triethylamine (0.9 mmol) in DMF (1 mL) was added to the reaction mixture over a 0.5-h period by means of a syringe pump. The reaction mixture was stirred at 2 °C for a further 0.5 h and then at room temperature for 2 h. The solvent was removed under reduced pressure and the residue was partitioned between ethyl acetate or methylene chloride (30 mL) and water (10 mL). The organic layer was separated, dried (anhydrous $MgSO_4$), and filtered. The filtrate was evaporated to dryness under reduced pressure and the residue worked up as described below.

2-Pivaloylpterin Cycloadduct 21a. The residue was chromatographed on silica gel, eluting with a mixture of 1% methanol in chloroform. The fractions containing the pure product were combined and the solvent was removed in vacuo to give 220 mg (65%) of a colorless solid, mp 222-223 °C: NMR ($CDCl_3$) δ 1.37 (s, 9 H), 3.67 (m, 1 H), 4.03 (m, 1 H), 5.88 (m, 1 H), 7.39 (m, 5 H), 8.38 (br, 1 H), 9.59 (s, 1 H), 12.48 (br, 1 H); IR (KBr) 3300-3680 (br), 3020-3300 (br), 1725, 1685, 1620 cm^{-1}; $C_{20}H_{20}N_6O_3$ m/z 392.1596, found m/z 392.1589. Anal. Calcd for $C_{20}H_{20}N_6O_3$: C, 61.22; H, 5.14; N, 21.42. Found: C, 61.15; H, 5.14; N, 21.37.

2-Pivaloylpterin Cycloadduct 22a. The residue was recrystallized from ethanol to give 208 mg (62%) of a colorless microcrystalline solid, mp 278-280 °C: NMR ($CDCl_3$) δ 1.38 (s, 9 H), 7.44 (s, 1 H), 7.53 (m, 3 H), 7.89 (m, 2 H), 8.46 (br, 1 H), 9.67 (s, 1 H), 12.50 (br, 1 H); IR (KBr) 3340-3680 (br), 3020-3320 (br), 1720, 1685, 1620 cm^{-1}; HRMS calcd for $C_{20}H_{18}N_6O_3$ m/z 390.1440, found m/z 390.1445. Anal. Calcd for $C_{20}H_{18}N_6O_3 \cdot 0.75H_2O$: C, 59.42; H, 4.83; N, 20.80. Found: C, 59.52; H, 4.72; N, 20.83.

2-Pivaloylpterin Cycloadduct 23a. The residue was chromatographed on silica gel, using ethyl acetate as eluent, the fractions containing the product were combined (R_f = 0.4 in ethyl acetate on silica gel plates), and the solvent was removed under reduced pressure. Recrystallization of the residue from ethanol gave 190 mg (62%) of a cream-colored microcrystalline solid, mp 232-233 °C: NMR ($CDCl_3$) δ 1.38 (s, 9 H), 3.48 (s, 3 H), 4.65 (s, 2 H), 7.15 (s, 1 H), 8.80 (br, 1 H), 9.61 (s, 1 H), 12.50 (br, 1 H); IR (KBr) 3360-3620 (br), 3020-3360 (br), 1725, 1685, 1620 cm^{-1}; HRMS calcd for $C_{16}H_{18}N_6O_4$ m/z 358.1389, found m/z 358.1379. Anal. Calcd for $C_{16}H_{18}N_6O_4$: C, 53.63; H, 5.06; N, 23.45. Found: C, 53.66; H, 5.08; N, 23.43.

2-Pivaloylpterin Cycloadduct 24a. The residue was chromatographed on silica gel, eluting with ethyl acetate. The fractions containing the product were combined (R_f = 0.5 in ethyl acetate using silica gel plates) and the solvent was removed under reduced pressure. The residue was triturated with diethyl ether and the solid was collected by vacuum filtration to give 200 mg (57%) of colorless microcrystals, mp >200 °C (gradual dec): NMR ($CDCl_3$) δ 1.36 (s, 9 H), 1.83 (s, 3 H), 3.78 (m, 2 H), 7.27-7.49 (m, 5 H), 8.65 (br, 1 H), 9.54 (s, 1 H), 12.48 (br, 1 H); IR (KBr) 3340-3680 (br), 3020-3320 (br), 1725, 1685, 1620 cm^{-1}; HRMS calcd for $C_{21}H_{22}N_6O_3$ m/z 406.1753, found m/z 406.1743. Anal. Calcd for $C_{21}H_{22}N_6O_3$: C, 62.06; H, 5.46; N, 20.68. Found: C, 61.96; H, 5.42; N, 20.62.

2-Pivaloylpterin Cycloadduct 25a. The residue was chromatographed on silica gel, using a mixture of 2% methanol in chloroform as eluent. The fractions containing the pure product were combined and the solvent was removed under reduced pressure to give 180 mg (58%) of a colorless solid, mp 270-271 °C: NMR ($CDCl_3$) δ 1.38 (s, 9 H), 2.45 (m, 2 H), 3.62 (m, 1 H), 4.07 (m, 1 H), 4.42 (m, 1 H), 6.41 (d, 1 H, J = 6 Hz), 8.45 (br, 1 H), 9.53 (s, 1 H), 12.48 (br, 1 H); IR (KBr) 3300-3680 (br), 3020-3300 (br), 1725, 1685, 1620 cm^{-1}; HRMS calcd for $C_{16}H_{18}N_6O_4$ m/z 358.1389, found m/z 358.1373. Anal. Calcd for $C_{16}H_{18}N_6O_4 \cdot 0.25H_2O$: C, 52.97; H, 5.10; N, 23.17. Found: C, 52.99; H, 5.13; N, 23.15.

2-Pivaloylpterin Cycloadduct 26a. The residue was recrystallized from absolute ethanol to give 137 mg (46%) of a cream-colored microcrystalline solid, mp 233-234 °C: NMR ($CDCl_3$) δ 1.37 (s, 9 H), 3.61 (m, 2 H), 3.68 (m, 2 H), 3.88 (m, 1 H), 5.01 (m, 1 H), 8.40 (br, 1 H), 9.50 (s, 1 H), 12.50 (br, 1 H); IR (KBr) 3300-3680 (br), 3020-3300 (br), 1725, 1685, 1620 cm^{-1}; HRMS calcd for $C_{15}H_{18}N_6O_4$ m/z 346.1389, found m/z 346.1390. Anal. Calcd for $C_{15}H_{18}N_6O_4 \cdot 0.25H_2O$: C, 51.31; H, 5.27; N, 23.94. Found: C, 51.40; H, 5.29; N, 23.97.

General Procedure for the Preparation of the Pterin Cycloadducts 21-24b by Hydrolysis of the Corresponding 2-Pivaloylpterin Cycloadducts 21-24a. A mixture of the 2-pivaloylpterin cycloadduct (100 mg), dioxane (10 mL), and 1.0 N hydrochloric acid (0.2 mL) was heated at 70-80 °C until all the starting material had been consumed (1-2 h). The progress of the hydrolysis was monitored by TLC. The solvent was removed under reduced pressure and the residue was triturated with water. The solid was collected by vacuum filtration, washed well with water, and ethanol, and then with diethyl ether, and dried at 80 °C in vacuo.

Pterin cycloadduct 21b: 58 mg (73%) of a cream-colored microcrystalline powder was obtained, mp >300 °C: NMR (Me_2SO-d_6/2 drops of CF_3CO_2D) δ 3.43 (m, 1 H), 4.0 (m, 1 H), 5.85 (m, 1 H), 7.32-7.53 (m, 5 H), 9.27 (s, 1 H); HRMS calcd for $C_{15}H_{12}N_6O_2$ m/z 308.1021, found m/z 308.1046. Anal. Calcd for $C_{15}H_{12}N_6O_2 \cdot 1.375H_2O$: C, 54.04; H, 4.35; N, 25.22. Found: C, 54.08; H, 4.04; N, 25.19.

Pterin cycloadduct 22b: 68 mg (78%) of a cream-colored microcrystalline powder was obtained, mp >300 °C: NMR (Me_2SO-d_6/2 drops of CF_3CO_2D) δ 7.55 (m, 3 H), 7.61 (s, 1 H), 8.0 (m, 2 H), 9.29 (s, 1 H). Anal. Calcd for $C_{15}H_{10}N_6O_2 \cdot 1.375H_2O$: C, 54.37; H, 3.63; N, 25.37. Found: C, 54.25; H, 3.45; N, 23.25.

Pterin cycloadduct 23b: 61 mg (80%) of a cream-colored microcrystalline powder was obtained, mp >300 °C: NMR (Me_2SO-d_6/2 drops of CF_3CO_2D) δ 3.30 (s, 3 H), 4.58 (s, 2 H), 7.05 (s, 1 H), 9.31 (s, 1 H). Anal. Calcd for $C_{11}H_{10}N_6O_3 \cdot 0.25H_2O$: C, 47.36; H, 3.76; N, 30.14. Found: C, 47.48; H, 3.74; N, 29.90.

