ORGANOMETALLICS

Volume 17, Number 25, December 7, 1998

© Copyright 1998
American Chemical Society

Downloaded by CARLI CONSORTIUM on June 30, 2009
Published on November 14, 1998 on http://pubs.acs.org | doi: 10.1021/om980801z

Communications

Iridium-Assisted, Enantiospecific Aliphatic C−H Activation/Iodination

Romano Dorta and Antonio Togni*

Laboratory of Inorganic Chemistry, Swiss Federal Institute of Technology, ETH-Zentrum, CH-8092 Zürich, Switzerland

Received September 24, 1998

Summary: The observation of an enantiospecific C−H bond activation followed by iodination at an allylic position of a coordinated 1,5-COD ligand in a chiral Ir(I) complex upon addition of I_2 in CH_2Cl_2 is reported. The same reaction carried out in THF affords an allylic η^3,η^2-COD derivative. Both reaction products were characterized by X-ray diffraction.

The development of systems capable of selective and eventually catalytic hydrocarbon activation/functionalization, taking place within the coordination sphere of a transition metal, is still a challenging objective. Nevertheless, stoichiometric C−H bond activation by metal complexes is well established,[1,2] and reports on C−C[3] and catalytic C−H[4] bond activation/functionalization are becoming more frequent. High selectivity in the activation of C−H bonds is observed in, for example, reactions catalyzed by cytochrome P-450 enzymes[5] and artificial analogues thereof.[6] Despite its potential importance, C−H activation followed by halogenation is an extremely rare reaction.[7]

Whereas there is some precedent in Rh- and Ir-mediated selective COD (1,5-cyclooctadiene) oxidation by H_2O_2[8] and by dioxygen,[9] respectively, no metal-mediated halogenation of a CH_2 group in this molecule has been reported. We describe here the first *enantiospecific* C−H bond activation/iodination of COD, formally corresponding to the transformation of eq 1. This is taking place in the coordination sphere of the

---

* To whom correspondence should be addressed. E-mail: togni@inorg.chem.ethz.ch.

[1] For a recent review, see: Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879, and references therein.

[2] For recent examples, see: (a) Bennett, J. L.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1997**, *119*, 10696. (b) Cook, J. K.; Mayer, J. M. *J. Am. Chem. Soc.* **1995**, *117*, 7139. (c) Wick, D. D.; Goldberg, K. I. *J. Am. Chem. Soc.* **1997**, *119*, 10235. (d) Brown, S. N.; Mayer, J. M. *J. Am. Chem. Soc.* **1994**, *116*, 2219. (e) Cook, G. K.; Mayer, J. M. *J. Am. Chem. Soc.* **1994**, *116*, 1855. (f) Ma, Y.; Bergman, R. G. *Organometallics* **1994**, *13*, 2548.

[3] (a) Gozin, M.; Weisman, A.; Ben-David, Y.; Milstein, D. *Nature* **1993**, *364*, 699. (b) Gozin, M.; Aizenberg, M.; Liou, S.-Y.; Weisman, A.; Ben-David, Y.; Milstein, D. *Nature* **1994**, *370*, 42. (c) Liou, S.-Y.; Gozin, M.; Milstein, D. *J. Am. Chem. Soc.* **1995**, *117*, 9774.

[4] (a) Lin, M.; Hogan, T.; Sen, A. *J. Am. Chem. Soc.* **1997**, *119*, 6048. (b) Periana, R. A.; Taube, D. J.; Evitt, E. R.; Löffler, D. G.; Wentrcek, P. R.; Voss, G.; Masuda, T. *Science* **1993**, *259*, 340. (c) Periana, R. A.; Taube, D. J.; Gamble, S.; Taube, H.; Satoh, T.; Fujii, H. *Science* **1998**, *280*, 560. (d) Belli, J.; Jensen, C. M. *Organometallics* **1996**, *15*, 1532. (e) Maguire, J. A.; Petrillo, A.; Goldmann, A. S. *J. Am. Chem. Soc.* **1992**, *114*, 9492.

[5] For a review, see: Woggon, W.-D. *Cytochrome P-450: Significance, Reaction Mechanisms and Active Sites Analogues*; Springer: Berlin, Heidelberg, 1996.

[6] Breslow, R.; Zhang, X.; Huang, Y. *J. Am. Chem. Soc.* **1997**, *119*, 4535.

