Table I. Precision of Measurements for Various Ions as a Function of the Magnitude of the Isotope Ratio

Compound	Ions monitored	Abundance of 2d as % of 1st ± 1σ	1σ/abundance × 100 = % precision
α-Methylallyl phenyl sulfide	164, 166	5.173 ± 0.009	0.18[a]
1,1,2-Trichloroethane	132, 134	93.82 ± 0.07	0.08[b]
	134, 136	31.80 ± 0.03	0.10[b]
	132, 130	5.483 ± 0.012	0.22[b]
Benzyl acetate	150, 152	1.014 ± 0.004	0.35[b]

[a] Based on 60 000 determinations of the isotope ratio. [b] Based on 10 000 determinations of the isotope ratio.

Torr/h) and reproducible source pressures (2 × 10^{-6} Torr).

The actual data acquisition was controlled by the computer using specially developed software. The objective was to sample the voltages corresponding to the parent and isotope peaks sufficiently close together in time to approximate simultaneous detection and to sample frequently enough to average out short term fluctuations in the electron beam or ion current. This was achieved by a technique of real time data collection in which the computer positioned the mass filter at the top of each peak and sampled the voltage of the ions in the order mass I, mass II, mass II, mass I. The voltages were summed, periodically verified against a set of threshhold conditions and stored for later retrieval and analysis. Following this procedure it is possible to make approximately 60 readings at each mass per second or 10 000–60 000 determinations of the isotope ratio in less than 20 min. This rate of data acquisition was limited only by the time required for equilibration of the detector when changing to a new mass setting. For a jump between two masses differing by 2 amu, the dead time was ~3 ms.

These data were evaluated off-line by means of a standard error analysis and a statistical treatment presented. A representative selection of isotope ratios for several compounds studied is presented in Table I. In general, statistics from individual runs and groups of determinations on a given day indicate a remarkable degree of instrument stability. This precision is characterized by a standard deviation (σ) of less than 0.2% for most measurements. It is only where the intensities of the ions being compared were greatly different from each other that the degree of precision deteriorates. Still, this precision is somewhat better than that found by Caprioli et al.[8] and far superior to that of Schoeller and Hayes.[9]

The question of accuracy, in the sense of absolute isotope ratio measurements, presented a problem for two reasons, isotope fractionation occurring during sample preparation, and mass discrimination resulting from the dependence of the quadrupole system's performance on tuning parameters (repeller voltage). For the α-methylallyl phenyl sulfide study, the difficulty was obviated by always referencing the ratio to that found in the starting material i.e.,

$$\text{fractionation} = \frac{{}^{34}\mathrm{S}_0/{}^{32}\mathrm{S}_0}{{}^{34}\mathrm{S}_t/{}^{32}\mathrm{S}_t}$$

Because the parent ion was used in the determinations, the isotope peak (p + 2) had to be corrected for ^{13}C and ^{2}H contributions. The data in Table II take this correction into account.

Table II. Variation of the Kinetic Isotope Effect with Approach to Equilibrium Composition of the Thioallylic Rearrangement

t (min)	% reaction	${}^{34}\mathrm{S}_0/{}^{32}\mathrm{S}_0/{}^{34}\mathrm{S}_t/{}^{32}\mathrm{S}_t \pm 1\sigma)$[a]
12.6	2.5	1.0041 ± 0.0027
25.5	5.0	1.0049 ± 0.0022
52.4	10.0	1.0036 ± 0.0025
80.9	15.0	1.0011 ± 0.0031
$\infty = (10t_{1/2})$[b]	equilibrium	0.99 ± 0.0027
$\infty = (20t_{1/2})$[b]	equilibrium	0.9959 ± 0.0024

[a] The value of 1.0040 ± 0.0016 is calculated for each % reaction listed when correcting for the inverse equilibrium isotope effect measured, $K_{32}/K_{34} = 0.9956$. [b] $t_{1/2}$ = a half life of reaction.

In this way, an average sulfur isotope effect of 1.0040 ± 0.0016 at 198° was calculated from the experimental fractionation and equilibrium data. When compared with the theoretical evaluation, the findings indicate a transition state of an associative nature (model 3) in which a clear increase in bonding is experienced by the sulfur seat of reaction. Moreover, the inverse equilibrium isotope effect of $K_{32}/K_{32} = 0.9956$, which has been determined, corresponds to a zero point energy difference of 4 cal/mol at 198°.

