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Synthesis of Dimethylsilyl Bis-Enol Ethers Derived from Aldehydes

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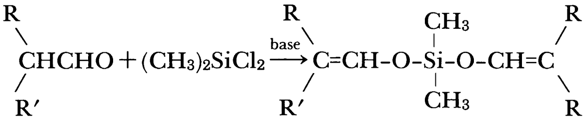
Two procedures for the prepation of dimethylsilyl bis-enol ethers from aldehydes, through enolization, are described. Dimethylsilyl bis-enol ethers, derived from propanal, butanal, 2-methylpropanal, pentanal, hexanal, and heptanal have been synthesized by refluxihg a mixture of triethylamine, dichlorodimethylsilane and the corresponding aldehyde in tetrahydrofuran for 18—38 h. The yields are in the range of 75—90%. Alternatively, a stronger base, lithium 2,2,6,6-tetramethylpiperidide (LiTMP) is used for deprotonation of the above mentioned aldehydes at −23 °C. The enolates are then quenched with dichlorodimethylsilane. The small aldehydes, propanal, butanal, and 2-methylpropanal fail to give the desired products, while the others gave a very good yields (56—85%). Ethanal fails to give the product in either of the two procedures. A competitive rate of polymerization with the rate of proton abstraction or with the rate of mixing of the reactants could explain these failures. The silyl bis-enol ethers have been characterized on the basis of their NMR, IR, and elemental analysis data.

Trimethylsilyl enol ethers were originally introduced as precursors for specific enolates[1,2] and much of their chemistry is like that of enol. Their usefulness surpasses that of all other derivatives,[3] because of their ease of preparation, clean reactions, and the mildness of desilylation processes: They also combine a reasonable reactivity with a high selectivity. Silyl enol ethers' reactions have been widely used as part of synthetic routes to natural products and other complex molecules[4] as well as simple coupling reactions.[5–7] Silyl enol ethers as synthetic reagents have been noted in the regeneration of enolates to react with electrophiles under basic conditions or direct reaction with electrophiles under neutral or acidic (Lewis acid) conditions. Although a great deal of attention has been paid to silyl enol ethers[4,8] derived from ketones and esters (silyl ketene acetals) very limited reports mentioned indirectly the silyl enol ethers derived from aldehydes.[8–10] The reason behind this ignorance of aldehydes is a theoretical problem. These reactions cannot be utilized with the enolates of reactive aldehydes, due to facile base-catalyzed polymerization of the starting material and/or product.[11] For this reason, various indirect methods have been developed for the alkylation of aldehydes, e.g., enamines[12] and imine anions.[13]

In earlier study[14] the preparation and characterization of some dimethylsilyl bis-enol ethers derived from ketones have been reported. The aim of the present work is to synthesize dimethylsilyl bis-enol ethers derived from aldehydes, in which two reactive aldehyde enolates are trapped in the same molecule as shown by Eq. 1. In this paper the preparation methods that we employed and the characterization of various dimethylsilyl bis-enol ethers derived from some aldehydes are described.



$$\mathrm{RR'CHCHO} + (\mathrm{CH_3})_2\mathrm{SiCl_2} \xrightarrow{\text{base}} \mathrm{RR'C{=}CH{-}O{-}Si(CH_3)_2{-}O{-}CH{=}CRR'} \qquad (1)$$

Results and Discussion

The first preparative method employed for dimethylsilyl bis-enol ethers derived from aldehydes involves preliminary treatment of a solution of LiTMP in tetrahydrofuran, generated from tetramethylpiperidine and butyllithium at 0 °C under nitrogen, with aldehydes to convert them completely into their enolate anions. Subsequent reaction of the enolate anions with dichlorodimethylsilane has produced the dimethylsilyl bis-enol ethers. Unfortunately the yields are low compared to yields in case of ketones. A better yield was obtained when the reaction temperature is changed to −23 °C instead of 0 °C and the aldehyde to dichlorodimethylsilane ratio is increased to 2 : 1. The results are summarized in Table 1. The small aldehydes fail to give the desired product. Dilution of these small aldehydes with tetrahydrofuran and then addition slowly to the base (LiTMP) do not produce any product either. It seees that in case of small aldehydes a competitive rate of aldol condensation and polymerization with the rate of proton abstraction or with the rate of mixing of the reactants. As the aldehydes get larger, the aldol condensation or polymerization is slowed down to such a degree that dimethylsilyl bis-enol ethers predominate.

