3-Bromo-3,3-difluoropropionic Anhydride (12). Phosphorus pentoxide (4.21 g, 29.6 mmol) and 3-bromo-3,3-difluoropropionic acid (9) (4.59 g, 24.3 mmol) were heated to 70 °C for 3 h under N_2. The reaction flask was equipped with a short-path distillation head, and product was distilled out of the reaction mixture to yield 3.9 g (89%) of a colorless oil, bp 80 °C (0.5 mmHg). This was used without further purification. IR (thin film): 1830, 1200–1050 cm^{-1}. ^1H NMR: δ 3.74 (t, J = 12.1 Hz, 2 H). ^{19}F NMR: δ 45.3 (t, J = 12.6 Hz, 2 F).

3,3-Difluoroacrylic Anhydride. 3-Bromo-3,3-difluoropropionic anhydride (12, 773 mg, 2.15 mmol) was dissolved in dichloromethane (5 mL) under N_2, and the mixture was cooled in an ice–water bath for 10 min. Triethylamine (480 μL, 3.4 mmol) was added by syringe over the course of 2 min with rapid stirring. The mixture was allowed to stir for 1 min a 0 °C. The flask was equipped with a vacuum adaptor, and the product was purified by dynamic vacuum transfer through a series of two traps, one at −20 °C and one at −196 °C. The product was collected as a white crystalline solid in the −20 °C trap and was further purified by a second fractionation to give 210 mg (65%) of a white solid, mp 42–42.5 °C. IR: (gas phase) 1760, 1720 cm^{-1}. ^1H NMR: δ 5.05 (dd J = 1.5, 20.2 Hz, 2 H). ^{19}F NMR: δ 58.2 (dd, J = 20.7, 31.2 Hz, 1 F), 63.3 (dd, J = 1.9, 32.6 Hz, 1 F). HR-MS (M + H^+) 198.9995, calcd for $C_6H_3F_4O_3$ 190.0018. Anal. Calcd: C, 36.36; H, 1.01. Found: C, 36.29; H, 1.11.

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Supplementary Material Available: ^1H NMR spectra for compounds 11, 12, and 2 (3 pages). Ordering information is given on any current masthead page.

Preparation of 1,2-Diketones from Nonenolizable Aliphatic and Aromatic Acyl Chlorides with Diethyl 1-Alkyl(aryl)-1-(trimethylsiloxy)-methanephosphonates1

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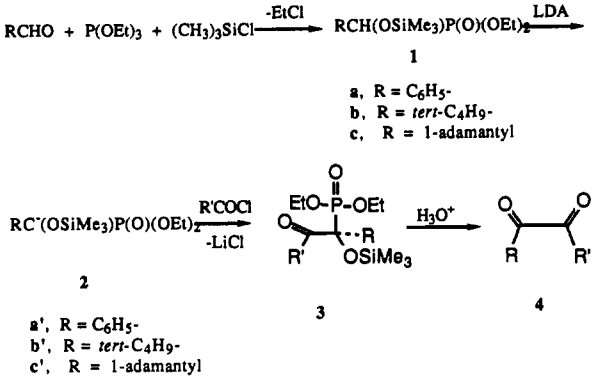
The methods for preparation of 1,2-diketones include acyloin condensation of esters with sodium metal and subsequent oxidation[3] and selenium dioxide oxidation of various monoketones.[3,4] Both methods involve multisteps. α-Diketones are also available through recent oxidative procedures such as the ene reaction of singlet oxygen with alkenes in the presence of titanium alkoxide[5] (followed by epoxide opening) or by the oxidation of acetylenes with $NaIO_4/RuO_2$.[6]

Scheme I



Masked acyl anions have become important synthons in organic synthesis. The most widely used methods for generation of masked acyl anions involve dithio acetals[7] and protected cyanohydrins.[8] More recently[9] the concept of charge affinity inversion[10] has also been applied.

Koenigkramer and Zimmer used the reaction of diethyl 1-phenyl-1-(trimethylsiloxy)methanephosphonate, the precursor of a desired acyl anion, in the presence of lithium diisopropylamide with various ketones to obtain the corresponding α-trimethylsiloxy ketones.[11] We report now a new simple preparation of 1,2-diketones by the reaction of the related acyl anion equivalents, **2**, with acyl chlorides.

