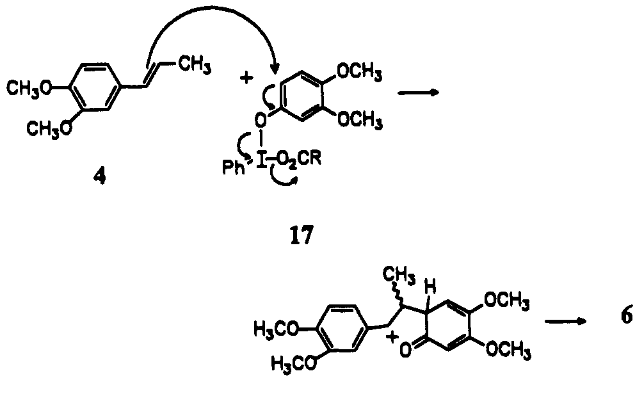


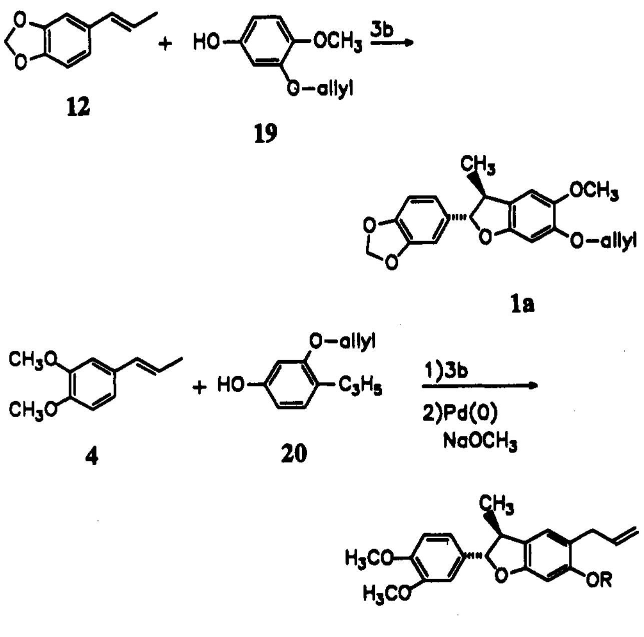
4

17

18

1a (69% yield). The product **1a** showed ^{1}H NMR and IR spectra in good agreement with those reported for the natural product.[1c] Finally, **4** was reacted with **20**[18] to furnish **21** (R = allyl, 30% yield) which was then deblocked[20] to **22** (R = H, 90% yield). The final product **22** showed a 200-MHz ^{1}H NMR spectrum identical with an authentic spectrum of the compound.[21] The dihydrobenzofuran **22** has been converted[5] to *kadsurenone* and *denudatin B*; thus, this serves as a formal synthesis of these natural products and rigorously establishes the *trans*-dihydrofuran stereochemistry. Since the position of the methyl resonance (trans isomer $\delta \approx 1.3$, cis isomer $\delta \approx 0.7$) is indicative of the stereochemistry in these dihydrobenzofurans,[22] the other adducts reported here are assigned as having the *trans*-dihydrobenzofuran stereochemistry based on the position of their methyl resonances in their ^{1}H NMR spectra.

The scope and mechanism of this oxidative cycloaddition reaction need to be studied further; however, this chemistry establishes a novel, convergent approach to *neolignans* containing the dihydrobenzofuran unit. Especially noteworthy is that the reaction involves a one-step procedure from readily available starting materials under conditions compatible with many sensitive functional groups. The synthesis of **1a** serves as a convenient entry into other compounds in this series. Thus, *neolignan* **1b** is related to **1a** via a Claisen rearrangement and **1c** is related to **1b** via a methylation. Further research will focus on defining the mechanistic aspects of this chemistry and the electrochemical version of this reaction.[23]



12

19

1a

4

20

21, R = allyl
22, R = H

Acknowledgment. We acknowledge support of this work from the National Science Foundation and Dr. K. Combrink for helpful discussions and references.

Supplementary Material Available: Experimental procedure for the preparation of **9a** and ^{1}H NMR spectra of **6** and **9a** (5 pages). Ordering information is given on any current masthead page.

