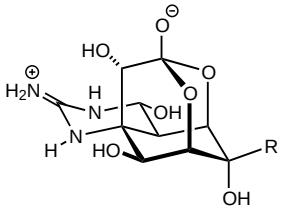
[10] For the nomenclature used to describe hexagonal plates, see Figure 2 and Reference [1].
[11] The thickness of the plates was controlled by cutting the oxidized hexagonal rod with a razor blade. The thickness is an average value since the hexagons vary slightly in their thickness ($\pm 0.1$ mm).
[12] We periodically changed the rate of agitation to 1.8 $s^{-1}$ to accelerate collisions, to break up weak structures, and to stimulate annealing.
[13] We repeated the experiment six times. The yield was calculated by counting the number of times structure $\mathbf{2}\cdot\mathbf{3}_3$ was formed, relative to the incomplete structures $\mathbf{2}\cdot\mathbf{3}_2$ and $\mathbf{2}\cdot\mathbf{3}_1$. For example, in the assembly of 1.4-mm-thick objects of **3** and 0.9-mm-thick **2** we counted 21 arrays of $\mathbf{2}\cdot\mathbf{3}_3$, 3 arrays of $\mathbf{2}\cdot\mathbf{3}_2$, and 6 arrays of $\mathbf{2}\cdot\mathbf{3}_1$. The yield of $\mathbf{2}\cdot\mathbf{3}_3$ was 21/30 or 70%.
[14] The structure $\mathbf{2}\cdot\mathbf{3}_3$ was not stable at $\omega = 1.5$ $s^{-1}$, but was stable at $\omega = 1.2$ $s^{-1}$. We agitated the objects at $\omega = 1.2$ $s^{-1}$ and periodically changed the frequency of agitation to 1.8 $s^{-1}$.
[15] We repeated the experiment five times with six objects of **2** and eighteen of **1** to get statistics for this self-assembly. We agitated the plates for one hour. The yields of the assembly of $\mathbf{2}\cdot\mathbf{1}_3$ were 67%, 100%, 83%, 67%, and 67%. The micrograph shown in Figure 3d is the most complete assembly (the highest yield) that we observed.
[16] S. A. Jenekhe, X. L. Chen, *Science* **1999**, *283*, 372–375.
[17] D. E. Ingber, *Sci. Am.* **1998**, *278*(1), 48–57.

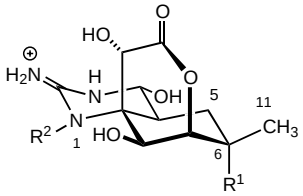
## Stereocontrolled Synthesis of (−)-5,11-Dideoxytetrodotoxin**

Toshio Nishikawa, Masanori Asai, Norio Ohyabu, Noboru Yamamoto, and Minoru Isobe*

Tetrodotoxin (**1**)[1] is a well-known marine natural product that is the toxic principle of puffer fish poisoning. Due to its highly selective inhibition of voltage-dependent sodium channels, tetrodotoxin has served widely as an important biochemical tool in neurophysiological studies.[2] Recently, tetrodotoxin analogues have been isolated from many kinds of animals.[3] These studies brought to light a number of new interesting problems associated with tetrodotoxin,[4] for example its biosynthesis, mechanisms of accumulation, detoxification, and binding to the sodium channel protein,[5] and its actual biological function.[6] In order to examine such new problems on a molecular level, suitably labeled tetrodotoxins are desirable. Such labeled compounds, however, are difficult to prepare from naturally occurring tetrodotoxin.[7] The complex structure, which has a variety of functional groups and unique chemical properties, has thwarted recent attempts at its total synthesis. In spite of many efforts,[8] no total synthesis of tetrodotoxin has been reported since the total synthesis of the racemate by Kishi, Goto, and co-workers in 1972.[9] During the course of our synthetic studies on tetrodotoxin, we have developed a stereocontrolled synthesis of polyhydroxylated cyclohexane,[10] the introduction of a nitrogen functionality by the Overman rearrangement,[11, 12] and a novel guanidine synthesis.[13] Here we describe the stereocontrolled synthesis of enantiomerically pure 5,11-dideoxytetrodotoxin (**2**), a tetrodotoxin analogue not yet found in natural sources.

