($CHCl_3$/hexane); $[\alpha]^{25}_D$ -189.1° (c 1.02, $CHCl_3$); IR (Nujol) 3350, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.60 (d, J = 7.2 Hz, 3 H), 2.57 (d, J = 6.8 Hz, 2 H), 2.80–3.50 (m, 2 H), 3.55–3.90 (m, 1 H), 4.30–4.78 (m, 1 H), 5.40 (q, J = 7.2 Hz, 1 H), 7.38 (s, 5 H). Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.09; H, 7.43; N, 5.78.

(4*R*,5*R*)-*N*-[(*S*)-1-Phenylethyl]-4-[(*tert*-butyldimethylsilyl)oxy]-5-[[(*tert*-butyldimethylsilyl)oxy]methyl]pyrrolidin-2-one (72): 98%; mp 62–65 °C (isopropyl ether); $[\alpha]^{25.5}_D$ -64.0° (c 1.05, $CHCl_3$); IR (Nujol) 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ -0.12 (s, 3 H), -0.08 (s, 3 H), 0.04 (s, 6 H), 0.85 (s, 9 H), 0.92 (s, 9 H), 2.64 (d, J = 7.0 Hz, 3 H), 1.64 (d, J = 7.0 Hz, 3 H), 2.40–2.70 (m, 2 H), 2.98–3.33 (m, 1 H), 3.40–3.77 (m, 2 H), 4.20–4.66 (m, 1 H), 5.40 (q, J = 7.0 Hz, 1 H), 7.18–7.60 (m, 5 H). Anal. Calcd for $C_{25}H_{45}NO_3Si_2$: C, 64.74; H, 9.78; N, 3.02. Found: C, 65.00; H, 9.74; N, 3.16.

(4*R*,5*R*)-*N*-(*tert*-Butoxycarbonyl)-4-[(*tert*-butyldimethylsilyl)oxy]-5-[[(*tert*-butyldimethylsilyl)oxy]-methyl]pyrrolidin-2-one (73): 60% from **72**; mp 89–90 °C (petroleum ether) (lit.[22c] mp 78–79 °C); $[\alpha]^{26}_D$ -49.8° (c 1.60, $CHCl_3$) [lit.[22c] $[\alpha]_D$ -43° (c 1.60, $CHCl_3$)]; spectral data (IR and ^1H NMR) were identical with those of **57**. Anal. Calcd for $C_{22}H_{45}NO_5Si_2$: C, 57.47; H, 9.87; N, 3.05. Found: C, 57.65; H, 9.95; N, 3.03.

(3*R*,4*R*)-Methyl 4-[(*tert*-butoxycarbonyl)amino]-3,5-bis-[(*tert*-butyldimethylsilyl)oxy]pentanoate (74): 75%; $[\alpha]^{25.5}_D$ 2.9° (c 2.77, $CHCl_3$); spectral data (IR and ^1H NMR) were identical with those of **58**.

(3*R*,4*R*)-Methyl 4-[(*tert*-butoxycarbonyl)amino]-3,5-dihydroxypentanoate (75): 47%; $[\alpha]^{25}_D$ 13.7° (c 2.17, $CHCl_3$); spectral data (IR and ^1H NMR) were identical with those of **59**.

(2*S*,3*R*)-Dimethyl 2-[(*tert*-butoxycarbonyl)amino]-3-hydroxyglutarate (76): 42%; $[\alpha]^{25.5}_D$ 30.5° (c 0.573, $CHCl_3$) [lit.[28] $[\alpha]^{20}_D$ 28.9° ($CHCl_3$)]; IR (neat) 1740, 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.46 (s, 9 H), 2.53–2.69 (m, 2 H), 3.30 (d, J = 3.4 Hz, 1 H), 3.73 (s, 3 H), 3.79 (s, 3 H), 4.34 (br d, J = 9.5 Hz, 1 H), 4.60 (br s, 1 H), 5.34 (br d, J = 9.5 Hz, 1 H); HRMS calcd for $C_{10}H_{18}NO_5$ ($M^+ - CO_2CH_3$) 232.1184, found 232.1155.

Acknowledgment. We are grateful for Dr. N. Ikota, National Institute of Radiological Sciences, for spectral data for **34** and **39**, to Professor T. Kunieda, Kumamoto University, for spectral data of **76**, and to Dr. N. Minami, Eisai, Inc., for NOE measurement. We acknowledge partial financial support from the Ministry of Education, Sciences and Culture, the Japanese Government (Scientific Research C No. 63570986).

Synthesis of Halothiophene *S,C*-Ylides and the Corresponding 1,4-Oxathiocines†,[1]

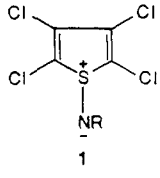
O. Meth-Cohn,*,‡ E. Vuorinen,*,§ and T. A. Modro*,⊥

Sterling Organics, Fawdon, Newcastle upon Tyne, NE3 3TT, U.K., Division for Processing and Chemical Manufacturing Technology, Council for Scientific and Industrial Research, Pretoria 0001, South Africa, and Department of Chemistry, University of Pretoria 0002, South Africa

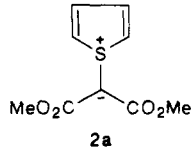
Received March 3, 1989

Crystalline halothiophenium *S,C*-ylides **2**, stabilized by α,α-biscarbonyl (or sulfonyl) substituents have been synthesized from the halo-substituted thiophenes and the corresponding diazoalkanes in the presence of rhodium(II) catalyst. Ylides **2** undergo smooth thermal rearrangement to 1,4-oxathiocines **3**, representing new hetero analogues (O,S) of an eight-membered 10π annulene system. NMR (^1H, ^{13}C) spectroscopy data are given for products **2** and **3**; for the latter no evidence of the aromatic character of the system was obtained.

