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POTENTIAL SYNTHETIC UTILITY OF [3,3]-SIGMATROPIC REARRANGEMENT OF S-ALLYL DITHIOCARBAMATES. NEW ROUTES TO α,β-UNSATURATED ALDEHYDES[1]

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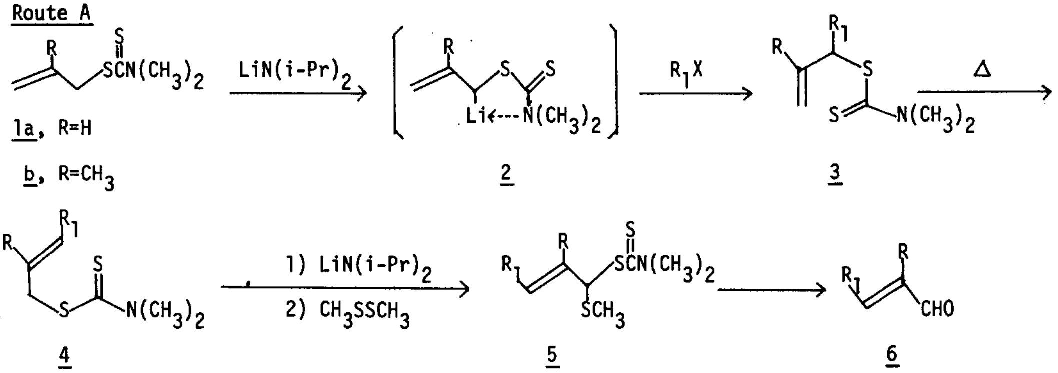
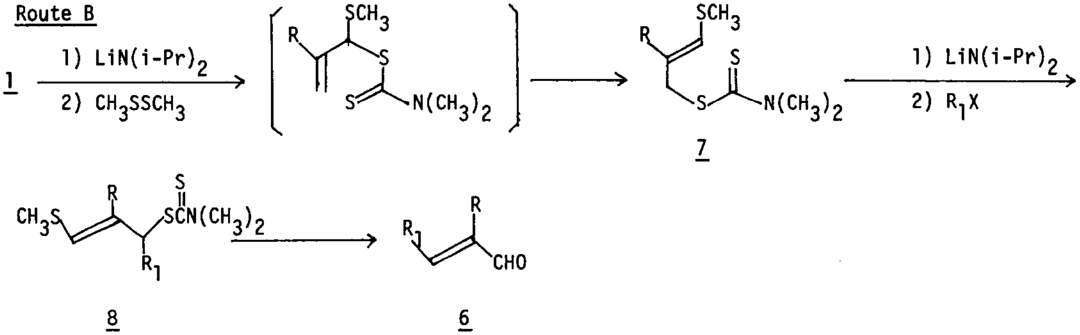
This communication describes two general sequences which permit the conversion of an alkyl halide (R_1X) to (E)-α,β-unsaturated aldehydes ($R_1CH{=}CRCHO$; R=H or CH_3), an important class of organic substances for which there exists only a limited number of methodology.[2] These involve S-α-lithioallyl dithiocarbamates[3] as the key intermediates and [3,3]-sigmatropic rearrangement[3,4] of S-allyl dithiocarbamates as the key process. The overall transformations are represented by route A and B as depicted below.

Route A



Route B

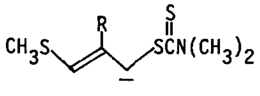


Treatment of 1a[5] with lithium diisopropylamide (LiIPA) (1 equiv) in THF at -78° produced the orange-colored solution of the lithium salt 2a which might be stabilized by chelation.[6] The salt 2a was alkylated immediately at -78° upon the addition of n-amyl iodide (1 equiv) to produce 3a(R_1=n-C_5H_{11}). The crude product is suitable for the next rearrangement, which was carried out by direct distillation or by heating in benzene at reflux for 3 hr to afford the desired trans-2-octenyl dithiocarbamate 4a(R_1=n-C_5H_{11})[7] in 92% overall yield. In a similar experiment, methyl iodide and benzyl bromide gave 4a($R_1=CH_3$) and 4a($R_1=CH_2C_6H_5$) in 92% and 90% overall yields, respectively. A similar two-step operation with the lithium salt 2b derived from 1b[5] and n-amyl iodide gave a mixture of E- and Z-4b(R_1=n-C_5H_{11}) (E, > 80%[7]) in 93% overall yield.

