^{3}J(H,H) = 7 Hz, 3H, OCH$_2$CH_3), 0.98 (t, ^{3}J(H,H) = 7 Hz, 3H, OCH$_2$CH_3); ^{13}C{^{1}H} NMR (75.47 MHz, CDCl$_3$): δ = 221.4 (CO), 173.5 (FeAr), 139.7 (Ar), 137.4 (Ar$_C$), 127.4 (Ar), 125.8 (*C*(OMe)(OEt)$_2$), 123.4 (Ar), 121.5 (Ar), 89.2 (*C*$_5$Me$_5$), 60.2 (O*C*H$_2$CH$_3$), 59.8 (O*C*H$_2$CH$_3$), 55.8 (OMe), 15.3 (OCH$_2$*C*H$_3$), 14.8 (OCH$_2$*C*H$_3$), 10.1 (C$_5$*Me*$_5$); IR (pentane): $\tilde{\nu}$ = 1914 cm^{-1} (CO); C,H analysis calcd for C$_{23}$H$_{32}$O$_4$Fe: C 64.49, H 7.53; found: C 64.82, H 7.47; HRMS (70 eV): *m/z*: 428.1641 [M^+], calcd for C$_{23}$H$_{32}$O$_4$Fe: 428.1649.

4 (65% yield): ^{1}H NMR (200 MHz, CDCl$_3$): δ = 7.84 (d, ^3J(H,H) = 7.6 Hz, 1H, Ar), 7.38 (dd ^3J(H,H) = 7.8, ^4J(H,H) = 1.7 Hz, 1H, Ar), 6.85 (td, ^3J(H,H) = 7.3, ^4J(H,H) = 1.4 Hz, 1H, Ar), 6.69 (td,^3J(H,H) = 7.3, ^4J(H,H) = 1.8 Hz, 1H, Ar), 3.29 (s, 9H, OMe), 1.65 (s, 15H, C$_5$Me$_5$), 1.12 (d, ^2J(P,H) = 8.4 Hz, 9H, PMe$_3$); ^{31}P{^{1}H} NMR (81 MHz, CDCl$_3$): δ = 36.51 (s, PMe$_3$); ^{13}C{^{1}H} NMR (75.47 MHz, CDCl$_3$): δ = 222.6 (d, ^2J(P,C) = 38 Hz, CO), 170.4 (d, ^2J(P,C) = 26 Hz, FeAr), 146.1 (d, ^2J(P,C) = 12 Hz, Ar), 145.8 (Ar$_C$), 129.2 (Ar), 122.6 (Ar), 119.3 (Ar), 117.7 (*C*(OMe)$_3$), 92.1 (*C*$_5$Me$_5$), 49.9 (OMe), 17.6 (d, ^1J(P,C) = 26 Hz, PMe$_3$), 10.2 (C$_5$*Me*$_5$); IR (CH$_2$Cl$_2$): $\tilde{\nu}$ = 1898 cm^{-1} (CO); C,H analysis calcd for C$_{24}$H$_{37}$O$_4$FeP: C 60.51, H 7.83; found: C 60.78, H 7.75.

