communication[19] and three typical reactions are described in the following section.

Table II also includes two terminal alkynes, phenylacetylene and 1-hexyne, which were known from previous work[8] to undergo conversion to the corresponding carboxylic acid with the loss of one carbon atom. A possible pathway for these reactions that is consistent with the other work reported here would involve the formation of dicarbonyl intermediates:

$$RC{\equiv}CH \xrightarrow{MnO_4^-} RC(O)C(O)H \xrightarrow{MnO_4^-} RC(O)COOH \xrightarrow{MnO_4^-} RCOOH + CO_2$$

Experimental Section

The Oxidation of 4-Octyne by Aqueous Permanganate. 4-Octyne (0.009 mol) was added to a 1% aqueous solution of $KMnO_4$ (250 mL) in a 500-mL flask. The mixture was stirred vigorously for 17 h and then acidified (50% H_2SO_4). The precipitated manganese dioxide was reduced by addition, in small portions, of the required amount of sodium bisulfite. The solution was saturated with sodium chloride and extracted with 3 × 50 mL of ether. The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated by rotary evaporation. Analysis of the resulting liquid residue by GLC indicated the presence of three compounds in addition to solvent–butyric acid, propionic acid, and 4-octyne. The calculated yields were 73, 6, and 6%, respectively.

The Phase Transfer Assisted Oxidation of 8-Hexadecyne in Dry Methylene Chloride. A 500-mL Erlenmeyer flask, equipped with a reflux condenser, was charged with methylene chloride (100 mL), acetic acid (5 mL), and 8-hexadecyne (2.0 g, 0.009 mol). The solution was heated to reflux temperature before 1.5 g of phase transfer agent (Adogen 464) and powdered potassium permanganate[7] (8.5 g, 0.054 mol) were added. The solution was stirred magnetically and refluxed for 4 h. After cooling, sodium bisulfite (5 g in 100 mL of water) was added to reduce any excess oxidant. After 15 min, the solution was acidified (50% H_2SO_4), and the precipitated manganese dioxide was reduced by addition, in small portions, of the required amount of sodium bisulfite. The aqueous layer was separated, saturated with sodium chloride, and extracted with 3 × 75 mL of methylene chloride. The combined organic extracts were washed with 2 × 50 mL of 10% aqueous NaOH solution, dried over anhydrous $MgSO_4$, and concentrated by rotary evaporation to give a yellow liquid which solidifed on cooling. Recrystallization of this solid from 15 mL of methanol gave 8,9-hexadecanedione (1.82 g, 0.007 mol, 80%), mp 51–52 °C (lit.[20] mp 49–50 °C).

The aqueous solutions were combined, acidified (50% H_2SO_4), and extracted with 3 × 75 mL of ether. The ether solution was dried over anhydrous $MgSO_4$ and concentrated by rotary evaporation, and on analysis (GLC) it was found to contain octanoic acid (5% yield) and a trace of heptanoic acid.

The Phase Transfer Assisted Oxidation of 7-Tetradecyne in "Wet" Methylene Chloride. A 500-mL Erlenmeyer flask was charged with $KMnO_4$ (8.2 g, 0.052 mol in 140 mL of water) and a solution consisting of 7-tetradecyne (5.0 g, 0.026 mol), acetic acid (35 mL), methylene chloride (100 mL), and Adogen 464 (1.8 g). The solution was stirred magnetically and refluxed for 5 h. The workup was performed as described above, and the resulting yellow liquid (obtained by evaporation of the organic solvents) was distilled under vacuum to give unreacted alkyne (10%) and a yellow liquid (bp 108–110 °C (5.5 torr)) which solidified on cooling. The yellow solid was recrystallized from methanol (15 mL) to give 7,8-tetradecanedione (3.2 g, 0.014 mol, 58%), mp 38–39 °C. The aqueous solutions were found to contain heptanoic and hexanoic acids in yields of 25 and 17%, respectively.

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Registry No. 8-Hexadecyne, 19781-86-3; 7-tetradecyne, 35216-11-6; 1-phenyl-1-pentyne, 4250-81-1; 5-decyne, 1942-46-7; 4-octyne, 1942-45-6; benzoic acid, 65-85-0; 1-phenyl-1,2-pentanedione, 20895-66-3; valeric acid, 109-52-4; 5,6-decanedione, 5579-73-7; butyric acid, 107-92-6; propionic acid, 79-09-4; 4,5-octanedione, 5455-24-3; phenylacetylene, 536-74-3; 1-hexyne, 693-02-7; diphenylacetylene, 501-65-5; 1-phenyl-1-hexyne, 1129-65-3; benzil, 134-81-6; 1-phenyl-1,2-hexanedione, 33720-29-5; 7,8-tetradecanedione, 6305-47-1; heptanoic acid, 111-14-8; hexanoic acid, 142-62-1; 8,9-hexadecanedione, 18229-29-3; octanoic acid, 124-07-2; $KMnO_4$, 7722-64-7.

