3× with 2 M sodium bisulfate solution followed by successive water washings until the aqueous layer remained clear. The ethyl acetate layer was then dried over magnesium sulfate. The drying agent was removed and the filtrate concentrated under reduced pressure to give an oil. The oil was dissolved in 3 mL of ethyl acetate and cooled to 0 °C. With stirring, dicyclohexylamine (62.5 μL, 0.314 mmol) was added. Five minutes later 15 mL of ether was added and the mixture placed in the freezer overnight. The product **26** was collected and washed with cold ether: 0.141 g (70%); mp 123–124 °C (lit.[1] mp 122–123 °C for the protonated analogue); R_f(**3a,b,c,e**)[19] 0.48; $[\alpha]^{20}_D$ (*c* 1.0, MeOH) −1.4° (−1.3°[1] for the protonated analogue).

The following compounds were synthesized by the procedures given for the unlabeled analogues.[1]

***N*-(Benzyloxycarbonyl)-α-(pentachlorophenyl)[ε-^{15}N,α-^{2}H]lysyl-*N*′-(*tert*-butyloxycarbonyl)[α-^{2}H]glutamic Acid Methyl Ester.** Physical data: mp 154–155 °C; $[\alpha]^{20}_D$ (*c* 1.0, MeOH) −20.5° (mp 154–155 °C; $[\alpha]^{20}_D$ (*c* 1.0, MeOH) −20.6° for the protonated analogue).[1]

***N*-(Benzyloxycarbonyl)-α-(pentachlorophenyl)[ε-^{15}N,α-^{2}H]lysyl[α-^{2}H]glutamic Acid Methyl Ester, Hydrochloride Salt.** Physical data: mp 123–125 °C; $[\alpha]^{20}_D$ (*c* 1.0, MeOH) −4.9° (mp 123–125 °C; $[\alpha]^{20}_D$ (*c* 1.0, MeOH) −4.9° for the protonated analogue).[1]

***N*-(Benzyloxycarbonyl)-*cyclo*([ε-^{15}N,α-^{2}H]lysyl[α-^{2}H]-glutamyl)Methyl Ester.** Physical data: mp 232–234 °C dec; $[\alpha]^{20}_D$ (*c* 1.0, TFE) −50.6° (mp 232–232.5 °C dec; $[\alpha]^{20}_D$ (*c* 1.0, TFE) −50.5° for the protonated analogue);[1] mass spectrum, *m/e* 409 (M + 1). Anal. Calcd for $C_{20}{}^{1}H_{25}{}^{2}H_{2}{}^{14}N_{2}{}^{15}NO_6$: C, 58.8; H, 7.2; N, 10.5. Found: C, 58.7; H, 7.0; N, 10.4.

Acetyl-*cyclo*([ε-^{15}N,α-^{2}H]lysyl[α-^{2}H]glutamyl) Methyl Ester. Physical data: mp 291–293 °C dec; $[\alpha]^{20}_D$ (*c* 1.0, TFE) −92.1° (mp 291–292 °C; $[\alpha]^{20}_D$ (*c* 1.0, TFE) −92.0° for the protonated analogue).[1]

***N*-Acetyl-*cyclo*([ε-^{15}N,α-^{2}H]lysyl[α-^{2}H]glutamyl) Hydrazide.** Physical data: mp 276–278 °C dec; $[\alpha]^{20}_D$ (*c* 1.0, TFE) −77.3° (mp 276–278 °C dec; $[\alpha]^{20}_D$ (*c* 1.0, TFE) −77.5°).[1]

***N*-Acetyl-*cyclo*(L-[ε-^{15}N,α-^{2}H]lysyl-L-[α-^{2}H]glutamyl)-*cyclo*(D-lysyl-D-glutamyl) *N*-Methylamide (I).** Physical data: mp >320 °C; $[\alpha]^{20}_D$ (*c* 0.5, TFE) −21.6° (mp > 320 °C; $[\alpha]^{20}_D$ (*c* 0.5, TFE) −21.8°);[1] mass spectrum, *m/e* 555 (M + 1). Anal. Calcd for $C_{25}{}^{1}H_{39}{}^{2}H_{2}{}^{14}N_{6}{}^{15}NO_7$: C, 54.1; H, 7.8; N, 17.9. Found: C, 53.9; H, 7.6; N, 17.6.

Acknowledgment. We gratefully acknowledge support from the National Institutes of Health through Grant GM-18694. We also acknowledge the Mass Spectrometry Facility located at the University of California, Riverside.

(α-Haloalkyl)phosphonium Salts and Sulfur Nucleophiles: A New Type of Reaction Mechanism[1a,b]

Remo Galli

Istituto di Biochimica e di Chimica, I-20133 Milano, Italy

Received November 3, 1986

Reaction between (α-haloalkyl)phosphonium salts and some sulfur nucleophiles leads to the substitution product $Ph_3P^+CH_2SR\ X^-$. Evidence is presented that this substitution is not a normal S_N2 reaction and that it occurs through formation of a phosphonium ylide and a disulfide, reaction between them, and action of the resulting salt on the starting phosphonium salt. Then RSX and $Ph_3P{=}CH_2$ reenter the sequence, giving rise to a three-step chain nucleophilic substitution.

Recently is has been shown that aryl[2] and alkyl thiolates[3] can be converted into difluorinated thioethers by reaction with fluorinated polyhalomethane (eq 1). This conversion

$$RSNa + CF_2BrX \rightarrow RSCF_2Br + NaX \qquad (1)$$

$$R = R, Ar;\ X = Br, Cl$$

occurs via a chain reaction with the intermediate formation of difluorocarbene.[2] It has been extended (albeit in low yield) to some dialkyldithiocarbamyl anions in order to test the fungicidal activity of the resulting compounds.[4] In contrast, the corresponding reaction with several nonfluorinated polyhalomethanes led to thiocarbamoyl disulfides and/or sulfides only (eq 2). Evidently, these

$$R_2NC(S)SNa + \left\{\begin{matrix} CCl_4,\ BrCCl_3,\ CHCl_3,\ CHBr_3 \\ CCl_2{=}CCl_2,\ BrCH_2Cl \end{matrix}\right\} \rightarrow [R_2NC(S)]_2Z \qquad (2)$$

$$Z = SS, S$$

polyhalomethanes do not sustain the chain reaction that occurs with CF_2BrX, since the decomposition rate of, e.g., CX_3^- (X = Cl, Br) is much lower than that of CF_2X^-.[5] The products obtained, however, are clearly formed through the intermediate sulfenyl halide, e.g. eq 3, pointing out the

$$RS^- + BrCCl_3 \rightarrow CCl_3^- + RSBr \xrightarrow{RS^-} RSSR \qquad RSBr \xrightarrow{-S} RBr \xrightarrow{RS^-} RSR \qquad (3)$$

$$RS^- = R_2NC(S)S^-$$

remarkable tendency of the dialkyldithiocarbamyl anion to undergo halogenophilic attack,[6] which is a soft–soft interaction. This tendency is greater than that of alkyl[7] and aryl[8] thiolates, since it occurs even with $BrCH_2Cl$, which undergoes the normal substitution of bromine by heteroaromatic thiophenols.[9] It was therefore expected that reaction between (α-iodomethyl)triphenylphosphonium iodide (**1a**) and sodium *N,N*-dimethyldithiocarbamate (**2**) would lead to a phosphonium ylide. Actually, by stirring **1a** and **2** (1:1 ratio) in chloroform

(1) (a) Presented in part at the 12th International Symposium on the Organic Chemistry of Sulfur, Nijmegen, The Netherlands, June-July 1986; paper OB15. (b) Taken from the dissertations of Lucia Pozzi and Maria Grazia Ghezzi, required for their University Degree respectively in Pharmacy (1984) and Pharmaceutic Chemistry and Technology (1985), University of Milan.

(2) Rico, I.; Wakselman, C. *Tetrahedron* **1981**, *37*, 4209.

(3) Suda, M.; Hino, C. *Tetrahedron Lett.* **1981**, *22*, 1997.

(4) Galli, R., unpublished results.

(5) Rico, I.; Cantacuzene, D.; Wakselman, C. *J. Org. Chem.* **1983**, *48*, 1979.

(6) Zefirov, N. S.; Makhon'kov, D. I. *Chem. Rev.* **1982**, *82*, 615.

(7) Baird, M. S.; Hoorfar, A.; Mitra, M. *Tetrahedron Lett.* **1981**, *22*, 2509.

(8) Hine, J.; Dowell, A. M.; Singley, J. E. *J. Am. Chem. Soc.* **1956**, *78*, 479.

(9) Goralski, G. T.; Burk, G. A. *J. Org. Chem.* **1977**, *42*, 3094.

