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Homogeneous Catalysis. Use of the [TiCp2(CF3SO3)2] Catalyst for the Sakurai Reaction of Allylic Silanes with Orthoesters, Acetals, Ketals and Carbonyl Compounds.

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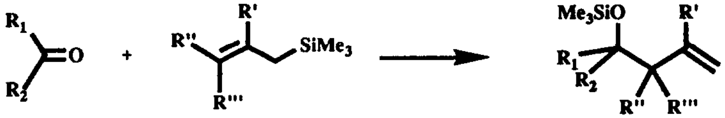
Key Words: Sakurai reaction, titanium based catalyst.

Abstract: *The effectiveness of the [TiCp$_2$(CF$_3$SO$_3$)$_2$] catalyst for the Sakurai reaction has been explored for a variety of allylic silanes reacting with orthoesters, acetals, ketals, aldehydes and ketones.*

The Sakurai reaction (eqs 1, 2) is promoted by a variety of Lewis acids[1-4] including $TiCl_4$, $AlCl_3$, BF_3, $SnCl_4$ and $ZnCl_2$. Generally, stoichiometric or greater amounts of these Lewis acids are required to obtain convenient rates for most electrophilis, and reactivity has only been demonstrated with allyltrimethylsilane. The Lewis acids, $Me_3SiO_3SCF_3$,[5] Me_3SiI,[6] Ph_3COClO_3[7] and $Ph_2BO_3SCF_3$,[7] on the other hand, are genuine catalysts which effect the Sakurai reaction at loadings of 5 to 10 mol%, but these catalysts have only been used for the reaction of allyltrimethylsilane with acetals and to a lesser extent ketals. Aside from trimethylorthoformate, orthoesters were generally found to be unreactive with any of the Lewis acids. Overall the promotion of Sakurai reaction has been limited by the necessity of employing stoichiometric amounts of the Lewis acid in order to encompass a wide range of substrates. Although a moderately successful boron based chiral catalyst has been reported[8] for a limited number of aldehydes, these types of Lewis acids are generally difficult to convert to chiral catalysts.



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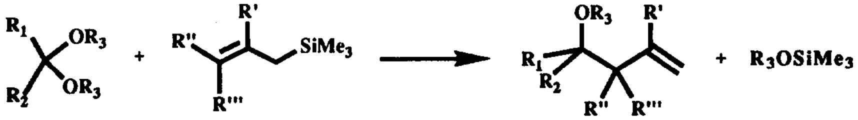


(2)

The purpose of this communication is to report on the effectiveness of the organometallic complex, [TiCp$_2$(CF$_3$SO$_3$)$_2$], for the Sakurai reaction. This catalyst is readily prepared in situ,[9] can alternatively be isolated as stable crystals,[10] can be modified into sterically well-defined chiral analogues,[11] and has proven effective at very low catalyst loading for a wider range of substrates than has hitherto been reported.

