permanganate. After 0.25 h, the resulting dark mixture was filtered, and the residue was washed with a tiny portion of water. The filtrate was adjusted to pH 4 with 6 N HCl, and a greenish solid precipitated. This solid was collected by filtration, washed with a small amount of water, and dried under vacuum (70 °C); yield 25 mg (65%), identified by direct comparison (UV, IR, NMR, and TLC) with the sample prepared above in method A.

7-Amino-1,2,3,4-tetrahydro-1-methyl-4-phenylpyrimido[4,5-*c*]pyridazin-5(6*H*)-one (14). To a stirred mixture of 0.51 g (2.0 mmol) of **13b** and 15 mL of liquid ammonia contained in a 50-mL round-bottomed flask equipped with a Dewar condenser containing dry ice/isopropyl alcohol was added 0.14 g (0.006 mol) of sodium as small chunks during a 45-min period. The solution was allowed to decolorize before each successive piece was added, and a water bath was used to ensure the continuous ebullition of ammonia. After all of the blue color had dissipated, the ammonia was evaporated with a continuous flow of nitrogen. The solid residue was dissolved in 30 mL of water, and the resulting alkaline solution was washed with ether (2 × 20 mL) and, subsequently, adjusted to pH 5 with glacial acetic acid. The precipitate was collected by suction filtration, washed with water and dried under vacuum (70 °C); yield, 0.44 g. An analytical sample was prepared by recrystallization from methanol/water: mp >260 °C dec; NMR (Me_2SO-d_6) δ 2.94 (m,[27] 2 H), 3.14 (s, 3 H), 3.88 (m,[27] 1 H), 4.42 (m,[20] 1 H), 6.16 (br s,[20] 2H), 7.15–7.25 (m, 5 H), 9.90 (br s,[20] 1 H); UV (CH_3OH) λ_{max} 225 nm (ϵ 20600), 282 (13400). Anal. Calcd for $C_{13}H_{15}N_5O$: C, 60.68; H, 5.88; N, 27.22. Found: C, 60.67; H, 5.91; N, 27.15.

Acknowledgment. We thank Dr. B. S. Hurlbert, Mr. A. Ragouzeos, and Mr. R. Crouch for NMR studies, Dr. D. A. Brent and Mr. R. Johnson for mass spectra data, and Ms. J. Miller and Ms. S. Wrenn for technical assistance.

Registry No. **1a**, 67873-21-6; **1b**, 6298-85-7; **1c**, 80082-11-7; **1c** (2-phenylhydrazino isomer), 80082-33-3; **2a**, 431-03-8; **2b**, 134-81-6; **2c**, 1074-12-0; **2d**, 78-98-8; **2e**, 70935-14-7; **2f**, 306-44-5; **2g**, 532-54-7; **2h**, 52143-74-5; **3a**, 70935-27-2; **3b**, 80082-12-8; **3c**, 70935-17-0; **3d** (R_3 = Me; R_2 = H), 80082-13-9; **3d** (R_2 = Me; R_3 = H), 80082-14-0; **3e** (R_3 = *m*-HO-C_6H_4; R_2 = H), 70935-18-1; **3e** (R_2 = *m*-HO-C_6H_4; R_3 = H), 80082-15-1; **3f**, 74482-47-6; **3g**, 80082-34-4; **3g**·HCl, 80082-16-2; **3i**, 80082-17-3; **3j**, 80082-18-4; **4**, 52764-58-6; **5**, 80082-19-5; **6**, 80082-20-8; **7**, 600-22-6; **8**, 80082-21-9; **9**, 67873-29-4; **10**, 80082-22-0; **11a**, 80082-23-1; **11b**, 80082-24-2; **12a**, 80082-25-3; **12a**·$NaHSO_3$, 80082-26-4; **12b**, 70311-96-5; **12c**, 67873-68-1; **13a**, 80082-27-5; **13b**, 80082-28-6; **13c**, 80082-29-7; **13d**, 80082-30-0; **13e**, 80082-31-1; **14**, 80082-32-2; 6-chloroisocytosine, 1194-21-4; phenylhydrazine, 100-63-0.

Supplementary Material Available: Full data available include the following: microanalyses on compounds **3a–c**, **3e–j**, **5**, **6**, **8**, **11a,b**, and **13b–e**; UV data on compounds **3a–c**, **3e** (4-aryl isomer), **3f**, **3h–j**, **11a,b**, and **13b–e**; ^1H NMR data on compounds **3a–j**, **10**, **11a,b**, and **13a–e**; ^{13}C NMR data on compounds **3a**,-**c**,**d**,**f–j**; and mass spectral data on **3a–c**,**g–j**, **11a,b**, and **13b**,**d** (8 pages). Ordering information is given on any current masthead page.

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[27] These protons exhibited a distinct ABX pattern after D_2O exchange. J_{AB}(gem) was measured as 13.5 Hz after decoupling at δ 3.88. The other coupling constants and chemical shifts for the geminal protons were determined by spin simulation to be δ 2.84 (J_{AX} = 2.2 Hz) and 3.04 (J_{BX} = 3.8 Hz).

