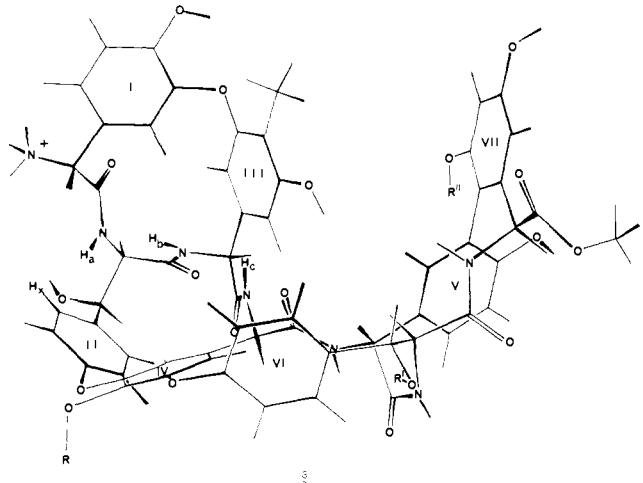
Table I. CD Spectra of *N*-Salicylidene Derivatives[a]

amino acid	λ, nm	[θ]	λ, nm	[θ]
1	*f*			
2	*f*			
3[b]	315	−2100	252	−8000
4[b]	316	−4300	262	−2200
5	315	+12800	255	+17700
6	320	+2100	262	+5000
7[b]	320	nil	252	−1400
(*R*)-phenylglycine[c]	315	+5600	277	+5500
(*R*)-*p*-hydroxyphenylglycine	315	+8900	260	+11700
(*R*)-cyclohexylglycine[b,d]	317	−1900	252	−11000
(*S*)-cyclohexylalanine[b,e]	320	+1100	252	+4900

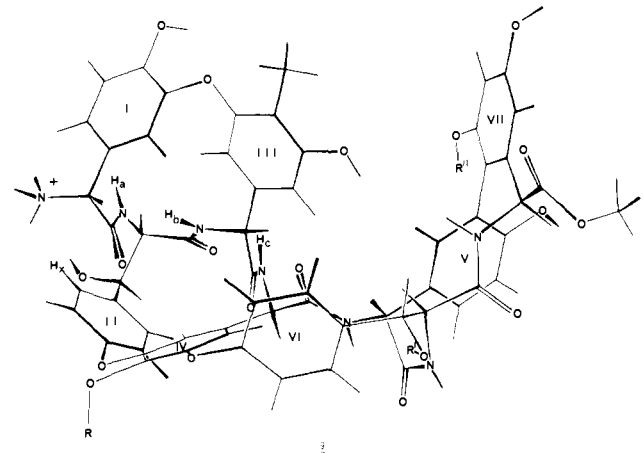
[a] *N*-Salicylidene derivatives were prepared in situ in MeOH by the method of Smith et al;[10] a 15% excess of sodium salicylaldehyde was used. [b] Also showed a band in the 275-nm region ascribed to a quinoid tautomer. [c] Lit.[10] 313 (+6000), 277 nm (+5800). [d] Prepared by reduction (PtO_2/H_2) of (*R*)-phenylglycine. [e] Prepared by reduction (PtO_2/H_2) of (*S*)-phenylalanine. [f] No measurable band in 350–300-nm region; broad band around 280 nm.

exchange to the extent of 70%. As expected the phenylalanyl β positions had each incorporated 1 equiv of D. The optical rotation, $[\alpha]^{28}_D$ −37° (*c* 0.7, 0.2 M HCl), of **5** and CD spectrum of derivatized **5**, dominated by the unracemized residue IV, are in agreement with Williams' *R* assignment. The CD spectrum for derivatized amino acid **6** was similar. The CD spectrum of derivatized **7** was too weak to be of significance, although it showed a slight excess of the *R* configuration. Thus, no independent assignments of residues II and VI can be made on the basis of this study. Further study is needed.



