Thiophilic Additions of Organometallics to Thiobenzophenones and of Phenyllithium to Phenyl Dithiobenzoate and Phenyl Trithiocarbonate

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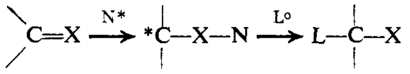
Received May 11, 1971

Abstract: The reaction of thiobenzophenone (**1**) with phenyllithium gives benzhydryl phenyl sulfide (**4**), the product of thiophilic addition. Analogous reactions occur between **1** and other organometallics and between phenyllithium and other diaryl thioketones. The formation of tetraarylethylene sulfides from diaryl thioketones and organometallics is proposed to proceed by initial thiophilic addition and this suggestion is supported by the observed increase in the episulfide:sulfide ratio as the concentration of 4,4′-dimethoxythiobenzophenone is increased in reaction with phenyllithium. Phenyl dithiobenzoate (**15**) gives bis(phenylthio)methane (**16**) and 1,2-bis(phenylthio)-1,2-diphenylethylene (**17**) on treatment with phenyllithium. Phenyl trithiocarbonate (**20**) reacts with phenyllithium to yield tris(phenylthio)methane (**21**) at −78°, but the same reactants produce **16** and tris(phenylthio)phenylethylene (**22**) at room temperature. The latter reaction is shown to be consistent with thiophilic addition followed by formation of bis(phenylthio)carbene. Possible mechanisms for thiophilic addition are noted.

Thiophilic addition, a recognized member of the novel heterophilic reactions[1] (eq 1), has been reported



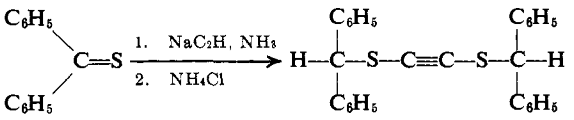
$$>C{=}X \xrightarrow{N^*} {}^*\overset{|}{\underset{|}{C}}{-}X{-}N \xrightarrow{L^\circ} L{-}\overset{|}{\underset{|}{C}}{-}X \qquad (1)$$

*, one, °, one electron or *, two, °, zero electrons

for the reactions of thiocarbonyl groups with phosphorous and sulfur nucleophiles,[2–5] carbon radicals,[6,7] cyanide,[8] and organometallics.[9,10]

In this paper, our preliminary note reporting the thiophilic reaction of thiobenzophenone and phenyllithium[10] is supplemented; and evidence is presented establishing that two apparenty anomalous reactions, the formation of episulfides from diaryl thioketones and organometallics[11] and the formation of bis(phenylthio)phenylmethane from diphenyl trithiocarbonate and phenyllithium at 25°, do involve initial bonding of carbon of the organometallic to the sulfur of the thiocarbonyl.

Thiophilic addition to a thiocarbonyl group by a formal carbon nucleophile has been observed by Proskow, who reported the addition of hydrogen cyanide to fluorotrithiocarbonates,[8] and by Schönberg, *et al.*, who reported that the reaction of thiobenzophenone (**1**) with excess sodium acetylide gives 1,2-bis(benzhydrylthio)acetylene (**2**).[9] The German authors noted the



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contrasting reactivity of carbonyl and thiocarbonyl groups toward electron-donating species.[9] Reaction of thioketones with diazoalkanes results in carbon–sulfur bond formation[12] and might be an example of thiophilic addition, although it is conceivable that reaction involves initial addition to carbon or an electrophilic attack on sulfur. The formation of products with new sulfur–carbon bonds by reaction of organolithiums with thiapyrilium salts[13] and sulfines[14] can be classified as thiophilic, and the production of thiocarbonyl groups by elimination from sulfides bearing an α-hydrogen and a leaving group on sulfur can be considered the reverse of thiophilic addition.[15] The process of thiaphilic addition, electron sharing by radicals or nucleophiles with sulfur which is singly bonded to carbon, is well documented.[16]

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[1] We suggest that bonding by an electron sharing species to the heteroatom of a carbon–heteroatom multiple bond constitutes heterophilic addition. Distinction between heterophilic and heteraphilic addition, the latter being addition to a heteroatom singly bonded to carbon, seems useful, as different reaction paths and stabilizations are available for the different processes. Until more information about heterophilic addition is available, the definition can be considered indicative of the structural transformations shown in eq 1.

