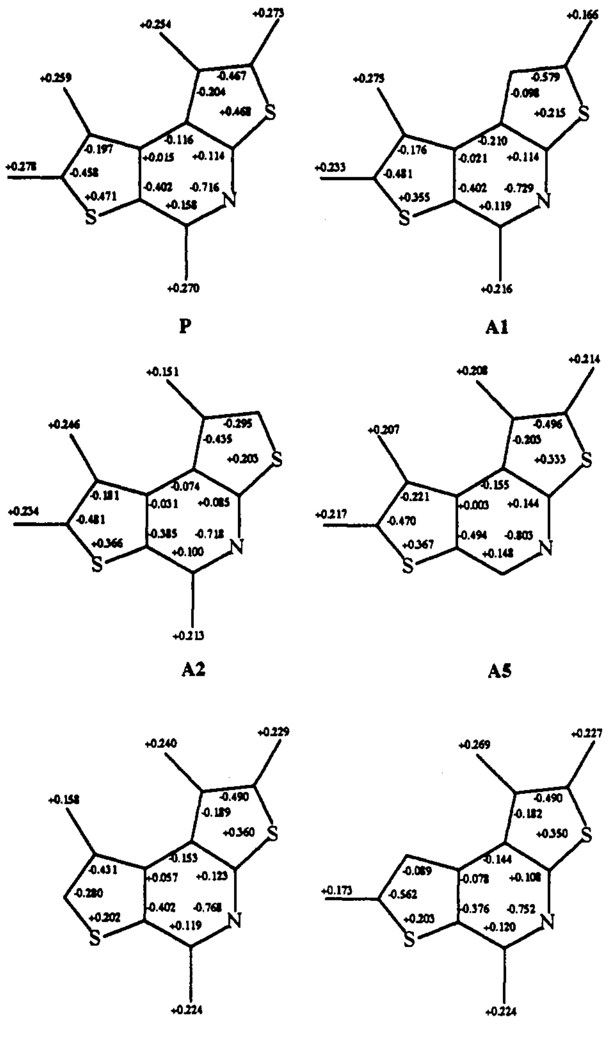

P **A1**

A2 **A5**

A7 **A8**

Figure 2. Aromic 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*]pyridine[3] 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 $C_{10}H_5NOS_2$ (**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 $C_{10}H_7NS_3$: 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 $C_9H_4NS_2Br$: C, 40.0; H, 1.5; N, 5.2. Found: C, 40.2; H, 1.3; N, 4.9.

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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

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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 ($TBAHSO_4$) (1 mol) to a solution of NaBr (3 mol) in aqueous NaOCl causes formation of an insoluble orange semisolid. When benzene, CCl_4, 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 ($TBABr_3$) but significant amounts of water, hypohalite and halide ions, and possibly Br_2 also appear to be present. A similar triphasic mixture forms when $TBABr_3$ is combined simply with aqueous hypochlorite.

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Table I. Reactions with TBAHSO/NaBr/NaOCl

reactants	products	% yield GLC	% yield isolated
cyclohexene	*trans*-1,2-dibromocyclohexane	40	
	trans-1-bromo-2-chlorocyclohexane	46	
phenylacetylene	phenylbromoacetylene	92	82
1-octyne	1-bromo-1-octyne	88	75
1-heptyne	1-bromo-1-heptyne	85	70
deoxybenzoin	α,α-dibromodeoxybenzoin		32
diphenylmethane	benzophenone	65	65
triphenylmethane	triphenylmethanol		69

The tendency for systems containing large amounts of electrolyte and tetrabutylammonium salts to form liquid third phases (coascervation) has been reported recently, and they are of some interest because of their ability to enhance reaction rates.[3]

Table I shows the results of the reaction of the alkaline TBAHSO$_4$/NaBr/NaOCl system (pH 12.4) with a range of compounds. To obtain these yields, a 2:1 molar ratio of TBAHSO$_4$/organic substrate was used. Prolonged reaction of a 1:1 molar ratio leaves much starting material unreacted, suggesting perhaps that less oxidizing agent is active in the interfacial layer in these cases.

In some respects, the reagent acts simply like TBABr$_3$ in that it adds bromine to alkenes[4] and ketones[5] in the usual way. However, note the high yield of chlorinated product formed in the addition to cyclohexene because the reaction takes place in a medium with a high concentration of chloride ion.

