Table I. Carbon 1s Binding Energies and Atomic Charge Differences in Oxocarbenium Ions

Compound	ΔE_b, eV	$E_b(C^+)$, eV	Rel areas, C^+/C	$\Delta q(C^+ - C)$
$CH_3CO^+SbF_6^-$	6.0 ± 0.5[b]	291.8[a]	1.0/1.5[b]	1.09 ± 0.08
$(CH_3)_2CHCO^+SbF_6^-$	6.4 ± 0.5[c]	290.0[a]	1.0/5.5[c]	1.16 ± 0.08
$C_6H_5CO^+SbF_6^-$	5.1 ± 0.3	289.9[a]	1.0/6.0	0.92 ± 0.05
p-$CH_3C_6H_4CO^+SbF_6^-$	5.3 ± 0.3	288.8[a]	1.0/7.0	0.96 ± 0.05
p-$CH_3OC_6H_4CO^+SbF_6^-$	5.0 ± 0.3	289.4[a]	1.0/7.0	0.90 ± 0.05
2,4,6-$(CH_3)_3C_6H_2CO^+SbF_6^-$	4.8 ± 0.3	288.5[a]	1.0/9.0	0.87 ± 0.05

[a] Absolute values always have a greater inherent uncertainty, due to surface potential (charging of the sample) and other solid state effects. [b] This was the best ratio we could obtain. The salt is very sensitive to moisture. [c] This compound decomposes under vacuum, which may account for the high degree of extraneous signal in the lower E_b region of the spectrum.

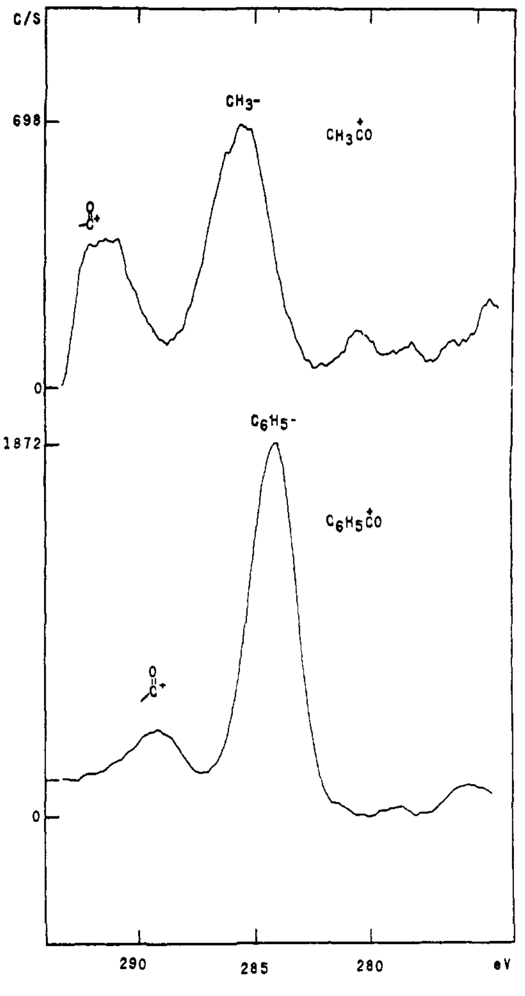

Figure 1. Carbon 1s electron spectra of methyloxocarbenium (a) and phenyloxocarbenium (b) hexafluoroantimonate.

for the isopropyloxocarbenium ion (for the difference between the C 1s levels of the α carbon and the carbonyl carbon). There is reasonable agreement between their calculated ΔE_b and our experimental results. The absolute values of the calculated binding energies are, however, higher (by 25–30 eV) than those found experimentally. The same calculations also predict that the β carbon C 1 signal in isopropyloxocarbenium ion should be 2.42 eV lower than that of the α carbon. We were unable to resolve these two carbon signals. Based on the ΔE_b of the corresponding C 1s levels in other isopropyl substituted compounds,[12] one would not expect to see such a large shift difference.

