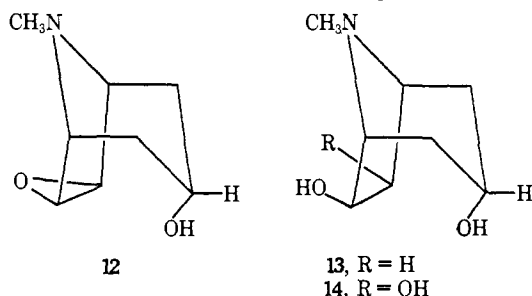


of tropinone (6) with either ordinary hydride reagents ( $\text{LiAlH}_4$ ,  $\text{NaBH}_4$ , etc.) or dissolving metals is known to give the  $\beta$  epimer **8** preferentially.<sup>14</sup> Equilibrium conditions also lead to the thermodynamically more stable isomer **8**.<sup>14</sup> Only the catalytic reduction has been employed for the selective production of the  $\alpha$  epimer **7**.<sup>15, 16</sup>

Synthetic methods for converting the key intermediate **10** to a variety of naturally occurring alkaloids have already been established.<sup>3</sup> Scopine (**12**), tropane-



diol (**13**), and telodine (**14**) which bear an oxygen function(s) at the C-6 (and C-7) position have become readily accessible. Thus the present method marks the realization of a novel, general synthesis of tropane family. Attractive features of the route outlined herein include (1) the directness, (2) the ready, economical availability of the starting materials, (3) the efficiency of the general synthesis of various alkaloids *via* a single, common intermediate,<sup>17</sup> and (4) the flexibility which allows the preparation of a number of artificial analogs not occurring in plant tissues.<sup>18</sup> Further refinements of the procedure are in progress.

**Acknowledgment.** Partial financial support from the Takeda Science Foundation is acknowledged.

(14) (a) R. Mirza, *Nature (London)*, **170**, 630 (1952); (b) A. H. Beckett, N. J. Harper, A. D. J. Balon, and T. H. E. Watts, *Tetrahedron*, **6**, 319 (1959).

(15) L. C. Keagle and W. H. Hartung, *J. Amer. Chem. Soc.*, **68**, 1608 (1946).

(16) Reduction of **6** with DIBAH under the comparable conditions gave a 97:3 mixture of **7** and **8**.

(17) The well-known Robinson procedure failed to prepare **2**: J. Kehrle and P. Karrer, *Helv. Chim. Acta*, **37**, 484 (1954); A. Stoll and E. Jucker, *Chimia*, **9**, 25 (1955). Direct synthesis of scopinone by this method was also unsuccessful.

(18) For instance, tropanes having alkyl groups at C-2 and C-4 positions are easily obtainable by the use of dibromo ketones having long alkyls.<sup>1</sup>

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### A Novel Isoquinoline Alkaloid Group. The Aporphine-Pavine Dimers<sup>1</sup>

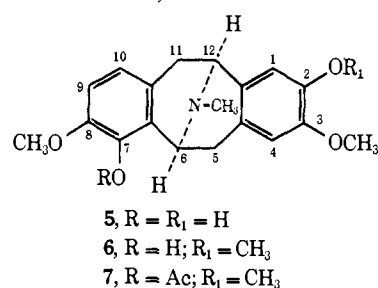
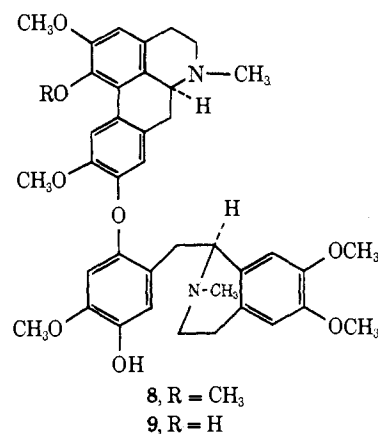
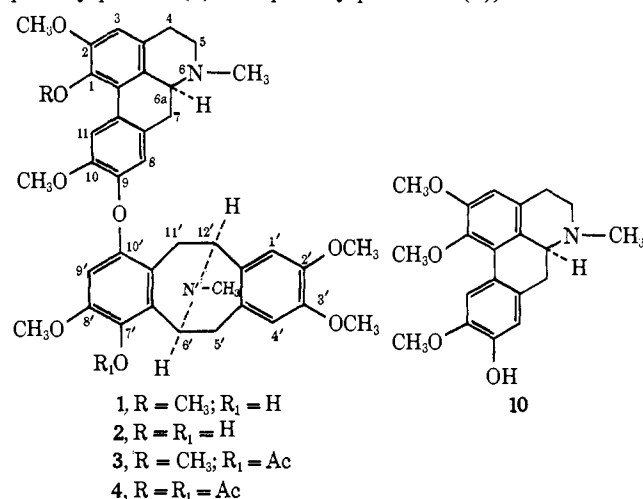
Sir:

