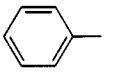
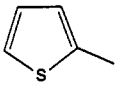
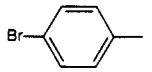
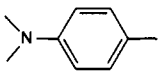
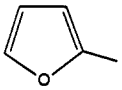
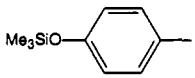
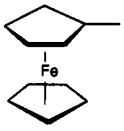
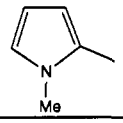
Table I. Summary of Results for the Rhodium-Catalyzed Silylformylation of Aldehydes[a]

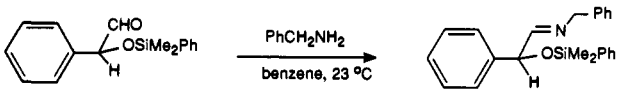
product	R	yield[b] (%)	product	R	yield[b] (%)
3a		74	**3f**		72
3b		84	**3g**[c]	$CH_3CH_2CH_2$-	60
			3h[c]	$(CH_3)_2CH$-	75
3c		80	**3i**		90
3d		50	**3j**		88
3e		60			

[a] A THF solution (8 mL) of the appropriate aldehyde (1.5 mmol) and Me_2PhSiH (0.20 g, 1.5 mmol) was degassed (freeze-pump-thaw ×3) and then cannulated into a glass vessel containing the $[(COD)RhCl]_2$ (1.8 mg, 0.5 mol %). The vessel was placed in the bomb, charged with carbon monoxide (250 psig), and allowed to react at ~23 °C for 24 h. [b] Yields reported were determined by NMR spectroscopy using an internal NMR standard (1,1,1-trichloroethane). Isolated yields were slightly lower but comparable. [c] 1000 psig of carbon monoxide pressure used.

α-silyloxyaldehyde. In the case of isobutyraldehyde we do see small amounts of enol ether formed, and at lower carbon monoxide pressures (250 psig) we observe hydrosilylation product.[13] The silylformylation reaction does not appear to tolerate strong electron-withdrawing substituents. For example, *p*-nitrobenzaldehyde shows only a 40% conversion with only some silylformylation product (20% yield). We find that pyridine carboxaldehydes (both the 2- and 4-) are completely unreactive under the reaction conditions.

Other monohydridic silane reducing reagents such as Et_3SiH and Ph_3SiH are not effective reagents for the rhodium(I)-catalyzed silylformylation of aldehydes at the mild temperatures employed in this study. Triethylsilane is recovered intact, and the triphenylsilane decomposes to unidentified products.

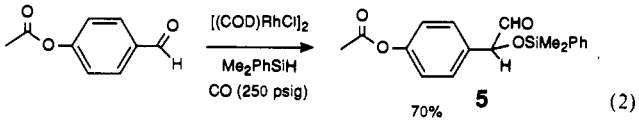
The utility of the α-silyloxyaldehydes is demonstrated by their facile conversion to α-silyloxyimine derivatives (eq 1).[14] The latter



100% **4** (1)

compounds are useful synthetic intermediates in the diastereoselective synthesis of β-amino alcohols.[15]

We find that the rhodium-catalyzed silylformylation is selective for the aldehyde functionality in the presence of an ester (eq 2).



70% **5** (2)

The highly functionalized aromatic compound **5** is isolated in 70% yield. Spectral data collected from the crude reaction mixture indicated complete chemoselectivity for the aldehyde group.

Studies are continuing in our research program to fully develop the tremendous potential of silylformylation, apply the novel methodology to selected synthetic targets, and explore the use of new catalytic systems.

Acknowledgment. We wish to express our gratitude to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Office of Naval Research for partial funding of this work.

Supplementary Material Available: Silylformylation procedure and complete spectroscopic data for compounds **3a-j**, **4**, and **5** (7 pages). Ordering information is given on any current masthead page.

(13) For aromatic aldehydes we find that carbon monoxide pressures of 125 psig produce slightly lower yields of the α-silyloxyaldehydes with concomitant formation of the hydrosilylation byproduct (~10%).