The known isolable S-substituted derivatives of thiophene comprise alkylthiophenium salts,[2] the mono-[3] and dioxides,[4] and the recently prepared *S,N*-ylides of tetrachlorothiophene **1**.[5] Porter et al. reported[6] that thiophenes react with diazoalkanes under rhodium acetate catalysis to give, depending on the diazo compound used, the ring substituted products or the remarkably stable *S,C*-ylides (e.g. **2a**).



1



2a

We have recently demonstrated[1] that *S,C*-ylides **2**, prepared according to the procedure reported by Porter,[6] undergo a smooth thermal rearrangement to the hitherto unknown 1,4-oxathiocines **3**. In view of the interest in the heteroanalogues of the eight-membered 10π annulenes,[7] and in view of the interesting fragmentation of some these compounds to give polysubstituted benzenes,[8] we report here the full synthesis of ylides **2** and their rearrangement products, 1,4-oxathiocines **3**.

† Parts of this work were presented at the 13th International Symposium on the Organic Chemistry of Sulfur, Odense, Denmark, August 1988.

‡ Sterling Organics.

§ Council for Scientific and Industrial Research.

⊥ University of Pretoria.

(1) Preliminary communication: Meth-Cohn, O.; Vuorinen, E. *J. Chem. Soc. Chem. Commun.* **1988**, 138.

(2) Brunlik, G. C.; Kosak, A. L.; Pitcher, P. *J. Am. Chem. Soc.* **1964**, *86*, 5360. Anderson, R. M.; Harrison, D. R. *J. Chem. Soc.* **1970**, 1764. Heldeweg, R. F.; Hoogeveen, H. *Tetrahedron Lett.* **1974**, 75.

(3) Mock, W. L. *J. Am. Chem. Soc.* **1970**, *92*, 7610. Cf. Geneste, P.; Grimaud, J.; Olivé, J. L.; Ung, S. N. *Tetrahedron Lett.* **1975**, 2345.

(4) Raasch, M. S. *J. Org. Chem.* **1980**, *45*, 856. See also: Gronowitz, S. *Adv. Heterocycl. Chem.* **1963**, *1*, 1. Van Tilborg, W. J. M. *Synth. Commun.* **1976**, *6*, 583.

(5) Meth-Cohn, O.; Van Vuuren, G. *J. Chem. Soc., Perkin Trans. 1* **1986**, 233.

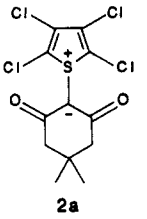
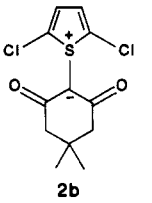
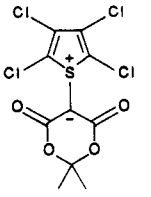
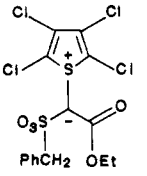
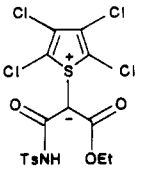
(6) Gillespie, R. J.; Murray-Rust, J.; Murray-Rust, P.; Porter, A. E. A. *J. Chem. Soc., Chem. Commun.* **1978**, 83. Gillespie, R. J.; Porter, A. E. A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2624.

(7) Fletschinger, M.; Zipperer, B.; Fritz, H.; Prinzbach, H. *Tetrahedron Lett.* **1987**, *28*, 2517 and literature cited therein.

(8) Vuorinen, E.; Cheney, D. L.; Modro, T. A., manuscript in preparation.

0022-3263/89/1954-4822$01.50/0

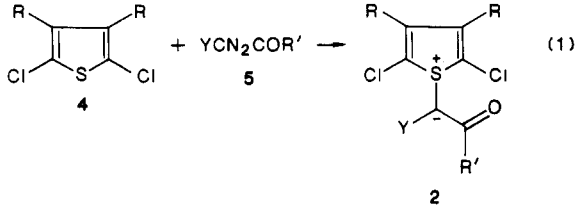
Table I. Synthesis of Chlorothiophene S,C-Ylides

substrates			reaction conditions				
4, R	5, Y	R^1	temp, °C	solvent	time	product (2)	yield, %
Cl	$COCH_2CMe_2CH_2$		rt[a]	none	1 week	 **2a**	67
Cl	$COCH_2CMe_2CH_2$		rt	DCE[b]	1 week	**2a**	31
H	$COCH_2CMe_2CH_2$		rt	none	1 week	 **2b**	24
Cl	$COOCMe_2O$		50–80	DCE	4 days	 **2c**	37
Cl	$PhCH_2SO_2$	EtO	rt	DCE	5 days	 **2d**	53
Cl	TsNHCO	EtO	75	none	16 h	 **2e**	88

[a] Rt = room temperature. [b] 1,2-Dichloroethane.

Results and Discussion

The synthesis of chlorothiophene S,C-ylides **2** is summarized in eq 1, and the results of these reactions are given in Table I. Ylides **2** are crystalline substances, relatively



(1)

stable when stored in a freezer, but some of them slowly decompose at room temperature. The structures of products **2a–e** were determined by their IR and NMR (^1H, ^{13}C) spectroscopy, mass spectrometry, and elemental analysis.[9] Infrared spectroscopy demonstrates for both keto **2a,b** and ester **2c,d,e** derivatives significant lowering of the carbonyl frequency, consistent with the presence of an electron-rich center (ylidic carbon) in the α-position. For **2a,b** the value of ν_{CO} = 1637 cm^{-1} lies in the range characteristic for such systems as α,β-unsaturated β-hydroxy ketones or tropolones.[10] Although this shift does indicate some participation of the enolate structure for **2a,b**, the observed ν_{CO} value is still much higher than that (ν_{CO} = 1508 cm^{-1}) found[11] for dimethylsulfonium C-benzoylmethylide, $Me_2S^+C^-HCOPh$, for which the fully enolic structure was accepted. Similarly, in **2c,d** the ester carbonyl group's absorbance (1719, 1749 cm^{-1}) corresponds to that observed for α,β-unsaturated carboxylic esters but occurs at higher wavenumbers than that (1650–1690 cm^{-1}) reported by Porter et al.[6] for thiophenium bis(alkoxycarbonyl) methylides. In **2e**, however, both carbonyl absorptions (ester and imide) occur at the unusually low frequencies (1665 and 1648 cm^{-1}). The low value of ν_{CO} (ester) in **2e** could be due to the intramolecular hydrogen bonding between this carbonyl group and the acidic hydrogen atom of the imide function, as further corroborated by the low-field ^1H NMR data of the NH proton (11.3 ppm). We have found that **2e** does not rearrange to the

(9) The structure of some ylides (2) has been also determined by X-ray crystallography: Dillen, J. L. M.; van Rooyen, P. H., to be published.