6b (80% yield, isolated at −40°C, yellow powder): ^{1}H NMR (300 MHz, CDCl$_3$, −30°C): δ = 7.58, 7.47, 7.17, 6.98 (Ar), 3.55, 3.40 (brm, OCH_2CH$_3$), 3.31 (s, OMe), 3.25, 3.05 (brm, OCH_2CH$_3$), 2.98 (s, OMe), 1.73, 1.64 (s, C$_5$Me$_5$), 1.35, 1.17 (brm, OCH$_2$CH_3); ^{13}C{^{1}H} NMR (75.47 MHz, CDCl$_3$, −30°C): δ = 219.1, 218.8, 218.2 (CO), 149.6, 147.9.(Ar$_C$), 131.3, 130.9 (Ar), 129.8, 129.2 (Ar$_{Cl}$), 128.0, 126.9, 126.5, 125.9, 125.6 (Ar), 116.5, 114.9 (C$_\alpha$), 97.9, 96.6 (*C*$_5$Me$_5$), 58.9, 57.1 (O*C*H$_2$CH$_3$), 51.5, 50.8 (OMe), 15.5, 15.0 (OCH$_2$*C*H$_3$), 10.0, 9.8 (C$_5$*Me*$_5$); IR (pentane): $\tilde{\nu}$ = 1997 (CO), 1947 cm^{-1} (CO). Two isomers were observed at −30°C owing to hindered C$^*_\alpha$–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, C$_6$D$_6$): δ = 7.75 (d, ^3J(H,H) = 6.6 Hz, 1H, Ar), 7.11 (t, ^3J(H,H) = 7.5 Hz, 1H, Ar), 6.96 (t, ^3J(H,H) = 7 Hz, 1H, Ar), 6.59 (d,^3J(H,H) = 6.6 Hz, 1H, Ar), 4.05 (brm, 2H, OCH_2CH$_3$), 3.92 (brm, 2H, OCH_2CH$_3$), 3.48 (s, 3H, OMe), 1.61 (s, 15H, C$_5$Me$_5$), 0.92 (brm, 6H, OCH$_2$CH_3); ^{13}C{^{1}H} NMR (75.47 MHz, CD$_2$Cl$_2$): δ = 263.8 (=C$_\alpha$), 226.6 (CO), 166.7 (FeAr), 154.3 (Ar$_{OMe}$), 143.9 (Ar), 122.5 (Ar), 119.8 (Ar), 108.2 (Ar), 95.5 (*C*$_5$Me$_5$), 66.7 (brs, O*C*H$_2$CH$_3$), 55.1 (OMe), 14.6 (OCH$_2$*C*H$_3$), 9.7 (C$_5$*Me*$_5$); IR (pentane): $\tilde{\nu}$ = 1936 cm^{-1} (CO); HRMS (70 eV): *m/z*: 383.1314 [M^+ − OEt], calcd for C$_{21}$H$_{27}$O$_3$Fe: 383.1310; 355.1355 [M^+ − OEt − CO], calcd for C$_{20}$H$_{27}$O$_2$Fe: 355.1361.

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Keywords: carbene complexes · C–C activation · C–Cl activation · iron

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[7] Crystal structure of **4**: Enraf-Nonius CAD4 diffractometer, Mo$_{K\alpha}$ radiation, $\mu = 6.91$ 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, $\alpha = 75.55(4)$, $\beta = 84.46(4)$, $\gamma = 67.88(3)°$, $V = 1246(1)$ Å^{-3}, $Z = 2$, $\rho = 1.270$ 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), $R = 0.046$, $R_w = 0.047$, $w = 1/\sigma(F_o)^2 = [\sigma^2(I) + (0.04F_o^2)^2]^{-1/2}$, $S_w = 0.890$ (residual $\Delta\rho < 0.44$ e Å^{-3}). Crystal structure of **8**: Enraf-Nonius CAD4 diffractometer, Mo$_{K\alpha}$ radiation, $\mu = 7.086$ 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, $\alpha = 99.64(5)$, $\beta = 89.89(2)$, $\gamma = 108.34(5)°$, $V = 1097(1)$ Å^{-3}, $Z = 2$, $\rho = 1.296$ 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), $R = 0.056$, $R_w = 0.051$, $w = 1/\sigma(F_o)^2 = [\sigma^2(I) + (0.04F_o^2)^2]^{-1/2}$, $S_w = 1.13$ (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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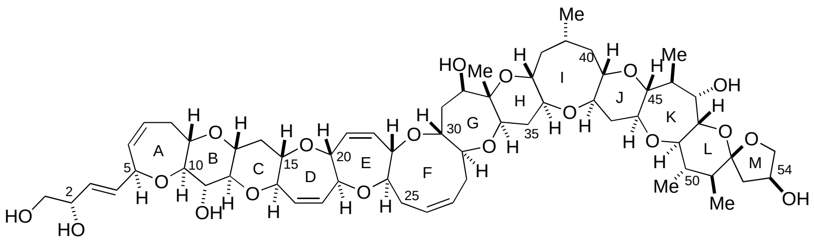

