Acknowledgment. This work was supported by the National Science Foundation. We thank Scott Horn for skilled technical assistance.

Supplementary Material Available: Synthetic procedures, NMR spectral data, and atomic positional and thermal parameters for $KZr_2(O^iPr)_9(MeOC_2H_4OMe)$ and $K_4Zr_2O(O^iPr)_{10}$ (7 pages). Ordering information is given on any current masthead page.

Template-Directed Phenolic Oxidative Coupling. A Stereocontrolled Route to Spiro Dienones

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Intramolecular oxidative coupling of phenols is a reaction of pivotal importance in alkaloid biosynthesis,[1] but its efficient simulation, particularly in stereochemical terms, has been a vexing problem for chemical synthesis.[2] Recent studies directed toward stereocontrolled oxidative coupling of benzyltetrahydroisoquinolines[3] have focused on conformational constraints that enforce proximity on reacting phenolic rings,[4] and on chiral appendages[5] and catalysts[6] that induce asymmetry in the coupled product. We describe herein a strategy for asymmetric phenolic coupling that employs a chiral oxazolidine as template and leads to the spiro dienone enantiomer **8** with extraordinary efficiency (Scheme I).

The chiral educt (*R*)-(−)-arterenol (norepinephrine, **1**) was N-acylated with 3-[[4-[(*tert*-butyldimethylsilyl)oxy]phenyl]-acetyl]thiazolidine-2-thione **2**[7] to yield amide **3** ($[\alpha]_D$ −25.2°).[8] After conversion to its methyl ether **4**, the hydroxy amide was treated with thionyl chloride and then with Hünig's base, to give oxazoline **6** ($[\alpha]_D$ +13.9°) with inverted configuration.[9] This stereochemical result is a consequence of participation by the amide function and, thus, retention of configuration[10] in the formation of the intermediate (unstable) chloride **5** ($[\alpha]_D$ −12.7°). The same configuration of **6** was obtained with *N*-chlorosuccinimide–dimethyl sulfide as halogenating agent.

Oxazoline **6** was acylated with 2,2,2-trichloroethyl chloroformate, and the intermediate salt was reduced with sodium cyanoborohydride to afford a mixture of cis and trans oxazolidines (3:1, respectively).[11] The mixture was subjected to tetra-*n*-butylammonium fluoride, furnishing the free phenols, which were separated chromatographically. The aryl rings in cis (2*R*,5*S*) isomer **7** ($[\alpha]_D$ +31.8°) are oriented in a manner that makes para–para coupling highly favorable, and when **7** was oxidized with vanadium oxytrifluoride[12] and trifluoracetic anhydride in a mixture of trifluoroacetic acid and dichloromethane, crystalline spiro dienone **8** ($[\alpha]_D$ +33.8°) was produced in quantitative yield.[13] The structure of **8** was established by means of an X-ray crys-

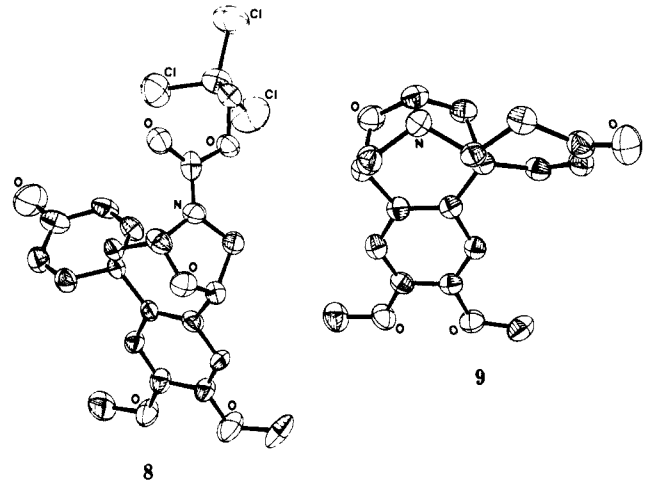
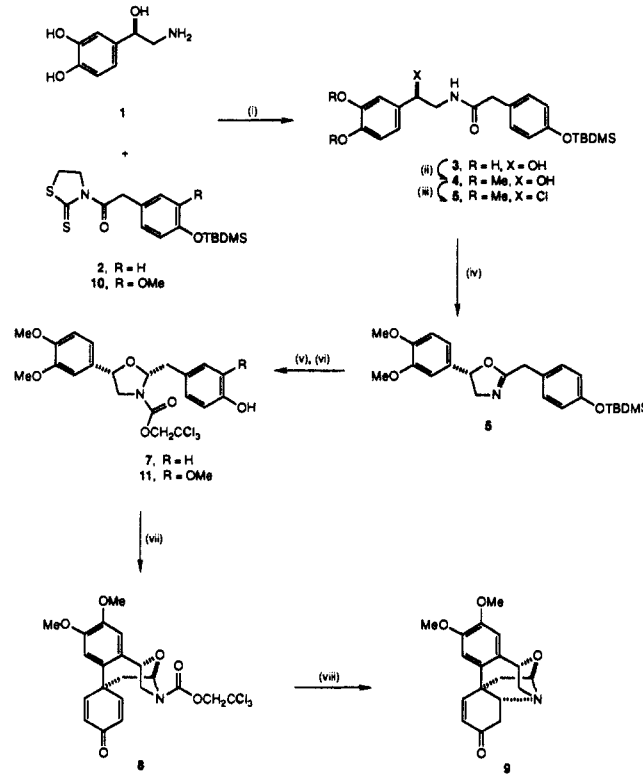