In an effort to produce products with the small aldehydes we examined an alternative method in which the quenching reagent, dichloromethylsilane, is added before enolate formation. In this case triethylamine as a base in tetrahydrofuran was the reagent of choice. The silyl bis-enol ethers were prepared by refluxing the mixture of the aldehyde, dichlorodimethylsilane, and three fold excess triethylamine in tetrahydrofuran for 18—38 h. The yields are in the range of 75—90%. In this way the preparation of dimethylsilyl bis-enol ethers (**1**—**6**) were accomplished regardless the size of the aldehyde. Evidently, in this case, the rate of the reaction of aldehyde enolates with dichlorodimethylsilane is faster than the

Table 1. Characterization and Properties of the Products (**1**—**6**)

Entry	Product R	Product R′	Preparative method[a] (reaction time/h) yield[b]/%	$\bar{\nu}_{C=C}$ (CCl$_4$) cm^{-1}	NMR spectrum δ (CDCl$_3$) vinyl[c] CH	(*Z* of *E*)
1	CH_3	H	B (18) 90	1660	4.60 (d of q, *J*=6 and 6.8)	*Z*
					5.07 (d of q, *J*=12 and 6.8)	*E*
2	CH_3CH_2	H	B (24) 84	1665	4.55 (d of t, *J*=5.9 and 7.1)	*Z*
					5.16 (d of t, *J*=12.1 and 7.1)	*E*
3	CH_3	CH_3	B (38) 77	1680	—	
4	$CH_3(CH_2)_2$	H	A (24) 56	1655	4.54 (d of t, *J*=6.2 and 7.2)	*Z*
			B (24) 82		5.06 (d of t, *J*=12.1 and 7.2)	*E*
5	$CH_3(CH_2)_3$	H	A (24) 85	1650	4.58 (d of t, *J*=5.9 and 7.2)	*Z*
			B (30) 75		—	
6	$CH_3(CH_2)_4$	H	A (24) 83	1655	4.54 (d of t, *J*=5.9 and 7.3)	*Z*
			B (30) 79		—	

a) In procedure A, the enolate, formed by initial reaction of the aldehyde with LiTMP in THF, was quenched with $(CH_3)_2SiCl_2$. In procedure B, the aldehyde was refluxed with a mixture of Et_3N and $(CH_3)_2SiCl_2$. b) GC yields. c) The aldehydic vinyl protons are shown in the experimental section.

rate of polymerization. Ethanal, however, fails to give product in either of the two methods. This result is not unexpected since it is reported[1)] that the indirect methods of enolization of aldehydes have never been successfully extended to the alkylation of ethanal, the simplest carbonyl compound having α-hydrogens.

It is interesting to note that the time required for synthesis of dimethylsilyl bis-enol ethers derived from aldehydes (1—2 days) is much shorter than the time required for the synthesis of dimethylsilyl bis-enol ethers derived from ketones (2—20 days).[14)] We believe that the reason behind this is the fact that aldehyde enolates are more reactive than ketone enolates.

