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Synthesis and Reactions of (4,5-Dicarbomethoxy-1,3-dithiolyl)tributylphosphonium Tetrafluoroborate†

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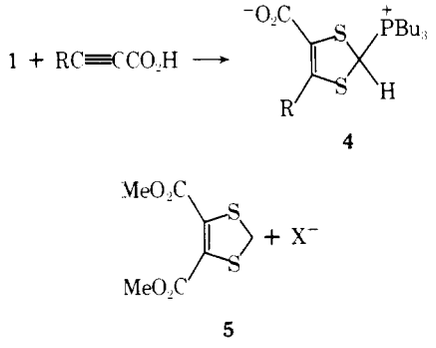
The title phosphonium salt (**7**) is readily prepared by the reaction of dimethyl acetylenedicarboxylate and fluoroboric acid with the adduct of carbon disulfide and tributylphosphine and serves as a stable precursor of the corresponding unstable phosphorane (**6**). A comparative study of the use of salt **7** in the Wittig reaction with various aldehydes and ketones is described. Attempts to effect the complete dehydrogenation of the bisfulvene **21** from cyclohexane-1,4-dione were unsuccessful.

In 1971, Hartzler reported that the carbon disulfide–tributylphosphine adduct (**1**) reacts with electron-deficient acetylenes to give poor yields of tetrathiafulvalenes. If adduct **1** is mixed with an aromatic aldehyde prior to the addition of the acetylene, excellent yields of 2-benzylidene-1,3-dithioles (**3**) are obtained, a result strongly suggesting the intermediacy of a highly reactive phosphorane **2**, the dipolar resonance contributor of which (**2b**) is a destablilized cyclic 8π-electron antiaromatic (Scheme I).[1] Additional support for this mechanism, as well as for a concerted 1,3-dipolar addition of **1** to the acetylene, was given by Pittman and Narita, who found that adduct **1** reacts smoothly with either propiolic acid or acetylenedicarboxylic acid to give a crystalline zwitterion (**4**).[2]

During the past few years, phosphoranes of the type **2** have become available in a very different manner from simple 1,3-dithiolium salts in cases where R equals H, alkyl, or a condensed benzene ring; these intermediates have proved very useful for the synthesis of a variety of dithiafulvenes,[3] as well as unsymmetrical tetrathiafulvalene derivatives.[4] This new method is not applicable, however, to the synthesis of phosphoranes containing electron-withdrawing groups since the required dithiolium salts (i.e., **5**) are not known.[5]

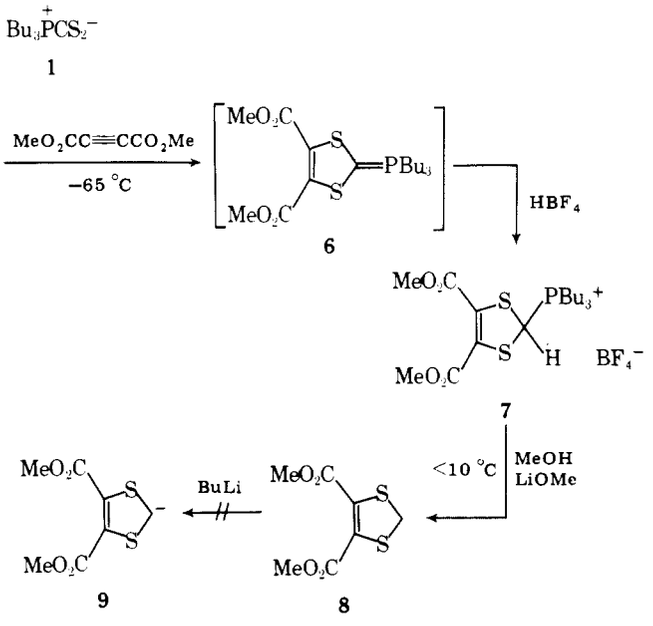
We now report a modification of the Hartzler reaction which provides a simple and convenient synthesis of the title phosphonium salt **7**, and which has enabled us to study in some detail the generation and Wittig reactions of the corresponding ester-substituted phosphorane **6**.



Results

When the carbon disulfide–tributylphosphine adduct (**1**) is treated with a mixture of dimethyl acetylenedicarboxylate and fluoroboric acid etherate at −65 °C, the initially produced phosphorane **6** is trapped by protonation, and the resulting cation can be isolated in yields of up to 72% as the stable, white, crystalline tetrafluoroborate **7**, mp 120–121 °C.

Treatment of salt **7** with dilute lithium methoxide in methanol at a low temperature, followed by an aqueous workup, led to a good yield (88%) of the previously unreported dephosphinated ester, 4,5-dicarbomethoxy-1,3-dithiole (**8**).



† Dedicated to Professor A. Dreiding on the occasion of his 60th birthday.

