

was then removed [pyridine-(HF)_x, THF, 98%]²⁰ in anticipation of macrolactonization.

Given **17b** possessing the *S* configuration at C(13), macrolactonization with inversion of configuration was required. Toward this end, Mitsunobu lactonization (4 equiv of DEAD/Ph₃P in benzene)⁸ proceeded smoothly to yield **18**¹² in 68% yield. The structure of **18** was confirmed by single-crystal X-ray analysis.^{16b}

Having successfully arrived at **18**, all that remained to complete a synthesis of latrunculin B was removal of the 4-methoxybenzyl group²¹ and hydrolysis of the mixed methyl ketal. The former was achieved with 2.0 equiv of Ce(NH₄)₂(NO₃)₆ at a concentration of 0.25 M²² [CH₃CN/H₂O (3:1); 68%], while the latter proceeded with mild acid [HOAc/THF/H₂O (3:1:1), 60 °C]; the yield for the two steps was 42%. That indeed (+)-latrunculin B (**2**) was in hand derived from careful comparison of synthetic material with the 250-MHz ¹H NMR spectrum of natural (+)-latrunculin B kindly provided by Professor Hiram,²³ the ¹³C NMR and [α]_D data available in the literature,^{3d,e} and TLC R_f values in four different solvent systems.

In summation, the first total synthesis of (+)-latrunculin B has been achieved via a highly convergent and stereocontrolled route (longest linear sequence, 14 steps). The synthesis serves both to confirm the structure and to establish the absolute stereochemistry of latrunculin B. Studies directed toward the total synthesis of latrunculin A (**1**) and related macrolides of potential biological interest are currently under way in our laboratory.

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(23) We thank Professor Hiram (Tohoku University) for the sample of natural latrunculin B, which in turn was received from Professor Kashman (Tel Aviv University). In addition, we thank Professor Kashman for the high-field ¹H NMR spectrum of latrunculin B.

Novel Cobalt(II)-Catalyzed Oxidative Cleavage of a Carbon-Carbon Double Bond

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We have recently reported two distinct reaction types for the cobalt-catalyzed, specific oxidation of organic substrates.^{1,2} In one, coordination of O₂ to the metal ion was shown to enhance the basicity³ and radical⁴ reactivity of the bound O₂. These features were shown to be important in the cobalt(II)-catalyzed oxidation of substituted phenols where it was demonstrated that metal-bound O₂ was a reactive intermediate. In the second reaction type, the metal complex is involved in the catalytic conversion of O₂ to H₂O₂ or M-O-O-H with accompanying solvent oxidation. Subsequent reactivity involves the reactivity of peroxides. In this paper we report a third type of O₂ activation which

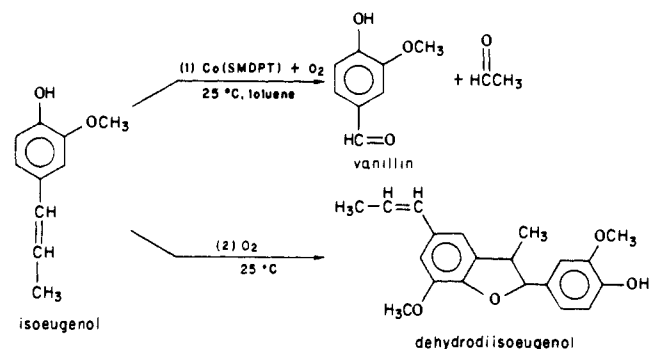
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Scheme I. Proposed Reactions in the Oxidation of Isoeugenol by CoSMDPT^a



^aThe formation of vanillin and acetaldehyde and the side product dehydrodiseugenol, the coupled dimer.

Table I. First Order CoSMDPT Dependence of the Oxidation of Isoeugenol

reaction ^a	molarity, M	initial rate ^b	conversion ^c	TO ^e
5.0 mg of CoSMDPT	2.44 × 10 ⁻⁴	2.25	27.9 (125)	562
11 mg of CoSMDPT	5.36 × 10 ⁻⁴	3.91	58.3 (345)	535
			60.8 (440)	558
20 mg of CoSMDPT ^d	9.75 × 10 ⁻⁴	8.10	58.3 (150)	294
			67.2 (365)	339
100 mg of CoSMDPT ^d	48.73 × 10 ⁻⁴	12.4	68.3 (195)	69
			74.7 (530)	75

^aReaction is run at 60 °C, in toluene, at P₀ = 75 psi, and 2.46 × 10⁻² mol of isoeugenol. 50-mL total volume of solution is used, which is 0.49 M in isoeugenol. ^bInitial rate is expressed as moles of O₂ absorbed per mole of substrate per minute. Reported values have been multiplied by 1 × 10³. ^cConversion is the moles of O₂ absorbed divided by the moles of isoeugenol present, expressed as a percent. The duration of the reaction, in minutes, is in parenthesis. ^dAn average of two runs. ^eNumber of turnovers based on moles of O₂ consumed per mole of catalyst.

results in a novel cleavage of a carbon-carbon double bond by molecular oxygen.

