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Selective Activation of Ar–Cl and Ar–C Bonds with Iron(II) Complexes[**]

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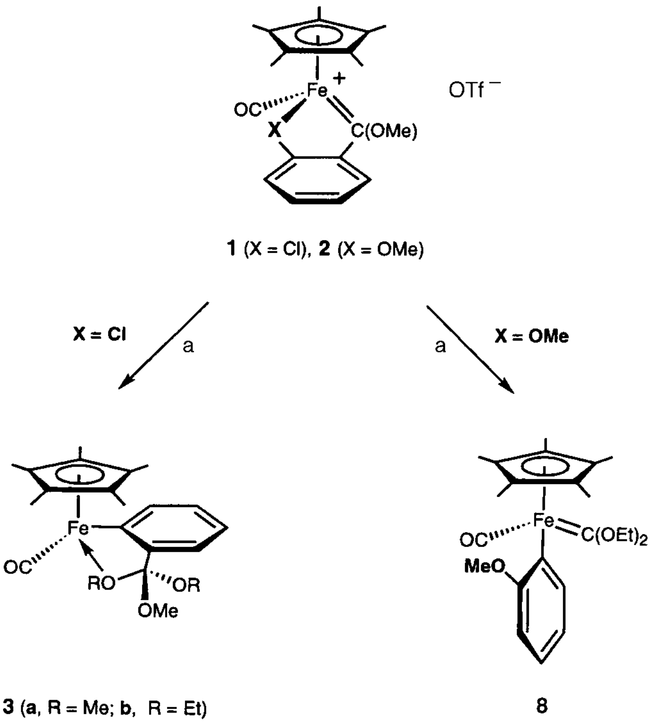
Selective bond-activation reactions mediated by transition metals are currently the focus of synthetic and mechanistic interest. These fundamental processes are particularly important in carbene and arene chemistry.[1, 2] In this context, the electrophilic arylcarbene chelate complexes **1** (X = Cl) and **2** (X = OMe) are good candidates for promoting new reactions within the coordination sphere, since the chelating group X can be activated by the Lewis acidic organo-iron fragment[3, 4] or dissociate to provide a vacant coordination site.[5, 6] Here we report on the reactivity of **1** and **2**[5] towards alkoxides. The outcome of the reaction depends on the nature of the chelate group; selective activation of Ar–Cl and Ar–C bonds was achieved.

Complex **1** reacts cleanly with alkoxides RONa to give the unexpected neutral chelate complexes **3a** (R = Me) and **3b** (R = Et), which were isolated as stable black crystals in 83–89% yield from pentane (Scheme 1). Both contain two additional alkoxy groups. The ^{1}H NMR spectrum (C_6D_6, 25 °C) of **3a** exhibits three broad signals for the methoxy substituents, one of which corresponds to the coordinated OMe group, while the other two methoxy groups are diastereotopic. The coalescence of these signals on warming (T_C(300 MHz) = 42 °C) to give a singlet at $\delta = 2.90$, indicates free exchange on the NMR time scale. For **3b**, the ^{1}H and ^{13}C NMR spectra each exhibit two well-resolved pairs of signals for the methyl and methylene groups, which indicates the presence of two different ethoxy groups. Moreover, in the ^{1}H NMR spectrum (25 °C) one of the methylene groups gives rise to an AB system at $\delta = 3.00$ and 2.78 ($^{2}J_{\mathrm{H,H}} = 10$ Hz) when the corresponding methyl signal at $\delta = 0.98$ is selectively ^{1}H-decoupled.



Scheme 1. a) RONa (3 equiv)/ROH, THF, −80 °C → room temperature. TfO = trifluoromethanesulfonate.

As expected the OMe ligand is labile, and treatment of **3a** with PMe_3 quantitatively yields orange crystals of **4**. In this

$[\mathrm{Fe(C_5Me_5)(CO)(PMe_3)\{\eta^1\text{-}C_6H_4\text{-}\mathit{o}\text{-}C(OMe)_3\}}]$ **4**

case, the three OMe groups are magnetically equivalent in the ^{1}H ($\delta = 3.29$) and ^{13}C ($\delta = 49.9$) NMR spectra (25 °C). An X-ray structure analysis confirms the proposed structure (Figure 1).[7] The $\mathrm{FeC{\equiv}O}$ unit deviates from the expected linear geometry (Fe-C-O 171.0(3)°). The bond angles at C_{ipso} of the aryl group are quite different owing to the presence of the bulky tris(methoxy)methyl substituent.