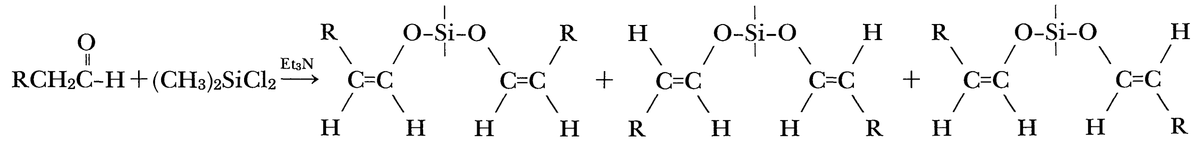
The dimethylsilyl bis-enol ethers derived from propanal, butanal, pentanal, and heptanal show geometrical isomers (Eq. 2). NMR analysis for the vinylic protons shows the predominance of *Z*-protons in these derivatives under thermodynamic conditions (triethylamine method). Under kinetic conditons, the NMR analysis for the vinylic protons of pentanal derivative showed the predominance of the *E*-protons which is in agreement with literature reports[14,15)] of ketone enolates under similar conditions.

Experimental

All boiling points are uncorrected. The infrared spectra were determined with a Pye-Unican SP3-100 spectrophotometer. The NMR spectra were determined at Bruker WP 80 EY spectrometer. Vapor phase chromatographic analysis and preparative work were carried out on a Varian Aerograph 1400 thermal conductivity chromatogram. The microanalysis were performed by M-H-W Laboratories, Phoenix AZ.

Commercial samples of aldehyses were purified by redistillation and stored over molecular sieve. Triethylamine and tetrahydrofuran were distilled from $LiAlH_4$ and stored under nitrogen over molecular sieve. Dichlorodimethylsilane was distilled prior to use. Commerical 2,2,6,6-tetramethylpiperidine and a solution of butyllithium were used without further purification.

Illustrative Procedures for the Preparation of the Dimethylsilyl Bis-Enol Ethers. Procedure A. A 250 ml round bottom flask equipped with a magnetic stir bar, septum and a reflux condenser fitted with a calcium chloride tube was flame dried while a stream of nitrogen gas was flowing through the system. 80 ml of tetrahydrofuran was introduced followed by 80 mmol (5.77 ml) of propanal, three fold excess of triethylamine (240 mmol) and 40 mmol (4.8 ml) of dichlorodimethylsilane. The resulting mixture was



(2)

refluxed and followed by GLC analysis (2.5% SE-30, 1/8 in×5ft column). After two hours a peak different from starting materials was noticed. Then the reaction was refluxed for 18 h. The reaction mixture was cooled, diluted with petroleum ether (40—60 °C) and washed with cold saturated solution of sodium hydrogen carbonate. The organic layer was separated and dried over anhydrous sodium carbonate. Then the solvent was removed by simple distillation and residue was vacuum distilled or chromatographed using 40 cm×2 cm column packed with 60/120 mesh silica gel and petroleum ether (40—60 °C). A sample for analysis was prepped from a GLC column (2.5% SE-30, 1/4 in×3 ft, 1 in=2.54 cm, 1 ft=30.48 cm).

Procedure B. A 50 ml flask equipped with a magnetic stir bar, septum, gas inlet valve and mercury bubbler, was flame dried under nitrogen. A 5.0 ml (8 mmol) of butyllithium (1.6 M, 15% in hexane, M=mol dm^{-3}) was added to the flask. The flask was immersed in an ice bath and 1.34 ml (8 mmol) of 2,2,6,6-tetramethylpiperidine was added dropwise over 2 min. Following the addition, the viscous mixture was stirred for an additional 10 min, after which the hexane was removed under reduced pressure at 0 °C. The flask was refilled with nitrogen and the residual white solid was redissolved in sufficient dry THF at 0 °C to give approximately 1 M solution. When dissolution was complete, the ice bath was replaced by CCl_4/liq N_2(−23 °C) bath. The reaction mixture was stirred for 10 min, and then 0.98 ml (8 mmol) of hexanal was added dropwise over 3 min. The mixture was stirred for 20 min, then quenched with 0.24 ml (2 mmol) of dichlorodimethylsilane all added at once at −23 °C. The reaction mixture was removed from the bath and to room temperature with stirring. An internal standard $C_{16}H_{34}$ (2 mmol) was added. The highest yield (85%) was obtained after 24 h of stirring at room temperature.

