrometrically showed <sup>18</sup>O in DMF. The identity of the formed benzoic acid was proven by isolation.

This acid could be isolated from the reaction mixture by either extraction with petroleum ether or carbon disulfide or alternately by direct filtration with subsequent washing with water. ] 8.4 g (0.1 m) of sodium bicarbonate was added to the reaction and when the evolution of carbon dioxide ceased the contents were extracted with acetone (3 x 15 ml). The acetone layer was dried over 5 g of anhydrous potassium carbonate and filtered. Acetone was removed under reduced pressure and the residual liquid was distilled at atmospheric pressure to obtain 6 g (81%) of  $^{18}\text{O}$ -dimethylformamide (153° C). The mole percentage of  $^{18}\text{O}$ -isotope in the so produced dimethylformamide was determined mass spectrometrically and was found to be 18% (90% incorporation, obtained as the average value of three experiments). The isotope abundances were as follows:

<u>m/e</u>	<u>% of P</u>
73(P)	100
75(P+2)	18

### $^{18}\text{O}$ -Exchange Studies

Equimolar quantities (0.01 m) of dimethylformamide (DMF),  $\text{H}_2\text{O}^{18}$  and concentrated HCl were heated at 60° C for 24 hours. When a sample of this solution was examined by mass spectrometry it showed no incorporation of  $^{18}\text{O}$  into DMF.

### DISCUSSION

From the data obtained above it is clear that the reaction between  $\text{H}_2\text{O}^{18}$  and the DMF-acyl chloride intermediate Ia (eq. 3) leads to  $^{18}\text{O}$ -DMF via an attack of the former at the immonium carbon (carbon #2) of the latter (Ia, eq. 3). The reaction, depicted by equation 3, appears to proceed to completion at 5° in about 5 min, as evidenced by the quantitative release of benzoic acid and the incorporation of  $^{18}\text{O}$  into its DMF fraction.

In contrast, however, the  $^{18}\text{O}$ -exchange studies show that the oxygen atom of DMF does not exchange with  $\text{H}_2^{18}\text{O}$  under strong acid conditions at  $60^\circ\text{C}$ , for prolonged periods of time (24 hours).

## REFERENCES

1. Kuhn, S. J. and McIntyre, J. S. — Can. J. Chem., **43**:375 (1965).
2. Kuhn, S. J. and McIntyre, J. S. — Can. J. Chem., **43**:995 (1965).
3. Garrard, W., Lappert, M. F., Pyrzora, H. and Wallis, J. W. — J. Chem. Soc., 2144 (1960).
4. Jones, R. A. Y. and Katritzky, A. R. — Chem. Ind., London, 722 (1961).
5. Hall, H. K. — J. Amer. Chem. Soc., **78**:2717 (1956).
6. Pattison, V. A., Colson, J. G. and Carr, R. L. K. — J. Org. Chem., **33**:1084 (1968).
7. Stephens, C. R., Branco, E. J. and Pilgrim, F. J. — J. Amer. Chem. Soc., **77**:1701 (1955).
8. Haszeldine, R. N. — J. Chem. Soc., 4150 (1954).
9. Koganty, R. Rao, Shambhu, M. B. and Digenis, G. A. — Tetrahedron Letters, 4511 (1973).