The change of configuration at residue I is the only major change we propose for the structure of ristocetin A. The assignment of the *S* configuration to residue I was made by Williams and co-workers on the basis of two NMR experiments which place the terminal amino group near one proton (H_x) on the aromatic ring of residue II.[2c] Their studies also place amide proton H_a close to H_x.[2b] In ristocetin A, having Williams' three-dimensional structure except that the configuration of I is *R* (i.e., **8**), H_a but not the amino group is close to H_x. If another conformation is chosen in which the I–II amide linkage has undergone a 180° rotation such that the carbonyl group is on the front (interior) side and amide proton H_a is on the back, i.e., structure **9**, then the amino group approaches H_x; H_a still remains reasonably close to H_x. Conformation **9** is analogous to that proposed for vancomycin on the basis of the X-ray structure of degradation product CDP-I[2e] and high-field NMR studies of the parent antibiotic.[13] With the proviso that the absolute configurations of all asymmetric centers are now correctly assigned, we conclude that ristocetin A lies either in conformation **9** or is in mobile equilibrium between **8** and **9**.

(13) Williams, D. H.; Kalman, J. R. *J. Am. Chem. Soc.* **1977**, *99*, 2768.



Ristocetin and related antibiotics exert their antibacterial action by complexing with bacterial cell wall constituents which contain peptides terminating in D-alanyl-D-alanine. Kalman and Williams[14] have proposed that peptide binding involves the cleft on the front face of the molecule and that amide protons (H_a, H_b, and H_c) are involved in intermolecular hydrogen bonds to the carboxyl group of the peptide. Thus, upon binding, ristocetin becomes fixed in conformation **8**. Kalman and Williams have also speculated upon the presence of a salt bridge between the N terminus of the antibiotic (in the ammonium form) and the C terminus of the peptide (as the carboxylate anion). With the reassigned configuration of residue I, the amino group is pointed away from the cleft. Nevertheless, it still lies approximately 5 Å from the peptide carboxyl group and may provide additional stabilization for the peptide–antibiotic complex. A similar but more extensive conformational change upon peptide binding has been proposed for vancomycin.[15,16] The additional degrees of freedom present in vancomycin because residue I is not cross-linked to residue III may allow the terminal ammonium ion to interact more closely with the peptide than in the case of ristocetin.

(14) Kalman, J. R.; Williams, D. H. *J. Am. Chem. Soc.* **1980**, *102*, 906.
(15) Convert, O.; Bongini, A.; Feeney, J. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1262.
(16) Williams, D. H.; Butcher, D. W. *J. Am. Chem. Soc.* **1981**, *103*, 5697.

Preparation and Crystal Structure of $[Mo_3S_8(NNMe_2)_2]^{2-}$, a Trinuclear Sulfido-Bridged Molybdenum Anion with Coordinated Isodiazene Ligands

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There has been intense recent interest in molybdenum complexes with sulfur ligands stimulated by the EXAFS studies[1] of nitrogenase and other molybdoenzymes. However, none of the complexes so far reported is able to bind or activate dinitrogen. There are very few examples of molybdenum–sulfur complexes which interact with the small molecules that can function as

(1) Cramer, S. P.; Hodgson, K. O.; Gillum, W. O.; Mortenson, L. E. *J. Am. Chem. Soc.* **1978**, *100*, 3398. Cramer, S. P.; Gillum, W. O.; Hodgson, K. O.; Mortenson, L. E.; Stiefel, E. I.; Chisnell, J. R.; Brill, W. J.; Shah, V. K. *Ibid.* **1978**, *100*, 3814.

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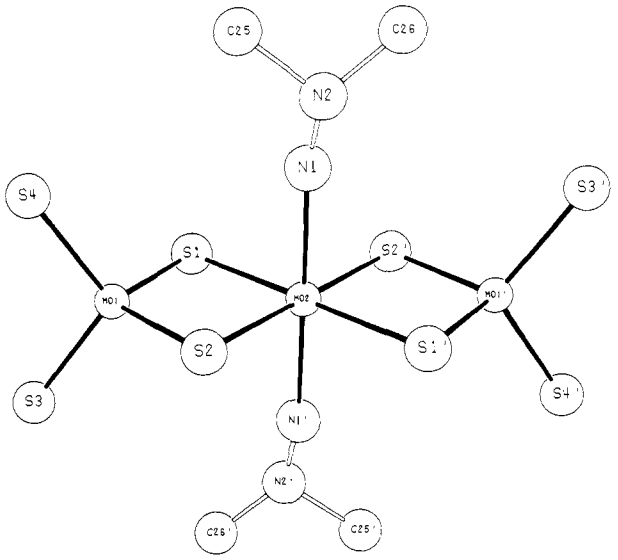


Figure 1. Perspective view of the molecular anion $[Mo_3S_8(NNMe_2)_2]^{3-}$.

inhibitors or alternative substrates for nitrogenase or indeed with any ligands relative to nitrogen fixation. Hydrazido(2-) complexes are proven intermediates in both the protonation[2] and the alkylation[3] of coordinated dinitrogen, and this paper reports their use to probe the properties of a molybdenum site predominantly ligated by sulfur.