The preparation of 1,2-diketones by the reaction of diethyl 1-phenyl(or alkyl)-1-(trimethylsiloxy)methanephosphonates **1** with acyl chlorides is outlined in Scheme I.

Similar to the preparation of diethyl 1-phenyl-1-(trimethylsiloxy)methanephosphonate,[12] diethyl 1-*tert*-butyl-1-(trimethylsiloxy)methane- and 1-(1′-adamantyl)-1-(trimethylsiloxy)methanephosphonates were prepared in nearly quantitative yield (94 and 96%, respectively) from trimethylacetaldehyde and 1-adamantanecarboxaldehyde, respectively, with chlorotrimethylsilane and triethyl phosphite. Subsequent treatment with lithium diisopropylamide (LDA) was carried out at −78 °C to afford the corresponding anions which were then reacted with acyl chlorides to give the desired 1,2-diketones.

Due to the bulk of diethyl 1-*tert*-butyl-1-(trimethylsiloxy)methanephosphonate and diethyl 1-(1′-adamantyl)-1-(trimethylsiloxy)methanephosphonate, the yield of the corresponding 1,2-diketones is subject to steric influence in the reactions with trimethylacetyl chloride and 1-adamantylcarbonyl chloride (Table I). On the other hand, a high yield of benzil was obtained in the reaction of diethyl 1-phenyl-1-(trimethylsiloxy)methanephosphonate with benzoyl chloride which suggests the absence of steric hinderence.

Unlike stronger nucleophiles, diethyl [1-alkyl(aryl)-1-(trimethylsiloxy)methyl]phosphonate anions, **2a–c**, behave as weak nucleophiles which are inert toward esters. Furthermore, **2a–c** also demonstrate unusual inertness toward **3a–c**, presumably due to steric bulkiness. However, the diethyl [1-alkyl-1-(trimethylsiloxy)methyl]phsphonate

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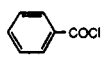
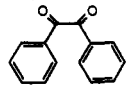
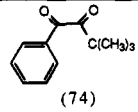
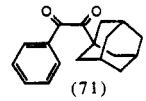
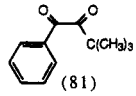
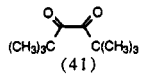
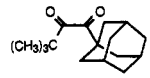
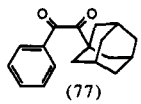
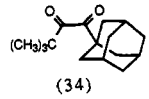
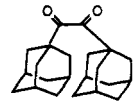
0022-3263/91/1956-0902$02.50/0

Table I. Preparation of 1,2-Diketones by Reaction of $RCH(OSiMe_3)P(O)(OEt)_2$ with Acyl Chlorides

substrate	product (% yield[a]) a, R = Ph	b, R = $(CH_3)_3C$	c, R = 1-adamantyl[b]
	 (83)	 (74)	 (71)
$(CH_3)_3CCOCl$	 (81)	 (41)	 (34)
	 (77)	 (34)	 (23)

[a] Isolated yield. [b] 1-adamantyl = 

anions **2a–c** react readily with acyl chlorides to give 1,2-diketones in good to moderate yields depending upon the bulk of the reactants.

The reaction of diethyl [1-alkyl(aryl)-1-(trimethylsiloxy)methyl]phosphonate anions with readily available acyl chlorides represents a simple, new alternative to available methodology for the preparation of 1,2-diketones. The reaction takes place under mild conditions with no further conversion of the products. At the same time, the competing generation of the corresponding ketenes via dehydrochlorination of enolizable acyl chlorides[15] limits the scope of the reaction to nonenolizable aliphatic and aromatic acyl chlorides.

Experimental Section

All chemicals used were commercially available and distilled prior to use. 1-Adamantanecarboxaldehyde was prepared according to the literature procedure.[13]

Gas chromatographic analyses were carried out on a quartz-silica capillary column coated with DB-1.

