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4-(*t*-BUTYLTHIO)-3-BUTEN-2-ONE. SYNTHON FOR α,β- AND α,β,γ,δ-UNSATURATED ALDEHYDE SYNTHESIS

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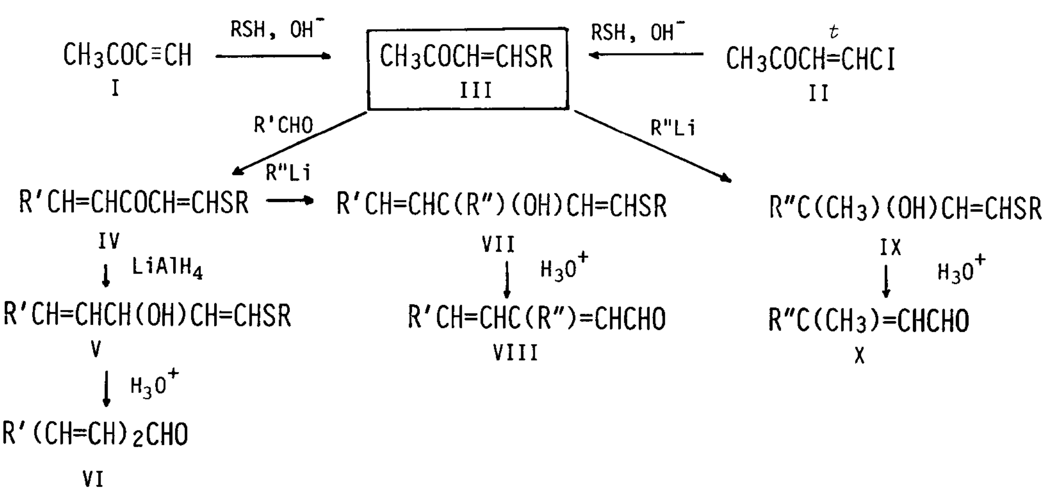
Summary: A convenient synthesis of α,β- and α,β,γ,δ-unsaturated aldehydes using readily accessible 4-(*t*-butylthio)-3-buten-2-one as synthon was described.

Thiovinyl ketone (vinylogous thioesters) have been used as useful synthetic intermediates for variety of transformation.[1)]

The preparation of highly unsaturated aldehydes as intermediates of synthesis of annulenoannulenes using readily accessible 4-(*t*-butylthio)-3-buten-2-one (III, R=*t*-Bu) has been reported in previous papers.[2)] In this communication we wish to report a wide applicability of III (R=*t*-Bu) to the synthesis of various types of α,β- and α,β,γ,δ-unsaturated aldehydes, and the new synthesis of isorenieratene, a carotenoid of animal origin bearing aromatic terminal groups, will be described in the subsequent paper.

The transformation of III (R=*t*-Bu) into unsaturated aldehydes (VI, VIII and X) is outlined in Scheme. The thiovinyl ketone (III) could be prepared by a nucleophilic addition of mercaptan to 3-butyn-2-one (I)[3),4)] or by a reaction of mercaptan with *trans*-4-chloro-3-buten-2-one (II).[5)] The latter route was found to be superior in view of the ease of preparation of II and exclusive

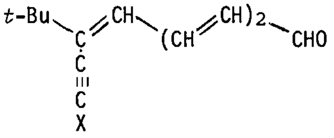
SCHEME



formation of *trans*-isomer of III. *t*-Butyl derivative of III (R=*t*-Bu) was used considering potentially high stability and crystallinity of the intermediate compounds.

The ketone (IV) obtained by the aldol condensation of aldehyde with III (R=*t*-Bu) (Table 1) was reduced with lithium aluminium hydride or alkylated with alkyllithium to yield alcohol (V or VII). The alcohol (V or VII) was treated without isolation with an acid to cause anionotropic rearrangement of the hydroxyl group accompanied with the elimination of *t*-butyl mercaptan. The unsaturated aldehydes (VI and VIII) thus obtained are tabulated in Tables 2 and 3 (VI and VIII). The dienaldehydes having methyl side chain (VIII, R''=Me) were obtained as a mixture of E- and Z-isomers. However, the mixture could be converted into pure E-isomer on irradiation in the presence of iodine. Alkylation of III (R=*t*-Bu) by means of alkyllithium afforded alcohol (IX) which could be transformed into β-methyl α,β-unsaturated aldehyde (X) (Table 4) on treatment with an acid.

