

version to fusidic acid then involves the loss of the 4β-methyl group, presumably *via* a 3-ketone analog (no tritium at C-3 in **5**). This contrasts with recent reports²⁴ that the demethylation of 4,4-dimethylcholestanol by a rat liver enzyme system and of cycloartanol by *Polypodium vulgare* Linn.²⁵ involves initial loss of the 4α-methyl group.

Acknowledgments. This work was supported by Grants No. AM12156, HE10566, and CA-K3-16614 from the National Institutes of Health. The authors are grateful to Dr. P. Diassi of the Squibb Institute for Medical Research, New Brunswick, N. J., and to Dr. W. O. Godtfredsen of Leo Pharmaceutical Products, Ballerup, Denmark, for specimens of *Fusidium coccineum* and for generous supplies of fusidic acid.

Chem. Commun., 530 (1969); G. P. Moss and S. A. Nikolaidis, *ibid.*, 1072 (1969).

(24) K. B. Sharpless, T. E. Snyder, T. A. Spencer, K. K. Maheshwari, J. A. Nelson, and R. B. Clayton, *J. Amer. Chem. Soc.*, **91**, 3394 (1969).

(25) E. L. Ghisalberti, N. J. de Souza, H. H. Rees, L. J. Goad, and T. W. Goodwin, *Chem. Commun.*, 1403 (1969).

E. Caspi, L. J. Mulheirn

The Worcester Foundation for Experimental Biology, Inc.
Shrewsbury, Massachusetts 01545

Received November 19, 1969

On the Probable Intermediacy of Tetrahedrane

Sir:

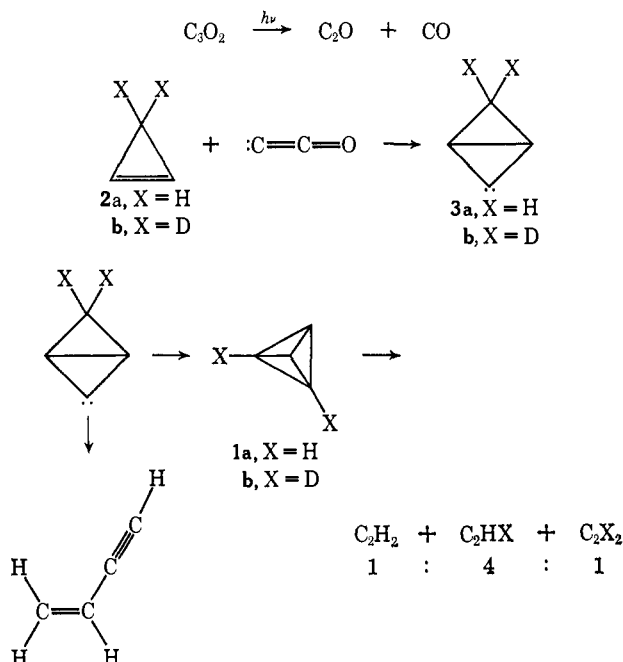
We wish to present evidence for the formation of tricyclo[1.1.0.0^{2,4}]butane (tetrahedrane, **1a**) as an intermediate in the gas-phase photolysis of carbon suboxide in the presence of cyclopropene. Attempts to prepare

tetrahedrane or its derivatives have thus far been unsuccessful.¹ However, recent mass spectral studies suggest structures of tetrahedral symmetry in the fragmentation of substituted cyclopentadienols.²

Carbon suboxide was generated by dehydration of malonic acid with phosphorus pentoxide and purified by gas chromatography. The cyclopropene, prepared from allyl chloride by the method of Closs and Krantz,³ was purified by gas chromatography on a dimethyl sulfolane column at -40° prior to use. A mixture of cyclopropene (2.18 × 10⁻² mmol) and carbon suboxide (4.72 × 10⁻² mmol) was placed in a 442-ml Pyrex photolysis flask. This mixture was photolyzed for 80 min at room temperature with a 200-W Hanovia medium-pressure lamp placed in a water-cooled immersion well in the center of the flask. The products condensable in liquid nitrogen were analyzed by gas chromatography.