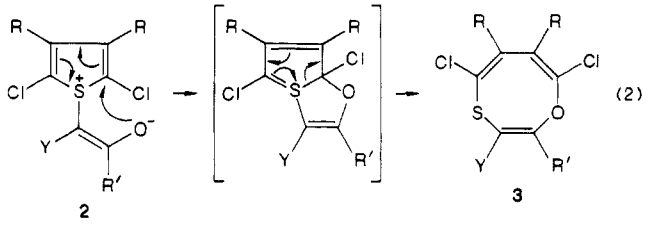
(10) Bellamy, L. J. *The Infra-red Spectra of Complex Molecules*, 2nd ed.; Methuen: London, 1958; Chapter 9.

(11) Johnson, A. W.; Amel, R. T. *J. Org. Chem.* **1969**, *34*, 1240.

corresponding 1,4-oxathiocine even upon prolonged heating; this reduced reactivity could result from the hydrogen bonding (vide infra).

^{13}C NMR spectra of ylides **2a–e** demonstrate small variations of the chemical shifts for the thiophene ring carbon atoms[12] but large variations (52–105 ppm) of the δ_C values for the ylidic carbon. The few ^{13}C NMR data of other sulfonium ylides available in the literature give values of 50.5[5] and 62.5 ppm[13] for the α-carbon atom; the similar range (50–80 ppm) was reported[14] for stabilized phosphonium ylides. It is interesting to note, however, that in **2e**, in which the ylidic carbon is most shielded (52 ppm), ^{13}C NMR spectroscopy revealed also the nonequivalence of the 2,5 and 3,4 carbon atoms of the thiophene ring. The high-field shift of the C_α signal implies the more carbanionic (as opposed to the enolate) structure of the ylide, hence stronger interactions with the sulfur center, resulting in the restricted rotation around the exocyclic S–C bond.

When reaction 1 was carried out with diazo compounds derived from acetoacetate esters or acetylacetone (**5**, R′ = OR or R; Y = COR), the corresponding ylides **2** were not stable enough to be isolated but rearranged spontaneously, giving the corresponding oxathiocines **3**. The same oxathiocine system **3** was obtained from stable ylides **2**, upon heating. We believe that the rearrangement involves the nucleophilic addition of the enolate oxygen atom to the thiophene α-carbon atom,[15] followed by the electrocyclic reaction, reminiscent of the sulfonium ylide rearrangement.[16] Table II lists 1,4-oxathiocines prepared directly



from **4** and **5**, without isolation of **2**. In some cases synthesis of **3** was repeated using the corresponding pure **2** as a substrate; in each case the product obtained was identical with that prepared directly. The structure of products **3a–h** was determined by NMR (^1H and ^{13}C) and IR spectroscopy, mass spectrometry, and, in some cases, elemental analysis. The structure of **3a** was determined previously[1] by X-ray diffraction. Compounds **3c** and **3d** have been prepared before, but erroneous structures were assigned to these products: **3c** was identified[17] as 1,3-dichloro-6-acetyl-6-(ethoxycarbonyl)-2-thiabicyclo[3.1.0]-hex-3-ene, while **3d** was believed[5] to be still its precursor **2b**. The X-ray crystal structure of **3a** revealed[1] a highly puckered eight-membered ring skeleton, indicative of the nonaromatic character of the 1,4-oxathiocine system. The absence of aromaticity in **3** can also be demonstrated by the comparison of the ^1H NMR spectra of oxathiocines and their precursors. The sequence of the structural conversion: 2,5-dichlorothiophene → **2b** → **3b** is followed by the change in the chemical shift of the 3,4-hydrogen atoms in the thiophene ring from δ 6.69 to δ 7.10, and δ 5.99, 6.77 ppm, respectively. The first deshielding (δ = +0.41 ppm) involves two aromatic systems and reflects the change in the electronegativity of sulfur upon the formation of the ylide, while the subsequent shielding (av δ = –0.72 ppm) results from the change into the nonaromatic product. The ^1H NMR chemical shift of the 6,7-hydrogen atoms in the unsubstituted 1,4-dioxocine was reported[18] to be δ 5.12 ppm; it is reasonable to expect that the introduction of two chlorine atoms at positions 5 and 8 will deshield these two hydrogen atoms in **3b** to the observed values of ca. 6 and 6.8 ppm.

As demonstrated earlier by Porter et al.,[17] and confirmed in our paper,[1] ylides **2** and oxathiocines **3** can undergo further thermal rearrangement, yielding finally polysubstituted benzene derivatives. Since this latter process involves ring contraction, sulfur extrusion, and a very unusual 1,2-chlorine atom shift, the mechanism of this reaction is currently being studied in our laboratories.

Experimental Section

Melting points were recorded on a Reichert hot-stage microscope and Reichert Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 883 spectrometer as liquid films or Nujol mulls. Mass spectra were recorded using a Varian MAT 188 spectrometer. ^1H NMR spectra were recorded on Varian E M 390, Bruker A M 300, and Bruker W M 500 spectrometers, and the ^{13}C NMR spectra were recorded on Bruker A M 300 and W M 500 instruments; in all cases solutions in chloroform-*d* or DMSO-d_6, containing TMS as internal standard, were used. Silica gel (Merck, Kieselgel 60) was used for column chromatography. TLC was conducted using Merck Kieselgel 60F-254 plates; for the preparative-layer chromatography Merck Kieselgel 60F-254 200 × 200 × 2 mm plates were used. Petroleum ether refers to the fraction of bp 60–80 °C. Mass spectra of halogeno compounds indicate only the major peak of the clusters of isotopic peaks.