We discovered the formation of vanillin from the cobalt(II) catalytic oxidation of lignin, a para-substituted polyphenolic polymer comprising 25-30% of the dry weight of trees⁵ whose biological function is to provide structural support in vegetation. We were surprised that the oxidation of lignin proceeded rapidly at 60 °C and 75 psi of O₂ pressure because previous reports indicated that oxidation of para-substituted phenols by cobalt dioxygen complexes was sluggish.⁶ Due to the complexity of lignin, we decided to probe this reactivity by changing substrates to the model compound isoeugenol,⁷ 2-methoxy-4-propenylphenol (see Scheme I). Rapid, catalytic oxidation of isoeugenol occurred in toluene solvent at 60 °C and 75 psi of O₂ to form vanillin (path 1). Several stoichiometric reactions resulting in the conversion of isoeugenol to vanillin are cited in the literature,⁵ but our reaction has the benefit of being catalytic while maintaining a high level of selectivity.

In a typical run, isoeugenol is oxidized by O₂ with [bis(salicylidene-γ-iminopropyl)methylamine]cobalt(II) (CoSMDPT) as the catalyst to form about 50% vanillin, 30% unreacted isoeugenol, and 20% dehydrodiseugenol, a dimerization product⁸ (path 1). The reaction occurs at room temperature in about 24 h and proceeds much more rapidly at 60 °C (see Table I). In this study,

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(7) For the experimentation, only *trans*-isoeugenol was used, which was obtained by catalytic isomerization of eugenol using RhCl₃ under nitrogen at room temperature.⁸ When a *cis-trans* mixture of isomers was used, less vanillin was produced and the catalyst was deactivated more rapidly.

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dimerization was found to occur by a side reaction involving molecular oxygen; therefore, the catalytic reaction resulting in vanillin formation can be credited with at least 75% selectivity. The rate of dehydrodiiisoeugenol formation in the uncatalyzed reaction with O₂ is about 10-20% as fast as the oxidation of substrate with CoSMDPT. Only at very low catalyst concentration or elevated reaction temperatures (≥ 60 °C) does the side reaction become important.

The formation of vanillin as a product has been unquestionably proven: NMR (singlet 9.8 ppm from Me₄Si), IR (carbonyl stretch), GC (co-injection experiment) and classical derivative analysis. Both the dinitropicrylhydrazyl, DNP, and semicarbazide derivatives of vanillin were prepared. The experimentally determined melting point of the DNP derivative and the semicarbazide derivative were found to be 268 and 227 °C, respectively, comparing favorably to the literature values of 271 and 230 °C.⁹ Comparison of elemental analysis data for synthesized vanillin semicarbazide (VSC) to that for purchased reagent grade vanillin semicarbazide was very close (reagent grade VSC, 51.40% C, 5.55% H, and 20.02% N; synthesized VSC, 51.69% C, 5.24% H, 19.85% N). Verification of acetaldehyde as a second product was confirmed by using NMR spectroscopy, which showed two singlets in the aldehydic region for samples removed during the oxidation reaction. Intensity of the one aldehydic peak was increased considerably by spiking of the samples with acetaldehyde. The principal oxidation reaction that occurs in the cobalt catalyzed oxidation is shown in path 1.

Reaction parameters such as solvent, temperature, catalyst concentration, and O₂ pressure were varied in the study. Solvent effects indicate that methanol > toluene > CCl₄ for the reaction rate. Although the rate in methanol is fourfold greater than in CCl₄, the total absorption of dioxygen is about 25% less in methanol than in toluene or CCl₄. These variances in reaction rate may be attributed to diminished lifetime of the cobalt catalyst.