Pterin cycloadduct 24b: 57 mg (72%) of a cream-colored microcrystalline powder was obtained, mp >300 °C: NMR (Me_2SO-d_6/2 drops of CF_3CO_2D) δ 1.72 (s, 3 H), 3.6 (m, 2 H), 7.27-7.5 (m, 5 H), 9.19 (s, 1 H). Anal. Calcd for $C_{16}H_{14}N_6O_2 \cdot 2H_2O$: C, 53.63; H, 3.91; N, 23.46. Found: C, 53.93; H, 4.23; N, 23.55.

Acknowledgment. We are deeply indebted to Dr. Thomas Shepard, who first demonstrated the cycloaddition reaction between **2a** and 2,3-dihydrofuran to give the cycloadduct **7**.

Model Studies Directed toward the Molybdenum Cofactor: 2-Alkylidene- and 2-(Phenylimino)-1,3-dithioles from Acetylenes

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The cycloaddition of activated alkynes, among them 6-alkynylpterins, with the tributylphosphine–carbon disulfide complex followed by a Wittig reaction of the resulting ylid with carbonyl compounds or nitrosobenzene affords novel 2-alkylidene- or 2-(phenylimino)-1,3-dithioles in moderate to very good yields. The pterin-substituted species are potential intermediates in the synthesis of the molybdenum cofactor.

The molybdenum cofactor (proposed structure **1** for the xanthine oxidase cofactor),[1] essential for the activity of several redox enzymes,[2] contains a molybdenum dithiolene ring which is, as well as the underlying enedithiol moiety,

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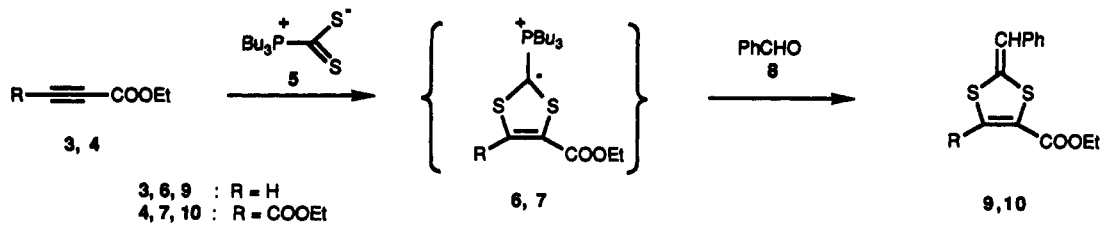
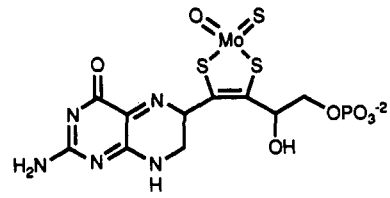
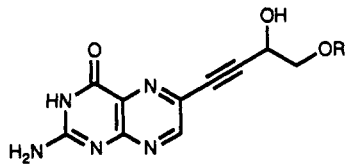
Scheme I



unique among biomolecules hithertofore known. These functional groups pose a challenging unsolved problem in natural product synthesis.

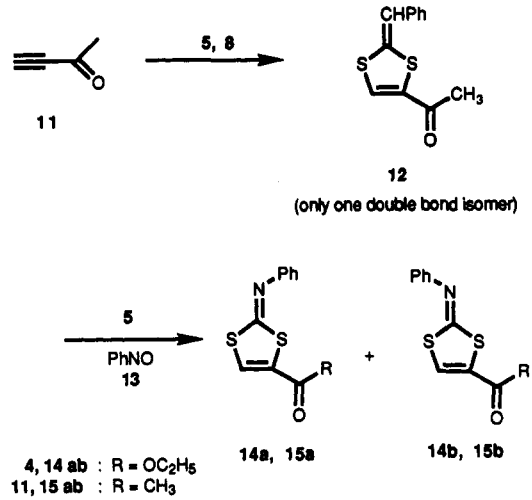




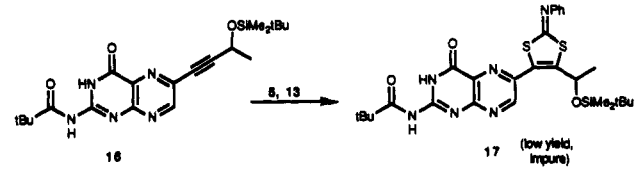
Taylor and Ray[3] have developed a method for generating 6-alkynylpterins which was later applied to the synthesis of dephospho-Form A (**2a**);[4] the phosphorylated molecule (**2b**) is an oxidative degradation product of the molybdenum cofactor 1.[1] The ready accessibility of this type of compound suggested introduction of the enedithiol functionality by dithiolation of the appropriate acetylene. Hartzler[5] has described the formation of 2-benzylidene-1,3-dithioles **9** and **10** from activated acetylenes **3**, **4** by reaction with the betainic tributylphosphine–carbon disulfide complex **5**[6] followed by a Wittig reaction of the initially formed ylids **6**, **7** with benzaldehyde **8**. Since these ylids are antiaromatic five-membered rings (8 π electron systems), they are very reactive and readily (<30 min) undergo the Wittig reaction even at temperatures between −50 °C and 0 °C.

In our first model system, 1-butyn-3-one **11** was converted to 2-benzylidene-4-acetyl-1,3-dithiole **12** which is formed, surprisingly, as only one of the two possible exocyclic double bond isomers (no assignment to a particular isomer was possible). Assuming that a dithiole bearing a more polarized exocyclic double bond might be more labile toward eventual hydrolysis, the above reaction was repeated with nitrosobenzene **13** in place of benzaldehyde. This heteroanalogous Wittig reaction[7] afforded the novel 2-(phenylimino)-1,3-dithioles **14**, **15** as mixtures of syn (**14a**, **15a**) and anti isomers (**14b**, **15b**) in good yields (see Scheme II).

Scheme II



Scheme III



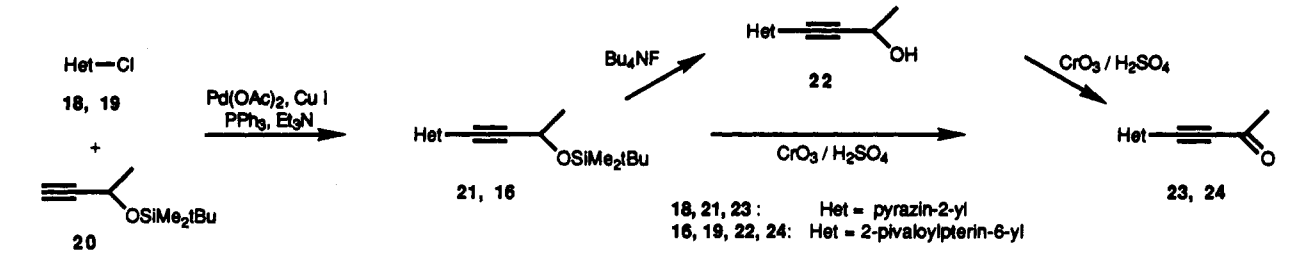
However, an attempt to apply this reaction to the pterin-substituted acetylene **16** (synthesis: see Scheme IV) resulted in only a minute yield of **17** alongside intractable material derived from the reaction of the phosphine complex **5** with nitrosobenzene **13** (as verified by mixing **5** and **13** without addition of the alkyne **16**). Apparently, the pterin system is not sufficiently electron deficient to activate the triple bond for reaction with **5** in a manner that overrides the side reaction.

Hence, the alkynylpyrazine **21** and the model alkynylpterin **16** (obtained from 2-chloropyrazine, **18**, and 2-pivaloyl-6-chloropterin, **19**, respectively, and the propargyl silyl ether **20**[8] by palladium-catalyzed coupling[9]) were oxidized to the ketones **23**, **24**, with Jones reagent[10] either directly or after cleavage of the silyl ether with tetrabutylammonium fluoride,[8] the two-step procedure via **22** affording the better yield (see Scheme IV).