A qualitative comparison of the ΔE_b values of studied alkyloxocarbenium ions with those of aryloxocarbenium ions (see Table I) reflects the ring and ring substituent participation in charge delocalization. Thus, 2,4,6-$(CH_3)_3C_6H_2CO^+$ presents the smallest ΔE_b (4.8 eV).

In an attempt to establish a first approximation for the C–O bond order in oxocarbenium ions we have plotted measured ΔE_b values *vs.* Δq, the difference in calculated atomic charge of the two types of carbon taken into consideration, for a series of 27 compounds. The atomic charge q was calculated using the Pauling electronegativity approach.[4,13] In this approach $q = \Sigma I + Q$, where I is the partial ionic character of the bond and Q is the formal charge. A reasonably linear correlation was found. Using the experimental ΔE_b of CH_3CO^+ (6.0 ± 0.5 eV) a $\Delta q = 1.09 \pm 0.08$ was found. The calculated Δq values for the methyloxocarbenium ion in its carbenium and oxonium forms are 1.3 and 1.15, respectively. This shows that the bond order is very much displaced toward 3, emphasizing the major contribution of the oxonium ion form. In spite of its high degree of approximation this result is in good agreement with X-ray crystal-structure determination[3d] and is complementary to existent ir data.[3b,c]

In arylcarbenium ions contribution from resonance forms involving charge delocalization into the ring decreases both E_b and ΔE_b. The overlapping of the O 1s and Sb $3d_{5/2}$ lines prevents the measurement of O 1s binding energies in hexafluoroantimonate salts. Oxygen chemical shifts will be obtained in continuing work using different counterions (BF_4^-, AsF_6^-, PF_6^-).

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(12) For example, the ΔE_b of diisopropyl ether is 1.4 eV. The C 1s levels of isopropyl groups bound to a neutral carbon are essentially identical.[4,10]

(13) L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960.

(14) NIH Postdoctoral Fellow.

(15) NDEA Predoctoral Fellow.

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Ratio of Terminal to Central Addition of Fluorine Atoms to Propylene

Sir:

Quantitative studies of the addition of fluorine atoms to simple asymmetric alkenes have been few because of the general experimental difficulties in the handling of fluorine atoms and the eventual reaction products.

Table I. Yields of ^{18}F-Labeled Products from HI-Scavenged Addiiton of ^{18}F Atoms to Propylene in Excess SF_6

			Product yield, absolute %			
			Radical			
Sample composition			$CH_3CH^{18}FCH_2^*$		$CH_3CHCH_2{}^{18}F^*$	
Pressure, Torr			Product[b]			
SF_6	Propylene	HI	$CH_2{=}CH^{18}F$	$CH_3CH^{18}FCH_3$	$CH_3CH_2CH_2{}^{18}F$	Ratio[a]
3800	191	19	0.77	18.4	25.9	1.35
3780	101	100	0.47	14.0	19.7	1.36
1920	48	48	0.62	13.7	19.3	1.34
1920	48	48	0.72	14.2	19.9	1.33
1060	26	26	1.02	14.2	20.7	1.36
360	18	19	2.29	10.5	17.4	1.36
360	18	18	2.22	10.0	16.7	1.36

[a] $(CH_3CH_2CH_2{}^{18}F)/(CH_2{=}CH^{18}F) + (CH_3CH^{18}FCH_3)$. [b] Also observed (from hot reactions of energetic ^{18}F atoms), yields in absolute per cent: $SF_5{}^{18}F$, 0.8–1.3%; $CH_3{}^{18}F$, 0.2%; traces of ^{18}F-fluoropropenes, <0.3% total.