The formation of complexes **3a–b** involves cleavage of the Ar–Cl bond. This cleavage is promoted by coordination of the chlorine atom, as shown by the following experiment. Treatment of the nonchelated complex $\mathbf{5}^{+}\mathrm{OTf}^{-}$[5] under the same conditions led to formation of the acetal complexes **6a** (R = Me) and **6b** (R = Et) by addition of RO^{-} to the electrophilic carbene carbon atom. Although stable in the

$[\mathrm{Fe(C_5Me_5)(CO)_2\{\eta^1\text{-}C(OMe)C_6H_4\text{-}\mathit{o}\text{-}Cl\}]OTf}$ $\mathbf{5}^{+}\mathrm{OTf}^{-}$

$[\mathrm{Fe(C_5Me_5)(CO)_2\{\eta^1\text{-}C(OMe)(OR)C_6H_4\text{-}\mathit{o}\text{-}Cl\}}]$ **6a, b**

solid state as a yellow powder, these species undergo thermal decomposition in solution at 0 °C. Addition of $HBF_4 \cdot OEt_2$ to a crude solution of **6a** led quantitatively to the carbene

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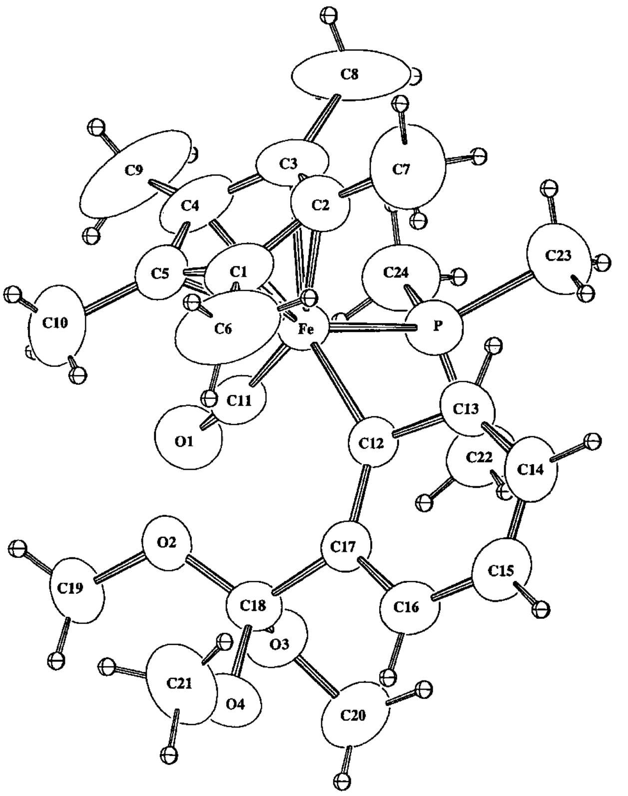

Figure 1. Crystal structure of **4**. Selected bond lengths [Å] and angles [°]: C17–C18 1.519(6), O2–C18 1.382(4), O3–C18 1.411(4), O4–C18 1.413(5), Fe–C12 2.033(3), Fe–P 2.187(1), Fe–C11 1.699(4), O2–C19 1.426(6), O3–C20 1.420(4), O4–C21 1.421(5); Fe-C11-O1 171.0(3), C11-Fe-C12 99.6, P-Fe-C11 85.9(1), P-Fe-C12 89.2(1), Fe-C12-C17 133.3(3), Fe-C12-C13 112.6(2).

complex $\mathbf{5}^+BF_4^-$, which still contains the chlorine atom, as confirmed by mass spectrometry.

Activation of an Ar–F bond by an iron complex with formation of an Ar–Fe bond has been previously postulated, but no spectroscopic evidence for an Fe–F interaction was obtained.[8] Halohydrocarbon complexes [M(η^1-XR)] (X = halogen; R = alkyl, aryl) undergo nucleophilic attack at the C_α atom.[3] However, similar activation is not observed for the chlorobenzene complex **7** on addition of Lewis bases.[9] In our

$[Re(C_5Me_5)(NO)(PPh_3)(\eta^1\text{-}ClC_6H_5)]BF_4$ **7**

case, the intermediate formation of an Ar–OMe bond by nucleophilic substitution[10] was ruled out by the investigation of the anisyl derivative **2**. The formation of the Fe–aryl bond and the subsequent rearrangement processes are not yet understood.