In other cases, the oxidizing power of the medium is important in the reaction. Of particular interest is the conversion of 1-alkynes to 1-bromo-1-alkynes which are usually prepared by the slow reaction of 1-alkynes with aqueous hypobromite[6] or by treating alkynyl organometallics with bromine.[7]

Alkynes slowly undergo addition reactions with TBABr$_3$ to give dibromoalkenes.[8] The present work reveals that TBABr$_3$ undergoes very little reaction with 1-alkynes in an alkaline medium of high ionic strength in a period of 1 h unless NaOCl is present. When it is, a clean and rapid reaction occurs to give the 1-bromo-1-alkyne.

Also of interest is the smooth conversion of diphenylmethane to benzophenone, presumably through the intermediate formation of diphenylmethyl bromide and benzhydrol followed by oxidation. The transformation occurs in diminished yield (see the Experimental Section) by action of hypochlorite and TBAHSO$_4$ initially at pH 8.5 but not by treatment with hypochlorite and tetra-*n*-butylammonium chloride (TBACl) at pH 12.2.

In the overall hydrolysis or oxidation reactions, TBABr$_3$ should act as a catalyst, being regenerated as hydrolysis of product occurs. The interfacial and aqueous layers are easily separated and recovered for repeat use. The interfacial layer can be used at least three times for the oxidation of diphenylmethane to give essentially the same yield of benzophenone. However, the repeat yields are somewhat erratic, and interestingly, the total amount of recovered neutral material is always less in the original reaction than in subsequent ones. Some changes take place in the physical characteristics of the interfacial layer, and the extent of degradation of product seems strongly dependent on the concentration and amount of oxidizing agent present.

The brominating/oxidizing system is quite reactive toward a number of compounds including primary amides, dichloromethane, and simple arylalkanes. However, in these cases reaction is extensive, leading to much degradation and formation of multiple products. For example, toluene reacts to give several compounds—the major identified ones being benzyl bromide and benzyl benzoate, presumably arising from reaction of a benzoate anion oxidative product with benzyl bromide. In this respect, the reactions of simple arylalkanes appear to be similar to those observed with NaOCl alone.[1b]

In conclusion, the triphasic system exhibits reactivity toward a variety of compounds. Convenient and successful syntheses appear to be possible in those cases where stable bromides are formed or where their transformation products are few in number.

Experimental Section

The quaternary ammonium salts were commercial grade (Aldrich Chemical Co.) and were used without further purification. The aqueous NaOCl was Mallinckrodt AR with 11% available chlorine. It was stored in a refrigerator, and the available Cl was checked periodically by iodometric titration. The 1-alkynes were purchased from Aldrich, and the other starting materials (except where otherwise indicated) were commercial materials which either had sharp melting points or were shown by GC to be free of interfering impurities.

GC analyses were performed on packed columns (1.5% OV-101, 1.5 m, 3-mm i.d. and 1.5% SP-2250/1.95% SP-2401, 2 m, 3-mm i.d.). All melting points are corrected.

Generation and Properties of the Third Phase. To a solution of 1.03 g (10 mmol) of NaBr in 8.0 mL (ca. 6.5 mmol) of aqueous NaOCl were added in succession 1.00 g (3 mmol) of TBAHSO$_4$ and 5.0 mL (4.4 g) of benzene. The resulting mixture (pH 12.4) was stirred vigorously at rt with a magnetic stirring bar for 10 min, after which the layers were separated in a separatory funnel and weighed. The interfacial layer was reddish in color and weighed 2.40 g; the benzene layer weighed 3.00 g. GC analysis showed that the interfacial layer contained about 55% benzene by weight. Solvent was evaporated from it, first at reduced pressure and then at high vacuum to give 0.75 g of an orange waxy solid which on long standing formed massive needles. An IR spectrum of the solid taken shortly after isolation was nearly identical to that of TBABr$_3$ with the exception of an intense, broad absorption band at 970 cm^{-1} characteristic of OCl$^-$ absorption.[9] Recrystallization of the solid from acetic acid–CCl$_4$ gave 0.40 g of crystals of mp 68–70 °C (lit.[10] mp 72.5–74 °C).

A similar interfacial layer can be formed with TBACl rather than TBAHSO$_4$, but this system is not as effective in subsequent reactions.

The behavior of the TBAHSO$_4$/NaBr/NaOCl system (without benzene) was also investigated as the pH was changed. Addition of 6 M NaOH caused the pH to rise until, at a pH of about 13.5, the aqueous layer became yellow in color and the original orange semisolid dissolved. If, instead, 3 M H$_2$SO$_4$ was added, the pH decreased and the semisolid became more granular, precipitating out of the mixture at about pH 9.