Figure 1. ORTEP plots of **8** and **9** with heteroatoms labeled. Thermal ellipsoids are drawn at the 50% level.

Scheme I[a]



[a] (i) DMF, 25 °C, 82%; (ii) CH_2N_2, ether–MeOH, 25 °C, 100%; (iii) $SOCl_2$, CH_2Cl_2, 0 °C; (iv) *i*-Pr_2NEt, CH_2Cl_2, 82% from **4**; (v) Cl_3CCH_2OCOCl, THF, −78 °C, then $NaBH_3CN$, THF–EtOH, 65%; (vi) *n*-Bu_4NF, THF, 25 °C, 76%; (vii) VOF_3, $(CF_3CO)_2O$, TFA, CH_2Cl_2, −78 °C → −10 °C, 98%; (viii) Zn, MeOH, reflux, 50%.

(1) Battersby, A. R. In *Oxidative Coupling of Phenols*; Battersby, A. R., Taylor, W. I., Eds.; Dekker: New York, 1967; pp 119–165.
(2) (a) Dhingra, O. P. In *Oxidation in Organic Chemistry*; Trahanovsky, W. S., Ed.; Academic Press: New York, 1982; Vol. 5-D, pp 207–278. (b) White, J. D.; Caravatti, G.; Kline, T. B.; Edstrom, E.; Rice, K. C.; Brossi, A. *Tetrahedron* **1983**, *39*, 2393 and references cited.
(3) Phillipson, J. D., Roberts, M. F., Zenk, M. H., Eds. *The Chemistry and Biology of Isoquinoline Alkaloids*; Springer-Verlag: Berlin, 1985. See also: Schwartz, M. A.; Pham, P. T. K. *J. Org. Chem.* **1988**, *53*, 2318 and references cited.
(4) Burnell, D. A.; Hari, D. J. *J. Org. Chem.* **1987**, *52*, 5662.
(5) Meyers, A. I.; Fuentes, L. M. *J. Am. Chem. Soc.* **1983**, *105*, 117. Meyers, A. I.; Fuentes, L. M.; Kubota, Y. *Tetrahedron* **1984**, *40*, 1361. Gawley, R. E.; Smith, G. A. *Tetrahedron Lett.* **1988**, *29*, 301.
(6) Noyori, R.; Ohta, M.; Hsiao, Y.; Kitamura, M.; Ohta, T.; Takaya, H. *J. Am. Chem. Soc.* **1986**, *108*, 7117 and references cited.
(7) Prepared from *p*-hydroxyphenylacetic acid by (i) protection with *tert*-butyldimethylsilyl chloride and imidazole in DMF, followed by workup with K_2CO_3 in aqueous MeOH, and (ii) exposure of the carboxylic acid to thiazolidine-2-thione, DCC, and DMAP in EtOAc (Burton, L. P. J.; White, J. D. *Tetrahedron Lett.* **1980**, *21*, 3147).
(8) Nagao, Y.; Kawabata, T.; Seno, K.; Fujita, E. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2470.
(9) The absolute configuration of **6** was established by its hydrolysis to the enantiomer of **4** (cf: Meyers, A. I.; Hoyer, D. *Tetrahedron Lett.* **1985**, *26*, 4687).
(10) Pines, S. H.; Kozlowski, M. A. *J. Org. Chem.* **1972**, *37*, 292.
(11) When the reduction was carried out with sodium borohydride, the stereoselectivity was reversed.
(12) Kupchan, S. M.; Liepa, A. J. *J. Am. Chem. Soc.* **1973**, *95*, 4062.
(13) The oxidative coupling of **7** could also be accomplished with $VOCl_3$ and $PhI(OCOCF_3)_2$, but neither reagent approached the efficiency of VOF_3.