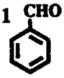
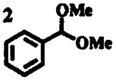
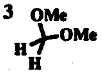
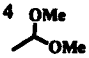
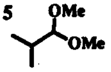
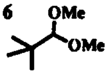
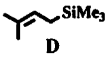
Some of the results are listed in Tables 1,2 and 3.[12] The reactions were carried out generally using 0.5 mol% catalyst at 25°C. In all cases but one, the reaction of **1** with **D**, ^1H NMR monitoring of the reactions established that only the expected product formed. Table 1 explores the effect of changing the allylic silane and the solvent for the reactions of benzaldehyde and a series of acetals. For aldehydes other than benzaldehyde the catalyst gave some of the expected product, accompanied by a variety of unidentified materials. Inspection of Table 1 indicates that the rate of reaction of the allylic silane is diminished by the presence of steric hinderance at the olefin terminus and that the more electron-rich olefin (**B**) reacts faster than the less electron-rich olefin (**A**). The catalysis occurs more slowly in dichloromethane than in nitromethane. Conductivity and ^{19}F NMR measurements[13] reveal that in nitromethane solutions the triflato ligands are extensively dissociated with a majority of the catalyst existing as the cationic mono-solvento species $[TiCp_2(CF_3SO_3)(CH_3NO_2)]^+$. No triflato dissociation is observed in dichloromethane solutions. In order to obtain catalysis, the oxygen atom of the electrophile has to bind to the titanium atom and, given the ability of nitromethante solvent to dissociate the triflato ligands, it is expected that the electrophiles will have a higher binding constant in nitromethane than in dichloromethane. Provided exchange is fast between substrate and catalyst as is observed for benzaldehyde[13] the higher binding constant will lead to a higher catalytic rate in nitromethane as observed. Assuming that the catalyst-electrophile adduct serves to activate the incipient carbocation toward attack by the allylic silane then the rate of catalysis will depend on the stability of the adduct, the stability of the incipient carbocation, the nucleophilicity of the allylic silane and the steric hinderance emanating from the two substrates. This variety of factors makes an analysis of the realtive rates difficult. Using the rates of acid hydrolysis as a guide[14] the order of electrophilicity should be $CH_2(OCH_3)_2 \ll RCH(OCH_3)_2 < R^1R^2C(OCH_3)_2 \lll RC(OCH_3)_3$. Thus the low rate observed for **3** parallels that observed for acid hydrolysis but because catalyst poisoning is observed it is not certain that this reaction is inherently slower. Silanes **A**, **B** and **C** initially react very quickly with **3** then the catalysis slows and even stops in some cases. None of the substrates alone cause poisoning; it arises during catalysis. In order to reach 90% reaction higher catalyst loadings were required. An interesting phenomenon is observed for electrophiles **4**, **5** and **6** reacting with silanes **A** and **B** in dichloromethane solution. With silane **A** the reaction becomes faster as the steric bulk of the acetal increases whereas the reverse is true for silane **B**. The diastereoselectivity of catalysis with silane **C** is generally high.

Table 2 contains the results for the reaction of a variety of ketones and ketals. Despite their faster acid hydrolysis rate the lower reactivity of ketals compared to acetals suggests that steric hinderance diminishes ketal reactivity in general relative to acetals. The low rate observed for **9** with **A** follows the relative acid hydrolysis rate but in this case there is also evidence of catalyst poisoning. Silane **A** does not react with ketones under the present conditions in contrast to the more electron-rich silane **B** which reacts well with both ketones and ketals in nitromethane solution, but is less effective in dichloromethane solution. Unlike the catalysis of acetals, silane **B** reacts faster with the more sterically hindered ketals in dichloromethane solution.

Table 3 presents the results obtained for the reaction of orthoesters. The least sterically hindered orthoester **13**, despite having the slowest acid hydrolysis rate, reacts much faster than other orthoesters. Neither silane **A** nor **B** reacts with acyclic orthoesters **14** and **16**. Cyclic orthoesters have greater rates of acid hydrolysis[15], and consistently, the more electron-rich silane **B** reacts with **15** and **17** to give the cyclic ketals.

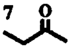
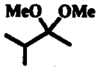
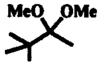
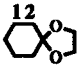
A consideration of the relative rates of catalysis of trimethyl orthoformate and of acetals allowed us to perform a clean sequential double allylation (eq 3).

Table 1 Catalytic Allylations of Aldehydes and Acetals Using 0.5mol% $[\mathrm{TiCp_2(CF_3SO_3)_2}]$ at 25°C.

		1 	2 	3 	4 	5 	6 
Silane	**Solvent**	**Time in minutes for 90% conversion^{a}**					
 A	CD_3NO_3	<5	<5	1100^{b}	<5	<5	<5
	CD_2Cl_2	[60% 68 hr]	28	[50% 70 hr]	2200	240	140
 B	CD_3NO_3	<5	<5	<5	<5	<5	<5
	CD_2Cl_2	<5	<5	500	13	100	670
 C	CD_3NO_3	40 (70:30)	<5 (80:20)	[70% 400 min]	6 (77:23)	19 (80:20)	23 (92:8)
 D	CD_3NO_3	[30% 45 hr]^{d,f}	570	[80% 250 min]^{e}	150	[30% 17 hr]^{f}	NR

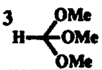
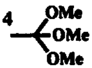
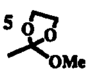
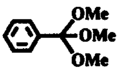
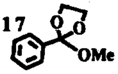
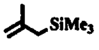
a. Diastereomeric ratio of the products are listed in parentheses under the conversion time where appropriate; unambiguous assignment of stereochemistry was not possible. Results listed in brackets represent maximum extent of reaction. NR=no reaction b. 1.5 mol% catalyst. At 0.5 mol% catalyst reaction stopped at 90% conversion. c. Silane was a 9:1 E:Z mixture. d. Unidentifiable side products also observed. e. 1.5 mol% catalyst. f. 1.5 mol% catalyst did not improve the yield.