These findings are offered to demonstrate a simple, new technique the availability of which could permit widespread application of the heavy atom isotope criterion of reaction mechanism. With the precision now realizable through use of the method described herein, it should be generally possible for one, previously deterred by instrumental limitations, to subject mechanistic proposals to the most searching "substituent effect" test for an unequivocal answer, namely, the kinetic isotope effect criterion. This applies particularly to reaction centers lighter than sulfur where the kinetic effects are much larger. Elaboration of this approach, presently under development in our laboratories, gives promise of improvements in the precision of measurement almost by another order of magnitude. This should make possible applications to reaction centers even heavier than sulfur.

References and Notes

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Received November 17, 1975

A New Diisocyanide of Novel Ring Structure from a Sponge

Sir:

Recent reports of the occurrence of sesquiterpene[1-5] and diterpene isocyanides[4] from sponges prompt us to report the structure of a diisocyanide obtained from a sponge of the genus *Adocia* collected near Townsville, Australia, on the Great Barrier Reef.

Concentration of the combined cold petroleum ether extracts of the milled freeze-dried sponge gave 2% of a crystalline

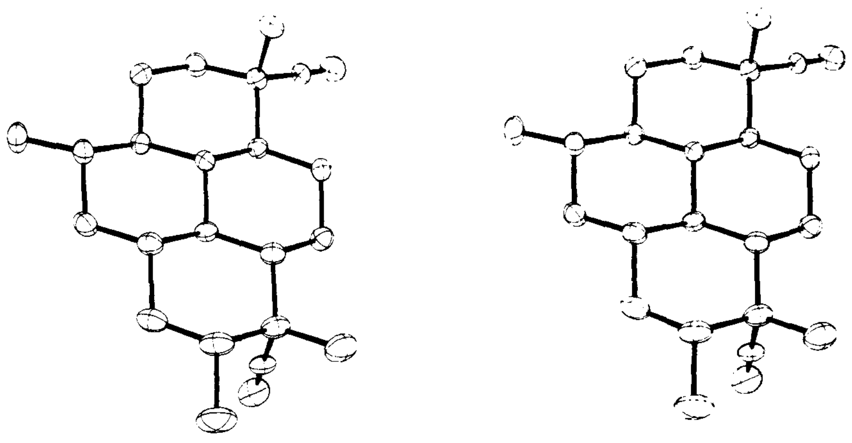


Figure 1.

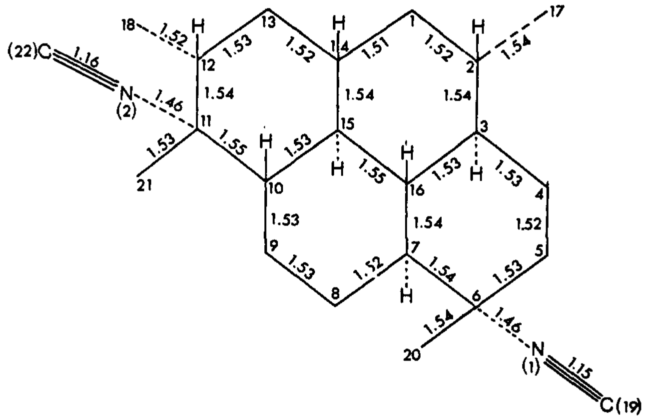


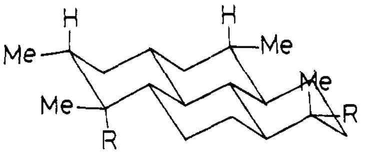
Figure 2. Bond lengths (esd ~0.005 Å) and numbering scheme used for the atomic coordinates.[6]

material, suitable for single-crystal x-ray structural determination after two further recrystallizations from hexane ($(\alpha)^{22}\text{D}$ + 47.4° (c 0.7, CH_2Cl_2)). High resolution mass spectrometry established the molecular formula of this compound (**1**), for which we suggest the name diisocyanoadociane, as $C_{22}H_{32}N_2$ (calcd mass, 324.2569; found, 324.2565; 77%). Major fragment ions occurred at m/e 282 ($M^+ - (CH_3 + HCN)$; 16%), 270 ($M^+ - 2HCN$; 100%), and 255 ($M^+ - (CH_3 + 2HCN)$; 31%).

The ir spectrum of **1** suggested the presence of an isocyanide moiety (λ_{max} 2130, 2140 cm^{-1} (s)) and the uv spectrum showed no absorption above 210 nm. The 100-MHz ^{1}H NMR spectrum demonstrated no resonances below δ 2.2. Two methyl doublets at δ 0.88 ($J = 6$ Hz) and 1.06 ($J = 6$ Hz), and two methyl multiplets at δ 1.29 and 1.37 which showed small couplings were the only resonances which could be definitely assigned.

