Table III. Distances and Angles[a] for 3b, $C_{30}H_{20}Cl_4$

C1–C2	1.465 (13)	C1–C4	1.531 (12)	C1–C5	1.332 (12)
C2–C3	1.518 (12)	C2–C6	1.355 (13)	C3–C4	1.604 (12)
C3–C19	1.505 (12)	C4–C25	1.514 (12)	C5–C7	1.478 (10)
C6–C13	1.468 (11)	C10–Cl(1)	1.722	C16–Cl(2)	1.717
C22–Cl(3)	1.712	C28–Cl(4)	1.718		

C2–C1–C4	92.0 (7)	C2–C1–C5	130.5 (9)
C4–C1–C5	137.4 (9)	C1–C2–C3	93.1 (7)
C1–C2–C6	131.8 (9)	C3–C2–C6	135.0 (9)
C2–C3–C4	87.3 (7)	C2–C3–C19	118.7 (7)
C4–C3–C19	117.3 (7)	C1–C4–C3	87.4 (7)
C1–C4–C25	120.8 (7)	C3–C4–C25	118.0 (7)
C1–C5–C7	130.5 (8)	C2–C6–C13	129.7 (9)
C5–C7–C8	116.7 (6)		

Angle between planes C1–C2–C3 and C1–C4–C3: 5.3°

[a] Units of distances are Å, of angles, deg. Esd in parentheses, in units of least significant digit of the corresponding value. C–C distances and angles in phenyl rings were restrained to ideal values; all C–H distances were also restrained (see Experimental Section). An approximate esd of the C–Cl distance is 0.007 Å (taking the restraints into account).

Photolysis. A mixture of dimers **4b** and **5b** (200 mg) in ether was photolyzed for 2 h. Preparative TLC on silica gel gave dimer **6b**, mp 179.5–181 °C, mass spectrum M^+ m/e 520 (4 chlorine isotope cluster). A second spot gave a glass that appeared to be mainly dimer **7b** on the basis of NMR.

For **6b**: ^{1}H NMR ($CDCl_3$, 60 MHz) δ 4.75 m (2 H), 6.15 m (1 H), 6.81–7.68 m (17 H).

For **7b**: ^{1}H NMR ($CDCl_3$, 60 MHz) δ 4.75 m (2 H), 6.34 m (2 H), 6.80–7.32 m (16 H).

1,3-Bis(*p*-bromophenyl)propyne was prepared from (*p*-bromophenyl)acetylene[11,13] and *p*-bromobenzyl bromide by the procedure used for **15**. The yield of pure product, mp 75.0–75.5 °C, was only 13% owing to the presence of less soluble material that was difficult to remove. No attempt was made to improve this yield: ^{1}H NMR (CCl_4 60 MHz) δ 3.73 s (2 H), 7.21–7.46 (8 H, 2 overlapping p-disubstituted benzene patterns). Anal. Calcd for $C_{15}H_{10}Br_2$: C, 51.47; H, 2.88. Found: C, 51.57; H, 2.91.

1,3-Bis(*p*-bromophenyl)allene, 1c, mp 90–91.5 °C, was prepared in 88% yield as described for **1b**: ^{1}H NMR (CCl_4 60 MHz) δ 6.47 (2 H), 7.05–7.40 (8 H, p-disubstituted benzene pattern). Anal. Calcd for $C_{15}H_{10}Br_2$: C, 51.47; H, 2.88. Found: C, 51.68; H, 2.89.

Dimerization of 1c was carried out as described for **1b**. From 1.4 g were obtained 0.3 g of **3c**, mp 189.5–190.5 °C, 0.2 g of **4c**, and 0.14 g of **5c**. Anal. Calcd for $C_{30}H_{20}Br_4$: C, 51.47; H, 2.88. Found for **3c**: c, 51.47; H, 3.08. For **4c**: 51.58; H, 2.91.

For **3c**: ^{1}H NMR (CCl_4, 60 MHz) δ 4.92 s (2 H), 6.91 s (2 H), 6.72–7.21 m (16 H).

For **4c**: ^{1}H NMR (CCl_4, 60 MHz) δ 3.80 dd (1 H), 4.14 dd (1 H), 6.08 d (1 H), 7.20 (1 H), 7.05–7.58 m (16 H).

For **5c**: ^{1}H NMR (CCl_4, 60 MHz) δ 4.21 s (2 H), 6.88–7.53 (18 H).

