reduction of the keto group upon treatment with 0.6 equiv of borane in THF at 23 °C for 2 min in the presence of 10 mol % of **2** as catalyst to give the 15-*R* alcohol **5** and the 15-*S* diastereomer **6** in a ratio of 91:9. Under the same conditions but with use of the enantiomer of **2** as catalyst the opposite stereochemical preference was observed with the 15-*S* diastereomer **6** predominating over the 15-*R* form **5** in a ratio of 90:10.[7] In our view this catalytic reduction represents a very practical solution to the problem of controlling C-15 stereochemistry in prostaglandin synthesis.

Recently a series of the racemic *trans*-2,5-diarylfurans has been found to be potent antagonists of platelet activating factor (PAF).[8,9] We report here the first enantioselective route to chiral *trans*-2,5-diarylfurans. Reduction of methyl 3-(3,4-dimethoxybenzoyl)propionate (**7**) with 0.6 equiv of borane and 2 mol % of **2** as catalyst at 0 °C for 30 min was highly selective for the keto function and produced the corresponding *R* secondary alcohol (98%, 95% ee), which upon treatment with 0.2 weight % of sodium hydride in THF at 23 °C for 1 h furnished the *R* lactone **8** (90%), mp 118-119 °C, $[\alpha]^{23}_D$ +17.15° (*c* 2, $CHCl_3$). Reduction of γ-lactone **8** with diisobutylaluminum hydride in toluene at −78 °C afforded the corresponding γ-lactol (88% as a 1:1 mixture of cis and trans isomers), which was converted to the corresponding α-bromo ether by reaction with trimethylsilyl bromide in methylene chloride at −78 °C. Coupling of this bromo ether with 3,4-dimethoxyphenylmagnesium bromide in THF at −100 °C afforded the trans 2*R*,5*R* product **9** selectively (ratio of **9** to the cis isomer, ca. 10:1), mp 115-116 °C, $[\alpha^{23}_D$ +54.2° (*c* 2, $CHCl_3$), in 70% yield. The 2*S*,5*S* enantiomer of **9** was synthesized similarly by using the enantiomer of **2** as catalyst for the CBS reduction of keto ester **7**. To demonstrate generality the same synthetic approach starting from **7** and employing β-napthylmagnesium bromide in the coupling step (86% yield, trans/cis selectivity 18:1) was used for the synthesis of (2*R*,5*R*)-diarylfuran **10**,[8c] mp 106-107 °, $[\alpha]^{23}_D$ +127° (*c* 2, $CHCl_3$). The *S*,*S* enantiomer of **10** was synthesized by a parallel process starting from the *S* enantiomer of **8**. These results demonstrate the outstanding effectiveness of the catalytic and enantioselective CBS reduction in the synthesis of medically interesting compounds such as **9**, **10**, and their enantiomers.[10]

The ligand (*S*)-(−)-2-(diphenylhydroxymethyl)pyrrolidine (DPP) and the *R* enantiomer are readily available from (*S*)- and (*R*)-proline, respectively. However, because (*R*)-proline is expensive, we have developed an alternative and economical route to both ligands. Racemic 2-(diphenylhydroxymethyl)pyrrolidine, mp 82-83 °C, was synthesized from the inexpensive pyroglutamic acid by the sequence (1) esterification with methanol containing 5 mol % hydrogen chloride (from acetyl chloride) at 23 °C for 24 h (95%), (2) reaction with phenylmagnesium chloride in THF at 23 °C for 24 h (70%), and (3) reduction with borane in THF (77%). A solution of the racemic DPP in ethanol was treated with (*S*)-(+)-*O*-acetylmandelic acid to give a solid which by a single recrystallization from methanol-ethanol afforded a salt, mp 226-228 °C, $[\alpha]^{23}_D$ +81.68° (*c* 2, in methanol), from which (*S*)-DPP, $[\alpha]^{23}_D$ −59° (*c* 2 in methanol) (99.3% ee),[11] was obtained (60% of the theoretical yield). The filtrates from the above operations were processed to give free DPP (enriched in the R isomer) which was treated with (*R*)-(−)-*O*-acetylmandelic acid to afford, after one recrystallization as described above, a salt, mp 226-228 °C, $[\alpha]^{23}_D$ −80.8° (*c* 2 in methanol) from which (*R*)-DPP, $[\alpha]^{23}_D$ +59° (*c* 2 in methanol) (99.5% ee),[11] was obtained in 65% yield. Both the resolving agent and unresolved DPP could be recovered efficiently for reuse.

We believe that the CBS methodology for enzyme-like, catalytic enantioselective reduction as elaborated by this research will prove to have many applications. Related research on the catalytic enantioselective addition of carbon to carbonyl groups also shows promise.[12,13]

(6) (a) Corey, E. J.; Albonico, S. M.; Koelliker, U.; Schaaf, T. K.; Varma, R. K. *J. Am. Chem. Soc.* **1971**, *93*, 1491-1493. (b) Corey, E. J.; Becker, K. B.; Varma, R. K. *J. Am. Chem. Soc.* **1972**, *94*, 8616-8618.