Synthesis and Reactions of 2,6-Diphenyl-4-(trimethysilyl)-4*H*-thiopyran[1]

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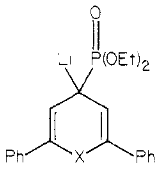
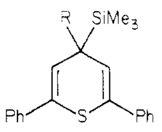
Received September 9, 1981

The title compound **3** was synthesized by trimethylsilyl chloride quenching of 2,6-diphenyl-4-lithio-4*H*-thiopyran (**7**), which was obtained by direct lithiation (*n*-BuLi) of either the 4*H*-thiopyran **10** or the 2*H* isomer **6**. Compound **6** was readily prepared in one step from the reaction of 2,6-diphenyl-4-hydroxy-4*H*-thiopyran (**5**) with NCS in 74% yield. Compound **3** was metalated to give **12** in 80–85% yield by using a combination of *n*-BuLi and *t*-BuOK in THF at an internal temperature slightly below -20 °C. The successful reaction of **12** with a variety of ketones and aldehydes provides an alternative synthesis of the Δ^4-2,6-diphenyl-4*H*-thiopyrans **16**. The scope and limitation of this Peterson-type reaction of **12** is compared with those of the corresponding Wittig–Horner reagent **2**.

Recently we reported the synthesis of the Wittig–Horner reagents of 2,6-diphenyl-4*H*-pyran 1[2] and thiopyran 2[3] and



1, X = O
2, X = S



3, R = H
4, R = M

their uses in the preparation of various *unsymmetrical* $\Delta^{4,4'}$-bi-4*H*-thiopyrans and *polyene-separated* $\Delta^{4,4'}$-bi-4*H*-pyrans and bithiopyrans.[4,5] The thio analogue **2**, however, is less stable than the pyran **1** and in many cases gives poorer yields in condensation reactions with aldehydes or ketones.[3–5] Since most of the interesting organic dark conductors of the bithiopyran class[6] are derived from **2**, an alternative reagent is desired to complement **2** in the synthesis of *unsymmetrical* bithiopyrans. One interesting modification is the Peterson type of reagent[7] **4** in which a trimethylsilyl group is substituted for the diethylphosphonyl group in **2**. This paper describes our synthesis of 2,6-diphenyl-4-(trimethylsilyl)-4*H*-thiopyran (**3**) and the generation of its metalated anion **4** from which a variety of *unsymmetrical* bithiopyrans were prepared in good yields. The scope and limitations of this reaction are

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[1] Presented in part at the 11th Northeast Regional Meeting of the American Chemical Society, Rochester, New York, Oct 18–21, 1981; Abstract NERM 11.

[2] Chen, C. H.; Reynolds, G. A. *J. Org. Chem.* **1980**, *45*, 2449.

[3] Chen, C. H.; Reynolds, G. A. *J. Org. Chem.* **1980**, *45*, 2453.

[4] Reynolds, G. A.; Chen, C. H. *J. Org. Chem.* **1981**, *46*, 184.

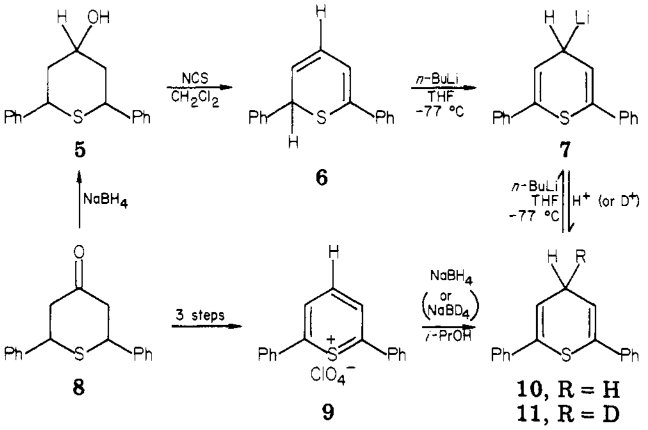
[5] Reynolds, G. A.; Chen, C. H. *J. Heterocycl. Chem.* **1981**, *18*, 627.

[6] Perlstein, J. H. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 519.

[7] Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780. Seebach, D.; Burstinghaus, R. *Synthesis* **1975**, 461.

0022-3263/82/1947-0680$01.25/0

Scheme I



discussed in comparison with the Wittig–Horner reaction of **2**.

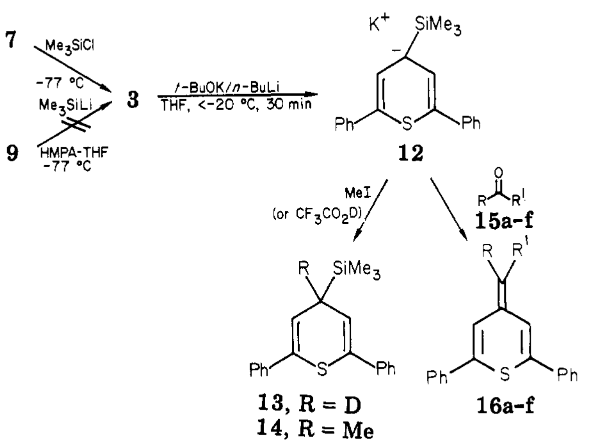
Results and Discussion

Synthesis and Lithiation of 2*H*- and 4*H*-2,6-Diphenylthiopyrans (6 and 10). The key intermediate in our approach toward the synthesis of **3** is the lithiated 2,6-diphenyl-4*H*-thiopyran (**7**), which can be satisfactorily prepared by two different routes from a common starting material, 2,6-diphenyl-4*H*-tetrahydrothiopyran-4-one (**8**),[8] as shown in Scheme I.