Recently we reported the synthesis of the binuclear bis[hydrazido(2-)] complexes $[S_2MS_2M'(NNMe_2)_2(PPh_3)]$ (M = M' = Mo or W; M = Mo, M' = W, M = W, M' = Mo).[4] The complex with M = M' = Mo (**1**) reacts rapidly with the thiophenolate ion.

Compound **1** (0.5 g, 1.4 nmol) and LiSPh (0.5 g, 4.3 nmol) were stirred at room temperature in MeCN (40 mL) for 1 h to give a deep orange solution. Addition of Ph_4PBr (1.2 g, 2.9 nmol) gave dark red-brown crystals of **2**. Elemental analysis[5] suggested the empirical formulation $[Ph_4P]_2[Mo_3S_8(NNMe_2)_2]$, and the UV spectrum[6] in CH_3CN implied the presence of coordinated $[MoS_4]^{2-}$.[7] The complex is diamagnetic in the temperature range 77-310 K.

Crystals of **2** suitable for an X-ray diffraction study crystallized as black needles, belonging to space group $P2_1/n$ with a = 9.937 (31) Å, b = 18.295 (2) Å, c = 15.851 (3) Å, β = 102.81 (2)°, V = 2809.94 Å^3, Z = 2, D_{calcd} = 1.58 g cm^{-3}, D_{obsd} = 1.60 g cm^{-3}, R = 7.2% for 1840 reflections. An ORTEP representation of the molecule is shown in Figure 1.

The central Mo atom, Mo2, sits at a crystallographic center of symmetry. The two Mo1S_4 fragments are thus identical, as are the $NNMe_2$ groups, and the symmetry also imposes planarity on the Mo2-S_4 unit. The terminal Mo1 and Mo1′ atoms are pseudotetrahedral. The average Mo-S (terminal) bond distance of 2.161 (5) Å is similar to that observed in other complexes containing coordinated MoS_4^{2-}, e.g., 2.146 (1) Å in $[S_2MoS_2Mo(NNMe_2)_2(PPh_3)]$[4] and 2.153 (6) Å in $[(PhS)_2FeS_2MoS_2]^{2-}$.[8] The Mo-S bridging distances of 2.242 (4) Å are again close to values found in other species where MoS_4 functions as a bidentate lignad, e.g., 2.246 (6) Å in $[Cl_2FeS_2MoS_2]^{2-}$.[8] The central molybdenum Mo2 is pseudooctahedrally coordinated by four coplanar sulfur atoms and two trans hydrazidonitrogens.

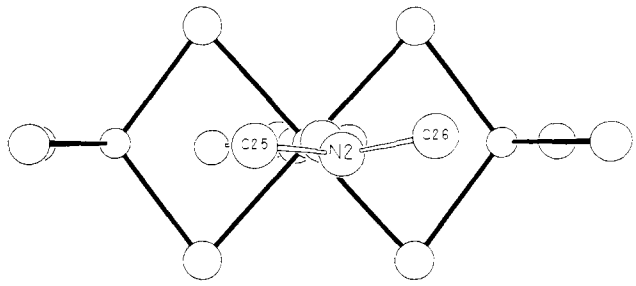
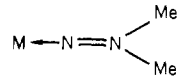


Figure 2. $[Mo_3S_8(NNMe_2)_2]^{3-}$ anion viewed down the N2-N1-Mo axis.