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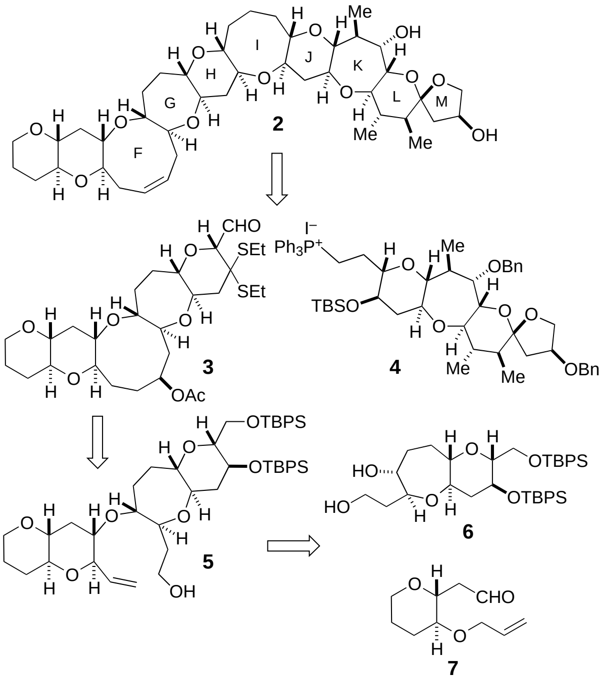
undergoes a slow conformational change in solution, which is thought to play a role in high-affinity binding to VSSC and/or VSSC activation.[1g] The structural complexity of the ciguatoxins and their exceptionally potent neurotoxicity together with their scarcity in natural sources make them prime targets for a total synthesis.[4, 5] In particular, construction of the hexahydrooxonin ring system represents a challenging synthetic problem. Despite recent advances in the synthesis of cyclic ethers,[6] there is still no general and convergent method for the assembly of a fused nine-membered ether ring system.[7]

We recently reported for the first time a convergent approach to the fused hexahydrooxonin ring system, one that features both an intramolecular reaction of a γ-alkoxyallylsilane with an acetal group to form an O-linked oxacycle and an SmI_2-mediated intramolecular Reformatsky reaction that leads to an oxonane ring.[5d] As part of our continuing investigation into the structural requirements for high-affinity binding of ciguatoxin to VSSC, we describe here the application of this strategy to a convergent synthesis of the decacyclic ciguatoxin mimic **2**, which contains the F–M ring framework but with the DE ring system of ciguatoxin replaced by a dioxadecalin unit.

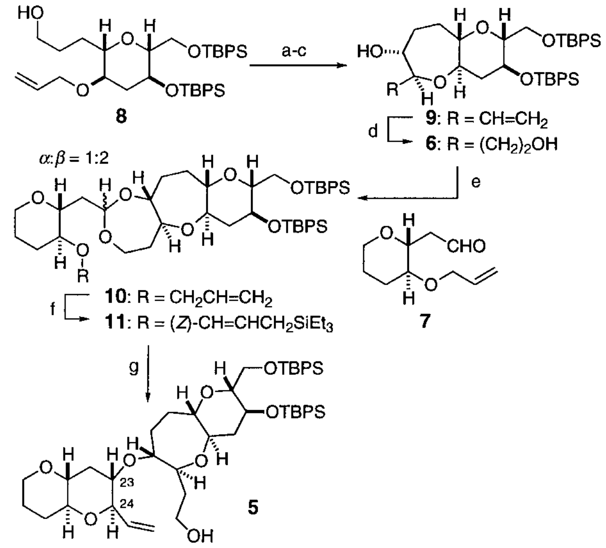
Based on a retrosynthetic analysis we anticipated that the target molecule **2**[8] could be prepared from aldehyde **3** and phosphonium salt **4** through a Wittig reaction followed by cyclization of the resulting hydroxy dithio acetal[9] (Scheme 1). The oxonane ring in **3** should be accessible from **5**, which in turn could be prepared from diol **6** and aldehyde **7** with the aid of our previously reported strategy.[5d]