(19) Lee, D. G.; Chang, V. S. *Synthesis* **1978**, 462.

(20) Burkin, A. R.; Preston, J. S. *J. Inorg. Nucl. Chem.* **1975**, *37*, 2187.

Comment on the Spectrum of Matrix-Isolated Thiirene and Characterization of New Matrix-Isolated Species

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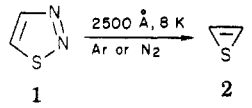
An analysis of the infrared bands of thiirene (**2**), generated from 1,2,3-thiadiazole (**1**), is offered in light of the comments of Torres et al. Some discrepancies and misinterpretations by Torres, as well as criteria for the characterization of matrix-isolated species by infrared spectroscopy, are discussed.

Torres et al.[1] recently described the photolysis of matrix-isolated 1,2,3-thiadiazole (**1**), confirming our report of



1 **2**

thiirene (**2**),[2] which can be detected by infrared spectroscopy when **1** is photolyzed through narrow-bandpass filters. We observed the following bands[2] for argon matrix-isolated thiirene: 3207, 3169, 3166, 1663, 912, and 563 cm^{-1} (Figure 1). Torres and co-workers have repeated the photolysis of **1** (they did not investigate isotopically labeled thiadiazoles) and list the following bands for **2**: 3208, 3170,

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(2) A. Krantz and J. Laureni, *J. Am. Chem. Soc.*, **99**, 4842 (1977).

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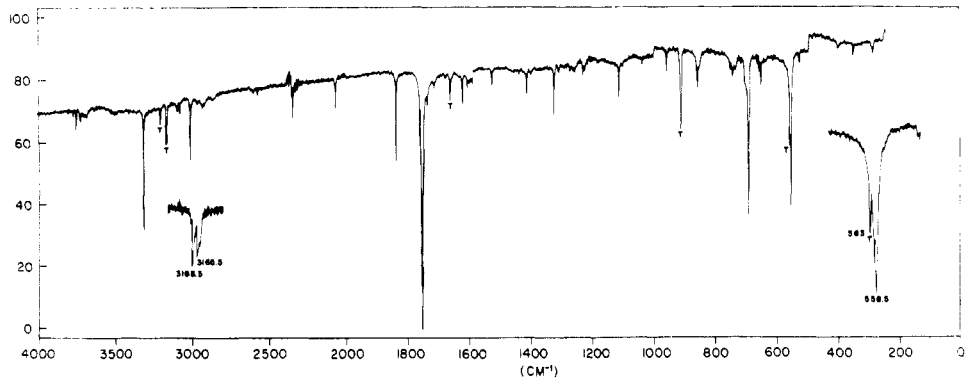

Figure 1. Infrared spectrum of argon matrix-isolated 1,2,3-thiadiazole (M/R 500, 44 mm) after irradiation for 40 min with a 100-W mercury–xenon lamp fitted with a 2500-Å interference filter. Oberve bands assigned to thiirene at 3205, 3169, 3166, 1663, 912, and 563 cm^{-1} indicated by the letter T. Note left inset of expansion of abscissa (10 times), which clearly shows resolution of bands at 3169 and 3166 cm^{-1}, and right inset showing bands at 563 and 558 cm^{-1} more clearly resolved.

1660, 912, 660, 563, and 425 cm^{-1}. Their report differs from ours in that we include a band at 3166 cm^{-1} and that they attribute additional bands at 660 and 425 cm^{-1} to **2**.

