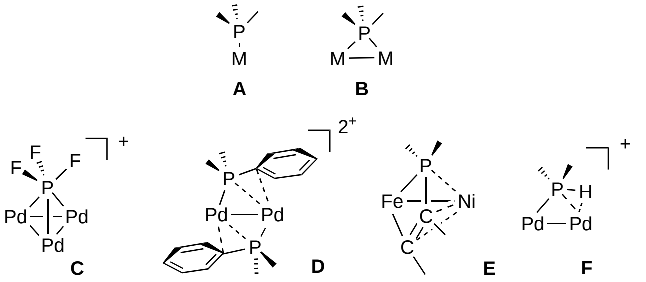
A Rare Phosphane Coordination Mode: A Symmetrically μ_2-Bridging Phosphole in a Dinuclear Palladium(I) Complex**

Mathieu Sauthier, Boris Le Guennic, Valérie Deborde, Loïc Toupet, Jean-François Halet,* and Régis Réau*

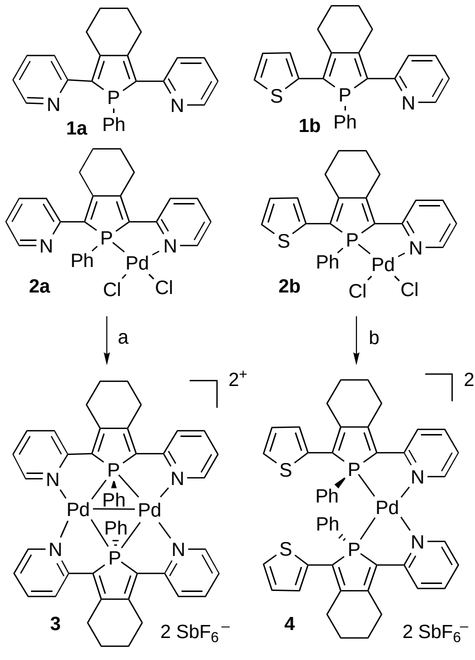
Tertiary phosphanes are the most common ancillary ligands associated with late transition metals in coordination chemistry and homogeneous catalysis. Among the immense variety of known transition metal complexes featuring σ^3,λ^3-phosphane ligands, very few exceptions to the terminal coordination mode **A** emerge (Scheme 1).[1] Trifluorophosphane can behave as a μ_3 donor towards a triangular palladium core (**C**[2a,b]), and extremely rare cases of unsymmetrically semibridging μ_2-P ligands—enforced by an agostic-like interaction of a P–C$_{sp^2}$ (**D**[2c,d] and **E**[2e]) or a P–H bond (**F**[2f–h]) with a coordinatively unsaturated Group 10 metal atom—have been described.[3] The symmetrically bridging μ_2-coordination mode **B**, which is typical for the other well-established transition metal ligands (e.g. CO, carbenes, hydride, alkyl groups), has little precedent for tertiary ligands based on Group 15 atoms. A symmetrically bridging μ_2-stilbine has been reported,[4a] but this coordination geometry has only been predicted by theoretical calculations for phosphanes.[4b–d] Herein, we describe the synthesis of a Pd^I dimer featuring a strongly bonded symmetrically bridging μ_2-phosphole unit, which is the first example of coordination mode **B** for a tertiary phosphane. After submission of this communication, Werner et al. reported dinuclear rhodium complexes with semibridging and bridging phosphane ligands.[18]



Scheme 1. Coordination modes of phosphanes.

Phospholes behave as classical two-electron donor tertiary phosphanes towards late transition metals.[5, 6] We thus became interested in 2-(2-pyridyl)phospholes[7] **1a** and **1b** (see Scheme 2) as new 1,4-chelates combining soft sp^3 phosphorus and hard sp^2 nitrogen centers.