[2] W. J. Middleton and W. H. Sharkey, *J. Org. Chem.*, **30**, 1384 (1965).

[3] G. H. Birum, U. S. Patents 3,116,335 (1963), *Chem. Abstr.*, **60**, 10549*d* (1964); 2,931,755 (1960), *ibid.*, **54**, 15245*b* (1960); and 3,172,803 (1965), *ibid.*, 62, 14727*c* (1965); N. H. Nilsson, C. Jacobsen, and A. Senning, *Chem. Commun.*, 658 (1970).

[4] E. J. Corey and G. Markl, *Tetrahedron Lett.*, 3201 (1967); D. Horton and C. G. Tindall, *J. Org. Chem.*, **35**, 3558 (1970).

[5] Analogous oxophilic additions have been reported for carbonyl groups with phosphorous nucleophiles: *e.g.*, F. Ramirez, *Accounts Chem. Res.*, **1**, 168 (1968); B. Miller, *J. Amer. Chem. Soc.*, **88**, 1842 (1966); Y. Ogato and M. Yamashita, *ibid.*, **92**, 4670 (1970); I. J. Borowitz, P. E. Rusek, and R. Virkhaus, *J. Org. Chem.*, **34**, 1595 (1969); J. S. Meek and L. Koh, *ibid.*, **35**, 153 (1970); D. M. Roundhill and G. Wilkinson, *ibid.*, **35**, 3561 (1970).

[6] K. Uneyama, T. Sadakaye, and S. Oae, *Tetrahedron Lett.*, 5193 (1969).

[7] A. Ohno, Y. Ohnishi, M. Fukyama, and G. Tsuchihashi, *J. Amer. Chem. Soc.*, **90**, 7038 (1968); G. Tsuchihashi, M. Tamauchi, and A. Ohno, *Bull. Chem. Soc. Jap.*, **43**, 969 (1970).

[8] S. Proskow, U. S. Patent, 3,117,985 (1964), *Chem. Abstr.*, **60**, 10549f (1964).

[9] A. Schönberg, E. Singer, E. Frese, and K. Praefcke, *Ber. Deut. Chem. Ges. B*, **98**, 3311 (1965).

[10] P. Beak and J. W. Worley, *J. Amer. Chem. Soc.*, **92**, 4142 (1970).

[11] A. Schönberg, A. Rosenbach, and O. Schutz, *Justus Liebigs Ann. Chem.*, **454**, 37 (1927).

[12] A. Schönberg, D. Cernik, and W. Urban, *Ber. Deut. Chem. Ges. B.*, **64**, 2577 (1930); A. Schönberg, B. Koenig, and E. Singer, *ibid.*, **100**, 767 (1967); W. J. Middleton, *J. Org. Chem.*, **34**, 3201 (1969); C. E. Diebert, *ibid.*, **35**, 1501 (1970).

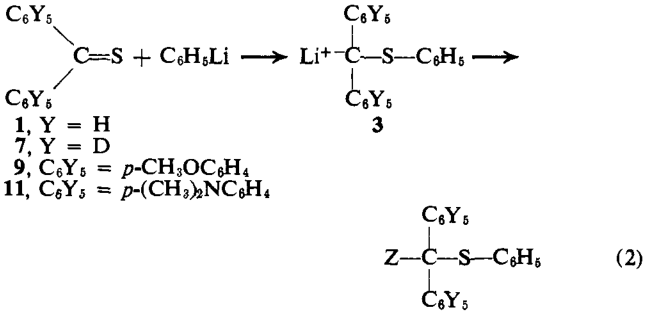
[13] M. Polk, M. Siskin, and C. C. Price, *J. Amer. Chem. Soc.*, **91**, 1206 (1969).

