10^{-6} and 1.4×10^{-4} M. None of these runs gave good first-order or second-order plots, and we therefore obtained the order of the reaction in naphthalene by analyzing the initial rates (r_i) as shown in Figure 2. By this method the order in napthalene was determined to be 1.5. This surprising result was verified by reexamination of the full kinetic runs, which were found to fit plots for a reaction 1.5 order in naphthalene. These results are in contrast to those of Ridd and Co-workers,[4] who found N(III)-catalyzed nitration of *N,N*-dimethylaniline to be first order in the aromatic. This finding is moreover obviously not in accord with the prenitrosation scheme.

The order of nitration in nitrous acid was also determined by the method of initial slopes and found to be 0.8 for the range of nitrous acid concentrations between 6.7×10^{-6} and 1.7×10^{-4} M (Figure 2). The order with respect to nitric acid changed in the range of concentrations studied. The reaction was zero order in nitric acid when the concentration of nitric acid was above 6.3×10^{-3} M. Below 10^{-4} M nitric acid, the order was approximately 1. Variation of the log initial rate with log initial nitric acid concentration is also shown in Figure 2.

From these kinetic data we can draw some conclusions regarding the mechanism of the reaction. The order of 1.5 in naphthalene can be explained in terms of a chain mechanism in which both initiation and propagation steps are first order in naphthalene. The changing order in nitric acid indicates a change in the rate-limiting step with changing N(V) concentration. We stipulate that nitric acid is involved in a propagation step following the step in which naphthalene is consumed. Zero order in nitric acid for high concentrations is consistent with the electron-transfer oxidation scheme of Ridd and co-workers,[4] and recently Main, Moodie, and Schofiled[5] found evidence for such a limiting kinetic form in the case of nitrous acid catalyzed nitration of 1,2,3-trimethoxy-5-nitrobenzene.

Further support for electron transfer is provided by the results of electrochemical nitration of naphthalene. Eberson et al.[7] and Achord and Hussey[8] reported that controlled potential electrolysis of naphthalene at +1.3 V (vs. Ag/Ag^+) in the presence of N_2O_4 produces nitronaphthalenes with an α/β isomer ratio of 23 ± 3, a value we have been able to reproduce, but significantly different from that reported by Perrin.[9]

However, the order of 1.5 in naphthalene cannot be reconciled with a simple scheme involving oxidation by NO^+, followed by reaction with NO_2. We support the idea of electron transfer being an important step, but the overall scheme must include a chain. So far we have not been able to identify the NO_x species involved in the reaction, primarily because at the acidity we have worked, several of the NO_x species are present in a significant quantities, including NO, HONO, NO^+, NO_2, N_2O_4, NO_3^-, and HNO_3.[9] We are currently studying the acidity dependence of N(III)-catalyzed nitration of naphthalene, with the hope to establish the identity of the oxidant and develop a detailed mechanism. However, it is clear that the nitration of simple hydrocarbons can be complex and the role of the lower nitrogen oxides can be significant.

Acknowledgment. We acknowledge the generous support of the U.S. Army Research Office. We also thank Professor R. B. Moodie for helpful discussion.

(7) Eberson, L.; Jonsson, L.; Radner, F. *Acta Chem. Scand., Ser. B* **1978**, *B32*, 749.
(8) Achord, J. M.; Hussey, C. L. *J. Electrochem. Soc.* **1981**, *128*, 255–261.
(9) Perrin, C. L. *J. Am. Chem. Soc.* **1977**, *99*, 5516.
(10) Ross, D. S.; Gu, C. L., to be published.

Registry No. Naphthalene, 91-20-3; nitrous acid, 7782-77-6.

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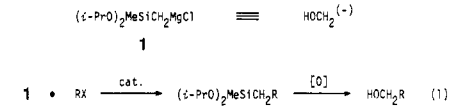
(Diisopropoxymethylsilyl)methyl Grignard Reagent: A New, Practically Useful Nucleophilic Hydroxymethylating Agent

Summary: The (diisopropoxymethylsilyl)methyl Grignard reagent serves as a new, versatile nucleophilic hydroxymethylating agent of organic halides via the metal-catalyzed cross-coupling and the subsequent oxidative cleavage of the silicon–carbon bond.

