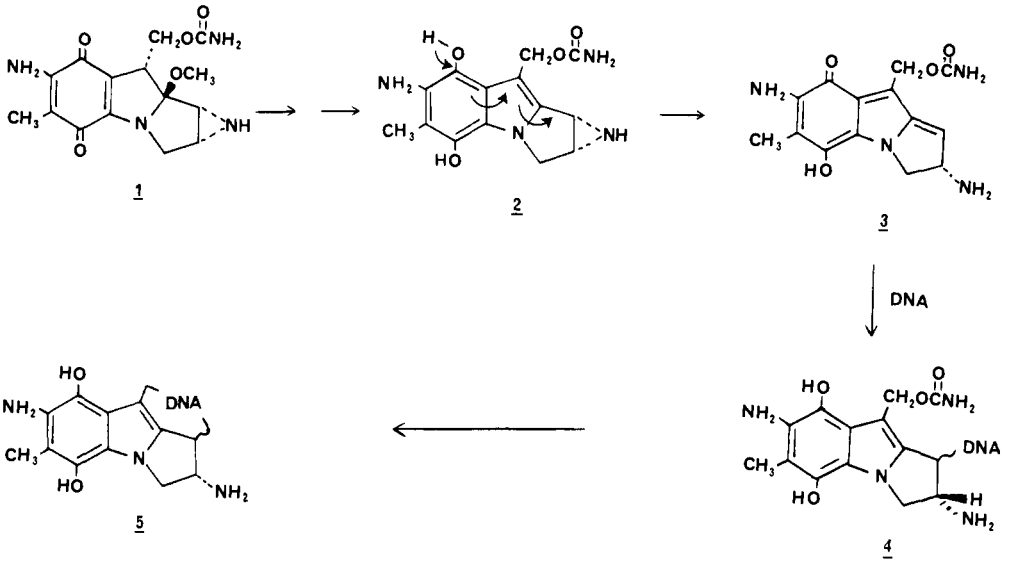
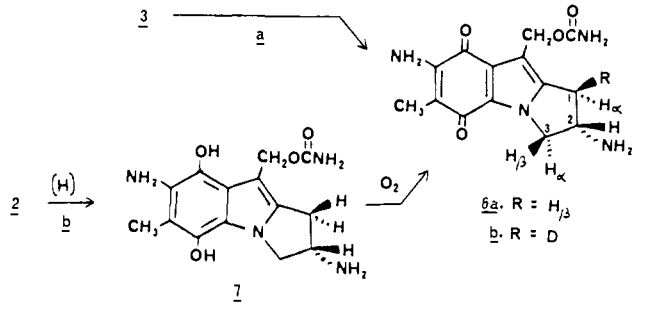
Scheme I



Scheme II



monodeuteration at carbon 1 in **6b** was greater than 80% by ^1H NMR analysis. Moreover, comparison of the ^1H NMR spectrum obtained from the product of this reaction to that obtained in the previous experiment showed the disappearance of the signal at δ 3.10 and the collapse of the doublet of doublets at δ 2.45 to a doublet. Thus, electrophilic substitution at carbon 1 in **1** proceeds with remarkably high stereoselectivity.

The signals at δ 2.45 and 3.10 in **6a** have been tentatively attributed to the C_1H_α and C_1H_β protons, respectively.[16] This assignment is based on analogy to the corresponding chemical shift differences observed for the C_3H_α and C_3H_β protons in a series of mitosenes.[9,17,18] In each case the chemical shift of the β-hydrogen appears downfield ($\Delta\delta \sim 0.5$ ppm) from the corresponding α-hydrogen. Furthermore, a similar analysis of the chemical shift values for the carbon 1 methine hydrogens in isomeric cis- and trans-1,2-disubstituted mitosenes indicated that the carbon 1 proton in the cis adduct (β-H) absorbs downfield ($\Delta\delta \sim 0.15$) from the trans derivative (α-H).[4,6,7,18] This analysis would require a reversal of the assignments previously made for the hydrogens at carbons 1 and 3 in **6a**.[4]

The results of this study provide evidence in favor of the previously proposed route for the formation of **6a**.[4] The high deuterium incorporation observed in the product for the reaction performed in Na_2DPO_4–D_2O suggests that this is the principal pathway leading to **6a**. Moreover, this series of experiments reinforces the overall bioreductive alkylation mechanisms for mitomycin C (**1**).[3d] Our finding that deuterium incorporation occurs selectively in mitomycin C (**1**) from the side opposite the carbon 2 amino group is contrary to the general results observed in nucleophilic substitution reactions that proceed at carbon 1.[5-12] In these latter reactions, substitution yields predominantly the cis adduct. Additional studies concerning this process are in progress.

