

0.05 mmol) gave **2e**⁹ (173 mg, 78%): ¹H NMR (200 MHz, CDCl₃) δ 1.55 (s, 6 H), 6.45 (s, 2 H), 7.19–7.45 (m, 10 H); ¹³C NMR (50 MHz, CDCl₃) δ 28.7, 40.8, 125.8, 125.9, 126.2, 126.7, 127.0, 128.2, 128.5, 137.7, 140.2, 148.7.

(*1E,3E*)-5,5-Dimethyl-1-phenyl-1,3-hexadiene (**2f**), (*4E*)-6-Phenyl-2-methyl-2,4-heptadiene (**8**), and (*1E*)-3,5-Dimethyl-1-phenyl-1,4-hexadiene (**9**). Via the general procedure, the reaction of **1f** (124 mg, 0.5 mmol), MeMgI (1.0 mL of a 2 M solution in ether, 2 mmol), and NiCl₂(dppe) (13.2 mg, 0.025 mmol) gave a mixture of **2f**, **8**, and **9** (74 mg, 80%, **2f**:**8**:**9** = 71:16:13). After chromatographic separation, **2f** and **8** were obtained. Compound **8** was extremely unstable in pure form. Attempts to separate **9** from **2f** were unsuccessful. **2f**:¹⁰ ¹H NMR (200 MHz, CDCl₃) δ 1.07 (s, 9 H), 5.85 (d, *J* = 15.4 Hz, 1 H), 6.14 (dd, *J* = 15.4, 9.9 Hz, 1 H), 6.46 (d, *J* = 15.7 Hz, 1 H), 6.75 (dd, *J* = 15.7, 9.9 Hz, 1 H), 7.17–7.39 (m, 5 H); ¹³C NMR (50 MHz, CDCl₃) δ 29.6, 33.4, 125.4, 126.1, 127.0, 128.5, 129.9, 130.2, 137.7, 146.8. **8**: ¹H NMR (200 MHz, CDCl₃) δ 1.37 (d, *J* = 7.0 Hz, 3 H), 1.73 (s, 3 H), 1.74 (s, 3 H), 3.50 (m, 1 H), 5.70 (dd, *J* = 15.1, 7.0 Hz, 1 H), 5.79 (d, *J* = 10.6 Hz, 1 H), 6.25 (dd, *J* = 15.1, 10.6 Hz, 1 H), 7.16–7.32 (m, 5 H); ¹³C NMR (75 MHz, CDCl₃) δ 18.3, 21.5, 25.9, 42.5, 124.9, 125.3, 126.0, 127.2, 128.4, 133.9, 136.2. **9**: ¹H NMR (200 MHz, CDCl₃) δ 1.12 (d, *J* = 6.9 Hz, 3 H), 1.66 (s, 3 H), 1.71 (s, 3 H), 3.20 (m, 1 H), 5.04 (d, *J* = 8.8 Hz, 1 H), 6.15 (dd, *J* = 16.1, 6.4 Hz, 1 H), 6.31 (d, *J* = 16.1 Hz, 1 H), 7.17–7.39 (m, 5 H).