(7) The analysis of mixtures of **5** and **6** was performed by HPLC with use of a DuPont Zorbax Sil column (4.6 mm × 25 cm) with 7:3 hexane-THF for elution (at a flow rate of 2 mL/min the 15*S* diastereomer **6** and the 15*R* diastereomer **5** eluted at 9.24 and 12.5 min, respectively.

(8) See: (a) Braquet, P.; Godfroid, J. J. *Trends Pharmacol. Sci.* **1986**, *7*, 397-403. (b) Hwang, S.-B.; Lam, M.-H.; Biftu, T.; Beattie, T. R.; Shen, T.-Y. *J. Biol. Chem.* **1985**, *260*, 15639-15645. (c) Biftu, T.; Hwang, S.-B.; Doebber, T. W.; Beattie, T. R.; Shen, T.-Y. Eur. Pat. Appl. EP 199 324; *Chem. Abstr.* **1987**, *106*, 50026r.

(9) In contrast the cis isomers are inactive as anti-PAF agents.

(10) The biological properties of the chiral 2,5-diarylfurans will be reported separately.

(11) Enantiomeric excess was determined by conversion to the amide using α-methoxy-α-(trifluoromethyl)phenylacetyl chloride and analysis by HPLC (Zorbax Sil column using 5% THF in hexane for elution).

(12) Corey, E. J.; Hannon, F. J. *Tetrahedron Lett.* **1987**, *28*, in press.

(13) This research was assisted financially by grants from the National Science Foundation and the National Institutes of Health.

Models for the Molybdenum–Phosphate Interactions in "Oxo-Type" Molybdoenzymes and Their Cofactors

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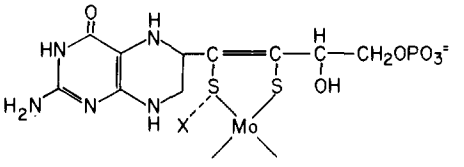
Molybdoenzymes such as xanthine oxidase, sulfite oxidase, and nitrate reductase have been intensively studied in recent years.[1] To date, however, the structures of these metalloproteins and their cofactors remain unsolved. A common cofactor I is proposed to



I

be present in all these molybdoenzymes,[2] and there is mounting chemical evidence that one or more covalently bound phosphate groups exist within ~10 Å of the catalytically active molybdenum atom of these enzymes.[3] Recent ^{31}P NMR studies show that xanthine oxidase contains three moles of acid-dissociable phosphorus per mole of catalytic center.[4] While several laboratories are engaged in research on molybdenum–thiolate[5] and molybdenum–pterin complexes,[6] to date no model compounds are available for molybdenum–phosphate interactions. We report here the syntheses (Scheme I) and properties of three oxo–molybdenum(V) complexes possessing pendant phosphate esters (**5a**, **5b**, **6**) with molybdenum–phosphorus interactions of less than 10 Å.[7]

The precursor Mo(V) complexes (**2a,b** and **4**) are obtained in good yields (50–95%) from the reaction between $LMoOCl_2$ (L = hydrotris(3,5-dimethyl-1-pyrazolyl)borate) and the appropriate hydroxy-substituted catechols in the presence of an equimolar

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(2) Johnson, J. L.; Rajagopalan, K. V. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 6856.

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(6) Burgmayer, S. J. N.; Stiefel, E. I. *J. Am. Chem. Soc.* **1986**, *108*, 8310.

(7) For **5a** and **5b** the Mo···P distance is a function of the rotation of the phosphate ester group about the C(cat)–O bond. The range is 4.1–6.0 Å for **5a** and 5.8–6.6 Å for **5b** as determined by molecular modeling calculations. For **6** the Mo···P distance depends on rotation about the C(cat)–CHMe bond and the CHMe–O bond. The maximum possible Mo···P distance is 6.8 Å, the minimum distance will be determined by repulsions between the phenyl groups of the pendant phosphate ester and the bulky 3,5-dimethylpyrazole rings of L and is 6.0 Å.

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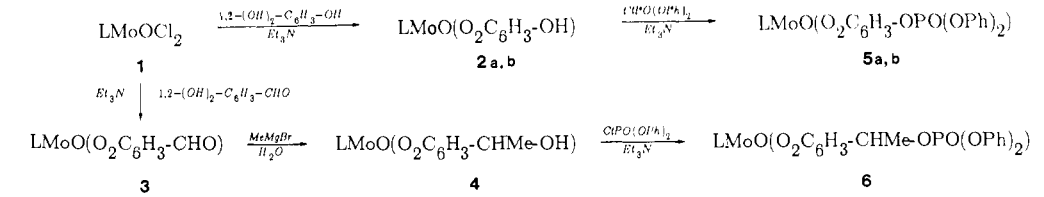
Scheme I



amount of triethylamine in refluxing toluene.[8] Phosphorylation of the free hydroxyl group of **2a,b** and **4** with diphenylchlorophosphate in refluxing toluene in the presence of triethylamine provides **5a,b** and **6** in ~90% yield.[9]