The following substrates were prepared according to the literature procedures: *p*-toluenesulfonyl azide,[19] 2,5-dichlorothiophene,[20] 2,3,4,5-tetrachlorothiophene,[21] 3,4-dibromo-2,5-dichlorothiophene,[22] diazodimedone,[23] ethyl diazoacetoacetate,[24] *tert*-butyl diazoacetoacetate,[19] 5-diazo-2,2-dimethyl-1,3-dioxane-4,6-dione,[23] ethyl α-(*p*-tosylamido)diazoacetate,[25] and α-acetyl-α-*p*-tosyldiazomethane.[26]

Preparation of Diaza Compounds.[28] **2-Diazodimedone:**[23]

(12) For the four derivatives of tetrachlorothiophene **2a,c,d,e**, the average chemical shifts of the more shielded and more deshielded ring carbon atoms are 127.8 ± 3.0 and 133.9 ± 1.9 ppm, respectively. For the parent 2,3,4,5-tetrachlorothiophene these values are 121.4 and 122.9 ppm.

(13) Bowles, T.; Jones, R.; Porter, A. E. A.; Rechka, J. A.; Rzepa, H. S.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1023.

(14) Albright, T. A.; Gordon, M. D.; Freeman, W. J.; Schweizer, E. E. *J. Am. Chem. Soc.* **1976**, *98*, 6249. Seno, M.; Tsuchiya, S.; Kise, H.; Asahara, T. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2001. Ostoja-Starzewski, K. A.; Dieck, H. T. *Phosphorus* **1976**, *6*, 177.

(15) The enolate oxygen atom represents a "hard" nucleophilic center and as such will be expected to react with the thiophene sp^2 carbon atom, substituted with two electron-withdrawing groups (Cl and S^+). Klump, G. W. *Reactivity in Organic Chemistry*; Wiley-Interscience: New York, 1982; Chapter 3.2. The first step of reaction 2 corresponds to the "8-Endo-Trig" ring closure, probably favored according to Baldwin's rules of cyclization: Deslongchamps P., *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press: Oxford, 1983; Chapter 6.

(16) Gill, G. B.; Willis, M. R. *Pericyclic Reactions*; Chapman and Hall, London, 1974; p 196.

(17) Gillespie, R. J.; Murray-Rust, J.; Murray-Rust, P.; Porter, A. E. A. *Tetrahedron* **1981**, *37*, 743.

(18) Vogel, E.; Altenbach, H. J.; Cremer, D. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 935.

(19) Regitz, M.; Hocker, J.; Liedhegener, A. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. 5, p 179.

(20) Hartough, H. D. *Thiophene and Its Derivatives*; Interscience: New York, 1952; p 182.

(21) Geering, E. J. *J. Org. Chem.* **1959**, *24*, 1128.

(22) Steinkopff, W. *Die Chemie des Thiophenes*; Verlag Von T. Steinkopf: Dresden, 1941; p 19.

(23) Regitz, M.; Stadler, D. *Ann. Chem.* **1965**, *687*, 214.

(24) Wulfman, D. S.; Mc Gibboney, B. G.; Steffen, E. K.; Thinh, N. V.; Mc Daniel, R. S., Jr.; Peace, B. W. *Tetrahedron* **1976**, *32*, 1257.

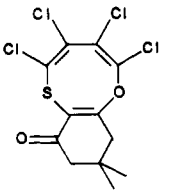
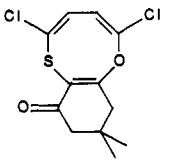
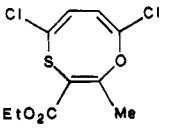
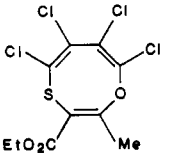
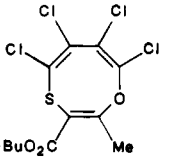
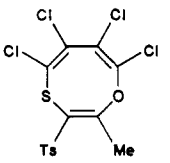
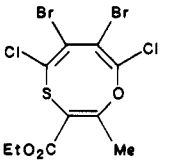
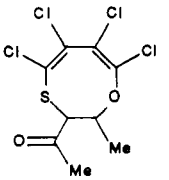
(25) Regitz, M. *Chem. Ber.* **1966**, *99*, 3128.

(26) Van Leusen, A. M.; Smid, P. M.; Strating, J. *Tetrahedron Lett.* **1965**, 337. Hodson, D.; Holt, G.; Wall D. K. *J. Chem. Soc. C* **1968**, 2201.

(27) For ylides **2** the melting points depend on the rate of heating. At slower rates (microscope) some rearrangement to products **3** takes place, and the melting point determined is usually significantly lower than that obtained with faster rate of heating (Kofler apparatus).

(28) Diazo compounds are toxic and potentially explosive and must be handled with caution. The preparations of diazo compounds should be carried out in a hood, and the distillations of diazo compounds should be conducted behind a safety shield.

Table II. Synthesis of 1,4-Oxathiocines

substrates			reaction conditions				
4, R	5, Y	R^1	temp, °C	solvent	time	product (3)	yield, %
Cl	$COCH_2CMe_2CH_2$		50	none	28 h	 **3a**	93
H	$COCH_2CMe_2CH_2$		reflux	dioxane	7 h	 **3b**	100
H	CO_2Et	Me	rt[a]	none	20 h	 **3c**	53
Cl	CO_2Et	Me	rt	none	5 days	 **3d**	94
Cl	CO_2-*t*-Bu	Me	rt	none	67 h	 **3e**	75
Cl	COMe	Me	10	DCE	6 days	 **3g**	11
Cl	Ts	Me	rt	DCE	2 weeks	 **3h**	26
Br	CO_2Et	Me	80	none	15 h	 **3f**	37

[a] Rt = room temperature.