0022-3263/87/1952-5349$01.50/0

suspension for 8–10 h at room temperature, the substitution product **3a** was formed in about 90% yield (eq 4).

$$\underset{\textbf{1a}}{Ph_3P^+CH_2I\ I^-} + \underset{\textbf{2}}{Me_2NC(S)SNa} \rightarrow \underset{\textbf{3a}}{Ph_3P^+CH_2SC(S)NMe_2\ I^-} + NaI \quad (4)$$

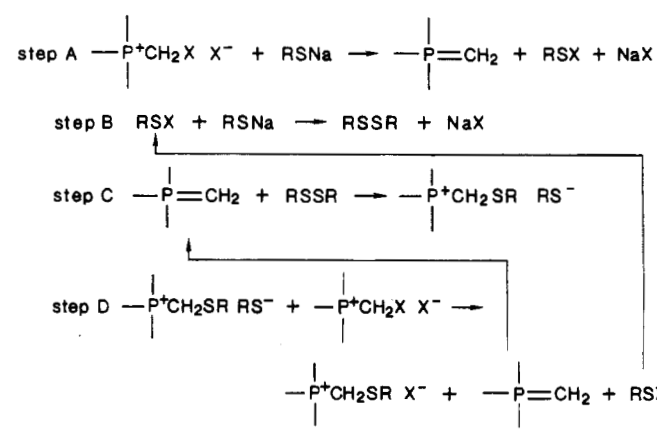
This reaction should not be an S_N2 process, as it might appear at first sight. No example is known of bimolecular substitution at the α-position of alkylphosphonium salts.[10] The replacement of a hydroxy group by chlorine is an internal substitution which occurs through the intermediate chlorosulfite,[11] and the two recent examples of halogen substitution by dithio-[12] and thiolcarboxylate groups,[13] for which no indication of mechanism is given, most probably follow the same pathway shown for reaction 4. In (α-haloalkyl)triphenylphosphonium salts the possible leaving groups are two, halogen and Ph_3P. Examples of Ph_3P displacements are known,[14] in which, however, there is not the concomitant presence of the halogen for a possible competition. In bimolecular nucleophilic displacements at saturated carbon the approximate order of decreasing leaving ability of R'_3N in comparison with halogens is[15] RI > RBr > RCl > $RN^+R'_3$. However, R'_3N is surely a more powerful nucleophile than Ph_3P, so that for (α-haloalkyl)phosphonium salts it is difficult to say a priori whether Ph_3P or halogen should be the leaving group. It may even be neither of them, as in the present case, in which the attacking nucleophiles are sulfur anions. Reaction 4 appears to be a pseudo-S_N2 reaction; it is not a simple bimolecular substitution but occurs instead through a more complex pathway, i.e., a three-step chain reaction of a new type.

Results and Discussion

The Reaction. When reaction 4 was carried out in chloroform the starting salts **1a** and **2** were in suspension; during the course of reaction they dissolved while NaI separated; filtration and evaporation of the solution left **3a** sufficiently pure. In dimethoxyethane (DME) or benzene, **3a** was also out of phase; it was obtained pure by simply washing with water–acetone. In DMF both starting and final salts were completely soluble. The optimum reaction time, 8–10 h at room temperature, could be shortened to 4–6 h by heating at 60 °C, with the same results. The yield of salt **3** was also equally good when Br or Cl replaced I in the starting salt **1** (**a** = I, **b** = Br, **c** = Cl). The sulfur nucleophile mostly used was a commercial product $Me_2NC(S)SNa{\cdot}2H_2O$. The other sulfur anions, commercially available or prepared as described in the literature, were used as sodium, potassium, or ammonium salts.

The Sulfur Anions. Reaction 4 easily occurred with several sulfur anions, such as $R_2NC(S)S^-$ (R = Me, Et) (**3a–d**), $(CH_2)_5NC(O)S^-$ (**3e**), $EtOC(O)S^-$ (**3f**), $EtOC(S)S^-$ (**3g**), $MeC(O)S^-$ (**3h**), NCS^- (**3i**), as well as the anions $ArC(S)S^-$[12] and $PhC(O)S^-$[13] (**3l**). On the contrary EtS^-, $PhCH_2S^-$, PhS^-, and other similar sulfur anions did not undergo reaction 4 but gave the corresponding disulfides and the phosphonium salt $Ph_3P^+Me\ X^-$. *Undoubtedly this result is contrary to expectation for a normal S_N2 reaction, since the weaker nucleophiles substitute while the more powerful ones do not.*

Scheme I



The Proposed Mechanism. The above result can be fully explained by assuming that reaction 4 occurs according to Scheme I.

Step A is the expected halogenophilic attack[6] by the sulfur anion. This is a new way for the generation of phosphonium ylides; it was previously observed to a minor degree with other non-sulfur nucleophiles in a very few cases.[16–18] Direct confirmation of the intermediate formation of the ylide $Ph_3P{=}CH_2$ came from its Wittig reaction with benzaldehyde to give styrene by reaction with EtS^- in DMF (eq 5). It was determined that the ylide was

$$Ph_3P^+CH_2I\ I^- + 2EtSNa + PhCHO \xrightarrow[DMF]{80\ ^\circ C,\ 2\ h} PhCH{=}CH_2 + EtSSEt + Ph_3PO + 2NaI \quad (5)$$

not formed under these conditions by action of EtS^- as a base on $Ph_3P^+Me\ X^-$. Moreover, a stabilized phosphonium ylide was obtained quantitatively, together with the disulfide, by reacting PhS^- with the corresponding brominated salt in methanol (eq 6).

$$Ph_3P^+CHBrCOMe\ Br^- + 2\ PhSNa \rightarrow Ph_3P{=}CHCOMe + PhSSPh + 2NaBr \quad (6)$$

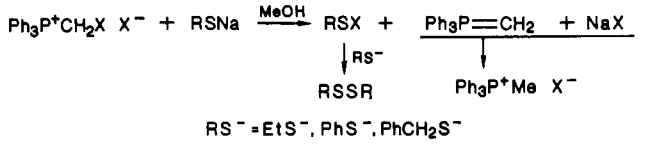
Step B is a known reaction of sulfenyl halides:[19] since the sulfur anion is the most powerful nucleophile present in the reaction mixture, its reaction with RSX prevails over other possible interactions, so that RSX cannot be captured by alkylating reagents such as alkenes or alkynes. However, it could be trapped by an arene sulfinate ion (vide infra).

Step C is also new. It is known that thiocarbamoyl disulfides are cleaved by vinyllithium,[20] enamines,[21] and Grignard reagents,[22] but, as far as phosphonium ylides are concerned, even the reactive methylene ylide is unable to cleave "normal" S–S bonds (e.g., PhSSPh and *n*-PrSSPr-*n*) under mild reaction conditions. The cleavage succeeds only under more severe conditions leading, however, to other products.[14]

The ease of attack under mild conditions is to be *attributed to the weak strength of the S–S bond in the*

(10) Beck, P. "*Quaternary Phosphonium Compounds*" *Organic Phosphorus Compounds*; Kosolapoff, G. M., Maier, L., Eds.; Wiley-Interscience: New York, 1972; Vol. 2, Chapter 4.
(11) Wittig, G.; Schlosser, M. *Chem. Ber.* **1961**, *94*, 1373.
(12) Ishida, M.; Sato, H.; Kato, S. *Synthesis* **1982**, 927.
(13) Ishida, M.; Iwata, T.; Yokoi, M.; Kaga, K.; Kato, S. *Synthesis* **1985**, *632*.
(14) Field, L.; Banks, C. H. *J. Org. Chem.* **1975**, *40*, 2774.
(15) March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley: New York, 1985; p 315.
(16) Seyferth, D.; Heeren, J. K.; Grim, S. O. *J. Org. Chem.* **1961**, *26*, 4783.
(17) Köbrich, G.; Trapp, H.; Flory, K.; Drischel, W. *Chem. Ber.* **1966**, *99*, 689.
(18) Ramirez, F.; Desai, N. B.; McKelvie, N. *J. Am. Chem. Soc.* **1962**, *84*, 1745.
(19) Schubart, R. "Sulfensäuren und deren Derivate" *Methoden der Organischen Chemie* (*Houben-Weyl*); Georg Thieme Verlag: Stuttgart, 1985; Band E11, p 90.
(20) Neumann, N.; Seebach, D. *Chem. Ber.* **1978**, *111*, 2785.
(21) Von Fanghänel, E. *J. Prakt. Chem.* **1975**, *317*, 123.
(22) Grunwell, J. R. *J. Org. Chem.* **1970**, *35*, 1500.

