protons in A·U and G·C hydrogen-bonded systems.

Comparison of GpCpA with UpGpCpA is significant. The chemical shift vs. temperature data for the aromatic and ribose H-1′ protons of UpGpCpA at 8.2 mM are contained in Table II, and its average T_m was 33 °C. Remarkably the GpCpA duplex which contains only two Watson–Crick base pairs and two dangling adenosine residues is equal in stability to the UpGpCpA duplex which contains four Watson–Crick base pairs. We consider that a combination of factors, base-stacking, hydrophobic interactions, solvation and entropic effects, as well as Watson–Crick hydrogen bonding, contribute to duplex stability.

Stability of the GpCpApA duplex was also studied and its T_m found to be 34 °C at 7.3 mM (Table IV). Behavior was similar to that for GpCpA, and its was noteworthy that the effects of 3′-terminal dangling adenosines were cooperative. However, the residue immediately adjacent to the base-paired region appears to make a major contribution to duplex stability.

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Synthesis of a Thiacyclopentyne

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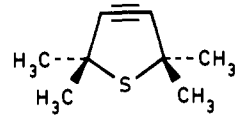
As a step in a program of generating and studying sulfur-containing reactive intermediates,[1,2] we undertook the synthesis of **1**. This was a reasonable objective since good evidence for



1

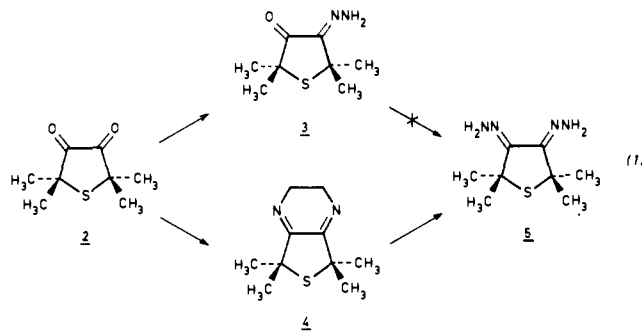
the existence of cyclopentyne as a short-lived intermediate is available.[3-5] Strained cycloalkynes and arenes remain matters of fundamental, theoretical, and synthetic interest to organic chemistry.[6] It seems likely that the ring strain in **1** will be less than in cyclopentyne owing to the longer carbon–sulfur bonds. The methyl groups should sterically shield the reactive triple bond much as in stable 3,3,6,6-tetramethyl-1-thiacycloheptyne[7] or 3,3,7,7-tetramethylcycloheptyne.[8] We also thought it possible that the carbon–sulfur–carbon σ bond segment could stabilize the heavily distorted in-plane π system wherein much of the strain is located.[9] On the negative side, the possibility is present that **1**, if generated, would immediately eliminate the sulfur bridge.

Table I. Yields of Products Obtained from Oxidation of Dihydrazone under Various Conditions

	yield, %[a]				
experiment	7	8	9	10	11
A[b]	28.4	15.3	9.4		
B[c]	7.4	7.8	4.1	6.9	
C[d]	10.8	6.3	3.6		12.6
D[e]			48.5		4.1
E[f]			54		

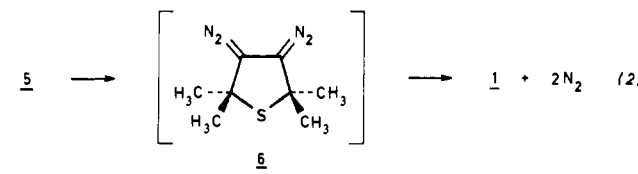
[a] Yields determined by ^{1}H NMR using $CH_3SO_2CH_3$ as internal standard; the balance of the materials consisted of intractable tar. [b] Oxidation with $Pb(O_2CCH_3)_4$ in CH_2Cl_2 under N_2 at 0 °C. [c] Oxidation with $Pb(O_2CCH_3)_4$ at 0 °C under N_2 in pure redistilled $C_6H_5N_3$. [d] Oxidation with $Pb(O_2CCH_3)_4$ at 20 °C under N_2 in pure redistilled 2,5-dimethylfuran. [e] Oxidation with MnO_2 at 20 °C under N_2 in pure redistilled 2,5-dimethylfuran. [f] Oxidation with MnO_2-$2H_2O$ in CH_2Cl_2 under N_2 at 20 °C.