Table 1. Preparation of Thiovinyl Ketones (R=*t*-Bu)

R'CHO	R'CH=CHCOCH=CHSR mp	yield(%)	lit.
C_6H_5CHO	[100∿100.5°C]	81	a
$C_6H_5CH=CHCHO$	[75.0∿76.5°C]	84	a
p-$CH_3OC_6H_4CHO$	[96∿99°C]	82	a
p-$CH_3OC_6H_4(CH=CH)_2CHO$	[141.5∿142.5°C]	61	a
2,3,6-$(CH_3)_3C_6H_2CHO$	[47.5∿48.5°C]	65	a
2,3,6-$(CH_3)_3C_6H_2CH=C(CH_3)=CHCHO$	liquid	67	a
1,4-$C_6H_4(CHO)_2$	[155.5∿157.6°C]	47	a
9-formylanthracene	[186∿187°C]	78	a
o-ethynylbenzaldehyde	[99.9∿101.4°C]	69	2d
p-$CH_3OC_6H_4CH=CHC(C\equiv CH)=CHCHO$	[115∿115.5°C]	61	a
 $t\text{-Bu}-C(C\equiv CX)=CH-(CH=CH)_2-CHO$			
n=0 (X=H)	[104.5∿105°C]	83	2a
n=1 (X=$SiMe_3$)	[107.5∿109.5°C](X=$SiMe_3$)	82	2b
n=2 (X=$SiMe_3$)	[87∿88°C](X=H)	46	2c

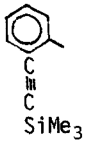
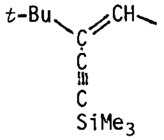
a: This work.

Table 2. Synthesis of Dienals (VI)

R'CH=CHCOCH=CHSR (IV, R=*t*-Bu)	R'$(CH=CH)_2$CHO mp	yield(%)	lit.
R'= C_6H_5	[38.5∿39.0°C]	69	a
R'= *p*-$CH_3OC_6H_4$	[75.5∿76.5°C]	84	a

a: This work.

Table 3. Synthesis of R'CH=CHC(R")=CHCHO (VIII)

R'CH=CHCOCH=CHSBu-*t* (IV) R'	R"	R'CH=CHC(R")=CHCHO (VIII) mp	yield(%)#	E : Z	lit.
C_6H_5-	CH_3	[209°C]*	68	45:55	a
C_6H_5-	C≡CH	[84.5∿85.5°C]	98	100:0	a
p-$CH_3OC_6H_4$-	CH_3	[90.0∿91.0°C]	81	80:20	a
p-$CH_3OC_6H_4$-	*n*-Bu	[180°C]dec.	83	50:50	a
p-$CH_3OC_6H_4$-	C≡CH	[94.0∿95.0°C]	90	100:0	a
2,3,6-$(CH_3)_3C_6H_2$-	CH_3	[190°c]dec.*	75	90:10	a
2,3,6-$(CH_3)_3C_6H_2CH{=}CHC(CH_3){=}CH$-	CH_3	[195.0∿195.5°C]*	60	75:25	a
	C≡CH	[64.1∿65.2°C]*	74	100:0	2d
	C≡CH	[225∿227°C]	72	100:0	2a

#: Yields of isolated aldehydes. *: Mp of 2,4-dinitrophenylhydrazone of E -isomer. a: this work.

Table 4. Synthesis of R"C(CH_3)=CHCHO (X)

R"	mp of DNP*	Yield(%)#	lit.
$(CH_3)_2C{=}CHCH_2CH_2$-	[90°C]dec.	51+	a
CH_3-	[173.5∿174.5°C]	69	a
n-Bu-	[167°C]	73	a

*: 2,4-dinitrophenylhydrazone. #: Yields of isolated aldehydes (X). +: geranial:neral = 65:35. a: This work.

Some representative examples of experimental procedures are given below:[6)]

trans-4-(*t*-Butylthio)-3-buten-2-one (III, R=*t*-Bu).

To an ice-cooled mixture of II (17.0 g, 0.16 mol) and *t*-butyl mercaptan (14.4 g, 0.16 mol) was added slowly an aqueous solution of sodium hydroxide (9.0 g, 0.23 mol in water, 40 ml). After the mixture had been stirred at room temperature overnight, the reaction mixture was extracted with ether, and worked up in the usual way. III (R=*t*-Bu) was obtained as a liquid, bp 106°C/25 mmHg, 22.3 g, 85%, which crystallized in a refrigerator, mp 31 ∿ 33°C; NMR ($CDCl_3$): δ 1.33 s (*t*-Bu), 2.18 s (Me), 6.11 d (J=16, olefinic-H) and 7.78 d (J=16, olefinic-H).