We now report a value of 1.35 for the ratio of terminal/central attack with propylene in the gas phase. An earlier estimate of 3.0 has been made for the same ratio from the respective yields of $CH_3CH(NF_2)CH_2F$ and $CH_3CHFCH_2NF_2$ in the gas-phase photolysis of N_2F_4–propylene mixtures.[1] The mechanism of this photodifluoramination reaction is believed to involve the direct photolysis of NF_2 (in equilibrium with N_2F_4) to F + NF; the addition of F to the olefin, and the further reaction of the adduct radical with NF_2 (either free or from N_2F_4) to give an observable stable product. Our experiments have involved the formation of tracer levels of ^{18}F atoms in SF_6 and the eventual identification and measurement of ^{18}F-labeled propyl fluorides. These studies have involved a much higher range of pressures (400–4000 Torr) and demonstrate that the radical from central addition, CH_3CHFCH_2, readily undergoes unimolecular decay to $CH_3 + CH_2{=}CHF$. Quantitative interpretation of relative ratios of attack by fluorine atoms on asymmetric olefins thus requires experimentation at several atmospheres pressure to avoid such decomposition problems.

The reaction sequence in our experiments is: formation of ^{18}F atoms in SF_6 by the (*n*, 2*n*) nuclear reaction; moderation of their initially high kinetic energy by collisions with excess SF_6; addition to propylene; and identification of the radical adducts, usually after subsequent abstraction of H from HI. The yields of the major volatile ^{18}F-containing products from such reactions are summarized in Table I. The basic experimental procedures have been described in detail earlier.[2–5]

The terminal addition of ^{18}F to propylene, as in (1), leads to a radical which may be expected to lose an H atom if not first stabilized by collision. The radical formed by central addition (2), on the other hand, can decompose by the much more exothermic pathway of methyl loss, as in (3). As the total pressure in the system was decreased, the results in Table I show an increasing yield of $CH_2{=}CH^{18}F$ from this decomposition. However, the yields of ^{18}F-fluoropropylenes were negligibly small at all pressures, indicating no appreciable decomposition of $CH_3CHCH_2{}^{18}F^*$ radicals in our system. At ≤500 Torr, the absolute yields in these ^{18}F experiments are diminished from nuclear recoil loss—insufficient total gaseous contents to remove the 10^5-eV energy from the initial nuclear reaction.[2] Most of the ^{18}F activity not identified in Table I can be found on the walls of the reaction vessels, presumably through reactions of $H^{18}F$ formed by abstraction of H from propylene.[5]

$$^{18}F + CH_3CH{=}CH_2 \longrightarrow CH_3CHCH_2{}^{18}F^* \tag{1}$$

$$^{18}F + CH_3CH{=}CH_2 \longrightarrow CH_3CH^{18}FCH_2^* \tag{2}$$

$$CH_3CH^{18}FCH_2^* \longrightarrow CH_3 + CH^{18}F{=}CH_2 \tag{3}$$

The ratio of terminal/central addition in propylene is 1.35 ± 0.02 for all of the experiments in Table I after correction for the formation of $CH_2{=}CH^{18}F$ at low pressures, in substantial disagreement with the value of 3.0 obtained earlier. A graph of D/S (decomposition/stabilization) *vs.* $(\text{pressure})^{-1}$ for $CH_3CH^{18}FCH_2^*$ radicals shows a straight line with near-zero intercept, indicating that ≥98% of these radicals were formed by the addition of ^{18}F atoms without extra kinetic energy, in agreement with other estimates of the essentially thermal nature of ^{18}F atom reactions in 95% SF_6.[3,4] Our experiments indicate almost 20% decomposition of $CH_3CH^{18}FCH_2^*$ radicals to CH_3 + $CH_2{=}CH^{18}F$ at 400 Torr total pressure of SF_6 and other reactants and imply even more of such radicals would have decomposed at the 150 Torr pressure used in the N_2F_4 photolyses.[1,6] No vinyl fluoride was reported in the N_2F_4 photolysis experiments, but the total yield of all identified volatile products amounted to only 50% recovery, and the vinyl fluoride could have been reacted further to form the polymeric material also reported.[1,7]

More than half of the ^{18}F atoms react with propylene to form $H^{18}F$ in our system. We do not experimentally observe the residual allyl radicals left by this abstraction since they are not labeled with ^{18}F. However, the abstraction reactions would be expected to lead to major yields for allyl plus radical terminator in unlabeled systems. The high yield of $CH_2{=}CHCH_2NF_2$ found in the N_2F_4 photolysis system has been attributed

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(1) C. L. Bumgardner, E. L. Lawton, K. G. McDaniel, and H. Carmichael, *J. Amer. Chem. Soc.*, **92**, 1311 (1970).