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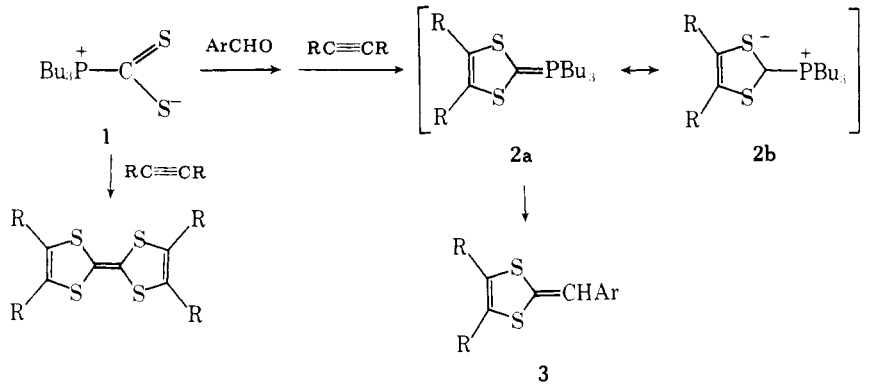
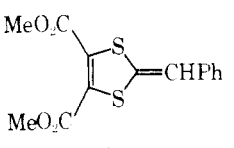
Scheme I



Ester 8 is an interesting compound in that the corresponding anion 9 represents an 8 π-electron, antiaromatic dithiolium anion, the instability of which might be somewhat tempered by electron-withdrawing carbomethoxyl groups. In fact, ester 8 proved to be highly resistant to proton abstraction; treatment of 8 with butyllithium at −78 °C, followed by quenching with deuterium oxide, led to a 60% recovery of starting material in which no deuterium had been incorporated.

Under aprotic conditions, salt 7 could be used for the in situ generation of the phosphorane 6. Thus, reaction of 7 with benzaldehyde and triethylamine at room temperature gave the dithiafulvene 10 in good yield (82%), while cinnamaldehyde afforded (41%) the corresponding extended fulvene



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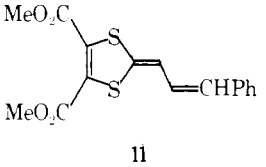

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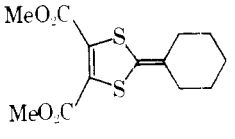

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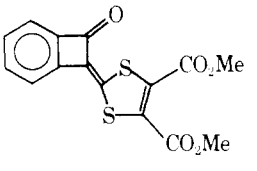

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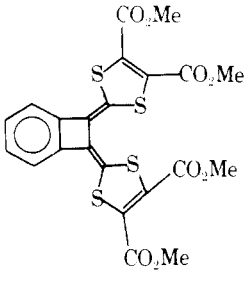

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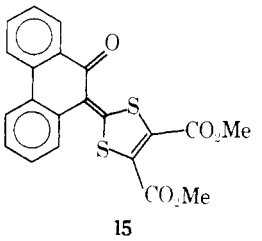

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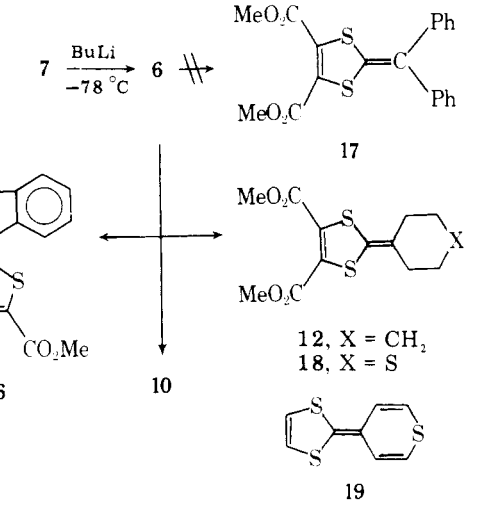
11. Under the same conditions (or even in refluxing toluene) none of fulvene 12 was formed from 7 and cyclohexanone, implying that phosphorane 6 decomposes too quickly at room temperature or above to be trappable by any but the most reactive of carbonyl groups. This interpretation is supported by the observation that the reaction of 2 equiv of 7 with 1 equiv of benzocyclobutenedione gives a virtually quantitative yield of the *mono*ketofulvene 13, none of the corresponding bisfulvene (14) being found. In a similar manner, 7 and 9,10-phenanthrenequinone gave the monoketofulvene 15.