X-ray Crystal Structure Analysis of 3b. Space group *Fdd2*, a = 51.101 (13) Å, b = 14.450 (4) Å, c = 14.015 (3) Å, V = 10348 Å^3, $C_{30}H_{20}Cl_4$, M_r = 522.27 g mol^{-1}, Z = 16, ρ_{calc} = 1.341, μ(Mo Kα) = 4.21 cm^{-1}, 3268 measured reflections, 2820 measured reflections (2807 unique, R_{merg} = 0.18) with h = 0–49, k = 0–18, l = 0–18, 1717 of these reflections with $F > 2\sigma(F)$, 1090 considered unobserved, 270 parameters refined, isotropic secondary-extinction factor 2×10^{-5}, maximum shift/error 0.04, peaks in final difference map 0.38/–0.40 e Å^{-3}, $w = 1/\sigma^2$, R = 0.092, R_w = 0.063, GOF = 1.35. Data were taken on a Syntex P1bar diffractometer with graphite monochromator; intensities were not corrected for absorption; structure solution by SHELX86;[14] refined with a locally-modified version of SHELX76.[15] The phenyl rings were refined as rigid bodies with ideal bond lengths and angles since there were very few significant intensities. Anisotropic displacement parameters were refined for all non-H atoms. All calculations were performed on the VAX 3100 using the UCLA Crystallographic Package[16] and the SHELX, local geometry and Cambridge Structural Database[17] programs.

Registry No. 1b, 143959-14-2; **1c**, 144345-78-8; **3b**, 144345-79-9; **3c**, 144408-50-4; **4b**, 144408-46-8; **4c**, 144345-80-2; **5b**, 144408-47-9; **5c**, 144408-48-0; **6b**, 144408-49-1; **7b**, 144489-50-9; **8b**, 144408-51-5; **15**, 144345-81-3; (*p*-chlorophenyl)acetylene, 873-73-4; *p*-chlorobenzyl bromide, 622-95-7; (*p*-bromophenyl)acetylene, 766-96-1; *p*-chloroacetophenone, 99-91-2; *p*-bromoacetophenone, 99-90-1.

Supplementary Material Available: Complete tables of atomic parameters, bond distances, angles and torsion angles, and least-squares planes for **3b** and further experimental details for preparation of the allenes and dimerization (6 pages). This material is contained in many libraries on microfiche, immediately following this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(13) Dufraisse, C.; Dequesnes, A. *Bull. Soc. Chim. Fr.* **1931**, *49*(4), 1880. Jacobs, T. L. The Synthesis of Acetylenes. *Organic Reactions*; John Wiley and Sons: New York, 1949; Vol. 5, Chapter 1, pp 50–51.

(14) Sheldrick, G. M. *Acta Crystallogr., Sect. A: Found. Crystallogr.* **1990**, *A46*, 467.

(15) Sheldrick, G. M. SHELX76, Program for crystal structure determination, University of Cambridge, England, 1976.

(16) *UCLA Crystallographic Package*: J. D. McCullough Laboratory of X-ray Crystallography, University of California, Los Angeles, 1984.

(17) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, S1.

Synthesis of β-Keto 1,3-Dithianes from Acetylenic Ketones

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β-Keto 1,3-dithianes are highly functionalized three-carbon units which are of much importance as potentially useful synthetic intermediates.[1] Procedures reported for the preparation of these compounds include α-alkylation of carbonyl compounds with 1,3-dithiane or its derivatives,[2] nucleophilic addition of 1,3-dithiane to epoxides followed by oxidation,[3] and conjugate reduction of α-oxo ketone dithio acetals.[4] In this paper we wish to disclose a new

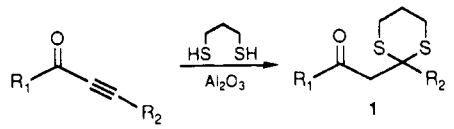
(1) (a) Corey, E. J.; Seebach, D. *Angew. Chem. Int. Ed. Engl.* **1965**, *4*, 1075. (b) Grobel, B.-T.; Seebach, D. *Synthesis* **1977**, 357.

(2) (a) Taylor, E. C.; LaMattina, J. L. *Tetrahedron Lett.* **1977**, 2077. (b) Hatanaka, K.; Tanimoto, S.; Sugimoto, T.; Okano, M. *Tetrahedron Lett.* **1981**, *22*, 3243. (c) Patterson, I.; Price, L. G. *Tetrahedron Lett.* **1981**, *22*, 2829.

(3) Stossel, D.; Chan, T. H. *J. Org. Chem.* **1988**, *53*, 4901.