Acknowledgment. We thank the National Institutes of Health (1R01CA29756) and The Robert A. Welch Foundation for their support of our work. We also express our appreciation to Dr. Douglas Dyckes of this department for help and use of his liquid chromatograph, Dr. Marvin Vestal of this department for his assistance in obtaining mass spectra, and Steven Silber of the Department of Chemistry, Texas A&M University, and Helga Cohen at the NSF sponsored NMR facility (University of South Carolina; CHE78-18723) for running the high-field NMR spectra. Grateful acknowledgment is made to both Dr. W. T. Bradner, Bristol Laboratories, Syracuse, NY, and Dr. I. Matsubara, Kyowa Hakko Kogyo Co., Ltd, Toyko, Japan, for gifts of mitomycin C.

Registry No. 1, 50-07-7; **6a**, 85827-92-5; PtO_2, 1314-15-4.

Supplementary Material Available: Select spectral properties for compounds **6a** and **6b** (1 page). Ordering information is given on any current masthead page.

(16) Karplussian analysis of the vicinal proton couplings in **6a** did not permit conclusions to be made concerning the relative orientations of the substituents at carbon 1 in relation to carbon 2.

(17) Hornemann, U.; Iguchi, K.; Keller, P. J.; Vu, H. M.; Kozlowski, J. F.; Kohn, H., submitted for publication in *J. Org. Chem.*

(18) Bean, M. B.; Kohn, H., submitted for publication in *J. Org. Chem.*

New Stereoselective Method for the Preparation of Vicinal Diamines from Olefins and Cyanamide

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The vicinal diamino group (**1**) is an ubiquitous structural entity in many naturally occurring compounds and medicinal agents. Surprisingly, few general methods exist for the preparation of this group. Most previous synthetic approaches are extensions of procedures developed to introduce a single amino moiety. These generally entail displacement reactions (i.e., with azides,[2] amino groups,[3] N-aromatic substituted amides[4]), rearrangements (i.e., Curtius[5]), and intramolecular cyclizations.[6] Recently, a series

(1) Alfred P. Sloan Foundation Fellow, 1977-1981. Camille and Henry Dreyfus Teacher-Scholar Grant Recipient, 1977-1982.