Table 2 Catalytic Allylations of Ketones and Ketals Using 0.5mol% $[\mathrm{TiCp_2(CF_3SO_3)_2}]$ at 25°C.

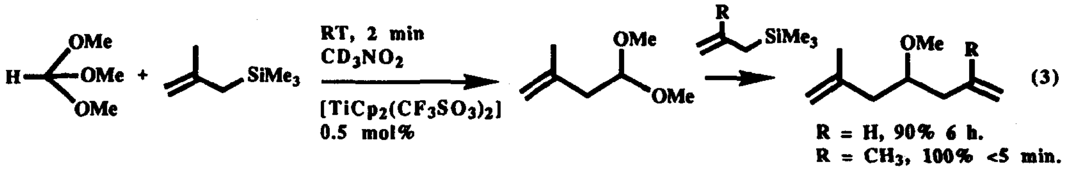
		7 	8 	9 	10 	11 	12 
Silane	**Solvent**	**Time in minutes for 90% conversion^{a}**					
 A	CD_3NO_3	NR	NR	1800^{b}	54	17	50
 B	CD_3NO_3	100	280	<5	<5	<5	<5
	CD_2Cl_2	NR	[35% 70 hr]	80	21	<5	1200

a. Results listed in brackets represent maximum extent of reaction. NR=No Reaction. b. 1 mol% catalyst was used. At 0.5 mol% catalyst the reaction reached only 50% in 45 hr.

Table 3 Catalytic Allylations of Orthoesters Using 0.5mol% $[\mathrm{TiCp_2(CF_3SO_3)_2}]$ at 25°C.

		13 	14 	15 	16 	17 
Silane	**Solvent**	**Time in minutes for 90% conversion^{a}**				
 A	CD_3NO_3	120^{b}	NR	NR	NR	NR
 B	CD_3NO_3	<5	NR	27	NR	60

a. NR=No Reaction. b. Both mono-allylated and di-allylated products obtained in a ratio of 1:1.



Overall the $[TiCp_2(CF_3SO_3)_2]$ catalyst is, in a number of respects, the most effective catalyst for the Sakurai reaction yet reported. It encompasses a wider range of substrates using very low catalyst loadings.

Acknowledgement. This work was supported by grants from the National Institutes of Health.

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9. **Typical in situ Preparative Procedure.** $AgCF_3SO_3$ (20.0 mg, 0.078 mmol) in CH_3NO_2 (2 mL) was injected under Argon into a solution of $[TiCp_2Cl_2]$ (9.5 mg, 0.039 mmol) in CH_3NO_2 (1 mL). The bright red mixture was stirred at 25°C in the dark for one hour, filtered through a fine frit under Argon and washed with CH_3NO_2 (1 mL). Trimethyl orthoformate (0.93 g, 7.8 mmol) was added, followed immediately by 2-methylallyltrimethylsilane (2.05 mL, 7.8 mmol) and the solution was stirred for 15 minutes. The solution was passed through a plug of florosil, and the solvent removed in vacuo. The spectroscopically pure product, 2-methyl-4,4-dimethoxybutene (0.74 g, 65%) was obtained as an oil. **Typical Catalytic Procedure.** The catalyst, $[TiCp_2(CF_3SO_3)_2]$ (1.4 mg, 0.0029 mmol), was weighed into an NMR tube under Argon. Dry CD_3NO_2 (400 µL) was injected. To the red/orange solution were added 3,3-dimethyl-2-butanone dimethyl ketal (95 µL, 0.58 mmol) and allyltrimethylsilane (93 µL, reaction was monitored by ^{1}H NMR integration of the product signals compared with the substrate signals.
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