Supplementary Material Available: Tables of atomic coordinates, thermal parameters, and bond distances and angles for $[Li(tmed)][Hf(C_2H_4)Et_4]$; $^{31}P\{^1H\}$ and $^{13}C\{^1H\}$ NMR spectra for **2** and **3** (9 pages); table of final observed and calculated structure factors (10 pages). Ordering information is given on any current masthead page.

Rhodium-Catalyzed Silylformylation of Aldehydes: A Mild and Efficient Catalytic Route to α-Silyloxyaldehydes

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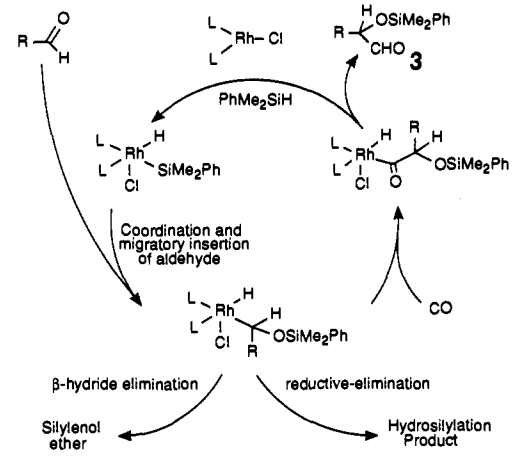
Hydroformylation is a widely used and well understood process catalyzed by a variety of transition metals.[1] The process incorporates an inexpensive source of carbon (i.e., carbon monoxide) and produces the aldehyde functionality, which is one of the most versatile and reactive functional groups in organic chemistry.[2] A variety of alkenes will undergo hydroformylation; however, carbon–oxygen double bonds (e.g., aldehyde) produce a formate ester and *not* the desired α-hydroxyaldehyde.[3] Murai and co-workers[4] in 1979 reported that treatment of aliphatic aldehydes (3-fold excess) with diethylmethylsilane and carbon monoxide (50 kg/cm^2) in the presence of $Co_2(CO)_8/PPh_3$ (100 °C, benzene) afforded α-silyloxyaldehydes in moderate yield.[4] More recently, Ojima and co-workers[5] and Matsuda and co-workers[6] independently reported the transition-metal-catalyzed "silylformylation" of alkynes.[7]

As part of our ongoing research effort to develop new chiral ligands and new reactions catalyzed by rhodium(I),[8] we have discovered that $[(COD)RhCl]_2$ is a very effective catalyst for the silylformylation of aldehydes. The rhodium(I)-catalyzed silylformylation of aldehydes appears very general, affords high yields of the α-silyloxyaldehydes, and does not require the use of excess aldehyde.

Scheme I



Initially our studies focused on the use of diphenylsilane, which is commonly used in rhodium(I)-catalyzed hydrosilylations.[9] Although at early stages in the reaction we could detect a new aldehyde group, at the completion of the reaction no α-silyloxyaldehyde could be isolated. We soon realized that an intramolecular hydrosilylation occurs after silylformylation, thus consuming the α-silyloxyaldehyde and producing the protected diol **1**.[10]

Utilization of the monohydric dimethylphenylsilane is found to work superbly in the rhodium(I)-catalyzed silylformylation of aldehydes (Scheme I, Table I). Since there is no evidence for the production of "diol" products, the relative rate of reaction for the starting aldehyde substrate must be much greater than that of the newly formed α-silyloxyaldehyde. A simple bulb-to-bulb distillation affords analytically pure α-silyloxyaldehydes.[11] Ketone substrates (e.g., acetophenone) yield silylenol ethers as the sole product. This result suggests that β-hydrogen elimination is much faster than migratory insertion of carbon monoxide.[12]

It can be seen from Table I that the reaction is quite general and works well for heterocyclic as well as aliphatic systems. The very mild reaction conditions permit discrimination of the starting aldehyde from the newly formed and more sterically demanding

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(5) Ojima, I.; Ingallina, P.; Donovan, R. J.; Clos, N. *Organometallics* **1991**, *10*, 38.