Scheme II



disulfides formed "in situ" from the sulfur anions which undergo reaction 4. Although the S–S bond strength seems not to be known, it is reasonable to assume that it is weaker when electron-withdrawing instead of electron-donating groups are linked to the S–S bond, since the S–S bond-dissociation energy drops from 74 kcal/mole in MeSSMe to 55 kcal/mole in PhSSPh.[23] On the other hand, when the sulfur anions give rise to disulfides with a strong S–S bond, the intermediate ylide is unable to cleave them, and thus it is protonated by the solvent methanol, DME, or DMF; chloroform was not used since it reacts with these sulfur anions[8] (Scheme II). Formation of $Ph_3P^+Me\ X^-$, therefore, supports the intermediate methylene ylide (step A) as does the disulfide for step B. When methanol was used instead of chloroform, even with $Me_2NC(S)S^-$ as anion, the intermediate ylide was partially protonated, so that **3a** and $Ph_3P^+Me\ X^-$ were formed in 40% and 60% yields, respectively.

Step D. In salt **3** the anion is X^- and not RS^- whether or not it is dissolved in the solvent at the end of the reaction. To account for the formation of **3**, in high yield (~90% for **3a**), starting from **1** and **2** in 1:1 molar ratio, the anion of the intermediate phosphonium salt must perform the same halogenophilic attack on **1** as it does in step A (vide infra).

In each one of the steps B and C of Scheme I there is generated a molecule which reacts in the next step, and in step D there are formed two such molecules which in turn enter the preceding steps, according to a sequence which by definition is a chain reaction. Step A is the initiation; steps B, C, and D are the propagation. Termination obviously occurs when the ylide and/or the sulfenyl halide are diverted by reaction with the solvent or with one another. It is a three-step chain reaction in which each one is a nucleophilic step. This chain reaction appears to be unprecedented, therefore it is suggested to name it *chain nucleophilic substitution.*

Further Evidence. (I) Since arenesulfinate ion is able to trap sulfenyl halides affording thiolsulfonates, it is used as a diagnostic tool for their formation.[24] However, when PhSNa was slowly added to a solution of **1c** and *p*-$MeC_6H_4SO_2Na$ in methanol, the main reaction product was the salt **4** (51.5% yield), identified by spectral data and an independent synthesis. Clearly, *S*-phenyl-*p*-toluenethiosulfonate was formed "in situ" and then cleaved by the methylene ylide (eq 7).

$$PhSCl + p\text{-}MeC_6H_4SO_2Na \rightarrow PhSSO_2C_6H_4Me\text{-}p \xrightarrow{Ph_3P=CH_2} \underset{\mathbf{4}}{Ph_3P^+CH_2SPh\ p\text{-}MeC_6H_4SO_2^-} \quad (7)$$

(II) Formation of a ylide which is able to cleave only certain disulfides and not others under the reaction conditions was also supported by a cross-over experiment. By reacting a thiophenolate anion with **1a** in the presence of a disulfide having a weak S–S bond (dimethylthiocarbamoyl disulfide), the salt obtained (55% yield) was **3a**, in accordance with Scheme I (RS = $Me_2NC(S)S$) (eq 8).

$$\underset{\mathbf{1a}}{2Ph_3P^+CH_2I\ I^-} + 2PhSNa + RSSR \rightarrow \underset{\mathbf{3a}}{2Ph_3P^+CH_2SR\ I^-} + PhSSPh + 2NaI \quad (8)$$

(III) The phosphonium salt $Ph_3P^+CH_2SC(S)NMe_2$ $Me_2NC(S)S^-$, which performs the last step D of the proposed mechanism, was never isolated as such, since it is involved in the reaction chain, nor can it be synthesized by obvious methods because the dithiocarbamyl anion attacks, e.g., $BrCH_2Cl$ by a halogenophilic mechanism.

However, in support of its supposed behavior, another phosphonium salt (benzyltriphenyl) was prepared with the same dimethyldithiocarbamyl anion (**5**) by anion exchange in benzene and was allowed to react with **1c**. The expected compounds were obtained with the yields indicated in eq 9 and 10. The result shows that a phosphonium dithiocarbamate indeed behaves like a sodium dithiocarbamate as far as halogenophilic attack is concerned.

$$Ph_3P^+CH_2Ph\ Cl^- + Me_2NC(S)SNa \xrightarrow{C_6H_6} \underset{\mathbf{5}}{Ph_3P^+CH_2Ph\ Me_2NC(S)S^-} + NaCl \quad (9)$$

$$\underset{\mathbf{1c}}{Ph_3P^+CH_2Cl\ Cl^-} + \mathbf{5} \rightarrow \underset{\mathbf{3c}\ (50\%)}{Ph_3P^+CH_2SC(S)NMe_2\ Cl^-} + \underset{(80\%)}{Ph_3P^+CH_2Ph\ Cl^-} \quad (10)$$

One could surmise that salt **3** may simply arise from the phosphonium salt and the dithiocarbamyl anion by anion exchange with sodium halide (eq 11) and that therefore step D would be the sum of such anion exchange with the initiation step A. However, this hypothesis would not alter the essence of the argument: it would always be a chain reaction with a further step in the chain sequence, since the sodium dithiocarbamate thus formed must necessarily enter another reaction cycle, on account of the high yield of **3** (~90%) starting from **1** and **2** in 1:1 molar ratio. But the above result shows that it is unnecessary to invoke such a further step because the phosphonium dithiocarbamate itself is able to attack the starting salt **1**. Furthermore an anion-exchange step is highly unlikely, since the anion exchange used for the preparation of **5** occurred in benzene in just the opposite direction.

$$Ph_3P^+CH_2SR\ RS^- + Na^+\ X^- \rightarrow \underset{\mathbf{3}}{Ph_3P^+CH_2SR\ X^-} + RS^-\ Na^+ \quad (11)$$

(IV) In principle, salt **3** could arise from direct interaction (step B′, eq 12) between the two intermediates formed in step A. The reaction is known, at least with phenylsulfenyl chloride.[25] However, if it occurred, it should also occur with EtS^-, $PhCH_2S^-$, and PhS^-, but this is not what happens. This fact means that the reaction of sulfenyl halide with sulfur anions (step B) is very fast and prevails over its reaction with the ylide. Moreover, starting from (chloromethyl)triphenylphosphonium iodide[26] (**6**), the reaction product was the phosphonium salt

step B′

$$Ph_3P{=}CH_2 + RSX \rightarrow Ph_3P^+CH_2SR\ X^- \quad (12)$$

(23) Benson, S. V. *Chem. Rev.* **1978**, *78*, 23.
(24) I am very grateful to Professor C. J. M. Stirling (Bangor) for this suggestion. Fishwick, B. R.; Rowles, D. K.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1171.
(25) Mukaiyama, T.; Fukuyama, S.; Kumamoto, T. *Tetrahedron Lett.* **1968**, 3787.
(26) Miyano, S.; Jzumi, Y.; Fuiü, K.; Ohno, Y.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1197.

with the iodide anion **3a** and not with the chloride anion **3c**, as would be required by the direct interaction B′ (eq 13). The salts **3a** and **3c** can be easily distinguished by

$$\underset{\mathbf{6}}{Ph_3P^+CH_2Cl\ I^-} + RSNa \rightarrow \underset{\mathbf{3a}}{Ph_3P^+CH_2SR\ I^-} + NaCl \quad (13)$$

$$RS^- = Me_2NC(S)S^-$$

the chemical shifts of their methylene hydrogens (see Experimental Section). The reaction was carried out in DMF, in which both starting and final salts are soluble, since the phosphonium chloride **3c** dissolved in chloroform undergoes anion exchange with solid NaI, and therefore **3a** might have been simply the result of a selective solubility in such solvent. After evaporation of the DMF in vacuo, the reaction product was identified by NMR analysis of the crude residue completely dissolved in DMSO. It was furthermore checked that **3a** did not result from an anion exchange between **3c** and NaI dissolved in DMF.

The above result also rules out another possible chain reaction, which would lead to a final salt with the Cl^- anion (**3c**), i.e., steps A and C of Scheme I followed by step D′ (eq 14).

step D′

$$Ph_3P^+CH_2SR\ RS^- + RSCl \rightarrow \underset{\mathbf{3c}}{Ph_3P^+CH_2SR\ Cl^-} + RSSR \quad (14)$$

(V) The radical nucleophilic substitution ($S_{RN}1$)[27,28] was ruled out because it does not explain all the above results. Furthermore, while a single electron transfer from a sulfur anion to salt **1** is conceivable, the next step which would involve separation of ions of opposite charge seems to be highly unlikely (eq 15). Also, the reaction was neither

$$Ph_3P^+CH_2X \xrightarrow[SET]{RS^-} (Ph_3PCH_2X)^\bullet \rightarrow Ph_3P^+CH_2^\bullet + X^- \text{ etc.} \quad (15)$$

catalyzed by light nor inhibited by oxygen or *p*-dinitrobenzene, as is the case for most reactions which follow such a mechanism.[29]