Synthesis of the O-linked tetracycle **5** began with alcohol **8**,[10] which was converted into bicyclic compound **9** by the method of Yamamoto et al.[11] (Scheme 2). Formation of the corresponding alkoxy-substituted allylic anion followed by a trapping reaction with tributyltin chloride afforded the γ-alkoxyallylstannane in 88% yield. Oxidation of the primary hydroxyl group to a formyl group and subsequent treatment with boron trifluoride etherate provided **9** as a single stereoisomer in high yield. Hydroboration of **9** with 9-borabicyclononane (9-BBN) followed by oxidative work-up led to diol **6** (86% yield over three steps). Reaction of **6** with aldehyde **7** was carried out in the presence of 0.1 equivalents of scandium trifluoromethanesulfonate[12] to give an epimeric mixture of seven-membered acetals **10** in an approximately 2:1 ratio, with the β-H isomer predominating (82% combined yield).[13]

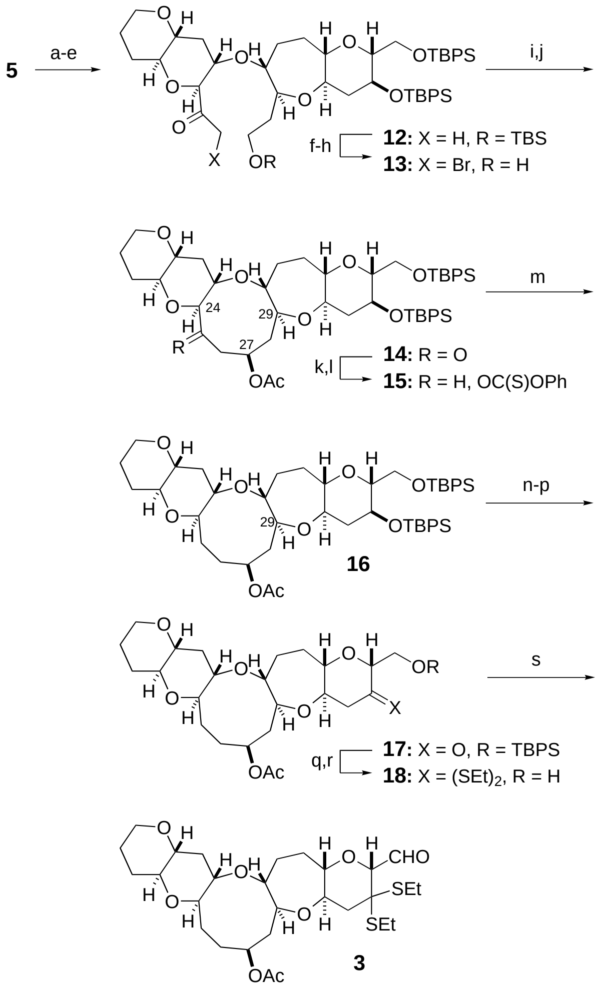
Metalation of **10** with *sec*-butyllithium followed by treatment with chlorotriethylsilane gave a mixture of γ-alkoxyallylsilanes **11** in 87% yield accompanied by recovered pure α-H isomer of **10** (12%). Use of the triethylsilyl group instead of the more common trimethylsilyl moiety in this reaction resulted in a higher yield and greater reproducibility.[14] Treatment of **11** with titanium(IV) chloride and triphenylphosphane[15] gave O-linked **5** with the desired stereochemistry as the major product, albeit in modest yield (36%), together with the (23*R*,24*R*) diastereoisomer (16%) and trace amounts of two other stereoisomers.[16]



Scheme 1. Retrosynthesis of the decacyclic polyether **2**. Bn = benzyl, TBPS = *tert*-butyldiphenylsilyl.



Scheme 2. Synthesis of the O-linked tetracycle **5**. a) *s*BuLi, nBu_3SnCl, THF, −78 °C, 88%; b) $SO_3\cdot$pyridine, Et_3N, DMSO, CH_2Cl_2, RT, 92%; c) $BF_3\cdot OEt_2$, CH_2Cl_2, −90 °C; d) 9-BBN, THF, RT, then H_2O_2, $NaHCO_3$, RT, 94% (2 steps); e) $Sc(OTf)_3$ (cat.), benzene, RT, 82%; f) *s*BuLi, Et_3SiCl, THF, −78 °C, 87%; g) $TiCl_4$, PPh_3, CH_2Cl_2, −78→0 °C, 36%. DMSO = dimethyl sulfoxide, 9-BBN = 9-borabicyclononane, OTf = trifluoromethanesulfonate.