(14) Spectroscopic data for **4**: ^1H NMR ($CDCl_3$) δ 7.66 (d, J = 5.9 Hz, 1 H, C*H*=N), 7.54 (d, J = 7.7 Hz, 2 H, phenyl CH), 7.43-7.15 (m, 13 H, phenyl CH), 5.33 (d, J = 5.9 Hz, 1 H, PhC*H*(OSiMe$_2$Ph)C=N—), 4.49 (s, 2 H, PhC*H*$_2$N=), 0.38, 0.37 (ss, 6 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$) δ 166.1 (*C*HN), 140.3, 138.6, 133.5, 129.7, 128.4, 128.0, 127.8, 127.7, 127.0, 126.2 (Ar C's), 76.8 (*C*H(OSiMe$_2$Ph)), 64.3 (*C*H$_2$N=), -1.0, -1.3 ($SiCH_3$); IR (CH_2Cl_2) $\nu_{C=N}$ 1655.

(15) Claremon, D. A.; Lumma, P. K.; Phillips, B. T. *J. Am. Chem. Soc.* **1986**, *108*, 8265. Yamamoto, Y.; Komatsu, T.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1985**, 814.

Structure of Maitotoxin

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Maitotoxin (MTX), with a molecular weight of 3422 Da, is one of the largest natural products known.[2] It exceeds palytoxin in size and lethality (LD_{50} 50 ng/kg, mouse, ip). Although scarcity of material has hampered full pharmacological evaluation, MTX is involved in Ca^{2+}-dependent mechanisms in a wide range of cell types.[3] It has been implicated in ciguatera food poisoning,[4] thus making its structural determination one of the most exciting challenges in natural products chemistry. We previously reported partial structures of MTX[5] (fragments A and C) and showed that the molecule consists mainly of fused polycyclic ethers. In this communication, we disclose the entire structure of MTX (**1**).

MTX (8.1 mg) was isolated from cultured dinoflagellates *Gambierdiscus toxicus* (strain GII-1) and was treated with $NaIO_4$ then with $NaBH_4$.[5] Subsequent HPLC yielded two major frac-

(1) (a) Tohoku University. (b) Suntory Institute. (c) The University of Tokyo.

(2) Yokoyama, A.; Murata, M.; Oshima, Y.; Iwashita, T.; Yasumoto, T. *J. Biochem.* **1988**, *104*, 184-187.

(3) Gusovsky, F.; Daly, J. W. *Biochem. Pharmacol.* **1990**, *39*, 1633-1639.

(4) Yasumoto, T.; Bagnis, R.; Vernoux, J. P. *Bull. Jpn. Soc. Sci. Fish.* **1976**, *42*, 359-365.

(5) Murata, M.; Iwashita, T.; Yokoyama, A.; Sasaki, M.; Yasumoto, T. *J. Am. Chem. Soc.* **1992**, *114*, 6594-6596.