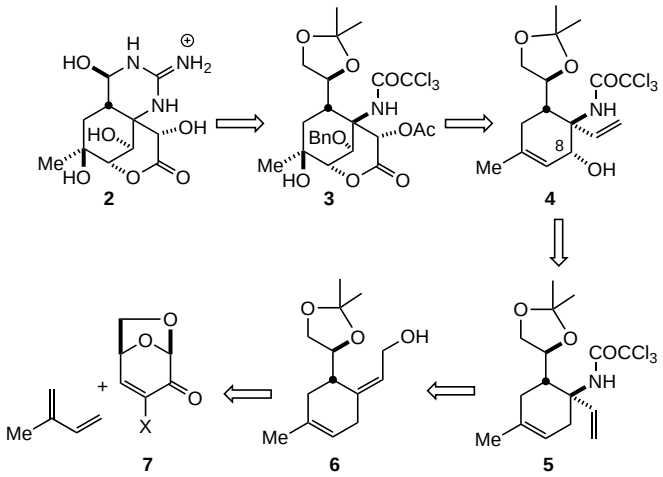


Tetrodotoxin **1** R = $CH_2OH$
11-Deoxytetrodotoxin R = $CH_3$



5,6,11-Trideoxytetrodotoxin $R^1$ = H $R^2$ = H
1-Hydroxy- 5,11-Dideoxytetrodotoxin $R^1$ = OH $R^2$ = OH
5,11-Dideoxytetrodotoxin **2** $R^1$ = OH $R^2$ = H

Our retrosynthetic plan for 5,11-dideoxytetrodotoxin (**2**) is shown in Scheme 1. The guanidine part of **2** is introduced at the latest stage of the synthesis because of the instability and low solubility of the intermediates. Lactone intermediate **3** was envisioned to be synthesized from trichloroacetamide diene **5** via diene alcohol **4** in a stereoselective manner. Compound **5** has already been synthesized from levoglucosenone **7** (X = H) as a chiral starting material[14] by means of a



Scheme 1. Retrosynthetic plan for 5,11-dideoxytetrodotoxin (**2**).

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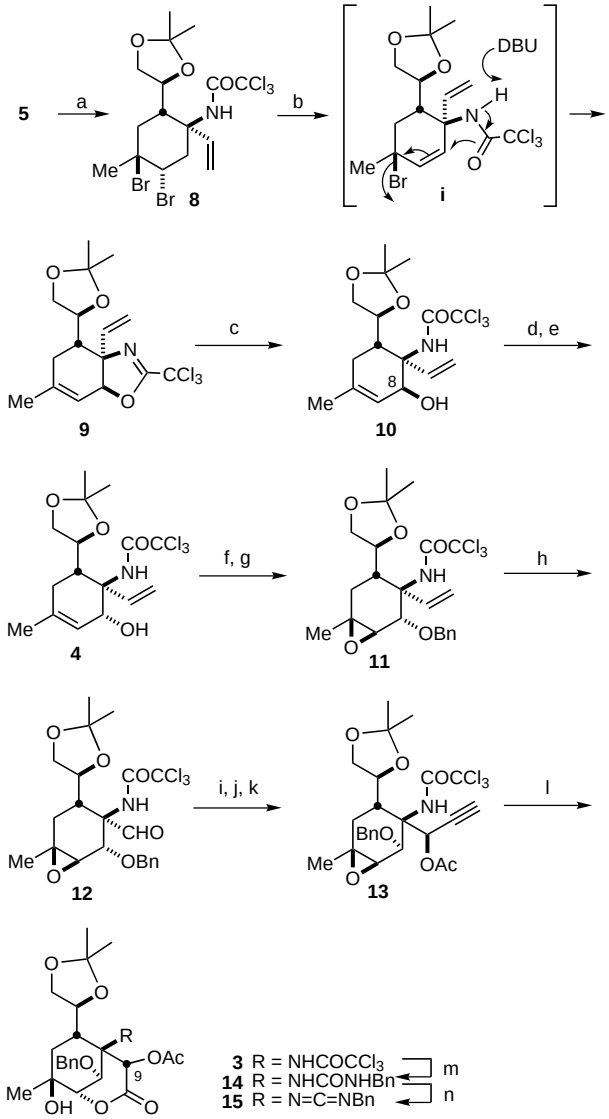
nine-step sequence that included the Diels – Alder reaction of bromolevoglucosenone **7** (X = Br) with isoprene and a highly stereoselective introduction of the amino group by the Overman rearrangement of the *exo*-allylic alcohol **6**[12, 15] as key steps.