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[18] This phenol was prepared by reaction of diethylaluminum chloride catalyzed Claisen rearrangement[19] of 1-(*tert*-butyldimethylsiloxy)-3-(allyloxy)benzene followed by allylation of the resulting phenol, silica gel chromatography, and desilylation with sodium methoxide.

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[20] Takahashi, K.; Miyake, A.; Hata, G. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 230.

[21] We thank Dr. M. Ponpipom of Merck Sharp & Dohme for the authentic ^{1}H NMR spectrum.

[22] Gregson, M.; Ollis, W. D.; Redman, B. T.; Sutherland, I. O. *J. Chem. Soc., Chem. Commun.* **1968**, 1394. See also ref 6a.

[23] All new compounds showed combustion analyses or exact mass measurements within acceptable limits. The melting points of solids were as follows: (±)-**1a**, 83–84.5 °C [lit.[1c] (2*S*,3*S*)-**1a**, oil]; (±)-**6**, 125.5–126 °C; (±)-**9a**, 99.5–100 °C; (±)-**9c**, 41–43 °C; (±)-**11**, 98–99 °C; (±)-**14**, mp 62–63 °C (lit.[4b] mp 67–69 °C); (±)-**21**, 51.5–52.5 °C (±)-**22**, mp 96–97 °C (lit.[5a] mp 98–99 °C).

Functionalization of Silica Gel: Application for the Catalytic Oxidation of Alkanes[1]

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Summary: Silica gel, functionalized by (*N,N*-dimethyl-3-aminopropyl)trimethoxysilane and complexed with Fe(II) or other metal ions in the presence of O_2 was effective for the aerobic, room temperature oxidation of a C–H bond in cyclohexane. The products were cyclohexanol and cyclohexanone.

The hydroxylation of inert C–H bonds in alkanes under mild conditions has remained a difficult challenge in organic chemistry. One possible approach to achieving this is to mimic biological conditions and systems. Mono-

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[1] Contribution 102 from the Center for Photochemical Sciences.

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Table I. Oxidation of Cyclohexand with Dioxygen in the Presence of Metal-Complexed Functionalized Silica (FS-1)

run	cyclohexane: g; mol	metal-complexed FS-1:[a] mg; metal atom × 10^3	Zn powder: g; mmol	CH_3COOH: g; mmol	time, h	yield based on cyclohexane, %	ratio cyclohexanol: cyclohexone	turnover[b]
1	19.2; 0.228	0	0.892 13.7	1.05 16.6	20.5	0.01		
2	13.4; 0.159	$FeSO_4\cdot 7H_2O$: 0.014; 0.050	1.07 16.4	1.98 28.0	16	0.19	8:1	6.04
3	19.5; 0.232	Fe: 23.6; 0.032	0.93 14.3	1.05 16.6	161.5	0.1	5:1	7.25
4	19.2; 0.228	Fe: 41.2; 0.056	2.16 33.0	3.55 59.1	32.5	1.4	15:1	57.0
5	19.3; 0.229	Mn: 61.8; 0.041	1.007 15.4	2.12 35.4	24	0.8	56:1	44.6
6	19.2; 0.228	Co: 56.0; 0.039	1.432 21.9	2.52 42.0	24	0.6	25:1	35.0
7	19.3; 0.229	Ni: 46.7; 0.049	0.98 15.0	1.98 33.0	24	0.7	18:1	32.7
8	19.2; 0.228	$CuSo_4\cdot 5H_2O$: 14.9; 0.6	0.998 15.1	2.30 38.3	24	0.6	8.8:1	2.28
9	19.3; 0.229	Cu: 29.8; 0.031	7.035 75.8	1.92 32.0	24	1.3	5.8:1	96.0
10	19.4; 0.231	Cu: 70.5; 0.074	1.223 18.8	1.97 32.8	67	4.3	3.3:1	134.2

[a] Metal complexed FS-1: Mn, 3.64; Co, 4.11; Ni, 6.16; Cu, 6.71 (%). [b] mol products/mol catalyst.

