acetoxy alkene **2b**, 89 mg (8%) of diacetate **3b**, 80 mg (8%) of phenyl alkene **10b**, and 58 mg of unreacted **1b** after chromatography on silica gel.

2b: IR (neat) 3040, 1735, 1640, 1250, 1230, 1040, 790 cm^{-1}; MS, *m/e* (relative intensity) 194 (M^+, 2), 134 (84), 119 (59), 105 (69), 92 (100), 91 (94); ^1H NMR ($CDCl_3$) δ 1.3–2.9 (m, 17 H, s at 1.96), 5.39 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 170.77 (s), 143.99 (s), 122.06 (d), 90.86 (s), 45.06 (t), 43.06 (t), 40.37 (t), 34.48 (t), 29.56 (t), 28.83 (t), 26.32 (t), 22.17 (q). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.92; H, 9.59.

3b: mp 52–53 °C; IR (KBr) 3010, 1730, 1250, 1230, 1090, 1065, 1015, 940, 860, 800, 780, 735 cm^{-1}; MS, *m/e* (relative intensity) 252 (M^+, not detected), 192 (38), 150 (68), 122 (68), 108 (66), 107 (100); ^1H NMR (CCl_4) δ 1.0–1.4 (m, 3 H), 1.5–2.3 (m, 13 H, s at 1.90), 2.49 (d, J = 15 Hz, 1 H), 2.83 (d, J = 15 Hz, 1 H), 6.11 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 170.11 (s, 2 C), 136.89 (d, 2 C), 92.37 (s, 2 C), 51.62 (t), 38.11 (t, 2 C), 28.13 (t, 2 C), 26.47 (t), 22.16 (q, 2 C). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.74; H, 7.99.

10b: IR (neat) 3040, 1640, 1600, 790, 760, 700 cm^{-1}; MS, *m/e* (relative intensity) 212 (M^+, 100), 169 (65), 156 (94), 155 (88), 129 (89), 91 (88); ^1H NMR ($CDCl_3$) δ 1.3–3.0 (m, 14 H), 5.52 (br s, 1 H), 7.04–7.42 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 151.06 (s), 144.97 (s), 128.04 (d, 2 C), 126.05 (d, 2 C), 125.35 (d), 123.04 (d), 54.13 (s), 48.93 (t), 46.29 (t), 42.96 (t), 35.69 (t), 29.52 (t), 28.95 (t), 26.60 (t). Anal. Calcd for $C_{16}H_{20}$: C, 90.50; H, 9.50. Found: C, 90.24; H, 9.73.

Oxidation of 1a with Lead Tetraacetate. Oxidation of **1a** (1.00 g, 6.02 mmol) was carried out with an excess of lead tetraacetate (6.65 g, 15.0 mmol) to afford 473 mg (33%) of **3a** after chromatography on silica gel.

3a: IR (neat) 1735, 1260, 1235, 1075, 1030, 780 cm^{-1}; MS, *m/e* (relative intensity) 238 (M^+, 3), 136 (100); ^1H NMR ($CDCl_3$) δ 1.4–1.7 (m, 4 H), 1.8–2.2 (m, 10 H, s at 1.98), 2.30 (d, J = 12 Hz, 1 H), 3.15 (d, J = 12 Hz, 1 H), 6.12 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 170.16 (s, 2 C), 135.82 (d, 2 C), 89.09 (s, 2 C), 47.70 (t), 35.42 (t, 2 C), 22.99 (t, 2 C), 21.92 (q, 2 C). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.28; H, 7.69.

Hydrogenation of 3a. Hydrogenation of **3a** (597 mg, 2.5 mmol) with a catalytic amount of palladium on charcoal in 10 mL of methanol at atmospheric pressure of hydrogen gave 500 mg (83%) of **4**: IR (neat) 1730, 1235, 1075, 1045, 1030, 1010, 940 cm^{-1}; MS, *m/e* (relative intensity) 240 (M^+, trace), 137 (100), 120 (79), 109 (58), 96 (68); ^1H NMR ($CDCl_3$) δ 1.4–2.3 (m, 19 H, s at 1.94), 2.85 (d, J = 12 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 170.21 (s, 2 C), 87.43 (s, 2 C), 46.58 (t), 38.46 (t, 2 C), 36.74 (t, 2 C), 23.04 (t, 2 C), 22.07 (q, 2 C). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.66; H, 8.21.