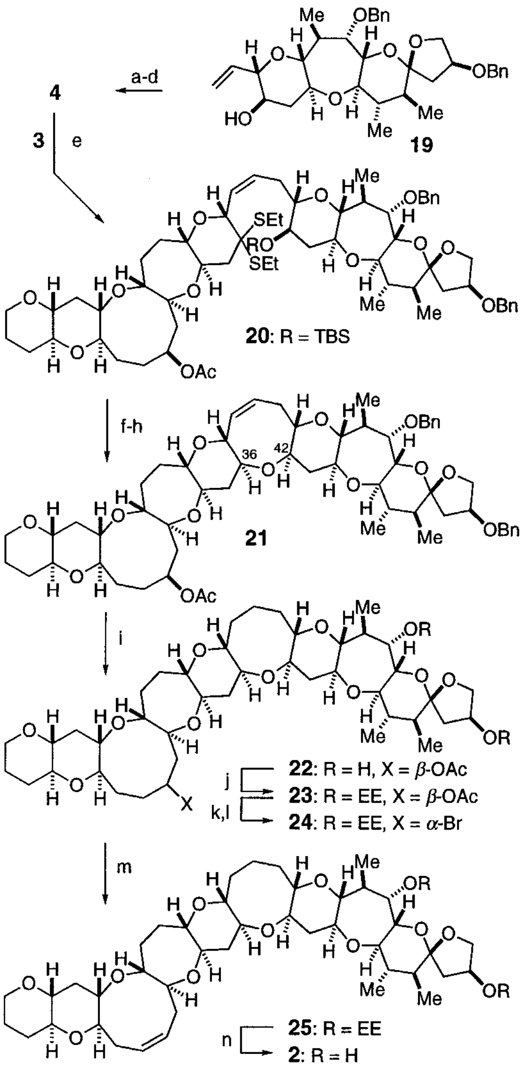
Scheme 3. Synthesis of pentacyclic aldehyde **3**. a) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 95 %; b) OsO_4, NMO, *t*BuOH/H_2O, RT; c) $Pb(OAc)_4$, benzene, RT, d) MeMgBr, THF, −78 → 0 °C, 91 % (3 steps); e) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C → RT, 94 %; f) LDA, Me_3SiCl, THF, −78 °C; g) NBS, THF, 0 °C; h) CSA (cat.), MeOH, RT, 83 % (3 steps); i) $SO_3\cdot$pyridine, Et_3N, DMSO, CH_2Cl_2, 0 °C; j) SmI_2 (5 equiv), THF, −78 °C, then Ac_2O, 4-DMAP, 0 °C; k) $NaBH_4$, CH_2Cl_2/MeOH, 0 °C; l) PhOC(S)Cl, 4-DMAP, CH_3CN, RT, 66 % (5 steps); m) *n*Bu_3SnH (20 equiv), Et_3B (cat.), benzene, RT, 80 %; n) *n*Bu_4NF, THF, RT; o) TBPSCl, imidazole, DMF, 0 °C, 82 % (2 steps); p) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C → RT, 94 %; q) EtSH, $TiCl_4$, CH_2Cl_2, −78 °C; r) *n*Bu_4NF, THF, RT, 97 % (2 steps); s) $SO_3\cdot$pyridine, Et_3N, DMSO, CH_2Cl_2, 0 °C. TBS = *tert*-butyldimethylsilyl, NMO = *N*-methylmorpholine *N*-oxide, DMF = dimethylformamide, LDA = lithium diisopropylamide, NBS = *N*-bromosuccinimide, CSA = 10-camphorsulfonic acid, 4-DMAP = 4-dimethylaminopyridine.