By use of a methodology which was developed earlier for the synthesis of diethyl (2,6-diphenyl-2*H*-thiopyran-4-yl)phosphonate,[3] 2,6-diphenyl-2*H*-thiopyran (**6**) can be prepared in one step by direct reaction of *N*-chlorosuccinimide (NCS) with the diastereoisomeric alcohol **5**[9] in methylene chloride. We improved the yield from 57% to 74% by running the reaction in the presence of 4A molecular sieves (ca. 3 times the weight of **5**) as a water scavenger. Presumably, the water generated as a byproduct, if not removed, can hydrolyze the oxidized intermediate chlorosulfonium salt, which is known to give sulfoxide upon hydrolysis.[10] The 2*H* isomer **6**, purified by passing the reaction mixture through a dry column of silica gel, is a yellowish oil which in methylene chloride solution is stable indefinitely in a freezer at ca. −15 °C. Treatment of **6** with *n*-BuLi in THF at −77 °C instantaneously produced a dark green solution, which was characterized as the 4-lithiated thiopyranyl anion **7** by quenching the reaction with a proton source to give 2,6-diphenyl-4*H*-thiopyran (**10**) in 70% yield. Quenching with deuterated methanol at −77 °C produced the 4-deuterio compound **11** which can be also prepared by reducing the thiopyrylium perchlorate **9** with sodium borodeuteride in isopropyl alcohol. For minimization of deuterium scrambling between the unreacted starting material **9** (which is not very soluble in isopropyl alcohol) and the reduced product **11**, the slow inverse addition of **9** to a solution of sodium borodeuteride is essential for the synthesis of pure **11**.

The 4*H* isomer **10**, which is a solid, also was prepared in 83% yield by sodium borohydride reduction of the corresponding thiopyrylium perchlorate **9**[11] in isopropyl alcohol. For large-scale runs, this latter procedure is preferred because it yields directly a solid product **10**, which is somewhat more stable and can be isolated readily without dry column chromatography. Lithiation of **10** in the manner described for **6** also produces the carbanion **7**, which is stable at −77 °C under argon but decomposes quickly at temperatures around −23 °C. The stability of this anion **7** is similar to that reported for the 2,4,6-triphenylthiopyranyl anion in THF.[12]

Scheme II



Synthesis and Metalation of 2,6-Diphenyl-4-(trimethylsilyl)-4*H*-thiopyran (3). Quenching the lithiated anion **7** with a large excess of trimethylsilyl chloride at −77 °C gave the 4-trimethylsilated thiopyran **3** in 98% yield. Attempts to prepare **3** by direct coupling of (trimethylsilyl)lithium generated in HMPA[13] with thiopyrylium perchlorate **9** in THF at −77 °C were not successful.

Direct lithiation of **3** with *n*-BuLi, *sec*-BuLi, *t*-BuLi, and lithium diisopropylamine (LDA) in THF under a variety of conditions was ineffective in generating any appreciable amount of **4** (M = Li). These results suggest that the 4*H* proton is rendered somewhat less acidic in **3** than in the parent 4*H*-compound **10** by the substitution of the trimethylsilyl group at C-4.[14] The carbon–silicon bond in **3** was also quite susceptible to cleavage by alkoxide ions. This was supported by treating a THF solution of **3** with 1.3 equiv of LDA at −77 °C, quenching the solution with excess CD_3OD to give mostly the 4-deuterio-4*H*-substituted compound **11** (71%) with essentially no 4-(trimethylsilyl)-4-deuterio compound **13** detectable by ^1H NMR. Under the same experimental conditions, quenching with methyl iodide resulted in the quantitative recovery of the starting material **3**.

Compound **3** was deprotonated *only* by the consecutive use of potassium *tert*-butoxide and *n*-butyllithium[15-17] in THF at a reaction solution temperature slightly below −20 °C under argon. Under these conditions, a dark green solution of the metalated species formed instantaneously. The optimum yields of **12** as determined by quenching with trifluoroacetic acid-*d* or methyl iodide to give the deuterio- and methyl-substituted derivatives **13** and **14**, respectively, were about 80% (Scheme II). We found that the addition of 2 equiv each of potassium *tert*-butoxide and *n*-BuLi gave the most reproducible results. When **3**

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[8] Chen, C. H.; Reynolds, G. A.; Van Allan, J. A. *J. Org. Chem.* **1977**, *42*, 2777.

[9] Chen, C. H.; Reynolds, G. A.; Zumbulyadis, N.; Van Allan, J. A. *J. Heterocycl. Chem.* **1978**, *15*, 289.

[10] Russell, G. A.; Mikol, G. J. In "Mechanism of Molecular Migrations"; Thyagarajan, B. S., Ed.; Interscience: New York, 1969; Vol. 2, pp 157–207.