Scheme I

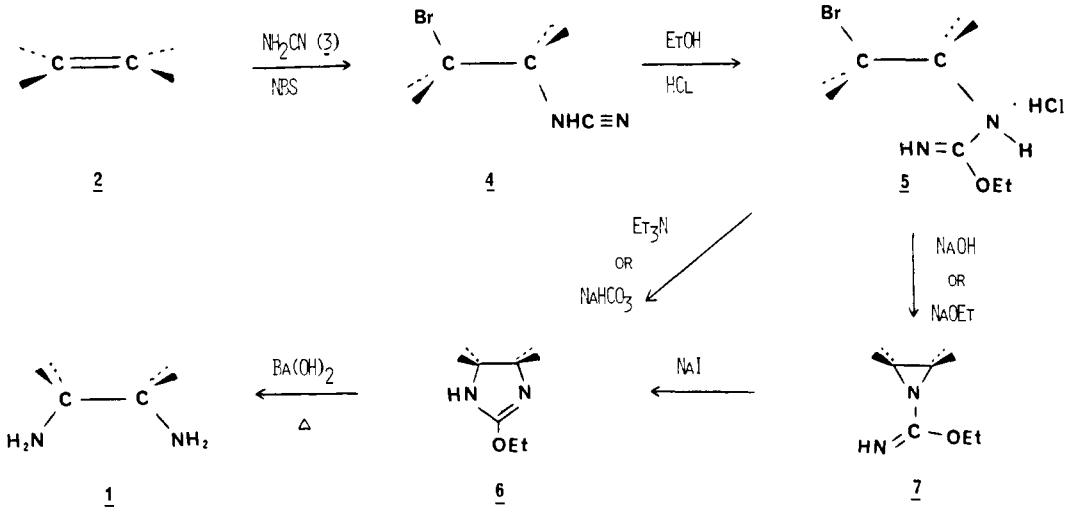

Table I. Vicinal Diamination of Olefins

entry	olefin	product	overall yield,[a] %
1	*trans*-2-butene (8)	*dl*-2,3-diaminobutane[b] (13)	51
2	*cis*-2-butene[c] (9)	meso-2,3-diaminobutane[b] (14)	53
3	1-hexene (10)	1,2-diaminohexane[d] (15)	63
4	cyclohexene (11)	*cis*-1,2-diaminocyclohexane[b] (16)	61
5	*trans*-4-octene (12)	*dl*-4,5-diaminooctane[b] (17)	71

[a] Purified yields. [b] The amine was characterized as the dihydrochloride salt. [c] The commerically available *cis*-2-butene contained approximately 5% of the trans isomer. The diamine 14 obtained after $Ba(OH)_2$ hydrolysis and conversion to the dihydrochloride salt but prior to final purification contained less than 5% of *dl*-2,3-diaminobutane (13). [d] The amine was characterized as the diacetyl derivative.

of procedures have also appeared that employ organometallic reagents[7-10] and select starting materials.[11-13] In many cases, the overall conversion to the desired vicinal diamine compound occurs in low yield, proceeds without stereochemical control,[14] is often accompanied by unwanted byproducts, and requires the generation of potentially hazardous intermediates. Despite these limitations the greatest disadvantage of most methods is that they are not tailored to convert readily accessible chemicals to product. In this communication, we report a direct procedure permitting the synthesis of vicinal diamines (**1**) from unactivated alkenes. The method is simple, inexpensive, and stereospecific and permits access to nitrogen-unsubstituted diamines.[15]

The procedure is outlined in Scheme I.[16] Addition of *N*-bromosuccinimide to an alkene (**2**) and cyanamide (**3**) in dichloromethane at ambient temperatures yields the corresponding alkyl cyanamide **4**.[17] Treatment of this adduct with ethanol and 1 equiv of HCl at 20 °C gives the corresponding protonated isourea salt **5**. Formation of the desired vicinal 1,2-diamino linkage is then accomplished in one of two ways. In the first method, treatment of **5** with mild base (Et_3N, EtOH or $NaHCO_3$, EtOH) produces the imidazoline **6** directly. In the second procedure, more basic conditions (EtONa, EtOH or NaOH, EtOH) are employed leading to the formation of aziridine **7**. Rearrangement of this adduct with NaI in DME, EtOH, or acetone yields **6**. Basic hydrolysis in the last step produces the vicinal diamine **1**. With this synthetic stategy, alkenes **8–12** were successfully transformed to the corresponding diamines **13–17**,[18,19] respectively (Table I). The overall purified yields for **1** ranged from 51% to 71%.

Several facts concerning each step in this procedure are worthy of comment. First, alkenes **8**, **9**, **11**, and **12** underwent reaction with *N*-bromosuccinimide and cyanamide (**3**) to produce a single product. The unsymmetrical alkene 1-hexene (**10**) gave a mixture

(2) (a) Parry, R. J.; Kunitani, M. G.; Vielle, O., III *J. Chem. Soc., Chem. Commun.* **1975**, 321–322. (b) Confalone, P. N.; Pizzolato, G.; Baggiolini, E. G.; Lollar, D.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1975**, *97*, 5936–5938. (c) Swift, G.; Swern, D. *J. Org. Chem.* **1967**, *32*, 511–517 and references therein.

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(5) Confalone, P. N.; Pizzolato, G.; Uskokovic, M. R. *J. Org. Chem.* **1977**, *42*, 135–139. Grüssner, A.; Bourquin, J. P.; Schnider, O. *Helv. Chim. Acta* **1945**, *28*, 517–527. Baker, B. R.; Querry, M. V.; Safir, S. R.; Bernstein, S. *J. Org. Chem.* **1946**, *12*, 138–154 and references therein.