(*E*)-1-Cyclohexyl-3,3-dimethyl-1-butene (**2g**), (*1E*)-1-Cyclohexyl-3-methyl-1,3-butadiene (**10**), and [(2-Methyl-1-propenyl)methylene]cyclohexane (**11**). Via the general procedure, the reaction of **1g** (228 mg, 1.0 mmol), MeMgI (2.0 mL of a 2 M solution in ether, 4 mmol), and NiCl₂(dppe) (26.3 mg, 0.05 mmol) gave a mixture of **2g**, **10**, and **11** (145 mg, 89%, **2g**:**10**:**11** = 77:9:14). After chromatographic separation, a mixture of **2g** and **11** was obtained as an oil. Attempts to separate **10** from **2g** were unsuccessful. **2g**: IR 2957, 2929, 2851, 1449, 976 cm⁻¹; ¹H NMR (200 MHz, CDCl₃) δ 0.96 (s, 9 H), 0.92–1.35 (m, 5 H), 1.57–1.72 (m, 5 H), 1.85 (m, 1 H), 5.23 (dd, *J* = 15.7, 6.3 Hz, 1 H), 5.37 (d, *J* = 15.7 Hz, 1 H); ¹³C NMR (50 MHz, CDCl₃) δ 26.2, 26.3, 29.9, 32.5, 33.5, 40.7, 130.8, 138.9; MS *m/z* (relative intensity) 166 (M⁺, 18), 151 (23), 110 (72), 95 (37), 83 (56), 69 (100); exact mass calcd for C₁₂H₂₂ 166.1721, found 166.1713. **10**:¹⁰ ¹H NMR (200 MHz, CDCl₃) δ 0.92–1.35 (m, 5 H), 1.57–1.91 (m, 6 H), 1.81 (s, 3 H), 4.85 (s, 2 H), 5.58 (dd, *J* = 15.8, 7.0 Hz, 1 H), 6.10 (d, *J* = 15.8, 1 H). **11**: IR 3050, 2921, 1630, 1610, 1460 cm⁻¹; ¹H NMR (200 MHz, CDCl₃) δ 1.54 (m, 6 H), 1.73 (s, 3 H), 1.77 (s, 3 H), 2.14 (bs, 2 H), 2.25 (bs, 2 H), 5.91 (d, *J* = 11.3 Hz, 1 H), 6.02 (d, *J* = 11.3 Hz, 1 H); ¹³C NMR (50 MHz, CDCl₃) δ 18.0, 26.3, 26.9, 27.8, 28.7, 29.0, 37.6, 118.0, 120.4, 132.6, 140.6.

Camphene (**14**). Via the general procedure, the reaction of **13** (198 mg, 1.0 mmol) with MeMgI (2.0 mL of a 2 M solution in ether, 4 mmol) in the presence of NiCl₂(dppe) (26.3 mg, 0.05 mmol) gave **14** (112 mg, 82%), which exhibited physical properties identical to those of the authentic sample.

(*E*)-4-Phenyl-1,3-pentadiene (**5**) and (*E*)-2-Phenyl-4-methyl-2-pentene (**6**). Via the general procedure, the reaction of **4** (118 mg, 0.5 mmol), MeMgI (1.0 mL of a 2 M solution in ether, 2 mmol), and NiCl₂(dppe) (13.2 mg, 0.025 mmol) gave a mixture of **5** and **6** (52 mg, 72%, **5**:**6** = 93.7). After chromatographic separation, a mixture of **5** and **6** was obtained as an oil. **5**:¹¹ ¹H NMR (300 MHz, CDCl₃) δ 2.18 (s, 3 H), 5.20 (d, *J* = 10.3 Hz, 1 H), 5.33 (d, *J* = 17.4 Hz, 1 H), 6.47 (d, *J* = 11.0 Hz, 1 H), 6.77 (ddd, *J* = 17.4, 11.0, 10.3 Hz, 1 H), 7.23–7.48 (m, 5 H); ¹³C NMR (75 MHz, CDCl₃) δ 16.0, 117.6, 125.7, 127.1, 127.7, 128.2, 133.5, 136.7, 143.0. **6**:¹² ¹H NMR (300 MHz, CDCl₃) δ 1.05 (d, *J* = 6.6 Hz, 6 H), 2.05 (s, 3 H), 2.70 (m, 1 H), 5.61 (d, *J* = 9.1 Hz, 1 H), 7.23–7.48 (m, 5 H).

Acknowledgment. This work has been supported by the National Science Council of the Republic of China.

(9) Zimmerman, H. E.; Steinmetz, M. G.; Kreil, C. L. *J. Am. Chem. Soc.* 1978, 100, 4147.

(10) Tamura, R.; Saegusa, K.; Kakihana, M.; Oda, D. *J. Org. Chem.* 1988, 53, 2723.

(11) Reich, H. J.; Wollowitz, S. *J. Am. Chem. Soc.* 1982, 104, 7051.

(12) Zioudrou, C.; Moustakali-Mavridis, I.; Chrysochou, P.; Karabatsos, G. *J. Tetrahedron* 1978, 34, 3181.