[7] (a) See, for example: (a) Horváth, I.; Cook, R. A.; Millar, J. M.; Kiss, G. *Organometallics* **1993**, *12*, 8. For a template-directed radical relay process, see: (b) Breslow, R.; Mehta, M. P. *J. Am. Chem. Soc.* **1986**, *108*, 2485. (c) Breslow, R.; Mehta, M. P. *J. Am. Chem. Soc.* **1986**, *108*, 6417.

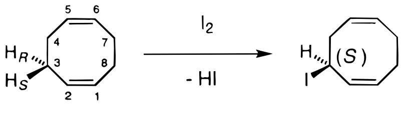
[8] de Bruin, B.; Boerakker, M. J.; Donners, J. J. J. M.; Christiaans, B. E. C.; Schlebos, P. P. J.; de Gelder, R.; Smits, J. M. M.; Spek, A. L.; Gal, A. W. *Angew. Chem.* **1997**, *109*, 2154.

[9] (a) Day, V. W.; Klemperer, W. G.; Lockledge, S. P.; Main, D. J. *J. Am. Chem. Soc.* **1990**, *112*, 2031. (b) Day, V. W.; Eberspacher, T. A.; Klemperer, W. G.; Zhong, B. *J. Am. Chem. Soc.* **1994**, *116*, 3119.

10.1021/om980801z CCC: $15.00 © 1998 American Chemical Society
Publication on Web 11/14/1998

Downloaded by CARLI CONSORTIUM on June 30, 2009
Published on November 14, 1998 on http://pubs.acs.org | doi: 10.1021/om980801z

chiral Ir(I) fragment [Ir((*R*)-(*S*)-PPFP(Xyl)$_2$)]$^+$ (serving also as a scavenger for the produced HI).[10]



(1)

Thus, 1 equiv of I$_2$ cleanly reacted with [Ir((*R*)-(*S*)-PPFP(Xyl)$_2$)(COD)]BF$_4$ (**1**) in THF at room temperature. The ^{31}P NMR spectrum showed the presence of a main product characterized by a new pair of doublets at δ -24.2 and -0.7 ppm (J_{PP} = 29 Hz). This cationic complex **3** could be isolated in pure form in 60−80% yield as a tetrafluoroborate salt.[11] An X-ray crystallographic analysis revealed the presence of an η^3,η^2-cyclooctadienyl ligand, as shown in the ORTEP represention of Figure 1B.[12] Compound **3** has the composition [IrI((*R*)-(*S*)-PPFP(Xyl)$_2$)(η^3,η^2-C$_8$H$_{11}$)]BF$_4$ (Scheme 1) and formally derives from the addition of I$_2$ to **1**, under extrusion of HI. The coordination sphere around the Ir(III) center is pseudooctahedral, with the η^3,η^2-cyclooctadienyl ligand occupying three coordination sites and the iodine atom being located in an *endo* position with respect to the ferrocene core. The bonding distances between the three carbon atoms C(36), C(37), and C(38), respectively, and Ir (2.336(10), 2.17(2), and 2.23(2) Å, respectively) clearly indicate the π-allyl nature of this fragment.

