Tetrahedron Letters No. 22 + 23, pp 1815 - 1818, 1975. Pergamon Press. Printed in Great Britain.

EFFICIENT SYNTHESIS OF DEUTERATED OLEFINS FROM ARENESULFONYLHYDRAZONES

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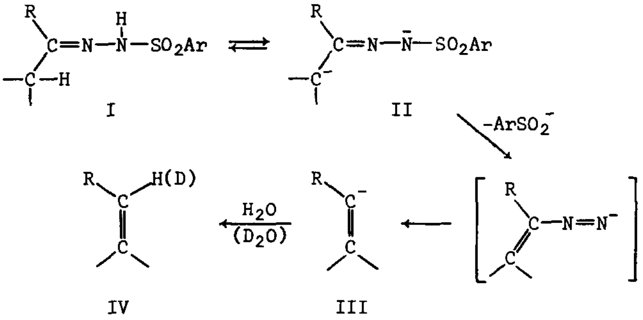
(Received in U.S.A. 6 January 1975; received in Uk for publication 16 April 1975)

The reaction of ketone tosylhydrazones with alkyllithium reagents (1) has become an important synthetic route to olefins (2). The mechanism originally proposed for the reaction involves



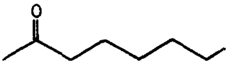
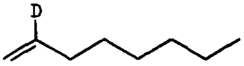
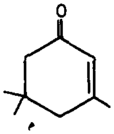
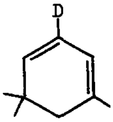
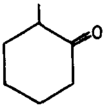
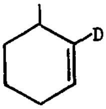
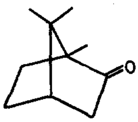
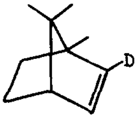
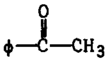
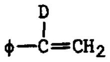
formation of dianion II, followed by loss of arenesulfinate anion to give the vinyl carbanion III, and ultimately the product IV by protonation. Low incorporation of deuterium upon D_2O workup (1,3) has led to a further study by Shapiro and Hornaman (4) which has shown that anion III abstracts β protons from ether solvents and, surprisingly, from the arenesulfonylhydrazone I when the reaction is run in hexane as solvent. Thus in only a few specific cases could vinyl deuterium be efficiently incorporated and this reaction in hexane resulted in low yields of olefin, presumably due to the heterogeneous nature of the reaction.

We wish to report that tetramethylethylenediamine (TMEDA) is an excellent solvent for this reaction and that near quantitative yields of olefins can be obtained as shown for a representative series of ketones in Table 1. More importantly, quenching of the reaction mixture with D_2O

gives the specifically deuterated olefins shown (5) with high deuterium incorporation. When hexane was used as the solvent under identical conditions, incorporation was significantly lower (0-50%) except with camphor. Use of less than 4 equivalents of n-BuLi also lowered the deuterium incorporation.

TABLE 1

Reaction of Phenylsulfonylhydrazones with 4 Equivalents of n-Butyllithium in TMEDA Followed by D_2O Quench

Phenylsulfonylhydrazone of	Product (5)	Yield	% d_1 (5)
		100	91
		98	93
		98	80
		∿100	95
 $\phi-C(=O)-CH_3$	 $\phi-C(D)=CH_2$	96	94

The reactions were run on benzenesulfonylhydrazones rather than the more common tosylhydrazones to eliminate the possibility of abstraction of benzylic hydrogens by III. In each case the benzenesulfonylhydrazone dissolved in TMEDA was treated with excess (4.0 equivalents) of commercial n-butyllithium in hexane (6) with cooling (ca. -50°), after which the reaction was allowed to warm to room temperature and stirred for about an hour before quenching. Decomposition of II to III occurs at room temperature and if cooling was not carried out deuterium incorporation was reduced, presumably by abstraction of hydrogen from tosylhydrazone I or its monoanion. No greater incorporation, however, was noted with inverse addition (3). The dianion derived from the sulfonylhydrazone of 2-methylcyclohexanone decomposes faster than the others possibly accounting for the lower deuterium incorporation.

Dimethyl ether was also investigated as a solvent for the reaction since it does not possess β hydrogens for abstraction. The decomposition proceeds too slowly, however, at its boiling point, though the reaction can be carried out in dimethyl ether-hexane mixtures in which the reaction is homogeneous. Yields of olefin are lower (40-60%), however, though high deuterium incorporation was noted. TMEDA is a much more convenient solvent to use, however.

It should be noted that in spite of the use of a large excess of n-butyllithium, no alkylated products of the type observed by Herz and Ortiz (7) were noted. The high directional specificity of the reaction was also confirmed for the first time in an acylic case. In the reactions of the derivative of 2-octanone, less than 2% of 2-octene was detected, confirming the previously noted specificity toward the less substituted olefin product. Use of _t_-butyllithium as the base gives essentially pure 1-octene.

We are studying the reactions of dianion II and vinyl carbanion III with other electrophiles (8).

Acknowledgment. The authors acknowledge financial support of this work by the National Science Foundation (Grant GP-33278).

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5. Deuterium incorporation was measured by mass spectroscopy. The position of deuterium incorporation was checked by nmr spectroscopy. Yields were determined by gas chromatography though isolated yields were also essentially quantitative.

6. Commercial n-butyllithium contains varying amounts of n-octane which interfered with some of the GC analyses.

7. J. E. Herz and C. V. Ortiz, J. Chem. Soc. (C), 2294 (1971); J. E. Herz, E. Gonzalez, and B. Mandel, Aust. J. Chem., 23, 857 (1970); R. H. Shapiro and T. Gadek, J. Org. Chem., 39, 3418 (1974).

8. We have just learned (see accompanying communication) of related, extensive work in this area by Shapiro and co-workers. We have also investigated alkylation of III as well as its reaction with other electrophiles.