[11] Reynolds, G. A.; Chen, C. H.; Van Allan, J. A. *J. Org. Chem.* **1979**, *44*, 4456.

[12] Schmidt, R. R.; Burkert, U. *Tetrahedron Lett.* **1973**, 4355.

[13] Still, W. C. *J. Org. Chem.* **1976**, *41*, 3063.

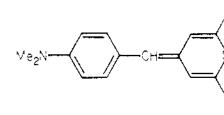
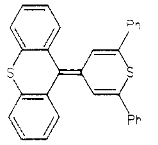
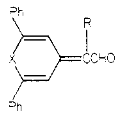
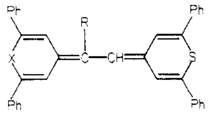
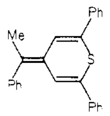
[14] McEwen, W. K. *J. Am. Chem. Soc.* **1936**, *58*, 1124.

[15] Trepka, W. J.; Favre, J. A.; Sonnenfeld, R. J. *J. Organomet. Chem.* **1973**, *55*, 221.

[16] An external cooling bath of 3-heptanone and dry ice (−35 °C) was adequate to keep the reaction temperature within this desired range.

[17] Schlosser, M.; Hartmann, J. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 508.

Table I. Comparison of the Reactions of 12 and 2 in the Synthesis of Δ^4-2,6-Diphenyl-4*H*-thiopyrans 16a-f

	starting carbonyl compd (15)	product (16)	mp, °C	% yield from 12	% yield from 2
a	*p*-(dimethylamino)benzaldehyde		145-146	78.5	67[3]
b	thioxanthen-9-one		256-257	47	43[3]
					
c	X = O, R = H		257-258	61	6[4]
d[4]	X = S, R = H		301-302	44	29[4]
e	X = O, R = Me		169-170	58	
f	acetophenone		166-167	0	15

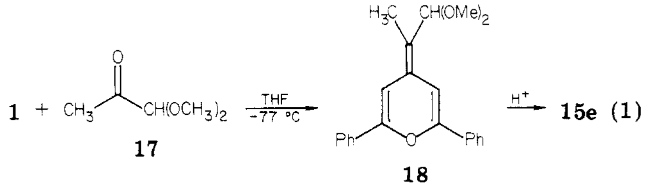
was deprotonated at a lower temperature (−42 °C) or by using 1.1 equiv each of potassium *tert*-butoxide and *n*-BuLi, the yields of 11 dropped to ca. 50%. Once generated, 12 is quite stable when kept at −42 °C or lower.

Synthesis of Δ^4-2,6-Diphenyl-4*H*-thiopyrans 16. Scope and Limitations. Dropwise addition of ketones or aldehydes 15a–f to the dark green solution of the carbanion 12 in THF at −25 to −20 °C resulted in rapid discoloration (to reddish brown). Slow equilibration of the reaction mixture to room temperature followed by aqueous ammonium chloride workup gave a variety of *unsymmetrical* Δ^4-2,6-diphenyl-4*H*-thiopyrans (16a–f) in good yields. Table I shows these results compared with those obtained by using the Wittig–Horner reagent 2.[3] In general, the Peterson reagent 12 produced somewhat better results than did 2, particularly in the synthesis of ethanediylidene $\Delta^{4,4'}$-bi-4*H*-thiopyrans 16c and 16d,[4] where the yields were improved from ca. 6% to 61% and from 29% to 44%, respectively. An exception is acetophenone (15f), which apparently has enolizable hydrogens that are acidic enough to quench the basic anion 12 before the desired nucleophilic addition can proceed at an appreciable rate. Other compounds that failed to add to 12 were 2,6-diphenyl-4*H*-tetrahydrothiopyran-4-one (8) and 5,6-dihydro-6-phenyl-4*H*-thiopyran-4-one.[18] Both of these compounds have α hydrogens adjacent to a ketone function.

These results further support the idea that the trimethylsilyl substitution at C-4, despite the stabilizing effect of the empty d orbitals of silicon,[7,19] actually increases the basicity of the 2,6-diphenylthiopyranyl anion 7. The net effect of the trimethylsilyl group is presumably a negative inductive effect ($\sigma_I = -0.11$)[20] which renders the tertiary carbanion 12 more basic than the parent 7, which is secondary. Thus, we conclude that the Peterson reagent 12 tends to react as a base in the presence of any carbonyl compounds with α hydrogens to generate the corresponding enolates, particularly at low temperature when the desired nucleophilic addition is slow.

Despite some undetermined differences imposed by the potassium counterion[21] on the reactivity of 12, the lithiated Wittig–Horner reagent 2 has the strong electron-withdrawing (Hammett $\sigma \sim +0.288$)[22] diethylphosphonyl group substituted at C-4 and is less basic than either the carbanion 12 or 7. Therefore, 2 is the reagent of choice for minimizing the proton-transfer reaction during the condensation with ketones or aldehydes with α hydrogens. The chemical shifts (δ) of the 4-H protons of diethyl (2,6-diphenyl-4*H*-thiopyran-4-yl)phosphonate,[3] 10, and 3, which decrease in the order 4.0, 3.1, and 2.8 ppm, respectively, appear to correlate also with the relative order of increasing pK_a values of these compounds.[23]

The new pyran aldehyde 15e used in Table I was synthesized by condensing 1 with the dimethyl acetal of pyruvaldehyde (17) to give 18, which, upon acid hydrolysis, afforded 15e in 35% yield (eq 1).



