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A CONVENIENT ROUTE TO VINYLLITHIUM REAGENTS

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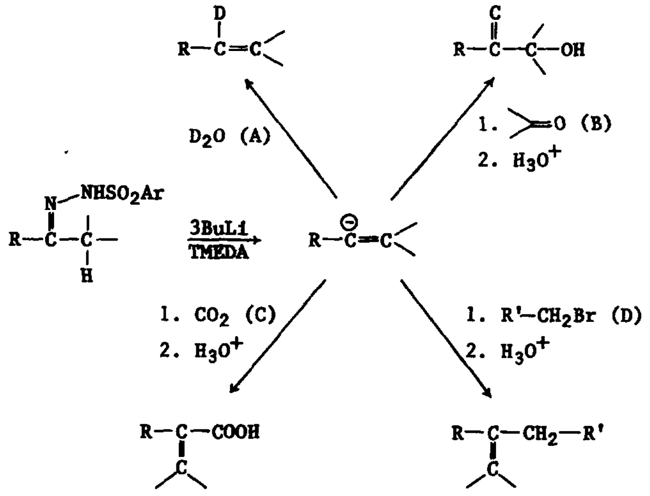
We (1), and Shapiro and co-workers (2), have recently reported a modification of the alkyl lithium-tosylhydrazone olefin synthesis (3) which allows the presumed vinyl carbanion intermediate (4) in that reaction to be efficiently trapped with D_2O. The sequence uses TMEDA as solvent and affords high yields of specifically deuterated olefins (Reaction IA). We report here our studies on the use of a variety of other electrophilic reagents which have been trapped in moderate to high yield (5). Electrophiles studied to date include ketones and aldehydes (Reaction B), carbon dioxide (C) and alkyl bromides (D) (2). The high yields in these reactions (see Tables B, C, and D for representative examples) demonstrate the utility of this method for the convenient preparation of vinyllithium reagents



Reaction I - Vinylcarbanion Trapping

Table B. Aldehyde and Ketone Reactions

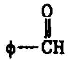
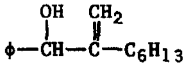
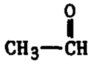
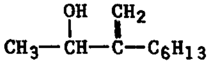
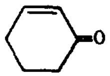
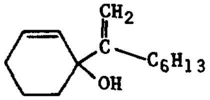
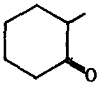
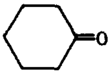
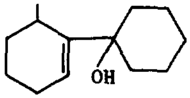
Ketone	Electrophile	Product	% Yield
2-octanone	 $\phi-\overset{O}{\overset{\|}{C}}H$	 $\phi-\overset{OH}{\overset{\mid}{C}}H-\overset{CH_2}{\overset{\|}{C}}-C_6H_{13}$	78
2-octanone	 $CH_3-\overset{O}{\overset{\|}{C}}H$	 $CH_3-\overset{OH}{\overset{\mid}{C}}H-\overset{CH_2}{\overset{\|}{C}}-C_6H_{13}$	75
2-octanone			67
			48

Table C. Carboxylation Reactions

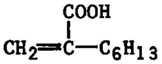
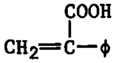
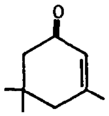
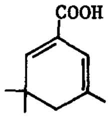
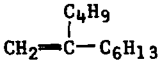
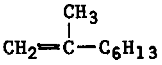
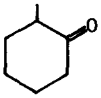
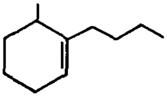
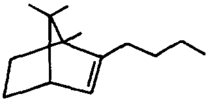
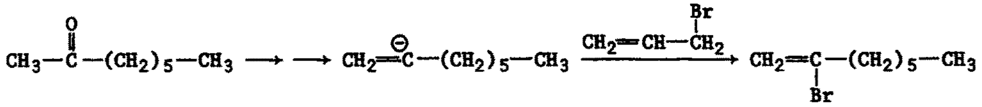
Ketone	Electrophile	Product	% Yield
2-octanone	CO_2	 $CH_2=\overset{COOH}{\overset{\mid}{C}}-C_6H_{13}$	52
Acetophenone	CO_2	 $CH_2=\overset{COOH}{\overset{\mid}{C}}-\phi$	61
	CO_2		45