The route followed to **1** is classical. Diketone **2**, the synthesis of which has been reported,[10] was converted to the dihydrazone **5** (eq 1). Direct treatment of **2** with H_2NNH_2,H_2O, $H_2NNH_3^+,HSO_4^-$ gave monohydrazone **3**, which was not stable to the required forcing conditions[11] and decomposed rather than providing **5**. An indirect route adapted from an earlier work of van Alpen[12] involving formation of dihydropyrazine **4**[13] and subsequent conversion (H_2NNH_2,H_2O, $H_2NNH_3^+,HSO_4^-$, ethylene glycol, 120 °C, 4 h) was successful and gave **5** in 65% overall yield.



(1)

The dihydrazone **5** was subjected to oxidation. Bis(diazo) compound **6** is assumed to be formed and this should be a precursor of **1** (eq 2).[2-5] Depending on the reaction conditions and additives used, the products **7**–**11** were obtained. All these



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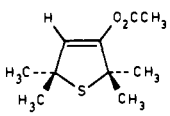
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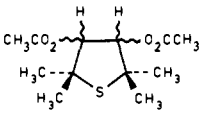
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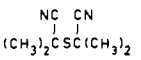
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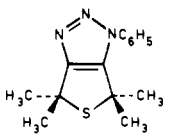
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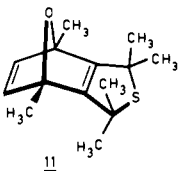
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products were completely characterized by spectral and analytical techniques.[14] The product distributions from various experiments are given in Table I.

The enol acetate **7** can be formed by trapping of **1** by acetic acid present in the reaction medium; there is precedent for such trapping.[11] The diacetate **8** (cis, trans mixture), probably formed by reaction of acetic acid with diazo functionalities, is stable under the reaction and workup conditions and does not provide **7**. Addition of dry pyridine to the reaction mixture of experiment A (Table I) led to decreased yields of **7** and the formation of an extremely unstable product that may be an addition product of **1** and pyridine, although its structure could not be established.

Even stronger evidence for the existence of **1** is the isolation of cycloadduct **10** (experiment B, Table I) and cycloadduct **11** (experiment C, Table I). The latter cycloadduct is surprisingly stable to acid, probably because of steric protection of the oxanorbornadiene by the methyl groups. The adduct **11** is also isolated on using MnO_2 as the oxidant (Experiment D). The isolation of two different cycloadducts under differing reaction conditions as well as the acetic acid addition product **7** are experimental observations that are difficult to explain except in terms of a free transient species **1**.

The efficiency of formation of **1** depends greatly on the reaction conditions. For example, in experiments D and E wherein MnO_2 is used as oxidant, the competing pathway of cleavage of **5** perhaps through bis(diazo) compound **6** to dinitrile **9** accounts for all or nearly all the isolated product. This mode of fragmentation also competes, but less well, in other experiments.

Acetylene **1** has, to the best of our knowledge, the smallest ring of any heteroatom-containing cyclic acetylene yet reported[15] (there is evidence for the five-membered heteroaryne, 2,3-thiophyne,[3d,f] but not for 3,4-thiophyne[16]). The ease of generation of **1** suggests that with optimalization of the synthetic approach that it should be quite readily available. The relative stability of **1** is also greatly encouraging, especially the fact that there is no noticeable tendency to eliminate the sulfur bridge to form 1,1,4,4-tetramethyl-1,2,3-butatriene. The synthesis of other five-membered acetylenes structurally related to **1** should be possible.

