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GENERAL SYNTHETIC ROUTES TO α,β-UNSATURATED CARBOXYLIC ESTERS AND KETONES VIA THE [3,3]SIGMATROPIC REARRANGEMENT OF ALLYLIC THIONCARBAMATES. STEREOSPECIFIC SYNTHESES OF TWO ANT MANDIBULAR GLAND SECRETIONS[1)]

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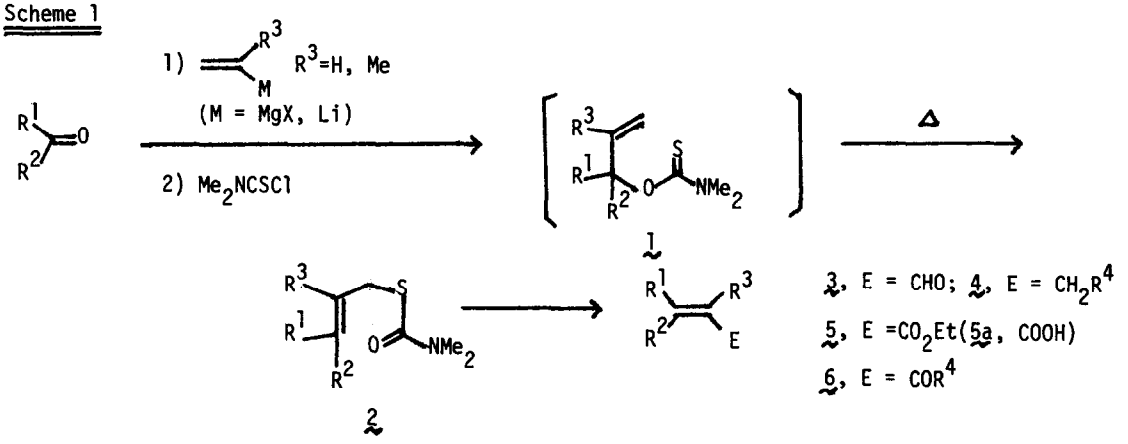
In our continuing investigation of the synthetic utilities of the [3,3]sigmatropic rearrangement of allylic thion-esters,[2)] we have recently reported the synthetic potentiality of the sigmatropic rearrangement in situ of allylic thioncarbamates (1) to the thiolcarbamates (2) which provides new synthetic routes to α,β-unsaturated aldehydes (3) and trisubstituted olefins (4) from carbonyl compounds[3)](Scheme 1). In the present communication, we wish to report versatile procedures for the elaborations of allylic thiolcarbamates (2) to α,β-unsaturated carboxylic esters (5) (or acids) and ketones (6), and their applications to the stereospecific syntheses of two ant mandibular gland secretions which have been identified as components of alarm pheromones.

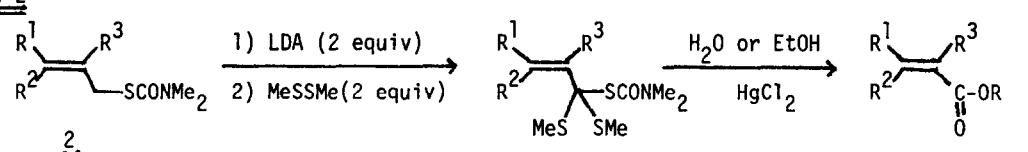
Scheme 1



First of all, thiolcarbamates 2, common precursors for both carboxylic esters 5 and ketones 6, were prepared in 62%~85% yields in one operation from allylic alcohols and N,N-dimethylthiocarbamoyl chloride[4)] according to the previously reported procedure.[3,5)]

The general procedure for the elaboration of thiolcarbamates 2 thus obtained into α,β-unsaturated carboxylic esters (5) or acids (5a) is as follows (Scheme 2). Treatment of 2 with

Scheme 2

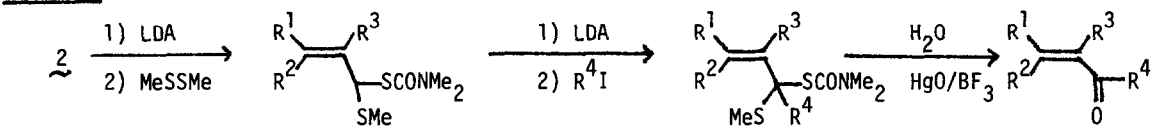


2 3 5, R=Et; 5a, R=H

? equiv of lithium diisopropylamide (LDA) in THF at -78°C followed by addition of dimethyl disulfide gave the α,α-bissulfenylated products (7)[6] in quantitative yields. Without purification, ethanolysis of 7 with mercuric chloride (5 equiv) in 95% aqueous ethanol[7] afforded the desired esters (5) in good yields (Table 1). Alternatively, hydrolysis of 7 with mercuric chloride in 80% aqueous acetonitrile[7] produced the corresponding acids (5a) (Table 1).

