Table II. Surface Coverages of Intermediates and Products

species	surf. residence time of C, s	$N_i^a \times 10^{-18}$	θ_i^b	intrinsic site TOF, s^{-1}
C_2H_6	3.1 ± 0.2^c	2.9 ± 0.2	0.29 ± 0.02	0.32 ± 0.09
CO_2	4.0	3.2	0.32	0.25
CO	2.4	1.4	0.14	0.42
CH_4	0.3	5.6	0.56	

^{a}Number of carbon atoms leading to products/gram of catalyst. ^{b}Based on an assumption of 1 × 10^{19} sites/g for the surface area of 1 m^2/g. ^{c}The error of ±0.2 s was determined from the average of three separate experiments. This relatively small error was made possible by a refinement in the data-acquisition technique, which increased the number of data points for each transient by an order of magnitude compared to those producing the results of Table I.

These results strongly suggest that surface carbonates are not involved significantly in this reaction on this catalyst. This contrasts with results for other catalyst systems such as Li/MgO and PbO/MgO[11,12] where the formation of surface carbonates was found to be important during the coupling of methane.

From the transients in Figure 1, the similarity in shape of the C_2H_6 and CO transients suggests that these product gases are formed via similar (parallel) surface reaction pathways. As seen in Table I, varying the catalyst bed length had no effect on these transients, indicating the lack of significant interaction of the product molecules with the catalyst surface.

The surface lifetimes cannot be attributed to adsorption/desorption of the product gases since the data in Table I indicates the lack of significant interaction of CO, CO_2, and C_2H_6 with the catalyst surface. Increasing the catalyst bed length had no effect on the holdup of the product gases, so readsorption of the product gases was not important. Thus, the surface lifetimes measured indicate the lifetime of formation of $\cdot CH_3/C_2H_6$, CO, and CO_2. Note that surface oxidation of C_2H_6 does not seem to be important under these conditions.

The commonly accepted mechanism for methane coupling assumes gas-phase coupling of surface-generated methyl radicals. In addition, there have been numerous suggestions made that CO and CO_2 may be produced primarily as a result of gas-phase oxidation of these methyl radicals. However, these isotopic transient results suggest that the role of the catalyst surface is more than just a methyl radical generator. Given that the product gases do not strongly interact with the surface under these conditions, if the catalyst surface served only to generate methyl radicals with subsequent reaction of these radicals in the gas phase, the surface lifetimes of all the intermediates leading to the formation of CO, CO_2, and C_2H_6 (as measured by the areas under the respective transients and taking into account experimental error) would be identical. As seen from the data presented, this is not the case under these reaction conditions.

However, nothing in these results led to a disagreement with the hypothesized role of methyl radicals in C_2H_6 production, nor can one rule out a significant role for homogeneous gas-phase oxidation at much higher reaction temperatures.

The surface concentration of reaction intermediates (N_i) can be calculated by integrating the transient curves after correcting each for the gas-phase holdup and applying the formula[13]

$$N_i = \text{(area)(rate of } CH_4 \text{ conversion)(product selectivity)}$$

Table II presents the results of the above calculation of surface concentrations and fractional surface coverages of intermediates leading to each product for the transients presented in Figure 1. The surface lifetimes presented in Table II are subject to a relatively small error of 0.2 s due to a refinement of the transient data acquisition technique, which increased the number of data points for each transient by an order of magnitude. In addition,

Figure 2. Proposed carbon reaction pathways for the oxidative coupling of methane over Sm_2O_3.

each transient is based on the average of three separate experiments.

On the order of 50% of the Sm_2O_3 working surface was involved in the formation of products. Of this 50%, approximately 3/5 was involved in CO_x formation, with the remaining 2/5 being active for C_2 formation. Since surface lifetime is inversely proportional to the intrinsic site TOF (turnover frequency), as can be seen in Table II, the sites active for C_2 formation had a lower activity than sites active for the formation of CO_x. The reason the calculated coverages total more than a monolayer is probably due to the number of assumptions made in arriving at these numbers.

Figure 2 summarizes the proposed carbon reaction pathways that are consistent with these findings. Dashed lines are used to indicate pathways that cannot be completely ruled out from this data.

In conclusion, it appears that the surface of a working Sm_2O_3 catalyst is much more than a methyl radical generator. It is active in the formation of CO, CO_2, and possibly even C_2H_6. Also, surface carbonates do not appear to be present in any large amount, and readsorption of the product gases is not important.