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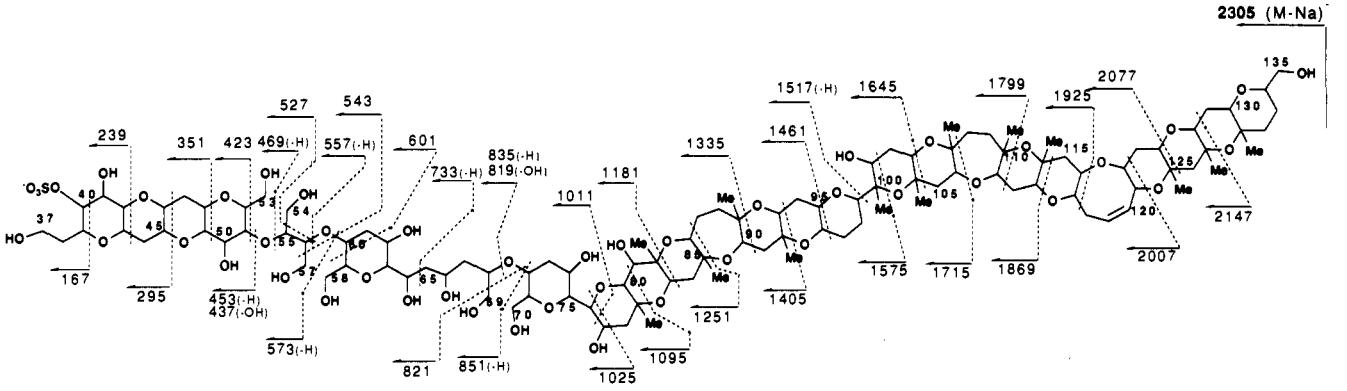
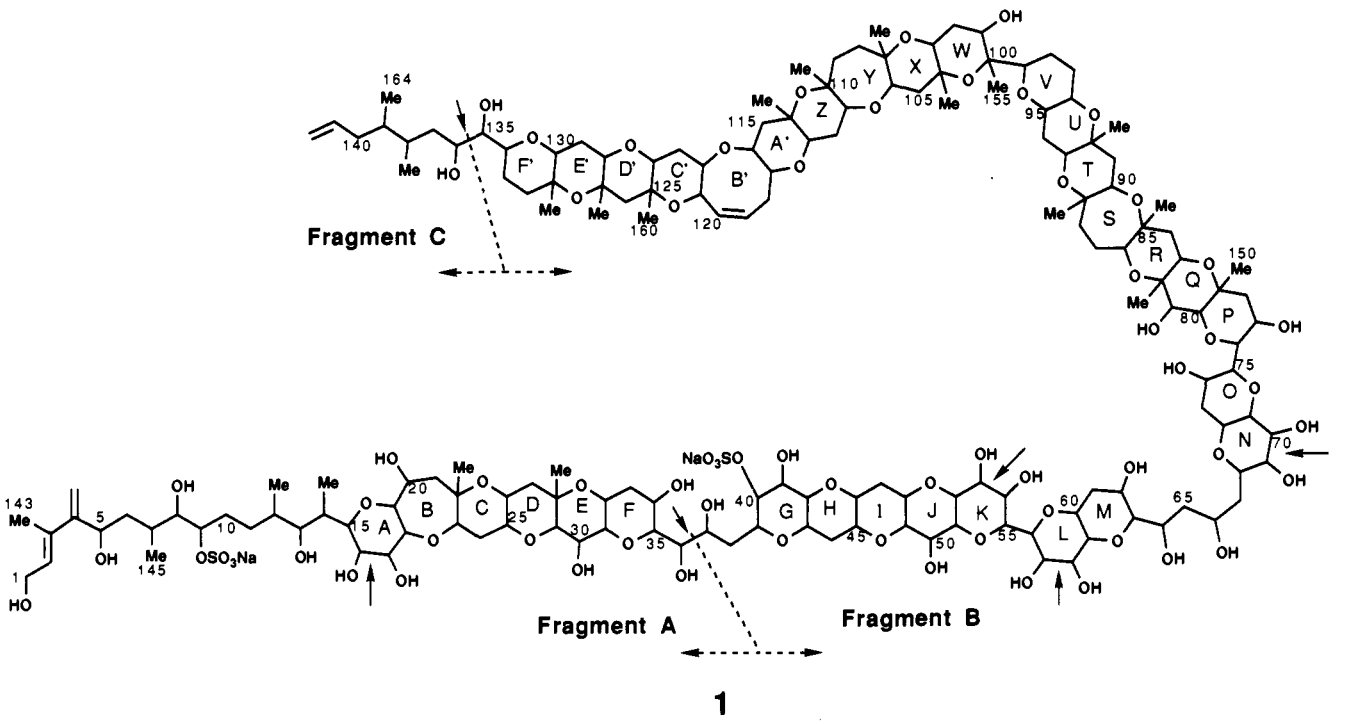


2

Figure 1. Structure of fragment B (**2**) and its fragmentations in negative FAB MS/MS experiments. The related molecular ion $(M - Na)^-$ at m/z 2305 (in nominal mass) was used as precursor. Mass numbers of the fragments are expressed in nominal mass.