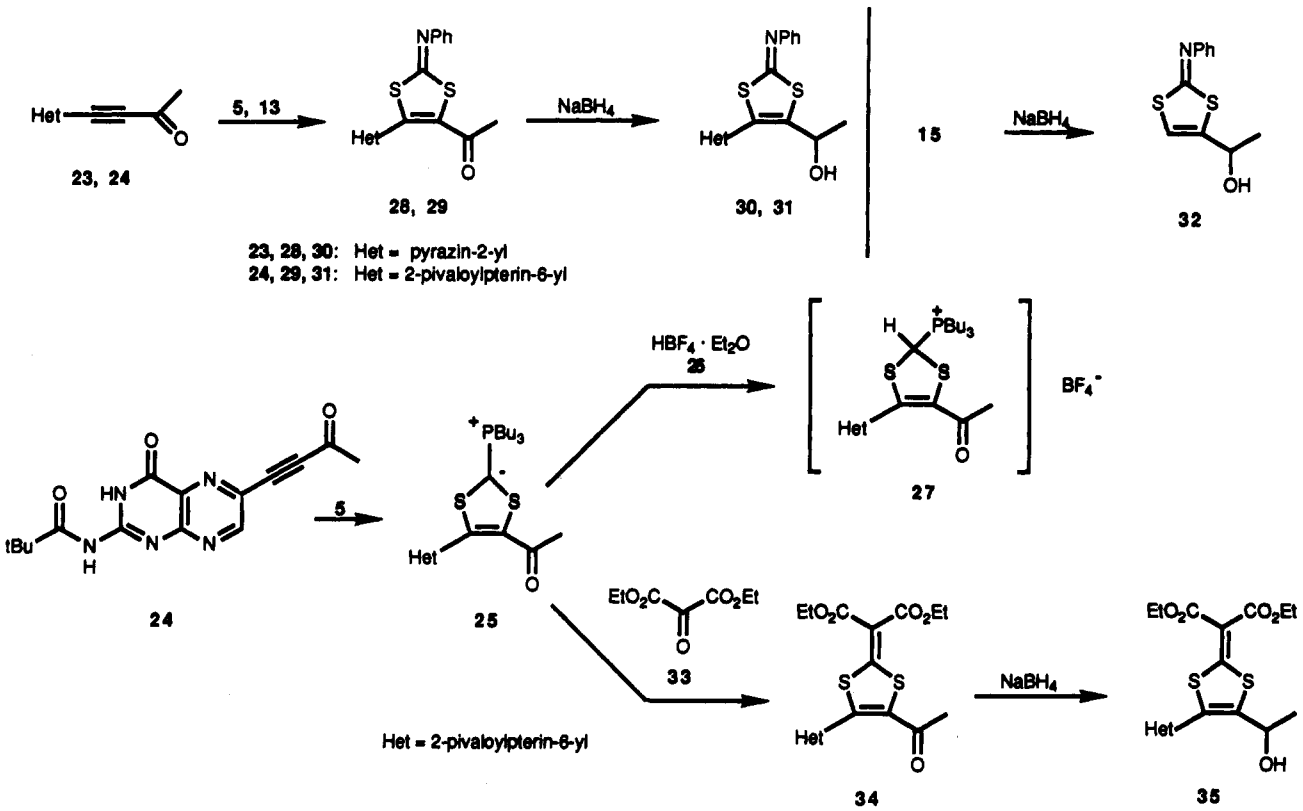
The ketones **23** and **24** reacted smoothly with **5** and **13** to give the 2-(phenylimino)-1,3-dithioles **28**, **29** in moderate to good yield (Scheme V). In the case of **24**, the intermediate ylid **25** proved to be stable at −50 °C and could thus be formed from **24** and **5** in the absence of nitroso-

(1) Gardlik, S.; Rajagopalan, K. V. *J. Biol. Chem.* **1990**, *265*, 13047.
(2) Reviews: (a) *Molybdenum and Molybdenum Containing Enzymes*; Coughlan, M. P., Ed.; Pergamon Press: New York, 1980. (b) *Molybdenum Enzymes*; Spiro, T. G., Ed.; Wiley-Interscience: New York, 1985. (c) Burgmayer, S. J. N.; Stiefel, E. I. *J. Chem. Ed.* **1985**, *62*, 443.
(3) Taylor, E. C.; Ray, P. S. *J. Org. Chem.* **1987**, *52*, 3997.
(4) Taylor, E. C.; Ray, P. S.; Darwish, I. S.; Johnson, J. L.; Rajagopalan, K. V. *J. Am. Chem. Soc.* **1989**, *111*, 7664.
(5) Hartzler, H. D. *J. Am. Chem. Soc.* **1971**, *93*, 4961.
(6) Davies, W. C.; Jones, W. J. *J. Chem. Soc.* **1929**, 33.
(7) Schönberg, A.; Brosowski, K. H. *Chem. Ber.* **1959**, *92*, 2602.
(8) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
(9) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. Modified procedure: Vigneswaran, M., personal communication. The direct synthesis of 1-substituted alkynyl ketones by Pd-catalyzed coupling of alk-1-yn-3-ones with aryl halides proved impossible because the ketones polymerize instantaneously upon contact with triethylamine.
(10) Veliev, M. G.; Guseinov, M. M. *Synthesis* **1980**, 461.

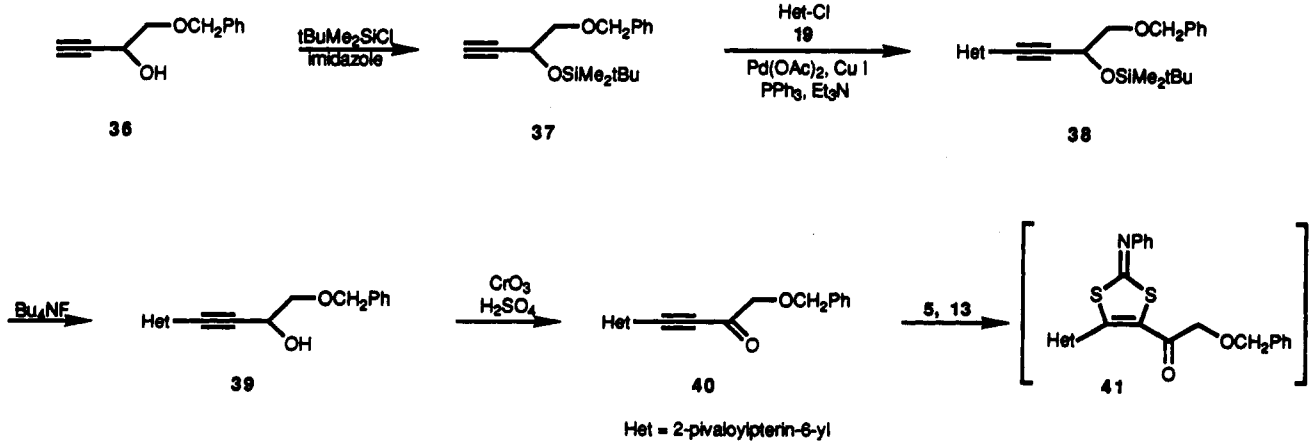
Scheme IV



Scheme V



Scheme VI

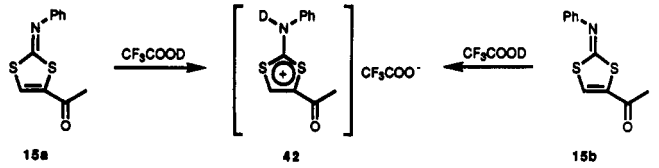


benzene 13, thus suppressing the reaction of the latter with 5; the intermediacy of 25 was established by quenching with tetrafluoroboric acid etherate 26[11] to yield the stable phosphonium salt 27. Compounds 15, 28, and 29 could be reduced to the corresponding alcohols 32, 30, and 31 with sodium borohydride in water/2-propanol/THF. In the same manner, 24 was converted to the push–pull alkene 34 by reaction with 5 followed by diethyl ketomalonate 33. Compound 34 was readily reduced to the alcohol 35 with sodium borohydride.

In analogy with the above reaction sequence, the model ketone 40, which bears the oxygen substituents in positions 3 and 4 of the side chain required in the target molecule,

(11) Sato, M.; Gonnella, N. C.; Cava, M. P. *J. Org. Chem.* **1979**, *44*, 930.

Scheme VII



was synthesized from **19** and the 3,4-disubstituted but-1-yne **37**[8,12] and then converted as described above into what we assume is the dithiole **41**. Contrary to the behavior of the methyl ketones **23**, **24**, **28**, and **29**, compounds **40** and its (presumed) derived phenylimino derivative **41** proved to be extremely acid-sensitive and did not survive attempted chromatographic purification.

Efforts to cleave the dithiole ring in the acetyl- or hydroxyethyl-substituted species (as reported for an analogous dimethylimmonium salt[13]) have failed thus far. Although the imino nitrogen atom in **15a,b** is deuterated by CF_3COOD to yield **42** (with resulting free rotation about the C–N bond, as evidenced by collapse of the separate peaks for the methyl groups in the NMR spectra of **15a,b**), **15a,b** were surprisingly unreactive toward alkylating agents like methyl iodide, iodoacetamide, and even triethyloxonium tetrafluoroborate. Further possible ways of cleaving the dithiole ring or exchanging the carbon atom in the 2-position of the dithiole system by a molybdenum-containing moiety are being investigated.

Experimental Section

General Procedures. Melting points were determined in open capillary tubes on a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1320 scanning and a Nicolet 730 FT instrument. ^1H NMR spectra were obtained on a General Electric GE 300 instrument (300 MHz), and chemical shifts are reported in ppm downfield from TMS. Mass spectra were obtained on AEI MS-902 and Kratos MS50TC spectrometers. Combustion analyses were performed at Eli Lilly and Co., Indianapolis, IN. Column chromatographic separations were carried out on Merck silica gel 60 (230–400 mesh), and TLC analyses were performed using Bakerflex IB-F plates, utilizing UV and potassium permanganate visualization.