On the other hand, the general procedure for the transformation of 2 into α,β-unsaturated ketones (6) is as follows (Scheme 3). Treatment of 2 with LDA (1 equiv) followed by addition of dimethyl disulfide (1 equiv) as described above gave the α-monosulfenylated products (8)[6]

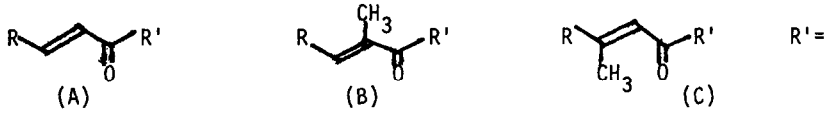
Scheme 3



8 9 6

in quantitative yields which were furhter lithiated with LDA followed by addition of a slightly excess of an alkyl iodide (R^4I) to give the α-alkylated products (9)[6] in excellent yields. Hydrolysis of crude 9 with mercuric oxide (1.2 equiv) and boron trifluoride (1.2 equiv) in 80% aqueous THF[8] afforded the desired ketones (6) in good yields (Table 2).

Of particular interest in Tables 1 and 2 are the stereochemical results; types of (A) and (B) possess only the E geometry while type(C)is obtained as the E, Z mixture for both esters 5 and ketones 6. The stereochemical features are consistent with the stereochemical analysis previously described for α,β-unsaturated aldehydes (3) derived from 2.[3,9]



(A) (B) (C) R'= OEt, Alkyl, H

As an example of applications of the present procedures, we carried out the stereospecific syntheses of the two alarm pheromones of ants, (E)-2,4-dimethyl-2-hexenoic acid (10)[10, 11] and (E)-4,6-dimethyl-4-octen-3-one (socalled manicone) (11)[11,12] (Scheme 4). Thus the allylic

Table 1. Synthesis of α,β-Unsaturated Carboxylic Esters (5) and Acids (5a)

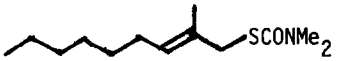
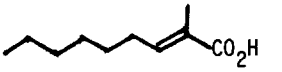
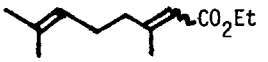
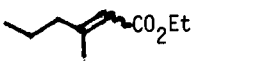
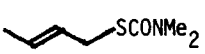
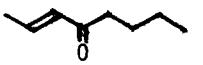
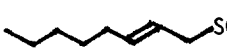
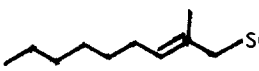
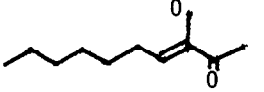
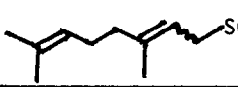
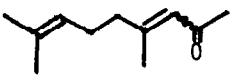
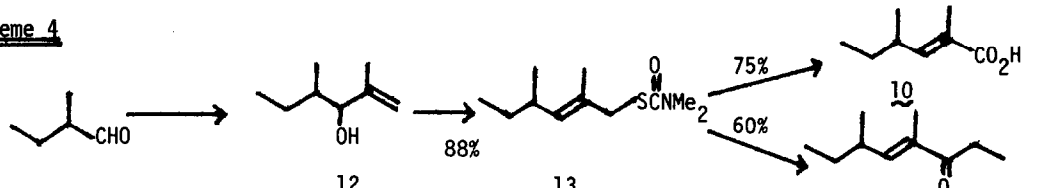
Thiolcarbamate (2)[a]	Esters (5) or Acids (5a)[b]	Yield[c]	Stereochemistry[d]
		17%[e]	E only
		57%	E only
		73%	E/Z =~3.0[f]
		57%	E/Z =~3.5[f]

Table 2. Synthesis of α,β-Unsaturated Ketones (6)