In contrast, the reaction of **2** with EtONa takes a completely different course: the new carbene–aryl complex **8** was isolated as a yellow solid in 80% yield (Scheme 1). The presence of the carbene ligand is indicated by the downfield signal at $\delta = 263.8$ in the ^{13}C NMR spectrum. The crystal structure (Figure 2) clearly shows that the geometry of the carbene ligand is distorted. There are two different Fe-C-O bond angles due to the presence of the anisyl ligand.[7]

We assume that the ethoxide ion initially adds to the carbene center and that the intermediate complex **9** then

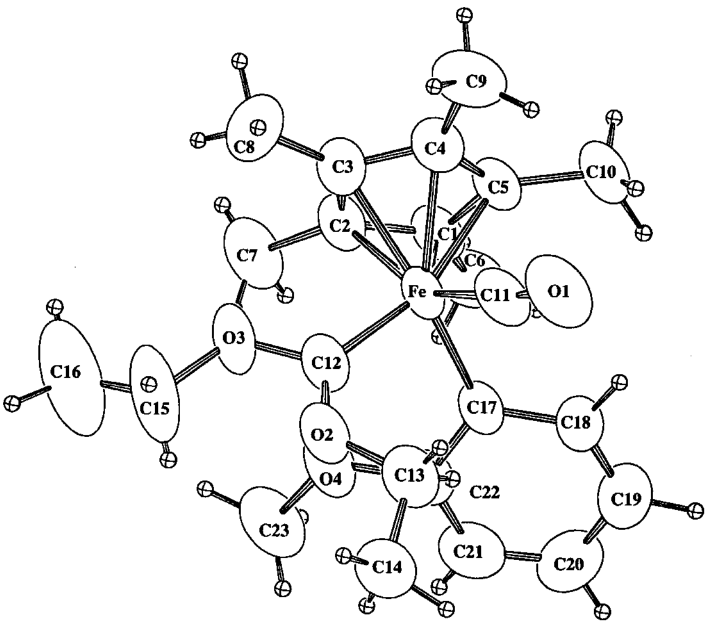

Figure 2. Crystal structure of **8**. Selected bond lengths [Å] and angles [°]: Fe–C17 1.990(6), Fe–C12 1.881(5), O2–C12 1.305(7), O3–C12 1.335(7), O4–C23 1.423(7); Fe-C11-O1 173.2(6), O2-C12-O3 108.8(4), Fe-C12-O2 133.4(4), Fe-C12-O3 117.8(4).

$(\eta^2\text{-}C,O)[Fe(C_5Me_5)(CO)\{\eta^2\text{-}C(OR)_2C_6H_4\text{-}o\text{-}OMe\}]$ **9**

rearranges by Ar–C_α bond cleavage, that is, α-aryl elimination. Examples of hydride, alkyl, and aryl migration to a carbene ligand are known;[11, 12] the reverse reaction is probably induced by the presence of the labile ligand[13] and/or the instability of the acetal complex (see above). Exchange of the alkyl group of the carbene ligand occurs in the presence of an excess of EtO^-/EtOH, a behavior already observed for vinyl ether complexes.[14]

This study illustrates the dichotomy of reactivity of iron complexes: exclusive Ar–Cl bond cleavage is promoted by the Lewis acid–base interaction, whereas the presence of a labile chelate ligand activates the Ar–C bond.

Experimental Section

A solution of **1**, **2**, or **5** (1 mmol) in THF was treated at −80 °C with a freshly prepared solution of RONa (3 equiv) in ROH (R = Me, Et). After stirring for 1 h, the solution was evaporated to dryness. The products were extracted with pentane and crystallized.