The elaboration of **5** to aldehyde **3** is outlined in Scheme 3. Protection of **5** as the *tert*-butyldimethylsilyl ether and oxidative cleavage of the double bond led to an aldehyde that reacted with methylmagnesium bromide. The resulting alcohol was oxidized under Swern conditions to afford methyl ketone **12** in an overall yield of 81 %. Formation of the silyl enol ether, treatment with NBS, and desilylation under acidic conditions gave alcohol **13** in 83 % yield over three steps. This was followed by oxidation of **13** with $SO_3\cdot$pyridine to the aldehyde, which was subjected to an SmI_2-mediated intramolecular Reformatsky reaction under the previously reported conditions.[5d] Thus, treatment of the aldehyde with five equivalents of SmI_2 in THF at −78 °C gave, after in situ acetylation, β-acetoxy ketone **14** in high yield as a single diastereomer,[17] which was immediately reduced with sodium borohydride.[18] The resulting alcohol was converted into phenyl thiocarbonate **15** (66 % overall yield based on **13**). A subsequent radical reduction of **15** proved to be problematic. When the reduction was carried out with *n*Bu_3SnH and AIBN under thermal conditions (benzene, 80 °C), formation of the undesired C29 isomer of **16** predominated, presumably due to transannular hydrogen abstraction. After considerable experimentation, an optimal result was achieved with a large excess of *n*Bu_3SnH in the presence of triethylborane[19] at room temperature; acetate **16** was obtained in 80 % yield. Removal of two silyl groups in **16** and selective reprotection of the primary hydroxyl group followed by oxidation of the secondary alcohol provided ketone **17** in an overall yield of 77 %. Formation of the thio acetal from **17** and desilylation gave alcohol **18** in 97 % yield. This was oxidized to the requisite aldehyde **3**, which was thereby available for coupling with **4**.

Phosphonium salt **4** was prepared from the previously reported JKLM ring fragment **19**[5b, c] by a four-step sequence of routine synthetic reactions (Scheme 4). Wittig reaction of the ylide generated from **4** with aldehyde **3** produced exclusively *Z* olefin **20** in 63 % yield. Desilylation of **20** followed by AgOTf-induced cyclization of the resulting hydroxy dithio acetal[9] and radical desulfurization[9] provided tetrahydrooxocin **21** and thus the desired decacyclic system.[20] Hydrogenation of the double bond in **21** and simultaneous hydrogenolysis of the benzyl groups gave diol **22**. Preliminary studies revealed that protection was required for the seriously hindered hydroxyl group at C47 to permit introduction of a *Z* double bond into the oxonane ring. Accordingly, **22** was protected as the bis(ethoxyethyl) ether **23** in quantitative yield. After deacetylation of **23** with diisobutylaluminum hydride, the alcohol product was treated with methanesulfonic anhydride in the presence of lithium bromide and Hünig base to give bromide **24** as a single stereoisomer, which upon exposure to potassium *tert*-butoxide in dimethyl sulfoxide[21] afforded the desired hexahydrooxonin **25** in a yield of 52 % based on **23**. Finally, removal of the ethoxy ethyl groups in **25** with pyridinium *p*-toluenesulfonate furnished the target compound **2**[22] in quantitative yield.

^1H and ^{13}C NMR signals due to the hexahydrooxonin ring of **2** were severely broadened at room temperature, which is consistent with the behavior of ring F in ciguatoxin. Dynamic NMR studies revealed that **2** exists as an approximately 1:1 equilibrium of two conformational states at the hexahydrooxonin ring. Preliminary investigation of the binding affinity of **2** to VSSC was conducted through a competitive inhibition assay.[3b] Synthetic **2** did not inhibit the binding of tritium-labeled dihydrobrevetoxin B (PbTx-3) to rat-brain synaptosomes at micromolar concentrations. Assay at higher levels proved impractical owing to low solubility of the compound in aqueous media. The possibility of noncompetitive binding is currently under investigation.