Registry No. **1a**, 107389-59-3; **1b**, 142039-23-4; **1c**, 142039-24-5; **1d**, 142039-25-6; **1e**, 142039-26-7; **1f**, 142039-27-8; **1g**, 142039-28-9; **2a**, 3846-66-0; **2b**, 142039-29-0; **2c**, 79958-53-5; **2d**, 142039-30-3; **2e**, 56763-59-8; **2f**, 114444-87-0; **2g**, 109660-16-4; **4**, 142039-31-4; **5**, 55177-38-3; **6**, 70303-26-3; **8**, 142039-32-5; **9**, 142039-33-6; **10**, 88001-23-4; **11**, 62412-27-5; **13**, 142039-34-7; **14**, 79-92-5; NiCl₂(dppe), 14647-23-5.

Supplementary Material Available: ¹³C NMR spectra of **2b–d, g, 8**, and **11** (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.

Experimental and Theoretical Study of the Orientation in Lithiation of Dithieno[2,3-*b*:3',2'-*d*]pyridine

Salo Gronowitz,* Kálmán J. Szabó, and Mohamed Ali Hassan[†]

Division of Organic Chemistry 1, Chemical Center, University of Lund, P.O. Box 124, S-221 00 Lund, Sweden

Received December 30, 1991

Several papers have recently been published on the regioselectivity in electrophilic substitution reactions of dithienopyridine ring systems^{1,2} with angular annelation. These publications have hitherto been focused on the experimental and theoretical investigation of nitration.^{1,2} The present study was undertaken in order to gain insight into the regioselectivity in the lithiation of dithieno[2,3-*b*:3',2'-*d*]pyridine. A comparison of the regioselectivity of this ring system with the mechanistically different electrophilic substitution reactions is especially interesting, because nitration (bromination) and lithiation might lead to different regioselectivity.

Experimental Results. Lithium diisopropylamide (LDA) in ether or THF was used as reagent in the lithiation reactions. In the second step dimethylformamide, dimethyl disulfide, or bromine were added as scavengers, resulting in the corresponding formyl (**1A**) methylthio (**2A**) and bromo (**3**) derivatives (Figure 1).

In the case of addition of DMF a minor product (~5%) could also be isolated. This product was identified as 7-(hydroxymethyl)dithienopyridine (**1B**). Its formation might be due to a Cannizzaro reaction of the formyl derivative in the basic medium of the reaction. However, the corresponding carboxylic acid derivative could not be isolated.

The substitution reactions were followed by GLC, and the reaction mixtures were also analyzed by NMR. Only products substituted in the 7-position could be detected. Besides this, the reaction mixture contained only unreacted starting material. Its recovery is the consequence of noncomplete lithiation and/or consecutive substitution reactions. By treating the dithienopyridine with a large (5-fold) excess of LDA followed by addition of dimethyl disulfide, the final reaction mixture consisted of 85% of the 7-substituted derivative (**2A**) and 15% of 2,7-bis-(methylthio)dithieno[2,3-*b*:3',2'-*d*]pyridine (**2B**).

The determination of the substitution position was achieved using 1D ¹H NMR, ¹³C NMR, and 2D COSY and HETCOR techniques. The ¹H NMR spectra of the isolated products show long-range coupling between H⁵ and

[†] On leave of absence from Ain Shams University, Abbassia, Cairo, Egypt.

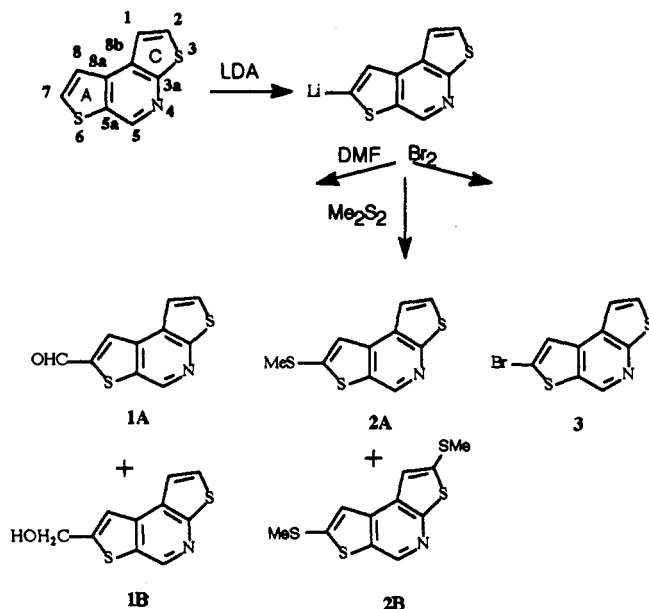


Figure 1. Survey of the lithiation reactions.