(2) T. Smail, G. E. Miller, and F. S. Rowland, *J. Phys. Chem.*, **74**, 3464 (1970).

(3) T. Smail, R. S. Iyer, and F. S. Rowland, *J. Amer. Chem. Soc.*, **94**, 1041 (1972).

(4) R. L. Williams and F. S. Rowland, *ibid.*, **94**, 1047 (1972).

(5) R. L. Williams and F. S. Rowland, *J. Phys. Chem.*, **75**, 2709 (1971).

(6) In unpublished experiments by R. L. Williams and F. S. Rowland, the efficiency of stabilization for $CH_2{}^{18}FCH_2^*$ radicals has been shown to be different by almost a factor of 2 for SF_6 and CF_4. Consequently, we are uncertain what equivalent pressure to use in comparisons of SF_6 with propylene–N_2F_4 mixtures.

(7) Evidence has since been obtained in the N_2F_4 system of the presence of small amounts of CH_3NF_2, expected from the CH_3 radicals in reaction 3; private communication, Professor C. L. Bumgardner.

to the combination of such allyl radicals with NF_2. Overall, after correction for the decay of CH_3CHFCH_2 radicals, our experiments are in excellent agreement with the analysis of the N_2F_4–propylene system through consideration of addition and abstraction of F atoms as the primary reactions with propylene.

The measured terminal/central ratio of 1.35 is in sharp contrast with the ratio of about 15 found for thermal hydrogen atom addition to propylene.[8] The former indicates a very moderate preference for reaction away from the CH_3 group of propylene, consistent with the characterization of atomic fluorine as a rather indiscriminate, highly reactive species. Relatively small directional preferences have also been found for ^{18}F atom addition to asymmetric fluoroethylenes.[3] Evaluation of the origin of this CH_3 orientation effect requires additional experiments with other asymmetric olefins, which depend in turn upon satisfactory resolution of the difficulty caused by the reactivity of HI with other substituted olefins under our experimental conditions.

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(9) This research was supported by AEC Contract No. AT-(04-3)-34, Agreement No. 126.

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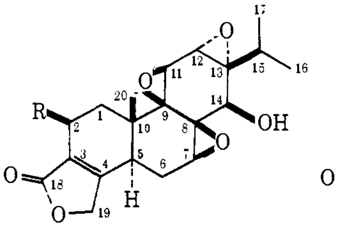
Triptolide and Tripdiolide, Novel Antileukemic Diterpenoid Triepoxides from *Tripterygium wilfordii*[1–3]

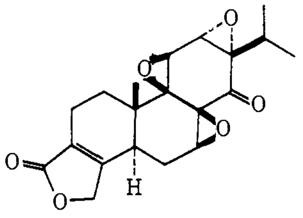
Sir:

The antileukemic activity of *Maytenus ovatus* and its active principle, maytansine,[2] prompted us to investigate other plants of the Celastraceae family. An alcoholic extract of *Tripterygium wilfordii* Hook F.[4] was found to show significant activity *in vivo* against the L-1210 and P-388 leukemias in the mouse and *in vitro* against cells derived from human carcinoma of the nasopharynx (KB).[5] We report herein the isolation and structural elucidation of triptolide (**1**) and tripdiolide (**2**), two novel antileukemic[6] diterpenoid triepoxides. These compounds and the companion cytotoxic ketone triptonide (**3**) appear to be the first reported natural products containing the 18(4→3) *abeo*-abietane skeleton and the first recognized diterpenoid triepoxides.