2-(2-Pyridyl)phospholes **1a** and **1b** react with [(CH$_3$CN)$_2$PdCl$_2$] to give rise to complexes **2a** (95% yield) and **2b** (94% yield), respectively, as air-stable solids (Scheme 2).[8] Under classical reducing conditions,[2c] in the presence of two equivalents of NaSbF$_6$, **2a** cleanly afforded the new complex **3** (82% yield), whereas complex **2b** decomposed to give "black palladium" and unidentified P-containing species.



Scheme 2. Synthesis of palladium complexes **3** and **4**. a) H$_2$ (20 bar), HC(OCH$_3$)$_3$, MeOH/CH$_2$Cl$_2$, 2NaSbF$_6$, 25 °C; b) **1b**, 2AgSbF$_6$, CH$_2$Cl$_2$.

Between room temperature and −80 °C, the ^{31}P{^{1}H} NMR spectrum of **3** in CD$_2$Cl$_2$ consists of one sharp line at low field ($\delta = +69.9$), and the simplicity of the ^{13}C{^{1}H,^{31}P} NMR spectrum[8] is in favor of a symmetric structure. An X-ray diffraction study[9] revealed that **3** is a $[\mathrm{Pd}_2(\mathbf{1a})_2]^{2+}\cdot 2\,\mathrm{SbF_6}^-$ complex (Figure 1), with normal van der Waals distances between the dication and the anions. The pseudo-centrosymmetrical dication consists of two planar 16-electron Pd^I atoms (maximum deviation from the mean plane 0.086 Å) joined by a rather long metal–metal single bond (**3**: 2.7870(19); **D**: 2.5833(7),[2c] 2.701(3);[2d] **F**: 2.611(1) Å[2g,h]) and capped by two

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[*] Prof. R. Réau, M. Sauthier, V. Deborde
Organométalliques et Catalyse: Chimie et Electrochimie Moléculaires
UMR 6509 CNRS-Université de Rennes 1
Institut de Chimie de Rennes, Campus de Beaulieu
35042 Rennes Cedex (France)
Fax: (+33) 2-99286939
E-mail: regis.reau@univ-rennes1.fr
Dr. J.-F. Halet, B. Le Guennic
Laboratoire de Chimie du Solide et Inorganique Moléculaire
UMR 6511, CNRS-Université de Rennes 1
Institut de Chimie de Rennes, Campus de Beaulieu
35042 Rennes Cedex (France)
Fax: (+33) 2-99635704
E-mail: halet@univ-rennes1.fr
Dr. L. Toupet
Groupe Matière Condensée et Matériaux
UMR 6626, CNRS-Université de Rennes 1
Campus de Beaulieu, 35042 Rennes Cedex (France)

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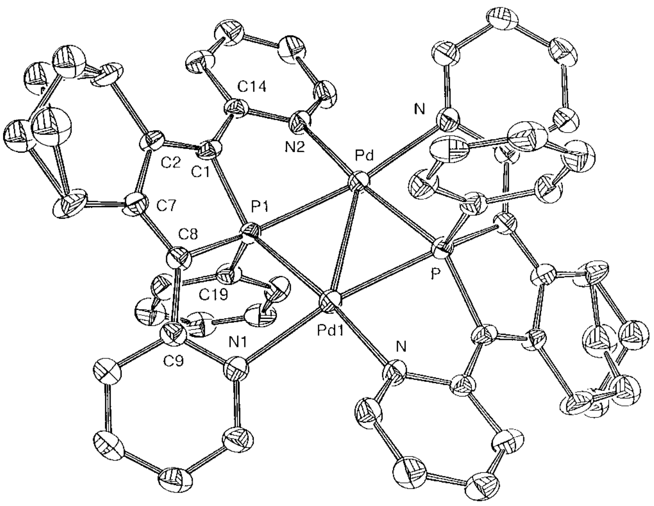

Figure 1. Molecular structure of the cation of complex **3** in the solid state (hydrogen atoms and solvent molecules have been omitted for clarity). Selected bond lengths [Å] and bond angles [°]: P1-C1 1.830(8), P1-C8 1.833(7), P1-C19 1.816(8), Pd1-N 2.162(6), Pd1-N1 2.177(6); P1-Pd1-N1 81.55(16), N1-Pd1-N 91.0(2), N-Pd1-P 80.50(10), P-Pd1-P1 107.40(6).

