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S-SILYLKETENE S,N-ACETALS. CROSS-ALDOL TYPE CONDENSATION REACTION WITH SCHIFF BASES.

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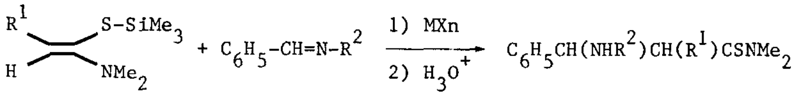
Abstract : S-silylketene S,N-acetals react with Schiff bases to afford β-aminothioamides in good yields. The reactivity of the title acetals is compared to that of corresponding lithium-enethiolates.

We have previously reported(1) that S-silylketene S,N-acetals undergo stereo- and regio selective aldol-type reaction with benzaldehyde and α-enones.

The area of applications of the reaction of silyl enol ethers and silyl ketene acetals with electrophiles activated with Lewis acids has been well reviewed(2) but Schiff bases have been far less studied(3). A recent communication of Dubois(4) on cross-aldol type reaction of ketene bis (trimethylsilyl) acetals with Schiff bases prompts us to report our results on the Lewis acid-mediated addition of S-silylketene S,N-acetals to several aldimines(5) :

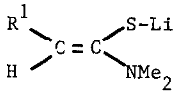


$$+\ C_6H_5\text{-CH=N-R}^2 \xrightarrow[2)\ H_3O^+]{1)\ MXn} C_6H_5CH(NHR^2)CH(R^1)CSNMe_2$$

1   2   3 (R^*R^* + R^*S^*)

β-aminothioamides 3 are obtained in good yields(table I).

The reaction of lithium enethiolates 4 with aldimines was also investigated because



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our previous study has shown striking differences of regio- and stereoselectivity between S-silylketene S,N-acetal 1 and lithium enethiolate 4.

Experimental procedures for reaction of aldimines with 4 are varied.

When $R^1 = CH_3$, condensation with benzilidene aniline ($R^2 = C_6H_5$) provides β-aminothioamides 3 in good yield (65 %) but the mixture 4 + 2 must be stirred 5 days at -70°C. With enolizable aldimines ($R^2 = CH_2\text{-}C_6H_5$, CH_3) no condensation product occurs whatever experimental conditions (temperature, solvent).

Lithium enethiolate 4 generated from methyl-3 butyrothioamide ($R^1 = CH(CH_3)_2$) does not react with Schiff bases whatever R^2 and experimental procedures.

Comparison of reactivity of 1 and 4 shows once more the superiority of S-silylketene S,N-acetals 1 over corresponding enethiolates 4 for synthetic views.

Table I : Reaction of 1 with aldimines 2

R^1	R^2	MX_n a)	Reactions conditions Temp.(°C)	Time (hr)	Yield 3 (%)	$(3\alpha/3\beta)$ b)
CH_3	C_6H_5	$ZnBr_2$ c)	-25	12	71	(45/55)
		$SnCl_4$ d)	0	0.15	74	(50/50)
			+20	2	75	(53/47)
CH_3	$CH_2-C_6H_5$	$ZnBr_2$ c)	20	12	45	(30/70)
		$SnCl_4$ d)	20	1	45	(40/60)
		$TiCl_4+Ti(O.iPr)_4$ e)	-20	12	70	(40/60)
$(CH_3)_2CH$	C_6H_5	$ZnBr_2$ c)			f)	
		$SnCl_4$ d)			f)	
		$TiCl_4+Ti(O.iPr)_4$ e)	20	12	70	(20/80)

a) Experimental procedure described in ref. 5

b) 3 is a diastereoisomeric mixture. Diastereoisomeric ratio $3\alpha/3\beta$ is determined by ^1H-NMR(6) and HPLC (silica gel Si-60, 25 cm, 15-25μ). 3α is assigned in all cases to the isomer with higher R_F and 3β to that with a lower R_F value.

c) Lewis acid added in catalytic amount ; $ZnBr_2$ to 1 was ≃ 0.05/1.

d) Ratio of $SnCl_4$ to 1 was 1/1.

e) The mixture forms a mixed ligand titanium compound $TiCl_2(O.iPr)_2$ by disproportionation(7). Ratio of MX_n to 1 was 1/1.

f) No reaction whatever experimental procedure.

References and footnotes.

1. C. Goasdoué, N. Goasdoué, M. Gaudemar, Tetrahedron Letters, 24, 4001 (1983) ; Tetrahedron Letters, 25, 537 (1984) ; J. Organomet. Chem., 263, 273 (1984).
2. For recent reviews see :
   a) T. Mukaiyama, Angew. Chem., Int. Ed. Engl., 16, 817 (1977).
   b) E. Colvin, Silicon in Organic Synthesis, Butterworths Ed., (1980).