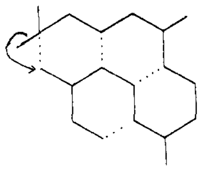
The presence of two isocyanide functions was established by the hydrolysis of **1** to the diformamide **2** under mildly acidic conditions. The MS of this product established the molecular formula ($C_{22}H_{36}N_2O_2$) and the ^{1}H NMR spectrum established the presence of two -NHCHO groups at δ 8.04 (1 H, s, NHC*H*O), 7.90 (1 H, s, NHC*H*O) and 3.0 (2 H, bs, -N*H*CHO exchanged by D_2O). The lack of any other functionality in **1** required that diisocyanoadociane must be tetracyclic with two secondary and two quaternary methyl groups. The appearance of two finely coupled quaternary methyl groups centered at δ 2.04 in the ^{1}H NMR spectrum of **2** indicated that each methyl group was bound to a carbon atom carrying an isocyanide moiety in **1**.

The diisocyanoadociane crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 7.086 \pm 0.004$ Å, $b = 21.630 \pm 0.011$ Å, $c = 13.104 \pm 0.007$ Å, $Z = 4$, $d_c = d_m = 1.079$ g/cm^3. The intensity data were measured with a four-circle diffractometer (Hilger and Watts Y.290) applying the Ω-scan technique with balanced filters. The crystal structure was solved by a multisolution method and tangent formula refinement. The refined structure (the hydrogen positions were included as constant parameters) yielded an R value of 5.9%.[6] The presence of the isocyanide functions was also proven by x-ray methods. The refinement of the opposite arrangement (nitrile) of the C and N atoms was performed yielding a significantly higher R-value of 7.6%. The structure of the material represents itself as a substituted fused polycyclic saturated hydrocarbon (Figure 1).[7] Four cyclohexane rings, all trans fused, form the body of the molecule with all rings in the chair conformation. Figure 1 does not necessarily give the correct absolute configuration.



(1) R= -N≡C

(2) R= NH-CHO



(3)

The bond lengths (Figure 2) and bond angles correspond to the expected values. The isocyanide groups show typical C—N≡C angles of 179.5°, N (**1**), and 178.1°, N (**2**), with standard deviations of 0.3° and 0.4°, respectively and N≡C bond lengths of 1.150 and 1.156 Å with standard deviations of 0.005 and 0.006 Å, respectively. The methyl hydrogens appear localized in the electron density map and take up staggered positions with respect to the following atoms: C_2-methyl with C_1, C_{11}-methyl with C_{22}, C_{12}-methyl with C_{13}, C_6-methyl with C_5.

The diisocyanoadociane is the first representative of a new class of compound containing a perhydropyrene ring system. The skeleton is extremely unusual in that the rings do not have any angular methyl substituents. The biosynthesis of such a compound is not straightforward. We suggest that **1** is terpene-derived and this can be accomplished formally by a single methyl shift of a unique cyclization of a geranyl-geraniol residue as illustrated in **3.** We have not been able to demonstrate the presence of any naturally occurring formamides, the suggested intermediates for diterpene isocyanide formation in another sponge[4] in this *Adocia* species. Other isocyanides have been extracted from the sponge and will be discussed in a subsequent publication.

Acknowledgments. The authors wish to thank Drs. W. Vetter and L. Chopard for valuable discussions.

Supplementary Material Available: A listing of structure factors and atomic coordinates (28 pages). Ordering information is given on any current masthead page.

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Received February 2, 1976

Ozonolysis of Fluoroalkenes: the Synthesis, Conformation, and Microwave Spectrum of 3-Fluoro-1,2,4-trioxolane

Sir:

Simple derivatives of ethylene ozonide with halogen substitution directly on the ring have not been synthesized until recently. Gillies[1] has isolated the cis/trans difluoroethylene ozonide isomers from ozonolysis of 1,2-difluoroethylene in isobutane and observed little dependence of the ozonide cis/trans ratio on the initial alkene configuration. He also observed that in CH_3Cl, *cis*-1,2-difluoroethylene oxide and HFCO were major products along with lesser amounts of the ozonides and a trace of *cis*-1,2,3-trifluorocyclopropane. In related studies, the ozonolysis of 2,3-dibromo-2-butene[2,3] and C_2F_4[4] in solution gave only trace amounts of the ozonides while emission from CF_2 was observed upon gas phase ozonolysis of C_2F_4.[5] Such results raise the question as to what extent the normal ozonolysis mechanism[6] is applicable to halogenated alkenes.