Table I. Proton NMR Shifts (ppm) and Coupling Constants (Hz) in CDCl₃

	H ¹	H ²	H ³	H ⁸	-CH ^a	-OH	² J ₁₂	⁴ J ₆₈	³ J _{8-CH}	² J _{-CH₂OH}
1A	7.68	7.75	9.13	8.36	10.25		5.8	0.8		
1B ^b	7.87	7.93	9.13	7.84	4.9	5.95	5.8	0.8	1.1	5.8
2A	7.52	7.58	8.88	7.45	2.71		5.9	0.7		
2B	7.34		8.75	7.33	2.69, 2.64					
3	7.53	7.63	8.90	7.70			6.0	0.7		

^a Proton shift of the corresponding substituent (-CHO, -CH₂OH, -SCH₃).

^b DMSO-d₆ was used as solvent.

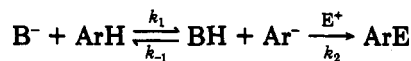
H⁸ (Table I). This proves that these positions remained unchanged. The small long-range coupling is characteristic of the dithienopyridine systems³ and also of their derivatives.² The COSY spectrum of **3**, using carefully chosen relaxation delay parameters to emphasize the long-range couplings, also shows interaction between protons H⁵ and H⁸. The thiophenic α and β carbons can be differentiated by measuring their C-H coupling constants. They are about 190 and 170 Hz for α and β carbon atoms respectively (Table II). The HETCOR spectrum of **3** shows C-H interaction between the carbon atom at 119.4 ppm, with CH coupling constant 170.7 Hz (characteristic for the thiophenic β position), and the proton doublet at 7.53 ppm, with coupling constant 6.0 Hz. On the basis of the above-mentioned considerations this carbon atom can be assigned as C¹. Further C-H interactions could be detected between ¹³C shifts at 124.3, 127.1, and 139.8 ppm and ¹H shifts at 7.7, 7.63, and 8.90 ppm, respectively, which can be assigned to C⁸, C², and C⁵. The information over C-H interactions of this HETCOR map were also exploited for the assignment of C¹ and C² for the rest of the products.

Characteristic thiophene α - β couplings (\approx 6 Hz) are missing in the proton spectrum of **2B** indicating that disubstitution has not taken place in the same thiophene ring. The thiophenic C-H coupling constants, 171.5 and 174.3 Hz, refer to intact β positions and 1,7-disubstitution. Besides the chemical shifts of the ring system a peak at 10.25 ppm in the ¹H NMR spectrum and at 186.4 ppm in

the ¹³C NMR spectrum of **1A** appear, which are characteristic for the formyl group. The ¹H NMR shift at 2.71 ppm and ¹³C NMR shift at 19 ppm in the spectra of **2A** could be assigned to the methyl group. Two upfield chemical shifts can be found in the proton spectrum of **1B**, a doublet at 4.90 ppm and a triplet at 5.95 ppm, with integral ratio 2:1. A new long-range coupling appears between the proton at 4.90 ppm and the ring proton H⁸. By these considerations **1B** can be identified as the 7-hydroxymethyl derivative.

The high regioselectivity in the lithiation is somewhat surprising, because the C_{2v} symmetry of the benzo analogue of the ring system is decreased only by a nitrogen atom. From a synthetic point of view this is, however, very fortunate as nitration² and bromination⁴ result in a mixture of 1- and 2-substituted products.