Pyrolysis of 4. A solution of **4** (455 mg, 1.90 mmol) in 50 mL of hexane was passed with a nitrogen flow through a Pyrex column packed with Pyrex chips which was heated at 400 °C (contact time about 20 s). Products were collected in a cold trap containing powdered potassium carbonate. The solvent was evaporated and the products were analyzed by GLC. Preparative GLC gave 144 mg (42%) of **2a**: IR (neat) 1730, 1260, 1240, 1035, 1020, 825, 790, 730 cm^{-1}; MS, *m/e* (relative intensity) 180 (M^+, 26), 120 (100), 96 (63), 92 (95), 91 (74); ^1H NMR ($CDCl_3$) δ 1.0–3.0 (m, 15 H, s at 1.95), 5.35 (br m, 1 H); ^{13}C NMR ($CDCl_3$) δ 170.97 (s), 143.28 (s), 125.47 (d), 90.25 (s), 41.90 (t), 41.79 (t), 36.19 (t), 31.79 (t), 25.39 (t), 22.64 (t), 22.10 (q). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 72.96; H, 8.86.

Pyrolysis of 2c. Pyrolysis of **2c** (236 mg, 1.13 mmol) was carried out as described above to afford 99 mg (59%) of **6a** after purification by preparative GLC. **6a**: IR (CCl_4) 3020, 1660, 915 cm^{-1}; MS, *m/e* (relative intensity) 148 (M^+, 80), 106 (63), 105 (77), 91 (100), 79 (59); ^1H NMR ($CDCl_3$) δ 1.0–3.2 (m, 14 H), 4.76 (dd, J = 5, 10 Hz, 1 H), 5.82 (dd, J = 2, 4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 151.63 (s), 149.19 (s), 132.01 (d), 114.84 (d), 38.78 (t), 33.62 (t), 33.26 (t), 27.53 (t), 23.51 (t), 23.27 (t), 19.65 (t). Anal. Calcd for $C_{11}H_{16}$: C, 89.12; H, 10.88. Found: C, 89.18; H, 10.93.

Registry No. *exo*-**1a**, 89398-38-9; *endo*-**1a**, 89460-83-3; *exo*-**1b**, 89398-39-0; *endo*-**1b**, 89460-84-4; *exo*-**1c**, 89398-40-3; *endo*-**1c**, 89460-85-5; **2a**, 88226-68-0; **2b**, 89398-41-4; **2c**, 89398-42-5; **3a**, 89398-43-6; **3b**, 89398-44-7; **4**, 89398-45-8; **6a**, 89398-46-9; **7a**, 22118-00-9; **7b**, 769-32-4; **7c**, 38262-50-9; **8a**, 20990-27-6; **8b**, 89398-47-0; **8b** semicarbazone, 89398-48-1; **8c**, 89398-49-2; **8c** semicarbazone, 89398-50-5; *exo*-**9a**, 89398-51-6; *endo*-**9a**, 89460-86-6; *exo*-**9b**, 89398-52-7; *endo*-**9b**, 89460-87-7; *exo*-**9c**, 89398-53-8; *endo*-**9c**, 89460-88-8; **10b**, 89398-54-9; **10c**, 89398-55-0; [4.3.1]-propell-8-en-7-one, 89398-56-1; 8-methoxy[4.3.1]propellan-7-one, 89398-57-2; 8-formyl[5.3.1]propellane, 89398-58-3; 8-formyl-[5.3.1]propellane semicarbazone, 89398-59-4; 7-formyl[4.3.1]-propellane, 89398-60-7; trimethyloxosulfonium iodide, 1774-47-6; lead tetraacetate, 546-67-8.

Generation of the Dianion of *N*-(Trimethylsilyl)acetamide and Reaction of the Dianion with Electrophilic Reagents

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Aliphatic esters are readily converted to enolate anions by strong bases, and numerous examples of condensations of the anions with electrophilic reagents have been reported.[1] These reactions are sometimes complicated by self-condensation leading to β-keto esters. One method for circumventing this problem involves enolate anions prepared from salts of the corresponding carboxylic acids;[2] the resulting dianions are more basic and nucleophilic than the corresponding ester anions.