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(7) (a) Barluenga, J.; Alonso-Cires, L.; Ansenio, G. *Synthesis* **1979**, 962–964. (b) Gômez Aranda, V.; Barluenga, J.; Aznar, F. *Ibid.* **1974**, 504–505. (c) Barluenga, J.; Aznar, F.; Liz, R. *J. Chem. Soc., Chem. Commun.* **1981**, 1181–1182 and references therein.

(8) Bäckvall, J. *Tetrahedron Lett.* **1978**, 163–166 and references therein.

(9) Chong, A. O.; Oshima, K.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 3420–3426 and references therein.

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(11) Sharpless, K. B.; Singer, S. P. *J. Org. Chem.* **1976**, *41*, 2504–2506 and references therein.

(12) Michejda, C. J.; Campbell, D. H. *J. Am. Chem. Soc.* **1974**, *96*, 929–930.

(13) Olsen, R. K.; Hennen, W. J.; Wardle, R. B. *J. Org. Chem.* **1982**, *47*, 4605–4611.

(14) The recent diamination technique of Bergman and co-workers[10] proceeds with moderate stereoselectivity.

(15) Recent approaches provide procedures for the preparation of fully substituted aryl,[9] alkyl, [10] and *N,N*-di-*tert*-butyl[11] vicinal diamines.

(16) A typical experimental procedure for the preparation of vicinal diamines **13**, **15**, and **17** entailed the addition of *N*-bromosuccinimide (1.1 equiv) to a dichloromethane solution containing the alkene (**2**; 1 equiv) and cyanamide (**3**; 4 equiv). The solution was maintained at room temperature (3 days) and then washed with water, dried, and concentrated in vacuo. The bromoalkyl cyanamide **4** was usually of sufficient purity (66–93% yield) for the next step. Analytical samples of these materials, however, could be obtained by distillation. Treatment of **4** with EtOH containing 1 equiv of HCl (20 °C, 6 h) gave **5** in situ. Addition of Et_3N (3 equiv) to the ethanolic solution containing **5** (reflux, 1 h) followed by NaOEt (2 equiv) workup and distillation led to **6** (average yield from **4**, 91%). Alternatively, $NaHCO_3$ (4 equiv) in EtOH (room temperature, 18 h) could be employed in this cyclization step. Basic hydrolysis of **6** with $Ba(OH)_2$ (10 equiv; 120 °C, 18 h) gave diamine **1** (79–99% yield). This synthetic procedure was modified for the preparation of diamines **14** and **16**. Treatment of **5** with stronger bases (EtONa [2 equiv], EtOH, room temperature, 18 h, or NaOH [2 equiv], EtOH, room temperature, 18 h) led to the formation of aziridine **7** after purification by distillation (average yield from **4**, 80%). Stereospecific conversion of **7** to **6** was then accomplished with NaI (2–4 equiv) in DME, EtOH, or acetone (reflux, 2 days). Removal of the solvent followed by trituration of the residue with Et_2O and distillation gave **6** in 83–90% yield.

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of two regioisomers. Second, conversion of the alkyl cyanamide **4** to the imidazoline **6** or aziridine **7** was accomplished without the isolation of the isourea salt **5**. This procedure was one of choice rather than need. Third, satisfactory yields were obtained only for the imidazoline adducts **6** in the cis-alkene series (**9** and **11**) by the initial generation of aziridine **7**.[20] Both aziridine ring formation (**5** → **7**) and rearrangement to the imidazoline[21] (**7** → **6**) proceeded stereospecifically. Fourth, the ring-cleavage reaction in the final step can be readily accomplished with $Ba(OH)_2$.[22]

The synthetic technology described herein readily permits stereospecific incorporation of the key vicinal diamino group within the framework of readily accessible molecules. Our approach should compliment existing diamination procedures. Moreover, useful routes for the preparation of both functionalized aziridines **7** and imidazolines **6** have also been developed. Research is now actively in progress to elaborate this method.

Acknowledgment. We thank the National Institutes of Health (Grant NS15604) and The Robert A. Welch Foundation for their support of our research program.

