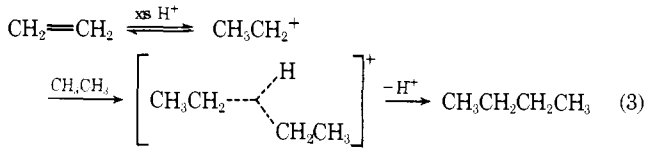
carbenium ion stabilities in acid and thus further substantiate the direct alkene–alkane alkylation and the existence of pentacoordinated carbocations. The reaction of polyethylene to give *tert*-butyl cation in FSO_3H–SbF_5 has been noted previously.[16]

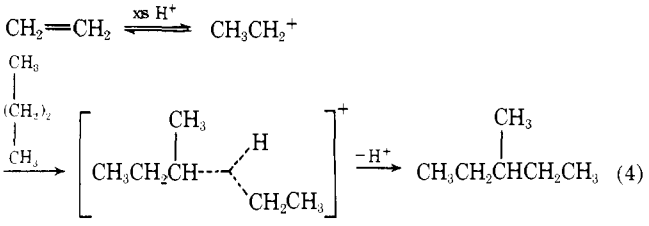
In another experiment, ethylene (17.9 wt %) reacted with ethane at 40 °C in a flow system to form *n*-butane as the only product (eq 3). This means that the ethyl cation is al-



(3)

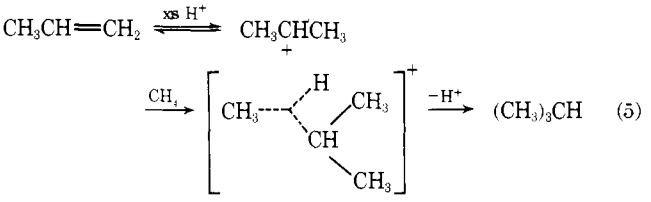
kylating a primary ethane position and supports the conclusion that there is no free primary butyl cation formed. *n*-Butyl chloride in acid reacts quantitatively with hydrogen in 1 h at 20 °C to yield isobutane via rearrangement, whereas *n*-butane does not undergo isomerization under any of the conditions noted.[17] Of more interest is the fact that *n*-butyl chloride reacts in the presence of excess ethane, also at 40 °C, to form butylenes (85%) and some isobutane (15%). These products lead to the conclusion that rearrangement of the free trivalent carbenium ion is more rapid than hydride abstraction from another *n*-butyl chloride molecule.[13] The *tert*-butyl cation ion thus formed, being too weak an acid to abstract a hydride, deprotonates to form butylene products. No isohexane alkylation products are formed. This example also provides direct evidence for the existence of pentacoordinated carbon.

Olah[2] has also reported the alkylation reactions at −10 °C with 1:1 FSO_3H–SbF_5 of *n*-butane with ethylene to yield 38 wt % of hexanes and alkylation of *n*-butane with propylene to yield 29 wt % of heptanes. The former reaction has also been reported by Parker[18] at 60 °C, but the product analysis in this case more nearly resembles polyethylene degradation products. In our work with 10:1 HF:TaF_5 at 40 °C, in a flow system, ethylene (14.1 wt %) reacts with *n*-butane to form 3-methylpentane as the initial product with 94% selectivity (eq 4). The less acidic secondary propyl cat-



(4)

ion, formed in the reaction of propylene (3.4%) at 40 °C in 10:1 HF–TaF_5, attacks methane (96.6%) to form isobutane (eq 5) with over 60% selectivity.



(5)

The formation of 3-methylpentane and *n*-butane in these alkylations provides strong evidence that cations, or tight ion pairs, of the pentacoordinated type in which the positive charge is distributed over three orbitals are more stable than the classical case in which the entire positive charge is localized in one vacant orbital. Work is now in progress to extend this chemistry to other olefins and to other "super acid" systems.