[14] A. G. Schultz and R. H. Schlessinger, *Chem. Commun.*, 747 (1970).

[15] N. A. Rosenthal and G. Oster, *J. Amer. Chem. Soc.*, **83**, 4445 (1961); J. P. Danehy, "The Chemistry of Organic Sulfur Compounds," Vol. 2, N. Kharasch and C. Y. Meyers, Ed., Pergamon Press, Oxford, England, 1966, pp 341–344; A. Ceccon, U. Miotti, U. Tonellato, and M. Padoun, *J. Chem. Soc. B*, 1084 (1969), and references cited therein.

Results and Discussion

Diaryl Thioketones. The addition of thiobenzophenone (**1**) to 2.2 equiv of phenyllithium in ether at room temperature followed by quenching with methanol and water gives a 70% yield of benzhydryl phenyl sulfide (**4**) (eq 2).[17] The product **4** was identified by



1, Y = H
7, Y = D
9, C_6Y_5 = p-$CH_3OC_6H_4$
11, C_6Y_5 = p-$(CH_3)_2NC_6H_4$
3

(2)

4, Y = Z = H
5, Y = H; Z = D
6, Y = H; Z = $Si(CH_3)_3$
8, Y = D; Z = H
10, C_6Y_5 = p-$CH_3OC_6H_4$; Z = H
11, C_6Y_5 = p-$(CH_3)_2NC_6H_4$; Z = H

spectral and physical comparisons with an authentic sample.

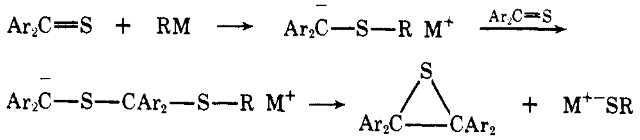
Intermediacy of the anion **3** (Y = H) is established by the formation of benzhydryl phenyl sulfide-d (**5**) on quenching with methanol-O-d and by formation of the silylated adduct **6** on quenching with chlorotrimethylsilane. That the course of reaction involves initial addition to the sulfur of the thiocarbonyl group, rather than initial addition to carbon followed by rearrangement, is revealed by the reaction of thiobenzophenone-d_{10} (**7**) with phenyllithium to give benzhydryl phenyl sulfide-d_{10} (**8**), which has at least 98% of the unlabeled phenyl bonded to the sulfur. The location of the deuterium in the above experiments was established by nmr and mass spectrometry.

Thiophilic addition of phenyllithium is also observed in the reactions of 4,4′-dimethoxythiobenzophenone (**9**) and 4,4′-bis(dimethylamino)thiobenzophenone (**11**) and 2.2 equiv of phenyllithium to give the corresponding sulfides **10** (70%) and **12** (4%) (eq 2). The low yield of **12** is attributed to losses in isolation, since nmr analysis of the crude reaction mixture indicates that *ca.* 65% of **12** is initially formed, and subsequent examination of pure **12** reveals its instability in solution and to chromatography.

Thiobenzophenone reacts with organometallics, other than phenyllithium[10] and sodium acetylide,[9] also by a thiophilic process. Phenylmagnesium bromide and phenylsodium give benzhydryl phenyl sulfide (**2**) upon reaction with **1** in 37 and 27% yields (glpc). Reaction of n-butyllithium with **1** gives benzhydryl n-butyl sulfide in 25% yield (glpc).