In this note we report the identification of the ozonide of vinyl fluoride, $\mathrm{HF\overline{COOCH_2O}}$ (I) and preliminary results of cross ozonide formation and foreign aldehyde insertion with *cis*-1,2-$C_2H_2F_2$. I is also reported to have the twisted half-chair conformation observed for other ozonides[6d,7] with the fluorine in the axial position.

I was synthesized by ozonolysis of vinyl fluoride in isobutane or CH_3Cl at −95° using standard techniques.[6d] The major volatile products were I and ethylene ozonide (about 5:1 in CH_3Cl) along with HFCO, H_2CO, and HCOOH. Not all products have been identified yet; whether 1,2-difluoroethylene ozonide, fluoroethylene oxide, or cyclopropanes are obtained requires further investigation. I was partially isolated at −95° by trap to trap distillation and further purified by VPC.[8] It was identified by its mass spectrum, ir, and microwave (MW) spectrum.[9,10]

I has also been isolated upon ozonolysis of mixtures of C_2H_4 (or *cis*-$C_2H_2D_2$) and *cis*-1,2-$C_2H_2F_2$ in CH_3Cl (−95°) or mixtures of H_2CO and *cis*-1,2-$C_2H_2F_2$ in isobutane (−45°). For the former reaction, the yield of the monofluoro cross ozonide was small (5–10%). The latter reaction was efficient enough to synthesize $\mathrm{HF\overline{COOCH_2{}^{18}O}}$ using labeled H_2CO (^{18}O, ~55%). The enriched ozonide was identified by its MW spectrum (cf. below). No MW spectrum for $\mathrm{HF\overline{CO^{18}OCH_2O}}$ could be assigned suggesting that insertion produced enrichment predominantly at the ether site.

Although further work is obviously desired, it is reasonable to propose from these preliminary experiments that formation of I from C_2H_3F and by aldehyde insertion and cross ozonide reactions with *cis*-$C_2H_2F_2$ very likely involves a Criegee mechanism. This could occur by the combination of the H_2COO zwitterion (or diradical)[11] plus HFCO (path A) and/or the HFCOO zwitterion plus H_2CO (path B). The synthesis involving H_2CO insertion (in isobutane) argues strongly that HFCOO must be considered a viable precursor (path B). The cross ozonide synthesis of I ($C_2H_4 + C_2H_2F_2$) can be rationalized by either pathway alone or both competing; since difluoroozonides are also formed from $C_2H_2F_2$[1] it seems likely that both pathways are occurring.

The production of I from C_2H_3F is also possibly occurring via both pathways. Thus, the identification of ethylene ozonide (a cross ozonide) implies both pathways; however, an ambiguity remains since the other cross ozonide (the difluoro) has not yet been identified. Therefore the possibility can not yet be eliminated that with C_2H_3F, path A predominantly leads to I and that the H_2CO necessary to produce ethylene ozonide arises from decomposition reactions rather than path B.

In summary, formation of fluorinated ozonides from C_2H_3F and $C_2H_2F_2$ can be rationalized by a Criegee mechanism; the existence of the HFCOO precursor is more clearly established as an intermediate from $C_2H_2F_2$ than from C_2H_3F. Also, it is not clear from this work what relevance these conclusions have towards rationalizing the more unusual products obtained[1] from ozonolysis of $C_2H_2F_2$.

The conformation of I was established by assignment of the MW spectrum of the normal isotopic species, $\mathrm{HF\overline{COOCH_2{}^{18}O}}$ and *cis*-$\mathrm{HF\overline{COOCHDO}}$.[10] The rotational constants can be readily correlated with the O_p–O_p twisted half-chair conformation reported for other ozonides but only if the fluorine occupies the axial site.[6d,7] Using structural parameters from ethylene ozonide (and d(C–F) = 1.33 Å), the rotational constants for the eq and ax isomers of the normal species were predicted to be respectively (in MHz): 8046, 3589, 2721 and 6610, 4030 and 3231. The observed constants[10] argue strongly for the axial conformer.

The rotational constants for the ^{18}O species are consistent with substitution at the ether site. The observed coordinates (Å) for this atom[12] are $a = 0.120$, $b = 1.162$, and $c = 0.211$. This is within 0.02–0.05 Å of values predicted with the assumed structural parameters noted above but differs by 0.25–0.80 Å for enrichment at the $O_p(CH_2)$ site. Similar good agreement between the model and data serves to identify the assigned deuterium species as the cis-D isomer. Several tentative transitions for the trans-D species have also been observed, but this assignment was not completed before sample