Dimethylsilyl Bis-Enol Ether Derived from Propanal (1): Bp 23 °C (2 mmHg, 1 mmHg=133.322 Pa); density=0.896 g cm^{-3}; NMR ($CDCl_3$) δ=0.26 (s, 6H), 1.55 (m, 6H), 4.60, 5.07 (two multiplets 70:30, 2H), 6.24 (m, 2H); IR(CCl_4) 3040, 2960, 1660, 1450, 1065, 875, and 815 cm^{-1}. Calcd for $C_8H_{16}O_2Si$: C, 55.76; H, 9.36%. Found: C, 55.87; H, 9.27%.

Dimethylsilyl Bis-Enol Ether Derived from Butanal (2): Bp 30—32 °C (0.7 mmHg), density=0.865 g cm^{-3}, NMR ($CDCl_3$) δ=0.25 (s, 6H), 0.96 (t, 6H), 2.11 (m, 4H), 4.55, 5.16 (two multiplets 80:20, 2H) 6.18 (m, 2H); IR(CCl_4) 3020, 2960, 1655, 1450, 1260, 1070, 850, and 810 cm^{-1}. Calcd for $C_{10}H_{20}O_2Si$: C, 59.95%; H, 10.06%. Found: C, 60.09; H, 9.93%.

Dimethylsilyl Bis-Enol Ether Derived from 2-Methylpropanal (3): Bp 34—36 °C (0.6 mmHg), density=0.865 g cm^{-3}, NMR ($CDCl_3$) δ=0.22 (s, 6H), 1.56 (d, 6H), 1.61 (d, 6H), 6.09 (m, 2H); IR (CCl_4) 2960, 1680, 1450, 1260, 1070, 890, and 800 cm^{-1}. Calcd for $C_{10}H_{20}O_2Si$: C, 59.95; H, 10.06%, Found: C, 60.15; H, 10.09%.

Dimethylsilyl Bis-Enol Ether Derived from Pentanal (4): Bp 48.51 °C (0.6 mmHg), density=0.861 g cm^{-3}, NMR ($CDCl_3$) δ=0.24 (s, 6H), 0.95 (t, 6H), 1.41 (m, 4H), 2.02 (m, 4H), 4.54, 5.06 (two multiplets 76:24, 2H), 6.25 (m, 2H); IR (CCl_4) 2960, 1655, 1450, 1260, 1050, 860, and 810 cm^{-1}. Calcd for $C_{12}H_{24}O_2Si$: C, C, 63.10; H, 10.59% Found: C, 62.91; H, 10.31%.

Dimethylsilyl Bis-Enol Ether Derived from Hexanal (5): Bp 58—60 °C (0.6 mmHg), density=0.893 g cm^{-3}, NMR ($CDCl_3$) δ=0.25 (s, 6H), 0.90 (t, 6H), 1.31 (m, 8H), 2.10 (m, 4H), 4.58 (m, 2H), 6.24 (m, 2H); IR (CCl_4) 2960, 1650, 1455, 1260, 1070, 865, and 810 cm^{-1}. Calcd for $C_{14}H_{28}O_2Si$: C, 65.56; H, 11.00%. Found: C, 65.44; H, 10.86%.

Dimethylsilyl Bis-Enol Ether Derived from Heptanal (6): Bp 68.73 °C (0.6 mmHg), density=1.104 g cm^{-3}, NMR ($CDCl_3$) δ=0.24 (s, 6H), 0.88 (t, 6H), 1.30 (m, 12H), 2.08 (m, 4H), 4.54 (m, 2H), 6.22 (m, 2H); IR (CCl_4) 3025, 2950, 1655, 1260, 1080, 865, and 810 cm^{-1}. Calcd for $C_{16}H_{32}O_2Si$: C, 67.54; H, 11.34%. Found: C, 67.38; H, 11.09%.

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