Chart I[a]



1

[a] Arrows denote cleavage sites by periodate.

tions, fragment A (1.6 mg) and fragment B (**2**, 5.1 mg)[5] (Chart I). The latter was subjected to extensive 2D NMR[6] and FAB MS/MS experiments.[7]

An acetyl derivative of **2** (3 mg) was prepared with Ac_2O/C_5H_5N to compare ^1H NMR chemical shifts to locate hydroxyl groups (see supplementary material). The ^{13}C DEPT spectrum of **2** coupled with ^1H NMR data of the acetate revealed eight methylenes, each bearing a hydroxyl group. Thus, three bonds (C53/54, C57/C58 and C69/C70) were cleaved by periodate in addition to both termini.

Fifteen sequences of ^1H spin systems in **2** were established by ^1H-^1H COSY, TOCSY, NOESY, and DQF-COSY:[6] C37–C53, C54–C57, C58–C69, C70–C78, C80–C81, C83–C84, C86–C88, C90–C91, C93–C99, C101–C103, C105–C106, C111–C113, C115–C124, C128–C130, and C132–C135. They are separated by acyclic ethers and by quaternary carbons. HMBC experiments[8] of **1** revealed that all quaternary carbons were adjacent to an oxygen atom and a methyl group, thereby suggesting that they were angular carbons of two fused cyclic ethers. Intense negative NOEs observed in the NOESY spectrum of **1** or **2** among adjacent methyls and/or angular protons enabled us to connect the segments beyond the quaternary carbons and to clarify the way the ether rings were fused. HMBC and NOE data permitted assembly of the last 12 segments separated by quaternary carbons into one piece (C70–C135).

Negative FAB MS/MS[7] provided essential information to confirm the structure of **2**. Since **2** has a sulfate ester at C40 near one terminus of the molecule, a negative charge was localized at that point, thereby allowing fragments arising from that part of **2** to appear in the spectrum.[9] Connectivity around acyclic ethers

(6) ^1H-^1H COSY, TOCSY, NOESY, and DQF-COSY of **2** were measured in CD_3OD or in CD_3OD–C_5D_5N, 1:1. ^1H-^1H COSY, TOCSY, and NOESY of an acetyl derivative of **2** were measured in CD_3OD. 2D spectra were recorded either on a 400-MHz (JEOL, GSX-400) or a 600-MHz spectrometer (Bruker, AM-600; see supplementary material).

(7) FAB MS/MS experiments[9] were carried out on a JMS HX-110/HX-110 instrument (JEOL) with the use of 2,2-dithiodiethanol as a matrix at a resolution of 2000.

(8) HMBC and 2D HMQC-TOCSY of **1** (10 mM) were measured with an Omega 500 (GE, 500 MHz) in CD_3CN–D_2O, 1:1. HMBC was optimized at 10 Hz. NOESY with a mixing time of 250 ms, TOCSY with a spin-locking time of 45 or 80 ms, and DQF-COSY were recorded with **1** in C_5D_5N–C_5D_5OD, 1:1, or in CD_3CN–D_2O, 1:1, on an AM-600 (Bruker, 600 MHz).

between C51/C55, C56/C60, and C68/C72 was established by the MS/MS experiments, in which the related molecular ion $(M - Na)^-$ at m/z 2306 (m/z 2305 in nominal mass) was selected as the precursor. Ion peaks at m/z 851/835 (821), 573/557 (543), and 469/453 (423) due to cleaved bonds at either side of the ether oxygens allowed us to sequence four blocks (C37–C53, C54–C57, C58–C69, and C70–C135, Figure 1). Characteristic fragmentations at specific sites of the rings[9] provided invaluable information about ring size (Figure 1). Particularly, they were of great help in assigning rings S and Y because ^{1}H NMR signals of C87/C88 and C108/C109 heavily overlapped and could not be interpreted with confidence.

