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CHEMISTRY OF 2-SUBSTITUTED THIOTHIAZOLINE. IV.1)

A NEW SYNTHETIC METHOD FOR IODO-METHYLATION AND IODO-PROPENYLATION(ICH$_2$C=C-)

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In the course of our study into the chemistry of 2-substituted thiothiazoline, we developed new and versatile iodo-methylation and iodo-propenylation methods from the corresponding alkylhalide using 2-methyl or 2-allylthiothiazolinelithium derivative.

The sequence for the homologation is as follows [Chart 1] :

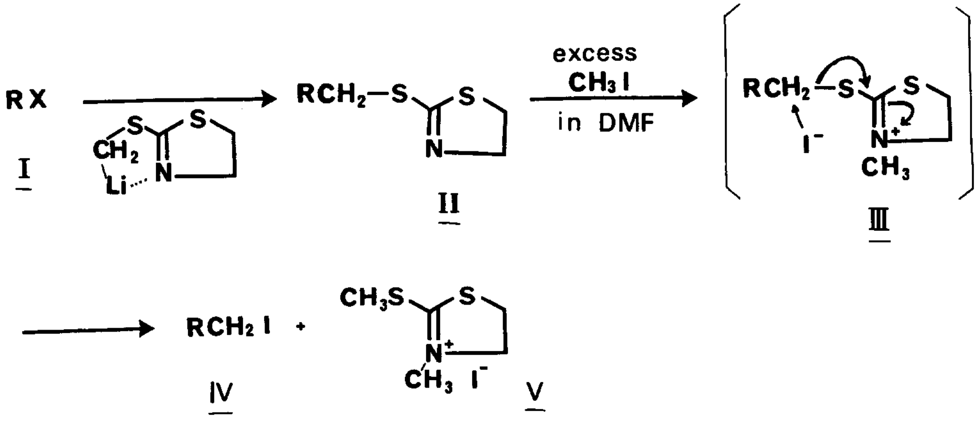

Chart 1

The 2-alkylthiothiazoline [1g] (II), which was prepared from alkylhalide (I) and 2-methylthiothiazolinelithium by the reported procedure2) was treated with excess methyl iodide [5 ml] in dimethylformamide(DMF) [3 ml] (or DMSO, HMPA) at r.t. overnight, or heating at 70° for one hour. A homologated iodide (IV) and crystalline, water-soluble N,S-dimethyl salt (V) [mp 132°]3) were produced. Extraction with ether, washing of the organic layer with 1% aq.

sodium hydrosulfite solution and water successively, and evaporation of the solvent gave almost pure IV in good yield[4] [Table 1]. The identity was proved by the comparison of the IR and NMR spectra with those of a reference sample.

Table 1

	RX	RCH_2I	Yield % (from II)
1.	$C_6H_5CH_2Br$	$C_6H_5CH_2CH_2I$	75
2.	$C_6H_5CH_2CH_2Br$	$C_6H_5CH_2CH_2CH_2I$	70
3.	$\underline{n}$-$C_9H_{19}Cl$	$\underline{n}$-$C_{10}H_{21}I$	68
4.		$C_6H_5CH_2I$	82 [from 2-benzylthiothiazoline]

Application of this method to the 2-allylthiothiazoline derivatives (VI) was studied (Chart 2). For example, 2-(1-tridecenyl-3-thio)-thiazoline (VIa) [1.1 g], which was prepared from n-decyl bromide and 2-allylthiothiazoline-lithium in an improved solvent system (THF:HMPA=10:1) in 70% yield, was dissolved in a solution of 5 ml of methyl iodide and 3 ml of DMF containing 10 mg of $NaHCO_3$ and the reaction mixture was kept standing overnight at r.t. The precipitated N,S-dimethyl salt (V) was filtered off and the filtrate was poured into water. Usual working up finally gave trans-tridec-2-en-1-yl iodide (VIIIa) in 72% yield. NMR[5] δ : 0.87 (CH_3, t.), 1.0-1.5 (CH_2x8), 1.8-2.2 (2H), 3.83 (2H, d., J=7.5 Hz), 5.5-5.9 (2H). Precise gas chromatography [30% DEGS on Chromosorb-W] showed the product (VIIIa) was isomer free. The IR showed strong CH_2-I absorption at 1150 and δ =CH absorption at 960 cm^{-1} which was characteristic of the trans-configuration of the disubstituted double bond as depicted in VIII. Further VIIIa was converted to the corresponding α,β-unsaturated-aldehyde (IXa) by Kornblum reaction (three minutes).[6] IXa [M^+ at m/e 196 ($C_{13}H_{24}O$)] showed characteristic NMR signals for the structure at δ 9.60 (1H, d. J=7.8 Hz, aldehyde H), 6.88 (1H, t. of d. J=6 and 16 Hz, β-H of $\alpha\beta$-unsaturated aldehyde), 6.10 (1H, d. of d. 7.8 and 16 Hz, α-H) and IR bands at 1690 cm^{-1} and UV maximum at 223 nm. The coupling constant (16 Hz) clearly indicated that IXa was trans-configuration. Thus IXa was determined as trans-tridec-2-en-1-al [2,4-dinitrophenylhydrazone, mp 117° (lit. 117-119°)[7]] .