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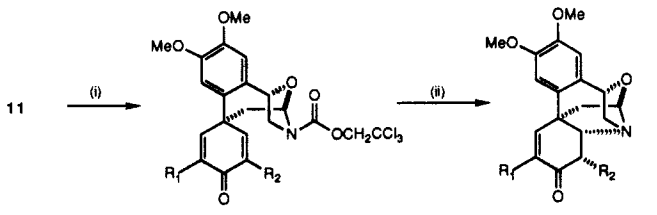
Scheme II[a]



12, R_1 = OMe, R_2 = H
13, R_1 = H, R_2 = OMe
14, R_1 = OMe, R_2 = H
15, R_1 = H, R_2 = OMe

[a] (i) VOF_3, $(CF_3CO)_2O$, TFA, CH_2Cl_2, - 78 °C (44%), **12**:**13**, 5:1; (ii) Zn, MeOH, reflux (46%).

tallographic analysis (Figure 1).[14] As expected, when the trans (2*S*,5*S*) isomer of **7** ($[\alpha]_D$ +24.8°) was exposed to VOF_3, no intramolecular phenolic coupling occurred. Reductive removal of the (trichloroethoxy)carbonyl group from **8** resulted in spontaneous addition of the liberated amine to the dienone in a process analogous to that observed previously.[15] The structure of the cyclization product **9**, which was also determined by X-ray crystallographic analysis (Figure 1),[16] possesses the cis-fused perhydroindole subunit in a configuration characteristic of the hasbanane alkaloids.[17]

With the aim of determining which of two diastereomeric products would predominate from oxidative coupling of a substrate in which the benzyl ring of the oxazolidine contained an additional substituent, a parallel sequence to that of Scheme I was initiated from homovanillic acid (**10**). This route led to cis oxazolidine **11** in excellent yield, which underwent phenolic coupling[18] to give **12** and **13** in the ratio 5:1, respectively (Scheme II). After deprotection, these diastereomeric dienones gave structurally isomeric pentacyclic amines **14** and **15**, which were readily distinguished on the basis of their ^1H NMR spectra.[19] Thus, the major stereoisomer **12** from phenolic coupling of **11** possesses a secoisosalutaridine framework antipodal to that found in most natural morphinans.

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(14) Compound **8** crystallized in a monoclinic space group ($P2_1/c$) with four molecules located within a unit cell of the following dimensions: a = 10.589 (8) Å, b = 19.221 (5) Å, c = 11.112 (5) Å; β = 104.72 (4)°; V = 2187 (2) Å^3. The structure was solved by using 927 observed unique reflections [$I > 3\sigma(I)$] for $2\theta \leq 40°$ with MITHRIL (Gilmore, G. J. *J. Appl. Crystallogr.* **1984**, *17*, 42), DIRDIF (Beurskens, P. T. Technical Report 1; Crystallography Laboratory: Toernooiveld, 6525 Ed Nijmegan, The Netherlands, 1984), and successive analysis of difference maps. Anisotropic full-matrix least-squares refinement of all non-hydrogen atoms afforded residuals of R = 0.043 and R_w = 0.042 with S = 1.29.

(15) White, J. D.; Chong, W. K. M.; Thirring, K. *J. Org. Chem.* **1983**, *48*, 2300.

(16) Crystals of **9** were triclinic ($P\bar{1}$), having two molecules located within a unit cell of the following dimensions: a = 9.648 (3) Å, b = 9.874 (2) Å, c = 8.791 (2) Å; α = 100.72 (2)°, β = 112.63 (2)°, γ = 84.22 (2)°; V = 759.1 (3) Å^3. The structure was solved by using MITHRIL,[14] DIRDIF,[14] and successive analysis of difference maps with 1750 observed unique reflections [$I > 3\sigma(I)$] and $2\theta \leq 50°$. Anisotropic full-matrix least-squares refinement of all non-hydrogen atoms afforded residuals of R = 0.042 and R_w = 0.048 with S = 1.53.

(17) Ito, S. In *Natural Products Chemistry*; Nakanishi, K., Goto, T., Ito, S., Natori, S., Nozoe, S., Eds.; Academic Press: New York, 1975; Vol. 2, pp 319-323.

(18) The diminished yield of **12** and **13** is due to subsequent dienone-phenol rearrangement (Kupchan, S. M.; Kim, C.-K. *J. Am. Chem. Soc.* **1975**, *97*, 5623).

(19) **14**: δ 6.09 (s, 1 H). **15**: δ 7.20 (d, J = 11 Hz, 1 H), 6.11 (d, J = 11 Hz, 1 H).

Supplementary Material Available: Spectroscopic data (IR, ^1H NMR, ^{13}C NMR, MS), optical rotations ($[\alpha]_D$), and combustion analyses (or HRMS) for **2**-**12** and **14** (4 pages). Ordering information is given on any current masthead page.

