A Novel Stereoselective Synthesis of Alkenol Sex Pheromones via [3,3]-Sigmatropic Rearrangement of Allylic Dithiocarbamates[1]

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Recently, we have reported the successive 1,3-dialkylation of the allyl group in allyl dimethyldithiocarbamate (**1**)[2]. In the course of study, it has been found that the dimethyldithiocarbamate group of **1** can be readily removed by reduction with alkali metal in liquid ammonia or ethylamine. This finding made it possible to apply the method to the stereoselective synthesis of di- and tri-substituted alkenes. We wish to report here a stereoselective synthesis of *trans*-alkenol sex pheromones having a general formula **2** which have already been isolated from various kinds of insects[3].

$H_3C-(CH_2)_m-CH=CH-(CH_2)_n-O-CO-CH_3$

2

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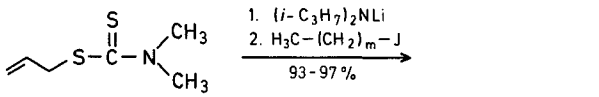
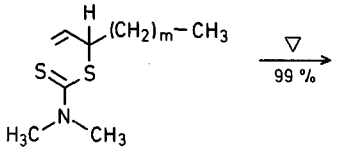
The advantages of our method lie in the high degree of stereoselectivity obtained, an excellent yield of each process, and the ready availability of the inexpensive starting material. Recently, Warthen and Jacobson have described the difficulties involved in the preparation of a *trans*-alkenol acetate with a C-chain longer than C_{13}[4]. However, our method afforded *trans*-7-tetradecen-1-ol acetate (**2c**) in an excellent yield. The sex attractants prepared in the present work are *trans*-6-nonen-1-ol acetate (**2a**), *trans*-7-dodecen-1-ol acetate (**2b**), and *trans*-7-tetradecen-1-ol acetate (**2c**), which are sex pheromones or attractants of lepidopterous insects[5-7].



1



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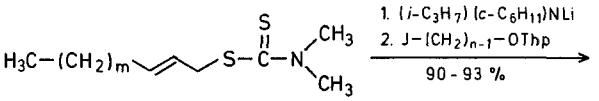

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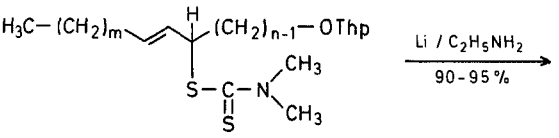

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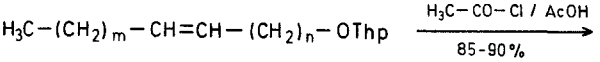

6

$H_3C-(CH_2)_m-CH=CH-(CH_2)_n-O-CO-CH_3$

2a m = 1, n = 5
2b m = 3, n = 6
2c m = 5, n = 6

The synthetic sequence is depicted above. The alkylation of **1** and **4** was carried out by a modification of the method previously described[2]. The rearrangement of **3** to **4** was affected by refluxing **3** in chloroform for 3 hours. The distillation of the rearranged product (**4**) afforded a *trans* isomer with no detectable trace of *cis* isomer. The C—C-coupled product (**5**) was stored in a refrigerator in order to avoid possible allylic rearrangement and migration of the double bond. The removal of the dimethyldithiocarbamate group could be performed in a better yield with lithium/ethylamine system than with sodium/ammonia system. The hydrogenation of the double bond by the former was almost negligible.

The synthetic sequence reported here should have wide applicability to the synthesis of other types of insect sex pheromones, such as alkadienols and alcohols having tri-substituted olefinic bonds.

***trans*-2-Alkenyl Dimethyldithiocarbamate (4); General Procedure:**
In an atomoshper of argon, *n*-butyl lithium (24 mmol) in *n*-hexane was added below −55° to a solution of **1** (22 mmol) and diisopropylamine (3.0 g) in tetrahydrofuran. To the resulting deep red solution was added below −55° a solution of alkyl iodide (30 mmol) in tetrahydrofuran (5 ml) and the solution was stirred for 15 min. after the red color completely disappearred. The solution was washed with 20% ammonium chloride solution, acidified with dilute hydrochloric acid, and again washed with 20% ammonium chloride solution. After the removal of the solvent, the product was refluxed in 40 ml of chloroform for 3 h. The product was subjected to distillation under reduced pressure. The results are summarized in Table 1.