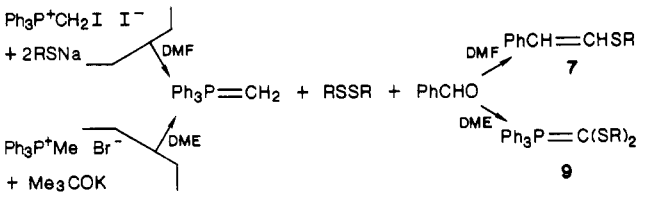
Reaction between 1a and 2 (1:2 Ratio) in the Presence of Aromatic Aldehydes. In attempting to capture the intermediate methylene ylide, the salts **1a** and **2** in 1:2 ratio were allowed to react in the presence of benzaldehyde. Styrene and dimethylthiocarbamoyl disulfide were the expected products. However, the reaction (DMF, 2.5 h, 80 °C) did not lead to styrene but instead to β-(*N*,*N*-dimethyldithiocarbamyl)styrene (**7a**) in low yield (~25%), together with several other products. The same result was observed with other aromatic aldehydes (reaction 16).

$$\underset{\mathbf{1a}}{Ph_3P^+CH_2I\ I^-} + \underset{\mathbf{2}}{2RSNa} + ArCHO \rightarrow \underset{\mathbf{7}}{ArCH{=}CHSR} + Ph_3PO + 2NaI + Ph_3PS + RSSR \text{ etc.} \quad (16)$$

$RS^- = Me_2NC(S)S^-$; Ar, **a** = Ph, **b** = 4-ClC_6H_4, **c** = 2,4-$Cl_2C_6H_3$, **d** = 3-Py

Evidently the salt **3a** is formed first, and the second mole of **2** acts as a base on it, affording the corresponding ylide, which eventually undergoes the Wittig reaction.[30] This

Scheme III



R = $R'_2NC(S)$; R′, **a** = Me; **b** = Et

sequence was separately verified (80% yield of **7a**). The amounts of detected products in reaction 16 make a poor material balance, most probably owing to partial extraction by the organic solvent from a mixture of water and DMF (see Experimental Section). However, the interesting feature of reaction 16 is that when faced with an aldehyde and a disulfide with a weak S–S bond in DMF, the methylene ylide first attacks the disulfide and then the resulting carbamylmethylene ylide undergoes the Wittig reaction.

Reaction of Phosphonium Ylides with Disulfides and Competition with the Wittig Reaction. Besides the methylene ylide, other more stabilized ylides also attack disulfides having a weak S–S bond, directly affording in benzene the corresponding substituted ylides **8** in high yield (~90%) (eq 17). To avoid consumption of 2 mol

$$Ph_3P{=}CHY + RS{-}SR \rightarrow (Ph_3P^+CHYSR\ RS^-) \rightarrow \underset{\mathbf{8}}{Ph_3P{=}CYSR} + RSH \text{ (dec)} \quad (17)$$

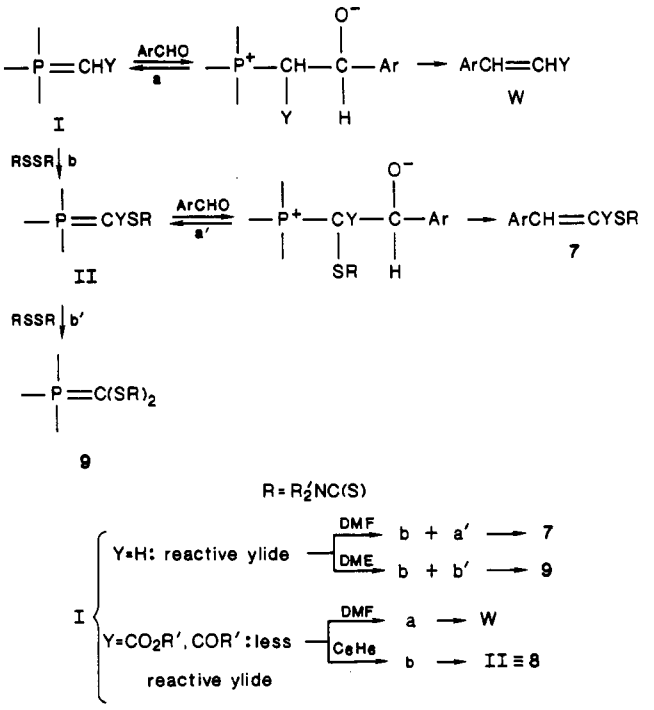
Y, **a** = COMe, **b** = CO_2Me; R = $R'_2NC(S)$, EtO_2C; R′ = Me, Et

of starting ylide, in early experiments a mole of Et_3N was also added, but it proved to be unnecessary, at least with the thiocarbamoyl disulfides. Evidently, the dithiocarbamyl anion itself is able to abstract the acidic hydrogen, like the carboxylate anion in the acylation of ester-stabilized ylides by anhydrides.[31] Dithiocarbamylation of phosphonium ylides cannot be accomplished by sulfenylation[25] since the necessary sulfenyl halides are unstable.[32,33] Reaction of similarly stabilized phosphonium ylides with dibenzoyl disulfide was observed previously; however, in this case transylidation consumed a second mole of starting ylide.[34] The ylides thus obtained, bearing two electron-withdrawing groups, are obviously more stabilized than the starting ones and poorly reactive.

These stabilized ylides, in the presence of both disulfide and benzaldehyde, led to ylides **8** in benzene and to Wittig products in DMF. Since styrene was never obtained from reaction 16, methylene ylide was separately prepared and allowed to react with the same mixture of disulfide and benzaldehyde. In DMSO[35] most of the reaction products were lost in the workup. However, in DME the bis(dithiocarbamyl)methylene ylide **9** was the main reaction product (~40%) (Scheme III). Clearly there is competition between benzaldehyde and thiocarbamoyl disulfide for the intermediate carbamylmethylene ylide, and the final product depends upon the solvent. Of course, the carbamylmethylene ylide can be formed from salt **3** by action of a base other than $R_2NC(S)S^-$, e.g., by NaH, and

(27) Kornblum, N. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 734.
(28) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.
(29) Bowman, W. R.; Rakshit, D.; Valmas, M. D. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2327.
(30) Galli, R. Presented at the 11th International Symposium on the Organic Chemistry of Sulfur, Lindau, FRG, September 1984; paper B1.25.P.
(31) Chopard, P. A.; Searle, R. J. G.; Devitt, F. H. *J. Org. Chem.* **1965**, *30*, 1015.
(32) Ritter, E. J. (Sharples Chem. Inc.). U.S. Pat. 2 466 276, *Chem. Abstr.* **1949**, *43*, 5038.
(33) Zumach, G.; Kühle, E. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 54.
(34) Kato, S.; Imamura, S.; Mizuta, M. *Int. J. Sulfur Chem., Part A* **1972**, *2*, 283.
(35) Drefahl, G.; Ponsold, K.; Schick, H. *Chem. Ber.* **1965**, *98*, 604.

Scheme IV



without isolation, it is able to attack dialkylthiocarbamoyl disulfides in nonpolar solvents. By this way the bis(dimethyl- and diethyldithiocarbamyl) methylene ylides **9** were prepared in 56% and 66% yields, respectively.

These results can be accounted for by considering that attack on the carbonyl group is reversible and rate determining for poorly reactive ylides,[36] while attack on the S–S bond should not be reversible. Furthermore, the intermediate betaine of the Wittig reaction is favored by the more polar solvent (DMF), while attack on the S–S bond and transylidation prevail in less polar solvents (DME, benzene). Therefore competition between attack on weak S–S bonds and on carbonyl groups depends upon the reactivity of the ylide and the polarity of the solvent[30] (Scheme IV).

Experimental Section

Melting points were determined on a Büchi apparatus and are uncorrected. Infrared spectra were recorded on liquid films or Nujol mulls on a Perkin-Elmer instrument Model 21. ^{1}H NMR spectra were recorded on a Bruker WP80 SY spectrometer in deuteriated solvents (chloroform, DMSO, acetone) and are reported in ppm (δ) downfield from internal standard tetramethylsilane. Gas–liquid chromatography was performed on a Dani 3600 instrument equipped with a column packed with 3% OV-17 on Chromosorb W AW-DMCS. Mass spectra were obtained on a Finnigan 4021 instrument equipped with an INCOS Data System (electron impact at 70 eV; emission current, 0.25 mA; ionization temperature, 250 °C) by direct inlet system or GC–MS analysis (fused silica column SE-52; 21 m X 0.25 mm i.d.; carrier gas; helium; splitter, 20:1; injector temperature, 280 °C; program, 100 °C (2 min), 10 °C/min to 270 °C; isotherm, 270 °C). Flash chromatography was performed on Merck Kieselgel 60 (230–400 mesh) and thin-layer chromatography on plates covered with Merck Kieselgel 60 F-254. All new compounds gave satisfactory elemental analyses, and their structural assignments are consistent with spectral data.