Two-dimensional NMR data of **1** enabled us to connect **2** with the rest of the molecule, fragments A and C. DQF-COSY and TOCSY[8] revealed spin connections due to H35/H36/H37/H38 and H134/H135/H136/H137. Three vicinal diols in rings K, L, and N cleaved by periodate were reconstructed on the basis of $^3J_{H,H}$ and NOESY data[8] of **1** (see supplementary material).

With these data, the entire structure of maitotoxin (**1**) is disclosed for the first time: It is a C142 carbon chain of composition $C_{164}H_{256}O_{68}S_2Na_2$ (molecular weight of 3422 in nominal mass as disodium salt),[10] encompassing 32 ether rings, 28 hydroxyl groups,[11] and two sulfate esters. Most of the ether rings are probably trans-fused as is the case with brevetoxin[12] except for rings L/M and N/O, for which NOE data suggested cis-fusion (see supplementary material).

Severe overlapping of both ^{13}C and ^{1}H NMR signals was overcome by repeated spectral measurements in different solvents[6,8] and by application of new NMR methods (e.g., 2D HMQC-TOCSY or HSQC). Even so, assignment of NMR signals was sometimes imperfect with only 10 mM of **1** or with 3 mM of **2**. Three-dimensional ^{1}H–^{13}C–^{1}H NMR experiments will be attempted with a ^{13}C-enriched sample, which should help to confirm the structure of MTX. Synthesis of labeled MTX in *G. toxicus* culture will also shed light on mechanisms of action, and on the intriguing relationship of MTX to its companion ciguatoxin.[13]

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Supplementary Material Available: Summary of NMR experiments showing connectivities assigned by NMR, stereochemical assignments of rings K–O of **1**, ^{1}H NMR assignments of **2** and its acetyl derivative, partial ^{1}H NMR assignments of **1**, NOESY and TOCSY of **2**, TOCSY of the acetyl derivative of **2**, negative FAB MS/MS of **2**, ^{1}H NMR 1D spectrum of **1**, NOESY of **1**, DQF-COSY of **1** in two different solvents, HMBC of **1** (21 pages). ^{1}H–^{1}H COSY, TOCSY, and NOESY of **1** in CD_3OD and 2D HMQC-TOCSY (^{13}C–^{1}H HOHAHA) of **1** in CD_3CN–D_2O, 1:1, are available as supplementary material to a previous paper.[5] Ordering information is given on any current masthead page.

(9) Naoki, H.; Murata, M.; Yasumoto, T. *Rapid Commun. Mass Spectrom.*, in press.

(10) The presence of nitrogen suggested in a previous paper[2] was ruled out by elementary analyses with **1**.

(11) The number of hydroxyl groups was determined on the basis of deuterium shifts in ^{13}C NMR signals between spectra obtained in CD_3CN–D_2O and in CD_3CN–H_2O, and of comparison of **2** with its acetyl derivative in ^{1}H NMR chemical shifts.

(12) (a) Lin, Y.-Y.; Risk, M.; Ray, S. M.; Van Engen, D.; Clardy, J.; Golik, J.; James, J. C.; Nakanishi, K. *J. Am. Chem. Soc.* **1981**, *103*, 6773–6775. (b) Shimizu, Y.; Chou, H.-N.; Bando, H.; Duyne, G. V.; Clardy, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 514–515.

(13) Murata, M.; Legrand, A.-M.; Ishibashi, Y.; Fukui, M.; Yasumoto, T. *J. Am. Chem. Soc.* **1990**, *112*, 4380–4386.