Theoretical Investigations. The base-catalyzed hydrogen-lithium exchange of aromatic compounds is classified as a B-S_E1 reaction.⁵ This mechanism involves base catalysis of the rate-determining ionization, which forms the aromatic anion, the latter reacts rapidly with the electrophile:



This mechanism has also been suggested for the lithiation of the thiophene ring.⁶ The reaction shows a large kinetic isotope effect⁷ ($k_H/k_T = 5.9$) proving that the rate-determining step is the attack on the hydrogen by the base. The B-S_E1 mechanism is assumed to be valid also for the lithiation reaction of the dithieno[2,3-b:3',2'-d]pyridine system. The regioselectivity is obviously decided in the rate-determining step of the reaction. Faster hydrogen-lithium exchange is expected if a more stable product can be formed. Since Schleyer et al.^{8,9} have shown that the relative energies of carbanions and their lithium salts are closely parallel to each other, it is assumed that the stability of the free carbanions can be correlated with the relative reactivity of the different ring positions. This model holds as long as the thermodynamical stability⁹ of the carbanions (or their lithium salts) determines the regioselectivity. However, if the lithium exchange was governed by kinetic control, and especially if it was accompanied by an early, reagent-like transition state, only investigation of the transition state and potential energy surface of the reaction should provide reliable results.

The GAUSSIAN 86¹⁰ and CADPAC¹¹ computer programs were used on a Cray X-MP/416 supercomputer to perform the calculations. Standard, single-determinant, restricted Hartree-Fock (RHF) calculations were carried out using the split valence 3-21G(*) and 3-21+G(*) basis sets. The d orbitals on the sulfur atoms were included. Stationary structures were optimized by using Schlegel's gradient

(4) Unpublished results.

(5) Taylor, R. *Electrophilic Aromatic Substitution*; Wiley: Chichester, 1990; pp 25-34 and 173-175.

(6) Taylor, R. *The Chemistry of Heterocyclic Compounds, Thiophene and Its Derivatives*; Gronowitz, S., Ed.; Wiley: New York, 1986; part 2, pp 28-30.

(7) Gronowitz, S.; Halvarson, K. *Arkiv Kemi* 1955, 8, 343. Shirley, D. A.; Barton, K. R. *Tetrahedron* 1966, 22, 515.

(8) Schleyer, P. R.; Chandrasekhar, J.; Kos, A. J.; Clark, T.; Spitznagel, G. W. *J. Chem. Soc., Chem. Commun.* 1981, 882.

(9) Schleyer, P. R.; Kos, A. J.; Clark, T.; Spitznagel, G. W.; Rohde, C.; Arad, D.; Houk, K. N.; Rondan, N. G. *J. Am. Chem. Soc.* 1984, 106, 6467.

(10) Frish, M. J.; Binkley, J. S.; DeFrees, D. J.; Fox, D. J.; Martin, R. L.; Flender, E. M.; Pople, J. A. GAUSSIAN 86; Carnegie-Mellon University, Pittsburgh, 1986.

(11) Amos, R. D.; Rice, J. E. CADPAC: *The Cambridge Analytical Derivative Package, Issue 4.0*, Cambridge, 1987.

(1) Szabó, K. J.; Hörnfeldt, A.-B.; Gronowitz, S. *J. Org. Chem.* 1991, 56, 1590.

(2) Gronowitz, S.; Szabó, K. J.; Oluwadiya, J. O. *J. Heterocycl. Chem.* 1991, 29, 351. Szabó, K. J.; Hörnfeldt, A.-B.; Gronowitz, S. *THEOCHEM*, in press.

(3) Yang, Y.; Hörnfeldt, A.-B.; Gronowitz, S. *Chem. Scr.* 1988, 28, 275.

Table II. Carbon NMR Shifts (ppm) and Carbon-Proton Coupling Constants (Hz) in CDCl₃

	C ¹	C ²	C ^{3a}	C ⁵	C ^{5a}	C ⁷	C ⁸	C ^{8a}	C ^{8b}	C ^{sub} ^a
1A										
δ	120.6	129.0	156.0	142.5	138.8	127.9	131.9	147.2	134.2	186.4
¹ J _{CH}	173.8	189.7		189.0			174.8			186.5
² J _{CH}	3.4	6.3		-			-			4.0 ^b
2A										
δ	119.5	126.3	156.8	140.0	140.5	126.0	119.2	148.4	132.7	19.2
¹ J _{CH}	170.3	186.2		184.2			171.5			141.2
² J _{CH}	3.0	5.5		-			-			
2B										
δ	119.6	126.8	157.1	139.2	140.3	139.3	119.1	148.4	133.1	c
¹ J _{CH}	174.3			184.7			171.5			
² J _{CH}	-			-			-			
3										
δ	119.4	127.1	156.9	139.8	134.1	122.4	124.3	138.9	126.0	
¹ J _{CH}	170.7	186.3		182.5			175.5			
¹ J _{CH}	3.0	5.4		-			-			