Thiolcarbamate (2)[a]	R^4I	Ketones (6)[b]	Yield[c]	Stereochemistry[d]
	n-C_4H_9I		59%	E only
	n-C_4H_9I		64%	E only
	CH_3I		61%	E only
	CH_3I		60%	E/Z =~3[f]

[a] Prepared from an appropriate allylic alcohol and Me_2NCSCl (see text). [b] All products exhibited spectral (NMR and IR) data in accord with the assigned structures and/or with the reported literature values. [c] Isolated yields (by TLC) based on 2, not optimized. [d] Determined by NMR assay unless otherwise noted. [e] The low yield was due to polymerization of the product. [f] Determined by VPC (DC 550, 190°C) analysis.

Scheme 4



alcohol (12)[13] from (±)-2-methylbutanal and 2-propenylmagnesium bromide was converted to the required common precursor (13).[14] The bissulfenylation-hydrolysis sequence performed on 13 produced the desired acid (10) in 75% overall yield while application of the sulfenylation-alkylation (with ethyl iodide)-hydrolysis sequence described above afforded manicone 11 in 60% overall yield, without any detectable traces of isomeric substances. The spectroscopic

properties of 10 and 11[15] are consistent with those reported for the natural products.[10,11,12]

In summary, this work coupled with the preceding one[3] demonstrates the synthetic potentiality of allylic thiolcarbamates (2) readily derived from allylic alcohols via the [3,3]sigmatropic rearrangement which permits ready access to a wide variety of olefins and α,β-unsaturated aldehydes, carboxylic esters (acids), and ketones.

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References and Notes

1) Part VII on Dithiocarbmates in Organic Synthesis.

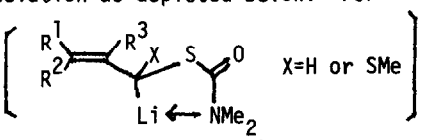
2) T. Nakai and A. Ari-izumi, Tetrahedron Lett., 1976, 2335; T. Nakai, H. Shiono, and M. Okawara, Ibid., 1974, 3625; T. Nakai, H. Shiono, and M. Okawara, Chem. Lett., 1975, 249.

3) T. Nakai, T. Mimura, and A. Ari-izumi, Tetrahedron Lett., 1977, 2425.

4) Commercially available and readily prepared from tetramethylthiuram disulfide and chlorine; M. S. Newman and F. W. Hetzel, J. Org. Chem., 34, 3604 (1973).

5) R. E. Hacker and T. W. Balko, J. Org. Chem., 38, 2106 (1973).

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



7) R. A. Ellison, W. D. Woessner, and C. C. Williams, J. Org. Chem., 37, 2757 (1972).

8) E. Vedejs and P. L. Fuchs, J. Org. Chem., 36, 366 (1971).

9) The stereochemistry of the final products (5 and 6) is not determined by the stereochemistry of 2, but by the relative stabilities of isomeric allyl cations, presumed intermediates of the mercury-catalyzed hydrolysis. For a full discussion on this point, see ref. 3.

10) J. M. Brand, R. M. Duffield, J. G. MacConnell, and M. S. Blum, Science, 179, 388 (1973).

11) For recent syntheses of 10 and its conversion to 11, see J. A. Katzenellenbogen and T. W. Utawanit, J. Am. Chem. Soc., 96, 6153 (1974) (stereoselective) and P. J. Kocienski, J. M. Ansell, and R. W. Ostrow, J. Org. Chem., 41, 3625 (non-stereoselective).

12) H. M. Fales, M. S. Blum, R. M. Crewe, and J. M. Brand, J. Insect Physiol., 18, 1077 (1972).

13) Yield, 60%; bp, 40-45°C/5 mmHg.

14) Bp, 84-86°C/0.2 mmHg;NMR (CCl_4), δ5.14 (d, olefinic), 3.5 (s, -S-CH_2-), and 3.00 (s, NCH_3).

15) 10: NMR (CCl_4), δ10.51 (br.s, 1H), 6.58 (d, 1H), 2.3 (m, 1H). 1.82 (s, 3H), 1.35 (m. 2H), 1.02 (d, 3H), 0.87 (t, 3H); 11, 6.27 (d, 1H), 2.62 (q, 2H), 1.77 (d, 3H), 1.4 (m, 2H),1.03 (t, 3H), 1.00 (d, 3H), 0.86 (t, 3H).