The most unusual features of the structure are the geometry and orientation of the $NNMe_2$ groups. They are bound in a near linear, end-on fashion, with Mo2-N1-N2 = 165.9 (16)°. However, the Mo2-N1 bond distances of 2.13 (1) Å are dramatically longer than those of 1.75-1.83 Å found in other molybdenum hydrazido(2-) complexes.[9] The N1-N2 distance is correspondingly very short at 1.16 (2) Å compared to about 1.3 Å for other known hydrazido(2-) complexes. These bond distances suggest that the $NNMe_2$ ligands are best described as coordinated isodiazenes with a valence-bond formulation



The central molybdenum is then formally described as Mo(II), with Mo1 and Mo1′ as Mo(VI).

The bond lengths imply an absence of Mo-N π bonding, and this is also supported by the relative orientation of the $NNMe_2$ groups, as shown in Figure 2. The $NNMe_2$ plane is rotated so as to bisect the S-Mo2-S′ vector whereby the N1 p orbitals have no net overlap with molybdenum t_2-type orbitals and there is no Mo-N π bonding. This orientation contrasts with that found in all other NNR_2 complexes studied[10] where the NNR_2 plane invariably eclipses the L1-Mo-L2 bond vector of the tetragonal plane, thereby maximizing π bonding. This complex illustrates both the electronic flexibility of the NNR_2 ligand and the very strong accepting propensities of the MoS_4 units which drain away all the electron density which might otherwise be available for π bonding to the $NNMe_2$ groups.

In view of the excess ligand used in the preparation of **2**, it is surprising that the product contains no thiophenolate, and any intermediate products containing it must disproportionate or degrade to the final product. Attempts to prepare the trimeric species **2** by direct reaction of dimer **1** with MoS_4^{2-} in refluxing MeCN gave a different crystalline product (**3**) which elemental analysis and ^1H NMR[11] spectroscopy suggest is $[PH_4P]_2[Mo_3S_8(NNMe_2)(CH_3CN)]$. There is no IR band assignable to ν(CN) of the coordinated acetonitrile, but this is not uncommon for acetonitrile complexes.[12]

Attempts to prepare the analogous tritungsten species by reaction of $[S_2WS_2W(NNMe_2)_2(PPh_3)]$ with $[Ph_4P]_2WS_4$ led to immediate bleaching of the purplish solution to very pale yellow, and the only isolable product to date is $[Ph_4P]_2[WS_4]$. However, reaction of $[WCl(NNMe_2)_2(PPh_3)_2]Cl$ with 2 equiv of $[Ph_4P]_2MoS_4$ in refluxing acetonitrile gave a red-brown crystalline

(2) Chatt, J.; Pearman, A. J.; Richards, R. L. *J. Chem. Soc., Dalton Trans.* **1977**, 2139.
(3) Chatt, J.; Diamantis, A. A.; Heath, G. A.; Hooper, N. E.; Leigh, G. J. *J. Chem. Soc., Trans. Dalton* **1977**, 688.
(4) Dilworth, J. R.; Zubieta, J. *J. Chem. Soc., Chem. Commun.* **1981**, 132.
(5) Anal. Calcd for $C_{52}H_{52}N_4Mo_8P_2S_8$: C, 46.6; H, 3.9; N, 4.2; P, 4.6; S, 19.1. Found: C, 46.0; H, 3.5; N, 4.0; P, 4.6; S, 18.5.
(6) The UV spectrum showed peaks at 464 (8900) and 535 (5760) μm; molar extinction coefficients in parenthesis.
(7) Coucouvanis, D.; Baenziger, N. C.; Simhon, E. D.; Stremple, P.; Swenson, D.; Siriopoulous, A.; Koskas, A.; Petrouleas, V.; Papaefthymiou, V. *J. Am. Chem. Soc.* **1980**, *102*, 1732.
(8) Coucouvanis, D.; Simhon, E. D.; Swenson, D.; Baenziger, N. C. *J. Chem. Soc., Chem. Commun.* **1979**, 361. Tieckelmann, R. H.; Silvis, H. C.; Kent, T. A.; Huynk, B. H.; Waszczak, J. V.; Teo, B.-K.; Averill, B. A. *J. Am. Chem. Soc.* **1980**, *102*, 5550.
(9) Chatt, J.; Dilworth, J. R.; Richards, R. L. *Chem. Rev.* **1978**, *78*, 589 and references therein.
(10) Dilworth, J. R.; Zubieta, J. A., unpublished results.
(11) Anal. Calcd for $C_{52}H_{49}N_3Mo_3P_2S_8$: C, 47.3; H, 3.8; N, 3.2. Found: C, 47.0; H, 3.9; N, 3.4. ^1H NMR in CD_2Cl_2: singlet at 2.10 ppm ($NNMe_2$) and singlet at 1.97 ppm (MeCN).
(12) $[ReCl_3(MeCN)(PPh_3)_2]$: Rouschias, G.; Wilkinson, G., *J. Chem. Soc.* **1967**, *19*, 993. $[Re(MeCN)(SPh_3)(PPh_3)]$: Dilworth, J. R.; Neaves, B. D., unpublished results.