^a ¹³C shift of the corresponding substituent (-CHO, -CH₂OH, -SCH₃). ^b ²J_{CH}. ^c In order to reduce the costs of the C-H coupling constants measurement, the rather insignificant coupling constants of the methyl groups were not determined.

Table III. Energies Calculated for the Dithienopyridine Anions

	A1	A2	A5	A7	A8
3-21G(*)					
//3-21G(*)					
E _{tot} (au)	-1186.627 713	-1186.642 102	-1186.620 117	-1186.651 009	-1186.633 472
E _{rel} (kJ/mol) ^a	61.2	23.4	81.1	0.0	46.0
3-21+G(*)					
//3-21G(*)					
E _{tot} (au)	-1186.697 525	-1186.708 029	b	-1186.718 099	-1186.703 211
E _{rel} (kJ/mol) ^a	54.0	26.4		0.0	39.1

^a Relative to the most stable anion. ^b The SCF iteration could not forced to convergence.

technique¹² on the ab initio 3-21G(*) level. The final optimization procedure was carried out with no restrictions on the internal coordinates and continued until the largest force was less than 0.001 au. In order to account for that portion of electron density which is allocated to diffuse lone pairs and high energy molecular orbitals, single point calculations were performed by the 3-21+G(*) basis set on the 3-21G(*) geometries.¹³ A single set of diffuse Gaussian s and p functions was applied on heavy atoms and sulfur atoms. The rest of the basis functions were taken from the 3-21G(*) basis set. As the so-constructed 3-21+G(*) basis set contains such basis functions, which are close to the linear dependence, the density matrix elements converge slowly or do not converge at all. This difficulty could be overcome for most of the calculated anions except the 5-deprotonated isomer.

The relative stabilities calculated for the deprotonated dithienopyridine isomers are in good agreement with the experimental findings (Table III). Most stable is the 7-dehydro derivative (A7), followed by the 2-dehydro anion (A2). Anions obtained by deprotonation at thiophenic α positions (A2, A7) are more stable than those deprotonated at the β-position (A1, A8) in accordance with the expectations.⁶ Although the 3-21+G(*) relative stability of the latter isomers are larger than those calculated by the 3-21G(*) basis set, the overall stability sequence is the same by both of the basis sets. It should be noted that the success of this rather simple theoretical model might be due to some fortunate properties of the dithienopyridine substrate: (1) the reactivity differences between the ring positions are relatively high, and (2) sterical hindrance or electron-donating substituents can not influence⁵ the deprotonation step of the heterocyclic α positions.

Most disadvantageous is apparently the deprotonation at position 5. A conceivable explanation of this might be the repulsion between the negative charge resulted from the deprotonation and the lone pair of the nitrogen atom.¹⁴ This is supported by the stretched bonds around position 5 in A5. Bond lengths C⁵C^{5a} and C⁵N⁴ are longer by about 0.07 Å than in the parent compound (P).

The Mulliken analysis was used to calculate the atomic charges (Figure 2). This method is strongly criticized, particularly because the resulting charges depend on the basis set applied.¹³ However, we believe that the comparison of the differences between the atomic charges of parent compound and carbanions can contribute to the rationalization of different stabilities of the deprotonated isomers.

Most of the negative charge, resulting from deprotonation, is localized at the neighboring atoms. The thiophenic α position bears a larger negative charge originally than the β one, as can be seen in the electron distribution of the parent system (Figure 2). As a consequence of this, the α position accepts less negative charge in case of β deprotonation than the β position does upon α deprotonation. The relative stabilities of the anions also depend on the ability of the ring system to delocalize the rest of the negative charge. As a consequence of the charge delocalization, the carbon atom C^{8a} gets negative charge in anions A1, A2, and A8. This is disadvantageous because it breaks off the charge alteration in the pyridine ring. Out of the four possible deprotonations of the thiophene rings only the 7-dehydro anion conserves the positive charge on the carbon atom C^{8a} (Figure 2).