Stereoselective $\alpha$-hydroxylation at the C8 position of the key intermediate **5** was critical because the hydroxy group has this configuration in all of the naturally occurring tetrodotoxin analogues. Bromination of **5** with pyridinium bromide perbromide gave dibromide **8**, which was treated with DBU in DMF to give oxazoline **9** in a high yield (Scheme 2; abbreviations are defined in the legend). This reaction involves regioselective dehydrobromination of the dibromide **8** and subsequent $S_N2'$ reaction of the resulting allylic bromide **i** with the neighboring trichloroacetamide group in a stereospecific manner. The product **9** was hydrolyzed with *p*TsOH in aqueous pyridine[16] to give trichloroacetamide **10** having an 8*S* hydroxy group without further hydrolysis. The hydroxy group of **10** was inverted by oxidation with PCC and highly stereoselective reduction with $NaBH_4/CeCl_3$ to afford largely the desired 8*R* alcohol **4** (20:1).[17] This high stereoselectivity is attributed to the steric hindrance of the axially oriented vinyl group of the cyclohexene ring, whose conformation is fixed by the bulky equatorial trichloroacetamide group.




Scheme 2. Synthesis of lactone **15**. a) Pyridinium bromide perbromide, $K_2CO_3$, $CH_2Cl_2$, 10 °C, 3 h, 87 %; b) DBU, DMF, rt, 6 h; c) *p*TsOH, pyridine – $H_2O$, 70 °C, 1.5 h, 71 % over two steps; d) PCC, MS 4 Å, $CH_2Cl_2$, rt, 11 h; e) $NaBH_4$, $CeCl_3(H_2O)_7$, EtOH – $CH_2Cl_2$, 0 °C, 2 h, →rt, 30 min, 75 % over two steps; f) MCPBA, $CH_2Cl_2$, rt, 24 h; g) NaH, BnBr, THF-DMF, rt, 22 h, 86 % over two steps; h) $O_3$, MeOH, −78 °C, 70 min, $Me_2S$, 96 %; i) $Me_3SiC{\equiv}CMgBr$, THF, rt, 2 h; j) $n Bu_4NF$, THF, rt, 2.5 h; k) $Ac_2O$, pyridine, rt, 5.5 h, 86 % over three steps; l) $RuO_2(H_2O)_n$, $NaIO_4$, $CCl_4$–$CH_3CN$–$H_2O$, rt, 4.5 h, 75 %; m) $BnNH_2$, $Na_2CO_3$, DMF, 125 °C, 30 min; n) $Ph_3P$, $CBr_4$, $Et_3N$, $CH_2Cl_2$, rt, 7 h, 87 % over two steps. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, DMF = dimethylformamide, rt = room temperature, *p*TsOH = 4-toluenesulfonic acid, PCC = pyridinium chlorochromate, MCPBA = *meta*-chloroperbenzoic acid.

Prior to the transformation of the terminal olefinic bond into a hydroxycarboxylic acid function, the trisubstituted C=C bond of **4** was epoxidized with MCPBA to give a $\beta$-epoxide as a sole product,[18] whose hydroxy group was protected as benzyl ether **11** in a high yield. In accord with our model studies,[19] the vinyl group of **11** was strongly shielded by the bulky trichloroacetamide group and therefore was extremely inert toward a variety of reagents. This C=C bond was, however, cleaved by ozonolysis to afford the aldehyde **12**, which was transformed into the hydroxycarboxylic acid by the addition of a carboxylic acid equivalent. Vinylmagnesium bromide, which we had employed previously,[19] did not react with the aldehyde **12**. On the other hand, a smaller sp nucleophile, an alkynylmagnesium bromide, added in a highly stereoselective manner to give a propargylic alcohol as a single stereoisomer. The resulting unstable product was immediately transformed into **13** by successive desilylation and acetylation in high yield. The acetylenic moiety was cleaved with ruthenium oxide[20] to give a carboxylic acid, which spontaneously opened the epoxide to furnish six-membered lactone **3**[21] in moderate yield.