product analyzing as $[Ph_4P]_2$ $[S_2MoS_2W(NNMe_2)_2S_2MoS_2]$[13] (**4**), presumably with a structure analogous to **2**.

Acknowledgment. We are grateful to the National Institute of Health for an award (to J.A.Z.) of Grant GM 22566 and to NATO for award (to J.R.D. and J.A.Z.) of Grant 274.80.

Supplementary Material Available: Final positional parameters, final temperature factors, and observed and calculated structure factors (14 pages). Ordering information is given on any current masthead page.

(13) Anal. Calcd for $C_{52}H_{52}N_4Mo_2P_2S_8W$: C, 44.1; H, 3.7; N, 3.9. Found: C, 43.6; H, 3.9; N, 3.7.

Annulated Sugars: The 1,2-*O*-Isopropylidene Ring as a Stereo-, Regio-, and Chemocontrolling Agent[1]

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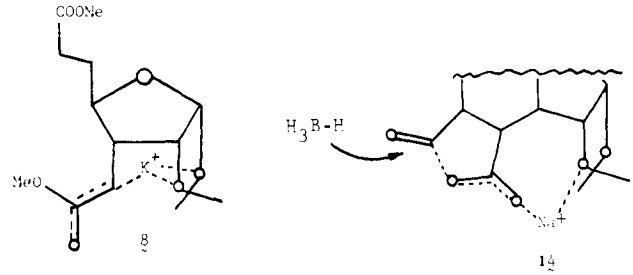
In a recent report from this laboratory we showed that 1,2-*O*-isopropylidenefuranoses such as **1**[4] could serve as precursors for α-methylene-γ-butyrolactones,[5] and consequently annulated furanoses such as **2** may be considered as synthons for sesquiterpene lactones. A survey of this broad family of substances[6] indicates that the absolute configuration at oxygen coincides (usually!) with that at C4 of **1** *whether the lactone is cis or trans fused*,[7] and thus the task is to prepare the 3β and 3α forms of **2** having, respectively, D-xylo and D-ribo configurations on the furanose moiety. In the course of this study we have uncovered remarkable stereocontrolling effects by which each of these forms of **2** may be *prepared and functionalized* with high selectivities.

The work of Rosenthal and Nguyen[8] has shown that the ester **4a** is formed exclusively during hydrogenation of **3**.[8] The derived aldehydic ester **4b**[8,9] was converted into the diester **5a**[10] as indicated in Scheme I. Dieckmann cyclization of **5a** can occur in two possible senses, and indeed treatment with potassium *tert*-butoxide gave a 90% yield of two crystalline compounds in the ratio 10:1. From the 220-MHz ^1H NMR spectra, it was clear that the major isomer was **6a**[10] because of the doublet at 3.44 ppm assignable to H8, the spacing of which (J_{38} = 13.5 Hz) indicated that the methoxycarbonyl group was equatorially oriented. The minor isomer existed entirely in the enolic form **7**[10] as indicated by the IR data (see Scheme I) and the exchangable proton at 12.84 ppm.



Compounds **6a** and **7** result from deprotonation of **5a** at C3[1] and C6, respectively, and one might have expected that the product ratio would be reversed since C3[1] is sterically hindered by the *O*-isopropylidene ring. However, if the influence of the latter were electronic rather than steric, the regiochemical outcome could be readily rationalized, seeing that the C3[1] enolate would be rendered more favorable by chelation of the dioxolane oxygens as in **8**. Thus the 1,2-*O*-isopropylidene ring of **5a** could control the regioselectivity of the cyclization.