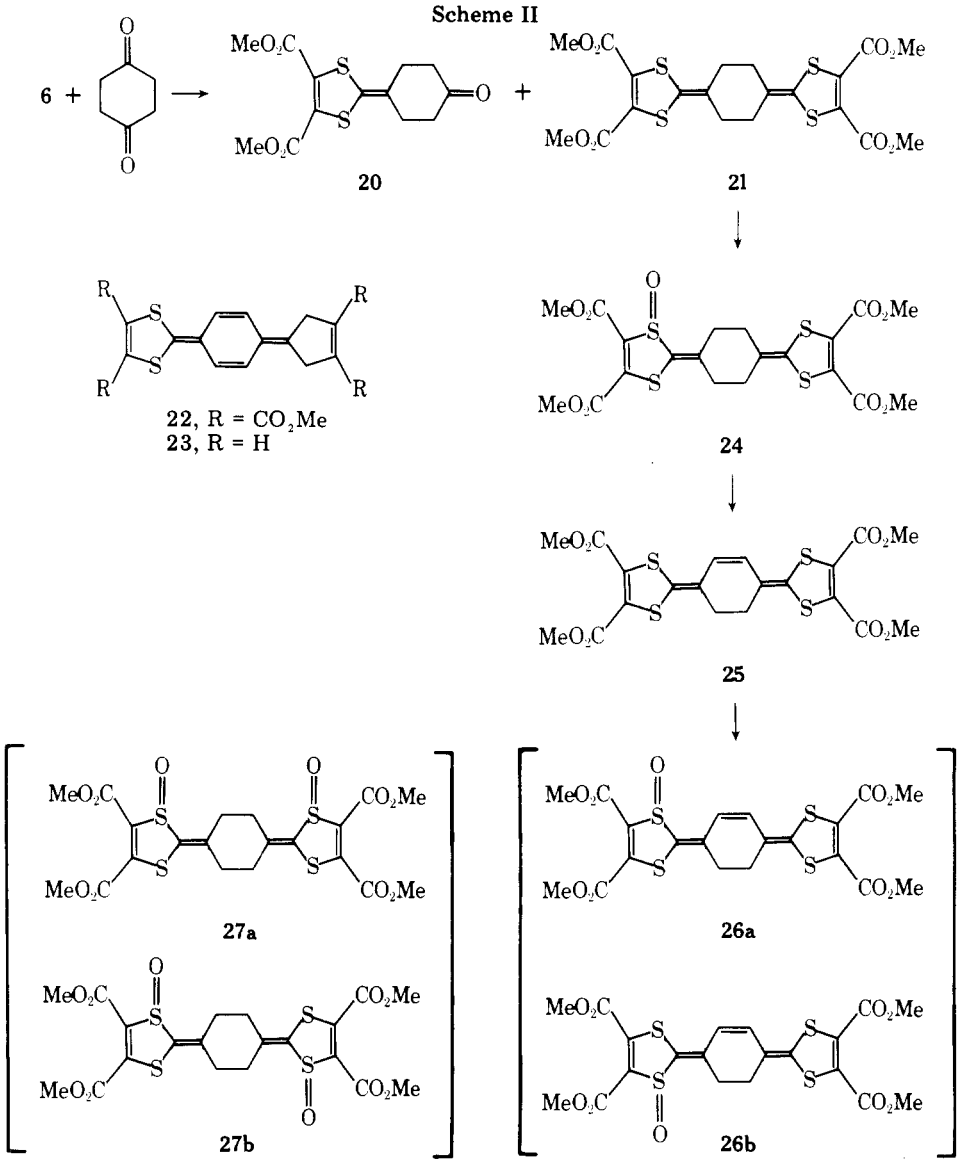
The reaction of salt 7 with butyllithium in tetrahydrofuran at −78 °C gave red solutions of phosphorane 6, which were quite stable at this low temperature. Such solutions not only reacted cleanly with benzaldehyde to give 10 (89%), but they also reacted well with a number of ketones. Thus, cyclohexanone gave fulvene 12 (60%), while 4-thiacyclohexanone gave fulvene 18 (84%). The latter compound, an intermediate in the synthesis of the unusual π-donor 19, was previously available only by a more laborious cross-coupling route.[6] On the other hand, the hindered ketone benzophenone gave none of the expected fulvene 17, although the more accessible carbonyl function of fluorenone coupled smoothly with 6 to give 16.



Condensation of phosphorane 6 with cyclohexane-1,4-dione gave a readily separable mixture of the oxofulvene 20 and the bisfulvene 21 (Scheme II). The latter compound was of particular interest since it is a tetrahydro derivative of the unknown vinylogous tetrathiafulvalene ester 22, a potential precursor of the equally unknown parent compound 23.[7] Attempts to dehydrogenate 21 to 22 using high potential quinones (DDQ, chloranil, or *o*-chloranil) always led to an inseparable mixture of starting material and the partially dehydrogenated compound 25, as shown by NMR analysis. It is of interest to note that, by contrast, the related fulvene ester 18 is smoothly dehydrogenated to its tetrahydro derivative under similar conditions.[5]

Oxidation of 21 with *m*-chloroperbenzoic acid afforded either the monosulfoxide 24 or a mixture of the isomeric disulfoxides 27, depending upon the conditions employed. Monosulfoxide 24 cleanly underwent a vinylogous Pummerer-type dehydration on heating with acetic anhydride containing diisopropylethylamine, affording the pure violet dehydrofulvene 25 in high yield. Similar treatment of disulfoxide 27, however, led only to a complex, unresolved reaction mixture, rather than to compound 22. Careful peracid oxidation of the violet fulvene 25 afforded a crystalline mixture of the isomeric sulfoxides 26. Attempted Pummerer dehydration of 26 to 22 in hot acetic anhydride afforded a solution containing a dark-red product which could not be isolated due to its sensitivity to air and silica gel. On the other hand, treatment of 26 with

Scheme II



trifluoroacetic anhydride and diisopropylethylamine led only to deoxygenation, with the regeneration of **25** in good yield.