Sir: Despite its anticipated potent utility in synthetic organic chemistry,[1] nucleophilic hydroxymethylation has only been described in a few scattered papers.[2] The previous approaches have limited applicability, because of the limited availability of starting materials and low functional group tolerance. We have now developed the (diisopropoxymethylsilyl)methyl Grignard reagent (1) as a new nucleophilic hydroxymethylating agent that is readily available, convenient to handle, and of general applicability (eq 1).



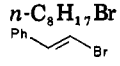
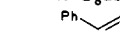
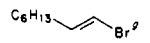
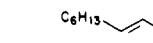
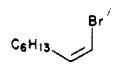
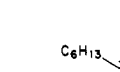
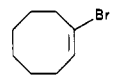
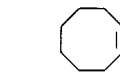
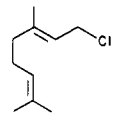
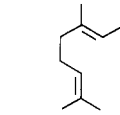
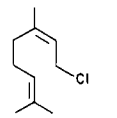
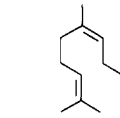
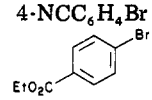
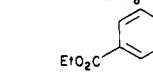
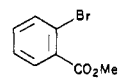
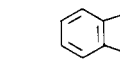
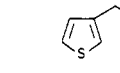
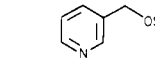
The present methodology is based on our recent observation that an alkoxysilyl group is synthetically equivalent to the hydroxy group.[3,4] Thus, the carbon–silicon bond in organoalkoxysilanes is readily cleaved by 30% H_2O_2[3] as well as MCPBA[4] in the presence of fluoride ions to form the corresponding alcohol. Such a unique reactivity of silicon–functional organosilicon compounds suggests a variety of new synthetic possibilities that are not possible with the more common trimethylsilyl derivatives.[5]

Despite the possible reactivity due to the coexistence of a reactive primary alkyl Grignard reagent and a labile alkoxy group on silicon, the Grignard reagent 1 could be prepared in a normal manner from $(i\text{-PrO})_2MeSiCH_2Cl$ (2)[6] and magnesium activated with dibromoethane in THF.[7]

(1) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.
(2) (a) $ArCO_2CH_2Li$/LAH: Beak, P.; McKinnie, B. G. *J. Am. Chem. Soc.* **1977**, *99*, 5213. (b) R_2BCH_2Li/[O]: Rathke, M. W.; Kow, R. *J. Am. Chem. Soc.* **1972**, *94*, 6854. (c) Ar_2BCH_2Li/[O]: Pelter, A. *Chem. Soc. Rev.* **1982**, *11*, 191. (d) Bu_3SnCH_2OH/2BuLi: Meyer, N.; Seebach, K. *Ber.* **1980**, *113*, 1290. See also: (e) Still, W. C.; Mitra, A. *J. Am. Chem. Soc.* **1978**, *100*, 1929. (f) $(Me_3SiO)CH{=}C(OSiMe_3)_2$: Wissner, A. *Tetrahedron Lett.* **1978**, 2749.
(3) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M., manuscript in preparation.
(4) Tamao, K.; Kakui, T.; Akita, M.; Iwahara, T.; Kanatani, R.; Yoshida, J.; Kumada, M. *Tetrahedron* **1983**, *39*, 983. See also: Hosomi, A.; Iijima, S.; Sakurai, H. *Chem. Lett.* **1981**, 243.
(5) Colvin, E. "Silicon in Organic Synthesis"; Butterworths: London, 1981.
(6) Andrianov, K. A.; Makorova, L. I.; Volkova, L. M.; Odinets, V. A. *Dokl. Acad. Nauk, SSSR* **1954**, *95*, 269; *Chem. Abstr.* **1955**, *49*, 3787.

0022-3263/83/1948-2120$01.50/0

Table I. Nucleophilic Hydroxymethylation of Organic Halides via the Silylmethylation-Oxidation Sequence