References and Notes

(1) Paper 2 in this series: M. Siskin, *J. Am. Chem. Soc.*, **96**, 3641 (1974).
(2) G. A. Olah, U.S. Patent 3 708 553, Jan 2, 1973.
(3) P. van Dijk, U.S. Patent 3 415 899, Dec 10, 1968.
(4) J. M. Oelderik, E. L. Mackor, J. C. Platteeuw, and A. van der Weil, U.S. Patent 3 201 494, Aug 17, 1965.
(5) R. D. Pinkerton, U.S. Patent 2 177 579, Oct 24, 1939.
(6) G. A. Olah and R. H. Schlosberg, *J. Am. Chem. Soc.*, **90**, 2726 (1968).
(7) G. A. Olah, G. Klopman, and R. H. Schlosberg, *J. Am. Chem. Soc.*, **91**, 3261, (1969).
(8) H. Hogeveen, J. Lukas, and C. F. Roobeek, *Chem. Commun.*, 920, (1969).
(9) G. A. Olah and Y. K. Mo, *J. Am. Chem. Soc.*, **94**, 6864 (1972).
(10) D. T. Roberts, Jr., and L. E. Calihan, *J. Macromol. Sci., Chem.*, **7**, 1629 (1973).
(11) L. Schmerling, *J. Am. Chem. Soc.*, **66**, 1422 (1944).
(12) Z. N. Vostroknutova and A. A. Shteinman, *Kinet. Katal.*, **13**, 324 (1972), reports that even at 50 °C in 1:1 HSO_3F–SbF_5, the ionization of methane is too slow to account for our results in terms of the traditional alkylation mechanism.
(13) F. H. Field and J. L. Franklin, "Electron Impact Phenomena and the Properties of Gaseous Ions", Academic Press, New York, N.Y., 1957, p 87.
(14) R. H. Schlosberg, M. Siskin, W. P. Kocsi, and F. J. Parker, *J. Am. Chem. Soc.*, in press.
(15) D. M. Brouwer and H. Hogeveen, *Prog. Phys. Org. Chem.*, **9**, 179 (1972).
(16) G. A. Olah and J. Lukas, *J. Am. Chem. Soc.*, **89**, 2227 (1967).
(17) D. M. Brouwer and J. M. Oelderik, *Recl. Trav. Chim. Pays-Bas*, **87**, 721 (1968).
(18) P. T. Parker, U.S. Patent 3 636 129, Jan 18, 1972.

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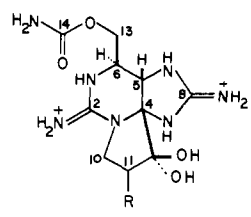
Structures of Gonyautoxin II and III from the East Coast Toxic Dinoflagellate *Gonyaulax tamarensis*

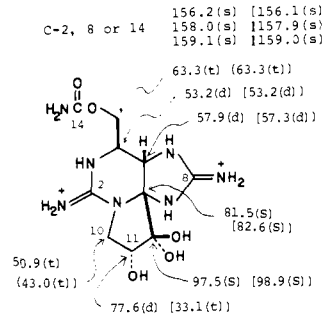
Sir:

Blooms caused by the toxic dinoflagellate, *Gonyaulax tamerensis*, have been creating serious health and economic problems along the North Atlantic coasts of Canada, the United States, and Great Britain. Although the nature of the shellfish poisoning resulting from the bloom is similar to the west coast paralytic shellfish poisoning (PSP) caused by *Gonyaulax catenella*, the toxic components of the east coast PSP are different from that of the west coast PSP, saxitoxin (STX, **1**),[1] the structure of which was recently established by x-ray crystallography,[2] and subsequently confirmed.[3] In a previous communication, we reported the isolation of saxitoxin and three new toxins from the infested softshell clams, *Mya arenaria*, and cultured organism itself.[4,5] In this communication, we wish to report the structures of gonyautoxin II (**2**) and III (**3**) (previously coded GTX-II and GTX-III, respectively).

