conformational interconversions. This is seen clearly from the observations that the ratio of naphthalene-localized emission (I_m) to excimer emission (I_e) varies with solvent polarity and that decreases in I_m/I_e are paralleled by decreased reaction yield (ϕ_{dis}).

The data presented here illustrate the delicate interplay between excited-state potential surface minima, populated by excitation of multiple ground-state molecular conformations, and the nature of the decay processes observed in complex multichromophoric systems. Changes in the relative orientation of interacting chromophores can dramatically alter the course of excitation decay. Scheme II summarizes our conclusions concerning the effect of conformation on the photochemistry of compounds **1**.

Structure Elucidation of a Potent Mutagen from Human Feces

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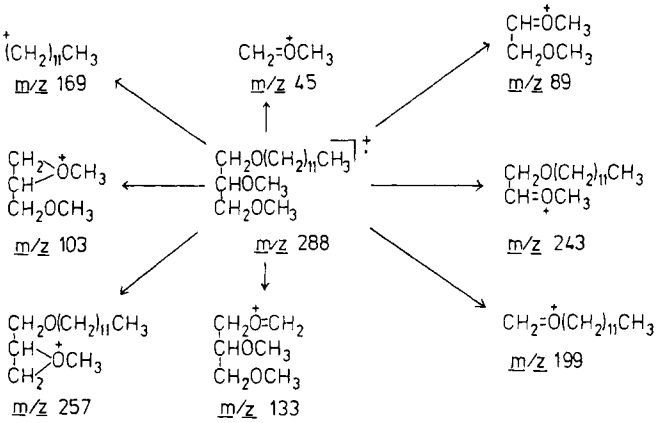
The occurrence of an ether-extractable strongly mutagenic agent in human feces was first reported by Bruce and his co-workers,[1,2] and their results have been confirmed and extended by ourselves[3-5] and others.[6] About 3% of the people in North America excrete feces that have a high level of mutagenic activity in their ether extracts as measured by the Ames test, and this activity has been shown to be due almost entirely to a single compound which has an intense UV absorption spectrum;[1,4,5,7] the purified compound is mutagenic at a level comparable to benzo[*a*]pyrene.[7] We now present evidence for the structure of this mutagen.[8]

The purified mutagen, prepared in microgram quantities as previously described,[7] is very unstable, decomposing rapidly on exposure to air or to traces of acid. It is a lipophilic compound, soluble in chloroform, benzene, and ether, and insoluble in water. Both acetylation and trimethylsilylation yield less polar substances, as determined by thin-layer chromatography, and *n*-butylboronation also yielded a less polar derivative, suggesting the presence of a diol function.[9]

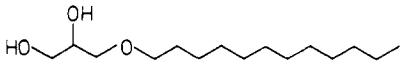
The UV absorption spectrum of the mutagen, with peaks at 325, 345, and 365 nm, is characteristic of a polyene. Simple pentaenes have their longest wavelength absorption at about 342 nm, while that for hexaenes is at about 380 nm,[10] so the mutagen must be a pentaene with some additional conjugation. The polyene nature is also indicated by the fact that purification by HPLC gave two closely related substances that could be collected separately but that interconverted on standing in solution at room temperature in daylight. We assumed that these substances were simple *E*–*Z* isomers of one or more of the double bonds, and all subsequent work was carried out with a mixture of these isomers.

Scheme I



Chemical ionization mass spectrometry (CIMS) of the mutagen gave a quasi-molecular ion at m/z 251. Hydrogenation (H_2/Pt) yielded a single major compound, which could be subjected to gas chromatography after derivatization with one of several reagents. CIMS of the hydrogenated compound itself showed a quasi-molecular ion (MH^+) at m/z 261, and corresponding ions were shown by the acetate, trimethylsilyl, and methyl derivatives at m/z 345, 405, and 289, respectively. Deuteration (D_2/Pt) of the mutagen followed by acetylation yielded a compound showing a molecular ion at m/z 354 on electron impact mass spectrometry.[11] These data indicate conclusively that the mutagen has two derivatizable hydroxyl groups and five double bonds.