In the next step, 4 thus obtained was again metalated with LiIPA using the same procedures as described above, and then the lithium salt so generated was quenched by dimethyl disulfide (1.1 equiv) at -78° to provide, after hydrolysis of the crude products (5) with mercuric ion in aqueous acetonitrile,[2a] good yields of the corresponding (E)-α,β-unsaturated aldehydes (6)[8] (Table 1).

Alternatively, route B is accomplished by initial sulfenylation followed by alkylation. The lithium salt 2a and 2b were quenched by dimethyl disulfide to produce, after extractive work-up at room temperature, the rearranged S-γ-methylthioallyl- (7a)[9] and S-γ-methylthiomethallyl dithiocarbamate (7b)[10] in 88% and 90% yields, respectively. In these reactions no special operation for rearrangement is neccessary since complete rearrangement takes place during the work-up.

In the next step, 7 thus obtained was metalated with LiIPA using the same procedures as described above giving the orange-colored solution containing the anion 9. In view of the structural analogy of 9 with the anion 10 recently developed by Corey and co-workers,[2a] it is easily expected that the anion 9 serves as the synthetic equivalent of unknown β-alkyl-β-formylvinyl anion 11. Thus the anion 9 so generated was alkylated by an alkyl halide (slightly less than 1 equiv) at -78° to provide, after hydrolysis of the crude products (8) with mercuric ion in aqueous acetonitrile,[2a,11] good yields of the corresponding (E)-α,β-unsaturated aldehydes (6)[8] (Table 1).



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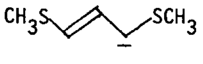

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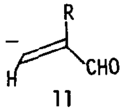

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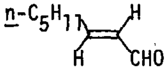
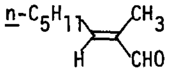
Table 1

Synthesis of α,β-Unsaturated Aldehydes

R in 1	Route	R_1X	Product[a]	Yield,[b]%
H	A	CH_3I	trans-$CH_3CH{=}CHCHO$[c]	95
H	A	n-$C_5H_{11}I$		78
H	B	n-$C_5H_{11}I$		67
H	A	$C_6H_5CH_2Br$	trans-$C_6H_5CH_2CH{=}CHCHO$	60
CH_3	B	----	$CH_2{=}C(CH_3)CHO$[c]	90
CH_3	A	n-$C_5H_{11}I$	 [d]	69
CH_3	B	n-$C_5H_{11}I$		68
CH_3	B	$C_6H_5CH_2Br$	(E)-$C_6H_5CH_2CH{=}C(CH_3)CHO$[d]	62

[a] All products exhibited spectral and physical properties in accordance with the assigned structure or with reported literature values. [b] The yields were based on 4 for route A and on 7 for route B. The yields are not neccessarily optimum since each run was performed only once. [c] Isolated as the 2,4-dinitrophenylhydrazone. [d] Homogeneous by vpc. The assignment of the E-configuration is based on the position of only one singlet due to the formyl proton in nmr ($CDCl_3$, TMS). For a detailed nmr discussion of (E)- and (Z)-β-alkyl-α-methylacroleins see K.C.Chan, R.A.Jewell, W.H.Nutting, and H.Rapoport, J. Org. Chem., 33, 3382 (1968).