Diethyl 1-Phenyl-1-(trimethylsiloxy)methanephosphonate. To a mixture of benzaldehyde (10.6 g, 0.1 mol) and freshly distilled triethyl phosphite (16.6 g, 0.1 mol) kept at 0 °C (ice bath) was added dropwise chlorotrimethylsilane (distilled from tributylamine; 10.8 g, 0.1 mol) with good stirring under a nitrogen atmosphere at 0 °C, during a period of 10 min. After the addition was completed, the ice bath was removed, and the reaction mixture was warmed to 120 °C (oil bath) for a period of 6–8 h and then distilled. Diethyl 1-phenyl-1-(trimethylsiloxy)methanephosphonate was obtained at 170 °C (10.0 mm) (**1a**; 29.1 g, 0.092 mol; 92% yield from benzaldehyde) as a colorless liquid. IR (neat): 1245 (m) cm^{-1}. ^{31}P NMR (81 MHz, D_3PO_4): δ -20.81. ^{13}C NMR ($CDCl_3$, 50 MHz): 137.12 (d), 127.86, 127.17, 127.06 (aromatics), 71.71 (CH, d, J_{cp} = 170.9 Hz), 62.94 (CH_2, d, J_{cp} = 7.3 Hz), 62.50 (CH_2 d, J_{cp} = 7.3 Hz), 16.28 (CH_3, d, J_{cp} = 5.0 Hz), 16.18 (CH_3, d, J_{cp} = 5.0 Hz), -0.25 (CH_3). ^1H NMR ($CDCl_3$, 200 MHz): δ 7.38 (m, 2 H), 7.21 (m, 3 H), 4.88 (CH, d, 1 H, J_{cp} = 14.7 Hz), 3.97–3.88 (m, 4 H), 1.12 (CH_3, t, 6 H, J = 6.8 Hz), 0.02 (s, 9 H). GC/MS (70 eV): m/e 316 (M^+, 0.5), 210 (46.7), 179 (100.0), 166 (5.9), 137 (2.1), 105 (7.0), 89 (3.4), (98.9), 45 (16.4), 29 (19.5).

Benzil. To a dry ice/acetone cold solution of diethyl 1-phenyl-1-(trimethylsiloxy)methanephosphonate (**1a**; 2.91 g, 10.0 mmol) and dry tetrahydrofuran (30 mL) under a nitrogen atmosphere was added lithium diisopropylamide (1.5 M in cyclohexane; 7.0 mL, 10.5 mmol) dropwise through a syringe with good stirring over a period of 5 min. After the addition of LDA had been completed, the reaction mixture was stirred for another 30 min. To the stirred reaction mixture was then added a solution of benzoyl chloride (1.41 g, 10.0 mmol) in dry THF (10 mL) dropwise over a period of 10 min. After the addition of benzoyl chloride was complete, the reaction mixture was stirred for another 30 min, the dry ice/acetone cold bath was removed, and the reaction mixture was stirred at ambient temperature for another 8 h. To the reaction mixture was added a 10% aqueous solution of hydrochloric acid (20 mL). The reaction mixture was stirred for several minutes and then extracted with ether (40 mL × 3). The combined ethereal layers were dried over anhydrous magnesium sulfate, filtered and evaporated in vacuo to leave crude material, which was further purified via column chromatography on silica gel (20% ethyl acetate/hexane as eluent) to give benzil (1.74 g, 83% yield from benzoyl chloride) as bright yellow microcrystals. All the spectral data was consistent with those given for benzil in the literature.

1-Phenyl-3,3-dimethyl-1,2-butanedione. The reaction of diethyl 1-phenyl-1-(trimethylsiloxy)methanephosphonate (**1a**; 3.16 g, 10.0 mmol), lithium diisopropylamide (1.5 M in cyclohexane, 7.0 mL; 10.5 mmol), and trimethylacetyl chloride (1.21 g, 10.0 mmol) and subsequent aqueous workup afforded 1-phenyl-3,3-dimethyl-1,2-butanedione (1.53 g, 81% yield from trimethylacetyl chloride) as a colorless liquid, bp: 87–88 °C (3.0 mm). IR (neat): 1710 (s), 1720 (s) cm^{-1}. ^{13}C NMR (50 MHz, $CDCl_3$): δ 209.96 (s), 194.63 (s), 134.32 (s), 129.27 (d), 128.72 (d), 128.23 (d), 34.77 (s), 26.35 (q). ^1H NMR (200 MHz, $CDCl_3$): δ 1.26 (s, 9 H), 7.14–7.25 (m, 5 H). GC/MS (70 eV): m/e 190 (M^+, 1.8), 105 (100.0), 85 (5.8), 77 (24.6), (25.8). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.79; H, 7.37. Found: C, 75.83; H, 7.43.