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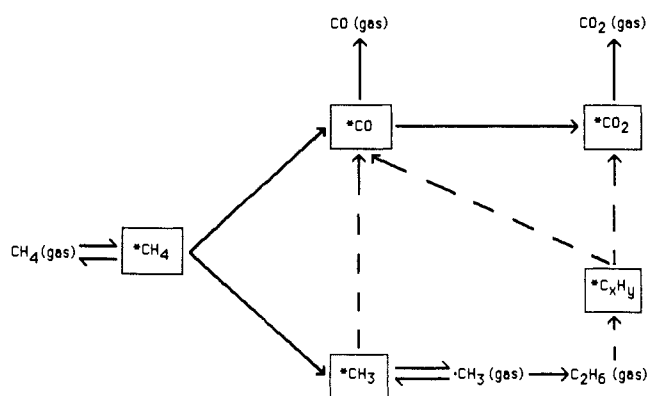
Are Chelates Truly Intermediates in Cram's Chelate Rule?

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In 1959, Cram and Kopecky[1] proposed that the steric outcome of additions of organometallic reagents to chiral α-alkoxy ketones rests on the ability of the reagent to chelate with the alkoxy substituent as well as the carbonyl oxygen. Reactions of this type are often highly stereoselective.[2-7] Recently, stable chelates

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Table I. Reactions between Ketones A and MgMe$_2$ (Eq 1)

			diastereomer composition	
ketone	R	rate constant k_2 ($\times 10^2$ M^{-1} s^{-1})[a]	found (B/C)[b]	calcd % B
A$_1$	OMe	~1000	>99/1	(100)
A$_2$	OSiMe$_3$	100 ± 30	99/1	99.7 ± 0.1
A$_3$	OSiEt$_3$	7.9 ± 1.0	96/4	96.7 ± 0.7
A$_4$	OSi(tBu)Me$_2$	2.5 ± 0.3	88/12	89 ± 2
A$_5$	OSi(tBu)Ph$_2$	0.82 ± 0.06	63/37	68 ± 5
A$_6$	OSi(iPr)$_3$	0.45 ± 0.04	42/58	(42)
A$_7$	H	0.54 ± 0.06		

[a] Measured at -70 °C in THF-d_8. [b] Measured at -78 °C in THF.

formed between alkoxy aldehydes and ketones and Lewis acids in CD$_2$Cl$_2$ were observed by static NMR spectra under equilibrium conditions.[8,9] In addition, Reetz has claimed direct evidence for a Cram chelate intermediate based upon ^{13}C NMR spectra recorded during the reaction of MeTiCl$_3$ with an α-alkoxy ketone.[10] However, it is not clear whether such chelates are kinetic intermediates in nucleophilic addition to alkoxy ketones or just products of a nonproductive equilibrium.[11] In 1987 the first kinetic evidence for a chelated transition state in reaction of α-alkoxy ketones with alkylmagnesium reagents was provided: the reaction of benzoxyacetone with dimethylmagnesium, as measured by rapid injection NMR at -70 °C, is 140 times faster than the corresponding reaction of [(triisopropylsilyl)oxy]acetone.[12] Rate enhancement of a ketone that can chelate versus one that cannot is a requirement of Cram's chelate rule:[1] If chelation is the cause of the high stereoselectivity observed in additions to alkoxy ketones, it must also be true that the chelated transition state provides a lower energy pathway to products than the less stereoselective reaction pathway not involving chelation which is available to all ketones. In this communication we now demonstrate that, indeed, alkoxy ketones that are highly stereoselective in reaction with dimethylmagnesium are also more reactive toward this reagent than similar nonstereoselective ketones.

The results of our investigation of the rates and products of addition of dimethylmagnesium[13,14] to propiophenone and various α-alkoxypropiophenones are shown in Table I. It is immediately obvious that addition of MgMe$_2$ to the most reactive α-methoxy ketone A$_1$ is much more stereoselective than addition to the least reactive (triisopropylsilyl)oxy ketone A$_6$, and that the stereoselectivity of the intermediate members of the series, (trimethylsilyl)oxy ketone A$_2$, (triethylsilyl)oxy ketone A$_3$, (*tert*-butyldimethylsilyl)oxy ketone A$_4$, and (*tert*-butyldiphenylsilyl)oxy ketone A$_5$, decreases with decreasing reactivity. The very large difference between the trimethylsilyl and triisopropylsilyl groups is remarkable, with the former one impeding chelation very little and the latter preventing it totally.[15-17]