(Triphenylphosphonio)methyl Dimethyldithiocarbamate Halides 3a–c. A suspension of (iodomethyl)triphenylphosphonium iodide[37] (**1a**, 1.06 g, 2 mmol) and sodium dimethyldithiocarbamate dihydrate (**2**, 0.36 g, 2 mmol) in chloroform (90 mL) was heated at reflux for 6 h. After the mixture was cooled, the solid NaI was filtered off and the solvent removed with a rotary evaporator. The greenish semisolid residue (1.35 g) was washed with acetone (8 mL), affording a white powder, mp 167–168 °C (**3a**, 0.88 g, 84.6%): ^{1}H NMR (DMSO) δ 3.35 (6 H, s, CH_3), 5.80 (2 H, d, CH_2, J = 7.5 Hz), 7.50–8.10 (15 H, m, H Ar).

When methanol (80 mL) was used instead of chloroform, the reaction mixture was heated at reflux for 1.5 h, turning into a complete solution. Removal of the solvent left a solid residue, which was shown to be a mixture of **3a** (40%) and methyltriphenylphosphonium iodide (60%) by ^{1}H NMR analysis and comparison with authentic samples.

Two runs were carried out in parallel in chloroform solution, one under irradiation by a halogen lamp (500 W) external to the Pyrex reaction flask. Formation of **3a** was monitored by ^{1}H NMR analysis at 30-min intervals and showed no acceleration of the reaction by light.

Similar comparison between two runs in chloroform, one with addition of *p*-dinitrobenzene (10 mol % of **1a**) clearly indicated no inhibition effect by the nitro compound.

Starting from (bromomethyl)triphenylphosphonium bromide[38] (**1b**), after stirring for 10 h at room temperature and workup as for **3a**, **3b** was obtained as a white crystalline solid: mp 216–217 °C dec (85.4% yield); ^{1}H NMR (DMSO) δ 3.32 (6 H, s, CH_3), 5.82 (2 H, d, CH_2, J = 7.5 Hz), 7.50–8.20 (15 H, m, H Ar).

In the case of (chloromethyl)triphenylphosphonium chloride (**1c**) the reaction mixture was stirred for 8 h at room temperature. Workup as above left **3c**, a white crystalline solid: mp 218–219 °C dec (86.2% yield); ^{1}H NMR (DMSO) δ 3.30 (6 H, s, CH_3), 5.90 (2 H, d, CH_2, J = 7.5 Hz), 7.50–8.20 (15 H, m, H Ar).

Another run with **1c**, in which oxygen was bubbled into the stirred mixture during the reaction, afforded practically the same yield of **3c** as above.

(Triphenylphosphonio)methyl Diethyldithiocarbamate Iodide (3d). From (chloromethyl)triphenylphosphonium iodide[26] (**6**) and sodium diethyldithiocarbamate trihydrate in chloroform, following the same procedure as above, **3d** as obtained as a white crystalline solid, recrystallized from acetone: mp 178–179 °C (72.7% yield); ^{1}H NMR ($CDCl_3$) δ 1.15 (6 H, br, CH_3), 3.80 (4 H, br, CH_2), 6.10 (2 H, d, CH_2P, J = 7.5 Hz), 7.55–8.05 (15 H, m, H Ar).

Reaction between 6 and 2. (Chloromethyl)triphenylphosphonium iodide[26] (**6** 1.10 g, 2.5 mmol) and sodium dimethyldithiocarbamate dihydrate (**2**, 0.45 g, 2.5 mmol) were dissolved in DMF (50 mL). The light yellow solution, after stirring for 5.5 h at room temperature, became opalescent but turned clear upon addition of water (4 mL). Removal of the solvents by heating (80 °C) in vacuo (3 Torr) left a residue containing NaCl in which **3a** was the only organic compound, as shown by ^{1}H NMR analysis of the crude material dissolved in DMSO.

A sample of **3c**, dissolved in chloroform and stirred for 3 h with solid NaI was completely converted into **3a**. On the contrary **3a**, dissolved in DMF with NaCl and stirred for 6 h at room temperature, remained unchanged (^{1}H NMR analysis in DMSO).

***S*-(Triphenylphosphonio)methyl *N*,*N*-Pentamethylenethiocarbamate Iodide (3e).** A solution of piperidinium *N*,*N*-pentamethylenethiocarbamate[39] (1.15 g, 5 mmol) in chloroform (50 mL) was added to a suspension of **6** (2.20 g, 5 mmol) in chloroform (100 mL) under stirring at room temperature. Stirring was continued for an additional 1.5 h, leading to a clear solution. The solvent was removed under reduced pressure, and the semisolid residue (4.20 g) was taken up in chloroform (25 mL). The chloroform solution was washed with water (2 × 20 mL), dried (Na_2SO_4), and evaporated on the rotary evaporator. The crude residue, a white-pink solid (3.10 g), was repeatedly washed with a mixture of *n*-hexane and ethyl acetate (3:1) until a hygroscopic powder was left (**3e**, 2.01 g, 73.1% yield): ^{1}H NMR ($CDCl_3$) δ 1.50 (6 H, br, CH_2), 3.25 (4 H, br, CH_2N), 5.37 (2 H, d, CH_2P, J = 7.5 Hz), 7.40–8.20 (15 H, m, H Ar).

(36) Gosney, I.; Rowley, A. G. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G.; Ed.; Academic: London, 1979; Chapter 2.

(37) Seyferth, D.; Heeren, J.; Singh, G.; Grim, S. O.; Hughes, W. *J. Organomet. Chem.* **1966**, *5*, 267.

(38) Erickson, K. L.; Wolinsky, J. *J. Org. Chem.* **1965**, *30*, 2208.

(39) Parrod, J. *C. R. Hebd. Seances Acad. Sci.* **1952**, *234*, 1062.

S-(Triphenylphosphonio)methyl O-Ethyl Thiocarbonate Iodide (3f). A suspension of **6** (2.20 g, 5 mmol) and potassium *O*-ethyl thiocarbonate[40] (0.72 g, 5 mmol) in chloroform (200 mL) was mechanically stirred for 4 h at room temperature. The undissolved solid was filtered off (0.50 g) and the solution evaporated under reduced pressure. The semisolid crude residue (3.0 g), was washed with ethyl acetate (10 mL), affording a pink solid, mp 116–117 °C (2.15 g, 84.6% yield), identified as **3f** by ^{1}H NMR ($CDCl_3$): δ 1.10 (3 H, t, CH_3), 4.00 (2 H, q, CH_2CH_3), 5.50 (2 H, d, CH_2P, J = 7.5 Hz), 7.50–8.15 (15 H, m, H Ar).

S-(Triphenylphosphonio)methyl O-Ethyl Dithiocarbonate Iodide (3g). A suspension of **6** (1.10 g, 2.5 mmol) and potassium *O*-ethyl dithiocarbonate (*O*-ethyl xanthate, 0.40 g, 2.5 mmol) in chloroform (110 mL) was stirred for 10 h at room temperature. Filtration of the undissolved solid (0.45 g) and removal of the solvent with a rotary evaporator left a semisolid residue (1.70 g) which was dried by a mechanical pump (3 Torr). The white solid (1.30 g) was successively washed with *n*-hexane, ethyl ether, and benzene to afford a white powder (0.80 g, 61.5% yield) which, after recrystallization from isopropyl alcohol, had mp 203–205 °C. It was identified as **3g** by the following: ^{1}H NMR ($CDCl_3$) δ 1.13 (3 H, t, CH_3), 2.80 (2 H, q, CH_2CH_3), 5.06 (2 H, d, CH_2P, J = 7.5 Hz), 7.50–8.20 (15 H, m, H Ar); IR 1110 cm^{-1} (CS).

S-(Triphenylphosphonio)methyl Thioacetate Iodide (3h). From **6** (1.10 g, 2.5 mmol) and potassium thioacetate (0.285 g, 2.5 mmol) following the same procedure as in **3g**, a crude reddish semisolid residue was obtained (1.35 g). It was washed with acetone (30 mL) to give a white solid, mp 183–185 °C (0.60 g, 50.4% yield) identified as **3h** by the following: ^{1}H NMR ($CDCl_3$) δ 2.20 (3 H, s, CH_3), 5.50 (2 H, d, CH_2, J = 7.5 Hz), 7.50–8.10 (15 H, m, H Ar); IR 1720 cm^{-1} (CO).

(Triphenylphosphonio)methyl Thiocyanate Iodide (3i). From **6** and potassium thiocyanate (2.5 mmol each) by the same procedure as in **3g**, a crude yellowish residue (1.16 g) was obtained which, after washing with ethyl acetate (20 mL), afforded a white-pink powder (0.90 g, 78.2% yield). A sample recrystallized from ethanol had mp 192–193 °C: ^{1}H NMR ($CDCl_3$) δ 5.97 (2 H, d, CH_2, J = 6 Hz), 7.50–8.25 (15 H, m, H Ar); IR 2060 cm^{-1} (SCN).