2-Benzylidene-4-acetyl-1,3-dithiole (12). To a solution of 2.02 g (10 mmol) of tributylphosphine in 10 mL of diethyl ether and 2 mL of THF were added, under nitrogen, 0.84 g (11 mmol) of carbon disulfide with stirring. A red solution of the tributylphosphine–carbon disulfide complex **5**[6] formed. The mixture was stirred at room temperature for 10 min and cooled to −15 °C, and 1.00 g (9.5 mmol) of freshly distilled benzaldehyde (**8**) and 0.66 g (9.8 mmol) of but-1-yn-3-one (**11**) were added in rapid succession. On adding the acetylene, a gold-yellow crystalline solid precipitated. The mixture was stirred at −15 °C for another 10 min, and the precipitate was collected by filtration. Evaporation of the solvent and column chromatography on silica with hexane/ethyl acetate (3:1) afforded additional product. Only one of the two possible double bond isomers was formed: overall yield 1.24 g (5.2 mmol, 54%); mp 179–180 °C; ^1H NMR ($CDCl_3$) δ 2.41 (s, 3 H, CH_3), 6.57 (s, 1 H, ring C*H*), 7.2–7.4 (m, 6 H, C_6H_5 and CHPh); FTIR (KBr) 3080, 2922, 2849, 1654, 1578, 1564, 1489, 1440, 1362, 1270, 1208, 1017, 830, 775, 748, 689, 585 cm^{-1}. Anal. Calcd for $C_{12}H_{10}OS_2$: C, 61.51; H, 4.30; S, 27.36. Found: C, 61.50; H, 4.16; S, 27.36.

2-(Phenylimino)-4-(ethoxycarbonyl)-1,3-dithiole (14a,b). In the same manner as described above, **5** was prepared from 1.01 g (5.0 mmol) of tributylphosphine and 0.42 g (5.5 mmol) of carbon disulfide in 10 mL of ether and 2 mL of THF and reacted with 0.54 g (5.1 mmol) of nitrosobenzene **13** and 0.56 g (5.2 mmol) of ethyl propiolate **4** at −15 °C. After the mixture was stirred for 15 min, the solvent was evaporated and the residue was purified by column chromatography on silica gel with hexane/ethyl acetate (4:1) to give 0.82 g (3.1 mmol, 62%) of brownish crystals, mp 59–61 °C. An analytical sample was obtained as white needles, mp 62 °C, by a second chromatography on silica (hexane/ethyl acetate, 9:1) followed by recrystallization from toluene/hexane. The product is a mixture of the syn and anti forms **14a,b** in a 2:1 ratio in favor of one of the isomers: ^1H NMR ($CDCl_3$) δ 1.30 and 1.35 (2 t, both J = 7.1 Hz, 3 H, OCH_2CH_3), 4.27 and 4.32 (2 q, both J = 7.1 Hz, 2 H, OCH_2CH_3), 6.99 and 7.04 (2 d, J = 8.1 and 7.7 Hz, 2 H, ortho-H), 7.17 (t, J = 7.5 Hz, 1 H, para H in both isomers), 7.35–7.45 (m, 2 H, meta H), 7.49 and 7.61 (2 s, 1 H, C*H*=C); FTIR (KBr) 3055, 2982, 1698, 1572, 1487, 1370, 1284, 1197, 1062, 937, 768, 731, 703 cm^{-1}; LRMS 265 (M^+, calcd for $C_{12}H_{11}NO_2S_2$), 237 (− ethylene), 192 (− COOEt), 134, 130, 116. Anal. Calcd for $C_{12}H_{11}NO_2S_2$: C, 54.32; H, 4.18; N, 5.28; S, 24.17. Found: C, 54.32; H, 4.19; N, 5.25; S, 24.26.

2-(Phenylimino)-4-acetyl-1,3-dithiole (15). To a solution of 6.9 g (24.8 mmol) of betaine **5** in 50 mL of THF were added under nitrogen and at −50 °C 2.8 g (26.2 mmol) of nitrosobenzene (**13**) and 1.7 g (25.0 mmol) of but-1-yne-3-one (**11**) in rapid succession. The mixture was stirred at −30 °C for 3 h and filtered through a short silica column. Pure hexane eluted several unidentified byproducts, while hexane/ethyl acetate (4:1) eluted the desired product. An additional amount of lower grade material was obtained by elution with hexane/ethyl acetate (1:1); this fraction was subsequently purified by stirring with neutral alumina in an ether/chloroform mixture. The combined yield of **15**, obtained as beige microcrystals, mp 86–87 °C, was 4.75 g (20.2 mmol, 82%). An analytical sample (mp identical) was obtained as white bushy needles by a second chromatography on silica gel (hexane/ethyl acetate, 9:1) followed by recrystallization from toluene/hexane. The product is a mixture of the syn and anti forms **15a,b**, in a 2:1 ratio in favor of one of the isomers: ^1H NMR ($CDCl_3$) δ 2.43 and 2.46 (2 s, 3 H, CH_3), 6.99 and 7.04 (2 d, J = 8.2 and 8.0 Hz, 2 H, ortho H), 7.18 (t, J = 7.4 Hz, 1 H, para H in both isomers), 7.35–7.45 (m, 2 $^1/_3$ H, meta H overlaying C*H*=C in minor isomer), 7.54 (s, $^2/_3$ H, overlying in major isomer); FTIR 3085, 3051, 2917, 1650, 1582, 1574, 1539, 1488, 1356, 1275, 1210, 1027, 1017, 946, 922, 800, 764, 697, 601, 591 cm^{-1}; LRMS 235 (M^+, calcd for $C_{11}H_9NOS_2$), 192 (− acetyl), 134, 132, 104. Anal. Calcd for $C_{11}H_9NOS_2$: C, 56.15; H, 3.86; N, 5.95; S, 27.25. Found: C, 56.34; H, 3.85; N, 5.92; S, 27.49.

1-(2-Pivaloylpterin-6-yl)-3-[(*tert*-butyldimethylsilyl)oxy]but-1-yne (16). To a suspension of 5.35 g (19.0 mmol) of 2-pivaloyl-6-chloropterin **19** in 75 mL of acetonitrile under nitrogen was added a mixture of 0.52 g (2.25 mmol) of palladium(II) acetate, 1.20 g (4.5 mmol) of triphenylphosphine, 0.22 g (1.13 mmol) of copper(I) iodide, 50 mL of triethylamine/acetonitrile (1:1), and 6.73 g (38 mmol) of **20**. On heating to reflux temperature, the reaction mixture darkens. Stirring under reflux was continued for 1 h, and the mixture was allowed to cool to room temperature, diluted with 200 mL of ether, and filtered through a silica pad first using ether as the eluent followed by chloroform/methanol (95:5). Chromatography of the brownish evaporation residue on silica with chloroform/methanol (97.5:2.5) yielded 6.6 g (15.4 mmol, 81%) of **16** as cream-colored microcrystals: mp 240–245 °C dec; ^1H NMR ($CDCl_3$) δ 0.18 and 0.19 (2 s, 6 H, $Si(CH_3)_2$), 0.95 (s, 9 H, $SiC(CH_3)_3$), 1.37 (s, 9 H, $(CH_3)_3CO$), 1.55 (d, J = 6.5 Hz, 3 H, $CHCH_3$), 4.81 (q, J = 6.5 Hz, 1 H, C*H*CH_3), 8.42 (br s, 1 H, tBuCON*H*), 8.86 (s, 1 H, ring C*H*), 12.40 (br s, 1 H, ring N*H*); IR (KBr) 3200, 2950, 2930, 2860, 2235, 1680, 1620, 1555, 1475, 1445, 1345, 1255, 1150, 1125, 1100, 925, 835, 780 cm^{-1}; LRMS 429 (M^+, calcd for $C_{21}H_{31}N_5O_3Si$), 414 (− CH_3), 372 (− tBu), 328 (− tBuMeSi=CH_2), 288, 243, 151, 97. Anal. Calcd for $C_{21}H_{31}N_5O_3Si$: C, 58.72; H, 7.27; N, 16.30. Found: C, 58.44; H, 7.01; N, 16.01.

1-Pyrazin-2-yl-3-[(*tert*-butyldimethylsilyl)oxy]but-1-yne (21). To a solution of 11.45 g (100 mmol) of 2-chloropyrazine **18** in 530 mL of dry acetonitrile under nitrogen was added a mixture of 2.73 g (12 mmol) of palladium(II) acetate, 6.33 g (24 mmol) of triphenylphosphine, and 1.13 g (6 mmol) of copper(I) iodide, followed by successive addition of 130 mL of triethylamine and

(12) Yadav, J. S.; Chander, M. C.; Joshi, B. V. *Tetrahedron Lett.* **1988**, *29*, 2737. It should be pointed out that although chirality is lost in the reaction sequence, the starting material (dimethyl L-tartrate) for the preparation of the optically active compound is no more expensive than its racemate. In addition, **38** and **39** are novel derivatives of the cofactor-derived oxidative degradation product form A (**2**).