Acetylene (24%)⁴ and vinylacetylene (33%) were the products. Vinylacetylene is an expected product, since the photolysis of carbon suboxide with 1,2-dimethylcyclopropene gives 2-methyl-1-penten-3-yne as the major product.^{1d}

The appreciable yield of acetylene suggests the presence of tetrahedrane (**1**) as an intermediate. Photolysis



of carbon suboxide produces ketocarbene (*cf.* ref 5 for a discussion of this intermediate) which may react with cyclopropene, to give an adduct leading to the bicyclic carbene intermediate **3**. This carbene may either rearrange to give vinylacetylene or it may undergo intramolecular carbon-hydrogen insertion to give tetrahedrane (**1**). In order to determine if the acetylene

(1) (a) M. P. Cava and M. J. Mitchell, "Cyclobutadiene and Related Compounds," Academic Press, New York, N. Y., 1967, p 69; (b) S. Masamune and M. Kato, *J. Amer. Chem. Soc.*, **87**, 4190 (1965); *cf.*, however, **88**, 610 (1966); (c) E. H. White, G. E. Maier, R. Graeve, U. Zirngibl, and E. W. Friend, *ibid.*, **88**, 611 (1966); (d) H. W. Chang, A. Lautzenheiser, and A. P. Wolf, *Tetrahedron Lett.*, 6295 (1966).

(2) M. M. Bursley and T. A. Elwood, *J. Amer. Chem. Soc.*, **91**, 3812 (1969).

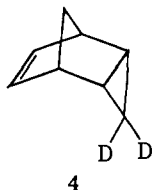
(3) G. L. Closs and K. D. Krantz, *J. Org. Chem.*, **31**, 638 (1966).

(4) All product yields are based on the amount of cyclopropene consumed.

(5) D. G. Williamson and K. D. Bayes, *J. Amer. Chem. Soc.*, **90**, 1957 (1968).

could arise from the decomposition of this tetrahedrane intermediate, the photolysis was carried out with a specifically labeled precursor (**1b**).

A test of the reaction scheme above requires the preparation of cyclopropene-3,3- d_2 . The synthesis was accomplished as follows. Allyl-3,3- d_2 alcohol⁶ was converted to allyl-3,3- d_2 chloride with thionyl chloride in tributylamine.⁷ The allyl-3,3- d_2 chloride was converted to cyclopropene-3,3- d_2 . The deuterium distribution in the cyclopropene was determined from the nmr spectra of the tricyclic hydrocarbon **4** resulting from addition of cyclopentadiene to **2b**.⁸ The nmr spectrum



of **4** showed that **2b** contains $87.1 \pm 3.2\%$ deuterium in the 3 position and that no deuterium was in the 1,2 positions. The expected ratio of acetylenes can be readily determined by adjusting the statistically expected ratio for the lack of unique deuterium substitution in the 3 position.

The specifically labeled cyclopropene was photolyzed in the presence of carbon suboxide (*vide supra*) and the product acetylenes were analyzed by mass spectrometry. In calibration runs it was found that a prepared mixture of C_2H_2 and C_2D_2 showed no hydrogen-deuterium exchange in the ions produced.

In the actual runs the ratio of acetylenes was calculated by correcting the mass 26 peak for a 21% contribution from C_2D (14% from C_2D_2 and 7% from C_2HD) and then taking the ratio 26:27:28. The accuracy of this method was confirmed by reduction of the acetylene mixture to the corresponding ethylenes and analyzing these ethylenes by gas chromatography (*vide infra*; cf. also ref 11).

Scrambling of the deuterium in the cyclopropene during photolysis was ruled out by adding recovered cyclopropene- d_2 to cyclopentadiene and analyzing the nmr spectrum of the adduct. It proved to be identical with that of **4**. The acetylene yields, which are the averages of three runs, are given in Table I. Table I

Table I. Acetylene Yields

	Observed av yield of acetylenes, %	Calculated yield of acetylenes, %
C_2H_2	23.7 ± 2.5	25.0
C_2HD	63.6 ± 1.2	62.4
C_2D_2	12.8 ± 1.4	12.6

also gives the calculated yields of the three acetylenes expected from the decomposition of a symmetrical tetrahedrane containing 43.55% deuterium. Thus, it appears that tetrahedrane is an intermediate in this reaction.

(6) K. D. McMichael, *ibid.*, **89**, 2943 (1967).

(7) S. H. Sharman, F. F. Caserio, R. F. Nystrom, J. C. Leak, and W. G. Young, *ibid.*, **80**, 5970 (1958).

(8) K. B. Wiberg and W. J. Bailey, *ibid.*, **82**, 6375 (1960).

To further substantiate the intermediacy of tetrahedrane, carbon-2- ^{14}C suboxide⁹ was photolyzed with cyclopropene-3,3- d_2 in a double label experiment. Carbon-2- ^{14}C suboxide of activity $89.5 \mu\text{Ci}/\text{mmol}$ produces acetylene of activity $44.8 \mu\text{Ci}/\text{mmol}$. The distribution of radioactivity among the product deuterated acetylenes was determined by converting the acetylenes to the deuterated ethylenes by reduction with chromous chloride and partially separating these ethylenes by gas chromatography.¹⁰ The distribution of activity among the three acetylenes is given in Table II; this table also contains the calculated activity distribution assuming a tetrahedrane intermediate. It can be seen that the experimental values correspond quite well to the calculated ones.