Within the complex skein of isoquinoline alkaloids, the aporphine-benzylisoquinoline dimers have so far been considered representatives of a terminal stage of development in the biogenetic tree.<sup>2</sup> We now wish to

(1) This research was supported by Grant CA-11450 from the National Institutes of Health. The authors are grateful to Professors J. Slavik and F. R. Stermitz for alkaloidal samples. All compounds were analyzed by high and low resolution mass spectroscopy. Nmr spectra were obtained in  $\text{CDCl}_3$ , CD curves in MeOH.

(2) For a discussion of the chemistry of isoquinoline alkaloids see M. Shamma, "The Isoquinoline Alkaloids," Academic Press, New York, N. Y., 1972.

report the isolation and structural elucidation of pennsylvavine (**1**) and pennsylvavoline (**2**), the first two



examples of a new group of dimeric alkaloids, the aporphine-pavines, probably derived from aporphine-benzylisoquinolines and thus extending the biogenetic locus.

The giant meadow rue, *Thalictrum polygamum* Muhl. (Ranunculaceae), endemic throughout Pennsylvania, yielded the weakly basic and monophenolic pennsylvavine (**1**), mp 122–123° (ether),  $[\alpha]^{25}_D -174^\circ$  (c 0.6, MeOH). The uv spectrum,  $\lambda_{\text{max}}^{\text{EtOH}}$  230, 280 sh, 288, 308 sh, and 320 sh nm (log  $\epsilon$  4.62, 4.38, 4.40, 4.23, and 4.15), was essentially that of a 1,2,9,10-tetrasubstituted aporphine (280, 308, and 320 nm) superimposed on that of a pavine or isopavine (288 nm).<sup>3</sup>

The mass spectrum of **1** (Scheme I) revealed a parent peak,  $M^+$  (R = CH<sub>3</sub>, R<sub>1</sub> = H,  $m/e$  680, 36%,  $\text{C}_{40}\text{H}_{44}\text{N}_2\text{O}_8$ ),<sup>4</sup> and a base peak E ( $m/e$  204, 100%,  $\text{C}_{12}\text{H}_{14}\text{NO}_2$ ).

(3) Among monomeric isoquinoline alkaloids, only pavines and isopavines show strong and selective absorption near 288 nm, see ref 2, p 112.

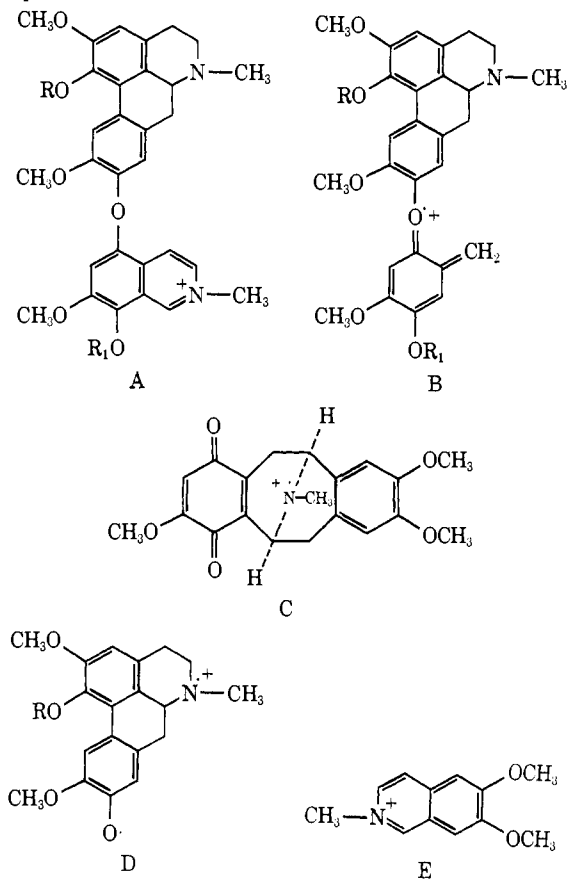
(4) The parent peak,  $M^+$ , for a monophenolic aporphine-benzylisoquinoline dimer of the thalicarpine series is  $m/e$  682; cf. M. Shamma, S. S. Salfgar, and J. L. Moniot, *Tetrahedron Lett.*, 1859 (1973).