Experimental Section

^{1}H NMR spectra were recorded on a Varian EM-390 spectrometer with tetramethylsilane as an internal standard. ^{13}C NMR spectra were recorded on a Varian CFT-20 spectrometer with Me$_4$Si as the internal standard; multiplicity was determined by the off-resonance proton decoupling. Melting points (uncorrected) were obtained on a Thomas-Hoover capillary melting point ap-

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[18] Chen, C. H.; Doney, J. J.; Reynolds, G. A. *J. Org. Chem.* **1981**, *46*, 4604.

[19] Covin, E. W. *Chem. Soc. Rev.* **1978**, *7*, 15.

[20] Taft, R. W.; Price, E., Fox, I. R.; Lewis, C. L.; Andersen, K. K.; Davis, G. T. *J. Am. Chem. Soc.* **1963**, *85*, 709. Ritchie, C. D.; Sager, W. F. *Prog. Phys. Org. Chem.* **1964**, *2*, 323.

[21] For example, see: Raucher, S.; Koolpe, G. A. *J. Org. Chem.* **1978**, *43*, 3794.

[22] Swain, C. G.; Lupton, E. C., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4328. Kabatschnik, M. I. *Z. Chem.* **1961**, *1*, 289.

[23] Farnum, D. G. *Adv. Phys. Org. Chem.* **1975**, *11*, 123.

paratus. Mass spectra were obtained on an AEI MS-30 mass spectrometer. Elemental analyses were done by the Analytical Sciences Division, Kodak Research Laboratories.

2,6-Diphenyl-2*H*-thiopyran (6). To a solution of 10.8 g (0.04 mol) of 2,6-diphenyl-4-hydroxy-4*H*-tetrahydrothiopyran (**5**, diastereoisomers)[9] in 400 mL of methylene chloride at room temperature was added 30 g of 4A molecular sieves, followed by 5.56 g (1 equiv) of *N*-chlorosuccinimide. The mixture was stirred overnight and was purified by passing it through a 38 cm × 7.5 cm column packed with dry silica gel (activity III), from which, on elution with more methylene chloride, was obtained 7.4 g (74%) of **6** as a yellowish, viscous oil: ^{1}H NMR ($CDCl_3$) δ 4.7 (dd, $J_{2,3} = 5.7$ Hz, $J_{2,4} = 1.2$ Hz, 1, H_2), 5.66 (dd, $J_{3,2} = 5.7$ Hz, $J_{3,4} = 9.3$ Hz, 1, H_3), 6.28 (ddd, $J_{4,3} = 9.3$ Hz, $J_{4,5} = 6.0$ Hz, $J_{4,2} = 1.2$ Hz, 1, H_4), 6.68 (d, $J_{5,4} = 6.0$ Hz, 1, H_5), 7–7.6 (m, 10, Ar H); mass spectrum, *m/e* 250 (M^+ for $C_{17}H_{14}S$), 249 ($M^+ - H$), 216 ($M^+ - H_2S$), 215.

Anal. Calcd for $C_{17}H_{14}S$: C, 81.6, H, 5.6. Found: C, 81.8, H, 5.6.

2,6-Diphenyl-4*H*-thiopyran (10). To a suspension of 10.5 g (0.03 mol) of 2,6-diphenylthiopyrylium perchlorate (**9**)[11] in 350 mL of 2-propanol was added 1.4 g of powdered sodium borohydride. The mixture was stirred at room temperature overnight, poured into 1.3 L of water, and stirred for 1.5 h until the excess sodium borohydride was destroyed. The precipitated dark gray solid was collected, washed thoroughly with distilled water, and dried in vacuo at room temperature to give 6.3 g (83%) of **10**:[24] ^{1}H NMR ($CDCl_3$) δ 3.1 (t, $J = 4.5$ Hz, 2, H_4), 5.85 (t, $J = 4.5$ Hz, H_2, H_6), 7.1–7.6 (m, 10, Ar H); mass spectrum, *m/e* 250 (M^+ for $C_{17}H_{14}S$), 249 ($M^+ - H$), 216 ($M^+ - H_2S$), 215; ^{13}C NMR ($CDCl_3$) δ 28.85 (C-4), 116.69 (C-3 and C-5), 126.46, 128.16, 128.47, 134.81, 138.59 (Ph). This material was pure enough to be used in subsequent reactions. An analytical sample was obtained by column chromatography over silica gel eluted with methylene chloride-/hexanes (1:3 v/v); mp 63–64 °C.

Anal. Calcd for $C_{17}H_{14}S$: C, 81.6; H, 5.6. Found: C, 82.0; H, 5.8.