GTX-II (**2**), the major component of the new toxins, was obtained as a highly hygroscopic amorphous substance. Al-



1 R:H Saxitoxin
2 R:α-OH Gonyautoxin-II
3 R:β-OH Gonyautoxin-III



4 GTX-II, cmr data for STX(11-H) shown in I [3]

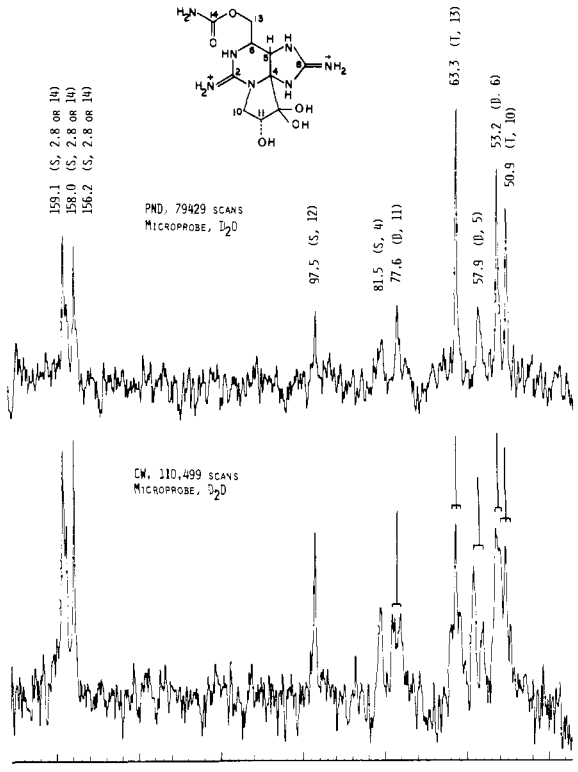


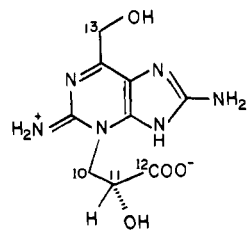
Figure 1. Gonyautoxin II in 20 μl. of D_2O, JEOL PS-100, microprobe: top run, proton-noise decoupled spectrum; bottom run, off-resonance decoupled spectrum.

though an exact determination of the toxicity was impossible due to its highly hygroscopic nature and the minute amount obtained, both GTX-II and -III exhibited very high toxicity, ca. 4800 mouse units/mg (as acetate salts).[6]

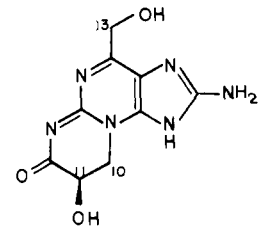
GTX-II (**2**) and -III (**3**) undergo slow equilibration in neutral waters to form a 3:1 mixture (separable by TLC employing a 75:25:30:15 mixture of pyridine–ethyl acetate–water–acetic acid), the equilibrium being remarkably enhanced by a trace of base, e.g., sodium acetate. GTX-II, ir (KBr) 3200 (br), 1700 cm^{-1} (br), gave a positive Weber reaction (for guanidium groups) and afforded guanidine upon drastic oxidation with H_2O_2. The molecular weight could not be determined by analyses or by various mass spectroscopic techniques[7] due to hygroscopicity, polarity, and scarcity (total of less than 2 mg) of material.

The proton-noise decoupled (79 429 scans) and continuous-wave decoupled (110 499 scans) ^{13}C NMR spectra[8] of GTX-II in D_2O were extremely revealing in that they showed close resemblance to STX as shown in structure **4.** The only clear differences were the replacements of the 33.1 ppm (11-C) and 43.0 ppm (10-C) triplets in STX by a 77.6 ppm doublet and 50.9 ppm triplet in GTX-II. Assuming that the 77.6 ppm signal is due to 11-C, then the 44.5 ppm downfield shift shows that this carbon bears a hydroxyl; the 7.9 ppm shift of the 10-C peak is also in agreement with such a substitution.[9] This 11-substitution is supported by further evidence.