1-(1′-Adamantyl)-2-phenyl-1,2-ethanedione. The reaction of diethyl 1-phenyl-1-(trimethylsiloxy)methanephosphonate (**1a**; 3.16 g, 10.0 mmol), lithium diisopropylamide (1.5 M in cyclohexane; 7.0 mL, 10.5 mmol) and 1-adamantanecarboxylic acid chloride (1.99 g, 10.0 mmol) afforded 1-(1′-adamantyl)-2-phenyl-1,2-ethanedione (2.06 g, 77% yield from 1-adamantanecarboxylic acid chloride) as colorless microcrystals, mp (from petroleum ether) 76–77 °C. IR (KBr): 1700 (s) cm^{-1}. ^{13}C NMR (50 MHz, $CDCl_3$): δ 209.95 (s), 195.33 (s), 136.61 (s), 127.70 (d), 126.78 (d), 126.58 (d), 48.31 (s), 38.68 (t), 36.17 (t), 28.97 (d). ^1H NMR (200 MHz, $CDCl_3$): δ 2.23–2.63 (m, 15 H), 7.14–7.28 (m, 5 H). GC/MS (70 eV): m/e 268 (M^+, 0.6), 163 (9.5), 135 (100.0), 105 (19.4), 77 (24.0). Anal. Calcd for $C_{18}H_{20}O_2$. C, 80.60; H, 7.46. Found: C, 80.83; H, 7.25.

Diethyl 1-*tert*-Butyl-1-(trimethylsiloxy)methanephosphonate. A reaction mixture of trimethylacetaldehyde (8.6 g, 0.1 mol), freshly distilled triethyl phosphite (16.6 g, 0.1 mol), and freshly distilled chlorotrimethylsilane (10.9 g, 0.1 mol) was warmed at 120 °C for 8 h and then distilled at 128–130 °C (5.0 mm) to give diethyl 1-*tert*-butyl-1-(trimethylsiloxy)methanephosphonate (**1b**; 27.8 g, 94% yield from trimethylacetaldehyde) as a colorless liquid. IR (neat): 1245(m) cm^{-1}. ^{31}P (81 MHz, D_3PO_4): δ -23.76. ^{13}C NMR (50 MHz, $CDCl_3$): δ 77.97 (CH, d, J_{cp} = 162.4 Hz), 61.98 (CH_2, d, J_{cp} = 7.3 Hz), 61.28 (CH_2, d, J_{cp} = 7.3 Hz), 34.90 (quat C, d, J_{cp} = 4.5 Hz), 26.74 (CH_3, d, J_{cp} = 6.2 Hz), 16.38 (CH_3, d, J_{cp} = 2.5 Hz), 16.27 (CH_3, d, J_{cp} = 2.5 Hz), 0.16 (CH_3). ^1H NMR (200 MHz, $CDCl_3$): δ 3.99 (CH_2, q, 4 H, J = 6.8 Hz), 3.48 (CH, d, 1 H, J_{HP} = 7.9 Hz), 1.18 (CH_3, t, 6 H, J = 6.8 Hz), 0.88 (CH_3, s, 9 H), 0.02 (CH_3, s, 9 H). GC/MS (70 eV): m/e 296 (M^+, 0.4), 281 (7.46), 210 (56.7), 159 (77.9), 121 (36.1), 73 (100.0). Anal. Calcd for $C_{12}H_{29}O_4PSi$: C, 48.65; H, 9.80. O, 21.62. Found: C, 48.46; H, 9.98; O, 21.52.

1-Phenyl-3,3-dimethyl-1,2-butanedione. The reaction of diethyl 1-*tert*-butyl-1-(trimethylsiloxy)methanephosphonate (**1b**;

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2.96 g, 10.0 mmol), lithium diisopropylamide (1.5 M in cyclohexane; 7.0 mL, 10.5 mmol) and freshly distilled benzoyl chloride (1.41 g, 10.0 mmol) gave 1-phenyl-3,3-dimethyl-1,2-butanedione (1.41 g, 74% yield from benzoyl chloride).