1-(*t*-Butylthio)-5-phenyl-1,4-pentadien-3-one (IV, R'=C_6H_5, R=*t*-Bu).

A solution of sodium hydroxide (1.5 g, 38 mmol in water, 5 ml) was added dropwise at -15°C to a solution of benzaldehyde (2.02 g, 19 mmol) and III (R=*t*-Bu, 2.98 g, 19 mmol) in ethanol (23 ml). After 2 hrs., crystals deposited were washed with ethanol-water and recrystallized from ethanol to give IV (R'=C_6H_5, R=*t*-Bu), mp 100∿100.5°C, 3.76 g, 81%.

5-(*p*-Methoxyphenyl)-1,3-pentadienal (VI, R'=*p*-$CH_3OC_6H_4$).

To a solution of IV (R'=*p*-$CH_3OC_6H_4$, 0.465 g, 1.7 mmol) in ether (40 ml) was added at -15°C a stock solution of lithium aluminium hydride (equiv. to 1.7 mmol) in the same solvent, and the mixture was kept for 3 hrs. at the same temperature. Diluted sulphuric acid (1M, 15 ml) was added below 0°C to the reaction mixture. After being stirred for 1 hr., the mixture was extracted with benzene. Chromatography of the extract on silica gel (15 g) followed by elution with benzene yielded VI (R'=*p*-$CH_3OC_6H_4$), mp 75.5∿76.0°C, 0.264 g, 84%.

5-Phenyl-3-ethynyl-1,3-pentadienal (VIII, R'=C_6H_5, R"= C≡CH).

A solution of IV (R'=C_6H_5, R=*t*-Bu, 0.146 g, 0.60 mmol) in THF (30 ml) was gradually added to a solution of lithium acetylide in the same solvent at -78°C. After the mixture had been stirred for 3 hrs. at -40 ∿ -45°C, 1M sulphuric acid (30 ml) was added, and worked up in the usual manner. Chromatography of the benzene extract on silica gel (10 g) followed by elution with the same solvent yielded VIII (R'=C_6H_5, R"= C≡CH), mp 84.5∿85.5°C, 0.108 g, 98%.

References and Notes

1) a) R. E. Irland and J. A. Marshall, *J. Org. Chem.*, 27, 1615, 1620 (1962); b) A. G. Schultz and D. S. Kashdan, *ibid.*, 38, 3814 (1973); c) R. M. Coates and R. L. Sowerby, *J. Am. Chem. Soc.*, 93, 1027 (1971); d) T. A. Bryson, R. E. Dardis, and R. B. Gammill, *Tetrahedron Lett.*, 743 (1978); P. R. Bernstein, *ibid.*, 1015 (1979).

2) a) S. Akiyama, M. Iyoda, and M. Nakagawa, *J. Am. Chem. Soc.*, 98, 6410 (1976); b) S. Nakatsuji, S. Akiyama, and M. Nakagawa, *Tetrahedron Lett.*, 3723 (1977); c) S. Nakatsuji, A. Akiyama, and M. Nakagawa, *ibid.*, 1483 (1978); d) K. Sakano, S. Akiyama, M. Iyoda, and M. Nakagawa, *Chem. Lett.*, 1019 (1978).

3) E. N. Prilezhaeva, G. S. Vasil'ev, I. L. Mikhelashvili, and V. S. Bogdanov, *Zh. Org. Khim.*, 7, 1349 (1971).

4) An ethanolic solution of I was added at -10 ∿ -15°C to a solution of mercaptan in the same solvent in the presence of Triton B to give III. Formation of minor amount of $CH_3COCH_2CH(SR)_2$ was observed except for *t*-BuSH. The ratio of *cis:trans* was found to be *ca.* 1:1 in the case of R= Me, Et and *n*-Bu, and *ca.* 7:3 in *t*-butyl derivative (yield 96%). A mixture consisting of predominantly *trans*-isomer (content 90 ∿ 95%) could be obtained on irradiation (diffused sunlight or tungsten lamp) of a solution of *t*-butyl derivative in the presence of iodine. Also, a mixture of III (R= Me) gave crystalline *trans*-isomer, mp 37∿37.5°C on irradiation.

5) V. T. Klimko, V. A. Mikahalev, and A. P. Skoldinov, *Zh. Obshch. Khim.*, 27, 370 (1957); A. E. Pohland and W. R. Benson, *Chem. Revs.*, 66, 161 (1966).

6) All new compounds described in this communication gave satisfactory elemental analyses and their NMR, IR and mass spectroscopic data are consistent with the assigned structures.

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