Anions of carboxamides have received relatively little study; many of the investigations have been with monoanions of *N,N*-disubstituted amides. Dianions of monosubstituted amides have been investigated by Hauser and co-workers.[3] Although the dianion of acetanilide could not be formed with KNH_2 in liquid ammonia, it was prepared satisfactorily with 2 equiv of *n*-butyllithium in ethereal solvent. Other monosubstituted amides formed dianions similarly; the anions reacted selectively with electrophiles at the α-methylene position. Problems arise with unsubstituted amides, other than special cases such as phenylacetamide.[4] The anions frequently have poor solubility in ethereal solvents, making it difficult to effect secondary ionization at the α position.[5] A second ionization at nitrogen may precede enolate anion formation. Furthermore, it has been reported that treatment of acetamide with strong bases under forcing conditions causes dehydration to form the anion of acetonitrile.[5,6] In cases where preparation of the N,C-dianion may be possible, it is not clear that electrophiles will react exclusively on carbon.

In synthetic studies of compounds related to pretetramide presently being carried out in this laboratory, the need arose for synthons that are equivalent to the enolate anion of acetamide for use in acylation reactions. The

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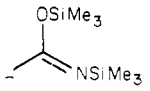
anions of mono- or dialkyl acetamide might have been satisfactory but dealkylation conditions compatible with sensitive functional groups could not be found. The lithium salt of *N,O*-bis(trimethylsilyl)acetamide (1) repre-



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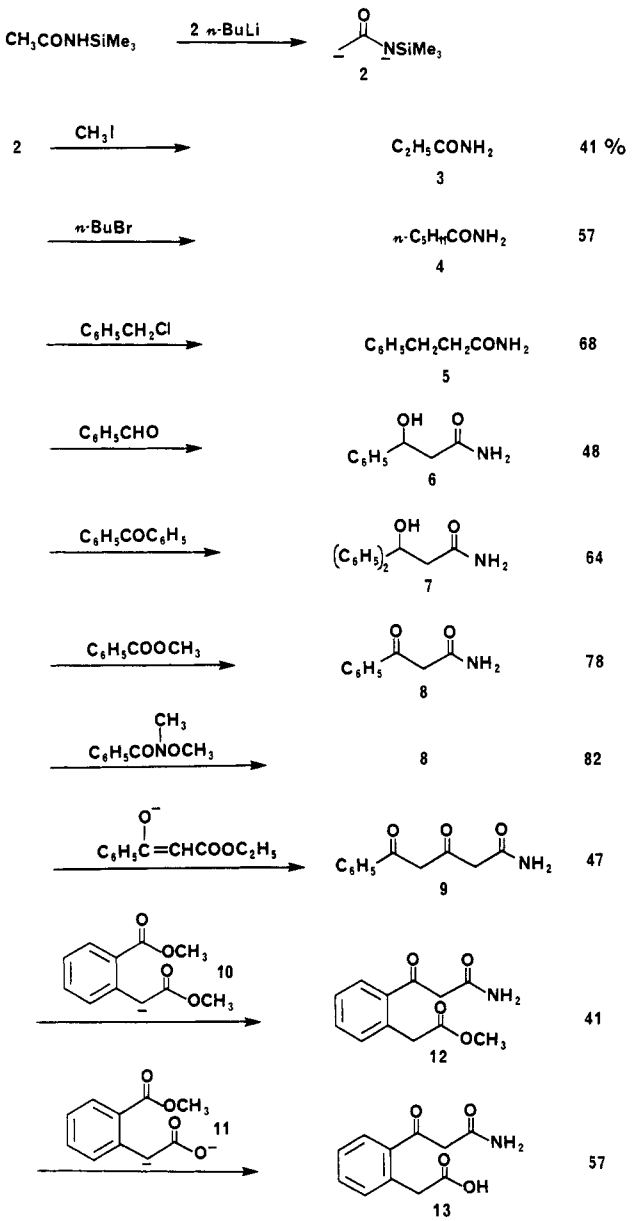
sented a potential solution to the problem since the silyl groups can easily be removed by hydrolysis. Condensation with ketones occur in excellent yield, but other reactions including alkylations and, most important for us, acylations are only marginally successful.[7] The enolate anion is thermally unstable; rearrangement to C-silylated derivatives competes with the desired condensation reactions in cases where the electrophile does not react instantaneously with the anion.