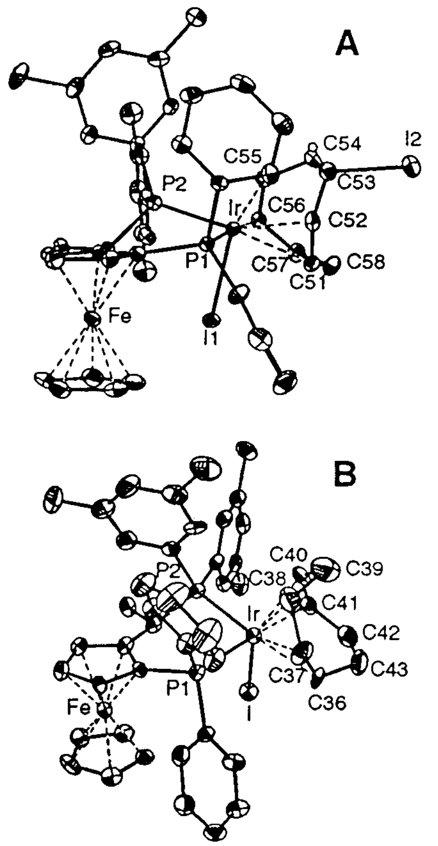
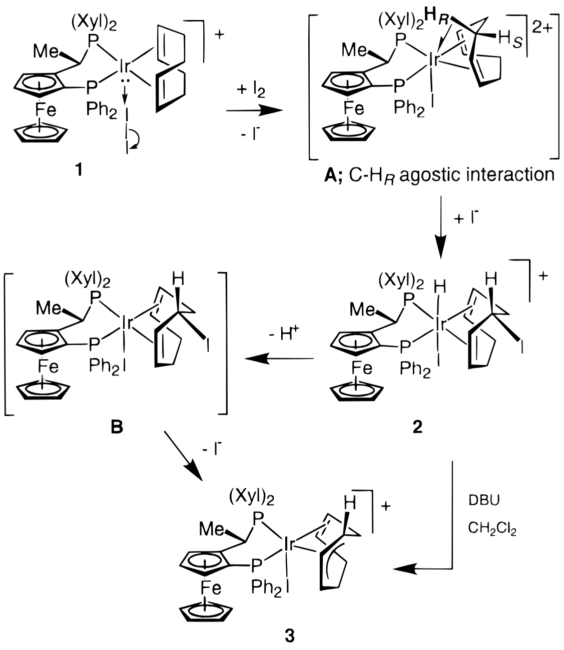


Figure 1. ORTEP views (30% probability ellipsoids) of the cations **2** (**A**) and **3** (**B**). The same absolute configuration (*R*)-(*S*) of the ferrocenyl ligands is shown for both complexes, although the structure of compound **3** has been determined using crystals containing the (*S*)-(*R*) enantiomer. For relevant bond distances and angles, see text.

Scheme 1



When the reaction was followed by NMR in THF-*d*$_8$, the transient formation of a major Ir-hydride species **2** (along with two minor Ir-hydrides, accounting for less than 15% of the mixture) was observed in the ^{1}H NMR spectrum at δ -13.8 ppm (dd, *J* = 16.0; 10.6 Hz), to which corresponded a new pair of doublets in the ^{31}P NMR spectrum (δ -33.3 and -1.9 ppm, J_{PP} = 22 Hz). This species could not be isolated from THF solutions even at low temperature. However, when the reaction of **1** with I$_2$ was run in CH$_2$Cl$_2$ at −78 °C, the same hydride species **2** was obtained in an analytically pure form and in excellent isolated yields (90−97%), as a tetrafluoroborate salt.[13] Once dissolved in THF-*d*$_8$, this Ir-hydride complex evolved to yield quantitatively **3** (based on NMR) over 1 h at 45 °C,[14] whereas it was stable in CD$_2$Cl$_2$ solution at room temperature. An

---

[10] We have previously shown that dinuclear Ir(I) complexes containing ferrocenyl diphosphines are able to undergo aliphatic C−H, O−H, and N−H bond activation. See: (a) Dorta, R.; Egli, P.; Zürcher, F.; Togni, A. *J. Am. Chem. Soc.* **1997**, *119*, 10857. (b) Dorta, R.; Togni, A. *Organometallics* **1998**, *17*, 3423.