Table D. Alkylation Reactions

Ketone	Electrophile	Product	% Yield
2-octanone	n-BuBr	 $CH_2=\overset{C_4H_9}{\overset{\mid}{C}}-C_6H_{13}$	65
2-octanone	CH_3I	 $CH_2=\overset{CH_3}{\overset{\mid}{C}}-C_6H_{13}$	71
	n-BuBr		86
camphor	n-BuBr		50

The reactions of vinyl anions reported here are not new (6). The particular attraction of this route to vinyllithium derivatives lies in the regioselectivity of the "Shapiro reaction" (3) which allows, for example, the conversion of 2-octanone into the octenyl anion 1 with formation of less than 2% of the 2-octenyl isomer. Synthesis of 1 by conventional methods would



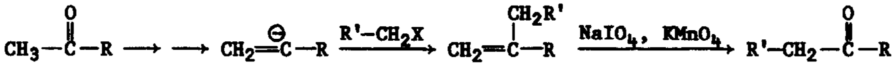
$$CH_3-\overset{O}{\overset{\|}{C}}-(CH_2)_5-CH_3 \longrightarrow \longrightarrow CH_2{=}\overset{\ominus}{C}-(CH_2)_5-CH_3 \xrightarrow{CH_2{=}CH-\overset{Br}{CH_2}} CH_2{=}\underset{Br}{C}-(CH_2)_5-CH_3$$

1 2

require the availability of 2-bromo-1-octene 2, the easiest synthesis of which is now reaction of 1 with allyl bromide! Yields shown in the tables are for isolated products of analytical purity.

To obtain good yields of the trapped products 3.0 or more equivalents of *n*-butyllithium in TMEDA must be used to generate the vinyl anion, or the olefin side product resulting from protonation of the vinyl anion is a major impurity. The source of the third proton appears to be the ring protons of the arenesulfonate group. Indeed, if the toluenesulfonylhydrazone of 2-octanone is treated with 3.0 equivalents of *n*-butyllithium in TMEDA at -78°, and then quenched with CH_3COOD, the recovered tosylhydrazone is labeled at C_1, at nitrogen and in the aromatic ring as shown clearly by NMR. Such ring metallation is not unexpected (7) in TMEDA solvent. The yields reported in Tables B-D were therefore obtained using an excess (3.0 equivalents) of electrophile. Side products derived from reaction of *n*-butyllithium with the electrophilic reagent were usually observed but easily separated. In general, the tosylhydrazone at -78° was treated in TMEDA with 3.5 equivalents of *n*-butyllithium. The solution was allowed to warm to room temperature and stirred for 4 to 24 hours under argon. The electrophile (3.0 equivalents) was then added dropwise with stirring and the reaction worked up in the usual manner. The tertiary allylic alcohols reported in Table B were only obtained free of dehydration side product by careful NH_4Cl workup and low temperature vacuum distillation. Numerous other ketones and aldehydes have been used in this reaction.

Epoxides are the only electrophilic reagents studied to date which do not appear to react cleanly in this sequence. Ethylene oxide and propylene oxide have been used with moderate success, but more hindered epoxides are either unreactive or give the allylic alcohol cleavage product. The reaction with alkyl halides (Table D) gives a very useful ketone homologation sequence starting with a readily available methyl ketone, followed by oxidation (8) of the



$$CH_3-\overset{O}{\overset{\|}{C}}-R \longrightarrow \longrightarrow CH_2=\overset{\ominus}{C}-R \xrightarrow{R'-CH_2X} CH_2=\overset{CH_2R'}{\overset{|}{C}}-R \xrightarrow{NaIO_4,\ KMnO_4} R'-CH_2-\overset{O}{\overset{\|}{C}}-R$$

olefin. Thus, 2-octanone and n-butyl bromide were converted to 5-undecanone in an overall yield of 58%.

One further limitation at present is that aldehyde tosylhydrazones cannot be used in the reaction. Indeed, we are unaware of the use of an aldehyde sulfonylhydrazone in a normal "Shapiro reaction." Otherwise, however, arenesulfonylhydrazones are proving to be extremely valuable reagents in organic synthesis. We are continuing our study on the utility of the vinyl anion intermediates, and their dianion precursors can be substituted with a variety of electrophiles in the less hindered α position (2,9). These sequences afford unsaturated products similar to the saturated derivatives recently reported from dimethylhydrazones (10) or oximes (11).

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