ESR Spectrum of a Stable Triplet π Biradical: Trioxytriangulene

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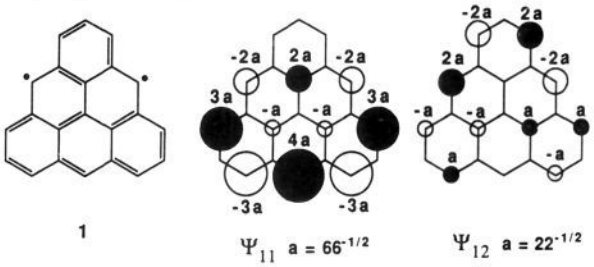
We report the first observation of the ESR spectrum of a non-Kekulé polynuclear aromatic compound: a derivative of triangulene **1**.[1-3] Like the non-Kekulé polyenes[4] and the non-Kekulé quinodimethanes,[5] the non-Kekulé polynuclear aromatics[6] are π biradicals for which it is impossible to write a structure in which each π electron is paired with one on a neighboring carbon. The non-Kekulé polyenes and non-Kekulé quinodimethanes have been known for some time. However, although attempts to make non-Kekulé polynuclear aromatics date back to the work of Clar in the 1950s,[1,7] so far they have escaped detection. Hückel molecular orbital calculations show that the simplest non-Kekulé polynuclear aromatic, triangulene, has a pair of nondisjoint[8] degenerate nonbonding molecular orbitals and as such should have a triplet ground state.



1 Ψ_{11} a = 66$^{-1/2}$ Ψ_{12} a = 22$^{-1/2}$

Our route to compounds of this type is based on the two-electron reduction of the diketone **2**.[1] The single-crystal structure of this compound, which has a vivid blue color, shows that the molecule is essentially planar with a 3-fold axis of symmetry.[9] Cyclic voltammetry[10] shows that the monoanion **2** undergoes two reversible one-electron additions ($E_{R1} = -2.04$ V, $E_{R2} = -2.37$ V) and hence that the dianion monoradical **3** and the trianion bi-

(1) Clar, E.; Stewart, D. G. *J. Chem. Soc.* **1951**, 3215. Clar, E.; Stewart, D. G. *J. Am. Chem. Soc.* **1953**, *75*, 2667. Clar, E.; Stewart, D. G. British Patent 760,912, Nov 7, 1956; *Chem. Abstr.* **1957**, *51*, 9699.

(2) Weiss, R.; Korczyn, J. *Monatsh. Chem.* **1924**, *45*, 207. Hellwinkel, D.; Aulmich, G.; Melan, M. *Chem. Ber.* **1981**, *114*, 86.

(3) The NMR spectrum of the dianion formally produced when two electrons are added to the biradical **1** and the NMR spectrum of a related dication have been reported: Hara, O.; Tanaka, K.; Yamamoto, K.; Nakazawa, T.; Murata, I. *Tetrahedron Lett.* **1977**, 2435.

(4) Bushby, R. J.; Jarecki, C. *Tetrahedron Lett.* **1988**, *29*, 2715. Bushby, R. J.; Jarecki, C. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2217.

(5) Platz, M. S. In *Diradicals*; Borden, W.T., Ed.; J. Wiley: New York, 1982. Berson, J. A. In *The Chemistry of the quinonoid compounds Vol. 2*; Patai, S, Rappoport, Z., Eds.; J. Wiley: New York, 1988.

(6) Clar, E.; Kemp, W.; Stewart, D. J. *Tetrahedron* **1958**, *3*, 325. Clar, E.; MacPherson, I. A. *Tetrahedron* **1962**, *18*, 1411. Clar, E.; MacPherson, I. A.; Schulz-Kiesow, H. *Justus Liebigs Ann. Chem.* **1963**, *669*, 44. Clar, E. *Chimia* **1964**, *18*, 375.

(7) Triangulene is also known as Clar's hydrocarbon.

(8) Borden, W. T.; Davidson, E. R. *J. Am. Chem. Soc.* **1977**, *99*, 4587.

(9) The small deviations from planarity and 3-fold symmetry seem to be attributable to lattice effects. Allinson, G.; Bushby, R. J.; Paillaud, J.-L.; Thornton-Pett, M. To be published.

(10) In DMF at a mercury drop cathode under an atmosphere of nitrogen with tetrabutylammonium tetrafluoroborate as the supporting electrolyte and a silver/silver nitrate reference electrode.

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