(13) Rowe, D. J.; Garner, C. D.; Joule, J. A. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1907.

36.9 g (100 mmol) of 3-[(*tert*-butyldimethylsilyl)oxy]but-1-yne **20**.[8] The reaction mixture, which rapidly turned black, was heated to 80 °C for 1 h and allowed to cool down to room temperature. Precipitated triethylamine hydrochloride was removed by vacuum filtration, and the filtrate was evaporated to a volume of ca. 100 mL. The residue was taken up in ether, extracted with water, dried over magnesium sulfate, filtered, and evaporated. The brown residue was filtered through a pad of silica using 500 mL of hexane, followed by 800 mL of hexane/ethyl acetate (4:1). The eluate was evaporated again and subjected to column chromatography on silica gel (hexane/ethyl acetate, 9:1) to yield 23.9 g (91 mmol, 91%) of **21** as a reddish oil. A small sample was purified by a second column chromatography on silica (hexane/ethyl acetate, 95:5) to afford **21** as a pale yellow liquid: ^{1}H NMR ($CDCl_3$) δ 0.17 and 0.20 (2 s, 6 H, $Si(CH_3)_2$), 0.95 (s, 9 H, $SiC(CH_3)_3$), 1.56 (d, J = 6.6 Hz, 3 H, $CHCH_3$), 4.80 (q, J = 6.6 Hz, 1 H, $CHCH_3$), 8.48 (d, J = 2.5 Hz, 1 H, pyrazin-H_6), 8.54 (m, 1 H, pyrazin-H_5), 8.65 (d, J = 1.1 Hz, 1 H, pyrazin-H_3); IR (KBr) 3060, 2980, 2955, 2930, 2885, 2230, 1460, 1390, 1270, 1255, 1140, 1120, 1100, 1075, 1050, 1010, 975, 900, 835, 810, 780 cm^{-1}; LRMS: 262 (M^+, calcd for $C_{14}H_{22}N_2OSi$), 261 (- H), 247 (- CH_3), 205 (- tBu), 161 (- tBuMeSi=CH_2), 131 ($OSiMe_2tBu$), 101, 75; HRMS calcd for $C_{14}H_{21}N_2OSi$ (M - 1) 261.1423, found 261.1411.

1-(2-Pivaloylpterin-6-yl)but-1-yn-3-ol (22). A solution of 1.72 g (4.0 mmol) of the silyl ether **16** in 25 mL of THF containing 4.5 mL (4.5 mmol) of 1 M tetrabutylammonium fluoride was stirred at room temperature for 3 h. The solvent was evaporated, and the residue was taken up in chloroform/methanol (95:5) and purified by column chromatography on silica gel to yield 1.18 g (3.7 mmol, 93%) of **22** as a slightly brownish powder, mp 250–255 °C. A small sample was stirred with toluene, suction-filtered, and washed with hexane to afford **22** as a colorless crystalline powder with the same melting point: ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 9 H, $(CH_3)_3CO$), 1.61 (d, J = 6.6 Hz, 3 H, $CHCH_3$), 4.84 (q, J = 6.6 Hz, 1 H, $CHCH_3$), 7.73 (br s, 1 H, tBuCONH), 8.85 (s, 1 H, ring CH), 12.75 (br s, 1 H, ring NH); IR (KBr) 3210, 2960, 2875, 1680, 1575, 1540, 1485, 1425, 1390, 1285, 1260, 1225, 1150, 1115 cm^{-1}; LRMS 315 (M^+, calcd for $C_{15}H_{17}N_5O_3$), 299 (- CH_4), 272 (- CH_3CO), 258 (- tBu), 230 (- tBuCO). Anal. Calcd for $C_{15}H_{17}N_5O_3$: C, 57.14; H, 5.43; N, 22.21. Found: C, 57.34; H, 5.34; N, 21.95.

1-Pyrazin-2-ylbut-1-yn-3-one (23). To a solution of 5.25 g (20 mmol) of the silyl ether **21** in 200 mL of methyl ethyl ketone was added from a pipette at 0 °C mL (37.6 mmol) of 1.88 M chromium trioxide in 25% aqueous sulfuric acid (Jones reagent). The mixture darkened, and green chromium(III) salt started to precipitate. The mixture was stirred for 30 min and diluted with 300 mL of ether, and the solid was dissolved by addition of 150 mL of water. The phases were separated, the aqueous layer was extracted twice with 100 mL of ether, and the combined organic extracts were washed with 100 mL each of saturated sodium hydrogen carbonate solution and water. After drying over sodium sulfate and evaporation of the solvent, a brownish, eye-irritating oil was obtained. Column chromatography with hexane/ethyl acetate (2:1) on silica gel and trituration with pentane afforded 1.28 g (8.8 mmol, 44%) of **23** as white hygroscopic crystals, mp 36 °C. The product decomposes upon standing and should only be prepared as needed: ^{1}H NMR ($CDCl_3$) δ 2.52 (s, 3 H, CH_3CO), 8.62 (d, J = 2.5 Hz, 1 H, pyrazin-H_6), 8.65 (m, 1 H, pyrazin-H_5), 8.81 (d, J = 1.0 Hz, 1 H, pyrazin-H_3); IR (KBr) 3075, 3020, 2240, 1700, 1475, 1415, 1380, 1295, 1200, 1175, 1160, 1070, 1030, 995, 870 cm^{-1}; LRMS 146 (M^+, calcd for $C_8H_6N_2O$), 131 (- CH_3), 118 (- CO), 103 (- acetyl).

1-(2-Pivaloylpterin-6-yl)but-1-yn-3-one (24). To a suspension of 1.81 g (5.74 mmol) of 2-(2-pivaloylpterin-6-yl)but-1-yn-3-ol (**22**) in 80 mL of methyl ethyl ketone was added via pipette and at 0 °C 4.5 mL (8.5 mmol) of 1.88 M Jones reagent (see above). The mixture was stirred for 2 h while allowed to warm up to room temperature, and it was then filtered through Celite. Chloroform (200 mL) and water (100 mL) were added, the phases were separated, and the organic layer was washed with 100 mL of saturated sodium bicarbonate solution and dried over sodium sulfate. The evaporation residue was subjected to column chromatography on silica gel with chloroform/methanol (99:1) to yield 1.06 g (3.34 mmol, 58%) of **24** as a pale yellow solid: mp 255–260 °C dec; ^{1}H NMR δ 1.38 (s, 9 H, $(CH_3)_3CO$), 2.53 (s, 3 H, CH_3CO), 8.47 (br s, 1 H, tBuCONH), 8.99 (s, 1 H, ring CH), 12.49 (br s, 1 H, ring NH); FTIR (KBr) 3256, 3202, 3127, 2967, 2932, 2201, 1679, 1620, 1552, 1480, 1439, 1344, 1299, 1266, 1177, 1138, 1108, 965, 826, 776, 615 cm^{-1}; LRMS 313 (M^+, calcd for $C_{15}H_{15}N_5O_3$), 256 (- tBu), 229, 214.

(*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-4-(benzyloxy)but-1-yne (37). Following the method of Yadav et al.[12] (*R*)-4-(benzyloxy)but-1-yn-3-ol was prepared from 10.82 g (40 mmol) of 2(*R*),3(*R*)-1-chloro-2,3-isopropylidene-4-(benzyloxy)butane and purified by column chromatography on silica gel (hexane/ethyl acetate, 3:1) to give 4.8 g (27 mmol, 68%) as a colorless viscous liquid: ^{1}H NMR ($CDCl_3$) δ 2.55 (d, J = 2.0 Hz, 1 H, HC≡C), 2.78 (d, J = 5.3 Hz, 1 H, OH), 3.68 and 3.76 (2 dd, J_{gem} = 9.9 Hz, J_{vic} = 3.6 and 6.9 Hz, 2 H, $CHOHCH_2OBn$), 4.62–4.69 (m, 1 H, CHOH), 4.71 and 4.72 (AA′ system, 2 H, OCH_2Ph), 7.36–7.46 (m, 5 H, phenyl protons); IR (liquid) 3420, 3275, 3045, 3010, 2965, 2890, 2845, 2095, 1485, 1440, 1365, 1235, 1105, 1035, 930, 730, 690 cm^{-1}; LRMS 176 (M^+, calcd for $C_{11}H_{12}O_2$), 146 (- CH_2O), 129, 117, 91 (benzyl$^+$); HRMS 176.0837, found 176.0833.