With the key intermediate **3** in our hands, we were ready for the crucial construction of the guanidine moiety. The trichloroacetamide group of **3** was difficult to deprotect to the amine, because the hydroxy group at the C9 position was easily epimerized even under mild basic conditions such as $K_2CO_3$ in MeOH. Consequently, we could not synthesize the guanidine unit in the usual way, from a nonprotected amine with one of a variety of guanylation reagents. To overcome this difficulty, we developed a novel guanidine synthesis from the trichloroacetamide group proceeding through a dibenzylguanidine.[13] This new route did not proceed through the corresponding free amine as an intermediate. First, we applied this route to the intermediate **3**, which was transformed into benzylurea **14** with benzylamine and $Na_2CO_3$ in DMF,[13, 22] and the resulting urea was dehydrated with $Ph_3P$ and $CBr_4$ to give benzylcarbodiimide **15** (Scheme 2). However, extensive examination under a variety of conditions revealed that the addition of an amine to carbodiimide **15** to obtain the corresponding dibenzylguanidine was very difficult because of the labile C9 acetoxy group.[23] Second, we planned an alternative route going through a stable tricyclic intermediate **17**, which could survive the guanidine synthesis. The synthesis of **17** is shown in Scheme 3. Oxidative cleavage of the ketal[24] in **3** was followed by protection of the resulting aldehyde and tertiary alcohol to give the dimethylacetal **16**, which was

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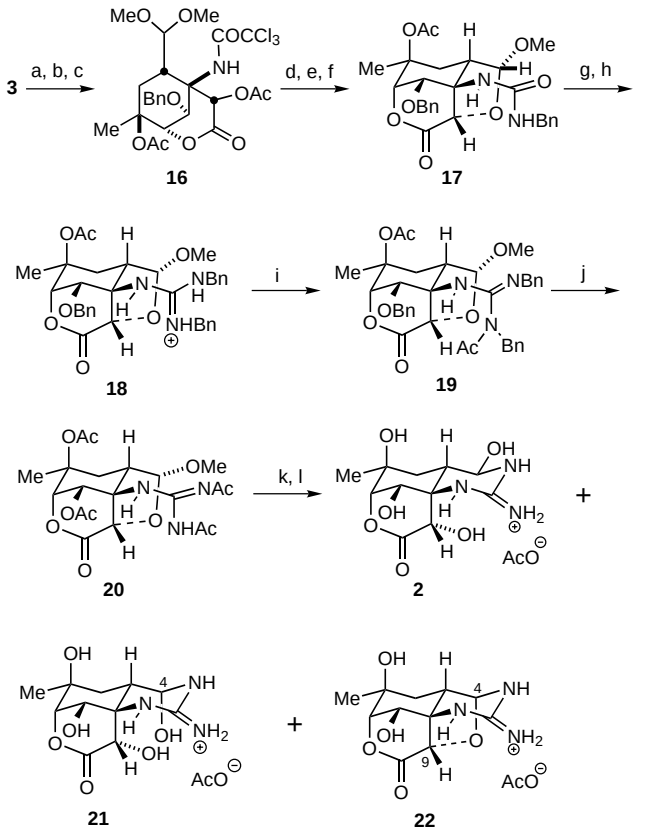

Scheme 3. Synthesis of 5,11-dideoxytetrodotoxin (**2**). a) $H_5IO_6$, AcOEt, rt, 24 h; b) CSA, $CH(OMe)_3$, MeOH, rt, 10 h; c) $Ac_2O$, pyridine, DMAP, rt, 24 h, 78% over three steps; d) $BnNH_2$, $Na_2CO_3$, DMF, 140 °C, 15 min; e) KCN, EtOH, rt, 1 h; f) CSA, acetone, rt, 2 h, 70% over three steps; g) $Ph_3P$, $CBr_4$, $Et_3N$, $CH_2Cl_2$, rt, 4 h; h) $BnNH_2 \cdot HCl$, pyridine, reflux, 5.5 h; i) $Ac_2O$, pyridine, $Et_3N$, rt, 4.5 h, 85% over three steps; j) $H_2$ (1 atm), $Pd(OH)_2/C$, $Ac_2O$, rt, 14 d, 81%; k) aq. $NH_3$, MeOH–$H_2O$, rt, 20 h; l) TFA, $H_2O$, rt, 34 h, 81% over two steps. CSA = 10-camphorsulfonic acid, DMAP = 4-dimethylaminopyridine, TFA = trifluoroacetic acid.