Table I. Nmr Spectra of Alkaloids and Their Acetates at 60 MHz ( $\delta$ )

	N-Me	N'-Me	O-Methyl groups					Aromatic hydrogens					Methine hydrogens			
			C-1	C-10	Other			C-9'	Other			C-11	C-6'	C-12'		
Pennsylvavine (1)	2.50	2.57	3.71	3.91	3.76	3.76	3.78	3.88	6.23	6.48	6.48	6.52	6.60	8.15	4.50 <sup>a</sup>	4.06 <sup>a</sup>
Pennsylvavine acetate (3)	2.49	2.55	3.70	3.90	3.68	3.77	3.78	3.84	6.43	6.48	6.46	6.51	6.60	8.15	4.35 <sup>a</sup>	4.15 <sup>a</sup>
Pennsylvavoline (2)	2.48	2.55		3.91	3.75	3.78	3.78	3.91	6.26	6.45	6.49	6.55	6.55	8.14	4.43 <sup>a</sup>	4.01 <sup>a</sup>
Pennsylvavoline diacetate (4)	2.50	2.55		3.86	3.67	3.78	3.79	3.86	6.42	6.46	6.52	6.56	6.66	7.60	4.21 <sup>a</sup>	4.11 <sup>a</sup>
Platynerine (6)		2.53			3.75	3.76	3.83		6.66 <sup>b</sup>	6.45	6.46 <sup>b</sup>		6.61		4.40 <sup>a</sup>	4.00 <sup>a</sup>
Platynerine acetate (7)		2.53			3.76	3.76	3.83		6.81	6.46	6.81		6.61		4.23 <sup>a</sup>	4.11 <sup>a</sup>

<sup>a</sup> dd,  $J = 6$  Hz. <sup>b</sup> dd,  $J = 9$  Hz.

Scheme I. Mass Spectral Fragmentation of Aporphine-Pavine Dimers



The spectrum was indicative of a trimethoxylated aporphine bonded through a diaryl ether bridge to a trimethoxylated and monophenolic pavine, with fragments D ( $R = \text{CH}_3$ ,  $m/e$  340, 20%,  $\text{C}_{20}\text{H}_{22}\text{NO}_4$ ) and C ( $m/e$  355, 28%,  $\text{C}_{20}\text{H}_{21}\text{NO}_5$ ) corresponding to cleavages on either side of the diaryl oxygen bridge.<sup>5</sup> The presence of ions A ( $R = \text{CH}_3$ ,  $R_1 = \text{H}$ ,  $m/e$  529, 22%,  $\text{C}_{31}\text{H}_{33}\text{N}_2\text{O}_6$ ) and B ( $R = \text{CH}_3$ ,  $m/e$  475, 5%,  $\text{C}_{28}\text{H}_{29}\text{NO}_6$ ) showed that the pavine moiety of pennsylvavine could undergo fission by two analogous pathways to yield either fragment B plus the base ion E or fragment A which contains both nitrogen atoms. Less intense ions were also present at  $m/e$  649, 648, and 637 for the loss of  $\text{CH}_3\text{NH}_2$ ,  $\text{CH}_3\text{NH}_3$ , and  $\text{CH}_3\text{N}=\text{CH}_2$  from  $\text{M}^+$ . The mass spectra of both aporphines and isopavines show ions for  $\text{M}^+ - \text{CH}_3\text{N}=\text{CH}_2$ , but not for  $\text{M}^+ -$

(5) The stronger intensity of fragment C as compared to that of D must be due to stabilization of the former ion by the *p*-quinoidal system.

$\text{CH}_3\text{NH}_2$  or  $\text{M}^+ - \text{CH}_3\text{NH}_3$ , so that ions  $m/e$  649 and 648 are indicative of a pavine moiety.