We have investigated the dianion (2) of *N*-(trimethylsilyl)acetamide as an alternative to the monoanion of *N,O*-bis(trimethylsilyl)acetamide. *N*-(Trimethylsilyl)-acetamide is easily prepared[8] and also available from commercial sources. It is convenient to handle being soluble in THF. The silyl group aids formation of anionic species by delocalization of charge into the d orbitals. Furthermore, the delocalization and perhaps steric hindrance lead to the amide anion of the dianion being much less nucleophilic than the enolate anion. Treatment of *N*-(trimethylsilyl)acetamide with 2 equiv of *n*-butyllithium at 0 °C for 30 min in THF gave the soluble, colorless dilithium salt. Ten different electrophilic reagents were condensed with the dianion, as shown in Scheme I; the condensations were carried out at temperatures ranging from 0 to 50 °C and included alkylation, aldol condensation, and acylation. In all cases the only product observed was that resulting from condensation on carbon rather than on the nitrogen or oxygen. The general workup procedure involved brief treatment with dilute aqueous acid to remove the trimethylsilyl group and thus give the unsubstituted amide. In no case was N → C rearrangement of the trimethylsilyl group detected.

Alkylation reactions with methyl iodide, *n*-butyl bromide, and benzyl chloride occurred in excellent yields with no indication of products other than the monoalkyl derivatives **3–5** being formed. The yields that are reported represent isolated materials and reflect losses that occur due to the high water solubility of the carboxamides. Aldol condensations were observed with benzaldehyde and benzophenone to give β-hydroxy carboxamides **6** and **7**.

The acylation reactions are of particular interest. The reactions of methyl benzoate and *N*-methyl-*N*-methoxybenzamide both proceeded efficiently to give keto amide **8**. In most cases the latter reagent, and analogues therof, would probably be the one of choice. In acylation reactions involving esters a 2:1 ratio of enolate anion to ester is commonly used, based upon studies that have shown that the second equivalent is needed to ionize the newly formed active methylene group of the condensation product.[9] Only a 1:1 ratio is required with the *N*-methyl-*N*-methoxy amide because methoxymethylamine is not eliminated until the reaction mixture is acidified.[10] *N*-Methyl-*N*-

Scheme I



methoxybenzamide is, however, significantly less reactive than methyl benzoate with nucleophiles.[10] The success of the condensation of *N*-(trimethylsilyl)acetamide dianion is indicative of the high reactivity of dianion **2**. The successful condensation of dianion **2** with the enolate anion of ethyl benzoylacetate to give diketo amide **9** is further evidence of the reactivity of the dianion because this relatively unreactive electrophile fails to react with enolate anions of low nucleophilicity such as the anion of acetophenone. Even with strong nucleophiles, reactions of ethyl benzoylacetate must be carried out at or above room temperature to achieve a satisfactory rate of reaction. Thus the anion of *N,O*-bis(trimethylsilyl)acetamide, which has low nucleophilicity and poor thermal stability, would not be expected to react with the β-keto ester. Reactions with homophthalate derivatives **10** and **11** gave keto amide **12** and **13**. Selectivity in attack on the aromatic carbonyl group was obtained in the first case by forming the enolate anion of the aliphatic ester and in the second one by employing the carboxylate anion.

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In summary, the trimethylsilyl group is uniquely well suited for modification of acetamide to create a synthetic equivalent of acetamide enolate anion because (1) it lends solubility to the amide, (2) it permits formation of the highly reactive dianion while at the same time solubilizing it and stabilizing the nitrogen anion against reaction with electrophilic reagents, and, finally, (3) it is readily removed under mild conditions.

