(6) A. R. Guseva, *Dokl. Akad. Nauk SSSR*, **82**, 757 (1952); **85**, 1353 (1952); **94**, 1137 (1954); A. R. Guseva and M. G. Borikhina, *Biokhimiya*, **20**, 106 (1955).
(7) The antihypertensive activity was measured according to the procedure described by F. R. Domer in "Animal Experiments in Pharmacological Analysis", Charles C Thomas, Springfield, Ill., 1971, p 61, except that the sample was introduced through the jugular vein of spontaneous hypertensive rats (SHR). The SHR rats (170–260 g, 9–10 weeks old) of the Okamoto-Aobi strain were purchased from Raconic Farms Inc., Germantown, N.Y.
(8) T. J. Mabry, K. R. Markham, and M. B. Thomas, "The Systematic Identification of Flavanoids", Springer-Verlag, New York, N.Y., 1970, p 25.
(9) R. J. Anderegg and J. W. Rowe, *Holzforschung*, **28**, 171 (1974).
(10) K. Kratzl and G. E. Miksche, *Monatsh. Chem.*, **94**, 434 (1963).
(11) K. Freudenberg and H. Dietrich, *Chem. Ber.*, **86**, 1157 (1953).
(12) E. E. Dickey, *J. Org. Chem.*, **23**, 179 (1958).
(13) K. Freudenberg and G. Grion, *Chem. Ber.*, **92**, 1355 (1959).
(14) C. F. H. Allen and J. R. Byers, *J. Am. Chem. Soc.*, **71**, 2683 (1949).
(15) K. Freudenberg and H. H. Hubner, *Chem. Ber.*, **85**, 1181 (1952).
(16) D. R. Morris and L. P. Hager, *J. Biol. Chem.*, **241**, 1763 (1966).
(17) Z. Rappoport, S. Winstein, and W. G. Young, *J. Am. Chem. Soc.*, **94**, 2320 (1972).
(18) S. D. Levine, S. L. Neidleman, and M. Oberc, *Tetrahedron*, **24**, 2979 (1968).
(19) C. H. Ludwig, B. J. Nist, and J. L. McCarthy, *J. Am. Chem. Soc.*, **86**, 1186 (1964).
(20) H. Pauly and K. Feuerstein, *Chem. Ber.*, **60**, 1031 (1927).
(21) The antihypertensive activity of the natural pinoresinol diglucoside (**1**) is expressed as the decrease in diastolic blood pressure (mmHg) of SHR rats: 30 mg/kg (25, 35[22] mm); 40 mg/kg (80 mm); 100 mg/kg (105, 90, 110, 120 mm).
(22) Each value given represents a single rat.

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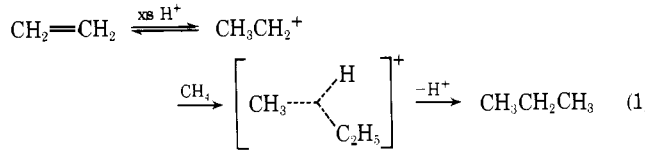
Strong Acid Chemistry. 3.[1] Alkene–Alkane Alkylations in HF–TaF_5. Evidence for the Presence of $C_2H_5^+$ in Solution

Sir:

Selective acid catalyzed alkylations of ethylene and propylene by the lower alkanes, methane, ethane, and propane, have never been clearly experimentally demonstrated, although the ability to carry out these reactions has been claimed.[2-5] The thermodynamics for these reactions to occur catalytically are very favorable below ~225 °C. Above this temperature antagonistic entropy effects become more important. Below this temperature acid catalyzed cleavage products from competing olefin oligomerization reactions must be distinguished from the simple alkylation products.

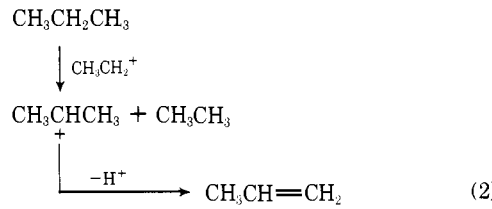
Olah discovered that the lower alkanes could be ionized at 50 °C and indeed could participate in further self-condensation (alkylation) reactions in antimony pentafluoride containing strong acid systems.[6] The door was opened to new chemistry through this activation of traditionally passive small molecules.[7-10]

We felt that a logical approach to achieve the catalytic reaction of methane would be to react it with a very energetic primary carbenium ion. The simplest way to generate such an ion is to dissolve ethylene, at moderate temperature in an excess of a strong acid. The ion would thus be available to react with the strongest base available, i.e., methane, in an alkene–alkane alkylation. This is in sharp contrast with the traditional alkane–alkene alkylations.[11] We have now found that such simple addition reactions can be selectively carried out in the HF–TaF_5 catalyst system. A methane–ethylene (85.9%:14.1%) gas mixture was passed at a rate of 42 standard cm^3/min through a 300-cm^3 Hastelloy C Autoclave Engineers autoclave containing 50 cm^3 of a 10:1 HF–TaF_5 (2.0 mol/0.20 mol) system stirred at 1000 rpm at 40 °C and maintained at 40 psig. In order to assure maximum protonation of the ethylene and minimize possible competition from ethylene oligomerization reactions a 40-fold excess of acid as well as efficient mixing was maintained and the temperature was not permitted to vary more than ±1°. Gas samples were taken from a system installed in the exit line and analyzed on a Perkin-Elmer Model 900 gas chromatograph using an 18 ft Silica Gel–10 ft DC-200 column connected in series and a flame ionization detector. After both 1.5 and 2.5 h the total C_3 in the reaction product amounted to 58% (eq 1). Mechanistically,