2,5-bis(2-pyridyl)phospholes **1a** acting as six-electron μ-1κN:1,2κP:2κN donors.

Dinuclear Pd^I complexes involving six two-electron donors arranged about the Pd–Pd bond are well-known,[10] but complex **3** exhibits two striking features: 1) In contrast to most Pd^I dimers,[10, 11] the Pd_2^{2+} core of **3** has an edge-bridged planar structure imposed by the topology of ligand **1a**; 2) the phosphorus atoms of both coordinated phospholes **1a** bridge almost symmetrically the Pd–Pd vector (Pd–P: 2.349(2) and 2.358(2) Å). The Pd atoms are coordinatively saturated, with the shortest Pd–C distance (2.949 Å) being considerably longer than the P–C_{ipso} distances reported in complexes **D** (2.385(16),[2c] 2.336(4) Å[2d]), indicating the lack of any Pd–C interaction.

The NMR data of **3** are in accordance with this solid-state structure. It is quite likely that the rigidity of the tridentate ligand **1a** enforces the symmetric μ_2 coordination mode and prevents any fluxional behavior. Complex **3** appears to be stable in coordinating solvents (CH_3CN, DMF), under a CO atmosphere, and even in the presence of a large excess of PPh_3. To evaluate whether this unusual coordination severely alters the structure of the ligand and/or the metal–heteroatom bonds, the synthesis of a classical monometallic Pd complex featuring two 2-(2-pyridyl)phosphole ligands was undertaken. All attempts to prepare a $[Pd(\mathbf{1a})_2]^{2+}$ complex by abstraction of the Cl^- ligands of **2a** by a silver salt in presence of one equivalent of **1a** failed. In marked contrast, this strategy was successful when complex **2b** and phosphole **1b** were employed (Scheme 2). According to multinuclear NMR spectroscopy,[8] complex **4** (75% yield) was obtained as a single diastereoisomer, and an X-ray diffraction study[9] revealed that, as expected, the P and N atoms are in a mutually *trans* configuration.

For both complexes the phosphole rings are almost planar (maximum deviation from the mean plane: **3**: 0.031; **4**: 0.02 Å) and the dihedral angles between the coordinated pyridine and phosphole moieties are comparable (**3**: 23.5° and 26.8°; **4**: 25.6°). The five-membered metallacycles of complexes **3** and **4** adopt a slightly distorted envelope conformation: The Pd, N, and the two C atoms lie almost in the same plane (maximum deviation: **3**: 0.068; **4**: 0.02 Å) with the P atoms being out of this plane (dihedral angles: **3**: 25.6–25.2°; **4**: 23.5–26.8°). The angles around the Pd atoms and the Pd–N bond lengths are similar for the two complexes (±5° and ±0.05 Å, respectively) and consistent with known literature values.[4c] The molecular geometry about the tetracoordinated P atoms in complex **4** can be regarded as a distorted tetrahedron with small endocyclic C-P-C angles (92.3(3), 91.7(4)°) and large C_{ipso}-P-Pd angles (114.6(3), 116.9(3)°). The bridging P atoms of **3** possess a very similar geometry when the midpoint of the Pd–Pd bond is considered as the coordination center (C-P-C 88.8(4)°, C_{ipso}-P-(Pd–Pd) 116.0°). This comparative study reveals that the symmetric μ_2 bridging mode of the P atoms does not dramatically perturb the structure of the ligand. Furthermore, the coordination spheres of the Pd centers in complexes **3** and **4**, although possessing different oxidation states, appear to be very similar. As expected, the only noticeable discrepancy between the two structures lies in the Pd–P bond distances: Those observed in complex **3** (2.349(2), 2.358(2) Å) are considerably longer than those in complex **4** (2.2494(18), 2.260(2) Å), but shorter than those reported for semibridging phosphanes (**D**: 2.690(4),[2c] 2.753(1),[2d] **F**: 2.393(3) Å[2g,h]).