(*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-4-(benzyloxy)but-1-yne (**36**) was then prepared from 4.8 g (27 mmol) of (*R*)-4-(benzyloxy)-but-1-yn-3-ol using the procedure described in ref 8; yield 7.6 g (26 mmol, 96%) as a colorless oily liquid. The product contained a small amount (<5%) of bis(*tert*-butyldimethylsilyl) oxide but was sufficiently pure for use in the following reaction. A small sample was purified by removing the side product in a Kugelrohr apparatus at 70–80 °C (1.5 mmHg): ^{1}H NMR ($CDCl_3$) δ 2.45 (d, J = 2.2 Hz, 1 H, HC≡C), 3.60 and 3.64 (2 dd, J_{gem} = 10.2 Hz, J_{vic} = 6.6 and 5.2 Hz, 2 H, $CHCH_2OCH_2Ph$), 4.59 (ddd, J = 6.6, 5.2, and 2.2 Hz, HC≡CCH(OtBDMS)CH_2), 4.65 (s, 2 H, OCH_2Ph), 7.25–7.40 (m, 5 H, C_6H_5); IR (liquid) 3300, 3055, 3020, 2950, 2920, 2850, 2110, 1465, 1365, 1255, 1180, 1155, 1030, 1005, 970, 940, 840, 780, 735, 700 cm^{-1}; LRMS: 290 (M^+, calcd for $C_{17}H_{26}O_2Si$) 289 (-H), 247, 179, 169, 123, 115 ($SiMe_2tBu$), 105, 91 (benzyl$^+$); HRMS calcd for $C_{17}H_{25}O_2Si$ (M - 1) 289.1623, found 289.1604; $[\alpha]_D$ = -25.7° (c = 1.01, $CHCl_3$).

(*R*)-1-(2-Pivaloylpterin-6-yl)-3-[(*tert*-butyldimethylsily)oxy]-4-(benzyloxy)but)-1-yne (38). To a suspension of 2.82 g (10 mmol) of 2-pivaloyl-6-chloropterin **19** in 30 mL of acetonitrile under nitrogen was added a mixture of 0.27 g (1.2 mmol) of palladium(II) acetate, 0.64 g (2.4 mmol) of triphenylphosphine, 0.12 g (0.6 mmol) of copper(I) iodide, 50 mL of triethylamine, and 4.35 g (15 mmol) of the 1-alkyne **37**. On heating to reflux, the reaction mixture darkened. Stirring under reflux was continued for 1 h, and the mixture was allowed to cool to room temperature, diluted with 200 mL of chloroform, and filtered through a silica pad. Chromatography of the brown evaporation residue on silica, first with chloroform followed by chloroform/methanol (98:2) afforded 4.05 g (7.6 mmol, 76%) of **38** as a pale yellow foam. A small sample was subjected to preparative TLC (silica gel, chloform/methanol, 97:3) to yield crystalline **37**: mp 175–180 °C dec; ^{1}H NMR ($CDCl_3$) δ 0.18 and 0.20 (2 s, 6 H, $Si(CH_3)_2$), 0.96 (s, 9 H, $SiC(CH_3)_3$), 1.36 (s, 9 H, $(CH_3)_3CO$), 3.69 and 3.75 (2 dd, J_{gem} = 10.0 Hz, J_{vic} = 6.8 and 4.9 Hz, 2 H, $CHCH_2OCH_2Ph$), 4.66 (m centered, 2 H, OCH_2Ph), 4.84 (dd, J = 6.8 and 4.9 Hz, 1 H, $CHCH_2OCH_2Ph$), 7.20–7.40 (m, 5 H, C_6H_5), 8.46 (br s, 1 H, tBuCONH), 8.82 (s, 1 H, ring CH), 12.39 (br s, 1 H, ring NH); IR (KBr) 3190, 2955, 2925, 2855, 2225, 1675, 1615, 1550, 1475, 1440, 1340, 1300, 1250, 1125, 1100, 965, 835, 780, 700 cm^{-1}; LRMS 535 (M^+, calcd for $C_{28}H_{37}N_5O_4Si$), 520 (- CH_3), 478 (- tBu), 414 (- CH_2OCH_2Ph), 362; HRMS calcd for $C_{28}H_{37}N_5O_4Si$ 535.2614, found 535.2630; $[\alpha]_D$ = -41.2° (c = 1.00, $CHCl_3$).

(*R*)-1-(2-Pivaloylpterin-6-yl)-4-(benzyloxy)but-1-yn-3-ol (39). To a solution of 535 mg (1.0 mmol) of the silyl ether **38** in 20 mL of THF was added 3.1 mL (3.1 mmol) of a 1 M solution of tetrabutylammonium fluoride in THF. The reaction mixture was stirred for 30 min, filtered through a short column of silica gel using chloroform/methanol (97:3), dried, and evaporated to yield 415 mg (0.99 mmol, 99%) of **39** as a cream-colored solid. A small sample was stirred with toluene and washed with hexane to afford a white powder: mp 202–204 °C dec; ^{1}H NMR ($CDCl_3$) δ 1.38 (s, 9 H, $(CH_3)_3CO$), 2.82 (br s, 1 H, OH), 3.77 and 3.80 (2 dd, J_{gem} = 9.8 Hz, J_{vic} = 6.7 and 3.7 Hz, 2 H, $CHOHCH_2$), 4.67 (AA′ system, 2 H, OCH_2Ph), 4.86 (dd, J = 6.7 and 3.7 Hz, 1 H, $CHOHCH_2$), 7.2–7.4 (m, 5 H, C_6H_5), 8.42 (br s, 1 H, tBuCONH), 8.86 (s, 1 H, ring CH), 12.41 (br s, 1 H, ring NH); IR (KBr) 3441, 3195, 2970, 2920, 2876, 2684, 1624, 1557, 1534, 1480, 1445, 1346,

1261, 1149 cm^{-1}; LRMS 421 (M$^+$, calcd for $C_{22}H_{23}N_5O_4$), 420 (- H), 403 (- water), 364 (- tBu), 300 (- CH_2OCH_2Ph), 216, 107. Anal. Calcd for $C_{22}H_{23}N_5O_4$: C, 62.70; H, 5.50; N, 16.62. Found: C, 61.99; H, 5.36; N, 16.19.

1-(2-Pivaloylpterin-6-yl)-4-(benzyloxy)but-1-yn-3-one (40). To a suspension of 680 mg (1.62 mmol) of the alcohol **39** in 20 mL of methyl ethyl ketone was added, at 0 °C and via pipette, 1.3 mL (2.5 mmol) of 1.88 M Jones reagent (see above). After 30 min of stirring, 50 mL of ether and 20 mL of water were added, the phases were separated, and the organic layer was washed with saturated sodium bicarbonate solution and dried over sodium sulfate. The resulting crude **40** (640 mg, 1.53 mmol, 94%) was obtained as a pale brown solid. During an attempt to purify the product by chromatography (silica gel, chloroform/methanol, 98.5:1.5), most of the product decomposed on the column, and only 80 mg of a reddish solid [pure by NMR], mp 160–165 °C, were isolated: ^{1}H NMR δ 1.38 (s, 9 H, $(CH_3)_3CO$), 4.40 and 4.71 (2 s, 2 H each, CH_2OCH_2Ph), 7.2–7.5 (m, 5 H, C_6H_5), 8.2–8.8 (br s, 1 H, tBuCONH), 8.95 (s, 1 H, ring CH), 12.40 (br s, 1 H, ring NH); FTIR (KBr) 3187, 2972, 2871, 2205, 1684, 1618, 1551, 1489, 1441, 1344, 1256, 1143, 1076 cm^{-1}; LRMS: 419 (M$^+$, calcd for $C_{22}H_{21}N_5O_4$), 362 (- tBu), 300, 108 (benzyl alcohol); HRMS 419.1594, found 419.1597.

2-(Phenylimino)-4-acetyl-5-(pyrazin-2-yl)-1,3-dithiole (28). To a solution of **5**, prepared from 1.71 g (8.5 mmol) of tributylphosphine and 0.68 g (9.0 mmol) of carbon disulfide in 40 mL of THF under nitrogen, were added at -50 °C in rapid succession 0.96 g (8.9 mmol) of nitrosobenzene (**13**) and 1.15 g (7.9 mmol) of 1-pyrazin-2-ylbut-1-yn-3-one (**23**). The mixture was stirred for 45 min during which time the temperature rose to -15 °C. It was then diluted with 40 mL of hexane and subjected to column chromatography on silica gel with hexane/ethyl acetate (1:1). The fractions containing the product were evaporated, and the oily residue was triturated with ether/pentane to induce crystallization of the product; yield 1.26 g (4.0 mmol, 51%), mp 92–95 °C. An analytical sample was prepared as yellow platelets, mp 96–97 °C, by recrystallization from hexane and a small amount of toluene. The product is an equimolar mixture of syn and anti isomers: ^{1}H NMR ($CDCl_3$) δ 2.16 and 2.25 (2 s, 3 H, CH_3), 7.02–7.07 (m, 2 H, phenyl ortho H in both isomers), 7.16–7.24 (m, 1 H, phenyl para H), 7.38–7.47 (m, 2 H, phenyl meta H), 8.60 (br s, 1 H, pyrazin-H_6 in both isomers), 8.67 (m centered, 1 H, pyrazin-H_5), 8.75 and 8.83 (2 s, 1 H, pyrazin-H_3); FTIR (KBr) 3042, 2916, 2852, 1679, 1599, 1589, 1530, 1487, 1460, 1404, 1356, 1299, 1258, 1198, 1151, 1063, 1016, 951, 857, 763, 696, 582 cm^{-1}; LRMS 313 (M$^+$, calcd for $C_{15}H_{11}N_3OS_2$), 270 (- acetyl), 210 (- PhNC), 168, 136, 123; HRMS calcd 313.0344, found 313.0336. Anal. Calcd for $C_{15}H_{11}N_3OS_2$: C, 57.49; H, 3.54; N, 13.41; S, 20.46. Found: C, 57.28; H, 3.33; N, 13.20; S, 19.84.