Fractionation of an ethanol extract, guided by assay against KB, L-1210, and P-388, revealed that the inhibitory activity was concentrated in the ethyl acetate layer of an ethyl acetate–water partition. Chromatography of the ethyl acetate soluble material on silica gel yielded a KB cytotoxic fraction (A) on elution with chloroform and an *in vivo* active fraction with 5% methanol in chloroform. The latter fraction was further chromatographed on SilicAR CC-7 to yield triptolide-enriched fraction (B) on elution with chloroform and tripdiolide-enriched fraction (C) with 1% methanol in chloroform. Further chromatography of fraction B on SilicAR CC-7 gave triptolide (**1**) (0.001%): $C_{20}H_{24}O_6$; mp 226–227°; $[\alpha]^{25}D$ −154° (c 0.369, CH_2Cl_2); uv max (EtOH) 218 nm (ϵ 14,000); ir (KBr) 2.89, 5.64, 5.93, 8.05, 8.52 μ; mass spectrum m/e 360.1600 (M^+) (calcd, 360.1573); nmr ($CDCl_3$) τ 9.03 (3 H, d, $J_{15,16} = 7$ Hz, 16-CH_3), 8.90 (3 H, d, $J_{15,17} = 7$ Hz, 17-CH_3), 8.78 (3 H, s, 20-CH_3), 7.17 (1 H, d, $J = 11$ Hz, OH), 6.54 (1 H, d, $J_{6\alpha,7} = 5$ Hz, 7-H), 6.48 (1 H, d of d, $J = 11$ Hz, $J_{12,14} = 1$ Hz, 14-H), 6.40 (1 H, d of d, $J_{11,12} = 3$ Hz, $J_{12,14} = 1$ Hz, 12-H), 6.00 (1 H, d, $J_{11,12} = 3$ Hz, 11-H), 5.22 (2 H, m, 19-CH_2).



1, R = H
2, R = OH



3

The structure and stereochemistry of triptolide (**1**) were determined by direct X-ray crystallographic analysis. Crystals of triptolide are monoclinic with space group $P2_1$ and $a = 13.420$ (1), $b = 6.256$ (1), and $c = 11.593$ (1) Å, and $\beta = 118.09$ (1)°. There are two molecules in the unit cell. The intensities of 1071 reflections, measured by counter diffractometry with monochromatic Cu Kα radiation, were used in the structure analysis. The phase problem was solved by the use of symbolic addition[7] and tangent formula refinement procedures,[8] and the atomic parameters were refined by block-diagonal least-squares methods to give $R = 0.078$. Isotropic thermal parameters were assumed for all atoms. Of the 24 hydrogen atoms 14 were identified from a final difference electron-density function and included with fixed parameters in the refinement process.

A consistent indication of the correct absolute configuration is provided both by the results of Hamilton's R-factor ratio test[9] and by the measurement of intensity differences in selected Friedel pairs of reflections.[10] For parameters corresponding to each of the two possible enantiomeric structures the values of R are 0.0785 and 0.0783, when the anomalous dispersion terms[11] for oxygen are taken into account, suggesting a significant distinction between the two configurations at the 90% confidence level. For the 13 structure amplitudes where the magnitude of the difference between $F(hkl)$ and $F(\bar{h}\bar{k}\bar{l})$ is calculated to be greatest, the observed

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(1) Tumor Inhibitors. LXXIV. Part LXXIII is ref 2.

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(3) Supported by grants from the National Cancer Institute (CA-11718 and CA-11760) and American Cancer Society (T-275 and T-541), and a contract with Chemotherapy, National Cancer Institute (NIH 71-2099).

(4) Roots were collected in Taiwan in Aug 1971. We thank Dr. Robert E. Perdue, Jr., U. S. Department of Agriculture, Beltsville, Md., for supplying the plant material. We gratefully acknowledge also the supply of a cytotoxic alkaloid fraction by Dr. M. Beroza, U. S. Department of Agriculture, Beltsville, Md.

(5) Cytotoxicity and *in vivo* activity were assayed as in *Cancer Chemother. Rep.*, 25, 1 (1962).

(6) Triptolide and tripdiolide showed significant antileukemic activity against the L-1210 and P-388 leukemias at the 0.1 mg/kg level, and cytotoxicity (ED_{50}) against KB cell culture at 10^{-3}–10^{-4} μg/ml.

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