It is of particular interest that the present methods starting with S-methallyl dithiocarbamate (1b) can be applied to the synthesis of (E)-β-substituted methacroleins as they appear in many natural products. Finally, it should be pointed out that route B is apparently most advantageous in comparison with route A and the previous ones[2a,b] from the points of the shorter length of the sequence, the accessibility of the starting materials, and the added flexibility in synthesis.

We are currently investigating further improvement in synthetic methods here outlined as well as the application to the synthesis of natural products.

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NOTES AND REFERENCES

1. Dithiocarbamates in Organic Synthesis. II. Part I: T.Nakai and M.Okawara, Chem. Lett., 731 (1974).
2. a) E.J.Corey, B.W.Erickson, and R.Noyori, J. Amer. Chem. Soc., **93**, 1724 (1971);b) A.I.Meyers, A.Nabeya, H.W.Adickes, J.M.Fitzpatrick, R.G.Malone, and I.R.Politzer, ibid., **91**, 764 (1969); c) A.F.Thomas, ibid., **91**, 3281 (1969);d) G.Wittig and H.Reiff, Angew. Chem. Int. Ed. Engl., **7**, 7 (1968).
3. Very recently Dr.Hayashi reported the results of his independent efforts on the formation of the lithium salt and its alkylation followed by allylic rearrangement: T.Hayashi, Tetrahedron Lett., 339 (1974). For a similar observation in our laboratory see K.Hiratani, Doctoral Dissertation, Tokyo Institute of Technology, 1974.
4. For [3,3]-sigmatropic rearrangements closely related to the present system see D.J.Faulkner and M.R.Peterson, J. Amer. Chem. Soc., **95**, 553 (1973) and H.Takahashi, K.Oshima, H.Yamamoto, and H.Nozaki, ibid., **95**, 5801 (1973).
5. The S-allyl dithiocarbamates 1a and 1b were obtained quantitatively by the reaction of sodium N,N-dimethyldithiocarbamate with allyl chloride and methallyl bromide, respectively.
6. For other examples of allyllithium stabilized by chelation see K.Hirai, H.Matsuda, and Y.Kishida, Tetrahedron Lett., 4359 (1971) and K.Narasaka, M.Hayashi, and T.Mukaiyama, Chem. Lett., 259 (1972).
7. The basis for the stereospecificity in this rearrangement can be explained by essentially the same arguments used to rationalize the stereochemical outcome of Claisen rearrangement: *cf*. P.Vottorelli, T.Winkler, H.J.Hansen, and H.Schmid, Helv. Chim. Acta, 51, 1457 (1967).
8. In all cases, no *Z*-isomers were detected by vpc and nmr. We believe that the exclusive formation of the *E*-isomers is due to rapid isomerization of unstable *Z*-isomers formed during hydrolysis under the hydrolytic conditions.
9. *Trans* only by nmr (CCl_4, TMS):δ 2.24 (s, SCH_3), 3.50 (bs, NCH_3), 4.50 (d, J=8 Hz, CH_2), 5.53 (dt, J=8 and 16 Hz, CH_2-C*H*=), 6.50 (d, J=16 Hz, S-CH=). Distillation at 138-143(1 mmHg) gave a mixture of *trans*/*cis* = 68 : 32 (by nmr assay).
10. *E*/*Z* = *ca*. 90 : 10 by nmr (CCl_4, TMS):δ 1.76 (s, *E*-CH_3), 1.89 (s, *Z*-CH_3), 2.27 (s, SCH_3), 3.48 (bs, NCH_3), 4.07 (s, CH_2), 6.13 (bs, S-CH=).
11. It is interesting to note that 8 was hydrolyzed much more rapidly than the corresponding 1,3-bis(methylthio)allylic compound[2a] under the same conditions; this is explained in terms of the stronger affinity of the dithiocarbamate moiety for mercuric ion. For hydrolysis of methylenebis(N,N-dimethyldithiocarbamate) *vs*. 1,3-dithiane see ref 1.