[11] A THF (2 mL) solution of I$_2$ (61.5 mg, 0.242 mmol) was added dropwise to a THF (3 mL) solution of [Ir(COD)((*S*)-(*R*)-PPF−P(Xyl)$_2$)]-BF$_4$ (**1**, 248.7 mg, 0.242 mmol). The resulting dark red solution was stirred for 60 h, whereupon it gradually turned orange. Addition of Et$_2$O (14 mL) caused precipitation of a red oil and a yellow solid. The supernatant mother liquor was syphoned off and the residue dried in vacuo. Redissolving the residue in THF (2 mL) caused almost immediate crystallization. The yellow precipitate was filtered off, washed with Et$_2$O, and dried in vacuo, yielding a yellow powder (192 mg, 69%). Anal. Calcd for C$_{48}$H$_{51}$BF$_4$P$_2$FeIIr: C, 50.06; H, 4.46; I, 11.02. Found: C, 49.84; H, 4.69; I, 11.30. ^{1}H NMR (CD$_2$Cl$_2$): δ 1.59 (m, 3 H), 2.14 (s, 6 H), 2.46 (s, 6 H), 3.94 (s and m, 5 and 1 H, respectively), 4.33 (m, 1 H), 4.88 (m, 1 H), 6.06 (m, 2 H), 6.22 (m, 1 H), 6.87 (m, 2 H), 6.99 (m, 2 H), 7.26 (m, 1 H), 7.61 (m, 2 H), 7.67 (m, 1 H), 8.43 (m, 2 H), 8.44 (m, 2 H), what follows are the resonances of the -η^3,η^2-C$_8$H$_{11}$ ligand (numbering scheme given in eq 1), 6.22 (m, 1 H−C(1)), 4.10 (m, 1 H−C(2)), 2.26 (m, 1 H−C(3)), 3.37 and 3.45 (m, 2 H−C(4)), 3.62 (m, 1 H−C(5)), 3.81 (m, 1 H−C(6)), 3.28 and 3.54 (m, 2 H−C(7)), 1.75 and 2.74 (m, 2 H−C(8)). ^{31}P NMR (CD$_2$Cl$_2$): δ -24.4 (d, $J = 28.6$ Hz), -0.7 (d, $J = 28.6$ Hz). Single crystals suitable for X-ray diffraction analysis were obtained by dissolving the complex in boiling THF followed by slow cooling to room temperature.

[12] Crystal data of **3**: IrFeIP$_2$C$_{48}$H$_{51}$·BF$_4$, fw 1151.59, monoclinic, space group $P2_1$ (No. 4), $a = 10.741(1)$ Å, $b = 15.295(2)$ Å, $c = 15.968(2)$ Å, $\beta = 104.99(2)°$, $V = 2534.0(5)$ Å^3, $Z = 2$, $F(000) = 1132$, Independent reflections 5949 (R(int) = 0.0364), R for $|F|^2 > 2\sigma(|F|^2) = 0.0474$, w$R$ for $|F|^2 > 2\sigma(|F|^2) = 0.1191$. The structure was solved by direct methods. For full details see the Supporting Information.

Downloaded by CARLI CONSORTIUM on June 30, 2009
Published on November 14, 1998 on http://pubs.acs.org | doi: 10.1021/om980801z

X-ray structural study confirmed the formulation of **2** shown in Scheme 1,[15] in particular the specific incorporation of an iodine atom at position 3 of the COD ligand, and the absolute configuration *S* of the newly formed stereogenic center, as shown in the ORTEP view of Figure 1A. The coordination environment of the Ir(III) center is distorted octahedral with the iodo ligand I(1) in an *endo*-apical position, as in derivative **3**. The Ir atom is displaced 0.23 Å along the Ir−I(1) vector out of the best plane defined by P(1), P(2), and the midpoints of the olefinic bonds C(51)═C(52) and C(55)═C(56). The hydride ligand could not be localized, but its position is inferred to be trans to I(1). The C(53)−I(2) distance of 2.212(10) is significantly longer than the typical expected average value of 2.159 for the $C(sp^3)$−I bond.[16] Further, the nonbonding distance between Ir and C(53) is 3.01 Å, therefore shorter than the corresponding distances to C(54), C(57), and C(58) (ranging from 3.17 to 3.26 Å). Thus, it seems that this structure anticipates the Ir−C(53) bond-making and C(53)−I bond-breaking process that leads to **3**.