To elucidate the bonding situation in **3**, extended Hückel (EH) calculations[12] were carried out on the model system $[Pd_2(NH_2)_4(\mu_2\text{-}PH_3)_2]^{2-}$ (**3'**), which is isoelectronic to the dication of complex **3**.[13] The resulting molecular orbital (MO) diagram built up from the interaction of the frontier orbitals (FO) of the dimetallic $[Pd_2(NH_2)_4]^{2-}$ and phosphane moieties is shown in Figure 2. An analysis reveals that the

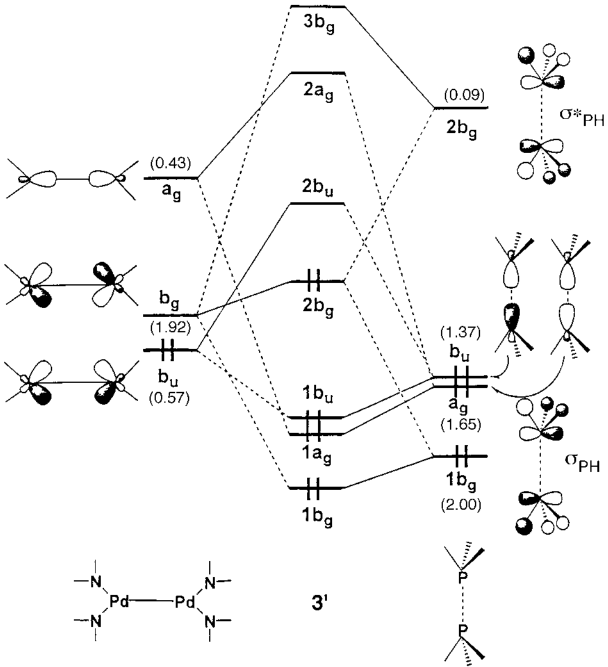

Figure 2. Qualitative MO interaction diagram of **3'**. Symmetry labels are given in C_{2h}. The FO electron occupations after interaction are given in parenthesis.

Pd–Pd and Pd–P bonding is highly delocalized and consists primarily of strong σ-type interactions between phosphane "lone pair" orbitals (a_g and b_u) and metallic orbitals of the same symmetry (σ donation). This bonding is somewhat supplemented by a π-type interaction between one component of the vacant σ^*_{PH} antibonding orbitals of the phosphanes ($2b_g$) and one metallic FO (b_g; back donation, negative hyperconjugation).[14] The latter stabilizing interaction is weakened by a destabilizing interaction between the same metallic FO and a low-lying component of the occupied σ_{PH} bonding phosphane orbitals ($1b_g$). Consequently, this metallic FO is weakly perturbed in energy after interaction and becomes the HOMO of **3′**. The Pd–Pd antibonding character partly explains the rather long Pd–Pd distance measured in complex **3**.[15] This bonding description is fully supported by density functional theory (DFT) calculations[16] carried out on $[Pd(\mathbf{1a})]_2^{2+}$, which indicate that the HOMO is Pd–Pd and Pd–N π-antibonding (Figure 3).

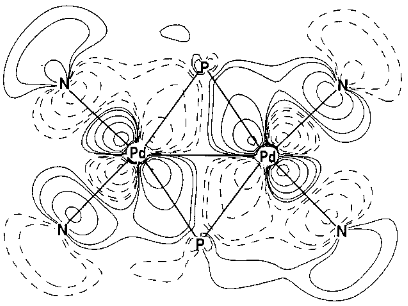

Figure 3. Contour plot of the HOMO (in the Pd_2P_2 plane) of the cation of complex **3**. Contour values are ±0.01, ±0.02, ±0.05, ±0.1, ±0.2, ±0.5 $e^{1/2}bohr^{-3/2}$.

