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INEPT-^{29}Si NMR STUDY OF A $TiCl_4$-MEDIATED REACTION OF AN ENOL SILYL ETHER

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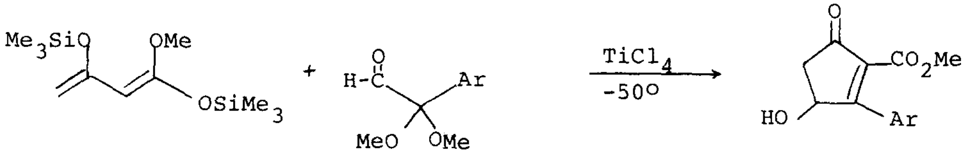
Abstract: Condensation of 1,3-bis(trimethylsiloxy)-1-methoxybutadiene (1) and 2-phenyl-2,2-dimethoxyethanal (2) under $TiCl_4$ condition gave the γ-hydroxycyclopentenone product 3. The reaction was followed by INEPT-^{29}Si NMR. Implication to the mechanism of the reaction was discussed.

Ever since the first report by Mukaiyama[1], the $TiCl_4$-mediated condensation of an enol silyl ether with a carbonyl electrophile to give the cross-aldol product has been used extensively in synthesis[2,3]. However, there is very little understanding of how this reaction occurs. Various suggestions have been made in the literature. These range from the formation of enol titanate[4], to a coordination of Ti(IV) with both the enol silyl ether and the carbonyl electrophile in a cyclic transition state[2,5], to the suggestion of an acyclic transition state without any intimate involvement between the enol silyl ether and the Lewis acid[6]. Attempts to examine the reaction mixture by ^{1}H nmr has been hampered by the complexity of the ^{1}H nmr encountered in this type of reaction involving several components. In principle, ^{29}Si nmr can provide a simple probe to study the reaction. However, because of the negative gyromagnetic ratio of ^{29}Si, normal acquisition of ^{29}Si nmr signal is time consuming and cannot be used to follow a reaction which may be completed in minutes. The recently introduced INEPT pulse sequence[7] allows the easy determination of ^{29}Si signal, especially for trimethylsilyl group where polarisation transfer from the hydrogen is particularly effective. We wish to report here the first ^{29}Si nmr study of a reaction between an enol silyl ether and a carbonyl component.

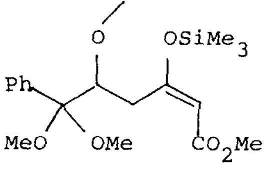
1,3-Bis(trimethylsiloxy)-1-methoxybutadiene(1)[8] was found to condense with 2-phenyl-2,2-dimethoxyethanal (2) and 3 moles of $TiCl_4$ to give the γ-hydroxycyclopentenone product **3**[9]. Similarly, compound **3** (Ar=p-methylphenyl) was obtained when 2-p-methylphenyl-2,2-dimethoxyethanal (**2**, Ar=p-CH_3-C_6H_4-) was used[9].



1 **2** **3**

In order to clarify this cyclization reaction, ^{29}Si-nmr using the INEPT pulse sequence was used (Fig. 1). Data accumulation of only seven minutes were required for each of the six spectra taken. The reaction was performed at -50° in an nmr tube by adding 0.5 mole of $TiCl_4$. After the third spectrum was taken, another 2.5 moles of $TiCl_4$ was added, and a further three spectra were taken. There was no change in the nmr following the acquisition of the sixth spectrum. The reaction was worked-up in a fashion similar to the preparative experiments to confirm the formation of the product **3**.

Several conclusions can be drawn from the ^{29}Si nmr experiment. Before $TiCl_4$ was added, the two signals observed at 16.2 and 21.8 ppm could be clearly assigned to the two siloxy groups in **1**[10]. With the addition of $TiCl_4$, the ^{29}Si chemical shifts of **1** remained little changed. This rules out a fast formation of enol titanate. It also suggests that if there were coordination between $TiCl_4$ and the siloxy groups, it was probably not strong enough to modify significantly the chemical shifts of the ^{29}Si nmr. With time, two new Si-containing species were formed. The one at 31.6 ppm was definitely assigned to trimethylchlorosilane. The remaining one at 26.1 ppm was an intermediate whose relative intensity increased first as more $TiCl_4$ was added and then diminished. At the end of reaction, trimethylchlorosilane was the only silicon-containing species in the reaction mixture. We assigned the 26.1 ppm to the siloxy group of structure **4**. The downfield shift of the siloxy group in **4** is consistent with the deshielding effect of the presence of an electron-withdrawing group at the γ-carbon. By comparison, the chemical shift of the siloxy group in **5** was found to be at 20.1 (for the E isomer) or 19.9 (for the Z isomer), but at 23.6 ppm for the siloxy group in **6**. The formation of the