In CD_2Cl_2 no incorporation of deuteride into the Ir−H position of **2** took place, ruling out hydride formation by solvent activation. Furthermore, the addition of a radical-trapping reagent such as 5,5-dimethyl-1-pyrroline-*N*-oxide[17] did not influence the course of the reaction. These findings strongly suggest a nonradical mechanism for the formation of **2** from **1**. As shown in Scheme 1, we assume that the starting complex **1** first reacts with iodine, giving free iodide and the dicationic Ir(III) intermediate **A**.[18] We postulate that this highly electrophilic species might be stabilized by undergoing an agostic interaction with one of the two accessible CH_2 groups of COD, i.e., either C(3)−H_R or C(4)−H_S (numbering of eq 1).[19] An alternative to this interpretation would be an intramolecular C−H oxidative addition involving the same C−H fragments, to afford an Ir(V) species. Although Ir(V) complexes formed by oxidative addition, mainly onto neutral species, are known,[20] it seems unlikely that the dicationic species **A** could be involved in such a reaction. Subsequently, the C−H-activated intermediate **A** could either undergo (1) an S_N2-type reaction, with iodide attacking C(3) to form directly **2**, or (2) a deprotonation affording the π-allyl complex **3** directly. The observation that **2** is both formed as final product in CH_2Cl_2 and observed as an intermediate in THF suggests that pathway 1 is operating. The formation of **3** from **2** observed in THF can largely be attributed to the higher basicity of THF, as compared to CH_2Cl_2. This favors the deprotonation of **2**, affording the pentacoordinated, electron-rich Ir(I) species **B**,[21] undergoing an S_Ni-type transformation to give **3**. Indeed, the immediate conversion of **2** to **3** in CD_2Cl_2 in the presence of 1 equiv of the strong nonnucleophilic base DBU is observed in an NMR control experiment. Attempts to reverse the latter reaction path (i.e., trying to generate **2** from **3**) by adding a 5-fold excess of $[Bu_4N]I$ and $HBF_4 \cdot Me_2O$ together to **3** in CD_2Cl_2 failed, leaving the π-allyl complex unchanged. The addition of iodide alone gave the same negative result, whereas the addition of strong acid alone led to slow decomposition. These experiments probably rule out proton-transfer reactions involving intermediate **A** and indicate that **3** is not readily susceptible to nucleophilic attack by iodide.

The origin of the stereospecificity in the formation of **2** remains a matter of speculation. Whereas the choice of the pro-*R* hydrogen at C(3) undergoing the agostic interaction is obvious because it is closer to Ir than its pro-*S* companion, we cannot provide arguments explaining why no reaction involving the adjacent diastereotopic $C(4)H_2$ group was observed.

We have demonstrated the possibility of enantiospecific aliphatic iodination via C−H bond activation within the coordination sphere of a chiral Ir complex. We are currently exploring ways of decoordinating the functionalized 3*S*-3-iodo-1,5-COD and of extending this new reaction to further substrates.

Acknowledgment. We thank Arianna Martelletti and Fabio Zürcher for the X-ray crystallographic studies of **2** and **3** and Lukas Hintermann for repeating key experiments. R.D. thanks Novartis Ltd. for financial support.

---

(13) Experimental details for the preparation of **2** are as follows: To a stirred red CH_2Cl_2 (60 mL) solution of $[Ir(COD)((S)\text{-}(R)\text{-}PPF{-}P(Xyl)_2)]BF_4$ (**1**, 1.475 g, 1.438 mmol) at 195 K was added dropwise a CH_2Cl_2 (60 mL) solution of I_2 (365 g, 1.438 mmol). The black-red solution was stirred and allowed to slowly reach room temperature overnight. The resulting orange-red solution was evaporated, affording a red glassy solid, which was slurried and washed with Et_2O (60 mL) and dried in vacuo, yielding a beige powder (1.806 g, 95%). Anal. Calcd for $C_{48}H_{52}BF_4P_2FeI_2Ir \cdot 0.5CH_2Cl_2$: C, 44.06; H, 4.04; I, 19.20. Found: C, 44.25; H, 4.07; I, 20.38. IR (Nujol) $\nu(Ir{-}H) = 2244\ cm^{-1}$. ^1H NMR (CD_2Cl_2): δ −13.82 (dd, $J_1 = 16.0$ Hz, $J_2 = 10.6$ Hz, 1 H), 1.69 (m, 3 H), 2.21 (s, 6 H), 2.46 (s, 3 H), 3.91 (m, 1 H), 4.12 (s, 5 H), 4.46 (m, 1 H), 4.96 (m, 1 H), 6.04 (s + m, 3 H + 1 H), 6.44 (m, 2 H), 6.54 (m, 1 H), 6.97 (m, 2 H), 7.07 (m, 2 H), 7.10 (m, 1 H), 7.17 (m, 1 H), 7.35 (m, 1 H), 7.60 (m, 2 H), 7.67 (m, 1 H), 8.21 (m, 1 H), 8.31 (m, 2 H), what follows are the resonances of the 3*S*-3-I-1,5-COD ligand (numbering scheme given in eq 1), 5.62 (m, 1 H−*C*(1)), 5.15 (m, 1 H−*C*(2)), 4.55 (m, 1 H−*C*(3)), 1.94 and 2.82 (m, 2 H−*C*(4)), 4.41 (m, 1 H−*C*(5)), 4.11 (m, 1 H−*C*(6)), 3.54 and 3.65 (m, 2 H−*C*(7)), 1.94 and 2.94 (m, 2 H−*C*(8)). ^{31}P NMR (CD_2Cl_2): δ −33.5 (d, 22 Hz), −2.1 (d, 22 Hz). Single crystals suitable for X-ray diffraction analysis were grown by vapor diffusion of Et_2O into a CH_2Cl_2 solution of the complex (0.50 g/4 mL).