The possibility for a tertiary phosphane to act as a symmetrically bridging ligand opens new perspectives in coordination chemistry for the construction of new architectures and the understanding of important mechanisms such as the intramolecular exchange of phosphane between two metal atoms.[17]

Experimental Section

A solution of **2a** (0.50 g, 0.92 mmol), $NaSbF_6$ (0.49 g, 1.90 mmol), and trimethylorthoformate (1.00 mL, 9.14 mmol) in CH_2Cl_2 (20 mL) and methanol (10 mL) was introduced under argon in a stainless-steel autoclave equipped with a magnetic stirrer. The autoclave was pressurized with H_2 (20 bar), and the solution was stirred for 12 h at room temperature. The autoclave was vented, and the volatile components were removed under vacuum. The brown residue was extracted with CH_2Cl_2 (50 mL), and the solution was concentrated to about 10 mL. After addition of $CHCl_3$ (40 mL), complex **3** precipitated at room temperature as an orange solid (0.53 g, 82% yield). Single crystals suitable for X-ray diffraction were grown from a solution in CH_2Cl_2/CH_3CN/heptane at −20 °C.

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[1] The coordination mode **B** is classical for phosphido groups (R_2P^-) and phosphorus species showing low coordination (phosphinidenes, T-shaped 10-P-3 derivatives, phosphaalkenes). a) K. B. Dillon, F. Mathey, J. F. Nixon, *Phosphorus: The Carbon Copy*, Wiley, Chichester, **1998**; b) D. W. Stephan, *Angew. Chem.* **2000**, *112*, 322; *Angew. Chem. Int. Ed.* **2000**, *39*, 314; c) A. J. Arduengo III, C. A. Stewart, *Chem. Rev.* **1994**, *94*, 1215.

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[8] Selected spectroscopic data (298 K, CD_2Cl_2): **1b**: ^{31}P NMR (81.014 MHz, H_3PO_4 80%): $\delta = +12.6$; **2a**: ^{31}P NMR (81.014 MHz, H_3PO_4 80%): $\delta = +55.2$; **2b**: ^{31}P NMR (81.014 MHz, H_3PO_4 80%): $\delta = +59.1$; **3**: $^{13}C\{^1H,^{31}P\}$ NMR (100.622 MHz, TMS): $\delta = 124.1$ (s, C_{5py}), 124.2 (s, C_{3py}), 127.2 (s, C_{iPh}), 129.3 (s, C_{mPh}), 132.3 (s, C_{pPh}), 133.4 (s, C_{oPh}), 140.6 (s, C_{4py}), 149.0 (PC_{phos}), 150.2 (PCC_{phos}), 151.7 (s, C_{6py}), 151.8 (s, C_{2py}); **4**: ^{31}P NMR (81.014 MHz, H_3PO_4 80%): $\delta = +69.7$; $^{13}C\{^1H\}$ NMR (75.469 MHz, TMS): $\delta = 124.3$ (m, C_{3py}), 125.7 (s, C_{5py}), 128.0, 128.7 (2 × s, C_{4thio} and C_{5thio}), 129.4 (m, C_{3thio}), 141.6 (s, C_{4py}), 151.3 (m, C_{6py}).