It is noteworthy to compare the electron distribution of A7 to that of the position 7 substituted Wheland intermediate of the nitration reaction.² In the latter case carbon

(12) Schlegel, H. P. *J. Comput. Chem.* 1982, 3, 214.

(13) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986; pp 86 and 336-345.

(14) Meot-Ner (Mautner), M.; Kafafi, S. A. *J. Am. Chem. Soc.* 1988, 110, 6297.

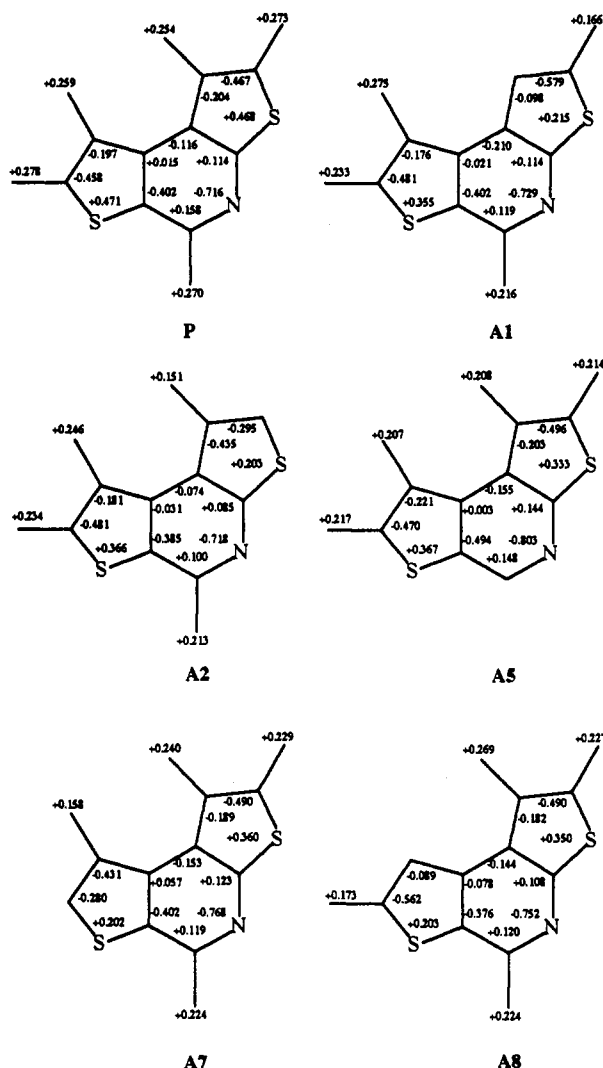


Figure 2. Aromatic charges (3-21G(*) calculated from the Mulliken population analysis.

atom C^{8a} is negatively charged making the electron distribution of the ring system markedly unbalanced. Consequently, this Wheland intermediate becomes less stable than any other Wheland intermediates substituted in thiophenic positions.

Experimental Section

General Procedure for the Substitution Reaction. To a stirred solution of 2.8 mmol of butyllithium in 10 mL of dry ether was added 2.8 mmol of diisopropylamine in 5 mL of dry ether dropwise under nitrogen at room temperature. The mixture was cooled to -70 °C whereupon 0.50 g (2.6 mmol) of dithieno[2,3-*b*:3',2'-*d*]pyridine³ in 50 mL of ether was added dropwise over 30 min. The reaction mixture was kept at -70 °C for 3 h with stirring, and then 2.8 mmol of the corresponding electrophile reagent in 5 mL dry ether was added. The mixture was stirred for an additional hour and then allowed to warm to room temperature. After addition of 10 mL of 2 N hydrochloric acid at 0 °C the solution was stirred for another 30 min. The phases were separated, and the aqueous phase was neutralized by saturated sodium carbonate solution followed by dichloromethane extraction. The organic phase was washed with water, dried, and evaporated. The solid residue was purified by column chromatography on silica gel 60.