Experimental Section

All glassware employed in the anion reactions was oven-dried at 150 °C and assembled while hot under a stream of N_2. Tetrahydrofuran (THF) was used immediately after distillation from Na–K alloy/benzophenone ketyl. Diisopropylamine, distilled from Na and stored over 4-Å molecular sieves, was converted to lithium diisopropylamide (LDA) by treatment with a stoichiometric quantity of *n*-butyllithium at 0 °C in THF under N_2. Flash column chromatography was carried out with silica gel 60 (E. Merck 9285, 230–400 mesh) deactivated by treatment with 6 N HCl followed by washing with H_2O to pH 5 and air-drying to a water content of approximately 25%. ^1H NMR spectra were taken on JEOL MH-100 and FX-90Q spectrometers; the latter was also used for ^{13}C spectra. IR spectra were taken on a Perkin-Elmer 727 spectrophotometer. Mass spectra (70 eV) were taken with an LKB 9000 spectrometer using the solids probe. Melting points (uncorrected) were taken in open capillaries. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

Preparation of Dilithium Salt 2 of *N*-(Trimethylsilyl)-acetamide. *N*-(Trimethylsilyl)acetamide (0.92 g, 7.05 mmol) dissolved in a minimum amount of THF was added slowly to a flask charged with 100 mL of THF and 14.09 mmol of *n*-butyllithium at 0 °C. The colorless solution was stirred for 30 min before use.

Propanamide (3). Methyl iodide (1.00 g, 7.05 mmol) was added slowly to 7.05 mmol of dianion **2** at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and quenched with excess acetic acid (1.20 g, 20 mmol). The solvent was evaporated at reduced pressure and the residue dried in vacuo. The residue was dissolved in 10 mL of H_2O and 75 mL of CH_2Cl_2. The pH of the suspension was adjusted to 1–2 with 6 N HCl. The organic layer and additional CH_2Cl_2 extracts (2 × 75 mL) were combined, dried ($MgSO_4$), and evaporated to leave a brown oil, which crystallized after being subjected to high vacuum. The solid was sublimed at 65 °C (0.01 mm) to yield 0.21 g (41% yield) of propanamide (**3**) as white crystals: mp 79 °C (lit.[11] mp 81 °C); ^1H NMR ($CDCl_3$) δ 1.12 (t, J = 7 Hz, 3 H), 2.26 (q, J = 7 Hz, 2 H), 6.50–7.10 (m, 2 H). The ^1H NMR spectrum of the aqueous layer showed a substantial amount of **3** to be present.

Hexanamide (4). 1-Bromobutane (1.00 g, 7.30 mmol) was added to 8.03 mmol of dianion **2** in 100 mL of THF at 0 °C. After 12 h at room temperature, the reaction mixture was quenched with acetic acid. Isolation as with **3** gave a solid, which was purified by flash chromatography[12] (hexane:EtOAc, 3:7) to give **4** (0.48 g, 57% yield) as white crystals: mp 100 °C (lit.[11] mp 100 °C); ^{13}C NMR ($CDCl_3$) δ 13.8 (q), 22.3 (t), 25.2 (t), 31.3 (t), 35.9 (t), 176.0 (s).

3-Phenylpropionamide (5). Benzyl chloride (1.00 g, 7.90 mmol) was added to 8.69 mmol of dianion **2** in 100 mL of THF at 0 °C. After 12 h at room temperature, the reaction mixture was quenched with excess acetic acid. Isolation as with **3** gave a solid, which was purified by flash chromatography (hexane:EtOAc, 1:9) to give 3-phenylpropionamide (**5**, 0.79 g, 68% yield) as white needles: mp 104 °C (lit.[11] mp 105 °C); ^{13}C NMR ($CDCl_3$) δ 31.3 (t), 37.4 (t), 126.2 (d), 128.2 (d), 128.5 (d), 140.7 (s), 174.8 (s).

3-Hydroxy-3-phenylpropionamide (6). Benzaldehyde (1.00 g, 9.42 mmol) was added to 10.36 mmol of dianion **2** in 100 mL of THF at 0 °C. After 3 h, the reaction mixture was quenched with excess acetic acid and the isolation procedure for **3** followed. However, much of amide **6** (0.3 g) failed to dissolve in either the H_2O or CH_2Cl_2 layer and was separated by filtration. The CH_2Cl_2 extracts were combined, dried ($MgSO_4$), and evaporated. The resulting brown liquid was purified by flash chromatography (EtOAc) to yield an additional 0.44 g of amide **6** to give a total yield of 0.74 g (48% yield): mp 118 °C (lit.[7b] mp 116–117 °C); ^{13}C NMR (CD_3SOCD_3) δ 45.2 (t), 69.6 (d), 125.7 (d), 126.7 (d), 128.0 (d), 145.3 (s), 172.4 (s).