53%; mp 108 °C (lit. mp 108 °C); IR (Nujol) 2141, 2188 (C=N_2), 1649 (C=O) cm^{-1}.

Ethyl diazoacetoacetate:[24] 91%; oil; IR (neat) 2142 (C=N_2), 1719, 1656 (C=O) cm^{-1}.

***tert*-Butyl diazoacetoacetate:**[19] 94%; oil; IR (neat) 2200, 2120 (C=N_2), 1705, 1655 (C=O) cm^{-1}.

5-Diazo-2,2-dimethyl-1,3-dioxane-4,6-dione:[23] 32%; mp 91 °C (lit. mp 87–91 °C); IR (Nujol) 2171 (C=N_2), 1725 (C=O) cm^{-1}.

Ethyl α-(*p*-tosylamido)diazoacetate:[25] 22%; mp 85 °C (lit. mp 85 °C); IR (Nujol) 2153 (C=N_2), 1702, 1679 (C=O), 1598 (Ar) cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.30 (3 H, t, J = 7.5 Hz, CH_3 of Et), 2.42 (3 H, s, CH_3Ar), 4.30 (2 H, q, J = 7.5 Hz, CH_2), 7.38 (2 H, d, J = 9.0 Hz, 3,5-H_2 of Ar), 7.92 (2 H, d, J = 9.0 Hz, 2,6-H_2 of Ar).

Diazoacetylacetone (prepared according to the modified procedure of Wulfman et al.[24]). A solution of acetylacetone (14.3

g, 0.143 mol), triethylamine (14.8 g, 0.147 mol), and *p*-toluenesulfonyl azide (28.6 g, 0.145 mol) in dry benzene (150 mL) was allowed to react at 0 °C for 1 h and then at room temperature for 3 h. The workup[24] gave the product: 10.5 g (58%); oil; IR (neat) 2129 (C=N_2), 1667 (C=O) cm^{-1}.

Ethyl α-(benzylsulfonyl)diazoacetate. Ethyl mercaptoacetate (28.8 g, 0.24 mol), benzyl alcohol (10.8 g, 0.10 mol), and ZnI_2 (15.9 g, 0.05 mol) were dissolved in dichloromethane (150 mL), and the solution was heated under reflux for 3 h. The solution was washed with water (3 times), brine (once), and water (once) and dried ($MgSO_4$), and the solvent was removed under reduced pressure. Benzyl carbethoxymethyl sulfide: 18.5 g (88%); oil; IR (neat) 1730 (br), 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (3 H, t, J = 7.5 Hz, CH_3), 3.02 (2 H, s, CH_2Ar), 3.78 (2 H, s, CH_2CO), 4.11 (2 H, q, J = 7.5 Hz, CH_2 of Et), 7.22 (5 H, m, Ph).

A 24.9-g (0.119-mol) portion of this product was dissolved in glacial acetic acid (50 mL), the solution was cooled in an ice bath, and 30% hydrogen peroxide (47.6 g, 0.420 mol) was added dropwise with stirring. The mixture was then heated under reflux for 2 h, acetic acid was removed under reduced pressure, and water was added to the residue. The pH of this mixture was brought to 5 with 10% solution of $NaHCO_3$, and the aqueous solution was extracted with chloroform. The organic phase was washed with water, brine, and water and dried over $MgSO_4$. After evaporation of the solvent under reduced pressure the product, benzyl carbethoxymethyl sulfone, was obtained: 9.9 g (35%); mp 100 °C; IR (Nujol) 3500 (br), 1700 (br) cm^{-1}.

The solution of this product (9 g, 0.037 mol), *p*-toluenesulfonyl azide (8.1 g, 0.041 mol), and triethylamine (7.5 g, 0.074 mol) in absolute ethanol (100 mL) was stirred at room temperature for 3 h. After removal of the solvent, ether was added to the residue, and the mixture was washed with 5% aqueous NaOH, water, brine, and water. After drying ($MgSO_4$) and removing ether under reduced pressure, the crude product (oil) was purified by column chromatography using hexane followed by chloroform as eluting agents: yield of the diazo compound 2.3 g (23%); oil; IR (neat) 2220 (C=N_2), 1705 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (3 H, t, J = 7.5 Hz, CH_3), 4.37 (2 H, q, J = 7.5 Hz, CH_2 of Et), 4.59 (2 H, s, CH_2Ar), 7.40 (5 H, m, Ph).

α-Acetyl-α-*p*-tosyldiazomethane:[26] 51%; mp 108–109 °C (lit. mp 109–110 °C); IR (Nujol) 2120, 2100 (C=N_2), 1660 (C=O), 1600 (Ar) cm^{-1}.

Synthesis of *S*,*C*-Ylides 2. 2,3,4,5-Tetrachlorothiophenium (4′,4′-dimethylcyclohexane-2′,6′-dione) 1′-*S*,*C*-ylide (2a): Diazodimedone (0.5 g, 0.003 mol) was added portionwise to a mixture of tetrakis(acetato)dirhodium(II) (5 mg) and 2,3,4,5-tetrachlorothiophene (5.35 g, 0.024 mol) at room temperature under nitrogen. The mixture was stirred at room temperature for 7 days, and dry hexane (20 mL) was added to dissolve the excess of tetrachlorothiophene. The insoluble product was collected and purified by column chromatography. Elution with petroleum ether (200 mL) gave tetrachlorothiophene and subsequent elution with chloroform (400 mL) gave the ylide **2a**: 0.72 g (67%), mp 115 °C (microscope), 155 °C (Kofler);[27] IR (Nujol) 1637 (C=O), 1609, 1574 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (6 H, s, 2 CH_3), 2.43, 2.53 (4 H, 2 s, ring hydrogens); ^{13}C NMR ($CDCl_3$) δ 28.05 (2 CH_3), 31.12 (C-4′), 51.41, 51.99 (2 CH_2), 75.12 (*C*-ylide), 133.16, 125.32 (C-2,3,4,5), 190.59, 193.89 (2 CO). Anal. Calcd for $C_{12}H_{10}Cl_4O_2S$: C, 40.48; H, 2.83. Found: C, 40.22; H, 2.65.