2,2,5,5-Tetramethyl-3,4-hexanedione. The reaction of diethyl 1-*tert*-butyl-1-(trimethylsiloxy)methanephosphonate (**1b**; 2.96 g, 10.0 mmol), lithium diisopropylamide (1.5 M in cyclohexane; 7.0 mL, 10.5 mmol), and trimethylacetyl chloride (1.21 g, 10.0 mmol) gave 2,2,5,5-tetramethyl-3,4-hexanedione (0.70 g, 41% yield from trimethylacetyl chloride) as a colorless liquid, bp 76–77 °C (3.0 mm). IR (neat): 1720 (s) cm^{-1}. ^{13}C NMR (50 MHz, $CDCl_3$): δ 210.46 (s), 37.51 (s), 26.06 (q). ^1H NMR (200 MHz, $CDCl_3$): δ 0.90 (s). GC/MS (70 eV): *m/e* 170 (M^+, 4.9), 85 (19.3), 57 (100.0). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.59; H, 10.59. Found, C, 70.54; H, 10.68.

1-(1′-Adamantyl)-3,3-dimethyl-1,2-butanedione. The reaction of diethyl 1-*tert*-butyl-1-(trimethylsiloxy)methanephosphonate (**1b**; 2.96 g, 10.0 mmol), lithium diisopropylamide (1.5 M in cyclohexane; 7.0 mL, 10.5 mmol), and 1-adamantanecarbonyl chloride (1.99 g, 10.0 mmol) gave 1-(1′-adamantyl)-3,3-dimethyl-1,2-butanedione (0.84 g, 34% yield from 1-adamantanecarboxylic acid chloride) as colorless microcrystals, mp (from petroleum ether) 82–83 °C. IR (KBr): 1740 (s), 1745 (s), cm^{-1}. ^{13}C NMR (50 MHz, $CDCl_3$): δ 210.33 (s), 209.31 (s), 46.31 (s), 38.02 (t), 36.00 (t), 35.48 (s), 28.03 (d), 26.92 (q). ^1H NMR (200 MHz, $CDCl_3$): δ 2.59–2.20 (n, 15 H), 0.91 (s, 9 H). GC/MS (70 eV): *m/e* 248 (M^+, 1.3), 163 (13.2), 135 (100.0), 85 (9.2), 57 (33.2). Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.42; H, 9.68. Found: C, 77.65; H, 9.41.

Diethyl 1-(1′-Adamantyl)-1-(trimethylsiloxy)methanephosphonate. A mixture of 1-adamantanecarbaldehyde[11] (16.4 g, 0.1 mol), freshly distilled triethyl phosphite (16.6 g, 0.1 mol), and freshly distilled chlorotrimethylsilane (10.9 g, 0.1 mol) was warmed at 120 °C for 8 h to give diethyl 1-(1′-adamantyl)-1-(trimethylsiloxy)methanephosphonate (**1c**; 35.9 g, 96% yield from 1-adamantanecarbaldehyde). Bp: 178–180 °C (0.05 mm) colorless oil. IR (neat): 1245 (m) cm^{-1}. ^{31}P NMR (81 MHz, D_3PO_4): δ −23.03. ^{13}C NMR (50 MHz, $CDCl_3$): δ 76.64 (CH, d, J_{cp} = 164.3 Hz), 60.78 (CH_2, d, J_{cp} = 7.5 Hz), 60.06 (CH_2, d, J_{cp} = 7.5 Hz), 43.03 (quat, C, d, J_{cp} = 4.8 Hz), 42.18 (CH_2, d, J_{cp} = 5.8 Hz), 36.85 (CH_2), 28.99 (CH), 16.33 (CH_3, d, J_{cp} = 2.4 Hz), 16.21 (CH_3, d, J_{cp} = 2.4 Hz), 0.16 (CH_3). ^1H NMR (200 MHz, $CDCl_3$): δ 3.98 (CH_2, q, 4 H, J = 6.8 Hz), 3.81 (CH, d, 1 H, J_{HP} = 8.6 Hz), 2.30–2.71 (m, 15 H), 1.20 (CH_3, t, 6 H, J = 6.8 Hz), 0.01 (CH_3, s, 9 H). GC/MS (70 eV): *m/e* 374 (M^+ 0.6), 237 (74.4), 210 (100.0), 195 (10.5), 183 (10.4), 135 (37.6), 121 (16.5), 91 (10.2), 73 (82.6). Anal. Calcd for $C_{18}H_{35}O_4PSi$: C, 57.75; H, 9.36; O, 17.11. Found: C, 57.46; H, 9.39; O, 16.98.