We have thus demonstrated that the SmI_2-mediated intramolecular Reformatsky reaction provides a general and powerful method for the construction of the *trans*-fused



Scheme 4. Synthesis of decacyclic polyether **2**. a) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 87 %; b) 9-BBN, THF, RT, then H_2O_2, $NaHCO_3$, RT, 85 %; c) I_2, PPh_3, imidazole, benzene, RT, 97 %; d) PPh_3, CH_3CN, 70 °C, 97 %; e) *n*BuLi, THF/HMPA, $-78\,^{\circ}C \rightarrow$ RT, 63 %; f) nBu_4NF, THF, RT, 90 %; g) AgOTf, $NaHCO_3$, 4-Å molecular sieves, silica gel, CH_3NO_2, RT, 76 % based on 70 % conversion; h) Ph_3SnH (10 equiv), AIBN (cat.), toluene, 110 °C, 82 %; i) H_2, $Pd(OH)_2/C$, EtOAc/MeOH/AcOH, RT; j) ethyl vinyl ether, PPTS, CH_2Cl_2, RT, 99 % (2 steps); k) DIBAL-H, CH_2Cl_2, $-78\,^{\circ}C$; l) Ms_2O, LiBr, iPr_2NEt, CH_2Cl_2, $0\,^{\circ}C \rightarrow$ RT; m) *t*BuOK, DMSO, RT, 52 % (3 steps); n) PPTS (cat.), MeOH, RT, quant. HMPA = hexamethyl phosphoramide, AIBN = 2,2′-azobisisobutyronitrile, PPTS = pyridinium *p*-toluenesulfonate, EE = ethoxyethyl, DIBAL-H = diisobutylaluminum hydride, Ms_2O = methanesulfonic anhydride.

hexahydrooxonin ring system found in ciguatoxins. Studies directed toward the total synthesis of ciguatoxin and its simplified analogues are currently underway.

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Keywords: ciguatoxin · cyclizations · natural products · polyethers · synthetic methods

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[17] The configuration at C27 of **14** was assigned on the basis of strong NOEs between 24-H/27-H and 27-H/29-H. The *syn* relationship between 23-H and 30-H was also confirmed by NOE experiments.

[18] β-Acetoxy ketone **14** underwent partial β-elimination during chromatography over silica gel to yield the α,β-unsaturated ketone.

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[22] Selected spectroscopic data for **2**: IR (film): $\tilde{\nu} = 3446, 2929, 2863, 1455, 1375, 1338, 1280, 1080, 939\,\mathrm{cm^{-1}}$; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 5.74-5.61$ (br, 2H; 26-H, 27-H), 4.48 (m, 1H; 54-H), 3.86 (dd, $J = 10.1$, 4.3 Hz, 1H; 55-H), 3.85 (m, 1H; 17-H), 3.77 (d, $J = 10.1$ Hz, 1H; 55-H), 3.67 (dd, $J = 3.7$, 1.5 Hz, 1H; 47-H), 3.66 (m, 1H; 44-H), 3.61 (dd, $J = 9.8$, 1.5 Hz, 1H; 48-H), 3.55 (br, 1H; 29-H), 3.43 (m, 1H; 30-H), 3.31 (m, 1H; 17-H), 3.22 (dd, $J = 9.8$, 9.8 Hz, 1H; 49-H), 3.19–3.13 (m, 3H; 34-H, 36-H, 42-H), 3.07 (m, 2H; 23-H, 24-H), 3.01 (m, 1H; 37-H), 2.94–2.89 (m, 4H; 20-H, 21-H, 33-H, 41-H), 2.83 (dd, $J = 10.1$, 5.2 Hz, 1H; 45-H), 2.80–2.56 (br, 2H; 25-H, 28-H), 2.34–1.35 (m, 27H; 18-H_2, 19-H_2, 22-H_2, 25-H, 28-H, 31-H_2, 32-H_2, 35-H_2, 38-H_2, 39-H_2, 40-H_2, 43-H_2, 46-H, 50-H, 51-H, 53-H_2), 1.11 (d, $J = 7.6$ Hz, 3H; 46-Me), 1.02 (d, $J = 6.4$ Hz, 3H; 50-Me), 0.98 (d, $J = 6.7$ Hz, 3H; 51-Me); HR-MS (FAB) calcd for $C_{42}H_{64}O_{12}Na$ [M+Na^+]: 783.4295, found: 783.4285.