[9] X-ray structural analysis: $\mathbf{3}\cdot 2\,CH_3CN\cdot 2\,C_6H_{12}$ ($C_{48}H_{42}N_4P_2Sb_2F_{12}Pd_2\cdot 2\,CH_3CN\cdot 2\,C_6H_{12}$): 0.38 × 0.21 × 0.18 mm, triclinic, space group $P\bar{1}$, $a = 9.389(2)$, $b = 11.793(9)$, $c = 14.079(5)$ Å, $\alpha = 70.33(3)$, $\beta = 88.03(2)$, $\gamma = 79.50(3)^\circ$, $\rho_{calcd} = 1.827\ Mg\,m^{-3}$, $2\theta_{max} = 54^\circ$, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, ω scans, 293 K, 4710 measured reflections, 3468 independent reflections, with $I > 2\sigma(I)$, Lp correction ($\mu = 16.79\ cm^{-1}$), 328 refined parameters with $R1 = 0.0588$ and $wR2 = 0.161$, max./min. residual electron density 1.090/−1.503 e Å^{-3}. Although the carbon atoms of the butyl bridges appear to be disordered, further studies in space group $P1$ show unambiguously that there is no disorder but a difference in the conformation of the six-membered ring. However, in this space group, the pseudo-symmetry of all the other atoms of **3** leads to important correlations, giving unsatisfactory geometry and estimated standard deviations. $\mathbf{4}\cdot 0.5\,C_2H_4Cl_2$ ($C_{46}H_{40}N_2P_2SbF_6PdS_2\cdot 0.5\,C_2H_4Cl_2$): 0.40 × 0.33 × 0.33 mm, triclinic, space group $P\bar{1}$, $a = 13.655(10)$, $b = 14.991(2)$, $c = 16.835(2)$ Å, $\alpha = 108.89(2)$, $\beta = 108.48(3)$, $\gamma = 90.10(3)^\circ$, $\rho_{calcd} = 1.584\ Mg\,m^{-3}$, $2\theta_{max} = 54^\circ$, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, ω scans, 293 K, 12920 measured reflections, 7587 independent reflections with $I > 2\sigma(I)$, Lp correction ($\mu = 15.28\ cm^{-1}$), 645 refined parameters with $R1 = 0.0735$ and $wR2 = 0.2112$, max./min. residual electron density 1.570/−0.971 e Å^{-3}. After Lorentz and polarization corrections, the structures were solved with SIR-97, and refined with SHELX97 by full-matrix least squares on $F2$. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data

Centre as supplementary publication nos. CCDC-149074 (**3**) and -149075 (**4**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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[13] $\mathrm{NH_2^-}$ was used to mimic the pyridine moieties of 2,5-bis(2-pyridyl)-phosphole. The DFT calculations[16] performed on **3'** indicate that the symmetrically bridging coordination of the P atoms is energetically preferred over an unsymmetrical semibridging coordination mode.

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[15] Complex **3** exhibits electronic absorptions at 326 ($\lg\varepsilon = 4.43$), 391 ($\lg\varepsilon = 4.08$), and 446 nm ($\lg\varepsilon = 3.96$) in $\mathrm{CH_2Cl_2}$. However, the absorption of lower energy cannot be unambiguously assigned to a Pd–Pd $\sigma \rightarrow \sigma^*$ excitation because of possible metal–ligand charge transfer bands. For comparison, complex **4** exhibits a maximum electronic absorption at 407 nm ($\lg\varepsilon = 3.96$).

[16] The DFT calculations (E. J. Baerends, D. E. Ellis, P. Ros, *Chem. Phys.* **1973**, *2*, 41) were carried out with the Amsterdam Density Functional (ADF) program (release 2.3, Vrije Universiteit, Amsterdam, The Netherlands, **1997**), using nonlocal exchange (A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098) and correlation (J. P. Perdew, *Phys. Rev. B* **1986**, *33*, 8822; Erratum: J. P. Perdew, *Phys. Rev. B* **1986**, *34*, 7406). Standard ADF STO basis set IV was used. The frozen-core approximation was considered.