The reaction was found to be first order in CoSMDPT concentration (Table I), over a defined range, at different O₂ pressure levels while constant temperature was maintained. At low cobalt concentrations, the reported rate of oxygen uptake tended to be higher than expected for first-order kinetics which can be attributed to the competing dimerization reaction. With concentrations of catalyst up to 0.5 mg/mL solution, the rate was first order in cobalt(II). Oxygen dependence in the CoSMDPT reaction was found to be first order in nature, as was the substrate dependence. A rate law for the reaction over the pressure and concentration range described can be written by using the obtained information:

$$\text{product formation} = K_1[\text{CoSMDPT}][\text{isoeugenol}][\text{O}_2]$$

Aliquots from a reaction in progress were taken at regular intervals and studied by EPR. As the reaction progressed, the intensity of the cobalt dioxygen signal decreased and so did the rate of the reaction.⁷ Addition of basic materials did not greatly alter the reaction, but the presence of acids or hydrogen bonding materials did inhibit the rate of vanillin formation. Thus, this reaction has many features in common with our earlier findings on the mechanisms of oxidation of substituted phenols by this catalyst system.¹

By analogy to earlier studies we propose that the phenolic group of isoeugenol is converted to a phenoxy radical by our catalyst as demonstrated for the oxidation of 2,6-dimethylphenol to the substituted benzoquinone. In this latter system, Co-O₂ attack on the phenoxy radical was the next step leading to quinone formation.¹ Unpaired electron delocalization in the isoeugenol radical can lead to an allyl type of π system (consisting of the para carbon and the C=C of the α - and β -carbons of the substituent) for the substituent. At this point we can only speculate about a reaction path that leads to the observed products to provide a basis for further experiments. Attack by Co-O₂ at the β -carbon

of the allyl substituent in the isoeugenol radical could occur leading to a dioxetane which decomposes into vanillin and acetaldehyde. By analogy with the substituted phenol oxidation the Co(III) resulting from this decomposition would then react with isoeugenol, forming the phenoxy radical and regenerating cobalt(II). Though speculative, the reaction sequence described above has precedence in the literature for all steps except the attack of the β -carbon by Co-O₂. Alternatively, a reaction sequence that involves conversion of dehydrodiiisoeugenol to products may occur. Research is under way to establish the mechanism.

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Optical Coupling of Surface Chemistry. Photoluminescent Properties of a Derivatized Gallium Arsenide Surface Undergoing Redox Chemistry

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Photoluminescence (PL) can be a powerful tool for examining semiconductor-derived interfaces. In recent studies, we have demonstrated that PL from semiconductor electrodes is influenced by applied potential¹ and that PL from semiconductors coated with Pd films is sensitive to hydrogen gas.² In both the semiconductor/liquid and semiconductor/metal interfaces, PL intensity conforms to a dead-layer model that permits the mapping of the electric field in the semiconductor: electron-hole pairs formed within a distance on the order of the depletion width do not contribute to PL.³

These results, which indicate that bulk PL can be influenced by interfacial chemistry, have prompted us to examine PL from a semiconductor/molecular interface. We report in this paper on the PL properties of n-GaAs derivatized with a redox-active film. In particular, we demonstrate that redox chemistry in the film can alter the depletion width of the underlying semiconductor by several hundred angstroms, as reflected in substantial changes in PL intensity satisfying a dead-layer model. Moreover, our results suggest a general strategy for designing optically coupled sensors with chemical specificity.

Samples of n-GaAs⁴ were derivatized with (1,1'-ferrocenediyl)dichlorosilane by the method of Wrighton et al. to yield the idealized structure shown in Scheme I; some polymerization may also occur.⁵ Surface attachment was verified by cyclic voltammetry under photoexcitation in CH₃CN with 0.1 M [*n*-Bu₄N]BF₄ as supporting electrolyte. Integration of the cyclic voltammetric waves shows the surface concentration of redox-active sites to be 1×10^{-9} mol cm⁻², corresponding to several monolayers. Samples were stored under Ar at -10 °C when not in use.

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(3) Hollingsworth, R. E.; Sites, J. R. *J. Appl. Phys.* 1982, 53, 5357 and references therein.

(4) Samples of n-GaAs:Te from Laser Diode Labs, Inc., had carrier concentrations of 3×10^{16} cm⁻³ and (100) orientation. Samples were etched in 4:1:1 H₂SO₄/H₂O₂ (30%)/H₂O at 50 °C for 30 s, rinsed in distilled water, immersed in 7 M KOH at 50 °C for 30 min, rinsed again, and air-dried prior to derivatization.

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