Solution pH: A Selectivity Switch in Aqueous Organometallic Catalysis—Hydrogenation of Unsaturated Aldehydes Catalyzed by Sulfonatophenylphosphane–Ru Complexes**

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Organometallic catalysis in aqueous medium offers an important possibility for avoiding the greatest problem of homogeneous catalysis: having to separate the catalyst from the product. In two-phase mixtures with an aqueous and an organic phase, soluble catalysts can be recovered by phase separation.[1] In many cases, water-soluble transition metal catalysts are prepared with sulfonated phosphane ligands such as (3-sulfonatophenyl)diphenylphosphane (TPPMS, **1**) and tris(3-sulfonatophenyl)phosphane (TPPTS, **2**); in general, both are used as their sodium salts.

Selective hydrogenation of α,β-unsaturated aldehydes to the corresponding allylic alcohols gives valuable products for fragrance, flavor, and vitamin chemistry. The most successful two-phase processes use ruthenium(II) complexes with sulfonated phosphane ligands as (pre)catalysts. Complex **3a** can be used for the reduction of citronellal to citronellol by hydrogen transfer from aqueous sodium formate,[2] and for the hydrogenation of cinnamaldehyde.[3] $RuCl_3$ and **2** form an in situ catalyst for the hydrogenation of 3-methyl-2-butenal (prenal).[4] Of the complexes **3b**, **4b**, and **5b**, the most active and durable catalyst precursor for the hydrogenation of cinnamaldehyde was **5b**.[5] In all these reactions the selectivity towards the unsaturated alcohol was at least 95%. As an apparent contradiction, in the hydrogenation of prenal with **4b** the C=C bond also became extensively hydrogenated.[5]

$[\{RuCl_2(tppms)_2\}_2]$	**3a**	$[\{RuCl_2(tppts)_2\}_2]$	**3b**
$[HRuCl(tppms)_3]$	**4a**	$[HRuCl(tppts)_3]$	**4b**
$[\{H_2Ru(tppms)_2\}_2]$	**5a**	$[\{H_2Ru(tppts)_2\}_2]$	**5b**

We are currently performing potentiometric studies on the formation and protic equilibria of water-soluble rhodium(I),[6] iridium(I),[7] and ruthenium(II) hydrides as a function of pH value to learn about the specific influence of water as solvent on the mechanism of catalyzed aqueous organometallic reactions. In several cases, such as with reactions (a) and (b), the equilibrium distribution of hydride complexes was strongly dependent on the pH of the solution.

$$1/2\underset{\mathbf{3a}}{[\{RuCl_2(tppms)_2\}_2]} + H_2 + TPPMS \rightleftharpoons \underset{\mathbf{4a}}{[HRuCl(tppms)_3]} + H^+ + Cl^- \qquad (a)$$

$$\underset{\mathbf{4a}}{[HRuCl(tppms)_3]} + H_2 + TPPMS \rightleftharpoons \underset{\mathbf{5a}}{[H_2Ru(tppms)_4]} + H^+ + Cl^- \qquad (b)$$

The amount of proton liberated during hydrogenation of **3a** (in the presence of three equivalents of **1**) was measured in solutions with different but constant pH values between 1 and 12 (static-pH hydrogenations). The major species in acidic solutions is **4a**, while in neutral and basic media **5a** can be found almost exclusively. This was confirmed by ^{1}H and ^{31}P NMR spectroscopy (Figure 1).[8] It is noteworthy that the shift in the hydride distribution occurs between pH 5 and 7.

Cinnamaldehyde was hydrogenated under the same experimental conditions used for the NMR measurements, except that the reactions were run at 80 °C instead of 50 °C. At pH values greater than 6, where the dominant ruthenium species is **5a**, exclusive hydrogenation of the aldehyde functionality occurred to yield cinnamyl alcohol. Conversely, **4a**, which forms below pH 5, was unreactive towards the aldehyde group but catalyzed a slow reduction of the C=C bond to furnish 3-phenylpropanal selectively.

The influence of the pH value on the selectivity of reactions catalyzed by [Ru(tppms)] complexes is demonstrated in

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