3,3-Diphenyl-3-hydroxypropionamide (7). Benzophenone (1.00 g, 5.49 mmol) was added to 6.04 mmol of dianion **2** in 100 mL of THF at 0 °C. After 3 h the reaction mixture was quenched with excess acetic acid. Isolation as for **3** gave a brown oil, which solidified after being subjected to high vacuum. The solid was purified by trituration with CH_2Cl_2 to give 0.84 g (64% yield) of amide **7** as white crystals: mp 233 °C (lit.[7b] 214–216 °C); ^{13}C NMR (CD_3SOCD_3) δ 44.2 (t), 75.9 (s), 125.2 (d), 126.2 (d), 127.7 (d), 147.1 (s), 174.1 (s).

Benzoylacetamide (8). Methyl benzoate (1.00 g, 7.35 mmol) was added to 16.26 mmol of dianion **2** in 100 mL of THF at 0 C. After 2 h the reaction mixture was quenched with excess acetic acid. Workup as with **3** gave an oil, which was purified by flash chromatography (hexane:EtOAc, 2:8) to yield amide **8** as white crystals (0.93 g, 78% yield): mp 111 °C (lit.[13] mp 111–113 °C); ^{13}C NMR ($CDCl_3$) δ 45.3 (t), 128.6 (d), 128.9 (d), 134.2 (d), 136.3 (s), 168.1 (s), 195.6 (s).

***N*-Methyl-*N*-methoxybenzamide** (1.00 g, 6.06 mmol) was added to 6.66 mmol of dianion **2** in 100 mL of THF at 0 °C. After 3 h the reaction mixture was quenched with excess acetic acid. Workup as with **3** gave an oil, which was purified by flash chromatography (hexane:EtOAc, 2:8) to give **8** (0.81 g, 82% yield) as white crystals: mp 111 °C, identical by ^1H NMR, ^{13}C NMR, MS, and TLC with material prepared from methyl benzoate.

3,5-Dioxo-5-phenylpentanamide (9). Ethyl benzoylacetate (1.00 g, 5.20 mmol) was added slowly to 10.41 mmol of NaH (prepared from a 50% oil dispersion, 0.50 g, by washing with pentane) in 50 mL of THF at room temperature; the mixture was stirred until evolution of H_2 had ceased (0.25 h). The clear yellow solution of the anion was added dropwise to 11.44 mmol of dianion **2** in 100 mL of THF at 0 °C. The mixture was heated at 50 °C for 24 h, cooled at 0 °C, and quenched with excess acetic acid. Isolation as for **3** gave an oil, which was purified by flash chromatography (hexane:EtOAc, 1:9) to give **9** (0.50 g, 47% yield) as white crystals: mp 120 °C (lit.[14] mp 121–122 °C). Amide **9** was identical by ^1H NMR, ^{13}C NMR, IR and MS with authentic material.[13]

Methyl 2-Malonamoylphenylacetate (12). Methyl 2-(methoxycarbonyl)phenylacetate[15] (1.00 g, 4.81 mmol) was added slowly to 4.81 mmol of LDA in 50 mL of THF at 0 °C, and the mixture was allowed to stir for 0.5 h. The resulting orange solution of anion **10** was added slowly to 10.57 mmol of dianion **2** in 100 mL of THF at 0 °C. The mixture was stirred at room temperature for 12 h, cooled to 0 °C, and quenched with excess acetic acid. Workup as with **3** gave an oil, which was purified by flash chromatography (hexane:EtOAc, 1:9) to give **12** (0.46 g, 41% yield) as white crystals: mp 115–116 °C; ^1H NMR (CD_3SOCD_3) major tautomer (keto form) δ 3.58 (s), 3.81 (s), 3.83 (s), 5.31 (s), 7.08 (br), 7.38–7.50 (m), 7.91–8.01 (m); ^{13}C NMR (CD_3SOCD_3) mixture of tautomers δ 39.2, 48.7 51.3, 51.4, 92.1, 127.2, 127.9, 129.6, 129.8 131.7, 131.9, 132.5, 132.6, 134.3, 135.3, 136.6 168.2, 171.1, 172.0, 174.1, 197.5; IR (KBr) 3450, 3320, 3215, 1720, 1700, 1680, 1660, 1615, 1585, 1435, 1400, 1360, 1305, 1225, 1200, 1175, 1110, 1000, 980, 760 cm^{-1}; MS, m/e (relative intensity) 235 (M^+, not observed), 203 (78), 186 (24), 175 (7), 160 (110), 149 (14), 131 (18), 118 (100), 90 (55), 77 (21). Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.25; H, 5.57; N, 5.96. Found: C, 61.17; H, 5.47; N, 5.84.