Reaction of GTX-II (**2**) with 0.1% H_2O_2 in 0.5 N NaOH at room temperature and Bio Gel P-2 chromatography of the reaction mixture gave two oxidation products, one of which was acid **5:** uv (H_2O) 337 (15 700), 252 (sh, 4400), 232 nm (12 100); CD (H_2O) 330 ($\Delta\epsilon$ − 0.51), 251 ($\Delta\epsilon$ − 1.06), 230 nm ($\Delta\epsilon$ + 1.14); ^1H NMR[10] (D_2O) 5.04 (s, 2 H, 13-H), 4.70 ppm (m, 3 H, 10-H and 11-H). The Cotton effect of the CD peaks is due to the perturbed transitions of the nucleus and is weak, thus indicating that the chiral center is not at a carbon directly linked to the nucleus. The highest MS peak of acid **5** was at *m/c* 250,[11] corresponding to the cyclized lactam **6,** which was also obtained upon leaving acid **5** in 1 N HCl at



5



6

room temperature for 18 h; uv 330 270 (sh) and 237 nm. Upon oxidation of STX with 0.8% H_2O_2, Wong et al.[12] obtained lactam **6** (no 11-OH) which played a crucial role in structural studies. When the oxidation of STX **1** was performed under conditions identical to those of GTX-II (**2**), one of the two products was the acid[13] corresponding to **5** (no 11-OH) (MS: 234 ($M - H_2O$); uv (H_2O) 335 (15 000), 252 (sh, 5300), 229 nm (12 950); ^1H NMR (D_2O)[10] 5.06 (s, 2 H, 13-H), 4.40 (t, J = 6 Hz, 2 H, 10-H), 2.70 ppm (t, J = 6 Hz, 11-H)) which cyclized to the lactam[12] (**6,** no 11-OH) upon acidification.

The second H_2O_2 oxidation products obtained from both GTX-II (**2**) and STX (**1**) are assigned structures having 8-OH instead of 8-NH_2 in **5,** with and without the 11-OH (from **2** and **1,** respectively), on the basis of MS, ^1H NMR, and uv data (ca. 2-nm blue shift of all peaks). GTX-II was oxidized slowly with $NaIO_4$ to afford a fluorescent compound, the λ_{max} (337 nm) of which was identical with that of the aromatized product **5;** the product is probably the 11-acid derived from **5.** These data establish the presence of 11-OH in GTX.

The complex ^1H NMR signals[10] of GTX-II (**2**) (in D_2O) could now be fully assigned. In STX (**1**) it is known that C-12 partly exists in the carbonyl form and that C-11 becomes deuterated upon exposure to D_2O via the enol.[14] This accounts for the 3:1 equilibrium between GTX-II (**2**) and GTX-III (**3**).[15] Although the 11-hydroxyl configurations in GTX-II and -III are not established, molecular models suggest the 11α configuration to be the less hindered; the α-configuration is thus assigned to GTX-II (**2**), the more favored of the two isomers. The acid strengthening 11-hydroxyl function in the gonyautoxins would lower the isoelectric point relative to that of saxitoxin as manisfested in the behavior upon electrophoresis[16] and on ion-exchange resins.

Acknowledgments. We thank Professor E. J. Schantz, University of Wisconsin, for his generious gift of saxitoxin. The work at the University of Rhode Island was supported by HEW GRANT FD-00619 and by the Sea Grant Program, University of Rhode Island R/D3. The work at Columbia University was supported by National Institutes of Health Grant CA-11572.

References and Notes

(1) E. J. Schantz, *Ann. N.Y. Acad. Sci.*, **90**, 843 (1960); M. H. Evans, *Br. J. Pharmacol.*; N. E. Ghazarosian, E. J. Schantz, H. K. Schnoes, and F. M. Strong, *Biochem. Biophys. Res. Commun.*, **59**, 1219 (1974); Y. Shimizu, M. Alam, and W. E. Fallon, Proceedings of the First International Conference on Toxic Dinoflagellate Blooms, 275 (1975); L. J. Buckley, M. Ikawa, and J. J. Sasner, Jr., *ibid.*, 423 (1975); Y. Shimizu, M. Alam, and W. E. Fallon, Food-Drugs from the Sea Proceedings, 1974, Marine Technology Society, Washington, D.C., in press.