In the hope of enhancing the formation of **7**, diester **5a** was treated with a variety of nonchelating bases (Et_3N, DBN, Bu_4NOH), but they all failed to induce cyclization. However, as indicated in Scheme I, *inclusion of two-tenth of an equivalent of 18-crown-6 caused complete suppression of* **6a**. This dramatic example of chelation-mediated regiocontrol was unfortunately soured by the low yield (20%) of **7**; but this reaction has not been optimized, and the direction which must be taken in our future studies is clearly apparent.

From the standpoint of sesquiterpene syntheses, better yields of **7** would have been appreciated since the carboxymethoxy functionality would make provisions for the ubiquitous C4 methyl group of sesquiterpene lactones.[6] Fortunately, this problem was readily solved by using the propionate $[Ph_3P{=}C(CH_3)COOMe]$ for the Wittig reaction to afford diester **5b**.[10] Cyclization as above led to **6b**.[10]

With the trans annulation of **1** thereby secured, we turned to the cis analogue in which the C3 attachment must be made anti to the 1,2-*O*-isopropylidene ring. A Diels-Alder strategy[11] was conceived which required the diene **9** whose preparation from **1** has been described by us elsewhere.[13] The α- face of compound **9** is rendered completely inaccessible by the *O*-isopropylidene ring, and we could therefore predict that the addition of a dieneophile would be β, forcing H3 into syn relationship with the acetonide. Crotonaldehyde, methyl crotonate, and even α-chloroacrylonitrile all failed to react with **9**. However, after 3 h with maleic anhydride in refluxing toluene, a single product (**10a**) was obtained in 86% yield. The material was crystalline, but it decomposed (retro Diels-Alder) on attempted melting point determination. The critical datum J_{23} = 0.4 Hz from the 360-MHz ^1H NMR spectrum confirmed that addition had indeed occurred from the β face, and the value J_{38} = 5.6 Hz showed that H3 and H8 were also cis related, indicating that the addition had also been exclusively endo. Thus the product of the reaction was established as **10a**.[10]

We now investigated the outcome of hydrogenating the double bond in **10**, and the role that the *O*-isopropylidene ring would play in this process was a source of speculation. In fact under atmospheric pressure and palladium/$BaSO_4$ catalysis, the hydrogenation went smoothly to give **11**[10] as the *exclusive* product isolated in 83% yield. The newly formed stereocenter was readily determined to be as shown in Scheme II in view of the coupling

(1) Presented in part at the "Third International Symposium on Organic Synthesis", Madison WI, June 1980. See "Organic Synthesis Today and Tomorrow"; Trost, B. M., Hutchinson, C. R., Eds.; Pergamon Press: New York, 1981.

(2) Holder of Merck, Sharp and Dohme Graduate Fellowship, University of Maryland. Taken in part from the Ph.D. Thesis of K-M.S., University of Maryland, 1981. Present address of K-M.S.: Shell Development Company, P.O. Box 4238, Modesto, CA 95352.

(3) Holder of an Ontario Graduate Fellowship, University of Waterloo. Taken in part from the Ph.D. Thesis of T.-F. Tam, University of Waterloo, 1980. Present address of T.-F.T.: Syntex Corporation, Missisauga, Ontario, Canada.

(4) 1,2-*O*-Isopropylidene-α-D-*xylo*-furanose, used for the study reported in ref 5, is homomorphous with **1**.

(5) Tam, T. F.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1980**, 556.

(6) Fischer, N. H.; Olivier, E. J.; Fischer, H. D. *Prog. Chem. Org. Nat. Prod.* **1979**, *38*, 47.

(7) C4 of **1** coincides with C6 of the trans-fused sesquiterpene lactones but with C8 of the cis-fused series.[6]

(8) Rosenthal, A.; Nguyen, L. *J. Org. Chem.* **1969**, *34*, 1029.

(9) Anderson, R. C.; Fraser-Reid, B. *J. Am. Chem. Soc.*, **1975**, *97*, 3870.

(10) This compound gave satisfactory spectroscopic, microanalytical, and/or high-resolution mass spectrum data.

(11) In other approaches to "annulated sugars" we have used the sugar residue as (chiral) dienophile, the diene being achiral.[12] In this present study the roles are reversed.

(12) Primeau, J. L.; Anderson, R. C.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1980**, *6*.

(13) Sun, K. M.; Fraser-Reid, B. *Synthesis*, in press.

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