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FACILE SYNTHESIS OF $\alpha$-DEUTERATED ACRYLICS AND ACTIVATED VINYLs

by

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**Facile Synthesis of α-Deuterated Acrylics and Activated Vinils**

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> A simple, direct exchange reaction has been discovered for vinyl groups in which the exchangeable deuterium of alcohols (e.g. CH₃OD) or water (D₂O) replaces only the α-hydrogen of activated vinyls under catalysis by DABCO (1,4-diazabicyclo-[2.2.2]octane). Acrylate esters, acrylonitrile, acrylamides and methyl vinyl ketone were found to go rapid exchange at room temperature to give easily isolated, pure and readily polymerizable α-deuterated compounds. This procedure is the most general efficient and cost-effective one available for obtaining such isotopically labeled materials.
FACILE SYNTHESIS OF α-DEUTERATED ACRYLATES AND ACTIVATED VINYLS

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Abstract

A simple, direct exchange reaction has been discovered for vinyl groups in which the exchangeable deuterium of alcohols (e.g. CH₃OD) or water (D₂O) replaces only the α-hydrogen of activated vinyls under catalysis by DABCO (1,4-diazabicyclo-[2.2.2]octane). Acrylate esters, acrylonitrile, and methyl vinyl ketone were found to undergo rapid exchange at room temperature to give easily isolated, pure and readily polymerizable α-deuterated compounds. This procedure is the most general, efficient and cost-effective one available for obtaining such isotopically labeled materials.
Introduction

Enormous capability exists for studying reaction mechanisms, and the solution and solid state behavior of small molecules and polymers by \(^{2}\)H NMR. In polymer characterization, for example, the molecular relaxation times available using variable temperature wide-line techniques spans the range of characteristic frequencies from ca. 10 MHz to 1 Hz\(^{1}\). New methods of deuterium incorporation at pivotal positions are vital for expanded use of these techniques.

An additional advantage in using deuterated reactants in synthesis is that \(^{2}\)H NMR can be used directly to follow conversion, monitor intermediate formation and disappearance, and examine side-reactions and by-products. The present discovery stems from the combined use of \(^{2}\)H, \(^{1}\)H and \(^{13}\)C solution spectroscopy to monitor the synthesis of a deuterated monomer needed for another study\(^{2}\). The specific reaction under investigation involved functionalization of acrylate esters by reaction with aldehydes in the presence of DABCO\(^{3}\). In the absence of acceptor aldehydes, and in the presence of a suitable exchangeable deuterium donor, rapid incorporation of deuterium at the \(\alpha\) position was observed for a number of activated vinyl species (1 - 2). The Table summarizes our initial results.
### Table

| Compound        | Reaction Conditions | % Deuterium*
|-----------------|---------------------|-------------
| Methyl acrylate | 30 min / CH$_3$OD   | 93.7        
| Butyl acrylate  | 30 min / CH$_3$OD   | 81.8        
| Acrylonitrile   | 30 min / CH$_3$OD   | 90.5        
|                 | 10 min / D$_2$O     | 82.0        

* Determined by integration of the vinyl region of the $^1$H NMR spectra.

We propose a DABCO-catalyzed equilibration (Figure 1) in which deuterium incorporation can be driven to high levels by use of a large excess of the deuterium donor. Levels of incorporation greater than 80% were obtained in minutes with a single exchange process. This procedure is straightforward in contrast to previously reported multistep methods of $\alpha$-deuteration of acrylates.$^4,5,6$

While either CH$_3$OD or D$_2$O served in the exchange for acrylonitrile, hydrolysis of the intermediate species formed from acrylate esters occurred in D$_2$O. In addition, higher alkyl esters underwent transesterification to methyl acrylate if the exchange reaction was extended. Exchange of methyl vinyl ketone was complete in a matter of minutes, although prolonged reaction led to Michael addition and aldol condensation products.$^7$

The general procedure involves simply mixing together excess deuterium donor with the activated substrate, adding DABCO, and monitoring the reaction with $^1$H or $^2$H NMR. Figure 2 gives...
representative spectra for methyl acrylate. The vinylic region of the $^1$H spectrum displays a typical ABX pattern with coupling constants $J_{AB} = 1.5$, $J_{AX} = 17.3$, and $J_{BX} = 10.2$ Hz. The deuterium spectrum displayed splitting of the $\alpha$-$^2$H by the cis and trans hydrogens with $J_{D-H}^a = 4.18$ and $J_{D-H}^b = 2.52$ Hz. Complete $^1$H-$^2$H a b a $^2$H a b a b a b a b equilibration was observed; eg, for methyl acrylate, 94% found vs. 92% theoretical.

These labeled materials, in addition to their value in forming specifically labeled polymers, should be useful in probing mechanisms in organic and natural product syntheses involving a variety of Grignard, Michael and Diels-Alder reactions.

**ACKNOWLEDGEMENT**

We gratefully acknowledge an instrumental grant from the Department of Defense through the Office of Naval Research for purchase of our Bruker MSL-200 NMR. This work was supported in part by the Office of Naval Research.
LIST OF FIGURES

Figure 1. Equilibrium of DABCO intermediate.

Figure 2. a) $^1$H spectrum of undeuterated methyl acrylate, b) $^1$H spectrum of $\alpha$-$d$-methyl acrylate, and c) $^2$H spectrum of $\alpha$-$d$-methyl acrylate.
REFERENCES

Figure 1.

\[
\begin{align*}
\text{H} \quad \text{Z} & \quad \xrightarrow{\text{DABCO}} \quad \text{D} \quad \text{Z} \\
1 & \quad 2 \\
\text{Z} &= \text{CO}_2\text{R, CN, COR}
\end{align*}
\]
Figure 2.
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