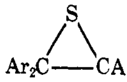
A unified relationship between the thiophilic additions described above and the reactions of some substituted thiobenzophenones with aryl and alkyl Grignard reagents to give tetraarylethylene sulfides[11] is outlined in Scheme I. It is suggested that the anion formed by

Scheme I



initial attack of the organometallic on sulfur subsequently attacks the thiocarbonyl of a second diaryl thioketone to give a species which can form episulfide by intramolecular loss of a thiolate group. An analogous scheme has been suggested to account for the formation of difluorenylidene *via* the corresponding episulfide from fluorenone sulfine and methyllithium.[18]

A consequence of the mechanism proposed in Scheme I is that the relative yields of sulfide and episulfide shoud be dependent on the relative concentrations of thioketone and organometallic. If, in a series of experiments, the concentration of thioketone is increased relative to that of the organometallic, the initially formed anion should be able to compete more successfully with the organometallic for thioketone, resulting in an increased yield of episulfide and a decreased yield of sulfide. Slow addition of slightly more than 1 equiv of phenyllithium to ether solutions of **9** and **11** gives the corresponding episulfides **13** and **14** in yields of 31 and



13, Ar = p-$CH_3OC_6H_4$
14, Ar = p-$(CH_3)_2NC_6H_4$

58%, respectively. In both cases the product precipitates from solution, and thus the possible subsequent conversion to the tetraarylethylene is avoided.[18] From the reaction of **9**, an 8% yield of the sulfide **10** is also obtained. Comparison of these yields of **10** and **13** with those obtained from the addition of **9** to 2.2 equiv of phenyllithium shows that the method of inverse addition decreases the yield of **10** by a factor of nine and increases the yield of **13** by a factor of at least eight. The direction of these changes supports the mechanism proposed in Scheme I for episulfide formation.

Schönberg, *et al.*, obtained **13** from **9** in 70% yield by allowing the Grignard reagent from 1.5 equiv of bromobenzene to react with **9**, partially dissolved and partially suspended in ether,[11] conditions which could maintain sufficient thioketone in solution to be considered consistent with the process suggested in Scheme I. Inverse addition does not assure formation of significant amounts of episulfide. Slow addition of phenyllithium to thiobenzophenone resulted in the formation of only a small amount of tetraphenylethylene sulfide and a 58% yield of the sulfide **4**. Several unsuccessful attempts were made to generate the anion **3** from its corresponding carbon acid or carboxylate anion and to investigate the reaction of the anion with thioketone in the absence of organometallic.

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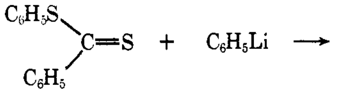
(16) J. C. Martin and R. J. Arhart, *J. Amer. Chem. Soc.*, **93**, 2339, 2341 (1971); B. M. Trost, W. L. Schinski, F. Chen, and I. B. Mantz, *ibid.*, **93**, 676 (1971); J. L. Kice, *Accounts Chem. Res.*, **1**, 58 (1968); D. C. Owsley, G. K. Helmkamp, and M. F. Rettig, *J. Amer. Chem. Soc.*, 91, 5239 (1969); C. R. Johnson and J. J. Rigau, *ibid.*, **91**, 5398 (1969); R. Tang and K. Mislow, *ibid.*, 91, 5644 (1969); M. P. Neuriter and F. G. Bordwell, *ibid.*, **81**, 578 (1959); U. Schmidt, A. Hochrainer, and A. Nikiforov, *Tetrahedron Lett.*, 3677 (1970); W. A. Pryor and K. Smith, *J. Amer. Chem. Soc.*, **92**, 2731 (1970), and references cited therein. These reactions are sometimes classed as thiophilic, a term which does not distinguish between singly and multiply bonded reactant sulfur.[1]

(17) This reaction, under different conditions and with a lower yield, and the following labeling data were communicated earlier.[10]

(18) A. G. Schultz and R. H. Schlessinger, *Chem. Commun.*, 748 (1970).