Experimental Section

Melting points are uncorrected. NMR ($CDCl_3$ containing Me_4Si as internal standard), infrared (KBr), ultraviolet, and mass spectra were determined using Varian A-60 and Perkin-Elmer 137, 202, and 270B spectrometers, respectively.

4,5-Dicarbomethoxy-1,3-dithiolyltributylphosphonium Tetrafluoroborate (7). A solution of tributylphosphine (5 mL, 0.02 mol) and carbon disulfide (1.2 mL, 0.02 mol) in ether (50 mL) was cooled to −65 °C. To the deep red complex was added at −65 °C a slight excess of fluoroboric acid etherate (3.5 g) and dimethyl acetylenedicarboxylate (2.5 mL, 0.02 mol). The solution immediately turned colorless and a gummy red solid precipitated. Manual stirring gave a gummy white solid. Recrystallization from acetonitrile–ether gave **7** as colorless needles (7.2 g, 72%): mp 120–121 °C; IR 2950 cm^{-1}, 1750, 1250, 1060. Anal. Calcd for $C_{19}H_{34}O_4S_2BF_4P$: C, 44.89; H, 6.69; S, 12.62. Found: C, 45.10; H, 6.76; S, 12.46.

2-Benzylidene-4,5-dicarbomethoxy-1,3-dithiole (10). A solution of the tetrafluoroborate salt (**7**) (1 g, 1.9 mmol) and benzaldehyde (0.201 g, 1.9 mmol) in THF (25 mL) was stirred at room temperature under argon. Triethylamine (1 mL) was added and the solution turned dark red. After 15 min the solvent was removed, giving a red oil. Chromatography on silica (hexane) afforded a red solid. Recrystallization from hexane gave shiny red needles of **10** (0.48 g, 82%): mp 90–91 °C; UV (CH_2Cl_2) λ_{max} 243 nm (log ϵ 3.96), 328 (4.16); NMR δ 3.95 (s, 6 H), 6.55 (s, 1 H), 7.2–7.5 (m, 5 H). Anal. Calcd for $C_{14}H_{12}O_4S_2$: C, 54.54; H, 3.89. Found: C, 54.32; H, 3.90.

When a solution of the fluoroborate salt (**7**) and triethylamine is stirred for 5 min followed by the addition of benzaldehyde, the yield is reduced to 52%.

2-Cinnamylidene-4,5-dicarbomethoxy-1,3-dithiole (11). Triethylamine (0.5 mL) was added to a solution of salt **7** (0.507 g, 1 mmol) and *trans*-cinnamaldehyde (0.132 g, 1 mmol) in THF (25 mL) under argon. The solution was stirred for 1 h. The solvent was removed and the residue was extracted with benzene. The benzene extracts were washed with water, dried (Na_2SO_4), and evaporated to give a red oil. Chromatography on silica (benzene) afforded after recrystallization (hexane) shiny red needles of **11** (136 mg, 41%): mp 124–125 °C; UV (CH_2Cl_2) λ_{max} 251 mm (log ϵ 3.92), 362 (4.22), 376 (4.21), 680 (2.53); NMR δ 3.87 (s, 6 H), 6.16 (m, 1 H), 6.4 (m, 2 H), 7.1–7.4 (m, 5 H). Anal. Calcd for $C_{16}H_{14}O_4S_2$: C, 57.48; H, 4.19; S, 19.16. Found: C, 57.20; H, 4.17; S, 18.90.

Monoketofulvene 13. A solution of salt **7** (0.507 g, 1 mmol) and benzocyclobutenedione (66 mg, 0.5 mmol) in THF (25 mL) was cooled to 5 °C. Triethylamine (1 mL) was added when the solution turned reddish orange. After 10 min the solvent was removed. Chromatography on silica (benzene) afforded after recrystallization (benzene) orange needles of **13** (167 mg, 100%): mp 175–177 °C; UV (CH_2Cl_2) λ_{max} 243 nm (log ϵ 4.08), 329 (4.06), 346 (4.02), 424 (3.92); NMR δ 3.9 (s, 6 H), 7.2–7.4 (m, 4 H). Anal. Calcd for $C_{15}H_{10}O_5S_2$: C, 53.89; H, 2.99; S, 19.16. Found: C, 53.72; H, 3.02; S, 18.95.