The nmr spectrum of pennsylvavine (1) (Table I) contained singlets for a C-1 methoxyl, a C-10 methoxyl, and a C-11 proton of an aporphine system,<sup>4</sup> two *N*-methyls, a phenolic exchangeable proton at  $\delta$  5.90, and four other *O*-methyl groups and five other aromatic protons. The most distinctive feature of the spectrum was two one-proton low field doublets at  $\delta$  4.06 and 4.50 ( $J = 6$  Hz), the same pattern as observed for the bridgehead protons at C-6 and C-12 of the unsymmetrically substituted pavines munitagine (5) and platynerine (6).<sup>6</sup>

Comparison of the nmr spectrum of pennsylvavine acetate (3),  $\text{C}_{42}\text{H}_{46}\text{N}_2\text{O}_9$ , mp 203–204° (ether),  $\nu_{\text{max}}^{\text{CHCl}_3}$  1760  $\text{cm}^{-1}$ , with that of 1 showed that in the former only one aromatic proton signal (C-9') had shifted downfield ( $\delta$  6.23  $\rightarrow$  6.43), and the magnitude of that shift (0.2 ppm) was indicative of a meta relationship to the acetate group.<sup>7</sup> A telling feature of the nmr spectrum of the acetate 3 was the upfield shift to  $\delta$  4.35 observed for the  $\delta$  4.50 doublet in the spectrum of 1, denoting a close spatial relationship between the phenolic hydroxyl and the C-6' bridgehead hydrogen in 1. Indeed, comparison of the nmr spectra of platynerine (6) and its acetate 7 (Table I) showed that the C-6 proton signal was also shifted upfield ( $\delta$  4.40  $\rightarrow$  4.23) upon acetylation.<sup>8</sup>

A companion alkaloid found in the same plant is the slightly more polar pennsylvavoline (2),  $[\alpha]_{\text{D}}^{25} - 245^\circ$  ( $c$  0.66, MeOH), mp 145–146° (ether),  $\lambda_{\text{max}}^{\text{EtOH}}$  230, 280 sh, 288, 306 sh, and 320 sh nm ( $\log \epsilon$  4.47, 4.06, 4.13, 4.01, and 3.96), whose mass spectrum paralleled that of 1. While ions C (25%) and E (100%) were the same as in the spectrum of 1, those ions assigned to fragments containing the aporphine unit ( $R = \text{H}$ ) were 14 mass units lower, e.g.,  $\text{M}^+$  ( $m/e$  666, 10%,  $\text{C}_{39}\text{H}_{42}\text{N}_2\text{O}_8$ ), D ( $m/e$  326, 22%,  $\text{C}_{19}\text{H}_{20}\text{NO}_4$ ), A ( $m/e$  515, 14%,  $\text{C}_{30}\text{H}_{31}\text{N}_2\text{O}_6$ ), and B ( $m/e$  461, 18%,  $\text{C}_{27}\text{H}_{27}\text{NO}_6$ ). The nmr spectra of 1 and 2 (Table I) were exceedingly similar, the only divergence being the absence, in the spectrum of 2, of the  $\delta$  3.71 singlet for the C-1 methoxyl.<sup>4,9</sup>

Pennsylvavoline diacetate (4),  $\text{C}_{43}\text{H}_{46}\text{N}_2\text{O}_{10}$ , mp 188–189° (ether),  $\nu_{\text{max}}^{\text{CHCl}_3}$  1770 and 1765  $\text{cm}^{-1}$ , exhibited an nmr spectrum (Table I) which as expected included an

(6) The signals for the bridgehead protons at C-6 and C-12 of the symmetrically substituted pavines argemone and norargemone are coincident near  $\delta$  4.0: F. R. Stermitz and J. N. Seiber, *J. Org. Chem.*, 31, 2925 (1966).

(7) R. J. Highet and P. F. Highet, *J. Org. Chem.*, 30, 902 (1965).

(8) The nmr spectra of nor- and bisnorargemone and their respective acetates revealed no upfield shifts for the bridgehead proton signals.

(9) P. L. Schiff, Jr., and R. W. Doskotch, *Lloydia*, 33, 403 (1970); M. Shamma and J. L. Moniot, *Tetrahedron Lett.*, 775 (1973).