7-Formyldithieno[2,3-*b*:3',2'-*d*]pyridine (1A). This compound was purified by column chromatography by using cyclohexane-acetone (3:1) as eluent mixture, yielding 0.32 g (55%) of 1A and 0.03 g (5%) of the hydroxymethyl derivative 1B. Mp: 177-8 °C (1A) and 147-8 °C (1B). Mass spectrum, M⁺, 219 (1A); 221 (1B). Anal. Calcd for C₁₀H₅NOS₂ (1A): C, 54.8; H, 2.5; N,

6.4. Found: C, 54.4; H, 2.9; N, 6.0.

7-(Methylthio)dithieno[2,3-*b*:3',2'-*d*]pyridine (2A). THF was used as solvent instead of ether. A mixture of heptane and chloroform (3:2) was used as eluent for the chromatography, yielding 0.37 g (61%) of 2A. Melting point: 90-91 °C. Mass spectrum, M⁺: 237. Anal. Calcd for C₁₀H₇NS₂: C, 50.6; H, 3.0; N, 5.9. Found: C, 50.3; H, 2.6; N, 5.7.

7-Bromodithieno[2,3-*b*:3',2'-*d*]pyridine (3). This compound was purified by column chromatography using a heptane-dichloromethane (1:1) eluent mixture yielding 0.34 g (48%) of product. Mp: 130-2 °C. Mass spectrum, M⁺: 269, 270. Anal. Calcd for C₉H₄NS₂Br: C, 40.0; H, 1.5; N, 5.2. Found: C, 40.2; H, 1.3; N, 4.9.

Acknowledgment. We thank NSC (National Superdatorcentrum vid Universitet i Linköping) for generous grants of computer time on the Cray X-MP/416. Grants from the Swedish Natural Science Research Council to S.G. are gratefully acknowledged.

Supplementary Material Available: COSY and HETCOR spectra, internal coordinate systems (in Z-matrix form), and optimized geometrical parameters (14 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.

A Triphasic Brominating/Oxidizing System

John Correia

Department of Chemistry, Saint Mary's College,
P.O. Box 4527, Moraga, California 94575

Received February 6, 1992

Aqueous sodium hypochlorite and phase-transfer agents have been used to chlorinate several kinds of compounds such as poly(*p*-methylstyrenes), arenes, alkenes, and various aromatics.¹ There have been fewer reports of bromination with sodium hypobromite.^{1a,2} The halogenations are usually performed at pH 8-9, and mixtures of products are frequently obtained.

This paper introduces a new system prepared from NaOCl which can act as a brominating agent and, in those cases where a reactive bromide is formed, lead to overall production of hydrolysis or oxidation products.

Addition of tetra-*n*-butylammonium hydrogen sulfate (TBAHSO₄) (1 mol) to a solution of NaBr (3 mol) in aqueous NaOCl causes formation of an insoluble orange semisolid. When benzene, CCl₄, or any other nonpolar organic substrate is stirred with this mixture, a third, reddish-colored liquid phase forms at the interface. This interfacial layer consists largely of organic solvent and tetra-*n*-butylammonium tribromide (TBABr₃) but significant amounts of water, hypohalite and halide ions, and possibly Br₂ also appear to be present. A similar triphasic mixture forms when TBABr₃ is combined simply with aqueous hypochlorite.

(1) (a) Fonouni, H. E.; Krishnan, S.; Kuhn, D. G.; Hamilton, G. A. *J. Am. Chem. Soc.* 1983, 105, 7672. (b) Qureshi, A. E.; Ford, W. T. *React. Polym.* 1988, 10, 279. (c) Arnold, J. T.; Bayraktaroglu, T. O.; Brown, R. G.; Heiermann, C. R.; Magnus, W. W.; Ohman, A. B.; Landolt, R. G. *J. Org. Chem.* 1992, 57, 391.

(2) Prokhorova, I. N.; Sirovskii, F. S.; Kartashov, L. M.; Chernysheva, T. V. *Khim. Prom-St.* 1989, 879; *Chem. Abstr.* 1990, 112 (14), 121059r.