Registry No. 3, 420-04-2; (±)-*trans*-**6** (4,5-dimethyl), 85782-25-8; *cis*-**6** (4,5-dimethyl), 85782-26-9; **6** (4-butyl), 85782-27-0; (±)-*trans*-**6** (4,5-dipropyl), 85782-29-2; *cis*-**7** (dimethyl), 85782-30-5; **8**, 624-64-6; **9**, 590-18-1; **10**, 592-41-6; **11**, 110-83-8; **12**, 14850-23-8; **13**, 20699-48-3; **13**·2HCl, 66427-25-6; **14**, 20759-15-3; **14**·2HCl, 28971-67-7; **15**, 13880-27-8; **15** (diacetyl), 85782-33-8; **16**, 1436-59-5; **16**·2HCl, 10027-80-2; **17**, 4853-59-2; **17**·2HCl, 85782-34-9; NBS, 128-08-5; (±)-(*R**,*S**)-(3-bromo-2-butyl)cyanamide, 85782-20-3; (*R**,*R**)-(3-bromo-2-butyl)cyanamide, 85782-21-4; (1-bromo-2-hexyl)cyanamide, 85782-22-5; (2-bromohexyl)cyanamide, 85782-32-7; *trans*-(2-bromocyclohexyl)-cyanamide, 85782-23-6; (±)-(*R**,*S**)-(5-bromo-4-octyl)cyanamide, 85782-24-7; 7-ethoxycarbimidoyl-7-azabicyclo[4.1.0]heptane, 85782-31-6; *cis*-2-ethoxy-3a,4,5,6,7,7a-hexahydrobenzimidazole, 85782-28-1.

Supplementary Material Available: Complete physical and spectral properties observed for all new compounds reported herein (8 pages). Ordering information is given on any current masthead page.

(18) Satisfactory spectral (^1H NMR, ^{13}C NMR, IR, and MS) data were obtained for all compounds in this procedure. Analytical (elemental analysis or high-resolution MS) data in agreement with the proposed structures were obtained for all new compounds except for the bromocyanamide derived from **10**. See supplementary material for details.

(19) (a) Strack, E.; Schwaneberg, H. *Chem. Ber.* **1934**, *67*, 1006-1011. (b) Minisci, F.; Galli, R.; Cecere, M. *Gazz. Chim. Ital.* **1964**, *94*, 67-90. (c) Brill, E.; Schultz, H. P. *J. Org. Chem.* **1963**, *28*, 1135-1137.

(20) Treatment of the protonated isourea salts derived from **9** and **11** with Et_3N or $NaHCO_3$ led to multiple products (TLC analysis).

(21) Variants of this stereospecific reaction have been previously reported; see: Heine, H. W.; Bender, H. S. *J. Org. Chem.* **1960**, *25*, 461-463. Dermer, O. C.; Ham. G. R. "Ethylenimine and Other Aziridines"; Academic Press: New York, 1969; p 283, and references therein.

(22) Cleavage of the imidazoline ring **6** can also be accomplished with 30% aqueous H_2SO_4 (reflux, 18 h).

Iron(II) Octaethylchlorin: Structure and Ligand Affinity Comparison with Its Porphyrin and Isobacteriochlorin Homologues

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A variety of heme-containing oxidoreductase enzymes[1-6] do not contain iron porphyrins but instead contain iron complexes of chlorins[7] or isobacteriochlorins[7] (hereafter collectively referred to as hydroporphyrins). The discovery of iron hydroporphyrins in these enzymes has prompted the examination of the properties of series of iron porphyrins, chlorins, and isobacteriochlorins[8-10] having identical or very similar peripheral substitution. To ascertain whether a given prosthetic group is optimally suited for a particular chemical task, it is necessary (although not sufficient[11]) to discover what features of the chemistry of iron hydroporphyrins differ from iron porphyrins. Metal-centered properties, such as Fe(II)/Fe(III) potentials,[8,9] CO stretching frequencies of carbonylated complexes,[9] and CO affinities of four-coordinate derivatives,[10] are not significantly macrocycle dependent. Here we report the first structure of an iron chlorin, Fe(OEC),[12] and show that the affinity for weak ligands, such as THF or ethanethiol (EtSH), is strongly macrocycle dependent. We further suggest this dependence to be a manifestation of structural relationships among the porphyrins and the hydroporphyrins.