3a (89% yield, dark brown crystals): ^1H NMR (300 MHz, C_6D_6): $\delta = 7.84$ (dd, $^3J(H,H) = 7.5$, $^4J(H,H) = 0.8$ Hz, 1 H, Ar), 7.35 (td, $^3J(H,H) = 7.4$, $^4J(H,H) = 1.6$ Hz, 1 H, Ar), 7.10 (td, $^3J(H,H) = 7.4$, $^4J(H,H) = 1$ Hz, 1 H, Ar), 6.99 (dd, $^3J(H,H) = 7.5$, $^4J(H,H) = 1.5$ Hz, 1 H, Ar), 3.02 (brs, 3 H, OMe), 2.88 (brs, 3 H, OMe), 2.73 (brs, 3 H, OMe), 1.42 (s, 15 H, C_5Me_5); $^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): $\delta = 221.7$ (CO), 174.6 (FeAr), 140.2 (Ar), 136.5 (Ar_C), 127.9 (Ar), 126.8 ($C(OMe)_3$), 123.9 (Ar), 121.9 (Ar), 89.6 (C_5Me_5), 56.3 (OMe), 52.7 (OMe), 52.5 (OMe), 10.8 (C_5Me_5); IR (pentane): $\tilde{\nu} = 1917\ cm^{-1}$ (CO); C,H analysis calcd for $C_{21}H_{28}O_4Fe$: C 63.01, H 7.05; found: C 62.78, H 7.12.

3b (83% yield, dark brown crystals): ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.57$ (d, $^3J(H,H) = 7.5$ Hz, 1 H, Ar), 7.17 (t, $^3J(H,H) = 6.7$ Hz, 1 H, Ar), 6.96 (t, $^3J(H,H) = 7$ Hz, 1 H, Ar), 6.84 (d, $^3J(H,H) = 7$ Hz, 1 H, Ar), 3.31 (q, $^3J(H,H) = 7$ Hz, 2 H, OCH_2CH_3), 3.15 (s, 3 H, OMe), 3.00 (m, 1 H, OCH_2CH_3), 2.79 (m, 1 H, OCH_2CH_3), 1.60 (s, 15 H, C_5Me_5), 1.14 (t,

$^3J(\mathrm{H,H}) = 7$ Hz, 3H, $\mathrm{OCH_2C}H_3$), 0.98 (t, $^3J(\mathrm{H,H}) = 7$ Hz, 3H, $\mathrm{OCH_2C}H_3$); $^{13}\mathrm{C}\{^1\mathrm{H}\}$ NMR (75.47 MHz, $\mathrm{CDCl_3}$): $\delta = 221.4$ (CO), 173.5 (FeAr), 139.7 (Ar), 137.4 ($\mathrm{Ar_C}$), 127.4 (Ar), 125.8 ($C(\mathrm{OMe})(\mathrm{OEt})_2$), 123.4 (Ar), 121.5 (Ar), 89.2 ($C_5\mathrm{Me_5}$), 60.2 ($\mathrm{O}C\mathrm{H_2CH_3}$), 59.8 ($\mathrm{O}C\mathrm{H_2CH_3}$), 55.8 (OMe), 15.3 ($\mathrm{OCH_2}C\mathrm{H_3}$), 14.8 ($\mathrm{OCH_2}C\mathrm{H_3}$), 10.1 ($\mathrm{C_5}Me_5$); IR (pentane): $\tilde{\nu} = 1914\ \mathrm{cm^{-1}}$ (CO); C,H analysis calcd for $\mathrm{C_{23}H_{32}O_4Fe}$: C 64.49, H 7.53; found: C 64.82, H 7.47; HRMS (70 eV): m/z: 428.1641 [M^+], calcd for $\mathrm{C_{23}H_{32}O_4Fe}$: 428.1649.