0022-3263/92/1957-7349$03.00/0

Table I. Preparation of β-Keto 1,3-Dithianes by Michael Addition of 1,3-Propanedithiol to α,β-Acetylenic Ketones on the Surface of Alumina



entry	R_1	R_2	reaction time (h)	yield[a] (%)
a	i-Pr	H	4	70[b]
b	Ph	H	5	82[c]
c	4-OMe-C_6H_4	H	5	85[c]
d	3,4-$(OMe)_2C_6H_3$	H	5	80[c]
e	i-Pr	CH_2OCH_3	5	80[b]
f	Ph	CH_2OCH_3	6	75[b]

[a] All yields refer to pure isolated products, fully characterized by IR and ^1H NMR. [b] The reaction was carried out without solvent. [c] The reaction was run in CH_2Cl_2.

approach for the synthesis of β-keto 1,3-dithianes through double Michael addition of 1,3-propanedithiol to α,β-acetylenic ketones on the surface of alumina.[5]

In a typical procedure, the Michael addition was carried out by stirring activated neutral alumina with a mixture of acetylenic ketone and 1,3-propanedithiol at room temperature. The product was isolated by simple extraction with CH_2Cl_2 followed by purification through column chromatography. The results are reported in Table I.

As shown in Table I, several structurally varied α,β-acetylenic ketones underwent clean additions with 1,3-propanedithiol[6] by this procedure to give the corresponding β-keto 1,3-dithiane derivatives. No other side products have been isolated. The experimental procedure is very simple. The reactions are reasonably fast, and the yields are good.

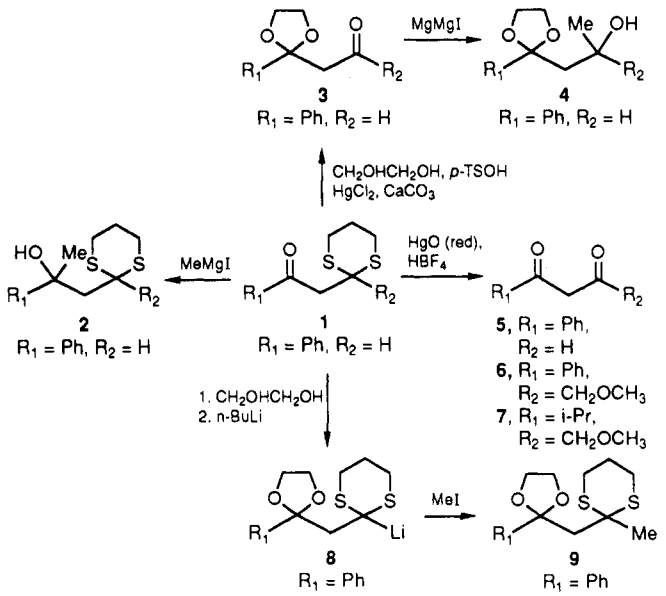
β-Keto 1,3-dithianes are versatile synthetic intermediates. For example, the 1,3-dithiane substituent may, if desired, be hydrolyzed to a carbonyl group or converted into a methyl group by reductive disulfurization.[2c] Alkylation with this three-carbon unit has also been utilized in several syntheses.[3] To illustrate a few synthetic potentialities of these dithianes, prepared by the present procedure, have been demonstrated in Scheme I. Moreover, this can be exploited in many more useful ways as an acyl carbanion equivalent.[1]

In conclusion, this novel route of double Michael addition of 1,3-propanedithiol to easily available[7] α,β-acetylenic ketones provides an easy and convenient access to β-keto 1,3-dithiane derivatives which have great potential for useful manipulations.

Experimental Section

General. Melting points were determined in a glass disk with an electrical bath (Reichert, Austria) and are uncorrected. ^1H NMR spectra were obtained at 60 MHz in CCl_4 solutions unless specified otherwise. TLC was done on precoated silica gel plates (E. Merck). Silica gel (60–120 mesh, SRL, India) was used for column chromatography. Alumina (neutral, Brockmann activity, grade 1 for column chromatography, SRL, India) was activated by heating at 200 °C for 4 h followed by cooling under N_2 and was used for all the reactions. (Activated alumina can be stored under N_2 for 1 week for subsequent uses without much loss of activity.) THF was distilled from benzophenone–sodium under N_2 immediately before use. Petroleum ether refers to the fraction boiling between 60 and 80 °C.

Scheme I



The starting α,β-acetylenic ketones were obtained by condensation[8] of acetylene or its derivative with an appropriate aldehyde followed by Jones oxidation.[9]

Representative Procedure for the Preparation of α,β-Acetylenic Ketones. 1-(3,4-Dimethoxyphenyl)prop-2-yn-1-one. To the suspension of sodium acetylide in liquid NH_3 (prepared in situ by the portionwise addition of sodium (580 mg, 25 mmol) into liquid NH_3 (250 mL) bubbled continuously with acetylene) was added dropwise 3,4-dimethoxybenzaldehyde (3.3 g, 20 mmol) in ether (20 mL) under stirring. The reaction mixture was stirred for an additional 4 h with continuous bubbling of acetylene. The reaction mixture was then quenched with solid NH_4Cl (2 g) and after evaporation of NH_3 the residue was extracted with CH_2Cl_2 (4 × 20 mL), washed with brine, and dried (Na_2SO_4). Evaporation of solvent produced the corresponding alcohol, 1-(3,4-dimethoxyphenyl)prop-2-yn-1-ol (3 g, 79%): mp 96 °C (ether); IR (KBr) 2110, 3240, 3100–3490 (broad) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.63 (1 H, d, J = 2 Hz), 3.89 (6 H, s), 5.40 (1 H, d, J = 2 Hz), 6.79–7.13 (3 H, m). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 69.02; H, 6.34.

