

α -Alkylation of Lithiated α,β -Unsaturated Aldehyde
N,N-Dimethylhydrazones. Synthesis of α -Alkylated
 β,γ -Unsaturated Aldehydes¹⁾

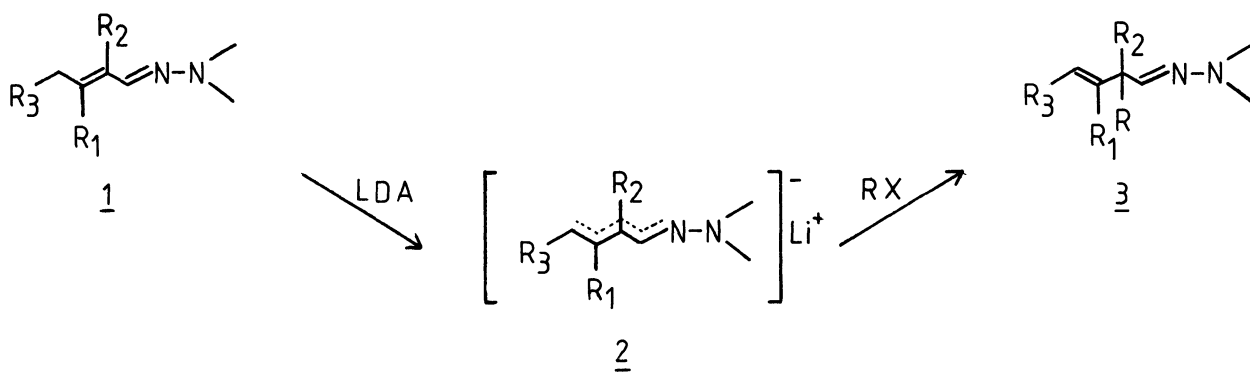
Masakazu YAMASHITA,* Kaoru MATSUMIYA, Ken-ichi NAKANO, and Rikisaku SUEMITSU
Department of Applied Chemistry, Doshisha University,
Kamikyo-ku, Kyoto 602

Lithiated α,β -unsaturated aldehyde N,N-dimethylhydrazones reacted with alkyl halides accompanying a double bond rearrangement to give α -alkylated β,γ -unsaturated aldehyde N,N-dimethylhydrazones in satisfactory yields. Using this reaction, the sesquiterpene, 2,5,9-trimethyl-2-vinyl-4,8-decadienal was synthesized.

Alkylation reactions of aldehydes or ketones via the corresponding imines²⁾ and hydrazones³⁾ have been widely utilized to synthesize a variety of organic compounds. In respect to alkylation of α,β -unsaturated aldehydes, the free aldehydes⁴⁾ and their aldimine derivatives⁵⁾ have been used.

Previously, we reported the alkylation of hydrazones of various ketones including cyclic α,β -unsaturated ketones.⁶⁾ In this communication, we wish to report the novel regioselective α -alkylation and rearrangement of α,β -unsaturated aldehyde N,N-dimethylhydrazones (1) to α -alkylated β,γ -unsaturated aldehydes (Scheme 1).⁷⁾

α,β -Unsaturated aldehyde N,N-dimethylhydrazones 1 were conveniently prepared from the corresponding aldehydes and N,N-dimethylhydrazine using trifluoroacetic acid as a catalyst.



Scheme 1.

Table 1. Reaction of α,β -unsaturated aldehyde *N,N*-dimethylhydrazones with alkyl halides

Run	Substrate	RX	Product a)	Yield/% b)
1				49
2				63
3				69
4				46
5				40
6		MeI		46
7				43
8				64
9				68
10				65
11				56
12				66

a) All compounds were identified by their IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, and mass spectra.

b) Isolated yields.