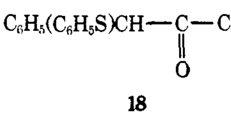
Phenyl Dithiobenzoate. The reaction of phenyl dithiobenzoate (**15**) with phenyllithium at −78° gives a 49% yield of bis(phenylthio)methane (**16**). Reaction of **15** with phenyllithium at room temperature gives a 34% yield of **16** and a 19% yield of 1,2-bis(phenylthio)-1,2-diphenylethylene (**17**). The dithio acetal **16** was identified by comparison with authentic material, and **17** was identified by spectral and analytical properties as well as by acidic hydrolysis to the same mixture of benzil, benzaldehyde, and diphenyl disulfide as is produced by hydrolysis of desyl phenyl sulfide (**18**), an anticipated product of the hydrolysis of **17**. The olefin **17** could be formed by desulfurization of the episulfide **19** by phenyllithium.



15

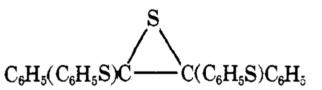
$$C_6H_5CH(S{-}C_6H_5)_2 + C_6H_5(C_6H_5S)C{=}C(C_6H_5S)C_6H_5$$

16 **17**



$$C_6H_5(C_6H_5S)CH{-}C({=}O){-}C_6H_5$$

18



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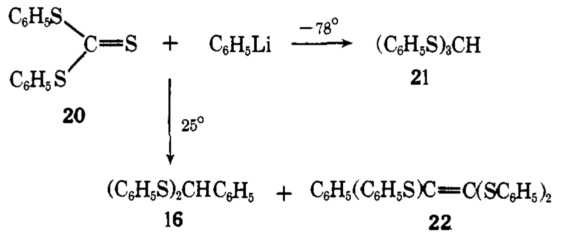
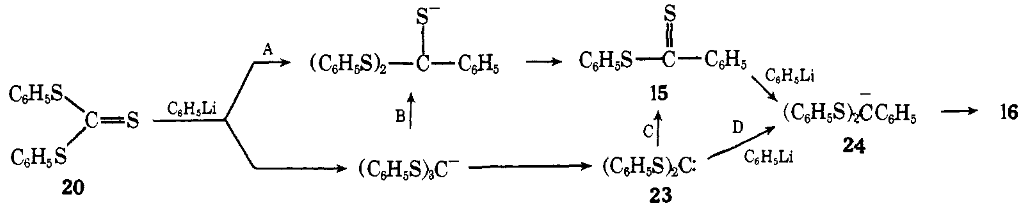
Phenyl Trithiocarbonate. The reaction of phenyl trithiocarbonate (**20**) with phenyllithium at −78° gives, after hydrolysis, a 66% yield of tris(phenylthio)methane[19] (**21**), which was characterized by comparison with an authentic sample. In contrast, the same reactants at room temperature yield 27% bis(phenylthio)phenylmethane (**16**) and 10% tris(phenylthio)phenylethylene (**22**). The olefin (**22**) was identified by acid hydrolysis to phenylthiophenylacetic acid as well as by its spectral and analytical properties.



Scheme II



The formation of **16** and **22** from **20** and phenyllithium appears to be anomalous in terms of thiophilic addition. Four pathways by which **16** might be produced are shown in Scheme II; three of these involve the intermediacy of phenyl dithiobenzoate (**15**), which does lead to **16** *via* **24** (*vide supra*) under the reaction conditions. If **15** is an intermediate, it could arise by either (1) direct addition of phenyl to the carbon of **20** (A), (2) initial addition of phenyl to the thiosulfur of **20** to give the tris(thiophenyl)methyl carbanion followed by 1,2-rearrangement (B), or (3) initial addition of phenyl to the thiosulfur of **20** followed by formation of the carbene **23** or reaction of the anion as a carbenoid and intramolecular insertion to **15** (C). A fourth possibility (D) which does not involve the formation of **15** is reaction of **23** or its equivalent with phenyllithium to give the anion **24**, a precursor of **16**.