Monoketofulvene 15. A solution of salt **7** (0.507 g, 1 mmol) and 9,10-phenanthrenequinone (0.104 g, 0.5 mmol) in THF (25 mL) was cooled to 5 °C. Triethylamine (1 mL) was added when the solution turned reddish orange. An orange solid formed which was filtered off. Chromatography on silica (benzene) afforded after recrystallization (benzene) shiny orange plates of **15** (200 mg, 97.5%): mp 210–212 °C; UV (CH_2Cl_2) λ_{max} 264 nm (log ϵ 4.35), 290 (4.07), 365 (3.73), 451 (4.17); NMR δ 3.95 (s, 3 H), 3.99 (s, 3 H), 7.1–7.4 (m, 8 H). Anal. Calcd for

$C_{21}H_{14}O_5S_2$: C, 61.46; H, 3.41; S, 15.60. Found: C, 61.36; H, 3.51; S, 15.56.

4,5-Dicarbomethoxyl-1,3-dithiole (8). To a solution of lithium methoxide prepared from lithium metal (15 mg) and methanol (20 mL) was added salt **7** (1.02 g, 2 mmol) below −30 °C under nitrogen. The suspension was gradually warmed under stirring to 10 °C for a period of 45 min. The resulting yellow solution was poured into water and extracted with dichloromethane. The extract was washed with water and dried over sodium sulfate. After evaporating the solution, the residue was chromatographed on silica, eluting with benzene, to give 4,5-dicarbomethoxy-1,3-dithiole as yellow oil (0.388 g, 88.3%). Sublimative distillation gave an analytical sample: NMR δ 3.77 (s, 6 H) and 4.49 (s, 2 H); UV (CH_2Cl_2) λ_{max} 296 nm (sh) (log ϵ 4.23) and 351 (4.67). Anal. Calcd for $C_7H_8O_4S_2$: C, 38.17; H, 3.66; S, 29.11. Found: C, 38.09; H, 3.88; S, 29.24.

To a solution of dithiole **8** (228 mg) in anhydrous THF was added a solution of butyllithium in hexane (2.5 M solution, 0.4 mL, 1 mmol) at −78 °C under nitrogen. The yellow solution was stirred for 1 h and deuterium oxide (0.1 mL) was added. The mixture was warmed to room temperature and evaporated. The residue was chromatographed on silica gel (benzene eluant) to give the starting material (134.4 mg). The NMR spectrum showed no incorporation of deuterium into **8**.

2-Cyclohexylidene-4,5-dicarbomethoxy-1,3-dithiole (12). To the suspension of the salt **7** (2.04 g, 4 mmol) in anhydrous tetrahydrofuran (50 mL) was added butyllithium solution (2.5 M in hexane, 1.6 mL, 4 mmol) at −78 °C over a period of 2 min, and subsequently cyclohexanone (0.42 mL, 4 mmol) dropwise. After being stirred for 1.5 h at −78 °C, the solution was warmed gradually to room temperature (2 h) and stirring was continued for 0.5 h at room temperature. The solution was poured into water and the mixture was extracted with dichloromethane. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica (benzene) to give a red oil (0.735 g), which was rechromatographed under the same conditions to give cyclohexylidene (4,5-dicarbomethoxy-1,3-dithiole) (0.715 g, 59.6%) as orange crystals. Recrystallization from methanol gave red needles: mp 70.5–72.5 °C; UV (CH_2Cl_2) λ_{max} 254 nm (log ϵ 4.07), 326 (2.99), 406 (3.26); NMR δ 3.69 (s, 6 H), 1.1–2.1 (m, 10 H); mass spectrum *m/e* (rel intensity) 300 (M^+, 100), 271 (39). Anal. Calcd for $C_{13}H_{16}O_4S_2$: C, 51.98; H, 5.39; S, 21.35. Found: C, 52.05; H, 5.50; S, 21.29.

2-(4-Thiacyclohexylidene)-4,5-dicarbomethoxy-1,3-dithiole (18). To the suspension of salt **7** (1.25 g, 2.4 mmol) in anhydrous tetrahydrofuran (20 mL) was added a solution of butyllithium (2.5 M in hexane, 0.96 mL, 2.4 mmol) dropwise at −78 °C under nitrogen. To the resulting red solution was added a solution of 4-thiacyclohexanone (0.232 g, 2 mmol) in anhydrous THF over a period of 10 min. After stirring at −78 ° for 1.5 h, the solution was warmed gradually to room temperature. The solution was poured into water and the mixture was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica (benzene) to give fulvene **18** (0.535 g, 84.2%) as red crystals, which were recrystallized from benzene–cyclohexane (1:1) to give orange needles: mp 121.5–122.5 °C (lit.[6] mp 124 °C); NMR δ 3.77 (s, 6 H), 2.2–2.8 m (8 H); UV (CH_2Cl_2) λ_{max} 262 nm (log ϵ 4.09), 327 (3.09), 402 (3.31). This material was identical (IR) with an authentic sample supplied by Dr. D. J. Sandman.