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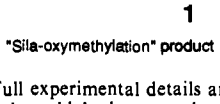
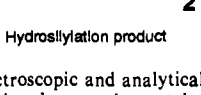
(9) Yamamoto, K.; Hayashi, T.; Kumada, M. *J. Organomet. Chem.* **1971**, *31*, C9. Dumont, W.; Poulin, J.-C.; Dang, T.-P.; Kagan, H. B. *J. Am. Chem. Soc.* **1973**, *95*, 8295. Ojima, I.; Kogure, T.; Nagai, Y. *Chem. Lett.* **1973**, 541.

(10) Compound **1** was independently synthesized from phenylethanediol and Ph_2SiCl_2 and found to be identical by GC-MS to the silyloxymethylation product. The hydrosilylation product **2** was unambiguously identified by comparison of ^1H NMR data.



1

"Sila-oxymethylation" product



2

Hydrosilylation product

(11) Full experimental details and spectroscopic and analytical data for the α-silyloxyaldehydes are deposited in the supplemental material. $C_6H_5CH(OSiMe_2Ph)CHO$ (3a) (74%, bp 130–140 °C at 0.1 mmHg): ^1H NMR ($CDCl_3$) δ 9.52 (s, 1 H, C*H*O), 7.55–7.28 (m, 10 H, Ar H), 4.99 (s, 1 H, –C*H*CHO), 0.43, 0.37, 0.33 (ss, 6 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$) δ 198.4 (CHO), 139.4 (Ar C), 136.3 (Ar C), 135.9 (Ar C), 133.3 (Ar CH), 132.8 (Ar CH), 132.7 (Ar CH), 130.0 (Ar CH), 129.7 (Ar CH), 129.0 (Ar CH), 128.5 (Ar CH), 128.3 (Ar CH), 128.2 (Ar CH), 128.1 (Ar CH), 128.0 (Ar CH), 127.8 (Ar CH), 127.5 (Ar CH), 126.5 (Ar CH), 126.2 (Ar CH), 79.9 (–CHCHO), 0.6, –1.4, –1.6, ($SiCH_3$); IR (CH_2Cl_2) $\nu_{C=O}$ 1736. Anal. Calcd for $C_{16}H_{18}O_2Si$: C, 71.06; H, 6.72. Found: C, 71.12; H, 6.94. It is noteworthy to mention that in each silaformylation reaction studied to date we observe at least two NMR signals for the prodiastereotopic silicon methyl groups. We also believe rotomers about the silicon–oxygen bond exist and have been indirectly supported by molecular mechanics analysis.

(12) Experimental data strongly suggests that the α-silyloxy moiety favors migratory insertion [see: Gladysz, J. A.; Selover, J. C.; Strouse, C. E. *J. Am. Chem. Soc.* **1978**, *100*, 6766]; however, its influence on the β-hydride elimination pathway has not been established.

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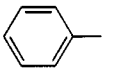
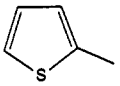
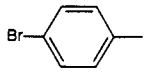
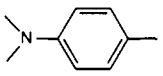
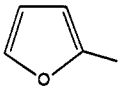
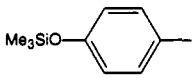
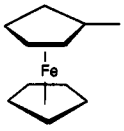
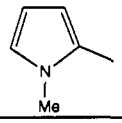
Table I. Summary of Results for the Rhodium-Catalyzed Silylformylation of Aldehydes[a]

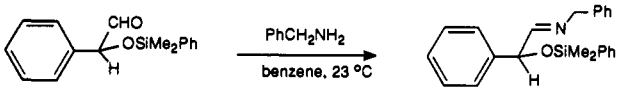
product	R	yield[b] (%)	product	R	yield[b] (%)
3a		74	**3f**		72
3b		84	**3g**[c]	$CH_3CH_2CH_2$-	60
			3h[c]	$(CH_3)_2CH$-	75
3c		80	**3i**		90
3d		50	**3j**		88
3e		60			

[a] A THF solution (8 mL) of the appropriate aldehyde (1.5 mmol) and Me_2PhSiH (0.20 g, 1.5 mmol) was degassed (freeze-pump-thaw ×3) and then cannulated into a glass vessel containing the $[(COD)RhCl]_2$ (1.8 mg, 0.5 mol %). The vessel was placed in the bomb, charged with carbon monoxide (250 psig), and allowed to react at ~23 °C for 24 h. [b] Yields reported were determined by NMR spectroscopy using an internal NMR standard (1,1,1-trichloroethane). Isolated yields were slightly lower but comparable. [c] 1000 psig of carbon monoxide pressure used.