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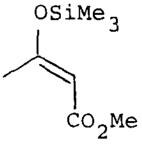

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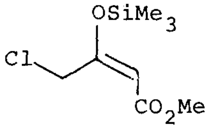

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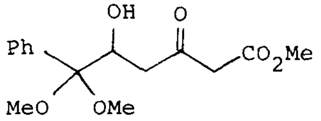
intermediate 4 was further supported by quenching experiment before the additional 2.5 moles $TiCl_4$ was added. It was possible to isolate the compound 7 after basic aqueous work-up. Compound 7 was clearly derived from the hydrolysis of 4[9].



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While it is premature to generalize conclusions drawn from this experiment to other Lewis acid-mediated reactions of enol silyl ethers, it is clear that ^{29}Si-nmr can provide a simple and direct probe of such reactions.

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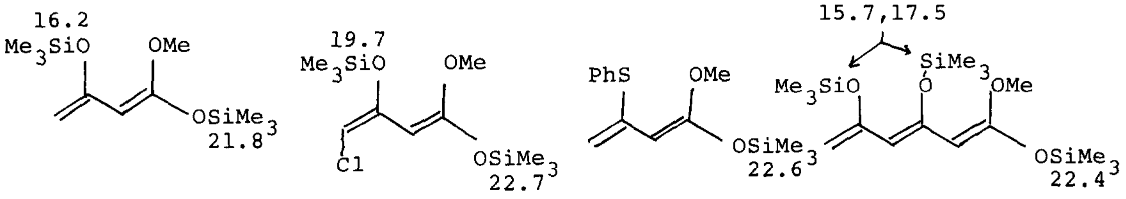
References

(1) T. Mukaiyama, K. Banno and K. Narasaka, J. Amer. Chem. Soc., 96, 7503 (1974).
(2) T. Mukaiyama, Angew. Chem. Int. Ed. Engl., 16, 877 (1977).
(3) P. Brownbridge, Synthesis, 1, (1983).
(4) (a) S. Inaba and I. Ojima, Tetrahedron Letters 2009 (1977).
(b) I.H.M. Wallace and T.H. Chan, Tetrahedron 39, 847 (1983).
(5) T.H. Chan, T. Aida, P.W.K. Lau, V. Gorys and D.N. Harpp, Tetrahedron Letters, 4029 (1979).
(6) C.H. Heathcock, K.T. Hug and L.A. Flippia, Tetrahedron Letters 25, 5973 (1984). See also J.-E. Dubois, G. Axiotis and E. Bertounesque, Tetrahedron Letters 25, 4655 (1984).
(7) G.A. Morris and R. Freeman, J. Amer. Chem. Soc., 101, 760 (1979); R.H. Helmer and R. West, Organomet., 1, 877 (1982).
(8) P. Brownbridge, T.H. Chan, M. Brook and G.J. Kang, Can. J. Chem. 61, 688 (1983).
(9) Experimental Conditions: Compound 2 (1.46 mmol) was dissolved in CH_2Cl_2 at -78° under argon atmosphere. To the solution, compound 1 (1.53 mmol) and then $TiCl_4$ (1.0 M solution in CH_2Cl_2, 5.0 ml) were added. The reaction was allowed to stir for 1 h at -78° and then warmed to 0° over 15 min. The mixture was quenched with a 5% aqueous bicarbonate solution and extracted with ether. The ether extract was washed with brine, dried ($MgSO_4$) and evaporated to give the crude product. Based on 'H nmr of the crude, yield of 3 was about 75-80%. Compound 3 can be purified by flash chromatography (16:2:1 hexane - EtOAc-Methanol) and the pure product was isolated in 40-50% yield. 'H nmr ($CDCl_3$) for 3a (Ar=Ph): δ = 2.59 (dd, 1H, J=2.3 Hz and 18.6 Hz), 3.04 (dd, 1H, J=5.9 Hz and 18.6 Hz), 3.64 (s, 1H), 3.79 (s, 3H), 5.45 (dd, 1H, J=2.3 Hz and 5.9 Hz), 7.7-7.8 (m, 5H); 3b (Ar=p-CH_3-C_6H_4-): 2.41 (s, 3H), 2.47 (dd, 1H, J=3.0 Hz and 18.0 Hz), 2.98 (dd, 1H, J=5.5 Hz and 18.0 Hz), 3.20 (s, 1H), 3.79 (s, 3H), 5.41 (dd, 1H, J=3.0 Hz and 5.5 Hz), 7.3-7.5 (AB, 4H). If only one mole of $TiCl_4$ was used in the reaction, compound 7 was isolated after work-up. 'H nmr for 7: 3.1-3.6 (m, 4H), 3.47 (s, 6H), 3.75 (s, 3H), 3.80 (s, 1H), 5.4-5.5 (m, 1H), 7.2-7.6 (m, 5H).
(10) The ^{29}Si nmr signals of 1 can be assigned by comparison of the following compounds:



^{29}Si NMR of some enol silyl ethers and their assignments (in ppm)

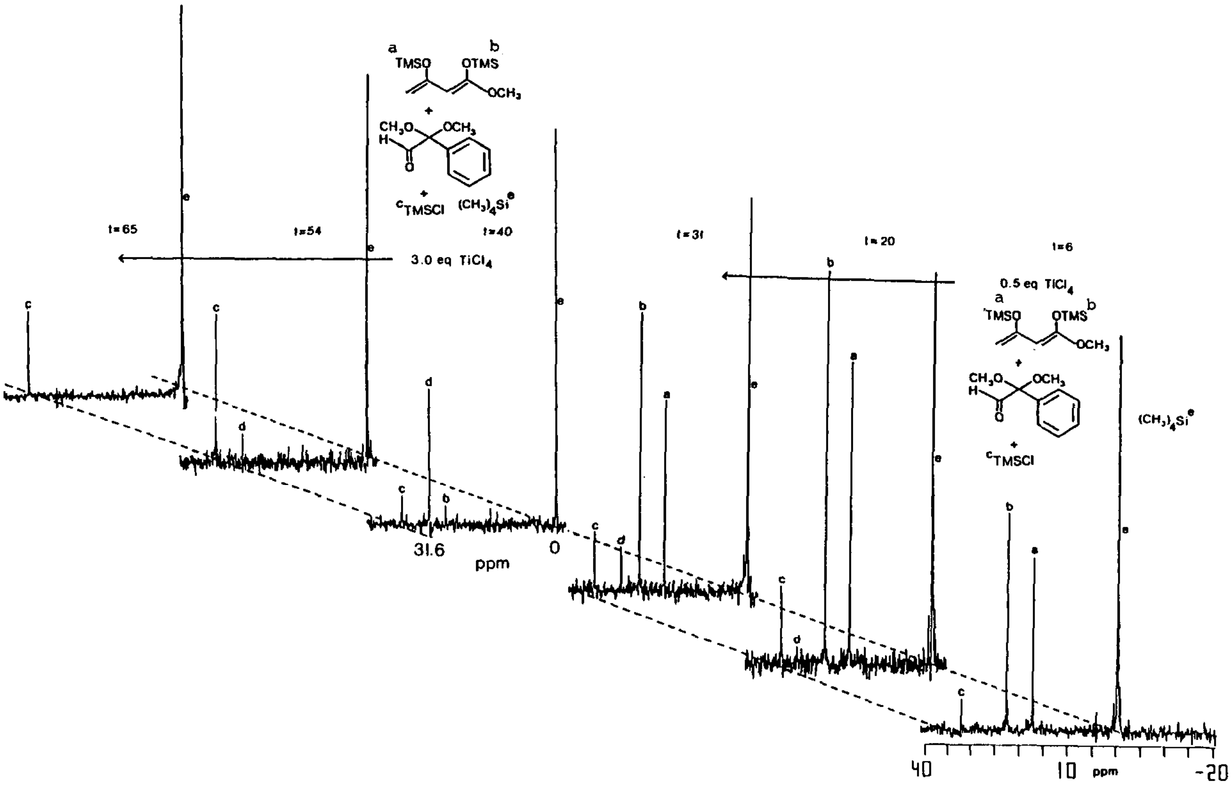


Figure 1: INEPT ^{29}Si NMR Spectra Following the Condensation Reaction

t refers to the time in minutes halfway through an aquisition.

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