General Procedure. Reactions were usually run on a small scale. To a mixture of 1.03 g (10 mmol) of NaBr in 8.0 mL (ca. 6.5 mmol) of aqueous NaOCl was added 2.00 g (6 mmol) of TBAHSO$_4$. Then 3 mmol of substrate was added directly or dissolved in 5.0 mL of benzene and the resulting mixture stirred

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vigorously with a magnetic stirring bar for the required period of time at room temperature.[11] At the end of the reaction, 5.0 mL of benzene were added if it was not used initially, and the benzene layer was separated. The interfacial layer was separated and washed simultaneously with saturated NaCl and additional benzene. Finally, the benzene extracts were all combined, washed with 10% $NaHSO_3$ and 5% $NaHCO_3$, and dried ($MgSO_4$). For purposes of isolation of products, the reaction was scaled up by a factor of five with no adverse effects.

1-Bromo-1-alkynes. 1-Octyne, dissolved in benzene, was reacted according to the small scale general procedure for 45 min. GC analysis showed an 88% yield of 1-bromo-1-octyne (1) with about 5% 1-octyne unreacted and the remainder higher brominated material.

The product was isolated in a scaled up procedure by distilling the benzene at reduced pressure through a short Vigreux column. After transferring to a microscale spinning band distillation apparatus, the product (1) (2.1 g, 75%) was collected at 81–83 °C (15 Torr) (lit.[12] bp 86 °C (12 Torr)): IR (neat, 0.1-mm cell) 2230 cm^{-1}; NMR (60 MHz, CCl_4) δ 0.90 (m, 3 H), δ 1.40 (m, 8 H), δ 2.22 (m, 2 H). Anal. Calcd for $C_8H_{13}Br$: C, 50.81; H, 6.93; Br, 42.26. Found: C, 50.54; H, 6.55; Br, 42.71.

1-Bromo-1-heptyne (2) and phenylbromoacetylene (3) (distilled under nitrogen[6]) were obtained in a similar fashion with yields as reported in Table I.

Experiments with 1-heptyne showed that when a 1:1 molar ratio of $TBAHSO_4$ and 1-heptyne was reacted for 1.5 h, 40% of the starting material was unreacted. Running the reaction for 2.5 h did not increase conversion. When TBACl was used in place of $TBAHSO_4$, the yield of 2 dropped to 40%. Use of $TBABr_3$ in the general procedure in place of $TBAHSO_4$ and NaBr gave results which were indistinguishable from the usual case. However, when aqueous NaOCl was omitted and $TBABr_3$ was used with only an alkaline solution of high ionic strength (20% NaCl), no reaction occurred.

Cyclohexane Dihalides. The reaction of cyclohexene, dissolved in benzene, was conducted according to the general procedure for 5 min. GC analysis indicated a yield of 46% *trans*-1-bromo-2-chlorocyclohexane (4) and 40% *trans*-1,2-dibromocyclohexane (5).

The products were isolated by distillation in a larger scale run to give 4 (1.5 g, 37%) (bp 85–90 °C (14 Torr)) (lit.[13] bp 76–77 °C (9 Torr)) and 5 (1.95 g, 36%) (bp 95–100 °C (14 Torr)) (lit.[14] bp 96.9–99.9 °C (13 Torr)). The products 4 and 5 were not completely separated, GC analysis showing them to be only about 80% pure. However, they were sufficiently pure to give spectra (IR and NMR) and GC behavior identical to the authentic samples prepared according to the published procedures.[13,15]

α,α-Dibromodeoxybenzoin (6). Deoxybenzoin,[16] in benzene, was reacted on a small scale according to the general procedure except that 1.5 times the normal amount of NaBr was used. The mixture warmed slightly, and reaction was carried out for 45 min. The benzene was removed under reduced pressure to give 720 mg of solid which was recrystallized from alcohol to give 320 mg (32%) of 6: mp 103–106 °C. This material showed one spot on TLC and gave IR and NMR spectra identical to that of a more highly purified sample (210 mg) obtained by three additional recrystallizations from 10% ethyl acetate–hexane: mp 109–111 °C (lit.[17] mp 112 °C); IR (Nujol mull) 1690 cm^{-1}; NMR (60 MHz, CCl_4) δ 7.5–8.0 (m, 10 H). Anal. Calcd for $C_{14}H_{10}Br_2O$: C, 47.49; H, 2.85; Br, 45.13. Found: C, 47.68; H, 2.77; Br, 45.21.