transformed into the acetal urea under the above-mentioned conditions. Mild deacetylation with potassium cyanide in ethanol,[25] and partial hydrolysis of the acetal gave the urea **17** (as a 5:1 diastereomeric mixture at the acetal carbon) as the precursor to the guanidine installation. The major isomer **17** was separated and dehydrated with $Ph_3P$ and $CBr_4$ to afford the carbodiimide, which was further treated with benzylamine hydrochloride in pyridine[26] to furnish the dibenzylguanidine **18** in a high yield. Our model studies revealed that the benzyl group of benzylguanidinium salts was difficult to remove under hydrogenolytic conditions, while the benzyl group of acetylbenzylguanidine could be easily removed under the same conditions.[12b] In the event, the corresponding acetylbenzylguanidine **19** was hydrogenolyzed in acetic anhydride under one atmosphere of hydrogen to give diacetylguanidine **20** in a good yield.[27] Under the reaction conditions, the benzyl ether in **19** was also converted to an acetyl group. At this stage, all the protective groups were unified to acetyl groups except for the acetal.

To complete the synthesis of 5,11-dideoxytetrodotoxin (**2**), two steps of deprotection were carried out. Thus, hydrolysis of the acetyl groups with ammonium hydroxide and then acid hydrolysis of the acetal with aqueous TFA was performed. The crude product was separated by HPLC with an ion-exchange resin (Hitachi gel 3013c)[3] to afford 5,11-dideoxytetrodotoxin (**2**), 4-*epi*-5,11-dideoxytetrodotoxin (**21**), and 4,9-anhydro-*epi*-5,11-dideoxytetrodotoxin (**22**)[28] in yields of 29, 16, and 36%, respectively. These structures were confirmed by full characterization by the NMR techniques COSY, HMBC, and HSQC, and by FAB mass spectrometry.

We have achieved a highly stereocontrolled synthesis of (−)-5,11-dideoxytetrodotoxin and its isomer. This is the first asymmetric synthesis of tetrodotoxin analogues and provides a practical route accessible to the labeled compounds for biochemical studies. Further studies toward naturally occurring tetrodotoxin (**1**) and other analogues are in progress in our laboratory.

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**Keywords:** asymmetric synthesis · natural products · synthetic methods · tetrodotoxins

[1] For the structure: a) T. Goto, Y. Kishi, S. Takahashi, Y. Hirata, *Tetrahedron* **1965**, *21*, 2059–2088; b) K. Tsuda, S. Ikuma, M. Kawamura, K. Tachikawa, K. Sakai, C. Tamura, O. Akamatsu, *Chem. Pharm. Bull.* **1964**, *12*, 1357–1374; c) R. B. Woodward, *Pure Appl. Chem.* **1964**, *9*, 49–74.

[2] T. Narahashi, *Physiol. Rev.* **1974**, *54*, 813–889.

[3] a) 5,6,11-Trideoxytetrodotoxin: M. Yotsu-Yamashita, Y. Yamagishi, T. Yasumoto, *Tetrahedron Lett.* **1995**, *51*, 9329–9332; b) 1-hydroxy-5,11-dideoxytetrodotoxin: Y. Kotaki, Y. Shimizu, *J. Am. Chem. Soc.* **1993**, *115*, 827–830; c) 6-*epi*- and 11-deoxytetrodotoxin: T. Yasumoto, M. Yotsu, M. Murata, H. Naoki, *J. Am. Chem. Soc.* **1988**, *110*, 2344–2345.

[4] "Tetrodotoxin, Saxitoxin, and the Molecular Biology of the Sodium Channel": *Ann. N.Y. Acad. Sci.* **1986**, *479* (review series).

[5] a) H. Nakayama, Y. Hatanaka, M. Takai, E. Yoshida, Y. Kanaoka, *Ann. N.Y. Acad. Sci.* **1993**, *707*, 349; b) G. M. Lipkind, H. A. Fozzard, *Biophys. J.* **1994**, *66*, 1–33.

[6] Tetrodotoxin was identified as a pheromonelike substance among the puffer fish. K. Matsumura, *Nature* **1995**, *378*, 563.

[7] For examples of some labeled tetrodotoxin derivatives, see: a) M. Balerna, A. Lombet, R. Chicheportiche, G. Romey, M. Lazdunski, *Biochim. Biophys. Acta* **1981**, *644*, 219–225; b) J. Bontemps, R. Cantineau, C. Grandfils, P. Leprince, G. Dandrifosse, E. Schoffeniels, *Anal. Biochem.* **1984**, *139*, 149–157; c) B. Q. Wu, L. Yang, C. Y. Kao, S. R. Levinson, M. Yotsu-Yamashita, T. Yasumoto, *Toxicon* **1996**, *34*, 407–416.