This alcohol (1.92 g, 10 mmol) was oxidized by Jones reagent at 0–5 °C under N_2[9] to furnish the acetylenic ketone, 1-(3,4-dimethoxyphenyl)prop-2-yn-1-one (1.5 g, 78%): mp 115 °C; IR (KBr) 1635, 2100, 3200 cm^{-1}; ^1HNMR ($CDCl_3$) δ 3.36 (1 H, s), 3.93 (3 H, s), 3.96 (3 H, s), 6.99 (1 H, d, J = 8 Hz), 7.53 (1 H, d, J = 2 Hz), 7.99 (1 H, dd, J = 8 Hz, 2 Hz). Anal. Calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.58; H, 5.26.

Representative Procedures for the Preparation of β-Keto 1,3-Dithianes. Method A. On the Surface of Alumina without Solvent: 1-(1,3-Dithian-2-yl)3-methylbutan-2-one (1a). To a stirred mixture of 4-methylpent-1-yn-3-one[9] (96 mg, 1 mmol) and 1,3-propanedithiol (108 mg, 1 mmol) was added neutral alumina (700 mg) in three portions during 5 min at 25 °C (if necessary, ice–water was used for cooling to avoid a rise in temperature). Stirring was continued for 4 h as monitored by TLC for complete reaction. The solid mass was then transferred

(4) (a) Gammill, R. B.; Sobieray, D. M.; Gold, P. M. *J. Org. Chem.* **1981**, *46*, 3555. (b) Choi, B.; Youn, I. K.; Pak, C. S. *Synthesis* **1988**, 792.
(5) Ranu, B. C.; Bhar, S.; Sarkar, D. C. *Tetrahedron Lett.* **1991**, *32*, 2811. (b) Ranu, B. C.; Bhar, S. *Tetrahedron* **1992**, *48*, 1327.
(6) 1,2-Ethanedithiol was also found to give a similar Michael adduct.
(7) Zweifel, G.; Polston, N. L. *J. Am. Chem. Soc.* **1970**, *92*, 4068. (b) Trost, B. M.; Schmidt, T. *J. Am. Chem. Soc.* **1988**, *110*, 2301. (c) Bartoli, G.; Cimarelli, C.; Palmieri, G.; Bosco, M.; Dalpozzo, R. *Tetrahedron Lett.* **1991**, *32*, 7091.
(8) (a) Jones, E. R. H.; McCombie, J. T. *J. Chem. Soc.* **1942**, 733. (b) Saunders, J. H. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. 3, p 416. (c) Lu, X.; Guo, C.; Ma, D. *J. Org. Chem.* **1991**, *56*, 6712.
(9) Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39.
(10) Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, *36*, 3553.
(11) Ranu, B. C.; Sarkar, D. C. *Synth. Commun.* **1987**, *17*, 155.
(12) Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231.

to a filtering column packed with a short plug of silica gel, and eluted with CH_2Cl_2. Evaporation of solvent furnished the crude product which was purified by column chromatography followed by crystallization (ether-petroleum ether) to furnish pure **1a** (140 mg, 70%): mp 51–52 °C (lit.[4b] 52–52.5 °C); IR (KBr) 1710 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 1.12 (6 H, d, J = 8 Hz), 1.72–2.24 (2 H, m), 2.48–3.00 (7 H, m), 4.54 (1 H, t, J = 8 Hz). Anal. Calcd for $C_9H_{16}OS_2$: C, 52.93; H, 7.90. Found: C, 53.15; H, 7.92.

This method was followed for liquid acetylenic ketones. The preparations of **1e** and **1f** refer to this procedure.

1-[2-(Methoxymethyl)-1,3-dithian-2-yl]-3-methylbutan-2-one (**1e**) was obtained as a viscous oil (400 mg from 280 mg of 1-methoxy-5-methylhex-2-yn-4-one, 80%): IR (neat) 1710 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 1.09 (6 H, d, J = 6 Hz), 1.84–2.12 (2 H, m), 2.52–3.12 (5 H, m), 3.04 (2 H, s), 3.4 (3 H, s), 3.9 (2 H, s). Anal. Calcd for $C_{11}H_{20}O_2S_2$: C, 53.21; H, 8.12. Found: C, 53.36; H, 8.09.