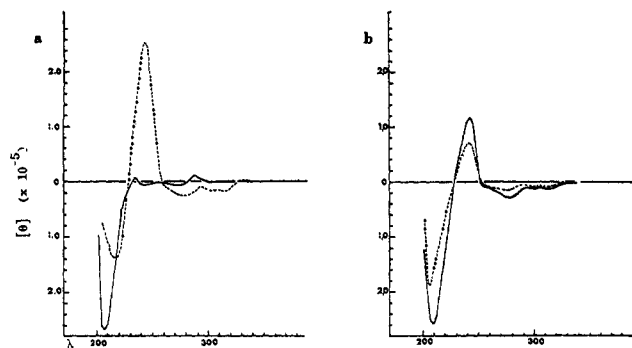


Figure 1. CD curves for: a, platycerine acetate (—), *N*-methyl-laurotetanine (10) (---); b, pennsylvanine (—), equimolar mixture of platycerine acetate and *N*-methyl-laurotetanine (---).

upfield shift of the C-6' bridgehead proton doublet to  $\delta$  4.21, and a still larger upfield shift of the C-11 proton signal to  $\delta$  7.60 due to the presence of acetoxy at C-1.<sup>9</sup>

The absolute configurations of **1** and **2** were determined by the aromatic chirality method.<sup>10</sup> The strong extrema at 242(+) and 209(−) nm in the CD curve of **1** (Figure 1) are associated with the <sup>1</sup>B transitions of the aporphine and pavine moieties, respectively, and lead to configurational assignments as shown in **1**.<sup>11</sup> The sum of the individual curves for **7** and **10** (Figure 1) shows no major deviation from that obtained for **1**. Additionally, the CD curve of **2** was virtually superimposable on that of **1**.

A felicitous event was the further isolation from *T. polygamum* of two additional alkaloids, (+)-pennsylvanine (**8**) and (+)-pennsylvanamine (**9**),<sup>12</sup> belonging to the (+)-thalicarpine series in which the absolute configurations of both asymmetric centers have been established. Comparison of structures **1**, **2**, **8**, and **9** furnishes *prima facie* evidence that in the plant alkaloids **8** and **9** could act as the biogenetic precursors of **1** and **2**, respectively.<sup>13</sup>

(10) N. Harada, K. Nakanishi, and S. Tatsuoka, *J. Amer. Chem. Soc.*, **91**, 5896 (1969).

(11) M. Shamma, J. L. Moniot, W. K. Chan, and K. Nakanishi, *Tetrahedron Lett.*, 4207, 3425 (1971).

(12) Alkaloids **8** and **9** will be discussed in a separate paper. Whenever a phenolic function is present at C-1 of an aporphine, this species whether monomeric or dimeric tends to oxidize in a protonic solvent and turn green (see ref 2, p 205). Alkaloids **2** and **9** showed such behavior.

(13) Conclusive evidence concerning the exact biogenesis of the aporphine-pavine dimers can come only from *in vivo* experiments using labeled precursors.

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Received February 1, 1974

### Stabilization of High Formal Oxidation States of the First-Row Transition Metal Series by *o*-Phenylenebis(dimethylphosphine)

Sir:

Primarily due to the investigations of Nyholm and his collaborators, the compound *o*-phenylenebis(dimethylarsine), *o*-C<sub>6</sub>H<sub>4</sub>{As(CH<sub>3</sub>)<sub>2</sub>}<sub>2</sub>, diars, has proved to be one of the most versatile ligands in coordination chemistry, capable of stabilizing transition metal ions in a variety of often unusual formal oxidation states and coordina-

tion environments.<sup>1</sup> Much less is known about the coordination chemistry of the analogous di(tertiary phosphine), *o*-C<sub>6</sub>H<sub>4</sub>{P(CH<sub>3</sub>)<sub>2</sub>}<sub>2</sub>,<sup>2-5</sup> diphos, mainly because the ligand is not easy to prepare in reasonable quantity. With the intention of making comparisons of arsenic and phosphorus as donor atoms to transition metal ions in a range of formal oxidation states, we have synthesized diphos in ~20% yield by a published procedure<sup>4</sup> and have examined some of its complexes with first-row transition metal ions of chromium through copper. These are obtained by treatment of the appropriate metal salt with the ligand in alcoholic solution, the cationic derivatives generally being isolated as their perchlorate salts.

