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α-Alkylation of Lithiated α,β-Unsaturated Aldehyde N,N-Dimethylhydrazones. Synthesis of α-Alkylated β,γ-Unsaturated Aldehydes[1)]

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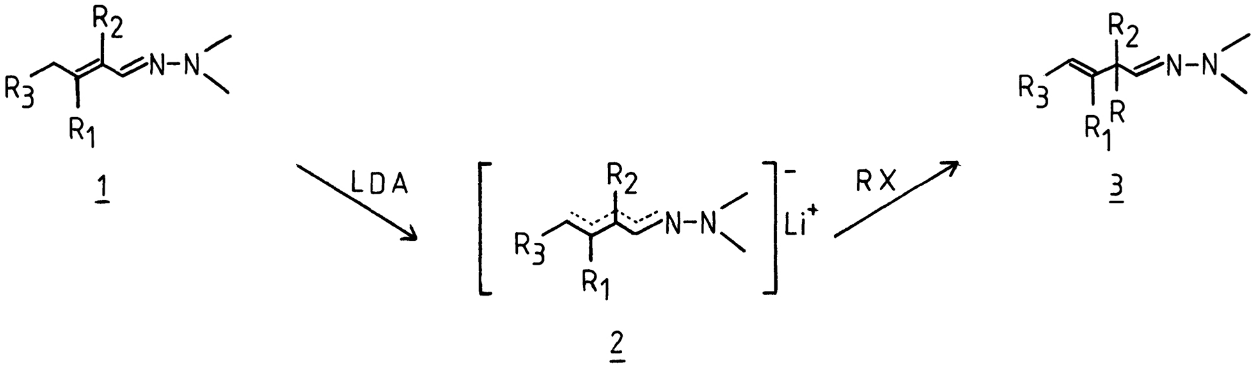
Lithiated α,β-unsaturated aldehyde N,N-dimethylhydrazones reacted with alkyl halides accompanying a double bond rearrangement to give α-alkylated β,γ-unsaturated aldehyde N,N-dimethylhydrazones in satisfactory yields. Using this reaction, the sesquiterpene, 2,5,9-trimethyl-2-vinyl-4,8-decadienal was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

Alkylation reactions of aldehydes or ketones via the corresponding imines[2)] and hydrazones[3)] have been widely utilized to synthesize a variety of organic compounds. In respect to alkylation of α,β-unsaturated aldehydes, the free aldehydes[4)] and their aldimine derivatives[5)] have been used.

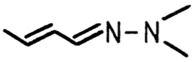
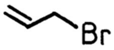
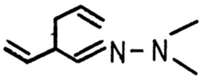
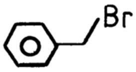
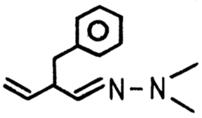
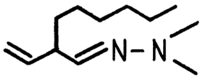
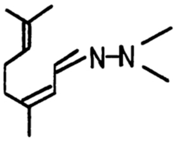
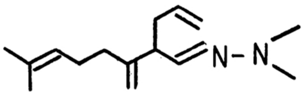
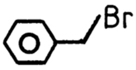
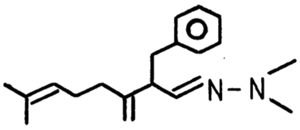
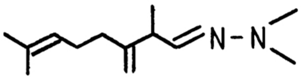
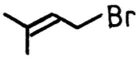
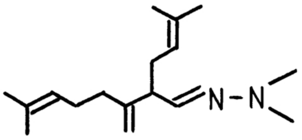
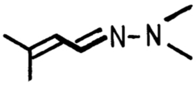
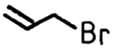
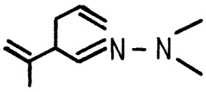
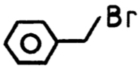
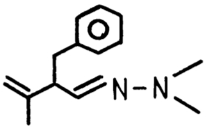
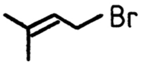
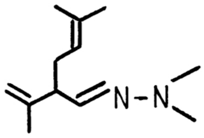
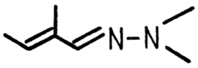
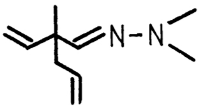
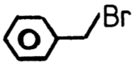
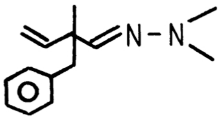
Previously, we reported the alkylation of hydrazones of various ketones including cyclic α,β-unsaturated ketones.[6)] In this communication, we wish to report the novel regioselective α-alkylation and rearrangement of α,β-unsaturated aldehyde N,N-dimethylhydrazones (1) to α-alkylated β,γ-unsaturated 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}H-NMR, ^{13}C-NMR, and mass spectra.
b) Isolated yields.

