Tetrahedron Letters No. 28, pp 2425 - 2428, 1977. Pergamon Press. Printed in Great Britain.

A NEW METHOD FOR THE BISHOMOLOGATION OF CARBONYL COMPOUNDS TO α,β-UNSATURATED ALDEHYDES VIA THE [3,3]SIGMATROPIC REARRANGEMENT OF ALLYLIC THIONOCARBAMATES[1]

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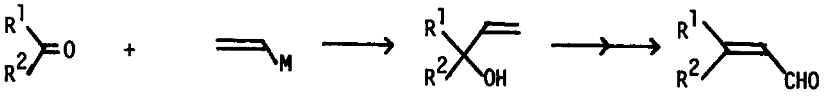
(Received in Japan 9 May 1977; received in UK for publication 27 May 1977)

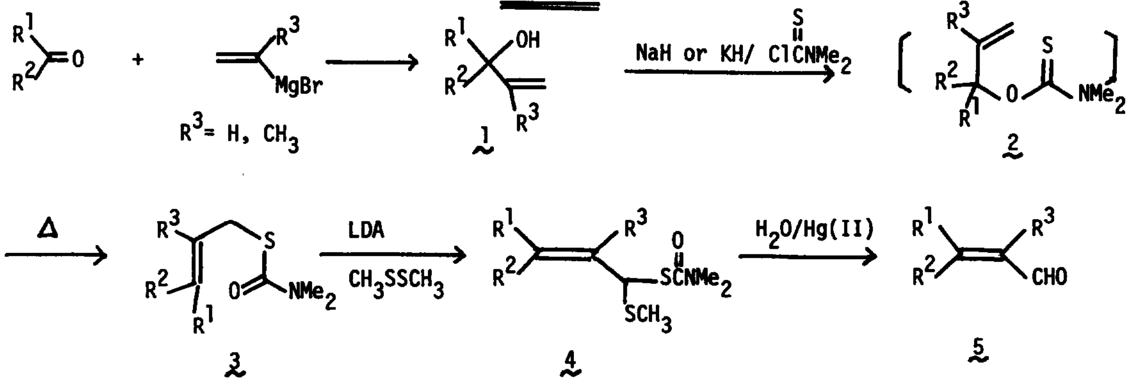
The aldol condensation continues to play a fundamental role in organic synthesis and many methods have recently been developed for directing the aldol condensation of nonidentical carbonyl partners.[2] A novel approach to the directed aldol condensation involves a two-carbon homologation of carbonyl groups which relies upon the initial addition of a vinyl anion followed by further elaboration to the directed aldol products (eq 1).[3,4]



(1)

In our continuing investigation of the synthetic utilities of the [3,3]sigmatropic rearrangements of allylic thion-esters,[5] we now wish to report a new, versatile procedure for the bishomologation of carbonyl compounds to α,β-unsaturated aldehydes which involves the [3,3]-sigmatropic rearrangement[5a,6] of allylic thionocarbamates as the key step. The complete scheme is depicted in Scheme I. The present procedure is comparable to the recent Trost's method[3] which relies upon the [2,3]sigmatropic rearrangement of allylic sulfenates.

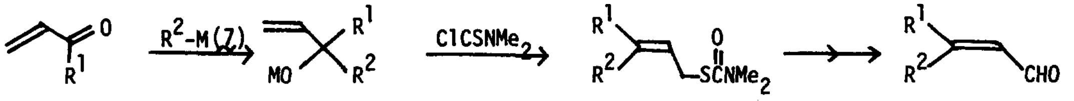
Scheme I



Typically, an allylic alcohol (1) prepared by the addition of a vinyl organometallic to the carbonyl group was treated with metal hydride (sodium hydride or potassium hydride[7]) in

THF followed by N,N-dimethylthiocarbamoyl chloride$^{8)}$ to produce, after distillation, the allylic thiolcarbamate 3 *via* the [3,3]sigmatropic rearrangement *in situ* of the thionocarbamate 2. Treatment of 3 thus formed with lithium diisopropylamide (LDA) in THF at -78° followed by addition of dimethyl disulfide gave the α-sulfenated product (4)$^{9)}$ quantitatively. Finally, hydrolysis of 4 with mercuric chloride (3 equiv) in the presence of calcium carbonate in aqueous THF afforded the desired α,β-unsaturated aldehydes in good yields (entries 1-5, Table 1). The conversion of carbonyl compounds to the rearranged thiolcarbamates 3 could be performed in one operation when one would employ lithium reagents instead of the Grignard reagents.

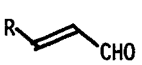
While the above procedure can be considered to be an *intermolecular* 1,3-carbonyl transposition, the availability of allylic alcohols by the organometallic addition to enone systems allows the above method to be utilized as an *intramolecular* 1,3-carbonyl transposition. The general scheme is represented by eq 2.



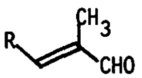
6 3 5 (2)

For example, addition of butyllithium (7, R^2= n-Bu) to acrolein (6, R^1= H) followed by treatment with the thiocarbamoyl chloride produced, after distillation, the thiolcarbamate 3. The sulfenylation-hydrolysis sequence performed 3 afforded 2-heptenal (entry 6, Table 1).