Despite the fact that the Canadian workers employed essentially the same conditions to irradiate **1**, they state "that the appearance of three absorptions in the C–H stretching region around 3000 cm^{-1} is inconsistent with the thiirene structure" and claim that "probably the low intensity of the spectrum attributed to thiirene, and its contamination with the intense spectra of thioketene (**3**), ethynylthiol (**4**), and possibly of unphotolyzed **1** made the analysis of the thiirene spectrum difficult and somewhat uncertain". These statements are misleading. Although theory predicts only *two fundamentals* corresponding to asymmetric and symmetric C–H stretches, the actual appearance of the spectrum can be significantly more complicated, because of the interaction between modes and owing to the interactions between the molecule and the local (matrix) environment.[3] (For example, cyclopropene has a more complicated spectrum than would be expected merely from absorption of fundamental modes.[4]) In fact, the spectrum published by Torres et al. also shows the two bands that we reported at 3166 and 3169 cm^{-1} but this "splitting" was totally ignored by these authors.

Although we do not claim to have observed the entire spectrum of thiirene **2** (symmetry modes of the thiirene molecule are indicated in Figure 2), we are confident in our assignments to thiirene. One major reason for assigning the above bands to **2** is because they all have the same kinetic dependence with respect to growth and destruction. We have been unable to collapse the bands at 3169 and 3166 cm^{-1} to a single absorption by annealing the argon matrix at higher temperatures. However, in a nitrogen matrix only one band is observed in this region for **2** at 3161 cm^{-1}. It is possible that the splitting of the band of the argon-matrix-isolated species is a consequence of the perturbing influence of the nitrogen molecule (in two distinct orientations relative to **2**) on the C–H symmetric stretch. Alternatively, intimate and host-separated pairs may be formed between the products upon photofragmentation of **1** and give rise to distinct absorptions.[5] In any event, as a general policy all bands that are resolved should be reported for a new species because the data may provide clues to its immediate environment.

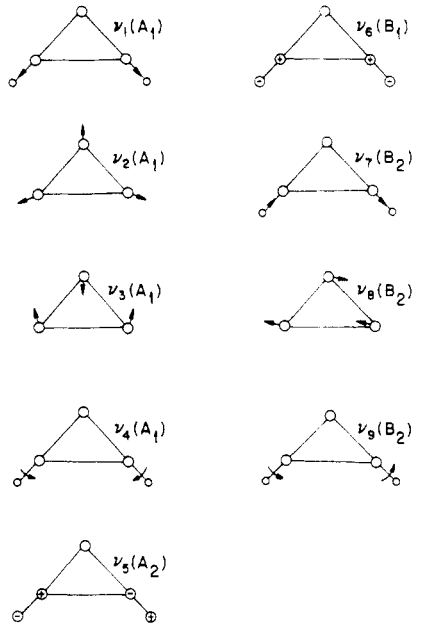

Figure 2. Symmetry modes of (C_{2v}) thiirene. In some cases, the compensating motions of hydrogens (or the carbon framework) are not shown for purposes of clarity.

Regarding the new bands reported by the Albertans it is difficult to measure the growth of the band at 660 cm^{-1} because it grows on top of two bands belonging to other molecules. Furthermore, difficulties arising from external carbon dioxide which often contaminates spectra of matrix-isolated species at cryogenic temperatures have to be considered. (The Albertans do not display the region around 2340 cm^{-1} where the C=O stretch of carbon dioxide absorbs, so it is difficult to determine if this is a factor in their case.) Although a band is present at 660 cm^{-1} during the photolysis, it is difficult to unambiguously determine if this absorption is kinetically competent to be assigned to thiirene because of the complicated pattern in this region.

However, the very intense band at 425 cm^{-1} reported by Torres et al. is definitely not present in our spectrum of photolyzed **1** (Figure 1). Presently we believe the assignment of the bands of **2** to fundamental modes of the molecule best be considered tentative until the entire spectrum can be observed for the parent (**2**) and its isotopically labeled derivatives. Only absorption corresponding to five modes is accounted for. Detectable absorption from **2** is found in regions typical of C–H

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stretching modes [3207 cm^{-1}, asymmetric stretch (ν_7); 3169 cm^{-1}, symmetric stretch (ν_1)], C=C stretching (1663 cm^{-1}), and of a C–H bending mode [563 cm^{-1} (ν_4 or ν_6)]. The most intense band at 912 cm^{-1} ostensibly shifts very little on deuterium substitution and is unlikely to be due to a C–H deformation mode but is perhaps an S-wagging mode, ν_8.

We also feel moved to comment on criteria of proof of structure for new matrix-isolated species. In many instances only infrared spectral evidence is available because of the difficulty of applying multiple spectroscopic probes and obtaining definitive chemical evidence for the species in situ. Proof of structure must at least be based on isotopic labeling experiments which establish the symmetry and molecular formula of the species.