Deuterium Quenching of 7. Synthesis of 4-Deuterio-2,6-diphenylthiopyran (11). To a cooled (−77 °C) solution of 250 mg (0.6 mmol) of **6** in 12 mL of dry THF was added 0.3 mL (1.2 equiv) of a 2.4 M solution of *n*-BuLi in hexane under argon. The reaction mixture immediately turned dark blue and was stirred at −77 °C for 1 h. Excess methanol-*d* (2 mL) was added, and the solution was allowed to equilibrate to room temperature, poured into aqueous ammonium chloride, extracted with ether, dried ($MgSO_4$), and evaporated to give 145 mg of crude **11** as a reddish brown gum: ^{1}H NMR ($CDCl_3$) δ 3.1 (m, 1, H_4), 5.85 (d, $J = 4.5$ Hz, 2, H_3, H_5) 7.1–7.6 (m, 10, Ar H); mass spectrum, *m/e* 251 (M^+ for $C_{17}H_{13}DS$). The ^{1}H NMR and mass spectra were identical with those of an authentic sample prepared as follows.

To a solution of 0.3 g of $NaBD_4$ (Ventron Corp.) in 70 mL of isopropyl alcohol was added slowly 1 g (2.87 mmol) of powdered thiopyrylium perchlorate **9**[11] over ca. 15 min at room temperature. The reaction mixture was stirred for about 2 h and poured into 500 mL of cold water. The precipitated yellow solid was collected by filtration, washed thoroughly with water, and dried in vacuo (25 °C) to give 0.34 g (47%) of **11**. An analytical sample was obtained by recrystallization from MeOH; mp 68–69 °C.

Anal. Calcd for $C_{17}H_{13}DS$: C, 81.3; H(D), 5.9. Found: C, 80.9; H, 5.7.

2,6-Diphenyl-4*H*-thiopyran (10) from the 2*H* Isomer 6. To a solution of 2,6-diphenyl-2*H*-thiopyran (**6**; 0.5 g, 2 mmol) in 50 mL of dry THF at −77 °C under argon was added dropwise by syringe (internal temperature kept at <−55 °C) 1.0 mL of *n*-BuLi (2.3 M in hexane). The dark blue anion formed immediately, and the mixture was stirred for 1 h at −77 °C, at which time 1.0 mL of methanol (excess) was added to quench the reaction. The reaction mixture was allowed to equilibrate to room temperature, poured into aqueous NH_4Cl, and stirred for 1 h. The precipitated solid was filtered, washed with water, and air-dried to yield 350 mg (70%) of crude **10** whose ^{1}H NMR, ^{13}C NMR, and mass spectra were identical with those of an authentic sample. This material, which had a small amount of yellow, nonpolar impurity (TLC), was suitable for use in subsequent reactions.

2,6-Diphenyl-4-(trimethylsilyl)-4*H*-thiopyran (3). To a solution of 2.0 g (8 mmol) of **10** in 50 mL of dry THF at −77 °C under argon was added dropwise by syringe (internal temperature kept at <−55 °C) 4.2 mL of *n*-BuLi (2.1 M in hexane). The dark blue anion immediately formed, the mixture was stirred for 5 min at −77 °C, and 4.0 mL (large excess) of freshly distilled chlorotrimethylsilane was added. The reaction mixture was allowed to warm to room temperature, poured into 400 mL of 5% aqueous NH_4Cl, and stirred for 1 h. The precipitated solid was filtered, washed with water, and air-dried to yield 2.52 g (98%) of crude **3**. This material, which had a small amount of reddish nonpolar impurity (TLC), was suitable for use in subsequent reactions.

An analytical sample was obtained by recrystallization of 2.52 g of this crude material in 35 mL of MeOH to yield 1.85 g (71% based on **10**) of pure **3**: mp 84–86 °C; mass spectrum, *m/e* 322 (M^+ for $C_{20}H_{22}SSi$); ^{1}H NMR ($CDCl_3$) δ 0.23 (s, 9), 2.80 (t, J_{AX_2} 6.5 Hz, 1), 5.87 (d, $J_{X_2A} = 6.5$ Hz, 2), 7.17–7.57 (m, 10, Ar H); ^{13}C NMR ($CDCl_3$; decoupled) δ −2.55 (sp^3, silyl methyl), 35.74 (sp^3, C-4 of pyran ring), 119.50 (sp^2, C-3 and C-5 of pyran ring), 126.09, 127.81, 128.41, 129.64, 139.03 (Ph).

Anal. Calcd for $C_{20}H_{22}SSi$: C, 74.48; H, 6.87. Found: C, 74.33; H, 6.96.

Procedure for the Generation of 12 from 3. To a stirred solution of 300 mg (2 mmol) of dry potassium *tert*-butoxide[25] in 25 mL of dry THF under argon in a 3-heptanone/dry ice cooling bath (−35 °C) was added a cooled solution of **3** (1 mmol) in 10 mL of dry THF via syringe (a light green color usually appeared as **3** was added). With the internal temperature kept slightly below −20 °C, 0.95 mL (2 mmol) of *n*-BuLi (2.1 M in hexane) was added dropwise via syringe, and the reaction mixture was stirred for 30 min. The resulting intensely dark green solution was then ready for reaction with the following electrophiles. Because of the presence of excess base, 2 mmol of the desired electrophile was required.