2-Fluorenylidene-4,5-dicarbomethoxy-1,3-dithiole (16). To a suspension of salt **7** (1.02 g, 2 mmol) and fluorenone (360 mg, 2 mmol) in anhydrous tetrahydrofuran (25 mL) was added a solution of butyllithium (2.5 M in hexane, 0.8 mL, 2 mmol) during a period of 10 min at −78 °C under nitrogen. After stirring for 3 h at −78 °C, the solution was warmed gradually to room temperature and poured into water. The usual workup afforded, after silica chromatography (benzene), red crystals of **16** (0.55 g, 72%), which were recrystallized from benzene to give red needles: mp 207.5–208.5 °C; NMR δ 3.84 (s, 6 H), 7.2–7.5 (m, 4 H), 7.55–7.85 (m, 4 H); UV (CH_2Cl_2) λ_{max} 245 nm (log ϵ 4.83), 377 (4.51), 396 (sh) (4.49). Anal. Calcd for $C_{20}H_{14}O_4S_2$: C, 62.81; H, 3.69; S, 16.77. Found: C, 62.62; H, 3.45; S, 16.92.

Ketofulvene 20 and Difulvene 21. To the ylide solution prepared from salt **7** (1.02 g, 2 mmol) was added a solution of cyclohexane-1,4-dione (0.112 g, 1 mmol) in tetrahydrofuran (5 mL) dropwise at −78 °C under nitrogen. The solution was stirred for 1.5 h at −78 °C and then warmed gradually to 0 °C for a period of 1 h. After stirring for an additional 1 h at 0 °C, the solution was poured into water. The usual workup, followed by silica chromatography (benzene), afforded two colored crystalline products. The red-orange difulvene **21** (198.5 mg, 38.6%) crystallized from benzene as red leaflets: mp 204–206 °C; NMR δ 2.13 (s, 8 H), 3.78 (s, 6 H); UV (CH_2Cl_2) λ_{max} 267 nm (log ϵ 4.58), 324 (3.62), 403 (3.67). Anal. Calcd for $C_{20}H_{20}O_8S_4$: C, 46.73; H, 3.97; S, 25.10. Found: C, 46.46; H, 3.90; S, 24.83. The yellow ketofulvene **20** (70.6 mg, 22.3%) crystallized from benzene–cyclohexane as yellow needles: mp 124.5–125.5 °C; NMR δ 2.40 (s, 8 H), 3.81 (s, 6 H); UV (CH_2Cl_2) λ_{max} 256.5 nm (log ϵ 4.10), 328 (3.11), 400 (3.35). Anal. Calcd for $C_{13}H_{14}O_5S_2$: C, 49.67; H, 4.49; S, 20.40. Found: C, 49.41; H, 4.25; S, 20.32. The mass spectra of **21** and **20** showed molecular ions at *m/e* 516 and 314, respectively.

The Oxidation of 21 with *m*-Chloroperbenzoic Acid. (a) To a mixture of **21** (1.03 g, 2 mmol), dichloromethane (50 mL), and 5% disodium hydrogen phosphate solution cooled in ice water was added an ice-cooled solution of *m*-chloroperbenzoic acid (70%) (0.50 g, 2 mmol) in dichloromethane (50 mL) during a period of 8.5 min. The mixture was stirred for a further 5 min. The organic layer was separated, washed with 5% aqueous disodium hydrogen phosphate, dried (Na_2SO_4), and evaporated. Chromatography of the residue on silica (dichloromethane–ethyl acetate 5:1) afforded starting material **21** (0.427 g, 41.5%) in addition to the more polar orange-yellow crystalline monosulfoxide **24** (0.356 g, 33.5%): mp 207–208 °C; NMR δ 2.0–2.6 (m, 6 H), 2.8–3.1 (m, 2 H), 3.79 (s, 6 H), 3.84 (s, 3 H), 3.91 (s, 3 H); UV (CH_2Cl_2) λ_{max} 260 nm (log ϵ 4.59), 337 (4.04). Anal. Calcd for $C_{20}H_{20}O_9S_4$: C, 45.10; H, 3.78; S, 24.08. Found: C, 44.83; H, 3.98; S, 24.01.

(b) To a cold mixture of **21** (66.2 mg, 0.13 mmol), dichloromethane (5 mL), and 5% aqueous disodium hydrogen phosphate solution (10 mL) was dropwise added an ice-cooled solution of *m*-chloroperbenzoic acid (70%) (128 mg, 0.52 mmol) in dichloromethane (10 mL). The organic layer was checked by TLC and when no more starting material was present, it was separated, washed with 5% aqueous disodium hydrogen phosphate, and dried over sodium sulfate. After evaporating the solution, yellow crystals of disulfoxide **27** (76 mg) were obtained. The crystals were dissolved in a small amount of chloroform, the solution was filtered, and cyclohexane was added to the filtrate. Yellow crystals of **27**, mp 228–230 °C dec, separated. Analysis was not possible, since this substance was unstable and decomposed on standing at room temperature for 1 day.