Table II. Activity Distribution in Acetylenes

	Observed % of total activity	Calculated % of total activity
C_2H_2	13.8 ± 5	12.9
C_2HD	59.4 ± 5	61.8
C_2D_2	26.8 ± 5	25.3

A set of competing mechanisms involving the formation of both 1,2- and 1,3-dideuteriocyclobutadiene as intermediates occurring independently can be postulated to explain the results. Such a sequence of events is unlikely for several reasons. Such a concurrence of mechanisms requires C-D insertion by C_2O to predominate over addition to the double bond. In addition, insertion into the "vinyl" C-H bond must also be taken into account. However, carbon-hydrogen insertion by C_2O at these wavelengths is a minor reaction if it occurs at all (*cf.* ref 5 and other references cited therein). At these wavelengths addition of C_2O to the double bond is the predominant reaction. A further argument which militates against cyclobutadiene as an intermediate is that the postulated decomposition of this intermediate to two molecules of acetylene has not been shown to occur in any of the reactions of cyclobutadiene (*cf.* ref 1a, p 69). Thus the experimental results cannot support a postulated cyclobutadiene intermediate.¹²

The data presented rule out all plausible mechanisms for the formation of acetylene other than *via* tetrahedrane. These results indicate that tetrahedrane has a finite lifetime at room temperature. Recent calculations¹³ report that tetrahedrane is unstable with respect to decomposition to two acetylene molecules by 70 to 100 kcal/mol. We are presently trying to isolate the elusive tetrahedrane molecule by low-temperature photolysis.

(9) R. T. Mullen and A. P. Wolf, *ibid.*, **84**, 3214 (1962).

(10) The gas chromatographic separation follows a recycling technique developed by Ache and Wolf.¹¹ Two 50-ft columns containing 7.3% saturated $AgNO_3$ -ethylene glycol on Firebrick were used.

(11) H. J. Ache and A. P. Wolf, *Z. Anal. Chem.*, **230**, 19 (1967).

(12) The cyclobutadiene intermediate was considered and rejected by the authors. It was felt necessary to include the reasons for rejecting this composite mechanism since it was raised as a possibility by one of the referees. Of the mechanisms considered, only an intermediate tetrahedrane was consistent with both the experimental data and the known chemistry of the reactants.

(13) R. J. Bunker and S. D. Peyerimhoff, *J. Amer. Chem. Soc.*, **91**, 4342 (1969).

Acknowledgment. We wish to thank Dr. David R. Christman for help in performing the mass spectral analysis and Miss Laura T. Ramer for assistance in the synthetic portion of the problem.

(14) Research performed under the auspices of the U. S. Atomic Energy Commission.

Philip B. Shevlin, Alfred P. Wolf
Chemistry Department, Brookhaven National Laboratory¹⁴
Upton, New York 11973
Received December 3, 1969

Labeling with Iodine-123. The Reactivity of Iodine-123 Formed by the Decay of Xenon-123¹

Sir:

Sodd, *et al.*,^{2,3} have recently described a "generator" system where 14-hr half-life iodine-123 is prepared as carrier-free iodide ion by the decay of 2-hr half-life xenon-123. The xenon-123 decay occurs in part by electron capture and in part by positron emission.⁴ The recoil energy imparted to the iodine may be sufficient for the iodine species formed to react with surrounding molecules. This study was carried out to investigate the reactivity of this generator-produced iodine and to compare this reactivity with that of the iodine species produced directly by nuclear recoil (*i.e.*, ¹²⁸I formed by the ¹²⁷I(n,γ)¹²⁸I reaction) and β⁻-produced iodine formed in uranium fission.

Natural tellurium was bombarded by the 25-MeV helium-3 beam of the Washington University 54-in. cyclotron and the xenon-123, formed by the ¹²²Te(³He, 2n)¹²³Xe reaction, was swept out of the bombardment chamber in a stream of helium gas and collected in a radiator trap cooled to liquid nitrogen temperature. The xenon was then transferred into various reaction vessels with the trap cooled to -80° to prevent distillation of iodine-123 already formed. No carrier xenon was added and each reaction vessel contained <10⁸ atoms of xenon.