oxygenation reactions are carried out in nature by enzymes called monooxygenases. Since some monooxygenases contain a heme protein (cytochrome P-450), metalloporphyrins have been used as models for cytochrome P-450 to mimic enzymatic monooxygenation.[2] On the other hand, methane monooxygenase, a non-heme monooxygenase, has catalytic activity for dioxygen oxidation of a number of simple alkanes.[3,4] The active site in methane monooxygenase has been suggested to consist of binuclear iron, and attempts to mimic this oxidation system have involved the use of an iron compound, to which are added metallic Zn as the reductant and acetic acid as a proton donor.[5]

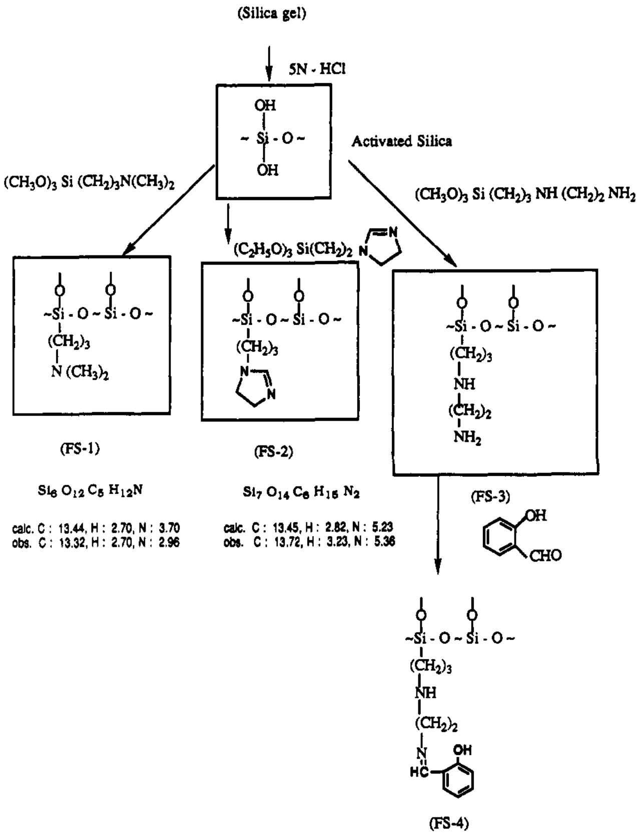
In view of our interest in polymer-immobilized reagents,[6] we have now synthesized a series of functionalized silica gels that should be able to complex metal ions. Our purpose was to convert these silicas to appropriate complexes and to test them as catalysts for the aerobic oxidation of alkanes. We have found that indeed at least one of the compounds is active as a catalyst for dioxygen oxidation, under very mild conditions.

Results and Discussion

Silica gel (Aldrich, 70–270 mesh, 60 Å) was activated by treatment with 5 N HCl and coupled with the functionalization reagents (*N,N*-dimethyl-3-aminopropyl)trimethoxysilane, *N*-(3-(trimethoxysilyl)propyl)-4,5-dihydroimidazole, or *N*-[[3-(trimethoxysilyl)propyl]ethylenediamine]. See Scheme I.

Metal complex formation with the functionalized silica was carried out by stirring a suspension of the silica in an aqueous solution of the required metal ion for 15 h. After filtration, the metal-complexed silica was dried at 50 °C and stored in a desiccator. The composition of the complex was determined by elemental analysis. Scheme II shows that FS-1 is a binuclear iron-oxygen-bridged structure while FS-2 is a mononuclear iron-oxygen-bridged complex.

Scheme I



The active site of methane monooxygenase consists of two complexed iron atoms, and to mimic the enzymatic oxidation, compounds containing two complexed iron atoms have been used.[7] It may be expected from these reports that complexes of FS-1 (Fe) would be active in the

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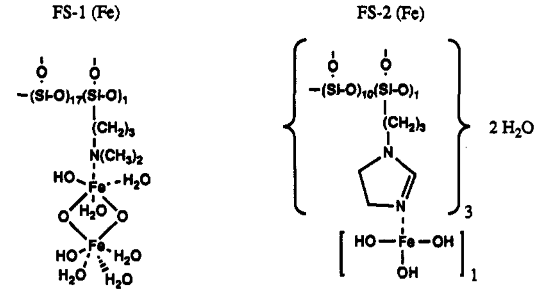
Scheme II. Plausible Structures for Fe Complexes FS-1 and FS-2