1-Phenyl-2-[2-(methoxymethyl)-1,3-dithian-2-yl]ethan-1-one (**1f**) was also obtained as a viscous oil (220 mg from 180 mg of 1-phenyl-4-methoxybut-2-yn-1-one, 75%): IR (neat) 1690 cm^{-1}; ^1H NMR δ 1.90–2.16 (2 H, m), 2.56–2.93 (4 H, m), 3.40 (3 H, s), 3.50 (2 H, s), 3.85 (2 H, s), 7.33–8.06 (5 H, m). Anal. Calcd for $C_{14}H_{18}O_2S_2$: C, 59.56; H, 6.43. Found: C, 59.42; H, 6.45.

Method B. On the Surface of Alumina in CH_2Cl_2: 1-Phenyl-2-(1,3-dithian-2-yl)ethan-1-one (1b). To a stirred solution of 1-phenylprop-2-yn-1-one[9] (130 mg, 1 mmol) and 1,3-propanedithiol (108 mg, 1 mmol) in CH_2Cl_2 (5 mL) was added activated neutral alumina (400 mg) in portions as above. After completion of the reaction (5 h, TLC) the reaction mixture was filtered through a short plug of silica gel followed by washing of the column with additional CH_2Cl_2 (25 mL). The filtrate and the washings were evaporated to give the crude product which was purified by column chromatography followed by crystallization (ether–petroleum ether) to yield **1b** (195 mg, 82%): mp 60–62 °C (lit.[3,4b] mp 59–61 °C); IR (KBr) 1690 cm^{-1}; ^1H NMR δ 1.67–2.23 (2 H, m), 2.76–2.96 (4 H, m), 3.23 (2 H, d, J = 8 Hz), 4.6 (1 H, t, J = 8 Hz), 7.33–8.00 (5 H, m). Anal. Calcd for $C_{12}H_{14}OS_2$: C, 60.50; H, 5.92. Found: C, 60.45; H, 6.09.

This procedure was followed for solid acetylenic ketones to prepare **1c** and **1d**.

1-(4-Methoxyphenyl)-2-(1,3-dithian-2-yl)ethan-1-one (**1c**) was isolated as a crystalline solid (230 mg from 160 mg of 1-(4-methoxyphenyl)prop-2-yn-1-one, 85%): mp 74 °C; IR (KBr) 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.76–2.16 (2 H, m), 2.83–3.03 (4 H, m), 3.30 (2 H, d, J = 7 Hz), 3.90 (3 H, s), 4.70 (1 H, t, J = 7 Hz), 6.96 (2 H, d, J = 9 Hz), 8.0 (2 H, d, J = 9 Hz). Anal. Calcd for $C_{13}H_{16}O_2S_2$: C, 58.20; H, 6.01. Found: C, 58.11; H, 5.89.

1-(3,4-Dimethoxyphenyl)-2-(1,3-dithian-2-yl)ethan-1-one (**1d**) was obtained as a crystalline solid (240 mg from 190 mg of 1-(3,4-dimethoxyphenyl)prop-2-yn-1-one, 80%): mp 92–93 °C; IR (KBr) 1680 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 1.76–2.26 (2 H, m), 2.84–3.02 (4 H, m), 3.32 (2 H, d, J = 8 Hz), 3.94 (3 H, s), 3.96 (3 H, s), 4.70 (1 H, t, J = 8 Hz), 6.92 (1 H, d, J = 8 Hz), 7.56 (1 H, s), 7.6 (1 H, d, J = 8 Hz). Anal. Calcd for $C_{14}H_{18}O_3S_2$: C, 56.37; H, 6.08. Found: C, 56.26; H, 6.13.

Although these procedures were shown for 1 mmol quantities, the reaction was also carried out on a multigram scale to afford similarly good yields.[13]

1-(1,3-Dithian-2-yl)-2-phenylpropan-2-ol (2). To a stirred solution of **1b** (238 mg, 1 mmol) in ether (5 mL) was added dropwise an ethereal solution of MeMgI (1.2 mL, 1.75 mmol) under argon. The reaction mixture was stirred at 0 °C for 1 h and left overnight. The mixture was then decomposed with cold saturated NH_4Cl solution and extracted with ether (3 × 10 mL). The ether extract was washed with brine, dried (Na_2SO_4), and evaporated to furnish the crude alcohol which was purified through a short column of silica gel to produce **2** as an oil, yield 216 mg (85%): IR ($CHCl_3$) 3300–3600 cm^{-1}; ^1H NMR δ 1.53 (3 H, s), 1.73–2.06 (2 H, m), 2.32 (2 H, d, J = 6 Hz), 2.66–2.83 (4 H, m), 3.3 (1 H, broad), 3.73 (1 H, t, J = 6 Hz), 7.03–7.33 (5 H, m). Anal. Calcd for $C_{13}H_{18}OS_2$: C, 61.40; H, 7.14. Found: C, 61.36; H, 7.16.