DCE can be used as a solvent for this synthesis, but **2a** was obtained in 31% yield. The same procedure was used for the preparation of other ylides.

2,5-Dichlorothiophenium (4′,4′-dimethylcyclohexane-2′,6′-dione) 1′-*S*,*C*-ylide (2b): 24%; mp (from ether–petroleum ether, 1:1) 129 °C (microscope), 156 °C (Kofler); IR (Nujol) 1637, 1596 cm^{-1}; MS m/z 290 (M^+, 30), 152 (45), 83 (100); ^1H NMR ($CDCl_3$) δ 1.10 (6 H, s, 2 CH_3), 2.40, 2.53 (4 H, 2 s, 2 CH_2), 7.10 (2 H, s, 3,4-H_2); ^{13}C NMR ($CDCl_3$) δ 29.02 (2 CH_3), 31.07 (C-4′), 51.51, 51.85 (2 CH_2), 76.12 (*C*-ylide), 131.45, 131.37 (C-2,3,4,5), 190.27, 193.76 (2 CO). Anal. Calcd for $C_{12}H_{12}Cl_2O_2S$: C, 49.84; H, 4.18. Found: C, 49.45; H, 3.71.

2,3,4,5-Tetrachlorothiophenium (4′,4′-dimethyl-3′,5′-dioxane-2′,6′-dione) 1′-*S*,*C*-ylide (2c): 37%; mp (from methanol) 196 °C (microscope), 215 °C (Kofler); IR (Nujol) 1719 (C=O), 1579 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 26.12 (2 CH_3), 49.08 (C-4′), 104.93 (*C*-ylide), 125.46, 134.11 (C-2,3,4,5), 159.51, 163.28 (2 CO). Anal. Calcd for $C_{10}H_6Cl_4O_4S$: C, 33.36; H, 1.68. Found: C, 33.03; H, 1.43.

2,3,4,5-Tetrachlorothiophenium *C*-(ethoxycarbonyl)-*C*-(benzylsulfonyl)methylide (2d): 53%; mp 156 °C (microscope), 159 °C (Kofler); IR (Nujol) 1749, 1664, 1579 cm^{-1}; MS m/z 307 (2), 279 (6), 222 (12), 194 (15), 91 (100); ^1H NMR ($CDCl_3$) δ 1.20 (3 H, t, J = 7.5 Hz, CH_3), 4.10 (2 H, q, J = 7.5 Hz, CH_2 of Et), 4.60 (2 H, s, CH_2Ar), 7.30 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 14.10 (CH_3), 61.13, 61.23 (2 CH_2), 61.97 (*C*-ylide), 128.52, 128.72, 130.11, 130.90 (phenylic carbons), 128.00, 131.72 (C-2,3,4,5), 161.22 (CO). Anal. Calcd for $C_{15}H_{12}Cl_4O_4S_2$: C, 39.32; H, 2.64. Found: C, 39.39; H, 2.81.

2,3,4,5-Tetrachlorothiophenium *C*-(ethoxycarbonyl)-*C*-[(*N*-tosylamino)carbonyl]methylide (2e): 88%; mp (from DMF) 165 °C (microscope), 214 °C (Kofler); IR (Nujol) 1665, 1648, 1597, 1578 cm^{-1}; MS m/z 305 (1), 279 (3), 222 (19), 187 (12), 155 (13), 44 (100); ^1H NMR ($CDCl_3$) δ 1.10, 1.30 (3 H, 2 t, J = 7.5 Hz, CH_3 of Et), 2.45 (3 H, s, CH_3Ar), 4.05, 4.25 (2 H, 2 q, J = 7.5 Hz, CH_2 of Et), 7.20–7.35 (2 H, m, 3,5-H_2), 7.80–8.10 (2 H, m, 2,6-H_2), 11.3 (1 H, s, NH); ^{13}C NMR ($CDCl_3$) δ 13.61, 14.15 (CH_3 of Et), 21.37, 21.43 (CH_3 of Ts), 51.95 (*C*-ylide), 61.10, 61.23 (CH_2), 126.12, 127.51, 128.09, 129.08, 129.20, 143.86, 144.11 (phenylic carbons), 132.01, 132.55, 136.61, 136.77 (C-2,3,4,5), 160.01, 162.80, 164.62, 167.49 (2 CO). Anal. Calcd for $C_{16}H_{13}Cl_4NO_5S_2$: C, 38.34; H, 2.61; N, 2.79. Found: C, 38.05; H, 2.86; N, 2.86.

Synthesis of 1,4-Oxathiocines 3. 3,4,5,6-Tetrachloro-11,11-dimethyl-2-oxa-7-thiabicyclo[6.4.0]dodeca-1(8),3,5-trien-9-one (3a). Diazodimedone (0.5 g, 0.003 mol) was added portionwise to a mixture of tetrakis(acetato)dirhodium(II) (5 mg) and 2,3,4,5-tetrachlorothiophene (5.35 g, 0.024 mol) at 50 °C in the atmosphere of dry nitrogen. The evolution of gas (N_2) commenced almost immediately after addition of diazodimedone; the mixture was then stirred at 50 °C for 28 h. After cooling, dry hexane was added, and the insoluble material was filtered off and purified by column chromatography. Elution with petroleum ether (200 mL) gave tetrachlorothiophene, and subsequent elution with chloroform (400 mL) gave the white crystalline product **3a**: 1.0 g (93%); mp 100 °C (microscope), 102 °C (Kofler); IR (Nujol) 1672 (C=O) cm^{-1}; MS m/z 360 (M^+, 2), 83 (100); ^1H NMR ($CDCl_3$) δ 1.16 (6 H, s, 2 CH_3), 2.43, 2.58 (4 H, 2 s, 4 ring hydrogens); ^{13}C NMR ($CDCl_3$) δ 26.22, 29.16 (2 CH_3), 31.68 (C-11), 45.28, 50.90 (2 CH_2), 112.56 (C-8), 122.71, 124.71, 135.15, 137.36 (thiophene carbons), 165.79 (C-1), 193.76 (CO). Anal. Calcd for $C_{12}H_{10}Cl_4O_2S$: C, 40.48; H, 2.83. Found: C, 40.04; H, 2.69.