Pummerer Reaction of Sulfoxide 24. A mixture of **24** (53.5 mg, 0.1 mmol), acetic anhydride (5 mL), and diisopropylethylamine (3 drops) was refluxed for 1 h under nitrogen. After evaporating the solution, the dark-violet crystalline residue was chromatographed on silica (dichloromethane) to give fulvene **25** (48 mg, 94%), which crystallized from 1:1 benzene–cyclohexane as deep violet needles: mp 202–204 °C; NMR δ 2.23 (s, 4 H), 3.79 (s, 12 H), 5.83 (s, 2 H); UV (CH_2Cl_2) λ_{max} 391 nm (log ϵ 4.59), 410 nm (4.61); mass spectrum *m/e* (rel intensity) 312 (M^+, 100). Anal. Calcd for $C_{20}H_{18}O_8S_4$: C, 46.68; H, 3.53; S, 24.92. Found: C, 46.87; H, 3.60; S, 25.08.

Oxidation of 25 with *m*-Chloroperbenzoic Acid. To a mixture of **25** (51.4 mg, 0.1 mmol), dichloromethane (5 mL), and 5% aqueous disodium hydrogen phosphate solution (10 mL) was added a solution of *m*-chloroperbenzoic acid (70%) (24.7 mg, 0.1 mmol) in dichloromethane (5 mL) with vigorous stirring and external ice cooling. The mixture was stirred for 5 min. The organic layer was separated, washed with 5% aqueous disodium hydrogen phosphate solution, dried (Na_2SO_4), and evaporated. Silica chromatography (4:1 dichloromethane–ether) afforded sulfoxide **26** (47.6 mg, 89.8%) as black-red crystals, which were recrystallized from chloroform–cyclohexane to give the analytical sample: mp 167 °C dec; NMR δ 2.2–3.3 (m, 4 H), 3.81 (s, 9 H), 3.91 (s, 3 H), 6.04 (d, J = 9.5 Hz), 6.41 (d, J = 9.5 Hz), 6.47 (d, J = 9.5 Hz), 6.86 (d, J = 9.5 Hz); UV (CH_2Cl_2) λ_{max} 257 nm (sh) (log ϵ 4.08), 343 (4.05), 456.5 (4.47); mass spectrum *m/e* (rel intensity) 530 (43), 514 (91), 469 (80), 324 (100). Anal. Calcd for $C_{20}H_{18}O_9S_4$: C, 45.27; H, 3.52; S, 24.17. Found: C, 44.88; H, 3.41; S, 23.65.

Attempted Pummerer Reaction of 26. To a solution of sulfoxide **26** (53.0 mg, 0.1 mmol) in dichloromethane (5 mL) was added diisopropylethylamine (0.1 mL, 0.6 mmol) and subsequently trifluoroacetic anhydride (0.05 mL, 0.35 mmol) under argon with external ice cooling. The solution was stirred for 10 min and then directly chromatographed on silica (dichloromethane) to give black-violet crystals of **25** (46.6 mg, 90.6%), the NMR spectrum of which was identical to that of an authentic sample.

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Registry No.—**1**, 58758-29-5; **6**, 68629-93-6; **7**, 68629-95-8; **8**, 68629-96-9; **10**, 51225-41-3; **11**, 68682-86-0; **12**, 68629-98-1; **13**, 68629-99-2; **15**, 68630-00-2; **16**, 68630-01-3; **18**, 65960-11-4; **20**, 68630-02-4; **21**, 68630-03-5; **24**, 68630-04-6; **25**, 68630-05-7; **25a**, 68630-06-8; **26b**, 68630-07-9; **27a**, 68630-08-0; **27b**, 68630-09-1; dimethyl acetylenedicarboxylate, 762-42-5; benzaldehyde, 100-52-7; *trans*-cinnamaldehyde, 14371-10-9; benzocyclobutenedione, 6383-

11-5; 9,10-phenanthrenequinone, 84-11-7; cyclohexanone, 108-94-1; 4-thiacyclohexanone, 1072-72-6; fluorenone, 486-25-9; cyclohexane-1,4-dione, 637-88-7.

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Catalytic Dipolar Micelles. 7. Catalytic Effects of Positively Charged Hydroxylic Micelles on the Hydrolysis of Phenyl and Benzoate Esters