That isothiazole and 1 are independent precursors to a common species X which is photoisomerized to **3** and **4** means that X must have the formula C_2H_2S. The fact that [4- and 5-^{13}C]-1,2,3-thiadiazoles are independent precursors to a single species ^{13}C–X, which is converted to ethynyl mercaptan and thioketene, both with randomized label, establishes the symmetry of X as C_{2v}. The effect of deuterium and methyl groups on the "double bond stretch" of X (–50 cm^{-1} per D, +125 cm^{-1} per methyl) is positive evidence for the cyclopropenoid nature of X. Such evidence raises the argument above a claim; it is proof of structure.

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Registry No. 1, 288-48-2; 2, 157-20-0.

Direct Synthesis of α-Halogenomethyl-α-amino Acids from the Parent α-Amino Acids

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A general approach to the preparation of α-halogenomethyl-α-amino acids **2**, **15**, and **16** which are potential enzyme-activated irreversible inhibitors of the parent α-amino acid decarboxylases is described. The key step in the synthesis is the regioselective alkylation of a Schiff base ester **6**, readily available from the parent α-amino acid, with poly(halomethanes) such as bromochloromethane, chlorofluoromethane, and chlorodifluoromethane to give the corresponding α-halogenomethylated adducts **8**, **9**, and **10**, respectively. Subsequent removal of the protecting groups from these adducts upon acidic treatment yields the corresponding α-halogenomethyl-α-amino acids **2**, **15**, and **16**. The mechanism of the key alkylation reaction appears to depend on the degree and the nature of the substitution of the halomethanes; it is suggested that bromochloromethane and chlorofluoromethane react via an S_N2 type mechanism, whereas chlorodifluoromethane reacts by a chain process involving the intermediacy of difluorocarbene.

We recently reported that α-halogenomethyl analogues of ornithine and 3,4-dihydroxyphenylalanine (DOPA) are potent and specific irreversible inhibitors[1,2] of pyridoxal phosphate-dependent ornithine decarboxylase (E.C. 4.1.1.17) and aromatic L-α-amino acid decarboxylase (E.C. 4.1.1.26), respectively. Kinetic studies indicated that these inactivators most probably belong to a novel class of inhibitors recognized by Bloch[3] 10 years ago which demand activation by the "target" enzyme. They are now referred to as k_{cat} inhibitors,[4] suicide enzyme inactivators,[5] or enzyme-activated irreversible inhibitors.[6] The mechanism of inhibition which we proposed[1,2] (depicted in Figure 1) has recently been demonstrated by Kollonitsch and coworkers for the inactivation of aromatic L-α-amino acid decarboxylase by (*S*)-α-monofluoromethyl-3,4-dihydroxyphenylalanine.[7] The high selectivity of these inhibitors results from the fact that they can act only on those enzymes which accept them as substrates. As all pyridoxal phosphate-dependent decarboxylases operate by a similar mechanism, it could be anticipated as already commented on by Kollonitsch and co-workers[7] that the specificity of α-halogenomethyl-α-amino acids as potential decarboxylase inhibitors will be determined essentially by the chain residue R. We detail now the synthesis of α-halogenomethyl analogues **2b,c,e–i**, **15b–g,i,k,l** and **16b,e** of the α-amino acids **5b,c,e–i,k,l** whose decarboxylases are known to have essential metabolic functions in mammals, bacteria, and/or plants.

These highly functionalized α-amino acid analogues constitute a class of compounds which thus far has seen very few representatives. The difficulty associated with the preparation of these molecules lies in the presence of halogen atom(s) on a carbon atom vicinal to a quaternary center bearing an amine and a carboxylic acid functionality. The classical Bucherer–Lieb or Strecker synthesis of α-amino acids does not appear as an attractive approach to this problem. These routes imply that the preparation of the key starting halogenomethyl ketones has to be tailored to each specific side chain of the α-amino acids and also to each specific halogenomethyl group. Furthermore, the formation of the intermediate hydantoins or α-aminonitriles has been reported to be troublesome with halogenomethyl ketones[8] in many instances. Moreover, the hydrolysis of these intermediates to the

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(5) R. H. Abeles and A. L. Maycock, *Acc. Chem. Res.*, **9**, 313 (1976).
(6) Reference 2b, pp 123, 221.
(7) J. Kollonitsch, A. A. Patchett, S. Maburg, A. L. Maycock, L. M. Perkins, G. A. Dolduras, D. E. Duggan, and S. D. Aster, *Nature (London)*, **274**, 906 (1978).
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