The identical product **3a** can be obtained in quantitative yield by heating under reflux a chloroform solution of ylide **2a**.

3,6-Dichloro-11,11-dimethyl-2-oxa-7-thiabicyclo[6.4.0]-dodeca-1(8),3,5-trien-9-one (3b): ylide **2b** (0.10 g) was dissolved in dioxane (10 mL), and the solution was heated under reflux for 7 h. After evaporation of solvent the product was purified by column chromatography using chloroform as eluting agent; **3b** was obtained in quantitative yield: mp 89–90 °C (microscope), 103 °C (Kofler); MS m/z 290 (M^+, 4), 255 (3), 207 (4), 83 (100); ^1H NMR ($CDCl_3$) δ 1.08 (6 H, s, 2 CH_3), 2.40, 2.52 (4 H, 2 s, 2 CH_2), 5.99 (1 H, d, J = 1.5 Hz, H-5), 6.77 (1 H, d, J = 1.5 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 28.16 (2 CH_3), 32.02 (C-11), 45.81, 51.39 (2 CH_2), 112.05 (C-8), 115.98, 125.24, 135.59, 136.10 (thiophene carbons), 163.87 (C-1), 193.29 (CO). Anal. Calcd for $C_{12}H_{12}Cl_2O_2S$: C, 49.84; H, 4.18. Found: C, 49.97; H, 4.09.

2-Methyl-3-carbethoxy-5,8-dichloro-1,4-oxathiocine (3c): prepared according to ref 17; oil; 53%; IR (neat) 2984, 1720, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (3 H, t, J = 7.0 Hz, CH_3 of Et), 2.34 (3 H, s, CH_3), 4.22 (2 H, q, J = 7.0 Hz, CH_2), 5.85 (1 H, d, J = 4.0 Hz, H-6), 6.67 (1 H, d, J = 4.0 Hz, H-7); ^{13}C NMR ($CDCl_3$) δ 13.97 (CH_3 of Et), 21.61 (CH_3), 61.91 (CH_2), 107.35 (C-3), 115.11, 125.32, 136.22, 137.35 (C-5,6,7,8), 159.44 (C-2), 164.80 (CO).

2-Methyl-3-carbethoxy-5,6,7,8-tetrachloro-1,4-oxathiocine (3d): prepared according to ref 5; oil; 94%; IR (neat) 1720 (C=O) cm^{-1}; MS m/z 350 (M^+, 2), 307 (5), 279 (13), 43 (100); ^1H NMR ($CDCl_3$) δ 1.33 (3 H, t, J = 7.5 Hz, CH_3 of Et), 2.42 (3 H, s, CH_3), 4.27 (2 H, q, J = 7.5 Hz, CH_2); ^{13}C NMR ($CDCl_3$) δ 14.02 (CH_3 of Et), 22.09 (CH_3), 62.29 (CH_2), 106.57 (C-3), 121.87, 123.62, 135.55, 138.44 (C-5,6,7,8), 160.49 (C-2), 164.11 (CO).

2-Methyl-3-(*tert*-butoxycarbonyl)-5,6,7,8-tetrachloro-1,4-oxathiocine (3e): prepared directly from the corresponding **4** and **5** (see Table II); oil; 75%; IR (neat) 1715 (C=O) cm^{-1}; MS

m/z 378 (M^+, 1), 277 (4), 43 (100); ^1H NMR ($CDCl_3$) δ 1.50 (9 H, s, t-Bu), 2.35 (3 H, s, CH_3); ^{13}C NMR ($CDCl_3$) 21.61 (CH_3 of t-Bu), 27.98 (CH_3), 83.58 (C of t-Bu), 107.90 (C-3), 121.67, 123.95, 135.76, 138.15 (C-5,6,7,8), 158.78 (C-2), 163.19 (CO). Anal. Calcd for $C_{12}H_{12}Cl_4O_3S$: C, 38.10; H, 3.17. Found: C, 38.00; H, 2.89.

2-Methyl-3-acetyl-5,6,7,8-tetrachloro-1,4-oxathiocine (3f). Diazoacetylacetone (1.0 g, 0.008 mol) was added dropwise during 2 h to a stirred and cooled (4 °C) solution of tetrakis(acetato)-dirhodium(II) (5 mg) and 2,3,4,5-tetrachlorothiophene (8.7 g, 0.04 mol) in DCE (5 mL). After addition, the mixture was left at 10 °C for 6 days. The solvent was removed under reduced pressure, dry hexane (20 mL) was added, and the solid product was filtered off and purified by column chromatography. Elution with petroleum ether (200 mL) gave tetrachlorothiophene, and subsequent elution with chloroform (400 mL) gave the white crystalline product **3f**: 0.28 g (11%); mp 82–83 °C (microscope), 83 °C (Kofler); IR (Nujol) 1687 (C=O) cm^{-1}; MS m/z 235 (1), 187 (1), 149 (4), 44 (100); ^1H NMR ($CDCl_3$) δ 2.29 (3 H, s, CH_3), 2.52 (3 H, s, CH_3); ^{13}C NMR ($CDCl_3$) δ 21.95, 29.91 (2 CH_3), 112.38 (C-3), 121.73, 122.59, 135.58, 138.73 (C-5,6,7,8), 160.06 (C-2), 196.98 (CO). Anal. Calcd for $C_9H_6Cl_4O_2S$: C, 34.21; H, 1.91. Found: C, 34.41; H, 1.81.