Coupling of Alkenyl Dimethyldithiocarbamate with 2-(ω-Iodo-*n*-alkoxy)-tetrahydropyran: General Procedure:
To a solution of the dimethyldithiocarbamate (**4**, 14 mmol) in tetrahydrofuran (20 ml) was added below −55° lithium *N*-isopropylcyclohexylamide (14 mmol) in *n*-hexane (10 ml). To the resulting deep red solution was added below −55° a solution of 2-(ω-iodo-*n*-alkoxy)-tetrahydropyran (20 mmol) in tetrahydrofuran (10 ml). Stirring was continued for 30 min. after the red color dissipated. The solution was worked up as usual and dried over sodium sulfate. After the solvent was removed in vacuo below 30°, the residue was chromatographed on a column of silica gel with dichloromethane as eluent; yield: 90–93%.

2-(*trans*-Alkenyl)-tetrahydropyran (6); General Procedure:
To dry ethylamine (80 ml) at −60° was added lithium wire (with 1% sodium; 423 mg, 60 mg-atom) as small pieces. The temperature of the blue solution was brought to 0° for 1.5 h to ensure dissolution and then decreased to −60°. The coupled product (**5**; 6 mmol) in tetrahydrofuran (20 ml) was added slowly and the resulting solution allowed to stir an additional 30 min at −20°. Maintaining the temperature at −60°, 3-hexyne was added until the blue color was totally dissipated and the resulting pale yellow solution was then treated with methanol and water. After attaining room temperature, the volatiles were carefully evaporated under reduced pressure. The resulting cloudy solution was extracted four times with ether and the combined organic layers washed with water and brine, dried over sodium carbonate, filtered and evaporated

Table 1. 2-Alkenyl Dimethyldithiocarbamates (**4**); $H_3C(CH_2)_mCH{=}CHCH_2SCSN(CH_3)_2$

Compound	m	Yield (%)[a]	B.p.	Elemental Analyses					
4a	1	93	117–121°/3.5 torr	$C_8H_{15}NS_2$ (189.2)	calc.	C 50.78	H 7.99	N 7.40	S 33.82
					found	50.95	8.05	7.38	33.51
4b	3	96	135–136°/3.5 torr	$C_{11}H_{21}NS_2$ (231.3)	calc.	C 57.12	H 9.15	N 6.06	S 27.67
					found	57.05	9.21	6.13	27.78
4c	5	94	152–154°/3.5 torr	$C_{12}H_{23}NS_2$ (245.3)	calc.	C 58.75	H 9.45	N 5.71	S 26.09
					found	58.66	9.62	5.66	26.20

[a] Based on allyl dimethyldithiocarbamate (**1**).

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Table 2. 2-(*trans*-Alkenyl)-tetrahydropyrans (**6**); $H_3C(CH_2)_mCH{=}CH(CH_2)_nOThp$

Compound	m	n	Yield (%)	Elemental Analyses			
6a	1	5	95	$C_{14}H_{26}O_2$ (226.4)	calc. found	C 74.28 74.03	H 11.58 11.38
6b	3	6	93	$C_{19}H_{32}O_2$ (268.4)	calc. found	C 76.06 76.13	H 12.02 12.05
6c	5	6	90	$C_{19}H_{36}O_2$ (296.5)	calc. found	C 76.97 76.70	H 12.24 12.30

Table 3. *trans*-Alkenol Acetates (**2**); $H_3C(CH_2)_mCH{=}CH(CH_2)_nOCOCH_3$

Compound	m	n	Yield (%)	B.p.	Elemental Analyses			
2a	1	5	90	65–70°/0.3 torr	$C_{11}H_{20}O_2$ (184.3)	calc. found	C 71.69 71.78	H 10.94 10.96
2b	3	6	87	78–82°/0.05 torr	$C_{14}H_{26}O_2$ (226.4)	calc. found	C 74.28 74.03	H 11.58 11.36
2c	5	6	85	112–117°/0.05 torr	$C_{16}H_{30}O_2$ (254.4)	calc. found	C 75.53 75.72	H 11.89 11.78