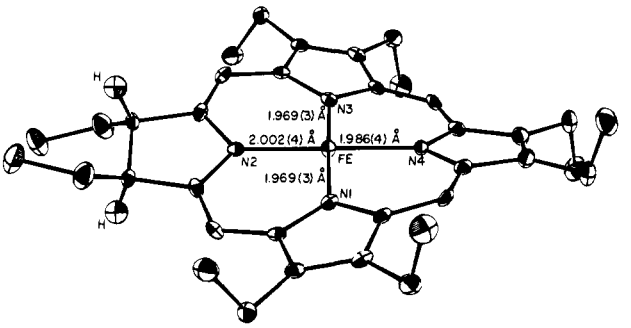

Figure 1. Drawing of the structure of Fe(OEC). Hydrogen atoms, except the two on the pyrroline C_b atoms, have been omitted for clarity. The pyrrole rings containing atoms N1 and N3 are crystallographically related by the 2-fold axis passing through atoms N2, Fe, and N4. Probability ellipsoids are drawn at the 50% level.

(1) (a) Siegel, L. M.; Singer, T. P.; Ondarza, R. N., Eds. "Mechanisms of Oxidizing Enzymes"; Elsevier: New York, 1978; pp 201-13, and references therein. (b) Janick, P. A.; Siegel, L. M. *Biochemistry* **1982**, *21*, 3538-47. (c) Krueger, R.; Siegel, L. M. *Ibid.* **1982**, *21*, 2892-904. (d) Siegel, L. M.; Rueger, D. C.; Barber, M. J.; Krueger, R. J.; Orme-Johnson, N. R.; Orme-Johnson, W. H. *J. Biol. Chem.* **1982**, *257*, 6343-50.

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(6) Brittain, T.; Greenwood, C.; Barber, D. *Biochim. Biophys. Acta* **1982**, *705*, 26-32 and references therein.

(7) Porphyrins that contain two reducing equivalents (hydrogen atoms or alkyl groups) across the vicinal C_b atoms of a single pyrrole ring are called chlorins. Porphyrins that contain two adjacent reduced pyrrole rings are called isobacteriochlorins.

(8) (a) Stolzenberg, A. M.; Spreer, L. O.; Holm, R. H. *J. Chem. Soc., Chem. Commun.* **1979**, 1077-8. (b) Richardson, P. F.; Chang, C. K.; Hanson, L. K.; Spaulding, L. D.; Fajer, J. *J. Phys. Chem.* **1979**, *83*, 3420-24. (c) Chang, C. K.; Fajer, J. *J. Am. Chem. Soc.* **1980**, *102*, 848-51. (d) Chang, C. K.; Hanson, L. K.; Richardson, P. F.; Young, R.; Fajer, J. *Proc. Natl. Acad. Sci.* U.S.A. **1981**, *78*, 2652-56.

(9) Stolzenberg, A. M.; Strauss, S. H.; Holm, R. H. *J. Am. Chem. Soc.* **1981**, *103*, 4763-78.

(10) Strauss, S. H.; Holm, R. H. *Inorg. Chem.* **1982**, *21*, 863-8.

(11) Ibers, J. A.; Holm, R. H. *Science* (*Washington, D.C.*) **1980**, *209*, 223-35.

(12) Abbreviations: OEP, 2,3,7,8,12,13,17,18-octaethylporphyrinato dianion; OEC, *trans*-7,8-dihydro-2,3,7,8,12,13,17,18-octaethylporphyrinato dianion; OEiBC, 2,3,7,8-tetrahydro-2,3,7,8,12,13,17,18-octaethylporphyrinato dianion, a mixture of the trans,trans,trans and trans,cis,trans isomers; TPP, 5,10,15,20-tetraphenylporphyrinato dianion; TMP, 5,10,15,20-tetramethylporphyrinato dianion; TMC, 7,8-dihydro-5,10,15,20-tetramethylphorphyrinato dianion; P = OEP, OEC, or OEiBC.

0002-7863/83/1505-4108$01.50/0