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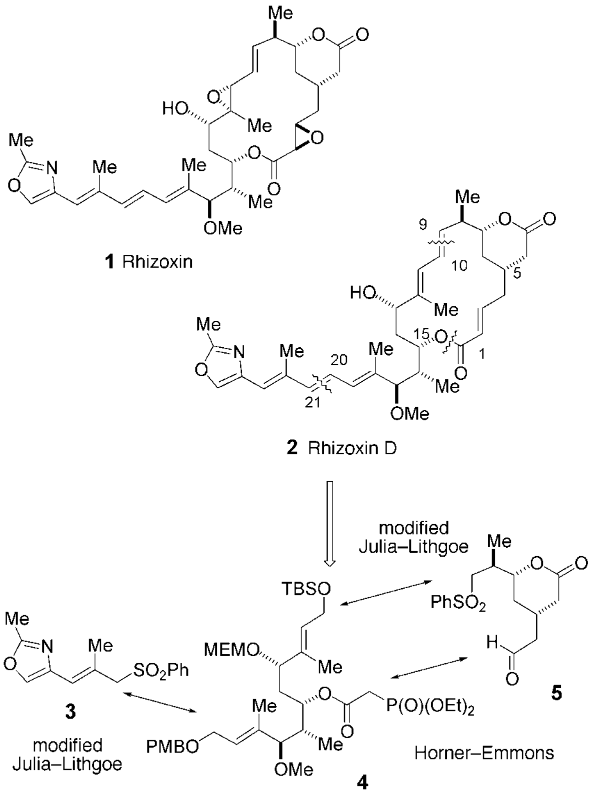
Asymmetric Total Synthesis of Rhizoxin D**

Gary E. Keck,* Carrie A. Wager, Travis T. Wager,
Kenneth A. Savin, Jonathan A. Covel,
Mark D. McLaws, Dhileep Krishnamurthy, and
Victor J. Cee



Scheme 1. Structures of rhizoxin and rhizoxin D and retrosynthesis of the latter (see ref. [6] for abbreviations).

Rhizoxin (**1**, Scheme 1) and five closely related compounds have been isolated from *Rhizopus chinensis* by Iwasaki and co-workers.[1] In addition to antibiotic and antifungal activity, these materials have been shown to possess potent antitumor activity,[2] including activity against vincristine- and adriamycin-resistant cells.[3] These compounds have attracted considerable interest with respect to synthesis, and one total synthesis of rhizoxin has been reported,[4] as well as three syntheses of rhizoxin D (**2**).[5] We describe herein the synthesis of rhizoxin D by an approach utilizing catalytic asymmetric allylation as a key strategic element.

The overall approach to this synthesis is illustrated in Scheme 1 and relied upon disconnections at the C9–C10 and C20–C21 disubstituted alkenes to yield the three major subunits indicated. In the route described herein, both of these alkene linkages are established by a modified Julia–Lithgoe protocol developed previously in our laboratories,[7] and the macrocycle is closed by an intramolecular Horner–Emmons reaction. This strategy provides inherent flexibility in the timing of the necessary operations and also allows for other ring closure options to be investigated using the same basic subunits.

In principle the "lactone" subunit could be utilized as either the sulfone component or the aldehyde subunit in the proposed Julia coupling; the choice shown was made based upon model studies. The synthesis of this subunit used a thermodynamic approach for control of stereochemistry at C5 as we have previously described.[8] Thus, condensation of the aldehyde **6** with the boron enolate of (*S*)-3-(1-oxopropyl)-4-(phenylmethyl)-2-oxazolidinone afforded the aldol product[9] as a single diastereomer, which was reduced with $\mathrm{LiBH_4}$ to afford the diol **7** (Scheme 2). Elaboration to the sulfone **8** followed by oxidative olefin cleavage provided, upon silyation with TBSCl, the all-equatorial protected lactol **9**. The stereochemistry at C5 is thus set in this sequence by the preference

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[*] Prof. G. E. Keck, C. A. Wager, T. T. Wager, K. A. Savin, J. A. Covel, M. D. McLaws, D. Krishnamurthy, V. J. Cee
Department of Chemistry, University of Utah
315 South 1400 East, Rm 2020
Salt Lake City, UT 84112-0850 (USA)
Fax: (+1) 801-581-7055
E-mail: keck@chemistry.utah.edu

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