Table 4. Spectroscopic Data for Products **4**, **6**, and **2**

Product	I.R. (ν, cm^{-1})	^{1}H-N.M.R. (δ ppm)	Mass spectrum (*m/e* for $M^{\oplus}$)
4a	1150 (s), 1500 (s), 1258 (s) (thioamide I, II, and III, resp.), 970 (—CH=CH—)	1.00 (CH_3), 3.40, 3.54 ($N(CH_3)_2$), 3.94 (—S—CH_2—C=), 5.51, 5.73 (—CH—CH—, J = 15.3 Hz)	—
4b	1148 (s), 1495 (s), 1258 (s) (thioamide I, II, and III, resp.), 970 (—CH—CH—)	0.89 (CH_3), 3.38, 3.53 ($N(CH_3)_2$), 3.93 (—S—CH_2—C=), 5.51, 5.73 (—CH—CH—, J = 15.5 Hz)	—
4c	1145 (s), 1495 (s), 1258 (s) (thioamide I, II, and III, resp.) 970 (—CH=CH—)	0.88 (CH_3), 3.38, 3.53 ($N(CH_3)_2$), 3.93 (—S—CH_2—C=), 5.51, 5.73 (—CH=CH—, J = 15.5 Hz)	—
6a	1125 (C—O), 970 (—CH=CH—)	0.94 (CH_3), 4.58 (—O—CH—O—), 5.42 (—CH=CH—)	
6b	1125 (C—O), 970 (—CH—CH—)	0.91 (CH_3), 4.58 (—O—CH—O—), 5.40 (—CH=CH—)	—
6c	1125 (C—O), 970 (—CH—CH—)	0.90 (CH_3), 4.56 (—O—CH—O—), 5.38 (—CH=CH—)	—
2a	1740 (C=O), 1240 (C—O), 968 (—CH=CH—)	0.96 (CH_3), 2.00 (H_2C—C=), 2.04 (—CO—CH_3), 4.06 (—CH_2—O—), 5.40 (—CH=CH—)	184
2b	1745 (C=O), 1240 (C—O), 968 (—CH=CH—)	0.90 (CH_3), 2.00 (H_2C—C=), 2.04 (—CO—CH_3), 4.06 (—CH_2—O—), 5.40 (—CH=CH—)	226
2c	1742 (C=O), 1240 (C—O), 968 (—CH—CH—)	0.90 (CH_3), 2.00 (H_2C—C=), 2.04 (—CO—CH_3), 4.06 (—CH_2—O—), 5.40 (—CH=CH—)	254

under reduced pressure affording a pale yellow oil. Chromatography on silica gel with dichloromethane as eluent afforded a clear colorless oil. The results are summarized in Table 2.

***trans*-Alkenol acetate (2); General procedure:**
2-(*trans*-Alkenyl)-tetrahydropyran (**6**) was converted in an excellant yield to *trans*-alkenol acetate according to the method described by Warthen and Jacobson[8]. Gas chromatographic analysis revealed a single peak. The results are summarized in Table 3.

We wish to thank Dr. Takeshi Nakai of Tokyo Institute of Technology for helpful suggestions.

October 8, 1974

[1] Synthesis with Dithiocarbamate Derivatives; IV. Part III is I. Hori, T. Hayashi, H. Midorikawa, *Synthesis* **1974**, 705.
[2] T. Hayashi, *Tetrahedron Lett.* **1974**, 339.
[3] S. Ishii, *Biologically Active Substances Produced by Insects*, Nankodo, Tokyo, 1974.
[4] J. D. Warthen and Jacobson, *Synthesis* **1973**, 616.
[5] M. Jacobson, K. Ohinata, D. L. Chambers, W. A. Jones, M. S. Fujimoto, *J. Med. Chem.* **16**, 248 (1973).
[6] J. S. Read, F. L. Warren, *Chem. Commun.* **1968**, 792.
[7] W. L. Roelofs, A. Comeau, *Pesticide Chemistry*, Vol. III, A. S. Tobotu, Ed., Gordon and Beach, New York, N.Y., 1971, p. 91.
[8] D. Warthen, M. Jacobson, *J. Med. Chem.* **11**, 1190 (1968).

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Errata:

T. HAYASHI, H. MIDORIKAWA, *Synthesis* **1975**, 100;

The boiling point and elemental analysis for compound **4b** (Table 1, page 101) should be:

131–132°/3.5 torr

$C_{10}H_{19}NS_2$	calc.	C 55.28	H 8.82	N 6.45	S 29.46
(217.26)	found	55.42	8.58	6.35	29.16

R. J. BORGMANN, R. V. SMITH, J. E. KEISER, *Synthesis* **1975**, 249;

Entry 2 in the Table (page 250) should be:

Ac_2O	r.t.	24 h	**3**	95

V. M. KAPOOR, A. M. MEHTA, *Synthesis* **1975**, 471;

The elemental analysis for 3,4-dihydro-6-methoxy-2-naphthyl 2-(2-furyl)-vinyl Ketone (**4**) should be:

$C_{18}H_{16}O_3$	calc.	C 77.13	H 5.75	
(280.3)	found	77.34	5.84	

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