3. a) I. Ojima, S. Inaba, K. Yoshida, Tetrahedron Lett., 3643 (1977).
   b) I. Ojima, S. Inaba, Tetrahedron Lett., 21, 2077 (1980) ; ibid, 21, 2081 (1980).
   c) J.F. Kerwin, S. Danishefsky, Tetrahedron Lett., 23, 3739 (1982).
4. J.E. Dubois, G. Axiotis, Tetrahedron Lett., 25, 2143 (1984).
5. General procedure :

To a stirred solution of aldimine (0.02 mol) in dry methylene chloride (10 ml) (under a N_2 atmosphere), cooled at -40°C, is added MXn (1 equivalent or in the ratio noted in table I). The mixture is then stirred for 15 mn at 0°C and then cooled at -40°C. A methylene chloride (10 ml) solution of 1 (0.02 mol)$^{(1)}$ is added dropwise to the solution and stirred for the time indicated in the table. After quenching with water at -80°C, desilylation is achieved with 1M HCl and then the aqueous phase neutralized with Na_2CO_3 or NaOH solution. After filtration of inorganic salts, 3 is extracted with CH_2Cl_2. The organic extracts are combined, dried over $MgSO_4$ and concentrated in vacuo. The purification of the oil is achieved by HPLC.

6. $C_6H_5\overset{3}{C}H(NHC_6H_5)\overset{2}{C}H(\overset{4}{C}H_3)\overset{1}{C}SNMe_2$

HPLC : ether/petroleum ether (50/50)

3α mp = 163°C   3β oil

3α RMN ^1H (250 MHz, $CDCl_3$, δppm, ref. TMS) : 7.5 to 6.45 (10H) ; 4.60 (1H, d, ^3J = 5.3 Hz); 3.64 (1H, m) ; 3.30 and 2.62 (6H, s, s) ; 1.46 (3H, d).

RMN ^{13}C (20.13 MHz, $CDCl_3$, δppm, ref. TMS) : 206.1 (C_1) ; 148.0 to 114.0 (aromatic ring C) ; 61.7 (C_3) ; 48.5 (C_2) ; 44.8 and 41.1 ($N(CH_3)_2$) ; 170 (C_4).

3β RMN ^1H : 7.5 to 6.45 (10H) ; 4.53 (1H, d, ^3J = 5.6 Hz) ; 3.45 (1H, m) ; 3.36 and 3.22 (6H, s, s) ; 1.34 (3H, d).

RMN ^{13}C : 204.4 (C_1) ; 142.4 to 113.4 (aromatic ring C) ; 62.7 (C_3) ; 47.0 (C_2) ; 44.8 and 41.1 ($N(CH_3)_2$) ; 20.6 (C_4).

$C_6H_5\overset{3}{C}H(NH\overset{5}{C}H_2C_6H_5)\overset{2}{C}H(\overset{4}{C}H_3)\overset{1}{C}SNMe_2$

HPLC : CH_2Cl_2, CH_3COOEt (70/30)

3α mp = 78°C   3β oil

3α RMN ^1H : 7.5 to 7.1 (10H) ; 4.03 (1H, d, ^3J = 6.9 Hz) ; 3.63 and 3.48 (2H, d, d (AB), ^2J = 13.2 Hz) ; 3.35 (1H, m) ; 3.25 and 2.96 (6H, s, s) 1.39 (3H, d).

RMN ^{13}C : 207.1 (C_1) ; 142.1 to 126.8 (aromatic ring C) ; 66.6 (C_3) ; 51.7 (C_5) ; 49.1 (C_2) ; 44.5 and 41.1 ($N(CH_3)_2$) ; 17.2 (C_4).

3β RMN ^1H : 7.5 to 7.0 (10H) ; 4.15 (1H, d, ^3J = 9.2 Hz) ; 3.50 and 3.36 (6H, s, s) ; 3.43 (2H, s) ; 3.25 (1H, m) ; 0.89 (3H, d).

RMN ^{13}C : 207.2 (C_1) ; 141.1 to 126.7 (aromatic ring C) ; 68.8 (C_3) ; 51.7 (C_5) ; 49.8 (C_2) ; 44.9 and 41.4 ($N(CH_3)_2$) ; 18.8 (C_4).

$C_6H_5\overset{3}{C}H(NHC_6H_5)\overset{2}{C}H(\overset{4}{C}H(\overset{5}{C}H_3)_2)\overset{1}{C}SNMe_2$

HPLC : CH_2Cl_2, petroleum ether (80/20)

3α mp = 178°C 3β mp = 205°C

3α RMN ^1H : 7.5 to 6.4 (10H) ; 4.75 (1H, d, ^3J = 4.3 Hz) ; 3.08 (1H, d x d) ; 3.22 and 2.52 (6H, s, s) ; 2.77 (1H, m) ; 1.12 and 0.86 (6H, d, d).

RMN ^{13}C : 203.7 (C_1) ; 146.8 to 112.8 (aromatic ring C) ; 60.1 (C_2) ; 57.5 (C_3) ; 44.5 and 41.3 ($N(CH_3)_2$) ; 32.2 (C_4) ; 21.7 and 20.1 (C_5 x 2).

3β RMN ^1H : 7.5 to 6.4 (10H) ; 4.87 (1H, d, ^3J = 7.9 Hz) ; 3.41 (1H, d x d) ; 3.24 and 3.11 (6H, s, s) ; 2.55 (1H, m) ; 1.12 and 1.01 (6H, d, d).

RMN ^{13}C : 204.1 (C_1) ; 147.2 to 114.2 (aromatic ring C) ; 6.16 (C_3) ; 59.2 (C_2) ; 44.5 and 41.7 ($N(CH_3)_2$) ; 31.5 (C_4) ; 20.9 and 20.1 (C_5 x 2).

7. C. Dijkgraaf, J.P.G. Rousseau, Spectrochim. Acta, A, 24, 1213 (1968).

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