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ERYTHRO OR THREO SELECTIVE ALDOL-TYPE REACTION VIA (Z)S-SILYL KETENE S,N ACETALS

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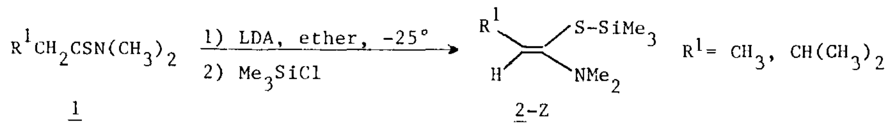
Summary : N-dialkyl thioamides can be converted stereoselectively into (Z) N-dialkyl S-trimethylsilylketene S,N acetals 2. *Condensation of* 2 *with benzaldehyde in the presence of TBAF or Lewis acids catalysis affords erythro* (R^*R^*) *or threo* (R^*S^*) *β-hydroxythioamides selectively.*

The development of highly stereoselective aldol and related C-C bond forming reactions continue to be a dominant theme of synthetic organic chemistry[1]. Most of them utilize enolate monoanions of a ketone, an ester or their equivalent. We established earlier that lithium enethiolates generated from N-dialkylthioamides $R^1CH_2CSN(R^2)_2$ provide modest erythro aldol selectivity when $R^1= CH_3$, C_2H_5 and threo aldol selectivity when $R^1= CH(CH_3)_2$[2]. More recently, several erythro selective reactions have been developed with nucleophicaly activated naked enolates and unactivated carbonyl compounds[3].

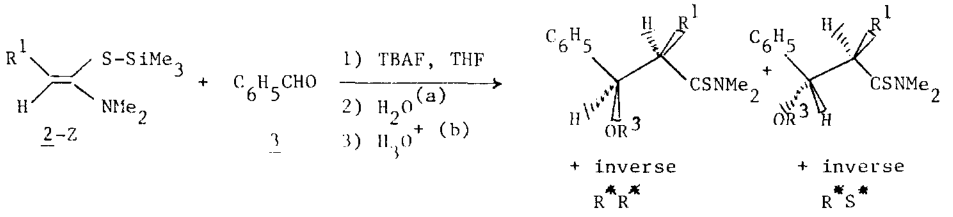
We report here high erythro aldol condensation with quaternary ammonium enethiolates generated from N-dialkyl S-trimethylsilylketene S,N acetals and threo aldol selectivity mediated with Lewis acid.

I - Fluoride ion catalyzed reaction between S-silylketene S,N acetals and benzaldehyde.

Thioamides $R^1CH_2CSN(CH_3)_2$ can be converted stereoselectively into geometrically pure (Z) N-dimethyl S-trimethylsilylketene S,N acetals via their lithium enethiolates. The stereochemistry was deduced from (^{1}H)N.M.R.-NOE measurements[4].



Under the influence of a catalytic amount (5 mol %) of tetrabutylammonium fluoride (TBAF), silylketene S,N acetals 2 react with an equimolar amount of benzaldehyde in THF smoothly at low temperatures, giving β-siloxy 4 or β-hydroxy 5 thioamides in good yields (table I).



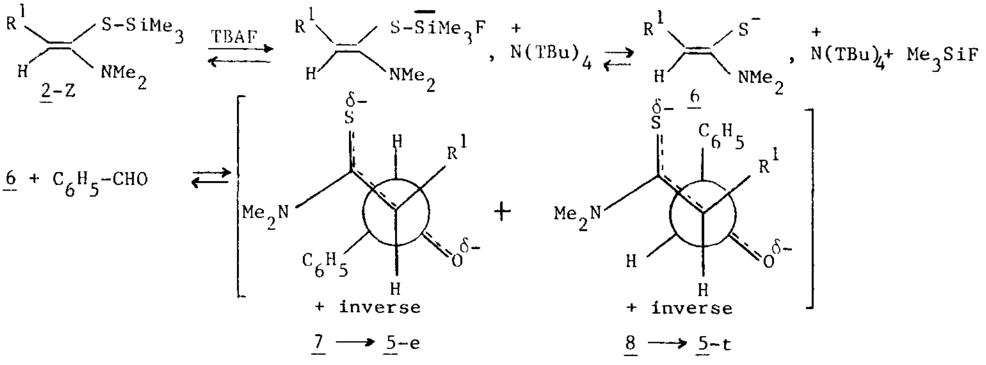
(a) R^3 = Me_3Si 4-e R^3 = Me_3Si 4-t

(b) R^3 = H 5-e R^3 = H 5-t

Table I : Diastereoselective β-hydroxythioamide formation catalyzed by fluoride ion.

entry	R^1	Reaction conditions Temp.(°C)	 time(mn)	Yield of 5	Ratio 5-e/5-t
1	CH_3	-80	2	83	95/05
2	CH_3	-70	30	90	95/05
3	CH_3	-10	2	86	85/15
4	$(CH_3)_2CH$	-80	2	55	80/20

In sharp contrast with the corresponding lithium enethiolates $R^1CH=C(SLi)NMe_2$, condensation of silylketene S,N acetals 2-Z show high erythro selectivity even when R^1 becomes bulky. Stereoselectivity improves with lower temperature. Likewise it was previously postulated[3,6] for enol silyl ethers, our results can be understood by considering the naked enethiolate of type 6 which undergoes addition to benzaldehyde by acyclic extented transition states of type 7 and 8 in which electrostatic repulsion is minimized. Transition state 7 leading to the erythro adduct is sterically favored over the diastereoisomeric threo transition state 8, because the latter suffers repulsive gauche R^1/C_6H_5 interactions.



II - Reaction of silylketene S,N acetals with benzaldehyde activated by Lewis acids.

The area of applications of reaction of enol silyl ethers and silyl ketene acetals with electrophiles activated with Lewis acids has been well reviewed[7]. Stereochemistry of Lewis acid mediated aldol reactions has not been systematically studied and stereoselectivities observed have not yet been fully eluciated.