2-(Phenylimino)-4-acetyl-5-(2-pivaloylpterin-6-yl)-1,3-dithiole (29). A solution of **5** in 10 mL of THF, prepared from 200 mg (0.98 mmol) of tributylphosphine and 114 mg (1.5 mmol) of carbon disulfide under nitrogen, was cooled to -40 °C, and 313 mg (1.0 mmol) of 1-(2-pivaloylpterin-6-yl)but-1-yn-3-one (**24**) was added. On stirring at -40 °C for 1 h, the color of the reaction mixture changed to a yellowish brown as the ylid formed (yellow base-line spot on TLC with chloroform/methanol, 98:2). Nitrosobenzene (**13**) (187 mg, 1.7 mmol) was added, and the mixture was allowed to warm up to 0 °C (ca. 1.5 h). The yellow base-line spot on TLC disappeared. The product mixture was filtered through a silica pad with chloroform, the solvents were evaporated, and the residue was purified by column chromatography on silica gel with chloroform/methanol (98.5:1.5) to afford 272 mg (0.57 mmol, 58%) of **29** as yellow microcrystals, mp 135–140 °C dec. The product is an equimolar mixture of syn and anti isomers: ^{1}H NMR ($CDCl_3$) δ 1.32 and 1.34 (2 s, 9 H, $(CH_3)_3C$), 2.19 and 2.32 (2 s, 3 H, CH_3CO), 6.98 and 7.02 (2 d, J = 8.1 and 8.5 Hz, 2 H, phenyl ortho H), 7.16 and 7.20 (2 t, both J = 7.3 Hz, 1 H, phenyl para H), 7.30–7.42 (m, 2 H, phenyl meta H), 8.37 and 8.40 (2 br s, 1 H, tBuCONH), 8.89 and 8.96 (2 s, 1 H, ring CH), 12.39 and 12.41 (2 br s, 1 H, ring NH); FTIR (KBr) 3150, 2969, 2920, 1718, 1684, 1618, 1583, 1576, 1553, 1486, 1437, 1353, 1256, 1145, 766, 696 cm^{-1}; LRMS 480 (M$^+$, calcd for $C_{22}H_{20}N_6O_3S_2$), 377 (- PhNC), 335, 319, 277, 135 (PhNCS); HRMS 480.1038, found 480.1035.

2-[Bis(methoxycarbonyl)methenyl]-4-acetyl-5-(2-pivaloylpterin-6-yl)-1,3-dithiole (34). As described above, 2.0 mmol of **5** in 20 mL of THF were reacted at -50 °C with 470 mg (1.5 mmol) of 1-(2-pivaloylpterin-6-yl)but-1-yn-3-one (**24**) (ylide formation controlled by TLC). After stirring for 1 h at -50 °C, 360 mg (2.05 mmol) of diethyl ketomalonate (**33**) were added. The yellow base-line spot on TLC (chloroform/methanol, 98:2) disappeared (over a 1.5-h period of stirring while allowing the mixture to warm to 0 °C) in favor of a yellow spot showing orange fluorescence at 366 nm with R_f = 0.15. The solvent was removed, and the residue was purified by column chromatography on silica gel with chloroform/methanol (99:1) to afford 560 mg (1.03 mmol, 69%) of **34** as a bright yellow microcrystalline solid: mp 215–220 °C dec; ^{1}H NMR ($CDCl_3$) δ 1.38 (s, 9 H, $(CH_3)_3C$), overlying 1.38, 1.40 (2 t, both J = 7 Hz, 6 H, both OCH_2CH_3), 2.47 (s, 3 H, CH_3CO), 4.33 and 4.37 (2 q, J = 7.0 and 7.1 Hz, 4 H, both OCH_2CH_3), 8.51 (br s, 1 H, tBuCONH), 9.02 (s, 1 H, ring CHN), 12.45 (br s, 1 H, ring NH); IR (KBr): 3291, 3201, 2978, 2932, 1720, 1683, 1620, 1552, 1429, 1287, 1145, 1033 cm^{-1}; LRMS 547 (M$^+$, calcd for $C_{23}H_{25}N_5O_7S_2$), 345 (- $(EtOOC)_2C{=}C{=}S$), 288, 246 (2-pivaloylpterin-6-yl$^+$), 122, 105; HRMS calcd 547.1195, found 547.1188.

[4-Acetyl-5-(2-pivaloylpterin-6-yl)-1,3-dithiol-2-yl]tributylphosphonium Tetrafluoroborate (27). A solution of **5** in 10 mL of THF, prepared from 202 mg (0.98 mmol) of tributylphosphine and 114 mg (1.5 mmol) of carbon disulfide under nitrogen, was cooled to -50 °C and stirred for 1 h. At this temperature, 200 mg (1.15 mmol) of 85% tetrafluoroboric acid etherate (**26**) were added dropwise from a syringe. Compound **27** precipitated as a reddish oil. After another 10 min of stirring, the solvent was decanted off, and the residue was treated with ether/hexane whereupon crystallization occurred. Suction filtration through a nitrogen-flushed fritted-glass funnel yielded 435 mg (0.63 mmol, 63%) of **27** as an orange microcrystalline powder: mp 122–127 °C dec; ^{1}H NMR δ 0.92 (t, J = 6.7 Hz, 9 H, P-$[(CH_2)_3CH_3]_3$), 1.38 (s, 9 H, $(CH_3)_3CCO$), 1.4–1.7 (m, 12 H, P-$[CH_2(CH_2)_2CH_3]_3$), 2.23 (s, 3 H, CH_3CO), 2.48 (m centered, 6 H, $P(CH_2C_3H_7)_3$), 6.32 (br s, 1 H, PCHS), 8.58 (br s, 1 H, ring NH), 8.93 (s, 1 H, ring CHN, 12.46 (br s, 1 H, tBuCONH); FTIR 3198, 2961, 2932, 2873, 1717, 1683, 1620, 1551, 1505, 1480, 1466, 1445, 1353, 1249, 1147, 1124, 1084, 1037, 825, 725, 533, 522 cm^{-1}; LRMS (FAB) 592 (M$^+$ for cation, calcd for $C_{28}H_{43}N_5O_3PS_2$) 562, 516 (- CS_2), 500.

2-(Phenylimino)-4-(1-hydroxyethyl)-1,3-dithiole (32). To a solution of 940 mg (4.0 mmol) of 2-(phenylimino)-4-acetyl-1,3-dithiole (**15**) in a mixture of 15 mL of 2-propanol and 10 mL of THF was added at room temperature a solution of 42 mg (1.1 mmol) of sodium borohydride in 5 mL of 2-propanol and 5 mL of water. The reaction was monitored by TLC (chloroform/methanol, 96:4; R_f (ketone) = 0.57, R_f (alcohol) = 0.19). After the mixture was stirred for 1 h, 10 mL of saturated aqueous ammonium chloride solution and 20 mL of ether were added, the layers were separated, and the aqueous layer was extracted twice with ether. The combined organic extracts were dried over magnesium sulfate and filtered, and the solvent was evaporated. The oily product was subjected to column chromatography on silica gel with chloroform/methanol (99:1 to 97:3), and recrystallized from ether/hexane to afford 802 mg (3.4 mmol, 84%) of **32** as pinkish bushy needles, mp 90–91 °C. The product is an approximately equimolar mixture of syn and anti isomers: ^{1}H NMR ($CDCl_3$) δ 1.35 and 1.44 (2 d, J = 6.3 Hz and 6.6 Hz, 3 H, $CHOHCH_3$), 2.39 and 2.47 (2 br s, 1 H, OH), 4.58 and 4.66 (2 q, J = 6.3 and 6.6 Hz, 1 H, $CHOHCH_3$), 6.24 and 6.33 (2 s, 1 H, CH-S), 6.93 and 6.94 (2 d, both J = 7.3 Hz, 2 H, phenyl ortho H), 7.07 (t, J = 7.3 Hz, 1 H, phenyl para H in both isomers), 7.26–7.33 (m, 2 H, phenyl meta H in both isomers); FTIR (KBr) 3204, 3058, 2980, 2879, 1575, 1550, 1482, 1450, 1203, 1131, 1104, 1049, 987, 949, 775, 766, 702, 632, 447 cm^{-1}; LRMS 237 (M$^+$ calcd for $C_{11}H_{11}NOS_2$), 219 (- water), 135 (PhNCS), 116, 104. Anal. Calcd for $C_{11}H_{11}NOS_2$: C, 55.67; H, 4.67; N, 5.90; S, 27.02. Found: C, 55.45; H, 4.65; N, 5.84; S, 26.84.