		coupling[a]		oxidation[b]		
entry	organic halide	cat.	yield,[c] %	oxidant (equiv)	product	yield,[c,d] %
1	n-$C_8H_{17}Br$	Cu	92	30% H_2O_2 (12)[e,f]	n-$C_8H_{17}CH_2OH$	88 [81]
2		Ni	100	30% H_2O_2 (12)		51 [51]
3		Ni	83	30% H_2O_2 (10) 90% H_2O_2 (10) CH_3CO_3H (3)		93 [79] 67 66
4		Ni	90	30% H_2O_2 (12)		76 [68]
5		Ni[k]	88	90% H_2O_2 (10)		70 [62]
6		Cu[l]	91	30% H_2O_2 (12)[e] 90% H_2O_2 (12)		52[m] 81 [74]
7		Cu[l]	96	90% H_2O_2 (12)[e]		91 [87]
8	4-$MeOC_6H_4Br$	Pd[n]	79	30% H_2O_2 (12) 90% H_2O_2 (12)	4-$MeOC_6H_4CH_2OH$	59 64 [50]
9	4-NCC_6H_4Br	Pd[n]	92	CH_3CO_3H (3)[o]	4-$NCC_6H_4CH_2OH$	51 [47]
10		Pd[n]	94	30% H_2O_2 (12) 90% H_2O_2 (12) CH_3CO_3H (3)[o]		trace[p] 48 75 [70]
11		Pd[n]	95	CH_3CO_3H (4)[o]		90 [86]
12		Pd[n]	77[q]	90% H_2O_2 (6)[f]		84 [65]
13		Ni	92	90% H_2O_2 (6)[f]		66 [61]

[a] 1/RX = 1.3/1. Catalyst: Cu = CuI (10 mol %), Ni = $NiCl_2$(dppp) (0.5 mol %), Pd = $PdCl_2$(dppf) (0.5 mol %). Unless otherwise stated, the coupling reaction was carried out in THF at 50–60 °C for 13–28 h. [b] Unless otherwise stated, the oxidation was carried out by addition of the oxidant to a mixture of the coupling product, KF (3 equiv), and DMF, followed by stirring at room temperature for ca. 40 h. [c] Isolated yield. [d] Overall yields based on RX are given in brackets. [e] KHF_2 (3 equiv) was used. [f] At 60 °C for 6 h. [g] E/Z = 93/7. [h] E only. [i] E/Z = 13/87. [j] E/Z = 22/78. [k] At 50 °C for 90 h. [l] At −50 to ~0 °C for 5.5 h. [m] Purity 85%. [n] 1 was converted to the zinc reagent by treatment with $ZnCl_2$ (1 equiv). [o] At room temperature for 14–18 h. [p] $EtO_2CC_6H_4CH_3$ was formed only. [q] Crude yield; contaminated with $[(i\text{-}PrO)_2MeSiCH_2]_2$. [r] Isolated after silylation of the crude product with $(Me_3Si)_2NH$.

The yield was high as determined by the GLC analysis after hydrolysis (91%), by titration (96%), and by deuterium incorporation (95%). The Grignard reagent 1 is surprisingly stable and can be stored at room temperature at least for 2 days with little decrease in activity.

The synthetic utility of 1 has been demonstrated by the nucleophilic hydroxymethylation of organic halides (eq 1). Representative results are shown in Table I. Several characteristics and significant features deserve comment.

The Grignard reagent smoothly underwent the cross-coupling with organic halides in the presence of CuI,[8] [$NiCl_2$(dppp)],[9] or [$PdCl_2$(dppf)].[10] For reaction with functional-group-substituted aromatic halides, 1 was converted to the corresponding organozinc reagent by treatment with $ZnCl_2$.[11] Stereo- and regiochemistry of allylic halides and configuration of alkenyl halides were retained.

Transformation of the coupling products to alcohols was achieved by oxidative cleavage of the silicon–carbon bond by using 30% H_2O_2, 90% H_2O_2, or 48% CH_3CO_3H in DMF in the presence of KF or KHF_2 as the essential additive.[3] Although the optimum conditions have not yet been determined, there seems to be the following trends: 30% H_2O_2 may be the first choice for the alkylsilanes (entry 1) and allylic oxidation (entries 3 and 4), for the homoallylic oxidation 90% H_2O_2 appears better than 30% H_2O_2 (entry 6), and benzylic, especially electron-withdrawing-group substituted, silanes give the most satisfactory results with

(7) It was essential to start the reaction by addition of ca. 50 μL of dibromoethane to *a hot mixture* of magnesium powder, ca. 1 mL of 2, and dry THF (ca. 2 mL for a 30-mmol scale), followed by addition of a solution of 2 in THF at 0 °C. In contrast, $(EtO)_2MeSiCH_2Cl$ reacted smoothly with Mg to 100% conversion, but the yield of the Grignard reagent was only 20%, intermolecular substitution readily occurring. Although $(t\text{-}BuO)_2MeSiCH_2MgCl$ was also obtained in a quantitative yield, it was not suitable for our present purpose, since the silicon–carbon bond in $(t\text{-}BuO)_2MeSi$–R was reluctant to the oxidative cleavage.[3]

(8) Cf.: (a) Tamura, M.; Kochi, J. K. *Synthesis* **1971**, 303. (b) Derguini-Boumechal, F.; Linstrumelle, G. *Tetrahedron Lett.* **1976**, 3225.