3,3-(Ethylenedioxy)-3-phenylpropan-1-al (3). A mixture of **1b** (1.5 g, 6.3 mmol), ethylene glycol (781 mg, 12.6 mmol), *p*-toluenesulfonic acid (100 mg), and dry benzene (30 mL) was stirred and refluxed under N_2 for 7 h with a Dean-Stark water separator. The reaction mixture was then washed with saturated aqueous $NaHCO_3$ solution and brine and dried over Na_2SO_4. Evaporation of solvent under reduced pressure followed by crystallization afforded the corresponding acetal (1.70 g, 98%): mp 72–73 °C; ^1H NMR ($CDCl_3$, 100 MHz) δ 1.72–2.2 (2 H, m), 2.32 (2 H, d, J = 8 Hz), 2.76–2.9 (4 H, m), 4.04 (1 H, t, J = 8 Hz), 3.72–4.2 (4 H, m), 7.28–7.52 (5 H, m). Anal. Calcd for $C_{14}H_{18}O_2S_2$: C, 59.56; H, 6.43. Found: C, 59.60; H, 6.42. This acetal (70 mg, 0.25 mmol) in 80% aqueous CH_3CN (2 mL) was added at 25 °C to a stirred suspension of $HgCl_2$ (271 mg, 1 mmol) and $CaCO_3$ (125 mg, 1.25 mmol) in the same solvent (4 mL).[10] This mixture was then refluxed for 5 h under argon and filtered through a sintered glass funnel. The organic phase was washed with 5 M aqueous ammonium acetate solution and brine, dried (Na_2SO_4), and evaporated to leave the crude product which was purified by chromatography through a short column of silica gel to afford **3** as an oil (40 mg, 80%): IR (neat) 1720 cm^{-1}; ^1H NMR δ 2.79 (2 H, d, J = 3 Hz), 3.63–4.26 (4 H, m), 7.16–7.46 (5 H, m), 9.70 (1 H, t, J = 3 Hz). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68.63; H, 6.21.

4,4-(Ethylenedioxy)-4-phenylbutan-2-ol (4). The alcohol **4** (40 mg, 90%) was obtained from **3** (40 mg, 0.208 mmol) as an oil following the same procedure as in **2**: IR (neat) 3300–3600 cm^{-1}; ^1H NMR δ 1.06 (3 H, d, J = 6 Hz), 1.95 (2 H, d, J = 6 Hz), 3.0 (1 H, broad), 3.6–4.2 (5 H, m), 7.2–7.5 (5 H, m). Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.28; H, 7.80.

1-Phenyl-2-formylethan-1-one (5).[14] To a stirred suspension of red HgO (108 mg, 0.5 mmol) and HBF_4 (48%, 0.1 mL, 0.5 mmol) in 85% aqueous THF (2 mL) was added a solution of **1b** (60 mg, 0.25 mmol) in THF (0.5 mL) at room temperature under N_2.[11] This mixture was stirred for 2 h, diluted with ether (10 mL), and filtered. The residue was also washed with additional ether (10 mL). The combined organic phase was washed with $NaHCO_3$ solution and brine, dried (Na_2SO_4), and evaporated to leave the crude product which was purified by column chromatography over silica gel to produce **5** (90% pure by ^1H NMR) as an oil (20 mg, 54%): ^1H NMR δ 6.13 (1 H, d, J = 4 Hz), 7.3–7.93 (5 H, m), 8.2 (1 H, d, J = 4 Hz).

1-Phenyl-4-methoxybutane-1,3-dione (6) (95% pure by ^1H NMR) (oil, 30 mg from 75 mg of **1f**, 62%): ^1H NMR δ 3.43 (3 H, s), 4.0 (2 H, s), 6.5 (1 H, s), 7.40–8.0 (5 H, m).

1-Methoxy-5-methylhexane-2,4-dione (7) (95% pure by ^1H NMR) (oil, 28 mg from 65 mg of **1e**, 66%): ^1H NMR δ 1.25 (6 H, d, J = 6 Hz), 2.26–2.76 (1 H, m), 3.4 (3 H, s), 3.9 (2 H, s), 5.73 (1 H, s).

In spite of several attempts, microanalytical data for these compounds 5–7 did not agree well with their elemental composition because of their tendency to decompose during purification.