A

1. R = OMe
3. R = OSiEt$_3$
5. R = OSitBuPh$_2$
7. R = H

B ("Cram Product") (RS/SR)

C (RR/SS)

2. R = OSiMe$_3$
4. R = OSitBuMe$_2$
6. R = OSi(iPr)$_3$

The data in Table I can be put on a quantitative basis, with the following simple hypothesis: Assume that the specific rate for traversing the unchelated transition state is that for A$_6$, k_u = 0.45 ± 0.04 × 10^{-2} M^{-1} s^{-1} (very similar to the specific rate for propiophenone, A$_7$ in Table I), and is constant for all members of the series. Further assume that the specific rate for traversing the chelated transition state is k_c = k_2 - k_u, k_2 being the total bimolecular rate constant. Morever, assume that the fraction of the reaction proceeding through the unchelated transition state gives B (the "Cram" product) and C in a ratio of 42:58, the actual ratio for A$_6$, and that the part of the reaction proceeding via the chelated transition state gives only B. The composition of the product may then be calculated as % B = 100(k_c + 0.42k_u)/k_2. The product composition so calculated is shown in the last column of Table I.[18] It is seen that except for ketone A$_2$, for which neither product composition nor rate can be determined with high accuracy, the calculated composition agrees with the experimental within the error of the rate determination. Thus a very simple hypothesis emerges: chelating ketones react via two competitive transition states, one chelated, the other not, with the former reaction being highly stereoselective and the latter very little so, such that stereoselectivity depends sensitively on what percentage of the reaction proceeds via the chelated transition state.[19]

In conclusion, formation of a chelate intermediate in additions of organometallic reagents to chiral α-alkoxy ketones on the one hand lowers the transition-state energy and thus increases the reaction rate and, on the other hand, restricts bond rotation and increases stereoselectivity. *The most reactive substrates are therefore the most selective!* The results here reported demonstrate directly that chelates are truly intermediates in the operation of Cram's chelate rule. Whether the cause for the variation in rates and product composition (Table I) is due to steric or electronic factors or both remains to be elucidated through further studies presently being undertaken, as does the relative importance of entropic vs enthalpic differences.

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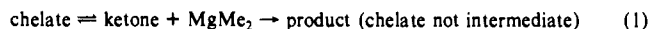
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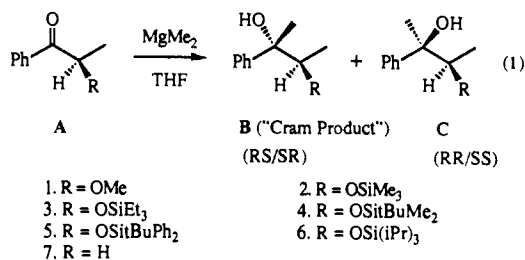
(11) Ashby has presented an excellent discussion of this problem (Laemmle, J.; Ashby, E. C.; Neumann, H. M. *J. Am. Chem. Soc.* **1971**, *93*, 5120). In the absence of appropriate kinetic studies, one cannot distinguish between the following alternatives (eq 1 or 2):

chelate ⇌ ketone + MgMe$_2$ → product (chelate not intermediate) (1)

ketone + MgMe$_2$ ⇌ chelate → product (chelate intermediate) (2)

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(14) House, H. O.; Oliver, J. E. *J. Org. Chem.* **1968**, *33*, 929.

(15) For another example of apparent chelation by OTMS, see: Reetz, M. T.; Hullmann, M. *J. Chem. Soc., Chem. Commun.* **1986**, 1600.

(16) The relative contributions to the steric and electronic effects of silicon substitution on the chelating ability of an ether oxygen are the subject of debate. For leading references, see: Shambayati, S.; Blake, J. F.; Wierschke, S. G.; Jorgenson, W. L.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 697. Stern, A. J.; Swenton, J. S. *J. Org. Chem.* **1989**, *54*, 2953.

(17) There is now considerable evidence that (*i*-Pr)$_3$SiO does not chelate; see ref 7 and the following: Bai, X. Ph.D. Dissertation, University of North Carolina, Chapel Hill, NC, 1990. The near-idential rate constants for propiophenone (Table I, entry A$_7$) and its α-triisopropylsiloxy analogue (A$_6$) provide additional evidence. α-Triisopropylsiloxy ketones do form simple complexes with MgBr$_2$ in CDCl$_3$: cf. footnote 12 in ref 12.

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(20) Katzenellenbogen, J. A.; Bowlus, S. B. *J. Org. Chem.* **1973**, *38*, 627.