S-(Triphenylphosphonio)methyl Thiobenzoate Iodide (31). A solution of sodium thiobenzoate, prepared from thiobenzoic acid (0.345 g, 2.5 mmol) and sodium hydride (80% dispersion in mineral oil, 72 mg, 2.5 mmol) in DME (15 mL), was added to a suspension of **1a** (1.33 g, 2.5 mmol) in chloroform (100 mL). The mixture was mechanically stirred for 4 h, monitoring the progress of the reaction by TLC (methanol/ethyl acetate, 1:2). Filtration of the undissolved solid (20 mg) and evaporation of the solvents in vacuo gave a yellow-orange residue (1.74 g). It was washed with acetone (4 × 2.5 mL) to afford a yellow powder: mp 193–194 °C (1.12 g, 82.9% yield); ^{1}H NMR ($CDCl_3$) δ 5.65 (2 H, d, CH_2, J = 7.5 Hz), 7.15–8.20 (15 H, m, H Ar).

Reaction of 1a with Sodium Thiophenoxide and Benzaldehyde. A solution of sodium thiophenoxide, prepared from thiophenol (1.10 g, 10 mmol) dissolved in methanol (20 mL) and sodium hydroxide (0.40 g, 10 mmol) in water (3 mL), was slowly dropped into a suspension of **1a** (2.65 g, 5 mmol) and benzaldehyde (1.06 g, 10 mmol) in methanol (90 mL) under stirring at room temperature. The suspended salt was completely dissolved at the end of the addition, and stirring was continued for 1 h. The solvents were removed under reduced pressure, and the oily yellowish residue was flash chromatographed. A mixture of benzaldehyde and diphenyl disulfide was first obtained (eluant *n*-hexane/ethyl acetate, 3:1), and then elution with methanol gave a hygroscopic solid, which was washed with *n*-hexane (1.62 g, 80% yield) and identified as methyltriphenylphosphonium iodide by comparison with an authentic sample and ^{1}H NMR ($CDCl_3$): δ 3.20 (3 H, d, CH_3, J = 14 Hz), 7.50–7.95 (15 H, m, H Ar).

Analogous runs carried out in DME and in DMF gave the same results. In the case of DMF as solvent, the workup was as follows: addition of water (300 mL), extraction with ethyl ether (3 × 100 mL), washing with water (3 × 80 mL) drying (Na_2SO_4), and removal of the solvent. Flash chromatography of the residue (*n*-hexane/ethyl acetate, 8:1) gave diphenyl disulfide (70% yield).

Similarly, in the absence of benzaldehyde, reaction of **1a** with *sodium thioethoxide* afforded the phosphonium salt in 95% yield (in MeOH) and ethyl disulfide in 64% yield (in DME) and with *sodium thiobenzyloxide* in DMF afforded the disulfide and the phosphonium salt in 98% and 97% yields, respectively.

Reaction of 1a with Sodium Thioethoxide and Benzaldehyde. A solution of sodium thioethoxide, prepared from ethanthiol (0.31 g, 5 mmol) and sodium hydride (80% dispersion in mineral oil, 0.144 g, 5 mmol) in anhydrous DMF (15 mL), was dropped into a solution of **1a** (1.33 g, 2.5 mmol) and benzaldehyde (0.53 g, 5 mmol) in anhydrous DMF (30 mL) under stirring and nitrogen atmosphere at room temperature. The solution soon turned light yellow and the color became more intense with time. Stirring was continued for 2.5 h. A TLC control (*n*-hexane/ethyl acetate, 5:1) revealed the presence of styrene, benzaldehyde, and methyltriphenylphosphonium iodide. Water (400 mL) was added to the solution and the mixture extracted with ethyl ether (3 × 200 mL). The ethereal extracts were washed with water (3 × 150 mL), dried over Na_2SO_4, and evaporated under reduced pressure to give a yellow liquid (0.80 g). It still contained styrene and benzaldehyde (TLC control), but an attempt to isolate the styrene by flash chromatography (*n*-hexane/ethyl acetate, 5:1) afforded only benzaldehyde, perhaps owing to polymerization of styrene in the column. However, GC analysis (3% OV17 column; program, 100 °C (2 min), 20 °C/min to 230 °C; isotherm, at 230 °C) confirmed the presence of styrene by comparison with an authentic sample.

It was checked that sodium thioethoxide and methyltriphenylphosphonium iodide (molar ratio, 2:1) in the presence of benzaldehyde do not lead to styrene under the above reaction conditions.

Reaction of 1-(Triphenylphosphonio)-1-bromopropan-2-one Bromide with Sodium Thiophenoxide. A solution of bromine (0.80 g, 5 mmol) in chloroform (25 mL) was slowly added to a solution of (acetylmethylene)triphenylphosphorane (1.59 g, 5 mmol) in chloroform (30 mL) under stirring at 0–5 °C. The clear yellow solution was stirred for an additional hour at room temperature. Addition of ethyl ether (140 mL) to the chilled solution (ice–water bath) separated a white solid, which was filtered and repeatedly washed with benzene (2.10 g, 88% yield): mp 125–128 °C (lit.[41] mp 127–130 °C); ^{1}H NMR ($CDCl_3$) δ 2.82 (3 H, d, CH_3, J = 2 Hz), 7.50–8.20 (15 H, m, H Ar), 9.70 (1 H, d, CH, J = 14 Hz).

A solution of sodium thiophenoxide, prepared from thiophenol (0.55 g, 5 mmol) and sodium hydride (80% dispersion in mineral oil 0.15 g, 5 mmol) in methanol (20 mL), was dropped into a solution of the salt above prepared (1.20 g, 2.5 mmol) in methanol (30 mL) under stirring at room temperature. Stirring was continued for 4.5 h, then the solvent was removed in vacuo, and the residue was flash chromatographed (eluant, ethyl acetate). Diphenyl disulfide was eluted first (0.34 g, 62.4% yield), then a mixture of diphenyl disulfide with an unidentified product (0.32 g), and finally (acetylmethylene)triphenylphosphorane (0.79 g, 98.5% yield), identified by comparison with an authentic sample.

Reaction of 1c with Sodium Thiophenoxide and Sodium p-Toluenesulfinate. A solution of sodium thiophenoxide (0.67 g, 5 mmol) in methanol (20 mL) and water (2 mL) was slowly dropped into a solution of **1c** (1.74 g, 5 mmol) and sodium *p*-toluenesulfinate (1.78 g, 10 mmol) in methanol (90 mL) under stirring at room temperature. The solution turned light brown, and stirring was continued for 8 h. Most of the methanol was removed by rotary evaporator, the temperature of the bath not exceeding 40 °C, water (200 mL) was added, and the solution was extracted with dichloromethane (3 × 60 mL). The organic phase was dried (Na_2SO_4) and evaporated to leave a crude semisolid material (2.30 g), which was thoroughly washed with ethyl acetate and a little acetone to afford a white powder (1.40 g, 51.5% yield), mp 135–138 °C dec. It was identified as salt **4** by the following: IR 680, 740, 815, 955, 1040, 1110, 1175, 1230, 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.30 (3 H, s, CH_3), 5.53 (2 H, d, CH_2, J = 9 Hz), 7.00–8.05 (24 H, m, H Ar).

(40) Holmberg, B. *J. Prakt. Chem.* **1906**, *73*, 242.

(41) Shevchuk, M. I.; Volynskaya, E. M.; Dombrovskii, A. V. *Zh. Obshch. Khim.* **1970**, *40*, 48; *Chem. Abstr.* **1970**, *72*, 100817b.

Salt 4 was separately synthesized for comparison. A suspension of triphenyl[(phenylthio)methyl]phosphonium chloride (2.0 g, 4.7 mmol) and sodium *p*-toluenesulfinate (2.50 g, 14.1 mmol) in benzene (50 mL) was magnetically stirred at room temperature for 29 h. The solid was filtered and extracted with dichloromethane (3 × 50 mL), the organic phase was rotary evaporated (bath temperature, 40 °C), and the oily residue (2.40 g) was thoroughly washed as above. The white solid obtained (1.80 g, 70% yield) had mp, mixed mp, IR, and ^{1}H NMR spectra identical with those of the salt obtained in the above reaction.

Reaction of 1a with Sodium Thiophenoxide and Dimethylthiocarbamoyl Disulfide. A solution of sodium thiophenoxide, prepared from thiophenol (0.44 g, 4 mmol) and sodium hydride (80% dispersion in mineral oil, 0.12 g, 4 mmol) in anhydrous benzene (20 mL) and DME (10 mL), was slowly dropped into a suspension of **1a** (2.12 g, 4 mmol) and dimethylthiocarbamoyl disulfide (0.48 g, 2 mmol) in anhydrous benzene (100 mL) under stirring and nitrogen atmosphere at room temperature. The mixture was heated at reflux for 2.5 h, and the suspended solids mostly dissolved. After cooling, the solid was filtered (1.70 g) and washed with water (10 mL). A white powder was left, identified as **3a** by comparison (mixed mp and ^{1}H NMR) with an authentic sample (1.15 g, 55% yield). The organic layer, washed with water (2 × 25 mL) dried over Na_2SO_4, and evaporated, gave a thick yellow oily residue (1.10 g), which contained (TLC comparison with authentic samples) diphenyl disulfide, dimethylthiocarbamoyl disulfide, and some other unidentified impurities.

