

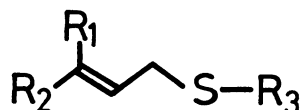
THE INFLUENCE OF ELECTROPHILES ON THE REGIOSELECTIVE ALKYLATION OF AMBIDENT CARBANION FROM DIHYDROTHIOPYRAN

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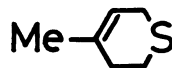
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The reaction of ambident carbanion derived from dihydrothiopyran (Id) with alkyl halides, epoxides, and carbonyl compounds was examined. The results demonstrate that in the cases of alkyl halides selectivity in producing 2-alkyl- Δ^3 -dihydrothiopyrans increases in the order, $\text{Cl} > \text{Br} > \text{I}$. On the other hand, the carbonyl compounds gave exclusively 4-alkyl- Δ^2 -dihydrothiopyrans in contrast to the results obtained from the epoxides.

The formation of products resulting from both α - and γ -alkylations on sulfur-stabilized allylic carbanions has been reported for allyl sulfides (Ia, Ib, and Ic).^{1,4)} The regioselective α -alkylation of the allyl sulfides has been found to depend on the structure of the sulfides,^{1a)} the solvent employed,^{1b)} the effect of metal ions,^{1c)} and others.^{1d)} This communication reports the results of our study on the alkylation of carbanions derived from dihydrothiopyran (Id) with alkyl halides, epoxides, and carbonyl compounds as electrophiles.



Ia $\text{R}_1 = \text{R}_2 = \text{Me}$, $\text{R}_3 = \text{Ph}$ or Alkyl
 Ib $\text{R}_1 = \text{R}_2 = \text{H}$, $\text{R}_3 = \text{Ph}$



Ic




Id

Typical experimental procedure is as follows: To a stirred solution of Δ^3 -dihydrothiopyran (Id)²⁾ (74.2 mg, 0.74 mmol) in dry THF (2 ml) was added slowly *sec*-butyllithium (2.4 ml, 0.95 mmol) for 1 hr at -78°C . To this mixture benzyl chloride (0.078 ml, 0.67 mmol) was added and the mixture was stirred for 2 hr at -78°C and then quenched with small amount of ice. The organic phase was extracted with ether and the extracts were washed with aqueous NH_4Cl , dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel. *n*-Hexane-dichloromethane (4:1) elution gave 90 mg (70.6%) of 2-benzyl- Δ^3 -dihydrothiopyran and 32.7 mg (25.7%) of 4-benzyl- Δ^2 -dihydrothiopyran. Instead of *sec*-butyllithium, *n*-butyllithium-tetra-methylethylenediamine complex³⁾ could be used without affecting the product yield. The reaction conditions and a summary of results are shown in the following Table.

Although 4-methyl- Δ^3 -dihydrothiopyran (Ic) has been shown to react with alkyl halides to give 2-alkyl- Δ^3 -dihydrothiopyrans preferentially,^{4a)} the absence of the methyl group in Ic resulted in loss of the regioselectivity of the alkylation reactions as shown in Runs 1-5 (see Table). The similar results have been reported on alkylations of Ia and Ib.^{1a)} On the other hand, our results (Runs 3-5) enable us to discuss the behavior of alkyl halides bearing Cl, Br,

Table Reaction Conditions and Results

Run	 mmol	Base mmol	Solvent (THF) ml	Temp °C	Time min	Substrate mmol	Yield,% ^c		
							2-Sub.	4-Sub.	
1	1.31	1.65 ^a	2.5	-49	120	Ph-CH ₂ -Cl	0.81	68.0	24.0
2	0.74	0.95 ^b	2.0	-78	120	Ph-CH ₂ -Cl	0.67	70.6	25.7
3	1.12	1.60 ^b	2.0	-78	120	n-Bu-Cl	1.10	68.5	1.3
4	1.15	1.60 ^b	1.5	-78	90	n-Bu-Br	1.20	72.5	6.5
5	0.52	0.88 ^b	2.0	-78	45	n-Bu-I	0.52	70.5	29.5
6	0.35	0.70 ^b	2.0	-78	180	Propylene Oxide	0.35	33.5	17.0
7	0.40	0.56 ^b	4.0	-78	60	Epichloro- hydrin	0.2 (ml)	95.0	trace
8	0.42	0.82 ^b	2.0	-78	135	2-Octanone	0.42	0.0	72.5
9	1.00	1.40 ^b	1.5	-78	60	Enanthaldehyde	1.00	0.0	94.0

^a n-Butyllithium-tetramethylethylenediamine complex was used.

^b sec-Butyllithium was used.

^c Yields are calculated on isolated product by column chromatography.

or I as a leaving group, since the relative ratios of C₂ and C₄ alkylation products decreased in the order as follows: chloride (C₂/C₄) 53/1; bromide 11/1; iodide 2.4/1. This indicates that electrophilic attack on the anions of Id may proceed predominantly at the C₂ position in the case of alkyl halide having a less electrophilic character.

We have also examined how the regioselectivity of the alkylation is affected by changes of a type of electrophile.⁴⁾ Thus, the reaction of both the ketone and the aldehyde with Id gave exclusively the corresponding 4-alkylation products, whereas epoxides afforded predominantly 2-substituted products (see Runs 6-9).

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