1-(1′-Adamantyl)-2-phenyl-1,2-ethanedione. The reaction of diethyl 1-(1′-adamantyl)-1-(trimethylsiloxy)methanephosphonate (**1c**; 3.74 g, 10.0 mmol), lithium diisopropylamide (1.5 M in cyclohexane; 7.0 mL, 10.5 mmol), and benzoyl chloride (1.41 g, 10.0 mmol) with subsequent aqueous workup gave 1-(1′-adamantyl)-2-phenyl-1,2-ethanedione (1.90 g, 71% yield from benzoyl chloride).

1-(1′-Adamantyl)-3,3-dimethyl-1,2-butanedione. the rection of diethyl 1-(1′-adamantyl)-1-(trimethylsiloxy)methanephosphonate (**1c**; 3.74 g, 10.0 mmol), lithium diisopropylamide (1.5 M in cyclohexane; 7.0 mL, 10.5 mmol), and trimethylacetyl chloride (1.21 g, 10.0 mmol) and subsequent aqueous workup gave 1-(1′-adamantyl)-3,3-dimethyl-1,2-butanedione (0.84 g, 34% yield from trimethylacetyl chloride).

1,2-Di-1′-adamantyl-1,2-ethanedione. The reaction of diethyl 1-(1′-adamantyl)-1-(trimethylsiloxy)methanephosphonate (**1c**; 3.74 g, 10.0 mmol), lithium diisopropylamide (1.5 M in cyclohexane; 7.0 mL, 10.5 mmol), and 1-adamantanecarbonyl chloride (1.99 g, 10.0 mmol) with subsequent aqueous workup gave 1-(1′-adamantyl)-2-phenyl-1,2-ethanedione (0.75 g, 23% yield from 1-adamantanecarbonyl chloride). Mp: 76–77 °C. The spectral data was identical with that reported for 1,2-di-1′-adamantyl-1,2-ethanedione.[14]

Acknowledgment. Support of our work by the National Institutes of Health is gratefully acknowledged.

The Crystal Structure of 2,3-Dithia-8-(*p*-nitrobenzoyl)bicyclo[3.2.1]octane and the First Bridged Bicyclic Thiosulfinate Ester

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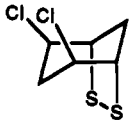
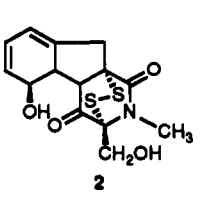
Bridged bicyclic disulfides are unique among the many examples of disulfides; the relatively rigid framework of the bicyclo-backbone forces the dihedral angle about the sulfur–sulfur bond (θ) to become, of necessity, close to 0°. Few systematic studies concerning the reactivity and structure of these compounds have been reported. The preferred conformation for the disulfide linkage has θ in the range of 90°, which minimizes the interaction between the two pairs of 3p, nonbonding electrons on the sulfur atoms. With θ near 0°, the chemical behavior of this class of compounds becomes markedly different from disulfides that have a larger dihedral angle, which absorb light at longer wavelengths in the ultraviolet[1] and have lower ionization potentials.[2] In fact, the first reported photoelectron spectrum of a bridged bicyclic disulfide, 2,4-dichloro-6,7-dithiabicyclo[3.2.1]octane (**1**), showed the largest sulfur lone pair energy gap ever observed for a simple, nonaromatic disulfide.[3]



1

Nature provides many examples of disulfides; naturally occurring bridged bicyclic disulfides are less common but one of the best known may be found in the family of fungal toxins characterized by the epidithiodioxopiperazine ring system. The crystal structure of gliotoxin (**2**), the first member of this family to be isolated,[4] has been reported,[5] and the dihedral angles were found to be 8.8° and 15.8° for the two distinct molecules in the unit cell. Other biologically active examples of bridged bicyclic disulfides may be found in the prostaglandin derivatives. The sulfur analogue of 13,14-dehydro-PGH_2 (**3**) has been synthesized[6] and found to have platelet aggregating properties.



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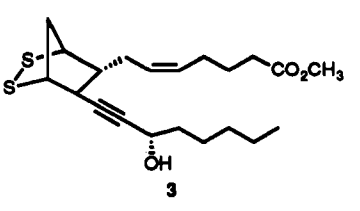

3

The synthesis of the relatively simple bridged bicyclic disulfide **4** has been achieved in only four steps from readily available precursors.[7] However, the stereochemistry of the OH group and the monomeric nature of the molecule was correctly inferred but not unambiguously

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