A convenient method for distinguishing among some of the possibilities is outlined in Table I, where the results of isotopic incorporation into bis(phenylthio)phenylmethane (**16**) for the reaction of phenyl trithiocarbonate (**20**) with phenyllithium-d_5 by each pathway, A–D in Scheme II is presented in terms of the deuterium distribution expected for the molecular ion and the base peak (M − thiophenyl)$^+$ in the mass spectrum. The predictions made in Table I are based on the assumptions that the steps in each reaction path are irreversible and that secondary isotope effects on the possible intramolecular rearrangement reactions are negligible. The deuterium incorporation reaction observed for the reaction of **20** and phenyllithium-d_5 is shown as the last entry in Table I and is consistent with reaction *via* pathway D only. Both the formation of **23**[20,21] and the reaction of dithia-substituted carbenes with organometallics[22] have precedent. In fact, Seebach and Beck[20c] have interpreted kinetic data for the conversion of the lithium salt of tris(phenylthio)methane to tetrakis(phenylthio)ethylene in terms of free bis(phenylthio)methylene (**23**).

Table I. Predicted Relative Intensities of Isotopic Ions in the Mass Spectra of Bis(phenylthio)phenylmethane (**16**) for the Reaction Pathways in Scheme II and the Reaction of Phenyl Trithiocarbonate (**20**) and Phenyllithium-d_5

Pathway Scheme II	Molecular ion[a] d_5	d_{10}	Base peak[b] d_0	d_5	d_{10}
A	0	100	0	50	50
B	33	67	17	67	17
C	33	67	17	67	17
D	33	67	0	67	33
Observed	39 ± 5	61 ± 5	0 ± 2	69 ± 2	31 ± 2

[a] The molecular ion is 0.14% of the base peak. [b] $(M - SC_6Y_5)^+$.

Possible routes for the formation of tris(phenylthio)phenylethylene (**22**) *via* **24** are shown in Scheme III. Attack of the anion **24** on the thiocarbonyl of **20** (E)

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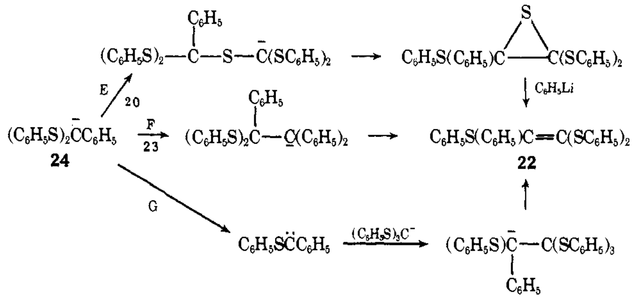
(19) This reaction has been observed independently by Dr. D. Seebach; private communication, September 1970.

(20) (a) A. Fröling and J. F. Arens, *Recl. Trav. Chim. Pays-Bas*, **81**, 1009 (1962); (b) J. Hine, R. P. Bayer, and G. G. Hammer, *J. Amer. Chem. Soc.*, **84**, 1752 (1962); (c) D. Seebach and A. K. Beck, *ibid.*, **91**, 1541 (1969); D. Seebach, *Angew. Chem. Int. Ed. Engl.*, **6**, 4421 (1967).

(21) D. L. Coffen, J. Q. Chambers, D. R. Williams, P. E. Garrett, and N. D. Caufield, *J. Amer. Chem. Soc.*, **93**, 2258 (1971), provide a summary of methods for producing dithiacarbenes.

(22) G. A. Wildshut, H. J. T. Bos, L. Brandsma, and J. F. Arens, *Monatsh. Chem.*, **98**, 1043 (1967); R. M. Carlson and P. M. Helquist, *Tetrahedron Lett.*, 173 (1969).

Scheme III



could lead to an episulfide precursor of **22**. Another possible route, reaction of **24** with **23** (F), could give an anion which could produce **22** by loss of thiophenolate; alternatively, another anion precursor of **22** could result from loss of thiophenolate from **24** (G) followed by reaction with tris(thiophenyl)methyl carbanion. Distinction between routes E and F and G can be provided by analysis of the mass spectrum of **22** from the reaction of phenyl trithiocarbonate-d_{10} and phenyllithium, as shown in Table II, if it is assumed that all steps are irreversible.[23] The observed result is shown in the last entry in the table and is consistent with reaction *via* pathway F or G.