1,1-(Ethylenedioxy)-1-phenyl-2-(2-methyl-1,3-dithian-2-yl)ethane (9). To a stirred solution of the acetal of **1b** (prepared during the preparation of **3**) (140 mg, 0.5 mmol) in anhydrous THF (3 mL) was added dropwise *n*-BuLi (38.4 mg, 0.6 mmol, 0.5 mL of 1.2 M solution in hexane) under N_2 at −20 °C.[12] Stirring was continued at that temperature for 2 h, and MeI (0.31 mL, 5 mmol) was added at −78 °C. After being stirred at −78 °C for another 2 h, the reaction mixture was allowed to attain rt and left overnight. This was then decomposed with cold water and extracted with ether (4 × 10 mL). The combined ether extract was washed with brine, dried (Na_2SO_4), and evaporated to leave the crude product which was purified by column chromatography over silica gel to furnish **9** as oil (88 mg, 60%): ^1H NMR δ 1.6–2.13 (m), 2.0 (s), 2.06 (s) (total 7 H), 2.33–2.83 (4 H, m), 3.43–4.13 (4 H, m), 7.13–7.6 (5 H, m). Anal. Calcd for $C_{15}H_{20}O_2S_2$: C, 60.80; H, 6.80. Found: C, 60.65; H, 6.87.

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(13) Compound **1b** (3.7 g, 78%) was obtained from the reaction (8 h) of 1-phenylprop-2-yn-1-one (2.6 g, 20 mmol) and 1,3-propanedithiol (2.16 g, 20 mmol) in CH_2Cl_2 (80 mL) in the presence of alumina (7 g) following method B.

(14) (a) Bhagwan, J.; Tyagi, A.; Joshi, Y. C.; Tyagi, R. P.; Joshi, B. *Chem. Abst.* **1983**, *98*, 179253h. C.; Mangal, H. N. *J. Inst. Chem.* **1982**, *54*, 266; *Chem. Abstr.* **1983**, *98*, 179253h. (b) Acheampong, Y. B.; Niger, J. *Pharm.* **1984**, *15*, 18; *Chem. Abst.* **1984**, *101*, 51579g.

EMR-II). S.B. and R.C. also thank CSIR for awarding them JRF and RA, respectively.

Supplementary Material Available: ^{1}H NMR data of 4-methylpent-1-yn-3-one, 1-phenylprop-2-yn-1-one, 1-(4-methoxyphenyl)prop-2-yn-1-one, 1-methoxy-5-methylhex-2-yn-4-one, and 1-phenyl-4-methoxybut-2-yn-1-one and ^{1}H NMR spectra of all the starting acetylenic ketones and compounds **1a-1f**, **2-7**, and **9** (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

New Preparation of Pyridines from Enamino Nitriles[1]

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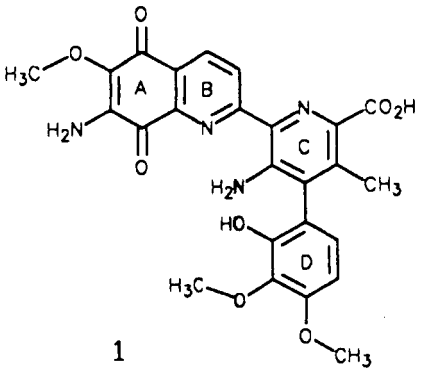
Numerous synthetic sources of the pyridine ring have been reviewed.[2-4] There remained a need for a pyridine preparation with few limitations. Indeed, the synthesis of the multisubstituted pyridine ring C of Streptonigrin (1),[5] with five different substituents, has presented quite



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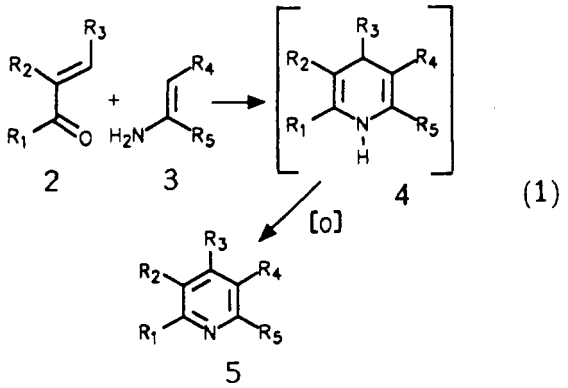
a synthetic challenge. It was the key to several reported total syntheses.[6,7] The construction of a pyridine ring C of Streptonigrin with five appropriate groups was best accomplished by sequential inverse electron demand aza Diels-Alder reactions.[6] However, these two steps achieved only a 28% yield of the desired pyridine due to lack of regiochemical control. Kelly and Liu[8] published an elegant "one-pot" but multiple-step pyridine synthesis from *N,N*-dimethylhydrazone enolates. Regioselective control was achieved, but the yields of products which had four or five substituents was low (14-45%). Therefore, we proposed to develop an alternate method for synthesizing multisubstituted pyridines which could similarly achieve regioselective control of all groups.