Analysis of the mass spectrum of the dimethyl ether of the hydrogenated mutagen indicated it to be the dimethyl ether of 3-dodecyloxy-1,2-propanediol (**1**), with major fragment ions of



1

m/z 257, 243, 199, 169, 133, 103, 89, and 45 (Scheme I). Although the 2-dodecyloxy isomer would show most of these same fragmentations, the occurrence of an intense peak at m/z 89 was only consistent with the 3-dodecyloxy formulation. Confirmation of this structural assignment was achieved by comparison with a sample of **1** prepared by standard methods.[12] The synthetic compound[13] and its dimethyl, diacetyl, and bis(trimethylsilyl) derivatives showed chromatographic behavior identical with the hydrogenated mutagen[14] and its corresponding derivatives.[15] Although a synthetic sample of 2-dodecyloxy-1,3-propanediol[12,13] had chromatographic properties very similar to **1**, its dimethyl ether had a retention time on gas chromatography different from the dimethyl ether of **1** and from that of the hydrogenated mutagen. The mass spectrum of the dimethyl ether of synthetic **1** was identical with that of the methylated hydrogenated mutagen while the mass spectrum of the dimethyl ether of 2-dodecyloxy-1,3-propanediol differed from both of these spectra in lacking an intense ion at m/z 89 and in other respects.

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(11) CIMS yielded a complex set of ions in the region m/z 345–355, presumably due to hydrogen exchange between the ionized reagent gas and the sample.
(12) Gupta, S. C.; Kummerow, F. A. *J. Org. Chem.* **1959**, *24*, 409–411.
(13) Satisfactory elemental analyses have been obtained for these compounds.
(14) Thin-layer chromatography on silica gel with elution by 93:7 dichloromethane:isopropanol.
(15) Gas chromatography under the conditions specified earlier.[8]

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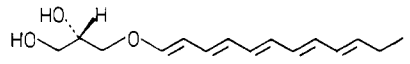
These data indicate conclusively that the hydrogenated mutagen has the structure **1**. Since the mutagen itself has five double bonds, it must either have the the structure **2** (excluding stereochemistry)



2

or an isomer in which the conjugated system is located at the 2,4,6,8,10- or 3,5,7,9,11-positions. Support for the assigned structure **2** is obtained from the compound's ^{1}H NMR spectrum. This shows signals at 6.56 (1 H, d, J = 12 Hz, OCH=), 5.5–5.8, and 5.9–6.3 (~8 H, C*H*=C*H*), 5.2 (1 H, m, OCH=C*H*), 3.5–3.9 (~5 H, m, CH_2O and CH(OH)), 2.05 (2 H, m, CH_2—CH=C), and 0.94 (3 H, t, J = 8 Hz, CH_3CH_2). Confirmation of the structural assignment was obtained by microozonolysis[16] of the mutagen, which yielded inter alia propionaldehyde, identified by comparison of its 2,4-dinitrophenylhydrazone with an authentic sample.[17] In addition, the formation of glycerol[18] on mild acid hydrolysis of the mutagen confirmed the presence of an enol ether linkage.

These data establish the structure of the mutagen as **2**, excluding stereochemistry. The enolic double bond must have the *E* configuration on the basis of the coupling constant of 12 Hz observed for one of its protons, and it seems probable that the remaining double bonds also have the stable *E* configuration.

The configuration of the glyceryl moiety was determined by derivatization with (+)-α-methoxy-α-(trifluoromethyl)-α-phenylacetyl chloride ((+)MTPA chloride).[19] Acylation of synthetic racemic **1** with (+)MTPA chloride yielded a mixture of two diastereomeric bis(+)MTPA esters that could be resolved by HPLC.[20] The bis(+)MTPA ester of the hydrogenated mutagen gave a single peak on HPLC corresponding to the faster eluting peak of the diastereomeric mixture, and the bis(+)MTPA ester of (*S*)-**1**[13,21] gave a single peak which also coincided with the first eluting peak on HPLC. The natural mutagen thus has the *S* configuration, as do naturally occurring ether lipids such as batyl alchol and chimyl alcohol,[22] and is hereby defined as (*S*)-3-(1,3,5,7,9-dodecapentaenyloxy)-1,2-propanediol (**2**).