In this study the xenon was mixed with gaseous methane, benzene frozen at 77°K, and serum albumin at 77°K. Two of these compounds were chosen to compare the iodine reactivity with the activity of recoil iodine produced directly by a nuclear reaction⁵⁻⁷ while the third compound (serum albumin) was chosen to investigate whether the active iodine would label a compound of biological interest.⁸

In the studies with methane the two gases were mixed in a 100-cc vessel at 760 mm pressure and the xenon was allowed to decay for 6-12 hr. A mixture of methyl iodide and dilute sodium thiosulfate was then added, the vessel shaken, and the mixture removed; the organic and aqueous layers were separated. It was found that 80 ± 9% (average of three experiments) of the activity⁹

remained in the organic phase. The integrity of the label was verified by forming pyridinium methiodide, where all the activity was found in the recrystallized salt. In nuclear recoil studies⁶ iodine vapor was mixed with the methane to produce the radioiodine and also to scavenge thermal iodine atoms. When ≈0.1 mm of iodine vapor was added to the xenon-methane mixture the organic yield dropped to 48 ± 5%.

In the studies performed with benzene and benzene were frozen together at 77°K and kept at this temperature for 6-12 hr before the aqueous and organic fractions were separated. In this case 54 ± 5% (average of three experiments) of the activity was organically bound.

A 0.1-g sample of recrystallized serum albumin was placed in an ampoule, the bottom of which was immersed in liquid nitrogen, and the xenon was frozen into the ampoule. The whole ampoule was then immersed in liquid nitrogen for 6-12 hr. After warming the ampoule, the albumin was dissolved in saline solution and the protein precipitated with trichloroacetic acid; it was found that 80 ± 10% of the iodine-123 activity was precipitated with the protein, and was therefore organically bound.

It appears from these studies that the iodine-123 species formed by the decay of xenon-123 are active and, with methane and benzene, have a reactivity similar to that of iodine atoms produced by nuclear recoil. The organic yield observed in the reaction with methane is much higher than that observed in the recoil case⁶ (54%); however, when the recoil studies were duplicated by adding small amounts of iodine scavenger to the reaction vessels the yield dropped. As all single displacement or abstraction reactions of thermal iodine atoms or ions with methane are endothermic,⁶ this drop in organic yield upon addition of iodine cannot be explained by the iodine scavenging thermal iodine atoms. The drop in yield can only be explained if the scavenger is competing for an excited species.

In the solid state, where scavengers will have less effect due to trapping of the active species in the matrix, the organic yield observed with benzene (54%) is very similar to that observed in the nuclear recoil case (59%).⁷ The similarity between the reactivity of the generator-produced species and iodine formed by nuclear recoil is in contrast to the reactivity of β⁻-produced iodine, where the reactivity was 0.5-0.75 that of iodine formed directly by nuclear recoil.^{10,11} This difference can be explained by the fact that the kinetic energy spectrum of species formed by β⁻ decay contains a larger fraction with low kinetic energy than does the spectrum from β⁺ decay. It is therefore to be expected that the generator-produced iodine, with a maximum kinetic energy ≈15 eV and with fewer low energy species, will resemble iodine produced by nuclear recoil more than will iodine produced by β⁻ decay.

The iodine-123 formed by the decay of xenon-123 is an active species which can be formed with a much lower radiation dose to the sample than can iodine formed

attached to a 400-channel analyzer. The ¹²³I activity was determined by measuring the area under the γ peak at 159 keV. This method was used to distinguish the ¹²³I activity from any ¹²⁵Xe, ¹²⁴I, and ¹²⁵I formed. If enriched ¹²²Te had been used as the target these impurities would be minimal (ref 2 and 3).

(10) H. O. Denschlag, N. Henzel, and G. Herrmann, *Radiochim. Acta*, **1**, 172 (1963).

(11) Y. Paiss and S. Amiel, *J. Amer. Chem. Soc.*, **86**, 233 (1964).

(1) This work was supported by Public Health Service Grant No. GM14889-06.

(2) V. J. Sodd and J. Blue, *J. Nucl. Med.*, **9**, 349 (1968).

(3) V. J. Sodd, J. W. Blue, and K. L. Scholz, *ibid.*, **10**, 371 (1969).

(4) C. M. Lederer, J. M. Hollander, and I. Perlman, "Table of Isotopes," John Wiley and Sons, Inc., New York, N. Y., 1968, p 71.

(5) G. Levey and J. E. Willard, *J. Chem. Phys.*, **25**, 904 (1956).

(6) E. P. Rack and A. A. Gordus, *ibid.*, **34**, 1855 (1961).

(7) R. L. Ayres, E. J. Lemnitz, R. M. Lambrecht, and E. P. Rack, *Radiochim. Acta*, **11**, 1 (1969).

(8) It has been suggested (R. L. Myers, AEC publication CONF-651111, April 1966, p 217) that for use as a biomedical tracer iodine-123 has the most desirable decay characteristics of all iodine isotopes.

(9) The samples were counted in a well-type scintillation counter