(1)

the ethyl cation appears to directly alkylate methane via a pentacoordinated carbonium ion such as proposed by Olah. It should be noted that methane alone does not react with HF–TaF_5 under these conditions[12] and that unless a flow system is used, the propane product, which is a substantially better hydride donor than methane, reacts further with the intermediate ethyl cation to ultimately form ethane and propylene in equal amounts (eq 2). Only ~1% of the propane formed in the flow system reacts with another molecule of methane to form isobutane. Also, based upon the results of acid quenching and analysis of hydrocarbons, only traces of isopentane and isohexanes, and no heavier materials, were present in the acid. No hydrogen could be detected in the product with a thermal conductivity detector.

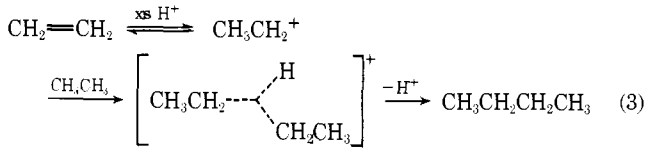


(2)

A less favorable mechanistic pathway is one in which an ethyl cation abstracts a hydride ion from a methane molecule to form a methyl cation (less stable than $C_2H_5^+$ by 39 kcal/mol).[13] The methyl cation can then alkylate a molecule of ethylene to produce propyl$^+$, etc. This alternative can be ruled out because the ethane thus formed includes a hydrogen needed to form propane product catalytically, and would consequently lead to increased formation of propylene and/or polymeric products. In an attempt to generate primary cations and to simulate the ethylene–methane alkylation, ethyl chloride was reacted with methane under alkylation reaction conditions. When no propane or propylene product was observed the reaction of methyl chloride with ethane was carried out. These latter two reactions[14] proceed without any involvement of the alkane and provide evidence that the ethylene–methane alkylation proceeds through a stabilized species such as a pentacoordinated carbonium ion. By this we mean a species having one three-centered two-electron bond, not a carbon having five directly bound ligands (see eq 1).[15] It should also be noted that propane formation, as a degradation product of polyethylene, can be ruled out because ethylene alone, diluted in helium, reacts, under these conditions, with no propane formation. Under similar reaction conditions, but in a hydrogen atmosphere, polyethylene (mol wt 20 000) reacts quantitatively with 10:1 HF–TaF_5 to form C_3–C_6 alkanes, with isobutanes and isopentanes constituting 85% of the product. Results of the polymer reaction are best understood in terms of known

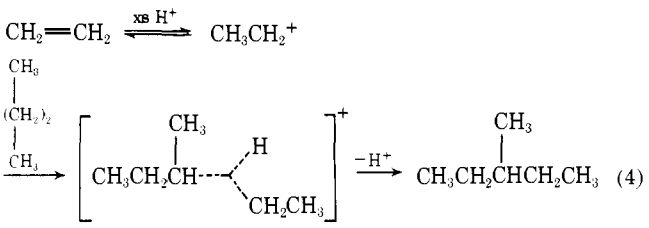
carbenium ion stabilities in acid and thus further substantiate the direct alkene-alkane alkylation and the existence of pentacoordinated carbocations. The reaction of polyethylene to give *tert*-butyl cation in FSO_3H-SbF_5 has been noted previously.[16]

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 alkylating 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.

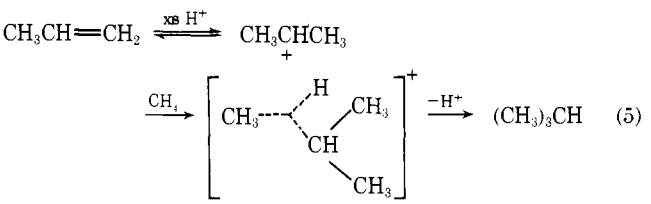


(3)

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 cation, 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.



(4)



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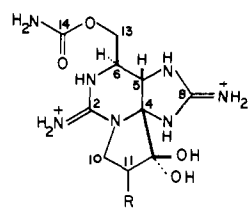
Structures of Gonyautoxin II and III from the East Coast Toxic Dinoflagellate *Gonyaulax tamarensis*

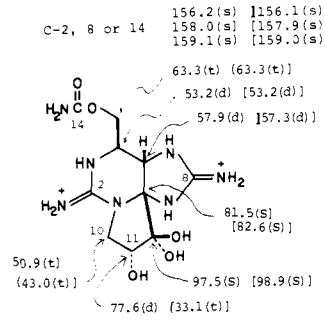
Sir:

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 [ ][3]