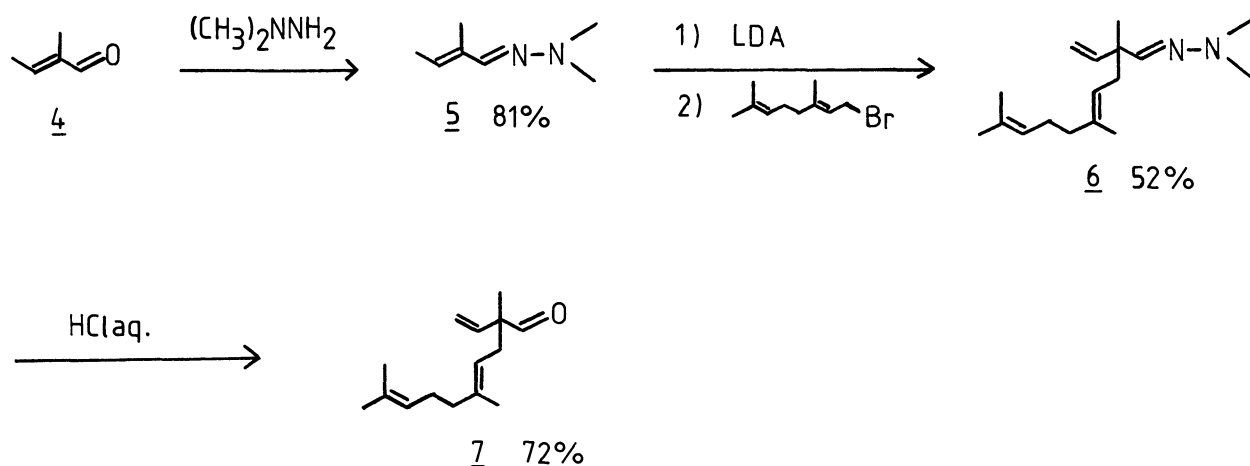
A typical procedure is as follows: To a solution of lithium diisopropylamide (LDA) (4.8 mmol) in tetrahydrofuran (THF) (10 ml) was added 3-methyl-2-butenal *N,N*-dimethylhydrazone (4.8 mmol) at $-5\text{ }^{\circ}\text{C}$ under argon atmosphere. After stirring for 1 h, the yellowish solution was cooled to $-5\text{ }^{\circ}\text{C}$ again, and benzyl bromide (4.8 mmol) was added. The reaction mixture was further stirred for 3 h at room temperature and then treated with water. After usual work up, 2-benzyl-3-methyl-3-butenal *N,N*-dimethylhydrazone was obtained in 68% yield by column chromatography as a colorless liquid.

Lithiated α,β -unsaturated aldehyde *N,N*-dimethylhydrazones (2) reacted with a variety of alkyl halides accompanying a double bond rearrangement to afford α -alkylated β,γ -unsaturated aldehyde *N,N*-dimethylhydrazones (3). The results of the alkylation of hydrazones 1 were listed in Table 1. It is noteworthy that, in the reaction of the hydrazone of citral (Runs 4-7), the α,β -double bond rearranged to the methyl carbon to give a terminal methylene group exclusively, and that even 2-methyl-2-butenal *N,N*-dimethylhydrazone, which has no α -hydrogen, was α -alkylated to give the corresponding compounds (Runs 11,12).

On the other hand, attempts to alkylate the *N,N*-dimethylhydrazone of cinnamaldehyde and benzaldehyde gave no identifiable product.

Using this new reaction, the synthesis of 2,5,9-trimethyl-2-vinyl-4,8-decadienal (7),⁸⁾ which is considered to be a component of an essential oil of a beefsteak plant, was conducted (Scheme 2). 2-Methyl-2-butenal (4) reacted with *N,N*-dimethylhydrazine to give 2-methyl-2-butenal *N,N*-dimethylhydrazone (5) in 81% yield. To the THF solution of 1 equiv. of LDA at $-5\text{ }^{\circ}\text{C}$, was added hydrazone 5, followed by 1-bromo-3,7-dimethyl-2,6-octadiene to provide the corresponding hydrazone (6) in 52% yield, which was readily converted to the desired aldehyde 7 after hydrolysis in 72% yield.

Application of this reaction to syntheses of more complex terpenoids are under investigation.



Scheme 2.

The authors wish to thank Takasago Co. for sending the spectral data of compound 7.

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(Received March 30, 1988)