(2) E. J. Schantz, V. E. Ghazarossian, H. K. Schnoes, F. M. Strong; J. P. Springer, J. O. Pezzanite, and J. Clardy, *J. Am. Chem. Soc.*, **97**, 1238 (1975).

(3) J. Bordner, W. E. Thiessen, H. A. Bates, and H. Rapoport, *J. Am. Chem. Soc.*, **97**, 6008 (1975).

(4) Y. Shimizu, M. Alam, Y. Oshima, and W. E. Fallon, *Biochem. Biophys. Res. Commun.*, **66**, 731 (1975). Since publication of this paper, three more new toxins have been isolated from both clam and organisms.

(5) Recently Buckley et al. have reported the isolation of two new toxins from *Mya arenaria:* L. J. Buckley, M. Ikawa, and J. J. Sasner, Jr., *J. Agric. Food Chem.*, **24**, 107 (1976). Comparisons showed them to be GTX-II and -III[4] (Buckley et al., unpublished work). Also GTX-II and -III were separated from a Japanese *Gonyaulax* species (Y. Oshima, W. E. Fallon, Y. Shimizu, T. Noguchi, and Y. Hashimoto, *Suisan Gakkaishi*, in press.

(6) One mouse unit is defined as an amount to kill a 20-g mouse within 15 min: H. Sommer and K. F. Meyer, *Arch. Pathol.*, **24**, 560 (1937).

(7) We thank Professor R. D. Macfarlane, Department of Chemistry, Texas A&M University for a trial with the plasma desorption MS employing ^{252}Cf: cf. R. D. Macfarlane and D. F. Torgerson, *Science*, **191**, 920 (1976).
(8) A JEOL micro ^{13}C NMR probe was used on a PS-100 instrument. Although **2** and **3** were separated by acetic acid containing solvent on TLC (see text), acetate was not the counterion (^{13}C NMR). The counterions are presumably chloride which could have been picked up during earlier stages of isolation.
(9) G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists", Wiley-Interscience, New York, N.Y., 1972, p 47; J. B. Strothers, "Carbon-13 NMR spectroscopy", Chapter 5, Academic Press New York, N.Y., 1972.
(10) JEOL PS-100, in D_2O; the HDO peak was removed by making it appear as an inverted sharp signal by partial relaxed Fourier transform, and completely moved upfield from overlapping positive signals around 4.70 ppm by warming the probe to 55 °C.
(11) Measured with a Finnigan 3300 instrument, multiple ion detection technique. We are grateful to Ms. Vinka Parmakovich for measurements.
(12) J. L. Wong, M. S. Brown, K. Matsumoto, R. Oesterlin, and H. Rapoport, *J. Am. Chem. Soc.*, **93**, 4633 (1971).
(13) The open acid form has so far not been isolated from STX by Rapoport and co-workers, presumably due to different workup procedures; their product is the lactam. However, the uv of the noncyclized monoanion has been reported: H. A. Bates and H. Rapoport, *J. Agric. Food. Chem.*, **23**, 237 (1975); our uv datum at pH 10 is identical.
(14) J. L. Wong, R. Oesterlin, and H. Rapoport, *J. Am. Chem. Soc.*, **93**, 7344 (1971).
(15) The 11-ene-11,12-diol, the intermediate in the GTX-II and -III equilibrium, could also tautomerize to the 11-ket-12-ol form. If this were GTX-III, the ^1H NMR should show a sharp singlet lower than 5 ppm (12-H). This was not the case.
(16) Relative mobility of gonyautoxin II to saxitoxin on cellulose acetate strip in pH 8.7 Tris buffer at 200 V was 0.56 (unpublished data).

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*Book Reviews**

Bibliography of Electrophoresis 1968–1972 and Survey of Applications. Edited by Z. DEYL, J. KOPECKÝ, J. DAVIDEK, M. JURICOVÁ, and R. HELM. Elsevier Scientific Publishing Co., Amsterdam. 1975. 861 pp. $83.50.