The observation that a simple glyceryl ether lipid has strongly mutagenic properties has potentially important implications for the etiology of colon cancer. We are currently in the process of synthesizing **2** in sufficient quantity to enable us to evaluate its biological and particularly its carcinogenic activity. We have previously shown that **2** is produced by colonic bacteria[5] and that there is a correlation between the excretion of this mutagen and populations at risk for colon cancer.[3] If it proves to be carcinogenic and to be involved in the initial lesion in colon cancer, then colon cancer may well turn out to be preventable by interfering with the biosynthesis of this compound by chemotherapy or by dietary methods.

Acknowledgment. This work was supported by Grant CA 23857 from the National Cancer Institute. Initial ^{1}H NMR spectra were obtained on a Bruker WH-400 spectrometer; we acknowledge the National Science Foundation Regional Facility at the University of South Carolina (CH78-18723). We acknowledge mass spectrometric assistance from Dr. J. D. Henion, Dr. R. D. Macfarlane, Dr. W. Garland, and K. Harich and ^{1}H NMR assistance from T. Glass.

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(20) μPorasil column, 3.9 mm × 30 cm, with elution by 1:1 dichloromethane:hexane.
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Cobalt-Catalyzed Carbalkoxylation of Olefins: A New Mechanism

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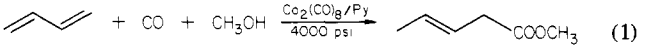
Transition-metal-catalyzed carbalkoxylation of olefins to esters, a synthetically very important reaction,[1] can, in principle, proceed by two main mechanisms, involving M–H or M–COOR addition to the double bond. Evidence for each one of these mechanisms has been presented for palladium-catalyzed olefin carbalkoxylations,[1–3] whereas only the hydrido route has been proposed for Co-catalyzed carbalkoxylation reaction.[1,4] We report here evidence that supports a mechanism involving both carbalkoxycobalt and hydridocobalt complexes synergistically in which addition of the carbalkoxy complex to the olefin is preferred.

We studied the $Co_2(CO)_8$/pyridine-catalyzed carbomethoxylation of butadiene to methyl 3-pentenoate (eq 1), a potential precursor for dimethyl adipate and nylon 66.[5]



(1)

To probe the plausibility of a route based on a carbomethoxycobalt complex in this reaction, we prepared the complex **1**[6] from methyl oxalyl chloride (eq 2). Methyl chloroformate does

(2)

1

not react with $NaCo(CO)_4$ or $TlCo(CO)_4$ because of insufficent electrophilicity of the carbonyl in this compounds.[7] **1** is a volatile liquid and can be isolated pure from the solvent dimethyl ether. **1** decomposes slowly at 25 °C ($\tau_{1/2} \approx 1$ h). When condensed into an ether solution of PPh_3, the complex $MeOC(O)Co(CO)_3PPh_3$ (**2**) is obtained, the crystal structure of which is presented in Figure 1.[8] The complex is trigonal bipyramid with the three carbonyls in the equatorial plane. All bond parameters appear reasonable;

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(6) This compound was unambiguously characterized on the basis of NMR and IR spectra. Satisfactory C, H analysis was obtained.
(7) Reaction of methyl oxalyl chloride with $NaCo(CO)_3PPh_3$ yields the first stable α,β-dicarbonylcobalt complex, $MeOC(O)C(O)Co(CO)_3PPh_3$: D. Milstein, to be submitted for publication.
(8) Crystal structure information: triclinic, space group $P\bar{1}$; at −100 °C, a = 10.349 (1), b = 21.095 (3), c = 10.271 (1) Å; α = 91.20 (1), β = 91.91 (1), γ = 76.72(1)°; V = 2180.9 Å^3; Z = 4. Syntex P3 diffractomer, graphite monochrometer, Mo Kα radiation, λ = 0.710 69 Å, ω scans of 1.0°, $4 < 2\theta < 50°$, 7695 reflections. An empirical absorption correction was applied; the "transmission factors" ranged from 0.958 to 0.999. The structure was refined by full-matrix least-squares techniques: 5280 reflections with $I > 3\sigma(I)$, 661 variables (non-hydrogen atoms with anisotropic thermal parameters, hydrogen atoms with isotropic parameters), R = 0.036, R_w = 0.038. The final difference Fourier map showed only residues, the largest having a magnitude of 0.33 e Å^{-3}. The mathematical and computational details may be found in the following: Nugent, W. A.; Harlow, R. L. *Inorg. Chem.* **1979**, *18*, 2030–2032.

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