[8] Recent reports: a) B. Noya, R. Alonso, *Tetrahedron Lett.* **1997**, *38*, 2745–2748; b) C. S. Burgey, R. Vollerthun, B. Fraser-Reid, *J. Org. Chem.* **1996**, *61*, 1609–1618; c) K. Sato, Y. Kajihara, Y. Nakamura, J. Yoshimura, *Chem. Lett.* **1991**, 1559–1562; d) J. F. W. Keana, J. S. Bland, P. J. Boyle, M. Erion, R. Hartling, J. R. Husman, R. B. Roman, G. Ferguson, M. Parvez, *J. Org. Chem.* **1983**, *48*, 3627–3631; J. F. W. Keana, P. J. Boyle, M. Erion, R. Hartling, J. R. Husman, J. E. Richman, R. M. Wah, *J. Org. Chem.* **1983**, *48*, 3621–3626.

[9] a) Y. Kishi, M. Aratani, T. Fukuyama, F. Nakatsubo, T. Goto, S. Inoue, H. Tanino, S. Sugiura, H. Kakoi, *J. Am. Chem. Soc.* **1972**, *94*, 9217–9219; b) Y. Kishi, T. Fukuyama, M. Aratani, F. Nakatsubo, T. Goto, S. Inoue, H. Tanino, S. Sugiura, H. Kakoi, *J. Am. Chem. Soc.* **1972**, *94*, 9219–9221; c) Y. Kishi, F. Nakatsubo, M. Aratani, T. Goto, S. Inoue, H. Kakoi, S. Sugiura, *Tetrahedron Lett.* **1970**, 5127–5128; d) Y. Kishi, F. Nakatsubo, M. Aratani, T. Goto, S. Inoue, H. Kakoi, *Tetrahedron Lett.* **1970**, 5129–5132.

[10] M. Isobe, T. Nishikawa, S. Pikul, T. Goto, *Tetrahedron Lett.* **1987**, *28*, 6485–6488.

[11] Reviews: a) L. E. Overman, *Acc. Chem. Res.* **1980**, *13*, 218–224; b) K. Ritter in *Stereoselective Synthesis* (*Houben-Weyl*) *Vol. 21/9* E21, *Vol. 9* (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Thieme, Stuttgart, **1996**, pp. 5677–5699.

[12] M. Isobe, F. Fukuda, T. Nishikawa, P. Chabert, T. Kawai, T. Goto, *Tetrahedron Lett*. **1990**, *31*, 3327 – 3330.
[13] a) N. Yamamoto, M. Isobe, *Chem. Lett.* **1994**, 2299 – 2302; b) T. Nishikawa, N. Ohyabu, N. Yamamoto, M. Isobe, *Tetrahedron* **1999**, *55*, 4325 – 4340.
[14] M. Isobe, N. Yamamoto, T. Nishikawa in *Levoglucosenone and Levoglucosans, Chemistry and Applications* (Ed.: Z. J. Witczak), ATL Press, **1994**, pp. 99 – 118.
[15] T. Nishikawa, M. Asai, N. Ohyabu, M. Isobe, *J. Org. Chem.* **1998**, *63*, 188 – 192.
[16] H. W. Pauls, B. Fraser-Reid, *Carbohydr. Res.* **1986**, *150*, 111 – 119.
[17] The original conditions described by Luche and Gamal using MeOH as a solvent gave a low yield of **4** and recovered starting material; J. L. Luche, A. L. Gamal, *J. Am. Chem. Soc*. **1979**, *101*, 5848. On the other hand, the reduction with the solvent system ($EtOH-CH_2Cl_2$) reported by Danishefsky et al. gave our desired product **4** in better yield and with higher selectivity; S. J. Danishefsky, H. G. Selnick, R. E. Zelle, M. P. DeNinno, *J. Am. Chem. Soc*. **1988**, *110*, 4368 – 4378.
[18] The stereochemistry was controlled by a steric factor rather than an orientation of the neighboring hydroxy group; see ref. [9d].
[19] N. Yamamoto, T. Nishikawa, M. Isobe, *Synlett* **1995**, 505 – 506.
[20] P. H. Carisen, T. Katsuki, V. S. Martin, K. B. Sharpless, *J. Org. Chem.* **1981**, *46*, 3936 – 3938.
[21] Determination of the configuration at the C9 position is included in the Supporting Information.
[22] J. Petrov, I. Atanassova, A. Balabanova, N. Mollov, *Izv. Khim.* **1990**, *23*, 53 – 57.
[23] Detailed analysis of the crude product revealed that one of the products lacked H9, indicating that an oxidation occurred at the C9 position. Kishi et al. reported on the lability of the acetoxy group at the C9 position in their total synthesis of tetrodotoxin. See: a) ref. [9b]; b) H. Tanino, S. Inoue, M. Aratani, Y. Kishi, *Tetrahedron Lett*. **1974**, 335 – 338.
[24] M. Xie, D. A. Berges, M. J. Robins, *J. Org. Chem.* **1996**, *61*, 5178 – 5179.
[25] K. Mori, M. Tominaga, T. Takigawa, M. Matsui, *Synthesis* **1973**, 790 – 791.
[26] Pyridine was indispensable in this addition, while we used DMF in our model studies.[13b]
[27] In this specific case, acetic anhydride was an indispensable solvent. This reaction was much slower or unreproducible when a mixture of acetic anhydride and triethylamine was employed as in our previous (successful) model studies.[13b]
[28] 4-*epi*- and 4,9-Anhydrotetrodotoxins have been found as minor constituents with tetrodotoxins from natural sources.[1, 3a, 3c] For example, 5,6,11-trideoxytetrodotoxin was also isolated with 4-*epi*-trideoxytetrodotoxin in the ratio (ca. 1:1.2).[3a] Compound **22** is the first example of 4,9-anhydrotetrodotoxin among a series of 5-deoxytetrodotoxin analogues.