The ^{31}P NMR spectra for **5a,b** and **6** (Figure 1) show substantial differences in both chemical shift and line width. The ^{31}P resonances for **5a** (−12.26 ppm) and **5b** (−15.16 ppm) are deshielded (downfield) relative to $PO(OPh)_3$ at −16.80 ppm. However, the most striking difference between **5a** and **5b** is the large difference in their line widths. The broad line for **5a** (207 Hz) indicates rapid relaxation of the ^{31}P nucleus by the unpaired electron on the Mo(V) center of the complex. For **5b** the broadening is much smaller (24 Hz). The chemical shift of **6** (−4.09 ppm) is significantly more deshielded than **5a**, **5b**, and than free benzyldiphenylphosphate at −11.55 ppm. The line width of **6** (10 Hz) is similar to that of a free phosphate triester, and the relatively poor signal-to-noise ratio for **6** suggests slow relaxation of the ^{31}P nucleus in this compound. The general dependence of the ^{31}P NMR linewidths on the Mo···P distance[7] is consistent with dipolar relaxation being the dominant process, but variations in spin density at the 3- and 4-positions on the catechol ring may also contribute to the observed line widths.

To our knowledge this is the first study of the broadening of ^{31}P NMR resonances by oxo–molybdenum(V) centers in discrete complexes. The observed line widths are consistent with those expected[10] for slow electron relaxation[11] and rapid molecular rotation.

These preliminary results demonstrate that ^{31}P NMR can be used to probe the interaction between an oxo-molybdenum(V) center and a pendant phosphate group and that the ^{31}P chemical shift and line width are both sensitive to the overall structure of the intervening ligand. Thus, ^{31}P NMR holds promise for probing the molybdenum–phosphate interactions of I. Recent EPR studies of solutions of the liberated molybdenum cofactor[12] show that the Mo(V) state of I is experimentally accessible.

The steric constraints of the ligands in **5a,b** and **6** preclude coordination of the phosphate group to the molybdenum atom. However, molecular modeling calculations on the proposed molybdenum cofactor I show that its phosphate group could actually coordinate to the molybdenum atom if a vacant coordination site were available. More detailed NMR studies of these initial models and of other models for the molybdenum–phosphate interactions of I are in progress.

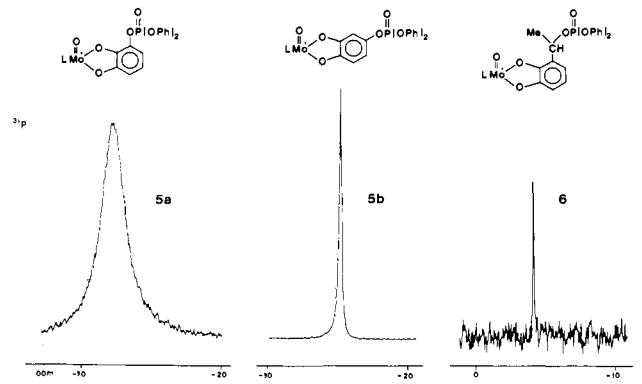


Figure 1. ^{31}P NMR spectra of the Mo(V) complexes **5a**, **5b**, and **6** (43.6 mMol) in $CHCl_3$ at 20 °C recorded on a Bruker WM-250 (4400 scans).

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Supplementary Material Available: Table of infrared data, EPR data, ^{31}P NMR data, elemental analyses, and cyclic voltammetric data (1 page). Ordering information is given on any current masthead page.

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(9) To 1 mmol of the hydroxy-substituted catechol complex (**2a**, **2b** or **4**) dissolved in 30 mL of toluene are added 0.15 mL (1.1 mmol) of triethylamine and 0.23 mL (1.1 mmol) of diphenylchlorophosphate. The mixture is refluxed for 15 h (30 h in the case of **4**), and the products are purified by chromatography on silica gel and recrystallization from dichloromethane/hexane to yield olive-green air stable microcrystals. All compounds give satisfactory elemental analysis. The physical properties—electronic spectra, EPR spectra, IR spectra—are available as Supplementary Material and are nearly identical with those of LMoO(cat).[8]

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σ-Assisted Exchange Interactions in Linear Adducts of Nitroxides with Dirhodium Tetrakis(trifluoroacetate)

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Recent reports on bis-nitroxyl adducts of tetrakis(trifluoroacetato)dirhodium,[1,2] ($Rh_2(tfac)_4$), show that efficient interactions between the two ligand based radicals are mediated by the Rh–Rh bond.

As part of our studies concerning the coordination chemistry of the nitronyl and imino nitroxides,[3,4] we have synthesized a series of discrete bis-nitroxyl complexes as well as extended linear adducts of these free radicals with $Rh_2(tfac)_4$. The O-bonded nitronyl complexes show moderate antiferromagnetic nitroxyl–nitroxyl interactions, while the N-bonded imino adducts exhibit either weak antiferro- or ferromagnetic couplings. The structural features of

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