Benzyltriphenylphosphonium Dimethyldithiocarbamate (5). Sodium dimethyldithiocarbamate dihydrate (**2**, 2.70 g, 15 mmol) was added to a solution of benzyltriphenylphosphonium chloride (1.94 g, 5 mmol) in benzene (50 mL). The mixture was mechanically stirred for 3 h at room temperature. The suspended solid soon began to change into a new one, whose amount increased with time. It was filtered (3.54 g), washed with water (10 mL), and dried in a desiccator. A yellow solid was left (1.89 g, 80% yield): mp 99–101 °C; ^{1}H NMR (CD_3COCD_3) δ 3.50 (6 H, s, CH_3), 5.48 (2 H, d, CH_2, J = 15 Hz), 7.70–8.05 (20 H, m, H Ar).

Reaction of 5 with 1c. **5** (0.46 g, 0.97 mmol) and **1c** (0.34 g, 0.97 mmol) were suspended in DME (55 mL), and the mixture was stirred for 2.5 h at room temperature. The solid was filtered and directly analyzed by ^{1}H NMR to be a mixture of benzyltriphenylphosphonium chloride (0.30 g, 80% yield) and **3c** (0.20 g, 50% yield).

β-(Dimethyldithiocarbamyl)styrenes 7a–d. (a) With Benzaldehyde (7a). A solution of **2** (3.58 g, 20 mmol) in DMF (30 mL) was dropped into a solution of **1a** (5.30 g, 10 mmol) and benzaldehyde (1.06 g, 10 mmol) in DMF (30 mL) under stirring at room temperature. The solution turned light yellow-green, and the temperature increased from 22 to 26 °C. Then it was heated at 85 °C for 2 h, and its color became reddish. After the mixture cooled, water (500 mL) was added and the solution extracted with ethyl ether (3 × 100 mL). A little suspended solid was identified as dimethylthiocarbamoyl disulfide (mixed mp compared with that of an authentic sample). The ethereal extracts were washed with water (3 × 50 mL), dried over Na_2SO_4, and evaporated. The residue (2.70 g), analyzed by GC–MS without an internal standard, was a mixture of benzaldehyde (14%), methyl dimethyldithiocarbamate (12%), β-(dimethyldithiocarbamoyl)styrene (**7a**, 22%; E/Z ratio, 2:1), triphenylphosphine oxide (39%), and triphenylphosphine sulfide (13%). With the limitations that there was no comparison with an internal standard and that dimethylthiocarbamoyl disulfide was not revealed under the GC conditions used, the above data indicate a 26.5% yield of **7a** (E/Z mixture). Flash chromatography of the crude residue (*n*-hexane/ethyl acetate, 10:1) afforded a pure sample of **7a** (E/Z mixture):[22] ^{1}H NMR ($CDCl_3$) δ 3.45 (6 H, br, CH_3), 6.75 (d, E isomer, J = 16 Hz) and 6.80 (d, Z isomer, J = 12 Hz) [integrated for 1 H], 7.15–7.60 (6 H, m, H Ar and vinylic); MS, m/z (relative intensity) 233 (M^+, 68), 88(100).

(b) With 4-Chlorobenzaldehyde (7b). The same procedure was used as in a, starting from the same moles of reagents dissolved in 75 mL of DMF, with some variation in the workup. Extraction of the crude residue with *n*-hexane (4 × 50 mL) separated some Ph_3PO. Evaporation of the hexane solution left a crude material (2.20 g), which, by GC–MS analysis carried out as in a, was a mixture of 4-chlorobenzaldehyde (40%), **7b** (40%; E/Z ratio, 3:1), triphenylphosphine oxide (11%), and triphenylphosphine sulfide (9%). Within the limitations mentioned above, the yield of **7b** was 34%. **7b**: MS, m/z (relative intensity) 259 (M^+, 3), 257 (M^+, 7), 134 (5), 101 (2), 88 (100).

(c) With 2,4-Dichlorobenzaldehyde (7c). The same procedure was used as in a, starting from the same moles of reagents dissolved in 80 mL of DMF. A transitory intense yellow color was noted during the addition of **2**. The crude residue was 4.30 g. It contained (by GC–MS analysis) **7c** (26%; E/Z ratio, 1.5:1), triphenylphosphine oxide (70%), and triphenylphosphine sulfide (4%), corresponding, with the limitations as above, to 39% yield of **7c**: MS, m/z (relative intensity) 293 (M^+, 7), 291 (M^+, 8), 168 (4), 88 (100).

(d) With 3-Pyridinecarboxaldehyde (7d). The same procedure and workup were used as in b, starting from the same moles of reagents. Triphenylphosphine oxide (0.70 g) was separated by extraction with *n*-hexane. The liquid crude residue (1.02 g), by GC–MS analysis, turned out to be a mixture of **7d** (63%; E/Z ratio, 2:1), triphenylphosphine oxide (29%), and triphenylphosphine sulfide (8%), indicating, with the same limitations as above, a 28% yield of **7d**: MS, m/z (relative intensity) 224 (M^+, 7), 136 (M − 88, 6), 88 (100).

Reaction of 3a with 2 and Benzaldehyde. Benzaldehyde (0.26 g, 2.5 mmol) and **2** (0.45 g, 2.5 mmol) were added to a solution of **3a** (1.31 g, 2.5 mmol) in chloroform (60 mL). The mixture was stirred at room temperature for 2 h and then heated at reflux for 3 h. A TLC control on silica gel and alumina plates (*n*-hexane/ethyl acetate, 3:1) showed that some **7a** was formed, but **3a** was still present. Then additional **2** (2.5 mmol) was added and the mixture heated at reflux again for 7 h. After cooling, the suspended solid was filtered off (0.65 g) and the solvent removed under reduced pressure. The semiliquid yellowish residue (2.0 g) was flash chromatographed (*n*-hexane/ethyl acetate, 3:1): a first fraction (0.90 g) was a mixture of **3a** and triphenylphosphine oxide; a second weighed 0.50 g, 90% of which was shown to be **7a** by GC–MS analysis, corresponding to 80.7% yield of **7a**. The third (0.10 g) and fourth (0.30 g) fractions contained unidenified products. Both the second fraction and the crude residue afforded directly pure **7a** by flash chromatography (*n*-hexane/ethyl acetate, 10:1).

Reaction of Phosphonium Ylides with Disulfides (8). Phosphonium ylide (10 mmol) and disulfide (10 mmol) partially dissolved in benzene (60 mL) were heated at reflux for 2–3 h: the initial mixture turned into a clear solution on heating. After the mixture cooled, addition of *n*-hexane (300 mL) separated the crude product in the case of the thiocarbamoyl disulfides. With ethoxycarbonyl disulfide,[42] the solvent was removed in vacuo; water (100 mL) was added to the residue and the mixture extracted with chloroform (3 × 50 mL). The organic layer was washed with water (2 × 100 mL), dried (Na_2SO_4), and evaporated to afford the crude material. The yields given are those before recrystallization (from ethanol, except as indicated).

8a (R′ = Me): 64.5% yield; mp 225–226 °C; IR 1540 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 2.21 (3 H, s, CH_3), 2.90–3.60 (6 H, br, CH_3N), 7.20–7.95 (15 H, m, H Ar); MS, m/z (relative intensity) 437 (M^+, 2), 365 (22), 350 (20), 349 (M − 88, 100), 262 (49), 183 (38), 108 (17), 88 (13).

8a (R′ = Et): 92% yield; mp 203–203.5 °C; IR 1550 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 0.80–1.35 (6 H, m, CH_2CH_3), 2.25 (3 H, s, CH_3), 3.15–4.40 (4 H, br, CH_2CH_3), 7.20–8.00 (15 H, m, H Ar); MS, m/z (relative intensity) 165 (M^+, 2), 365 (18), 350 (21), 349 (M − 116, 100), 262 (26), 183 (21), 108 (9).

8a (R = CO_2Et): 76.5% yield; mp 182–184 °C; IR 1700, 1690 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.12 (3 H, t, CH_2CH_3), 2.25 (3 H, s, CH_3), 4.10 (2 H, q, CH_2CH_3), 7.20–7.90 (15 H, m, H Ar); MS, m/z (relative intensity) 422 (M^+, 12), 349 (M − 73, 100), 262 (34), 183 (33), 108 (14).

8b (R′ = Me): 92.5% yield; mp 231–232 °C; IR 1660 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 3.25 and 3.62 (altogether 9 H, br, CH_3), 7.20–8.00 (15 H, m, H Ar); MS, m/z (relative intensity) 453 (M^+, 8), 365 (M − 88, 100), 262 (40), 183 (61), 108 (27), 88 (36).