Background

The so-called "3 + 3" pyridine synthesis,[4] using α,β-unsaturated carbonyls **2** as the 3-carbon component and primary enamines **3** as the 2-carbon component, had the potential to meet our goals (eq 1).[9] Unsaturated ketones **2** are easily prepared with a variety of substituents R_1-R_3.[10,11] The Michael addition of enamines **3**, to these propenones **2**, followed by ring closure to **4**, allows regioselective control of substituents R_1-R_5.[12,13] This method has previously been only marginally successful. The dihydropyridines **4** initially formed often underwent further reactions, including disproportionation, to a mixture of products. Subsequent oxidation of the isolated dihydropyridines **4** with HNO_3, or other reagents, also gave pyridines **5** but with overall poor yield.



(1)

Primary enamines of type **3** are not stable unless conjugated with an electron-withdrawing group on the β-carbon. Before now, this has been the nature of substituent R_4. We envisioned including one additional leaving group on either substrate, **2** or **3**. For example, reaction of **2** with a **3** that was modified to include another elimination would directly afford an aromatic ring. Aromatization would also provide driving force for the reaction.

Oxime[2] and hydrazone derivatives[4,8] of 1,5-diketones **6** have been employed to provide for this type of elimination. Acidic conditions were required for ring closure as well as protonation of the leaving group for the final elimination to the aromatic pyridine **5**. There are far fewer examples of pyridines synthesized with leaving groups that are not attached to nitrogen.[4,12,14,15] Kronke's[15] use of the pyri-

(1) Presented in part at the 42nd Southeast/46th Southwest Combined Regional Meeting of the American Chemical Society, New Orleans, LA; December 1990; Abstr. 393.

(2) (a) Brody, F.; Rudy, P. R. In *Pyridine and Its Derivatives*; Klingsberg, E., Ed.; Interscience: New York, 1960; Vol. 14, Part 1, Chapter 2. (b) Boodman, N. S.; Hawthorne, J. O.; Masciantonio, P. X.; Simon, A. W. In *Pyridine and Its Derivatives*; Abramovitch, R. A., Ed.; Wiley-Interscience: New York, 1972; Vol. 14, Supplement Part 1, Chapter 2.

(3) Newkome, G. R.; Paudler, W. W. *Contemporary Heterocyclic Chemistry*; Wiley: New York, 1982.

(4) *Pyridine and Its Derivatives*; Newkome, G. R., Ed.; Wiley: New York, 1984; Vol. 14, Part 5.

(5) Rao, K. V.; Biemann, K.; Woodward, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2532.

(6) Boger, D. L.; Panek, J. S. *J. Am. Chem. Soc.* **1985**, *107*, 5745.

(7) (a) Weinreb, S. M.; Basha, F. Z.; Hibino, S.; Khatri, N. A.; Kim, D.; Pye, W. E.; Wu, T.-T. *J. Am. Chem. Soc.* **1982**, *104*, 536. (b) Kende, A. S.; Lorah, D. P.; Boatman, R. J. *J. Am. Chem. Soc.* **1981**, *103*, 1271.

(8) Kelly, T. R.; Liu, H.-t. *J. Am. Chem. Soc.* **1985**, *107*, 4998.

(9) Substituent groups are represented generically: R is not limited to alkyl.

(10) The Perkin, Claisen-Schmidt, and Knoevenagel condensations have been extensively reviewed: (a) Johnson, J. R. *Org. React.* **1942**, *1*, 210. (b) Jones, G. *Ibid.* **1967**, *15*, 204. (c) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin: Menlo Park, CA, 1972; Chapter 10.

(11) A typical example is the preparation of chalcone (**10**): Kohler, E. P.; Chadwell, H. M. *Organic Syntheses*; Wiley: New York, 1941; Collect. Vol. I, p 78.

(12) (a) Meyer, V.; Irmscher, J. *J. Prakt. Chem.* **1908**, *78*, 497. (b) Courts, A.; Petrow, V. *J. Chem. Soc.* **1952**, 1, 334. (c) Chatterjea, J. N.; Prasad, K. *J. Indian Chem. Soc.* **1955**, *32*, 371. (d) Chatterjea, J. N.; Prasad, K. *J. Sci. Ind. Res. (India)* **1955**, *14B*, 383.

(13) Chatterjea, J. N. *J. Indian Chem. Soc.* **1952**, *29*, 323.

0022-3263/92/1957-7352$03.00/0