2-(Phenylimino)-4-(1-hydroxyethyl)-5-pyrazin-2-yl-1,3-dithiole (30). To a solution of 550 mg (1.75 mmol) of the ketone **28** in 35 mL of THF was added a solution of 20 mg (0.53 mmol) of sodium borohydride in 3.5 mL of 2-propanol and 3.5 mL of water. The resulting mixture turned a brownish color. TLC control (chloroform/methanol, 98:2) showed total disappearance of **28** within 10 min. Saturated ammonium chloride (5 mL) and

10 mL of ether were added, the layers were separated, and the aqueous layer was extracted twice with ether. The combined extracts were dried over magnesium sulfate, the solvent was evaporated, and the residue was subjected to column chromatography on silica with chloroform/methanol (99:1) to afford **30** as a yellow foam. Recrystallization from cyclohexane yielded 234 mg (0.74 mmol, 42%) of light yellow microcrystals, mp 118–119 °C. The product is an equimolar mixture of syn and anti isomers: ^{1}H NMR ($CDCl_3$) δ 1.47 and 1.60 (2 d, both J = 6.6 Hz, 3 H, $CHOHCH_3$), 4.43 and 4.54 (2 d, J = 4.0 and 3.0 Hz, 1 H, O*H*), 4.95–5.05 (m, 1 H, $CHOHCH_3$, become two quartets with J = 6.6 Hz upon D_2O exchange), 7.06 (d, J = 7.7 Hz, 2 H, phenyl ortho H), 7.20 (t, J = 7.3 Hz, 1 H, phenyl para H), 7.42 (m, centered, 2 H, phenyl meta H), 8.55–8.75 (m, 3 H, pyrazinyl-H); FTIR (KBr) 3204, 3065, 2974, 2923, 1578, 1559, 1539, 1516, 1402, 1145, 1101, 1066, 1011, 853, 762, 693 cm^{-1}; LRMS 315 (M^+, calcd for $C_{15}H_{13}N_3OS_2$), 314 (- H), 270 (- $CHOHCH_3$), 211 (- PhNCH$^+$), 180 (- PhNCS); HRMS calcd 315.0500, found 315.0484. Anal. Calcd for $C_{15}H_{13}N_3OS_2$: C, 57.12; H, 4.15; N, 13.32; S, 20.33. Found: C, 57.15; H, 3.99; N, 13.21; S, 20.46.

2-(Phenylimino)-4-(1-hydroxyethyl)-5-(2-pivaloylpterin-6-yl)-1,3-dithiole (31). Reduction of the ketone **29** (160 mg, 0.33 mmol) was carried out with 4 mg (0.10 mmol) of sodium borohydride, as described above for the preparation of **30**. Column chromatography on silica gel with chloroform/methanol (98:2) afforded the alcohol **31** as a yellow oil. Upon addition of hexane, the compound crystallized to yield 107 mg (0.22 mmol, 67%) of a yellow crystalline powder, mp 230–235 °C dec. The product is an equimolar mixture of syn and anti isomers: ^{1}H NMR δ 1.37 and 1.39 (2 s, 9 H, both $(CH_3)_3C$), 1.50 and 1.64 (2 d, both J = 6.6 Hz, $CHOHCH_3$), 4.85–4.92 (br d, 1 H, O*H*), 5.04 and 5.13 (2 m centered, 1 H, $CHOHCH_3$, become doublets with J = 6.6 Hz upon D_2O exchange), 7.05–7.08 (m, 2 H, phenyl ortho H), 7.20 (t, J = 7.6 Hz, 1 H, phenyl para H), 7.43 (m centered, 2 H, phenyl meta H), 8.48 and 8.59 (2 br s, 1 H, tBuCON*H*), 8.78 and 8.91 (2 s, 1 H, ring C*H*), 12.46 (br s, 1 H, ring N*H*); FTIR (KBr): 3220, 2970, 2922, 1686, 1620, 1578, 1560, 1448, 1356, 1262, 1143, 961, 764, 698 cm^{-1}; LRMS 482 (M^+, calcd for $C_{22}H_{22}N_6O_3S_2$), 481 (- H), 464 (- water), 438 (- isobutene), 361, 331, 304, 135 (PhNCS); HMRS 482.1194, found 482.1167. Anal. Calcd for $C_{22}H_{22}N_6O_3S_2$: C, 54.76; H, 4.61; N, 17.42; S, 13.29. Found: C, 54.54; H, 4.61; N, 17.25; S, 13.64.

2-[Bis(methoxycarbonyl)methenyl]-4-(1-hydroxyethyl)-5-(2-pivaloylpterin-6-yl)-1,3-dithiole (35). The ketone **34** (274 mg (0.50 mmol) was reduced with 6 mg (0.15 mmol) of sodium borohydride, as described above for the preparation of **30**. Part of the product **35** precipitated directly from the reaction mixture and was collected by filtration and washed with pentane. An additional amount of product was obtained by triturating the filtrate with pentane; combined yield 246 mg (0.45 mmol, 89%) of a yellow crystalline powder: mp >260 °C; ^{1}H NMR δ 1.24 (s, 9 H, $(CH_3)_3C$, overlapping 2 t, 6 H, OCH_2CH_3), 1450 (d, J = 6.5 Hz, 3 H, $CHOHCH_3$), 4.15–4.23 (m, 4 H, OCH_2CH_3), 5.15–5.25 (m, 1 H, $CHOHCH_3$), 5.82 (br s, 1 H, O*H*), 8.90 (br s, 1 H, tBuCON*H*), 8.93 (s, 1 H, ring C*H*), 12.45 (br, 1 H, ring N*H*); IR 3420, 2980, 2930, 1710, 1630, 1540, 1495, 1445, 1410, 1290, 1160, 1035, 945, 795, 760 cm^{-1}; LRMS 549 (M^+, calcd for $C_{23}H_{27}N_5O_7S_2$), 548 (- H), 531 (- water), 502 (- EtOH), 346 (- $(EtOOC)_2C{=}C{=}S$), 304, 246 (2-pivaloylpterin-6-yl$^+$), 202, 85 (tBuCO$^+$).

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Organometallic Reactions of ω-Heterosubstituted *N*-Acyl Lactams. A New Route to γ-Keto Aldehydes from 5-Ethoxy-2-pyrrolidinone

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A new route to γ-keto aldehydes has been developed in which 5-ethoxy-2-pyrrolidinone is the key intermediate, easily available from 2-pyrrolidinone or succinimide. The lactam undergoes the selective ring opening, previous "in situ" N-acylation reaction with pivaloyl chloride or di-*tert*-butyl dicarbonate and attack of Grignard reagents or pyridyllithium compounds, whereupon the γ-keto aldehydes are produced by acidic hydrolysis. By this way the γ-keto aldehydes, which are precursors of natural compounds, such as dihydrojasmone and methyl dihydrojasmonate, a feromone component of the peach fruit moth *Carposina niponensis*, and nicotine derivatives have been prepared. A practical synthesis of pyridyl-substituted pyrroles (α- and β-nicotyrine and the nor derivatives) can be achieved without purification of the intermediates. N-Acylated 6-ethoxy-2-piperidinone is less reactive toward the organometallic attack, affording in low yields 5-phenyl-5-oxopentanal using phenylmagnesium chloride, and 2-pentylcyclohex-2-en-1-one using *n*-hexylmagnesium bromide.

It has been recently reported by one of us[1] that five- to eight-membered lactams **1** (X = H), through their *N*-pivaloyl and *N*-Boc derivatives **2**, undergo regioselective ring-opening reaction with organometallic reagents, affording in good yields the N-substituted ω-amino ketones **3** (Scheme I). In the case of *N*-Boc derivatives, the cyclic imines **4** can be obtained by treatment with trifluoroacetic acid. Aiming to develop a new route to synthetically useful ω-keto aldehydes **5**, we have examined the possibility to perform the same synthetic sequence starting from ω-heterosubstituted lactams **1** (X = hetero group).

Preparation of ω-Heterosubstituted Lactams. The ethoxy lactams **8a,b** are easily prepared by the anodic oxidation of *N*-hydro lactams **6a,b** in ethanol[2] or by the reduction of cyclic imides **7a,b** with sodium borohydride in ethanol at controlled pH, followed by treatment with ethanolic solution of hydrochloric acid[3] (Scheme II). The benzyloxy and ethylthio lactams **9b** and **10b** were obtained by the reaction of the ethoxy lactam **8b** with benzyl alcohol

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