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A CONVENIENT METHOD FOR THE PRODUCTION OF DIAZOMETHANE-d_2

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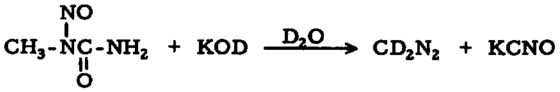
Published procedures for the preparation of diazomethane-d_2 include at least four methods based upon the exchange of diazomethane with D_2O in basic solution[1-4], one method utilizing exchange in an acidic medium[5], and two methods utilizing deuterated precursors.[1,6] The exchange reactions carried out in heterogeneous solution involve thorough mixing of the phases to approximate a homogeneous solution, the best results being obtained by the "violent agitation"[3] for 30 min of the two phases containing this potentially explosive compound. The exchanges carried out in acid or neutral solution resulted in the destruction of substantial amounts of diazomethane through the formation of methanol, while the generation of diazomethane-d_2 from deuterated chloroform and hydrazine was reported to afford impure diazomethane in low yield.[6]

We wish to report a convenient method for the production of diazomethane-d_2 in high isotopic purity and yield. This method utilizes a homogeneous solution of 1,2-dimethoxyethane-D_2O in which diazomethane is generated from N-nitrosomethylurea by the action of potassium deuteroxide. After the diazomethane has undergone deuterium exchange, the solution is cooled in dry ice to freeze the water from the homogeneous solution, according to the method of Robins and coworkers,[7] as modified by Gin and Dekker.[8,9] The resulting solution of diazomethane in 1,2-dimethoxyethane can be utilized directly.



$$CH_3\text{-}\overset{\overset{NO}{|}}{N}\underset{\underset{O}{\|}}{C}\text{-}NH_2 + KOD \xrightarrow{D_2O} CD_2N_2 + KCNO$$

In a typical experiment, a solution of 1,2-dimethoxyethane (30 ml) and KOD-D_2O (20 ml, 0.6 N) at ice bath temperature was treated dropwise with N-nitrosomethylurea (0.5 g, 4.9 mmoles) in 5 ml of 1,2-dimethoxyethane. The diazomethane solution was stirred for several minutes at 0°C and then immersed in a dry-ice-acetone bath (drying tube). The resulting solution of diazomethane in 1,2-dimethoxyethane was decanted from the frozen aqueous phase and was again cooled to -78°C to remove traces of water. Treatment of the reactants in Table I with this sample of diazomethane afforded the corresponding methylated products in theoretical yield and with the isotopic purity indicated in the Table.

We will report shortly on the use of a single phase system for the *in situ* generation of diazomethane.

Table I. Incorporation of Deuterium into Methylated Products

Reactant	% D in methylated product[a]	D exchange as % of theoretical[b]
m-nitrobenzoic acid-*d*$_1$	89	93
p-nitrogenzoic acid-*d*$_1$	90	94
m-nitrophenol-*d*$_1$	86[c]	90
p-nitrophenol-*d*$_1$	83[c]	87

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[a] Determined by mass spectrometry and nmr spectrometry. Since 99% D_2O and undeuterated N-nitrosomethylurea were utilized in the reaction, the theoretical level of deuterium incorporation was 96%, rather than 100%. [b] Based on the presence of 4% H introduced into the reaction mixture as HOD and undeuterated N-nitrosomethylurea. [c] These values are probably slightly low due to incomplete exchange of the starting material with D_2O.

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9. WARNING - Although we have not encountered any difficulties with this procedure, the separation of crystals from solutions containing diazomethane has been reported to facilitate explosions (e.g., see Org. Syn., 41, 16) and adequate precautions should be taken.