Triphenylmethanol (7) and Benzophenone (8). Triphenylmethane, suspended in 10.0 mL of benzene, was reacted according to the general procedure for 4 h. Removal of the benzene at reduced pressure gave a white solid whose IR spectrum showed that it was essentially crude 7. Two recrystallizations from 10% ethyl acetate–cyclohexane gave 0.54 g (69%) of 7: mp 158–160 °C. The material was identical in all respects (IR, NMR) to authentic 7 which melts at 160–162 °C. When triphenylmethyl bromide was carried through the general procedure, an 80% yield of 7 was obtained.

Diphenylmethane was reacted without a benzene solvent for 4 h according to the small scale general procedure except that twice the amount of aqueous NaOCl was used. GLC analysis showed a yield of 65% of 8 with 8% starting material unreacted. No other neutral material was present. Use of only 20% excess NaOCl or a reaction period of only 2 h gave substantially reduced yields of 8 (50% and 32%, respectively) with much unreacted starting material.

Removal of the benzene at reduced pressure gave an oil (0.44 g) which slowly crystallized at rt: mp 45–48 °C. The material was identical (IR, NMR, mixed mp) with authentic 8. When benzhydrol was used as starting material for the reaction, 8 was obtained in 87% yield.

During the course of these reactions, the pH of the aqueous phase decreased from 12.4 to 8.5. When a phosphate buffer was used, the pH at the end was 10.5 but there was no significant change in yield or amount of loss. It was observed that when 8 was exposed to the reaction conditions for 4 h only 83% was recovered.

For repeated use of the interfacial layer, there was a modification in the reaction work up. The original aqueous phase and the interfacial layer together were extracted three times with benzene. Benzene was evaporated from the interfacial layer at reduced pressure, and then the original aqueous phase and interfacial layer were recharged with an additional 8.0 mL of aqueous NaOCl and 3 mmol of diphenylmethane. The reaction was carried out for another 4 h. At the completion of the process, GC analysis showed 31% starting material unreacted and a 60% yield of 8. In the third, repeated use of the catalyst only the interfacial layer was combined with fresh NaOCl and diphenylmethane. The results were 65% 8 and 25% unreacted.

When diphenylmethane was reacted with aqueous NaOCl and TBACl (pH 12.2), no reaction occurred. Reaction did occur with aqueous NaOCl and $TBAHSO_4$ (pH 8.5) to give a 38% yield of 8, but 18% of starting material was unreacted.

Miscellaneous Reactions. The general procedure was used for reactions with benzamide, acetophenone, toluene, ethylbenzene, and cumene. Benzamide reacted rapidly in minutes to undergo extensive degradation. Only a small amount (10%) of phenylbenzoylurea, often found as a side product in the Hofmann reaction of amides,[18] was isolated and identified.

Acetophenone probably underwent the haloform reaction. Reaction for a few minutes led to decolorization and destruction of the interfacial layer. Upon reaction workup, the only neutral material isolated was acetophenone (80% recovery). Dichloromethane (45 min), ethylbenzene (4 h), and cumene (4 h) reacted to give five, two, and four products, respectively, when they were used as solvents in place of benzene in the general procedure. The products of these reactions were not identified except to show that acetophenone was not a reaction product from ethylbenzene.

The reaction of toluene was investigated. Little reaction occurred when it was used in equimolar amounts in the general procedure, but it did react extensively over a 4 h period when it was used as a solvent. Four products were formed, two of them comprising about 85% of the total. These were identified as benzyl bromide and benzyl benzoate by comparison (GC, IR) with authentic samples.

Registry No. 1, 38761-67-0; 2, 19821-84-2; 3, 932-87-6; 4, 13898-96-9; 5, 7429-37-0; 6, 15023-99-1; 7, 76-84-6; 8, 119-61-9; $TBAHSO_4$, 32503-27-8; $TBABr_3$, 38932-80-8; NaBr, 7647-15-6; NaOCl, 7681-52-9; 1-octyne, 629-05-0; PhC⋮CH, 536-74-3; 1-heptyne, 628-71-7; cyclohexene, 110-83-8; deoxybenzoin, 451-40-1; triphenylmethane, 519-73-3; benzamide, 55-21-0; phenylbenzoylurea, 1821-33-6; acetophenone, 98-86-2; toluene, 108-88-3; benzyl bromide, 100-39-0; benzyl benzoate, 120-51-4; diphenylmethane, 101-81-5.

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[11] Room temperature must be above 15 °C to allow good development of the interfacial layer in the absence of solvent.

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