(9) dppp = $Ph_2P(CH_2)_3PPh_2$. Tamao, K.; Sumitani, K.; Kiso, Y.; Zembayashi, M.; Fujioka, A.; Kodama, S.; Nakajima, I.; Minato, A.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1979**, *49*, 1958.

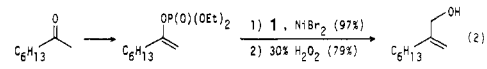
(10) dppf = 1,1′-Bis(diphenylphosphino)ferrocene. Cf.: Hayashi, T.; Konishi, M.; Kumada, M. *Tetrahedron Lett.* **1979**, 1871.

(11) Negishi, E.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821.

peracetic acid (entries 9–11). In the last case 30% H_2O_2 gave only the protonolysis product (entry 10).

One of the most characteristic features is that the OH group is introduced exclusively onto the carbon atom to which the silicon atom has been attached, even in allylic silanes. Thus, this reaction provides the first successful procedure for the direct conversion of allylsilanes to allyl alcohols without an allylic transposition.[12] Also noteworthy is the stereo- and regiocontrolled hydroxymethylation of allylic halides. For example, geranyl and neryl chlorides are converted to the corresponding homoallylic alcohols with the highest efficiency ever reported (entries 6 and 7).[13] Furthermore, under these oxidation conditions neither epoxidation of olefin nor oxidation of amine, nitrile, and thiophene was observed.

While the present method cannot be applied to carbonyl groups since the Peterson olefination[14] may result, the regioselective, reductive hydroxymethyltion of ketones has been accomplished via a nickel-catalyzed Grignard coupling with the enol phosphate,[15] as exemplified by eq 2.



In view of the ready availability of the starting material, compatibility of several functional groups, high regio- and stereoselectivity, mildness of oxidation step, and high overall yields, the present method may prove to be of great use for nucleophilic hydroxymethylation of various kinds of compounds.

Acknowledgment. We thank Shin-etsu Chemical Industrial Co., Ltd., for partial support and a gift of chlorosilanes, and Mitsubishi Gas-Chemical Industrial Co., Ltd., for a gift of 90% hydrogen peroxide.