Copper(I) forms a white diamagnetic d<sup>10</sup> [Cu(diphos)<sub>2</sub>]<sup>+</sup> species which is oxidized by concentrated nitric acid to the pale yellow diamagnetic square-planar d<sup>8</sup> [Cu(diphos)<sub>2</sub>]<sup>3+</sup> trication. Its perchlorate salt, which behaves as a 3:1 electrolyte in acetonitrile solution<sup>6</sup> ( $\Lambda_M = 360 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$ ), reacts with chloride ion to generate the five-coordinate yellow dication [CuCl(diphos)<sub>2</sub>]<sup>2+</sup>; the conductivity value for this perchlorate salt ( $\Lambda_M = 286 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$ ) falls within the range for 2:1 electrolytes in acetonitrile solution.<sup>5</sup> The less stable diars analogs, yellow [Cu(diars)<sub>2</sub>]<sup>3+</sup> and orange [CuCl(diars)<sub>2</sub>]<sup>2+</sup>, were obtained similarly starting from [Cu(diars)<sub>2</sub>]<sup>+</sup>. These appear to be the first described complexes of formal copper(III) containing tertiary phosphines and arsines. Interestingly, no copper(II) species has been observed in either of these systems.

Like copper(III), isoelectronic nickel(II) gives the diamagnetic yellow square-planar [Ni(diphos)<sub>2</sub>]<sup>2+</sup> and orange five-coordinate [NiX(diphos)<sub>2</sub>]<sup>+</sup> (X = Cl, Br) ions. Oxidation of the latter (X = Cl) with ferric chloride generates the six-coordinate green paramagnetic d<sup>7</sup> nickel(III) species [NiCl<sub>2</sub>(diphos)<sub>2</sub>]<sup>+</sup> [ $\mu_{\text{eff}} = 1.90 \text{ BM}$ ]<sup>7</sup> and with concentrated nitric acid the diamagnetic deep purple formal d<sup>6</sup> nickel(IV) complex [NiCl<sub>2</sub>(diphos)<sub>2</sub>]<sup>2+</sup>. The nickel(III) species also undergoes a reversible, one-electron electrochemical oxidation ( $E = +0.80 \text{ V vs. Ag|AgClO}_4$ ) in acetonitrile to nickel(IV); the reversibility suggests that the integrity of the complex is retained in the two oxidation states. With cobalt, six-coordinate greenish d<sup>7</sup> [CoCl<sub>2</sub>(diphos)<sub>2</sub>]<sup>0</sup> ( $\mu_{\text{eff}} = 1.97 \text{ BM}$ ) and purple d<sup>6</sup> [CoCl<sub>2</sub>(diphos)<sub>2</sub>]<sup>+</sup> (diamagnetic) have been characterized. Further oxidation to a cobalt(IV) species is not observed chemically or electrochemically. Iron(II) affords light green diamagnetic d<sup>6</sup> [FeCl<sub>2</sub>(diphos)<sub>2</sub>]<sup>0</sup>, which is oxidized by ferric chloride to the deep red low-spin d<sup>5</sup> iron(III) complex [FeCl<sub>2</sub>(diphos)<sub>2</sub>]<sup>+</sup> ( $\mu_{\text{eff}} = 2.22 \text{ BM}$ ). This undergoes reversible, one-electron electrochemical oxidation ( $E =$

(1) For a partial listing of diars complexes, see F. P. Dwyer and D. P. Mellor, Ed., "Chelating Agents and Metal Chelates," Academic Press, New York, N. Y., 1964, Chapter 3.

(2) F. A. Hart, *J. Chem. Soc.*, 3324 (1960).

(3) J. Chatt and F. A. Hart, *J. Chem. Soc.*, 1378 (1960).

(4) R. J. H. Clark, R. H. U. Negrotti, and R. S. Nyholm, *Chem. Commun.*, 486 (1966).

(5) We use the abbreviation diphos by analogy with the well-established usage of diars for *o*-C<sub>6</sub>H<sub>4</sub>{As(CH<sub>3</sub>)<sub>2</sub>}<sub>2</sub>, although diphos also conventionally refers to 1,2-bis(diphenylphosphino)ethane, (C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>PCH<sub>2</sub>-CH<sub>2</sub>P(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>.

(6) Di- and trivalent electrolytes exhibit molar conductance values of ~200-300 and ~340-420 ohm<sup>-1</sup> cm<sup>2</sup> mol<sup>-1</sup>, respectively, in acetonitrile.

(7) All reported magnetic susceptibilities were measured by the Gouy method at room temperature. Satisfactory elemental analyses have been obtained for all compounds described herein.