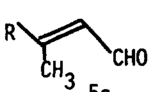
Of particular interest are the stereochemical results of α,β-unsaturated aldehydes thus obtained (see Table 1); types of 5a and 5b derived from aldehydes possess only the E geometry while 5c derived from methyl ketones was obtained as E : Z mixtures.$^{10)}$



5a

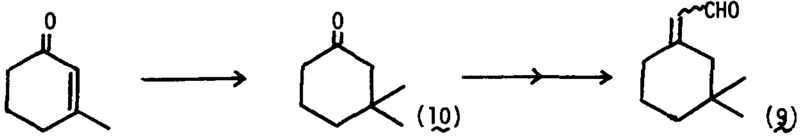


5b



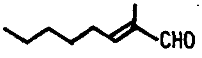
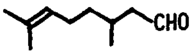
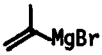
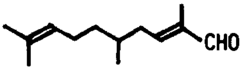
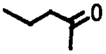
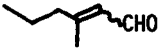
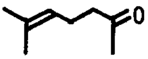
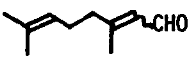
5c

As an example of synthetic application of the present procedure, we carried out a simple synthesis of isomeric aldehydes 9, two of the four components of the male boll weevil sex attractant$^{11)}$(eq 3). Thus 3,3-dimethylcyclohexanone (10) prepared from 3-methylcyclohex-2-enone and lithium dimethylcopper$^{12)}$ was converted using the above procedure to a 1 : 1 mixture of E : Z stereoisomeric aldehydes (9) in 54% overall yield.



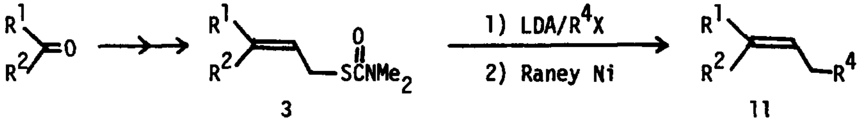
(10) (9) (3)

Table 1. Synthesis of α,β-Unsaturated Aldehydes

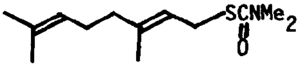
Entry	Carbonyl	Organometallic	Thiol-ester 3,%[a] (metal hydride[b])	Unsaturated Carbonyl (%)[a]	Geometry[c]
1			76 (NaH)	 (78)	E only
2			54 (NaH)	 (79)	E only
3			63 (NaH)	 (65)[d]	E only
4			37 (KH)	 (75)	E/Z = 2.3
5			51 (KH)	 (65)[d]	E/Z = 2.4
6			55 (--)	 (80)	E only

[a] No attempt has been made to optimize yields. [b] Metal hydride employed for the thiocarbamoylation of allylic alcohols. [c] Determined by nmr analysis. [d] The mercuric ion promoted hydrolysis was carried out in the presence of 4 equiv of $CaCO_3$. Otherwise the aldehyde yield considerably decreased due to the formation of cyclization products.

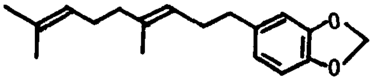
Finally, it should be noted that another elaboration of thiolcarbamates 3 in the above sequence provides an efficient method for trisubstituted olefin synthesis (eq 4). Thus the regiospecific α-alkylation[9)] of 3 followed by reductive desulfurization afforded olefins 11 in good yields. For example, thiolcarbamate 3a obtained in entry 5 was lithiated with LDA followed by alkylation with piperonyl bromide gave the α-alkylated product which was further treated with Raney Ni (W-2) in acetone, finally the trisubstituted olefin 12, a juvenile hormone mimic[6,13)] (96% overall yield, E/Z = ca. 3 : 1).



3 11 (4)



3a



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Acknowledgment. --- We wish to thank Professor Nobuo Ishikawa for his encouragement and helpful discussion throughout the investigation.

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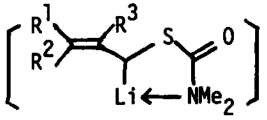
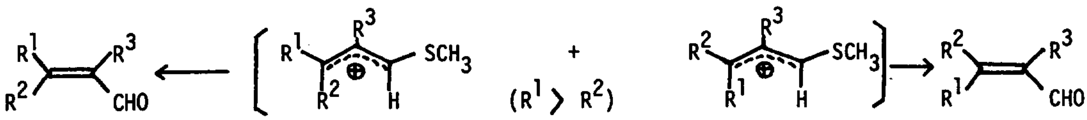
9) The observed α-regiospecificity is explained in terms of intramolecular chelation as depicted below. For other examples of allyllithium stabilized by chelation see T. Nakai, H. Shiono, and M. Okawara, Tetrahedron Lett., 1975, 4027, and references cited therein.



10) Stereochemical comparisons of 5 with 4 (or 3) indicates that the stereochemistry of the final product 5 is not determined by the stereochemistry of 4, but by the relative stabilities of the presumed intermediates of hydrolysis, 8E and 8Z. For a similar stereochemical argument see ref 3.



5E 8E 8Z 5Z

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