This soft-bound volume is published as Supplement No. 4 to the *Journal of Chromatography*, and is complementary to previously published bibliographies that covered column, paper, and thin-layer chromatography. The organization is similar to them and consists of a General Part and a Special Part. The former includes books and reviews, treatments of theory and principle, and all aspects of technique. The references, which number no less than 8236, are given with their full titles. The table of contents is detailed, and there is an author index and an extensive subject index entitled "List of Compounds Electrophoresed". The Czechoslovak team that compiled this work has made a most valuable contribution to separation chemistry.

Biophysical Chemistry. Readings from "Scientific American". Selected and introduced by V. A. BLOOMFIELD and R. E. HARRINGTON. W. H. Freeman & Co., San Francisco, Calif. 1975. viii + 231 pp. $12.00 cloth; $6.95 paper.

This is another in the useful series of collections of the excellently produced articles in "Scientific American". The articles date from 1951 to 1973, and include many great names among the authors. They are grouped in sections: Basic Biomolecular Structure; Macromolecular Aggregates and Organized Structures; Enzymes: Macromolecular Catalysts; and Methods to Characterize Macromolecules. Each section is begun by a unifying introduction. Four pages of bibliographies, a name index, and a subject index complete the work.

Chemical Tables. By BÉLA A. NÉMETH. Wiley/Halsted, New York, N.Y. 1976. 477 pp. $27.00.

The very general title misleadingly represents the restricted scope of this work, which the author states is intended for "graduate and non-graduate laboratory and plant workers and technicians of the chemical industry". It seems to be designed only for those engaged in classical analytical control chemistry, and it ignores instrumental methods and spectrometry, except for a table of spectral lines of the elements. One-third of the book is devoted to tables of densities of inorganic solution, and nearly one-quarter to a table of the simplest properties of inorganic compounds. It will be of no use in a research laboratory, but might be of use in restricted types of relatively unsophisticated control laboratories.

* Unsigned book reviews are by the Book Review Editor.

Chemistry Decoded. By LEONARD W. FINE (Housatonic Community College). Oxford University Press, New York, N.Y. 1976. xvi + 446 pp. $11.50 (an Instructor's Manual, 131 pp, is available).

This book is fun, and will probably be so even for those who are not scientists at all. Indeed, that is the author's aim, to produce a book to introduce the student who has no technical background to chemistry in such a way as to leave him with a good feeling. This book is reviewed here because it is rather different from other general chemistry textbooks. Its approach is not simply the currently fashionable one of interlarding ecology into chemistry, but it follows the broader canon that "the student needs to be shown how chemistry fits into the whole framework of human knowledge". That is a big order, but it seems to have been fulfilled remarkably well. The numerous illustrations, their extraordinary variety (from medieval paintings to modern cartoons), and the ingenuity of their selection are an outstanding feature. They make the book enjoyable for anyone to browse in. A rich spicing of history is an integral part of the writing throughout, in contrast to the footnote treatment usually found. The author brings out what is so often disguised, that man is as much a part of chemistry as are molecules.

Dissolution Technology. Edited by L. J. LEESON and J. T. CARSTENSEN. Academy of Pharmaceutical Sciences, Washington, D.C. 1974. 197 pp. $8.50.

This is a most peculiar book. It has no preface and no index. The editors are not identified as such, and one would infer that they were the authors, unless one examined the six main papers, five of which are contributed by others. The book is the proceedings of a conference, held in 1973, but that fact is nowhere stated in the book. The clue is the inclusion of a ten-page appendix, "Abstracts from an Evening Session".

The subject of the conference was dissolution of medicinal agents and the relation of formulation thereto. Chemical engineers attracted by the misleadingly general title are likely to be much disappointed, although two of the papers do deal with the fundamental theories of dissolution of particles. One of them has a group of "Selected Problems", followed by their answers, appended to the bibliography. It is not explained what role these are intended to play (or whether they were perhaps set as a homework task for the conferees?).

Environmental Quality and Safety. Volume 4. Edited by F. COULSTON and F. KORTE. Academic Press, New York, N.Y. 1975. viii + 276 pp. $19.50.

This is a serial publication, devoted to reports of original research