2-Malonamoylphenylacetic Acid (13). 2-(Methoxycarbonyl)phenylacetic acid[15] (1.00 g, 5.15 mmol, was added slowly to 10.31 mmol of NaH (prepared from 0.50 g of 50% oil dispersion of NaH by washing with pentane) in 100 mL of THF at room temperature; the mixture was stirred until evolution of H_2 had ceased (0.25 h). The resulting grey gel of anion (presumably dianion **11**) was added slowly to 10.30 mmol of dianion **2** in 100 mL of THF at 0 °C. The mixture was stirred for 12 h at room temperature, cooled to 0 °C, and quenched with excess acetic acid.

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Workup as with **3** gave a brown oil, which crystallized after being subjected to high vacuum for 12 h. The material was washed with Et_2O, EtOAc, CH_2Cl_2, $CHCl_3$, and H_2O to yield **13** (0.65 g, 57% yield) as white crystals: mp 162 °C; ^1H NMR (CD_3SOCD_3) major tautomer (keto form) δ 3.78, 3.80, 7.00 (br), 7.24–7.98; ^{13}C NMR (CD_3SOCD_3) tautomeric mixture δ 48.8, 56.0, 92.1, 126.9, 127.8, 129.5, 131.5, 131.6, 132.5, 133.2, 134.9, 135.3, 137.0, 168.2, 172.1, 174.1, 197.5; IR (KBr) 3450, 3200, 1720, 1700, 1670, 1640, 1600, 1565, 1385, 1280, 1250, 1170, 1000, 980, 740, 670 cm^{-1}; MS, *m/e* (relative intensity) 221 (M^+, not observed), 203 (51), 186 (19), 160 (34), 149 (16), 135 (20), 119 (24), 118 (100), 90 (69), 77 (33). Anal. Calcd for $C_{11}H_{11}NO_4$: C, 59.71; H, 5.01; N, 6.13. Found: C, 59.52; H, 5.20; N, 6.13.

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Registry No. **2**, 89462-29-3; **3**, 79-05-0; **4**, 628-02-4; **5**, 102-93-2; **6**, 705-59-9; **7**, 52042-99-6; **8**, 3446-58-0; **9**, 87318-70-5; **10**, 89462-30-6; **11**, 89462-31-7; **12**, 89462-32-8; **13**, 89462-33-9; $CH_3CONHSiMe_3$, 13435-12-6; CH_3I, 74-88-4; *n*-BuBr, 109-65-9; $C_6H_5CH_2Cl$, 100-44-7; C_6H_5CHO, 100-52-7; $C_6H_5COC_6H_5$, 119-61-9; $C_6H_5COOCH_3$, 93-58-3; *N*-methoxy-*N*-methylbenzamide, 6919-61-5; ethyl 3-hydroxy-3-phenyl-2-propenoate sodium salt, 39113-53-6; ethyl benzoylacetate, 94-02-0; methyl 2-(methoxycarbonyl)phenylacetate, 716-43-8; 2-(methoxycarbonyl)phenylacetic acid, 14736-49-3.