Registry No. 1, 85719-58-0; 2, 2212-08-0; *n*-$C_8H_{17}Br$, 111-83-1; (*E*)-PhCH=CHBr, 588-72-7; (*E*)-$C_6H_{13}CH$=CHBr, 51751-87-2; (*Z*)-$C_6H_{13}CH$=CHBr, 42843-49-2; (*E*)-$(CH_3)_2C$=$CHCH_2CH_2C(CH_3)$=$CHCH_2Cl$, 5389-87-7; (*Z*)-$(CH_3)_2C$=$CHCH_2CH_2C(CH_3)$=$CHCH_2Cl$, 20536-36-1; 4-$MeOC_6H_4Br$, 104-92-7; 4-NCC_6H_4Br, 623-00-7; 4-$EtO_2CC_6H_4Br$, 5798-75-4; 2-$MeO_2CC_6H_4Br$, 610-94-6; (*i*-PrO)$_2$MeSiCH_2-*n*-C_8H_{17}, 85719-59-1; (*E*)-(*i*-PrO)$_2$MeSiCH_2CH=CHPh, 85719-60-4; (*E*)-(*i*-PrO)$_2$MeSiCH_2CH=CHC_6H_{13}, 85719-61-5; (*Z*)-(*i*-PrO)$_2$MeSiCH_2CH=CHC_6H_{13}, 85719-62-6; (*E*)-(*i*-PrO)$_2$MeSiCH_2CH_2CH=$C(CH_3)CH_2CH_2CH$=$C(CH_3)_2$, 85719-64-8; (*Z*)-(*i*-PrO)$_2$MeSiCH_2CH_2CH=$C(CH_3)CH_2CH_2CH$=$C(CH_3)_2$, 85719-65-9; (*i*-PrO)$_2$MeSi$CH_2C_6H_4$-*p*-OMe, 85719-66-0; (*i*-PrO)$_2$MeSi$CH_2C_6H_4$-*p*-CN, 85719-67-1; (*i*-PrO)$_2$MeSi$CH_2C_6H_4$-*p*-CO_2Et, 85719-68-2; (*i*-PrO)$_2$MeSi$CH_2C_6H_4$-*o*-CO_2Me, 85719-69-3; *n*-$C_8H_{17}CH_2OH$, 143-08-8; (*E*)-PhCH=$CHCH_2OH$, 4407-36-7; (*E*)-$C_6H_{13}CH$=$CHCH_2OH$, 31502-14-4; (*E*)-$(CH_3)_2C$=$CHCH_2CH_2C(CH_3)$=$CHCH_2CH_2OH$, 459-88-1; (*Z*)-$(CH_3)_2C$=$CHCH_2CH_2C(CH_3)$=$CHCH_2CH_2OH$, 74380-61-3; 4-$MeOC_6H_4CH_2OH$, 105-13-5; 4-$NCC_6H_4CH_2OH$, 874-89-5; 4-$EtO_2CC_6H_4CH_2OH$, 15852-63-8; (*Z*)-$C_6H_{13}CH$=$CHCH_2OH$, 41453-56-9; 1-bromocyclooctene, 4103-11-1; 3-bromothiophene, 872-31-1; 3-bromopyridine, 626-55-1; methylbis(1-methylethoxy)(1-cyclooctenylmethyl)silane, 85719-63-7; methylbis(1-methylethoxy)(3-thienylmethyl)silane, 85719-70-6; methylbis(1-methylethoxy)(3-pyridylmethyl)silane, 85719-71-7; 1-methanol-1-cyclooctene, 56900-55-1; 1(3*H*)-isobenzofuranone, 87-41-2; 3-thiophenemethanol, 71637-34-8; 3-[(trimethylsilyloxy)methyl]pyrideine, 85719-72-8.

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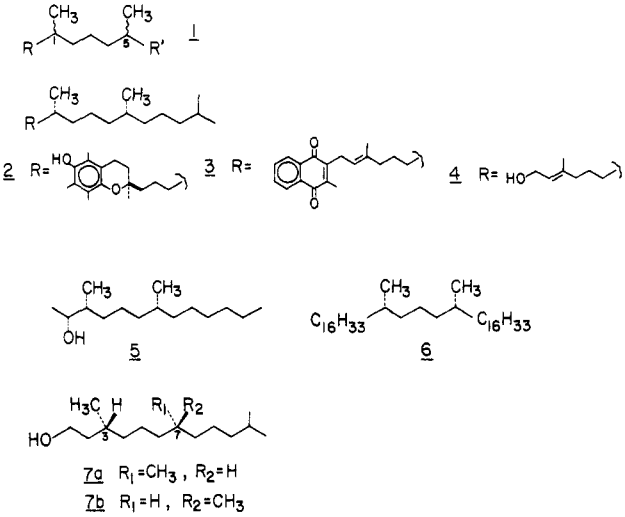
Chirality Transfer in Stereoselective Synthesis. A Highly Stereoselective Synthesis of Optically Active Vitamin E Side Chains

Summary: Employing the Carroll reaction as a means of chirality transfer, a highly efficient, stereochemically controlled, and generally applicable synthesis of optically active 1,5-dimethylated acyclic chains has been developed; as an example, the synthesis of the optically active C-15 vitamin E side chains **7a** and **7b** from (+)-pulegone in 12.6% and 11.7% overall yields, respectively, is described.

Sir: Stereocontrol originating from remote chiral centers during the construction of acyclic systems remains a central theme in the total synthesis of complex natural products.[1] One attractive solution to this end involves chirality transfer mediated by mechanistically well-defined, highly stereocontrolled rearrangement reactions.[2] Among the target molecules to which one could apply such methodology are the 1,5-dimethylated acyclic units **1**,



present in a number of biologically important natural products such as vitamin E (α-tocopherol, **2**), vitamin K (**3**), phytol (**4**), and insect pheromones of pine sawflies (**5**)[3]

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