By the same procedure 2-(1-pentene-5-phenyl-3-thio) thiazoline (VIb) was also coverted to the corresponding *trans*-2-penten-5-phenyl-1-iodide (VIIIb) in 70% yield [NMR δ : 7.2 (5H), 5.5-5.9 (2H), 3.75 (2H, d., J=6.2 Hz), 2.2-2.8 (4H). IR ν_{max}^{film}: 1660, 1600, 1150 and 960 cm^{-1}], and to the α,β-unsaturated aldehyde (IXb) [NMR δ : 7.2 (5H), 9.52 (1H, d., J=7.8 Hz), 6.82 (1H, t. of d., J=6 and 16 Hz), 6.10 (1H, d. of d., J=7.8 and 16 Hz), 2.5-2.9 (4H). IR ν_{max}^{film}: 2720, 2830, 1690 and 1640 cm^{-1}. UV λ_{max}^{EtOH}: 221 nm. 2,4-dinitrophenylhydrazone, mp 173°].

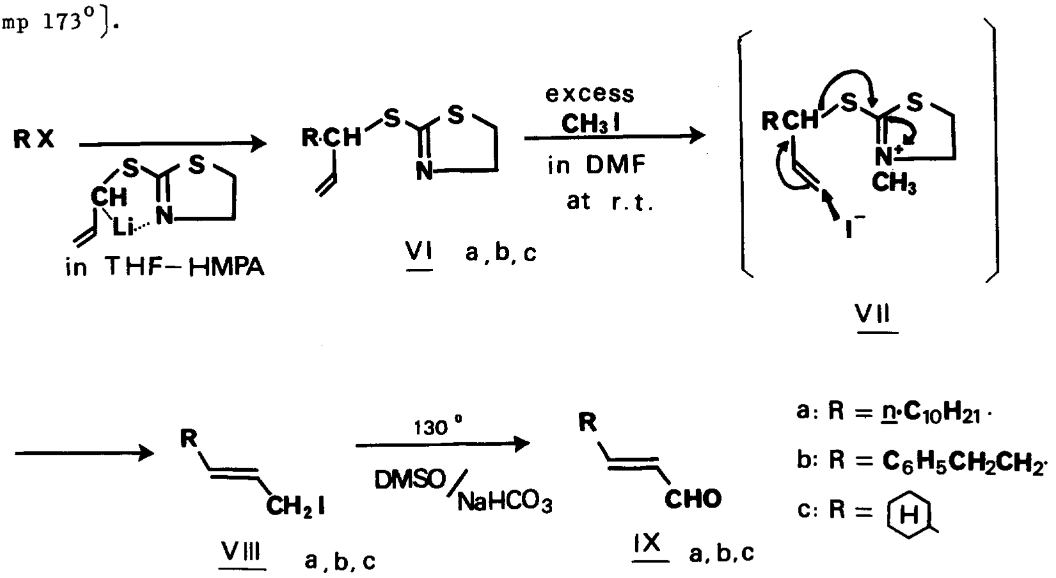

Chart 2

In the case of secondary halide such as cyclohexyl bromide, the 2-(1-propene-3-cyclohexyl-3-thio)thiazoline (VIc) was obtained in 52% yield and the convertion to the corresponding halide (VIIIc) was also effected by the same reaction conditions as VIa in 76% yield. [NMR δ : 5.4-6.0 (2H), 3.88 (2H, d., J=7 Hz), 0.9-2.4(11H). IR ν_{max}^{film}: 1650, 1150 and 960 cm^{-1}]. In this case the product (VIIIc) was also isomer free and was converted easily to the *trans*-cyclohexaneacrolein (IXc) by Kornblum reaction. [NMR δ : 9.57 (1H, d., J=7.8 Hz), 6.88 (1H, d. of d. J=6 and 16 Hz), 6.10 (1H, d. of d. J=7.8 and 16 Hz), 0.9-2.4 (11H). IR ν_{max}^{film} : 2720, 2850, 1690 and 1640 cm^{-1}. UV λ_{max}^{film}: 224 nm. 2,4-dinitrophenylhydrazone, mp 215°. *Anal.* Calcd. for $C_{15}H_{18}N_4O_4$: C, 56.59;

H, 5.70; N, 17.60. Found: C, 56.61; H, 5.70; N, 17.60.)

Plausible paths for the formation of trans-iodo-propenylated product are described in Chart 2. The stage of attacking of I^- in an intermediate, VII, would proceed to forming thermodynamically more stable trans-disubstituted olefins (VII).

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