α-silyloxyaldehyde. In the case of isobutyraldehyde we do see small amounts of enol ether formed, and at lower carbon monoxide pressures (250 psig) we observe hydrosilylation product.[13] The silylformylation reaction does not appear to tolerate strong electron-withdrawing substituents. For example, *p*-nitrobenzaldehyde shows only a 40% conversion with only some silylformylation product (20% yield). We find that pyridine carboxaldehydes (both the 2- and 4-) are completely unreactive under the reaction conditions.

Other monohydridic silane reducing reagents such as Et_3SiH and Ph_3SiH are not effective reagents for the rhodium(I)-catalyzed silylformylation of aldehydes at the mild temperatures employed in this study. Triethylsilane is recovered intact, and the triphenylsilane decomposes to unidentified products.

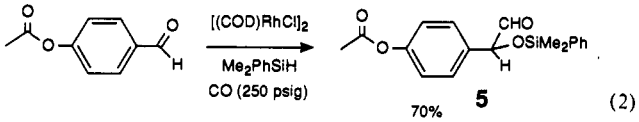
The utility of the α-silyloxyaldehydes is demonstrated by their facile conversion to α-silyloxyimine derivatives (eq 1).[14] The latter



100% **4** (1)

compounds are useful synthetic intermediates in the diastereoselective synthesis of β-amino alcohols.[15]

We find that the rhodium-catalyzed silylformylation is selective for the aldehyde functionality in the presence of an ester (eq 2).



70% **5** (2)

The highly functionalized aromatic compound **5** is isolated in 70% yield. Spectral data collected from the crude reaction mixture indicated complete chemoselectivity for the aldehyde group.

Studies are continuing in our research program to fully develop the tremendous potential of silylformylation, apply the novel methodology to selected synthetic targets, and explore the use of new catalytic systems.

Acknowledgment. We wish to express our gratitude to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Office of Naval Research for partial funding of this work.

Supplementary Material Available: Silylformylation procedure and complete spectroscopic data for compounds **3a-j**, **4**, and **5** (7 pages). Ordering information is given on any current masthead page.

(13) For aromatic aldehydes we find that carbon monoxide pressures of 125 psig produce slightly lower yields of the α-silyloxyaldehydes with concomitant formation of the hydrosilylation byproduct (~10%).

(14) Spectroscopic data for **4**: ^1H NMR ($CDCl_3$) δ 7.66 (d, J = 5.9 Hz, 1 H, C*H*=N), 7.54 (d, J = 7.7 Hz, 2 H, phenyl CH), 7.43-7.15 (m, 13 H, phenyl CH), 5.33 (d, J = 5.9 Hz, 1 H, PhC*H*(OSiMe$_2$Ph)C=N—), 4.49 (s, 2 H, PhC*H*$_2$N=), 0.38, 0.37 (ss, 6 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$) δ 166.1 (CHN), 140.3, 138.6, 133.5, 129.7, 128.4, 128.0, 127.8, 127.7, 127.0, 126.2 (Ar C's), 76.8 (C*H*(OSiMe$_2$Ph)), 64.3 (CH_2N=), -1.0, -1.3 ($SiCH_3$); IR (CH_2Cl_2) $\nu_{C=N}$ 1655.

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Structure of Maitotoxin

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Maitotoxin (MTX), with a molecular weight of 3422 Da, is one of the largest natural products known.[2] It exceeds palytoxin in size and lethality (LD_{50} 50 ng/kg, mouse, ip). Although scarcity of material has hampered full pharmacological evaluation, MTX is involved in Ca^{2+}-dependent mechanisms in a wide range of cell types.[3] It has been implicated in ciguatera food poisoning,[4] thus making its structural determination one of the most exciting challenges in natural products chemistry. We previously reported partial structures of MTX[5] (fragments A and C) and showed that the molecule consists mainly of fused polycyclic ethers. In this communication, we disclose the entire structure of MTX (**1**).

MTX (8.1 mg) was isolated from cultured dinoflagellates *Gambierdiscus toxicus* (strain GII-1) and was treated with $NaIO_4$ then with $NaBH_4$.[5] Subsequent HPLC yielded two major frac-

(1) (a) Tohoku University. (b) Suntory Institute. (c) The University of Tokyo.

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