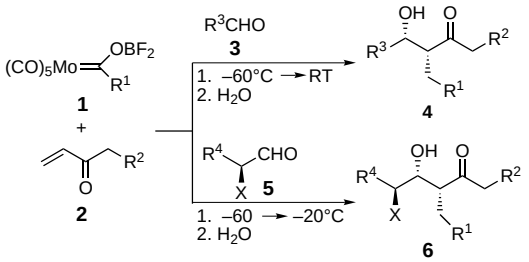
# Regio- and Diastereoselective Aldol Products through Three-Component Coupling Reactions of Difluoroboroxy Fischer Carbene Molybdenum Complexes**

José Barluenga,* Félix Rodríguez, Francisco J. Fañanás, and Eduardo Rubio

The formation of a large number of carbon – carbon bonds with high efficiency in the minimal number of chemical steps is the requirement of modern synthetic design.[1] In this context, radical and carbanion chemistry has become a valuable tool in organic synthesis. However, both reactive intermediates can be used in a complementary manner and sequential reactions have been devised to prepare complex molecules.[2, 3] On the other hand, despite the importance of Fischer carbene complexes for the development of novel organic transformations[4] there is only a very limited number of examples in which these complexes have been used as precursors of radicals. Thus, tetramethylammonium acyl chromate complexes are adequate precursors for alkyl and acyl radicals, which are formed by oxidation with manganese(III)[5] and copper(II)[6] salts.

In 1997 we reported a simple method for generating acyl radicals from difluoroboroxy Fischer carbene molybdenum complexes in very mild reaction conditions and in the absence of an oxidant.[7] Herein we describe a sequential radical-anionic three-component coupling reaction of difluoroboroxy Fischer carbene molybdenum complexes, vinyl ketones, and aldehydes to give *syn*-$\beta$-hydroxyketones diastereoselectively. This process is amenable for synthesizing enantiomerically pure compounds.

The treatment of pentacarbonyl(difluoroboroxycarbene)-molybdenum complexes **1** (formed by reaction of lithium pentacarbonyl acyl molybdate and boron trifluoride diethyl ether complex)[7] with vinyl ketones **2** and aldehydes **3** in diethyl ether at temperatures from $-60$ to 20 °C led to $\beta$-hydroxyketones **4**. According to the NMR studies the *syn* products were formed exclusively (Scheme 1 and Table 1).[3a, 8]




Scheme 1. Reaction of difluoroboroxycarbenemolybdenum complexes with vinyl ketones and aldehydes—Formation of *syn*-$\beta$-hydroxyketones **4** or **6**.

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