Deuterium Quenching of 2 with Trifluoroacetic Acid-*d*. To a stirred solution of the carbanion **12** prepared above, 0.3 mL of trifluoroacetic acid-*d* was added dropwise. The solution immediately changed from the intense green color of the anion to orange-red, and the solution was poured into a two-phase 1:1 mixture of hexane and 5% aqueous NH_4Cl. The mixture was stirred for 5 min at <−22 °C, the hexane layer was separated and dried ($MgSO_4$), and the solvent was removed. The crude orange-red oily residue contained 2,6-diphenyl-4-deuterio-4-(trimethylsilyl)-4*H*-thiopyran (**13**) as the major product: ^{1}H NMR ($CDCl_3$) δ 0.23 (s, 9), 5.85 (br m, 2), 7.71–7.57 (m, 10, Ar H); mass spectrum, *m/e* 323 (M^+ for $C_{20}H_{21}DSSi$).

Because of some additional unidentified byproducts and the overlapping absorptions in the ^{1}H NMR from the starting material, the quenching of **12** with MeI gave a far superior quantitative estimate of the carbanion formation.

Quenching of 12 with MeI. To a stirred solution of the carbanion **12** prepared above was added 0.5 mL of MeI (excess) dropwise. The reaction was worked up as described for the deuterium quenching experiment to yield a crude orange-red oil. Assay by ^{1}H NMR of this crude material gave estimated yields of 75–85% (over four experiments) of the methylated product, with the balance of the material being the starting material **3**. The structure of the methylated product **14** was supported by spectral analyses: ^{1}H NMR ($CDCl_3$) δ 0.20 (s, 9), 1.30 (s, 3), 5.52 (s, 2), 7.17–7.57 (m, 10, Ar H); mass spectrum, *m/e* 336 (M^+ for $C_{21}H_{24}SSi$).

General Procedure for the Addition of Carbonyl Compounds 15 in the Synthesis of 16 (Peterson Reaction). The preparation of **16c** is an example. A solution of 550 mg (2 mmol) of **15c**[26] in 20 mL of dry THF was added with stirring to **12** at −35 °C. Thirty minutes after the addition, the reaction mixture was allowed to equilibrate to room temperature for 30 min, poured into 400 mL of 5% aqueous NH_4Cl, and stirred for 1 h. The precipitate was collected, washed with water, dried in air, and purified by recrystallization from 50 mL of dry methanol to yield

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[24] 2,5-Diphenyl-4*H*-thiopyran (10), though mentioned in the Russian literature, has never been isolated and characterized. See Kharchenko, V. G.; Chalaya, S. N. *J. Org. Chem. USSR (Engl. Transl.)* **1975**, *11*, 1518.

[25] Dry powdered potassium *tert*-butoxide (alcohol free) was purchased from MSA Research Corp.

[26] Reynolds, G. A.; Van Allan, J. A. *J. Org. Chem.* **1969**, *34*, 2736.

309 mg (61% based on **3**) of **16c**. Compound **16c** was characterized by comparison (TLC, ^{1}H NMR, IR, and mass spectra) with an authentic sample prepared from the Wittig–Horner reagent **2**.[4]

2-[4-(2,6-Diphenyl-4*H*-pyranylidenyl)]propanaldehyde (15e). A solution of the Wittig–Horner reagent **1**[2] was prepared by dropwise addition of 2.85 mL (1 equiv) of *n*-BuLi (2.1 M in hexane) to a stirred solution of 2.0 g (0.0058 mol) of diethyl (2,6-diphenyl-4*H*-pyran-4-yl)phosphonate[2] in 50 mL of THF at −77 °C. The dark green anion solution was stirred for 5 min at −77 °C and then added slowly (over 5 min) through a transfer needle with positive argon pressure into a stirred solution of 1.4 mL (2 equiv) of distilled pyruvaldehyde dimethyl acetal in 10 mL of THF at −77 °C. The reaction mixture was allowed to equilibrate to room temperature and stirred for 1 h. Acetic acid (2 mL) was added slowly. The mixture was stirred for 15 min and poured into a stirred two-phase mixture of 200 mL of saturated Na_2CO_3 and 200 mL of ether. Water (100 mL) was added, the mixture was partitioned, separated, dried over $MgSO_4$, and filtered, and the solvent was removed on a rotary evaporator. The residue was recrystallized from 30 mL of cyclohexane to yield 580 mg (35%) of **15e**: mp 194–195.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.85 (s, 3, Me), 6.78 (d, 1, J = 2 Hz), 7.60 (d, 1, J = 2 Hz), 7.43 (m, 6), 7.75 (m, 4), 10.10 (s, 1); mass spectrum, *m/e* 288 (M^+ for $C_{20}H_{16}O_2$).

Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.3; H, 5.6. Found: C, 82.8; H, 5.7.