(14) Concentrated THF solutions of **1** + I_2 tended to become viscous as the reaction progressed toward **3**. This is probably due to HI-induced polymerization of THF.

(15) Crystal data of **2**: $IrFeI_2P_2C_{48}H_{52} \cdot BF_4 + 3 \cdot CH_2Cl_2$, fw 1534.27, monoclinic, space group $P2_1$ (No. 4), $a = 10.4216(5)$ Å; $b = 17.2104(8)$ Å; $c = 15.9880(7)$ Å, $\beta = 102.101(1)°$, $V = 2803.9(2)$ Å^3, $Z = 2$, $F(000) = 1492$, independent reflections 13386 ($R(\text{int}) = 0.0353$), R for $|F|^2 > 2\sigma(|F|^2)$ 0.0510, wR for $|F|^2 > 2\sigma(|F|^2)$ 0.1226. The structure was solved by direct methods. For full details see the Supporting Information.

(16) (a) Orpen, A. G.; Brammer, L.; Allen, F. H.; Kennard, O.; Watson, D. G.; Taylor, R. *J. Chem. Soc., Dalton Trans.* **1989**, Supplement S1−S83. (b) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, Supplement S1−S19. See also: (c) Bürgi, H.-B., Dunitz, J. D., Eds. *Structure Correlation*; VCH: Weinheim, **1994**; Vol. 2, Appendix A.

(17) It was verified that **1** did not react with 5,5-dimethyl-1-pyrroline-*N*-oxide, before iodine was added.

(18) Examples of well-characterized reactive pentacoordinate Ir(III) complexes have recently been reported. See, for example: (a) Esteruelas, M. A.; Lahoz, F. J.; Oñate, E.; Oro, L. A.; Rodríguez, L. *Organometallics* **1996**, *15*, 823. (b) Gupta, M.; Hagen, C.; Kaska, W. C.; Cramer, R. E.; Jensen, C. M. *J. Am. Chem. Soc.* **1997**, *119*, 840.

(19) An agostic interaction of a C−H group adjacent to a coordinated olefin has been previously observed. See: Green, M. *Polyhedron* **1986**, *5*, 427. For a review, see: Brookhart, M.; Green, M. L. H.; Wong, L.-L. *Prog. Inorg. Chem.* **1988**, *36*, 1.

(20) See, for example: (a) Ricci, J. S., Jr.; Koetzle, T. F.; Fernandez, M.-J.; Maitlis, P. M.; Green, J. C. *J. Organomet. Chem.* **1986**, *299*, 383. (b) Hay-Motherwell, R. S.; Wilkinson, G.; Hussain-Bates, B.; Hursthouse, M. B. *Polyhedron* **1993**, *12*, 2009. For the oxidative C−H addition of a coordinated propene in an Fe system, see: Barnhart, T. M.; McMahon, R. J. *J. Am. Chem. Soc.* **1992**, *114*, 5434.

(21) The analogous complex corresponding to **2** but bearing a nonfunctionalized COD ligand was prepared and fully characterized, including a solid-state structure. Reactivity studies confirmed the relatively high acidity of this hydride: it is converted to **1** upon addition of, for example, pyridine: Dorta, R.; Togni, A. Unpublished results.

Supporting Information Available: Preparation and characterization details for compounds **1**−**3**. Tables of crystallographic parameters, atomic coordinates, complete listing of bond distances and angles, tables of anisotropic displacement coefficients, coordinates of hydrogen atoms, and ORTEP representations with complete atom numbering schemes for **2** and **3** (31 pages). Ordering information is given on any current masthead page.

OM980801Z

Downloaded by CARLI CONSORTIUM on June 30, 2009
Published on November 14, 1998 on http://pubs.acs.org | doi: 10.1021/om980801z