4 (65% yield): ^{1}H NMR (200 MHz, $\mathrm{CDCl_3}$): $\delta = 7.84$ (d, $^3J(\mathrm{H,H}) = 7.6$ Hz, 1H, Ar), 7.38 (dd $^3J(\mathrm{H,H}) = 7.8$, $^4J(\mathrm{H,H}) = 1.7$ Hz, 1H, Ar), 6.85 (td, $^3J(\mathrm{H,H}) = 7.3$, $^4J(\mathrm{H,H}) = 1.4$ Hz, 1H, Ar), 6.69 (td,$^3J(\mathrm{H,H}) = 7.3$, $^4J(\mathrm{H,H}) = 1.8$ Hz, 1H, Ar), 3.29 (s, 9H, OMe), 1.65 (s, 15H, $\mathrm{C_5Me_5}$), 1.12 (d, $^2J(\mathrm{P,H}) = 8.4$ Hz, 9H, $\mathrm{PMe_3}$); $^{31}\mathrm{P}\{^1\mathrm{H}\}$ NMR (81 MHz, $\mathrm{CDCl_3}$): $\delta = 36.51$ (s, $\mathrm{PMe_3}$); $^{13}\mathrm{C}\{^1\mathrm{H}\}$ NMR (75.47 MHz, $\mathrm{CDCl_3}$): $\delta = 222.6$ (d, $^2J(\mathrm{P,C}) = 38$ Hz, CO), 170.4 (d, $^2J(\mathrm{P,C}) = 26$ Hz, FeAr), 146.1 (d, $^2J(\mathrm{P,C}) = 12$ Hz, Ar), 145.8 ($\mathrm{Ar_C}$), 129.2 (Ar), 122.6 (Ar), 119.3 (Ar), 117.7 ($C(\mathrm{OMe})_3$), 92.1 ($C_5\mathrm{Me_5}$), 49.9 (OMe), 17.6 (d, $^1J(\mathrm{P,C}) = 26$ Hz, $\mathrm{PMe_3}$), 10.2 ($\mathrm{C_5}Me_5$); IR ($\mathrm{CH_2Cl_2}$): $\tilde{\nu} = 1898\ \mathrm{cm^{-1}}$ (CO); C,H analysis calcd for $\mathrm{C_{24}H_{37}O_4FeP}$: C 60.51, H 7.83; found: C 60.78, H 7.75.

6b (80% yield, isolated at $-40\,^\circ$C, yellow powder): ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$, $-30\,^\circ$C): $\delta = 7.58$, 7.47, 7.17, 6.98 (Ar), 3.55, 3.40 (br m, $\mathrm{OC}H_2\mathrm{CH_3}$), 3.31 (s, OMe), 3.25, 3.05 (br m, $\mathrm{OC}H_2\mathrm{CH_3}$), 2.98 (s, OMe), 1.73, 1.64 (s, $\mathrm{C_5Me_5}$), 1.35, 1.17 (br m, $\mathrm{OCH_2C}H_3$); $^{13}\mathrm{C}\{^1\mathrm{H}\}$ NMR (75.47 MHz, $\mathrm{CDCl_3}$, $-30\,^\circ$C): $\delta = 219.1$, 218.8, 218.2 (CO), 149.6, 147.9.($\mathrm{Ar_C}$), 131.3, 130.9 (Ar), 129.8, 129.2 ($\mathrm{Ar_{Cl}}$), 128.0, 126.9, 126.5, 125.9, 125.6 (Ar), 116.5, 114.9 (C_α), 97.9, 96.6 ($C_5\mathrm{Me_5}$), 58.9, 57.1 ($\mathrm{O}C\mathrm{H_2CH_3}$), 51.5, 50.8 (OMe), 15.5, 15.0 ($\mathrm{OCH_2}C\mathrm{H_3}$), 10.0, 9.8 ($\mathrm{C_5}Me_5$); IR (pentane): $\tilde{\nu} = 1997$ (CO), $1947\ \mathrm{cm^{-1}}$ (CO). Two isomers were observed at $-30\,^\circ$C owing to hindered $\mathrm{C}_\alpha^* - \mathrm{Ar}$ rotation at low temperature. No coalescence was observed up to the decomposition temperature of O °C.