1-[4-(2,6-Diphenyl-4*H*-thiopyranylidenyl)]-1-phenylethane (16f). A solution of the Wittig–Horner reagent **2**[3] was prepared from 6.5 g (0.0186 mol) of thiopyrylium perchlorate **9**[11] in 60 mL of THF and 11 mL (1.2 equiv) of a solution of diethyl sodium phosphonate in benzene (1.9 M) at −77 °C followed by 1.2 equiv of *n*-BuLi under argon (2.4 M in hexanes). A solution of 2.68 g (0.022 mL) of acetophenone in 10 mL of THF was added, and the reaction mixture was allowed to equilibrate to room temperature in 4 h. The reddish brown mixture was poured into a beaker containing 500 mL of water. The precipitated gum was removed from the water by decantation and then stirred in ether. The insoluble solid was collected by filtration and recrystallized from 100 mL of acetonitrile to give 1 g (15%) of pure **16f**: mp 166–167 °C; ^{1}H NMR ($CDCl_3$) δ 2.13 (s, 3, Me), 6.75 (s, 1), 6.86 (s, 1), 7.15–7.64 (m, 15, Ar H); mass spectrum, *m/e* 352 (M^+).

Anal. Calcd for $C_{25}H_{20}S$: C, 85.2; H, 5.7. Found: C, 84.8; H, 5.7.

Registry No. **1**, 75548-91-3; **2**, 75548-92-4; **3**, 80160-61-8; **5**, 55221-37-9; **6**, 71750-06-6; **7**, 80160-62-9; **9**, 13586-29-3; **10**, 57094-07-2; **11**, 80160-63-0; **12**, 80160-64-1; **13**, 80160-65-2; **14**, 80160-66-3; **15a**, 100-10-7; **15b**, 492-22-8; **15c**, 20399-89-7; **15d**, 75548-93-5; **15e**, 40564-75-8; **15f**, 98-86-2; **16a**, 73453-38-0; **16b**, 73453-37-9; **16c**, 75548-95-7; **16d**, 51829-03-9; **16e**, 80160-67-4; **16f**, 80160-68-5; **17**, 6342-56-9.

Effect of Metal Ions in Organic Synthesis. Part 10. Synthesis and X-ray Crystal Structure of Some 1-(Arylamino)pyrrole Derivatives by Reaction of (Arylazo)alkenes and β-Dicarbonyl Compounds in the Presence of Copper(II) Chloride

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Received August 18, 1981

A mild, simple, and convenient method for the synthesis of some 1-(arylamino)pyrrole derivatives by reaction of (arylazo)alkenes and β-dicarbonyl compounds is reported. This reactivity appears to be catalyzed by copper(II) chloride dihydrate, takes place in very mild conditions, does not require a strong acid or base, seems to be successfully applicable to different (arylazo)alkenes and β-dicarbonyl derivatives, and frequently provides good yields. In particular, the reaction products of [(*p*-nitrophenyl)azo]cyclohexene and (phenylazo)stilbene with ethyl acetoacetate were examined. The X-ray diffraction study unambiguously demonstrated that the molecular structures of these compounds contain a pyrrole ring instead of a dihydropyridazine ring, as previously reported for analogous products. The details of the molecular parameters are presented and discussed.

In our previous papers some effects of metal ions in certain organic synthesis have been presented.[1] In particular, we reported the stereospecific 1,4 addition reactions of certain alcohols, water, and phenol to the azo-ene system of (phenylazo)stilbene in the presence of copper and iron ions. The role of the metal ions in these reactivities was also discussed.[2]

In continuation of these investigations, the reaction of some (arylazo)alkenes (**1a–c**) and β-dicarbonyl compounds (**2**) in the presence of copper(II) chloride dihydrate (M) has been studied.[3] While in the absence of this inorganic salt no reaction was observed, in the presence of copper(II) ions the above-mentioned reaction easily occurs, providing the 1-(arylamino)pyrrole derivatives (**4a–e**), as shown in Table I. The molecular ratio between the (arylazo)alkene derivative and copper(II) chloride (1:M), the reaction times and procedures, the yields and melting points of the reaction products are also listed in Table I.

In accordance with previous findings on this matter, the reaction probably occurs by 1,4 addition of the β-dicarbonyl compounds to the azo-ene system of the (arylazo)alkene derivatives (**3**), followed by ring closure and elimination to give the pyrrole ring (**4a–e**).[2-5] Since the

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[1] O. Attanasi and S. Gasperoni, *Gazz. Chim. Ital.* **108**, 137 (1978); O. Attanasi, S. Gasperoni, and C. Carletti, *Chim. Ind.* (*Milan*), **60**, 654 (1978); *J. Prakt. Chem.*, **322**, 1063 (1980); O. Attanasi and F. Serra-Zanetti, *Synthesis*, 314 (1980); *Org. Prep. Proced. Int.*, **13**, 170 (1981), and references therein.

[2] O. Attanasi, *Stud. Urbinati, Fac. Farm.*, **17**, 123 (1975); O. Attanasi, P. Battistoni, and G. Fava, *Synth. Commun.*, **9**, 465 (1979); *J. Org. Chem.*, **46**, 447 (1981), and references therein.

[3] O. Attanasi and P. Bonifazi, 12th Convegno Nazionale Chimica Organica, Società Chimica Italiana, Ancona, Sept 14–19, 1980 p 131.

[4] L. Bernardi, P. Masi, and G. Rosini, *Ann. Chim.* (*Rome*), **63**, 601 (1973).

[5] S. Brodka and H. Simon, *Justus Liebigs Ann. Chem.*, **745**, 193 (1971).

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