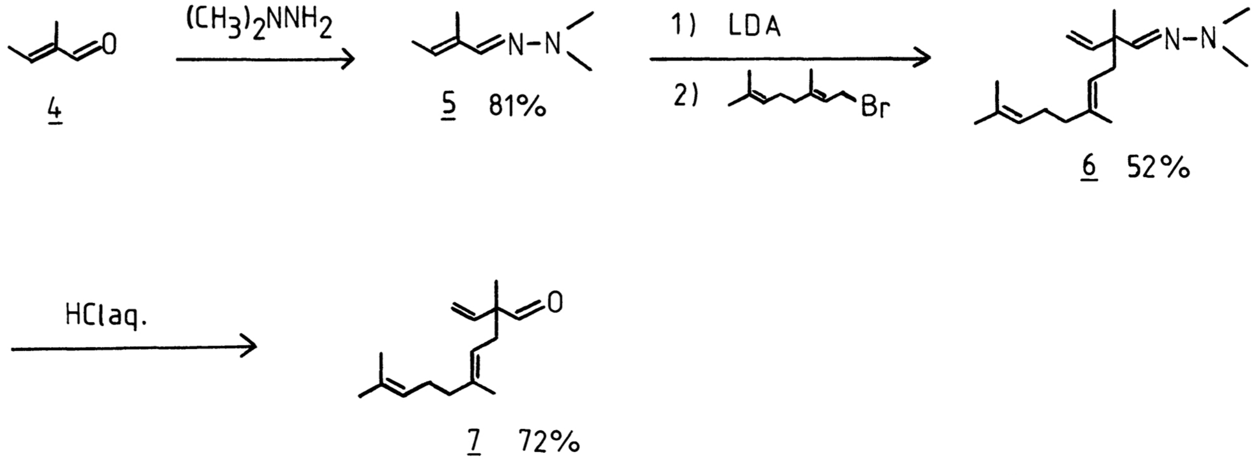
A typical procedure is as follows: To a solution of lithium diisopropylamide (LDA) (4.8 mmol) in tetrahydrofuran (THF) (10 ml) was added 3-methyl-2-butenal N,N-dimethylhydrazone (4.8 mmol) at -5 °C under argon atmosphere. After stirring for 1 h, the yellowish solution was cooled to -5 °C again, and benzyl 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 °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.

References

1) Organic synthesis via dialkylhydrazones, Part 4. For Part 3, see Ref. 6.
2) G. Stork and S. R. Dowd, J. Am. Chem. Soc., 85, 2178 (1963).
3) E. J. Corey and D. Enders, Chem. Ber., 111, 1337 (1978); E. J. Corey and D. Enders, ibid., 111, 1362 (1978).
4) S. A. G. de Graaf, P. E. R. Oosterhoff, and A. van der Gen, Tetrahedron Lett., 1974, 1653; P. Groenewegen, H. Kallenberg, and A. van der Gen, Tetrahedron Lett., 1978, 491; L. A. Kheifits, A. V. Gurevich, N. V. Lepikhina, and N. A. Novikov, Maslo-Zhir. Prom-st., 1980, 24.
5) K. Takabe, H. Fujiwara, T. Katagiri, and J. Tanaka, Tetrahedron Lett., 1975, 1237; G. R. Kieczykowski, R. H. Schlessinger, and R. B. Sulsky, Tetrahedron Lett., 1976, 597.
6) M. Yamashita, K. Matsumiya, M. Tanabe, and R. Suemitsu, J. Jpn. Oil Chem. Soc. (Yukagaku), 37, 245 (1988); M. Yamashita, K. Matsumiya, M. Tanabe, and R. Suemitsu, Bull. Chem. Soc. Jpn., 58, 407 (1985); M. Yamashita, K. Matsumiya, K. Tanji, and R. Suemitsu, J. Jpn. Oil Chem. Soc. (Yukagaku), 35, 1041 (1986).
7) Alkylation of crotonaldehyde N,N-dimethylhydrazone has been reported: see Ref. 3.
8) Y. Uji, T. Toyoda, and S. Muraki, 31st Symposium on the Chemistry of Terpenes, Essential Oils, and Aromatics, Kyoto, September 1987, Abstr., No. 1I02.

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