2-Methyl-3-(*p*-tolylsulfonyl)-5,6,7,8-tetrachloro-1,4-oxathiocine (3g). α-Acetyl-α-(*p*-tolylsulfonyl)diazomethane (0.71 g, 0.003 mol) was dissolved in DCE (1 mL) and added slowly at room temperature to a solution of tetrakis(acetato)dirhodium(II) (5 mg) and 2,3,4,5-tetrachlorothiophene (5.33 g, 0.024 mol) in DCE (5 mL), and the mixture was stirred at room temperature for 2 weeks. After evaporation of the solvent dry hexane was added, and the solid product was purified by column chromatography. Elution with petroleum ether (200 mL) gave tetrachlorothiophene, and subsequent elution with chloroform (400 mL) gave the product **3g**: 0.33 g (26%); mp (from $CHCl_3$) 181–182 °C (microscope); IR (Nujol) 1615 cm^{-1}; MS m/z 432 (M^+, 6), 277 (16), 235 (34), 91 (100); ^1H NMR ($CDCl_3$) δ 2.35, 2.51 (6 H, 2 s, 2 CH_3), 7.27 (2 H, d, J = 9.0 Hz, 3,5-H_2), 7.85 (2 H, d, J = 9.0 Hz, 2,6-H_2); ^{13}C NMR ($CDCl_3$) δ 21.68, 21.70 (2 × CH_3), 128.40, 129.77, 139.19, 145.32 (aromatic carbons), 118.01 (C-3), 122.12, 123.48, 135.05, 136.27 (C-5,6,7,8), 161.59 (C-2). Anal. Calcd for $C_{14}H_{10}Cl_4O_3S_2$: C, 39.27; H, 2.35. Found: C, 39.42; H, 2.06.

2-Methyl-3-carbethoxy-6,7-dibromo-5,8-dichloro-1,4-oxathiocine (3h). Ethyl diazoacetoacetate (0.78 g, 0.005 mol) was added dropwise to a mixture of tetrakis(acetato)dirhodium(II) (5 mg) and 3,4-dibromo-2,5-dichlorothiophene (12.36 g, 0.04 mol) at 80 °C under nitrogen. The mixture was stirred at 75–80 °C for 15 h and cooled, and petroleum ether was added. The crude product was purified by column chromatography. Elution with petroleum ether (200 mL) gave 3,4-dibromo-2,5-dichlorothiophene, and subsequent elution with petroleum ether–ether (1:1) (400 mL) gave the product **3h**: 0.81 g (37%); oil; IR (neat) 1721 (C=O) cm^{-1}; MS m/z 440 (M^+, 3), 395 (7), 367 (7), 43 (100); ^1H NMR ($CDCl_3$) δ 1.28 (3 H, t, J = 7.5 Hz, CH_3 of Et), 2.33 (3 H, s, CH_3), 4.25 (2 H, q, J = 7.5 Hz, CH_2); ^{13}C NMR ($CDCl_3$) δ 14.01 (CH_3 of Et), 22.03 (CH_3), 62.21 (CH_2), 106.17 (C-3), 113.98, 124.75, 131.23, 136.05 (C-5,6,7,8), 160.40 (C-2), 164.02 (CO).

Acknowledgment. Financial assistance from the CSIR and the University of Pretoria is gratefully acknowledged.

Synthesis of Quaternary Ammonium Fluoride Salts by a Solid–Liquid Halogen Exchange Process in Protic Solvents

Salman Dermeik and Yoel Sasson*

Casali Institute of Applied Chemistry, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

Received February 27, 1989

Both hydrophilic and lipophilic quaternary ammonium fluoride compounds are prepared by direct exchange of the corresponding halides with solid potassium fluoride containing an optimized amount of water (4.0 mol %). The procedure is most effective when methanol is applied as a solvent. A variety of quaternary ammonium fluorides were prepared in 75–97% yield.

Introduction

Quaternary ammonium fluoride salts are an important group of compounds with numerous synthetic applications, mainly as fluorinating agents and as mild bases.[1,2] Four major methods were reported in the literature for the preparation of these compounds:[3] (a) Neutralization of quaternary ammonium hydroxides with aqueous hydrogen fluoride.[4,5] (b) Reaction of silver fluoride with quaternary ammonium chlorides, bromides, or iodides.[6] (c) Anion exchange of aqueous quaternary ammonium halides with solid anion exchangers in fluoride form.[7] (d) Anion exchange between aqueous potassium fluoride (in large excess) and quaternary ammonium hydrogensulfates in organic phase.[3] These techniques suffer several limitations as follows: (a) The first three methods are limited to water-soluble starting materials and therefore cannot be applied to quaternary salts with more than 20–22 carbons. (b) The first two methods utilize relatively expensive reagents. (c) The product of method a is always contaminated with the side product bifluoride salt $R_4N{\cdot}HF_2$. (d) The last method is limited to lipophilic quaternary ammonium fluorides and requires large excess of reagent (30 equiv). Also, since the exchange is conducted in the presence of water, the ammonium fluorides are obtained as trihydrates which are rather difficult to dry.

Results and Discussion

We have examined the formation of quaternary fluorides by the direct heterogeneous liquid–liquid or solid–liquid halide exchange process (eq 1) where R is a normal alkyl

$$R_4NX + MF \rightleftharpoons R_4NF + MX \quad (1)$$

group, X is a halide, typically bromide or chloride, and M is an alkali metal, sodium, or potassium. These anion exchange reactions are relatively fast processes, and equilibrium is usually obtained within a few minutes at room temperature in liquid–liquid systems. Longer periods of time are required for solid–liquid systems.

(1) Clark, J. H. *Chem. Rev.* **1980**, *80*, 429.
(2) Kuwajima, I.; Nakamura, E. *Acc. Chem. Res.* **1985**, *18*, 181.
(3) Landini, D.; Molinari, H.; Penso, M.; Rampoldi, A. *Synthesis* **1988**, 953.
(4) Harmon, K. M.; Gennick, I. *Inorg. Chem.* **1975**, *14*, 1840.
(5) Nakayama, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3717.
(6) Hayami, J.; Ono, N.; Kaji, A. *Tetrahedron Lett.* **1968**, 1385.
(7) Pless, J. *J. Org. Chem.* **1974**, *39*, 2644.

0022-3263/89/1954-4827$01.50/0