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The catalytic effects of 13 hydroxylic micelles on the hydrolysis of positively charged benzoate esters and on long-chain phenyl esters were measured. The micelles are of the general structure: $CH_3(CH_2)_nN^+(R_1)_2C(R_2)_2CHR_3(CH_2)_mOH\ Br^-$, where $R_3 = R_2 = H$, $R_1 = CH_3$, $m = 0$, $n = 9$ (I); $m = 0$, $n = 11$ (IA); $m = 0$, $n = 13$ (IB); $m = 0$, $n = 15$ (IC); $m = 1$, $n = 13$ (IIB); $m = 1$, $n = 15$ (IIC); $R_3 = R_2 = H$, $m = 0$, $R_1 = Et$, $n = 9$ (III); $R_1 = Et$, $n = 15$ (IIIC); $R_3 = H$, $R_1 = R_2 = CH_3$, $m = 0$, $n = 9$ (IV); $R_1 = R_3 = CH_3$, $R_2 = H$, $m = 0$, $n = 9$ (V); $n = 13$ (VB); $n = 15$ (VC). Noncatalytic micelles were employed for comparison purposes where the functional group OH was replaced by hydrogen and $R_1 = CH_3$, $R_2 = R_3 = H$, $m = 0$, $n = 9$ (VI) or $n = 15$ (VIC). The benzoate esters studied possessed the above alkoxide catalysts as leaving groups. The corresponding *p*-nitrobenzoate esters were IE, IIE, IIIE, IVE, IVE, VE, ICE, IICE, IIICE, and VCE, and the corresponding *p*-methylbenzoate esters were IEM and IIEM. *p*-Nitrophenyl decanoate (NPD) and 2,4-dinitrophenyl decanoate (DNPD) were also included in the study. The cmc values of micelles I–IIIC and those of V–VC were determined. In each of these micelles it was found that the contribution of the head groups to the cmc is negligible. The free energy of micellization per methylene group in hydroxylic micelles was found to be 590 cal. The *trans*-benzoylation stage in the hydrolysis of benzoate esters was established. From the rate–pH profile of the least reactive esters IEM and IIEM in highly basic solutions and in the presence of micelle I, the apparent pK_a value of the micellized alkoxide I was estimated to be 13.4–13.5. All other pK_a values of micelles I–VC were also estimated either from the catalytic rates of NPD and DNPD or from the substituent effect on the dissociation constants of analogous compounds. The results from the first-order rate constants of the nucleophilic attack by the micellized alkoxide ions (I–VC) in the substrate–micelle complex (k_c) on benzoate esters indicated that relative to the basicity, the catalytic efficiency of micelle I was low. However, micelle II exhibited a high catalytic reactivity. These phenomena were explained by proximity factors. The second-order rate constants (k_{mH}) of the specific base catalysis in the hydrolysis of IE, IIE, IIIE, IVE, VE, ICE, IICE, IIICE, and VCE at moderate basic pH values were measured. The β Brønsted coefficient (0.55) found for these esters was higher than that (0.3) previously observed for the substituted phenyl esters and is consistent with the higher basicity of the leaving groups.

Surfactants containing imidazole,[1] amine,[2] thiol,[3] hydroxamate,[4] hydroxyl,[5] and carboxy[6] head groups catalyzed effectively ester hydrolyses. This phenomenon has focused general attention on micellar systems as probable models for the enzymatic processes.

In order to provide a closer analogy with the mechanistic features of the enzyme-catalyzed hydrolysis of esters, bifunctional micelles[7] have also been used in several studies.

One of the models for the acylation reaction of the serine oxygen in esteratic enzymes is the hydroxylic micelle. Bunton et al.[5b,c] have demonstrated that zwitterionic cholinium micelle exhibited phosphoryl transfer in the hydrolysis of phosphate esters. This finding is in accordance with our previously reported results,[5b] in which we established the involvement of the benzoyl transfer stage in the hydrolysis of benzoate esters within an identical micellar system.

In our continued investigations on micellar systems, it has become important to elucidate some microenvironmental and conformational parameters which affect the benzoyl transfer reaction at the interfaces of various types of cholinium micelles. Therefore, in this present study, 13 hydroxylic surfactants possessing substituted head groups of variable chain lengths were employed as catalysts.

Experimental Section

Materials. Phenyl esters, benzoate esters, and detergents (Chart I) were prepared by standard methods as previously described.[5j,h,6] Melting point data of the various detergents are given in Table I.

Kinetics. Hydrolytic reactions were followed spectrophotometrically at 30 ± 0.1 °C using a Unicam SP-800 spectrophotometer with a water-jacketed cell compartment. The release of *p*-nitrophenolate, *p*-nitrobenzoate, and *p*-methylbenzoate anions was detected at 350, 300, and 262 nm, respectively. The surfactant concentration in the reaction cells was 0.1 M, and the substrate concentration in most cases was $1–5 \times 10^{-5}$ M. The kinetic measurements were carried out at several pH values (9.3–10.5) with 0.05 M potassium carbonate buffer. The pH of the medium was measured on a Radiometer pH meter 26, with a combined glass electrode, before and after each run.

Rate Constants. At a moderate pH range of 9.3–10.5 the reaction rates of (i) phenyl esters in micelles I–VIC, (ii) the ester IE in micelles I–IC and III–VIC, (iii) the ester IIE in micelles II–IIC, VI, and VIC, and (iv) the esters IIIE, IVE, and VE in micelles III, IV, and V fol-

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