Ring-Opening Reactions. 20. Synthesis of Polyunsaturated Vinyl Sulfides

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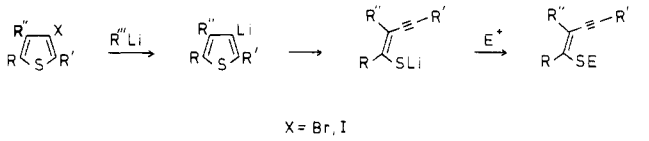
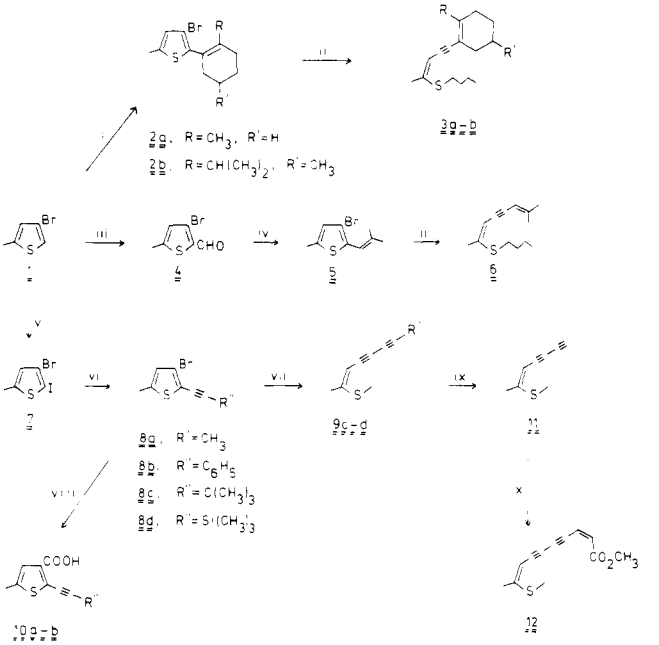
The ring-opening reaction of 3-thienyllithium derivatives constitutes a regio- and stereospecific synthesis of acetylenic vinyl sulfides (Scheme I). This kind of substance has attracted increased attention due to the possibilities presented to replace an alkyl- or arylthio group with carbon–carbon bonds.[1,2] Furthermore, the facile oxidation of sulfur to the corresponding sulfoxides and sulfones with *m*-chloroperbenzoic acid[3] presents an additional possibility of replacing the sulfur with carbon substituents.[4] This ring-opening reaction has recently been used for the total synthesis of naturally occurring substances from the plant genus *Anthemis*.[5] The scope and limitations of the reaction have been investigated rather extensively in our laboratories and have been reviewed.[6–10] It has been found that different substituents in the 2-position of the thiophene ring have more important effects on the rate of

Scheme I



Scheme II[a]



[a] (i) LDA, then 2-methylcyclohexanone or (–)-menthone, then *p*-TsOH, toluene, reflux; (ii) BuLi, 25 °C; BuBr; (iii) ref 13; (iv) $(CH_3)_2C{=}PPh_3$, THF; (v) I_2, HIO_3; (vi) RC≡CZnCl, $Pd(OAc)_2$, PPh_3; (vii) BuLi, 25 °C, MeI; (viii) BuLi, 0 °C, CO_2(s); (ix) KF·$2H_2O$, DMF; (x) (*Z*)-$BrCH{=}CHCO_2CH_3$, $Pd(OAc)_2$, PPh_3.

ring opening than 5-substituents. The rate is decreased by –I substituents in the 2-position or the reaction can be completely inhibited, whereas +I substituents have the opposite effect.

The effects of vinylic and acetylenic substituents have been investigated only very briefly. 2,5-Dimethyl-4-cyclohexenyl-3-thienyllithium derivatives with different cyclohexenyl substituents in the 4-position[11] ring-opened smoothly to give cross-conjugated polyunsaturated vinyl sulfides. Likewise, 5-(1-propynyl)-2-(trimethylsilyl)-3-thienyllithium underwent ring-opening to produce an enediynic sulfide.[5]

As pointed out earlier a more profound effect could be envisaged by introducing vinylic and acetylenic substituents in the 2-position. This would give a further possibility of making highly conjugated vinyl sulfides. A ring-opening would be expected to occur in view of the only very weak –I effect of these substituents. We now report our results on this matter.

Results and Discussion

The syntheses of the vinyl- and ethynylthiophenes are shown in Scheme II. 4-Bromo-2-methylthiophene (**1**)[12] was used as a common starting material.

The 2-cyclohexenylthiophenes **2** were obtained after metalation of **1** and reaction with 2-methylcyclohexanone and (–)-menthone, followed by dehydration. The iso-

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