8b (R′ = Et): 93% yield; recrystallized from ethyl acetate; mp 187–188 °C; IR 1610 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.10 (6 H,

(42) Murphy, C. N.; Winter, G. *Aust. J. Chem.* **1973**, *26*, 755.

br, CH_2CH_3), 3.00–4.10 (7 H, br, CO_2CH_3 and CH_2), 7.10–8.00 (15 H, m, H Ar); MS, m/z (relative intensity) 481 (M^+, 10), 365 (M − 116, 100), 262 (24), 183 (33), 116 (12), 108 (32), 88 (26), 60 (37).

8b (R = CO_2Et): 91.5% yield; mp 124–125 °C; IR 1710, 1660 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.13 (3 H, t, CH_2CH_3), 3.50 (3 H, s, CH_3), 4.06 (2 H, q, CH_2), 7.15–7.95 (15 H, m, H Ar); MS, m/z (relative intensity) 438 (M^+, 14), 365 (M − 73, 100), 262 (31), 183 (35), 108 (15).

[Bis(dimethyldithiocarbamyl)methylene]triphenylphosphorane (9a). (A) Potassium *tert*-butoxide (1.12 g, 10 mmol) was added to a suspension of methyltriphenylphosphonium bromide (3.57 g, 10 mmol) in DME (45 mL) under magnetic stirring and nitrogen atmosphere at room temperature. The solution soon turned light yellow, and the color became more intense with time. Stirring was continued for 3 h. Then a solution of dimethylthiocarbamoyl disulfide (1.20 g, 5 mmol) and benzaldehyde (2.12 g, 2 mmol) in DME (15 mL) was added, and the solution was heated at reflux for 3.5 h. The solvent was removed in vacuo, and the residue was washed with acetone (10 mL) and water (5 mL), affording a light yellow solid (1.0 g, 38.5% yield). A sample recrystallized from benzene had mp 233–235 °C: IR 1490, 1370, 1245, 980, 755, 710, 695, 685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.25 (12 H, br, CH_3), 7.30–8.10 (15 H, m, H Ar); MS m/z, (relative intensity) 514 (M^+, 0.2), 426 (M − 88, 2), 294 (4), 293 (3), 262 (6), 183 (18), 108 (10), 88 (100).

(B) Sodium hydride (80% dispersion in mineral oil 0.15 g, 5 mmol) was added to a suspension of **3a** (1.31 g, 2.5 mmol) and dimethylthiocarbamoyl disulfide (0.60 g, 2.5 mmol) in anhydrous DME (45 mL) under stirring and nitrogen atmosphere at room temperature. Stirring was continued for 1 h; then the mixture was heated at reflux for 1.5 h, turning into an almost complete solution, which was concentrated to 20 mL and cooled. The separated solid was filtered and washed with water (5 mL). Yellow crystals were left, mp 235–236 °C, identified as **9a** by comparison with a sample from A (0.72 g, 56.2% yield; part of **9a** remained in DME solution).

9b was similarly obtained from **3d** and diethylthiocarbamoyl disulfide. **9b**: yellow crystals; mp 139–141 °C; 66.5% yield; ^1H NMR ($CDCl_3$) δ 1.05 (12 H, br, CH_3), 3.75 (8 H, br, CH_2), 7.25–8.15 (15 H, m, H Ar).

Acknowledgment. I am very grateful to Dr. Alberto Griffini for GC–MS spectroscopic analysis and to Leonardo Scaglioni for recording ^1H NMR spectra. This work was made possible by support of the Italian National Research Council, Rome (CNR, Progetto Finalizzato Chimica Fine e Secondaria).

Registry No. **1a**, 3020-28-8; **1b**, 1034-49-7; **1c**, 5293-84-5; **2**, 72140-17-1; **3a**, 110637-62-2; **3b**, 110637-63-3; **3c**, 110637-64-4; **3d**, 110637-65-5; **3e**, 110637-66-6; **3f**, 110637-67-7; **3g**, 110637-68-8; **3h**, 110637-69-9; **3i**, 110637-70-2; **3l**, 110637-71-3; **4**, 110637-72-4; **5**, 110637-73-5; **6**, 68089-86-1; (*E*)-**7a**, 23846-99-3; (*Z*)-**7a**, 110637-74-6; (*E*)-**7b**, 110637-75-7; (*Z*)-**7b**, 110637-76-8; (*E*)-**7c**, 110637-77-9; (*Z*)-**7c**, 110637-78-0; (*E*)-**7d**, 110637-79-1; (*Z*)-**7d**, 110637-80-4; **8a** (R′ = Me), 110637-83-7; **8a** (R′ = Et), 110637-84-8; **8a** (R = CO_2Et), 110637-85-9; **8b** (R′ = Me), 110637-86-0; **8b** (R′ = Et), 110637-87-1; **8b** (R = CO_2Et), 110637-88-2; **9a**, 110637-81-5; **9b**, 110637-82-6; $Ph_3P{=}CHCOMe$, 1439-36-7; $Ph_3P{=}CHCO_2Me$, 2605-67-6; EtO_2CSSCO_2Et, 6365-90-8; MeSSMe, 624-92-0; EtSSEt, 110-81-6; sodium diethyldithiocarbamate, 148-18-5; piperidinium *N*,*N*-pentamethylenethiocarbamate, 98-77-1; potassium *O*-ethyl thiocarbonate, 35832-93-0; potassium *O*-ethyl xanthate, 140-89-6; potassium thioacetate, 10387-40-3; potassium thiocyanate, 333-20-0; sodium thiobenzoate, 51066-54-7; thiobenzoic acid, 98-91-9; sodium thiophenoxide, 930-69-8; benzaldehyde, 100-52-7; methyltriphenylphosphonium iodide, 2065-66-9; diphenyl disulfide, 882-33-7; sodium thioethoxide, 811-51-8; ethyl disulfide, 110-81-6; dibenzyl disulfide, 150-60-7; styrene, 100-42-5; thiophenol, 108-98-5; triphenyl[(phenylthio)methyl]phosphonium chloride, 13884-92-9; dimethylthiocarbamoyl disulfide, 137-26-8; triphenylphosphine, 603-35-0; 4-chlorobenzaldehyde, 104-88-1; 2,4-dichlorobenzaldehyde, 874-42-0; 3-pyridinecarboxaldehyde, 500-22-1; methyltriphenylphosphonium bromide, 1779-49-3; diethylthiocarbamoyl disulfide, 97-77-8; triphenylphosphine oxide, 791-28-6; methyl dimethyldithiocarbamate, 3735-92-0.

Mechanistic Studies on the Basic Hydrolysis of 2,2,2-Trichloro-1-arylethanones

César Zucco,* Claudio F. Lima, Marcos C. Rezende, Jose F. Vianna, and Faruk Nome*

Departamento de Química, Universidade Federal de Santa Catarina, 88.001 Florianopolis, SC, Brazil

Received May 4, 1987

The basic hydrolysis of 2,2,2-trichloro-1-phenylethanone (**1a**), 2,2,2-trichloro-1-(*p*-methoxyphenyl)ethanone (**1b**), and 2,2,2-trichloro-1-(*p*-chlorophenyl)ethanone (**1c**) has been studied in the pH range 5.5–13.2. In all cases the reaction products were chloroform and the corresponding benzoate. The reaction is first order toward both the ethanone and hydroxide ion and proceeds via an addition–elimination-type mechanism. The initial addition step forms the corresponding ethanone hydrates, which, depending on the pH, will form the mono- and dianionic intermediates, the elimination of CCl_3 from the mono- and/or dianionic species being the rate-limiting step of the reaction.

Introduction

Organic reactions in which the trichloromethyl is a leaving group have long been known, the haloform reaction being a classical example found in any textbook of organic chemistry.[1] In spite of this, systematic studies on the leaving group ability of the CCl_3 group, as compared to other more common groups, are scarce.

We have been interested for some years in exploiting the trichloromethyl as a leaving group in synthetic transformations and in investigating in detail the mechanisms involved in these reactions.[2-5] As an example, 1,1-diaryl-2,2,2-trichloroethanols undergo a base-catalyzed oxidative cleavage to yield chloroform and the corresponding benzophenone derivatives. This elimination proceeds via

(1) March, J. *Advanced Organic Chemistry*, 2nd ed.; McGraw-Hill: New York, 1977; p 575.

(2) Nome, F.; Erbs, W.; Correia, V. R. *J. Org. Chem.* **1982**, *46*, 3802.

(3) Nome, F.; Schwingel, E. W.; Ionescu, L. G. *J. Org. Chem.* **1980**, *45*, 705.

(4) Lins, H. S.; Nome, F.; Rezende, M. C.; de Souza, I. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1521.

(5) Uieara, M.; Zucco, C.; Zanette, D.; Rezende, M. C.; Nome, F. *J. Chem. Soc., Perkin Trans. 2* **1987**, 463.

0022-3263/87/1952-5356$01.50/0