8 (80% yield, yellow crystals): ^{1}H NMR (300 MHz, $\mathrm{C_6D_6}$): $\delta = 7.75$ (d, $^3J(\mathrm{H,H}) = 6.6$ Hz, 1H, Ar), 7.11 (t, $^3J(\mathrm{H,H}) = 7.5$ Hz, 1H, Ar), 6.96 (t, $^3J(\mathrm{H,H}) = 7$ Hz, 1H, Ar), 6.59 (d,$^3J(\mathrm{H,H}) = 6.6$ Hz, 1H, Ar), 4.05 (br m, 2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 3.92 (br m, 2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 3.48 (s, 3H, OMe), 1.61 (s, 15H, $\mathrm{C_5Me_5}$), 0.92 (br m, 6H, $\mathrm{OCH_2C}H_3$); $^{13}\mathrm{C}\{^1\mathrm{H}\}$ NMR (75.47 MHz, $\mathrm{CD_2Cl_2}$): $\delta = 263.8$ ($=\mathrm{C}_\alpha$), 226.6 (CO), 166.7 (FeAr), 154.3 ($\mathrm{Ar_{OMe}}$), 143.9 (Ar), 122.5 (Ar), 119.8 (Ar), 108.2 (Ar), 95.5 ($C_5\mathrm{Me_5}$), 66.7 (br s, $\mathrm{O}C\mathrm{H_2CH_3}$), 55.1 (OMe), 14.6 ($\mathrm{OCH_2}C\mathrm{H_3}$), 9.7 ($\mathrm{C_5}Me_5$); IR (pentane): $\tilde{\nu} = 1936\ \mathrm{cm^{-1}}$ (CO); HRMS (70 eV): m/z: 383.1314 [$M^+ - \mathrm{OEt}$], calcd for $\mathrm{C_{21}H_{27}O_3Fe}$: 383.1310; 355.1355 [$M^+ - \mathrm{OEt} - \mathrm{CO}$], calcd for $\mathrm{C_{20}H_{27}O_2Fe}$: 355.1361.

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[7] Crystal structure of **4**: Enraf-Nonius CAD4 diffractometer, $\mathrm{Mo_{K\alpha}}$ radiation, $\mu = 6.91\ \mathrm{cm^{-1}}$, $F(000) = 508$, $T = 294$ K, triclinic, space group $P\bar{1}$, $a = 9.601(5)$, $b = 10.711(5)$, $c = 13.600(6)$ Å, $\alpha = 75.55(4)$, $\beta = 84.46(4)$, $\gamma = 67.88(3)^\circ$, $V = 1246(1)$ Å^{-3}, $Z = 2$, $\rho = 1.270\ \mathrm{g\,cm^{-3}}$. Of 4402 reflections, 3524 with $I > 2\sigma(I)$ were observed ($\omega/2\theta = 1$, hkl: 0.11, -12.12, -16.16). Lorentzian and polarization corrections (DEFLT 1990), $R = 0.046$, $R_w = 0.047$, $w = 1/\sigma(F_o)^2 = [\sigma^2(I) + (0.04\,F_o^2)^2]^{-1/2}$, $S_w = 0.890$ (residual $\Delta\rho < 0.44$ e Å^{-3}). Crystal structure of **8**: Enraf-Nonius CAD4 diffractometer, $\mathrm{Mo_{K\alpha}}$ radiation, $\mu = 7.086\ \mathrm{cm^{-1}}$, $F(000) = 456$, $T = 294$ K, triclinic, space group $P\bar{1}$, $a = 8.773(6)$, $b = 9.185(9)$, $c = 14.572(9)$ Å, $\alpha = 99.64(5)$, $\beta = 89.89(2)$, $\gamma = 108.34(5)^\circ$, $V = 1097(1)$ Å^{-3}, $Z = 2$, $\rho = 1.296\ \mathrm{g\,cm^{-3}}$. Of 4133 reflections, 2364 observed with $I > 4\sigma(I)$ ($\omega/2\theta = 1$, hkl: 0.10, -10.10, -17.17), Lorentzian and polarization corrections (DEFLT 1990), $R = 0.056$, $R_w = 0.051$, $w = 1/\sigma(F_o)^2 = [\sigma^2(I) + (0.04\,F_o^2)^2]^{-1/2}$, $S_w = 1.13$ (residual $\Delta\rho < 0.46$ e Å^{-3}). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100931. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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Synthetic Studies on Ciguatoxin: A Convergent Strategy for Construction of the F–M Ring Framework[**]

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Kazuo Tachibana*

Ciguatoxin (CTX1B, **1**) and its congeners, naturally occurring polycyclic ethers found in marine unicellular algae, are the principal toxins associated with ciguatera fish poisoning.[1, 2] These potent neurotoxins reportedly bind to the same sites on voltage-sensitive sodium channels (VSSC) as brevetoxins, another class of structurally related marine toxins.[3] An important structural characteristic is the fact that the hexahydrooxonin ring (the F ring) in **1** and its congeners

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