(14) Spectral and analytical data for **7–11**. **7**: ^{1}H NMR ($CDCl_3$) δ 1.48 (s, 6, $2CH_3$), 1.51 (s, 6, $2CH_3$), 2.18 (s, 3, CH_3), 5.63 (s, 1, vinyl H); ^{13}C NMR ($CDCl_3$) δ 21.0 (q, J_{C-H} = 132 Hz, CH_3), 30.6 (q, J_{C-H} = 128 Hz, CH_3), 33.4 (q, J_{C-H} = 128 Hz, CH_3), 51.3 (s, quaternary C), 56.0 (s, quaternary C), 121.3 (d, J_{C-H} = 168 Hz, vinyl C), 149.8 (s, vinyl C), 168.0 (s, C=O); IR (neat) 1775 (C=O) and 1670 cm^{-1} (C=C); exact mass, calcd. *m/e* for $C_{10}H_{16}O_2S$ 200.088; found *m/e* 200.087. **8** (isolated as cis–trans mixture), **8** (cis): ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 6, $2CH_3$), 1.50 (s, 6, $2CH_3$), 2.08 (s, 6, $2CH_3CO$), 5.29 (s, 2, tertiary H). **8** (trans): ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 12, $4CH_3$), 2.08 (s, 6, $2CH_3CO$), 5.35 (s, 2, tertiary H); IR (cis–trans mixture, neat) 1750 cm^{-1}; exact mass (cis–trans mixture), calcd. *m/e* for $C_{12}H_{20}O_4S$ 260.108; found *m/e* 260.108. **9**: ^{1}H NMR ($CDCl_3$) δ 1.82 (s, CH_3); ^{13}C NMR ($CDCl_3$) δ 28.2 (q, J_{C-H} = 130 Hz, CH_3), 37.2 (s, quaternary C), 122.4 (s, C≡N); IR (neat) 2230 cm^{-1} (C≡N); exact mass, calcd *m/e* for $C_8H_{12}N_2S$ 168.072; found *m/e* 168.074. **10**: ^{1}H NMR ($CDCl_3$) δ 1.62 (s, 6, $2CH_3$), 1.87 (s, 6, $2CH_3$), 7.55 (br s, 5, aromatic); ^{13}C NMR ($CDCl_3$) δ 31.8 (q, J_{C-H} = 128 Hz, CH_3), 32.1 (q, J_{C-H} = 128 Hz, CH_3), 47.3 (s, quaternary C), 48.1 (s, quaternary C), 125.8 (d, J_{C-H} = 162 Hz, aromatic C), 129.1 (d, J_{C-H} = 162 Hz, aromatic C), 129.9 (d, J_{C-H} = 162 Hz, aromatic C), 136.2 (s, quaternary aromatic C), 144.0 (s, vinyl C, 158.4 (s, vinyl C); IR (KBr) 1043 and 1008 cm^{-1} (triazole); exact mass, calcd. *m/e* for $C_{14}H_{17}N_3S$ 259.114; found *m/e* 259.112. **11**: ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 6, $2CH_3$), 1.63 (s, 6, $2CH_3$), 1.66 (s, 6, $2CH_3$), 6.97 (s, 2, vinyl H); ^{13}C NMR ($CDCl_3$) δ 15.7 (q, J_{C-H} = 128 Hz, CH_3), 27.7 (q, J_{C-H} = 128 Hz, CH_3), 30.7 (q, J_{C-H} = 132 Hz, CH_3), 54.2 (s, quaternary C), 89.5 (s, quaternary C), 147.3 (d, J_{C-H} = 175 Hz, vinyl C), 163.9 (s, vinyl C); IR (KBr) 1310, 1285, 1220, 1150, 1134, 877, 861, and 731 cm^{-1} (not specifically assigned); exact mass, calcd. *m/e* for $C_{14}H_{20}OS$ 236.123; found *m/e* 236.125.

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One-Electron Electrochemical Reduction of a Ferrous Porphyrin Dioxygen Complex

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Despite the fact that cytochromes P-450 have been known for less than two decades,[1] considerable information concerning their modes of action as monoxygenases is known.[2] In the case of P-450$_{cam}$ the resting enzyme is a low-spin ferric hemoprotein[3] which upon binding of substrate changes to high spin in order to facilitate the first of two one-electron reductions. The first one-electron reduction generates a low-spin ferrous complex which reversibly can bind both dioxygen and carbon monoxide. The unusual optical spectrum of the CO complex allowed us,[4] and others,[5] to show that the sixth axial ligand is a thiolate anion. Moreover, it is now known that the binding of dioxygen to the ferrous heme, which is the next step in the enzymatic cycle, leaves the thiolate coordinated as the sixth axial ligand.[6,7] To this stage in the enzymatic cycle the rates and nature of the axial ligation and electronic configurations around the heme are reasonably well understood. The next step is the second one-electron reduction of the O_2 complex. Little is known and even less is understood about this and the subsequent steps leading to the oxygenation of substrate. The ferrous porphyrin dioxygen complex readily autoxidizes to ferric porphyrin, likely via generation of superoxide,[7] suggesting that there is some charge transfer from iron to oxygen and that this oxygenated porphyrin has some ferric superoxide character.[8] One might then envisage the additional electron from the second reduction going into an orbital in either the iron, to give formally a ferrous superoxide complex, or the dioxygen, to give formally a ferric peroxide complex.[9,10]

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