Carbon Monoxide Dependent Solid-State Electrochemistry of Ferrocenylferraazetine: En Route to a Molecule-Based Carbon Monoxide Sensor

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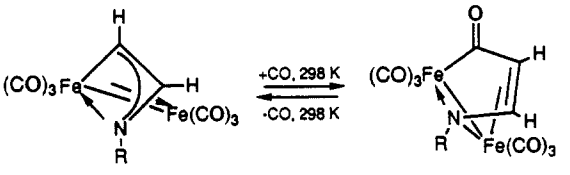
We report the solid-state reaction of CO with a ferrocenylferraazetine complex, **1a**, showing a possible entry into a new class of molecule-based CO detectors. Ferraazetine complexes **1b**,**c** show facile, reversible CO insertion to form ferrapyrrolinone complexes **2b**,**c**, eq 1.[1] Complex **1a** was synthesized with the aim



(1)

1a R = ferrocene
1b R = t-butyl
1c R = phenyl

2a, **b**, **c**

of demonstrating a reversible redox active molecule that undergoes CO insertion to give a product with a different redox potential. Like **1b** and **1c**, **1a** does insert CO to form a ferrocenylferrapyrrolinone complex, **2a**, in the dark. Importantly, while **1a** is photosensitive, **1a** at 25 °C is chemically inert to 1 atm of the following gases: air (not containing CO), pure H_2, O_2, or CO_2. Using a microelectrode array,[2] the solid ionic conductor MEEP (poly[bis(2-(2-methoxyethoxy)ethoxy)phosphazene]),[3] and compound **1a**, we have been able to investigate the solid-state electrochemistry of **1a** and **2a**, Scheme I. Such solid-state microelectrochemical systems have been pioneered by Murray and coworkers.[4]

Complex **1a** was isolated as a microcrystalline solid from the reaction of ferrocenylphosphinimine, $(FcN{=}PPh_3)_2$,[5] and $Fe_2(\mu\text{-}CH_2)(CO)_8$[6] and has spectral features similar to those of **1b**

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(1) (a) Mirkin, C. A.; Lu, K.-L.; Geoffroy, G. L.; Rheingold, A. L.; Staley, D. L. *J. Am. Chem. Soc.* **1989**, *111*, 7279. (b) Mirkin, C. A. Ph.D. Thesis, Pennsylvania State University, Dec 1989.

(2) (a) White, H. S.; Kittlesen, G. P.; Wrighton, M. S. *J. Am. Chem. Soc.* **1984**, *106*, 5375. (b) Paul, E. W.; Ricco, A. J.; Wrighton, M. S. *J. Phys. Chem.* **1985**, *89*, 1441. (c) Talham, D. R.; Crooks, R. M.; Cammarata, V.; Leventis, N.; Schloh, M. O.; Wrighton, M. S. *Lower-Dimensional Systems and Molecular Electronics*, Proceedings of NATO ASI, Spetses, Greece; Metzger, R. M., Day, P., Papavassiliou, G., Eds.; Plenum Press, in press.

(3) (a) Allcock, H. R.; Austin, P. E.; Neenan, T. X.; Sisko, J. T.; Blonsky, P. M.; Shriver, D. F. *Macromolecules* **1986**, *19*, 1508. (b) Austin, P. E.; Riding, G. J.; Allcock, H. R. *Macromolecules* **1983**, *16*, 719. (c) Blonsky, P. M.; Shriver, D. F.; Austin, P. E.; Allcock, H. R. *J. Am. Chem. Soc.* **1984**, *106*, 6854. (d) Blonsky, P. M.; Shriver, D. F.; Austin, P. E.; Allcock, H. R. *Solid State Ionics* **1986**, *18*, 258.

(4) (a) Pinkerton, M. J.; Mesl, L. E.; Zhang, H.; Watanabe, M.; Murray, R. W. *J. Am. Chem. Soc.* **1990**, *112*, 3730. (b) Geng, L.; Longmire, M. L.; Reed, R. A.; Parker, J. F.; Barbour, C. J.; Murray, R. W. *Chem. Mater.* **1989**, *1*, 58. (c) Geng, L.; Longmire, M. L.; Reed, R. A.; Kim, M.-H.; Wooster, T. T.; Oliver, B. N.; Egekeze, J.; Kennedy, J. W.; Jorgenson, J. W.; Parker, J. F.; Murray, R. W. *J. Am. Chem. Soc.* **1989**, *111*, 1614.

(5) $FcN{=}PPh_3$: Anal. Calcd: C, 72.89; H, 5.26. Found: C, 72.95; H, 5.25. MS (EI): m/z 461 (M^+). ^1H NMR ($CDCl_3$): δ 7.46-7.43 (m, Ph, 15 H), 3.78 (m, CpH, 2 H), 3.75 (m, CpH, 5 H), 3.73 (m, CpH, 2 H). $E_{1/2}$ = 170 mV vs $AgNO_3$/Ag. Yield = 98%.

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