$Si_{18}O_{46}C_5H_{24}NFe_2$

calc. C: 4.13, H: 1.66, N: 0.97, Fe: 7.69
obs. C: 4.09, H: 1.72, N: 0.81, Fe: 7.60

$Si_{33}O_{75}C_{18}H_{48}N_6Fe$

calc. C: 9.37, H: 2.09, N: 3.64, Fe: 2.42
obs. C: 8.42, H: 2.77, N: 3.07, Fe: 2.32

oxidation of C–H bonds with dioxygen whereas those of FS-2 (Fe) would be inactive.

Cyclohexane oxidation was investigated with several complexes prepared from the functionalized silica gels.[8] It was observed that the compound which contains the dimethylamino group and two iron atoms [FS-1 (Fe)] is effective but that the compounds synthesized from other complexing ligands [FS-2 (Fe), FS-3 (Fe), and FS-4 (Fe)] were not active catalysts for oxidation (see Scheme I). The results of FS-1 are given in Table I.

Different metal complexes show different reactivities. The results are also shown in Table I. Runs 1, 2, and 8 are blanks. (Runs with various metals are 5, 6, 7, 8, 9, and 10.) The order of reactivity is Cu > Fe ≈ Mn ≈ Ni ≈ Co.

The stability constants for complex formation of metal ions with ethylenediamine diacetate as a ligand are known:[9] Fe^{2+} = 14.33; Co^{2+} = 16.21; Ni^{2+} = 18.52; Cu^{2+} = 18.79; and Fe^{3+} = 25.1. Making use of these constants and using for iron a mean value of Fe^{2+} and Fe^{3+}, Cu(II) might form the most stable complex with FS-1 compared with the other metals. When a stable complex reacts with dioxygen, a new reactive metal–oxygen complex is produced that is active as oxidizing catalyst.

The main product obtained from the oxidation of cyclohexane by the present method is cyclohexanol. In contrast, Barton[10] and co-workers observed cyclohexanone as the main product. This suggests that the mechanisms of the oxidations by these two reactions are different. We are investigating the mechanism by means of substituted cyclohexanes.

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(8) Representative oxidation procedure: To cyclohexane in a 100-mL round-bottom flask were added metal complexed FS, Zn powder, and acetic acid, and the suspension was stirred magnetically for a given time at room temperature under a static pressure of oxygen provided by a balloon. (A reviewer has suggested caution since a potentially explosive mixture could be generated. We experienced no problems, however, and add that the balloon was thin and the pressure was never greater than 1 atm. The system was always in the hood.) After the reaction, the contents of the flask were filtered and washed thoroughly with anhydrous ethyl ether. The combined organic extracts were distilled to a constant residual volume and this was analyzed by GC. Recovered cyclohexane was weighed. The only products were cyclohexanone and cyclohexanol. Quantitative GC analysis was carried out by the comparison of a standard cyclohexane–cyclohexanol–cyclohexanone calibration curve.

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Powerful Dienophiles for Asymmetric Diels–Alder Reactions: α-(2-*exo*-Hydroxy-10-bornylsulfinyl)maleimides

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Summary: Enantiomerically pure *N*-substituted α-(2-*exo*-hydroxy-10-bornylsulfinyl)maleimides 1 have been synthesized diastereoselectively, and these dienophiles undergo Diels–Alder reactions readily with furan to give the corresponding cycloadducts with high diastereoselectivity.

The asymmetric Diels–Alder reactions using chiral dienes or dienophiles or chiral Lewis acid derivatives as promoters have received wide-spread attention during the past decade.[2] A number of applications of chiral dienophiles have been reported, including our studies in the area of chiral sulfoxides.[3-5] High asymmetric induction in the cycloadditions with reactive dienes such as cyclopentadiene has been achieved. In sharp contrast, few reports concerning asymmetric Diels–Alder reactions with furan have appeared because of its low reactivity.[4,5] Generally, the use of furan in a Diels–Alder reaction requires high-pressure conditions.[6] Although the high-pressure meth-

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(1) (a) Toyama Medical and Pharmaceutical University. (b) Shionogi Research Laboratories.

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