Table II. Predicted Relative Intensities of Isotopic Molecular Ions in the Mass Spectra of Tris(phenylthio)phenylethylene (**22**) for the Reaction Pathways in Scheme III and the Reaction of Phenyl Trithiocarbonate-d_{10} and Phenyllithium

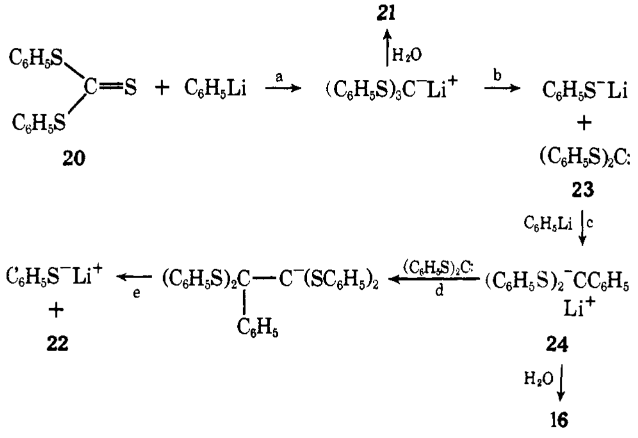
Pathway in Scheme III	Molecular Ion		
	d_5	d_{10}	d_{15}
E	0	33	67
F	22	56	22
G	22	56	22
Observed	21 ± 2	55 ± 2	22 ± 2

Further supposition leads to the suggestion that F is the reaction pathway. If the anion **24** generated in the reactions of **20** and **15** with phenyllithium loses thiophenolate to produce a carbene or carbenoid as specified in pathway G, that species would be expected to react with the excess phenyllithium to generate benzhydryl phenyl sulfide (**4**). As little as 5% benzhydryl phenyl sulfide would have been detected, and in neither case was **4** observed, consistent with reaction *via* pathway F rather than G.

A key intermediate in the formation of both **16** and **22** is the tris(thiophenyl)methyl carbanion. Formation of this anion by the reaction of tris(phenylthio)methane (**21**) with phenyllithium at room temperature[20] gives a 27% yield of **16** and a 17% yield of **22**, comparable to the 27 and 10% yields of the products obtained upon reaction of **20** with phenyllithium at room temperature.[24]

The results of the reaction of **20** with phenyllithium at −78° and at room temperature, of the deuterium labeling experiments at room temperature, and of the reaction of **21** with phenyllithium are consistent with the reaction processes outlined in Scheme IV. At −78° reaction ceases after step a, while at room temperature the steps b–e are operative.

Scheme IV



The possibility that some of the steps in Scheme IV are reversible can be evaluated from the results of the deuterium labeling experiments. Reversibility in step a, but no reversibility in the other steps, would make all phenyl groups of the diphenyl trithiocarbonate and phenyllithium equivalent. The net effect in the reaction of 1 equiv of phenyl trithiocarbonate-d_{10} with 2.2 equiv of phenyllithium would be to produce **16**, with a d_0:d_5:d_{10}:d_{15} ratio of 14:39:36:11, which would give a base peak, $(M - SC_6Y_5)^+$, in the mass spectrum with a d_0:d_5:d_{10} ratio of 27:50:23. The isotopic ratio observed for the base peak in the mass spectrum of **16**, formed in the reaction of phenyl trithiocarbonate-d_{10} and phenyllithium, is 33 (± 2):67 (± 2):0 (± 2).[23] Accordingly, reaction a is less than 7% (2/23·50/67) reversible under these conditions.

Application of the same type of analysis to the question of reversibility for the carbene forming step b in Scheme IV, with all other steps considered irreversible, shows that the necessary distinction can be made by deuterium labeling only on the basis of the isotope ratios for the molecular ion in the mass spectrum of **16**. The low intensity of this ion suggests that conclusions based on the relative intensities of its isotope peaks are unlikely to be of value. To clarify this point, the reaction of **20** and phenyllithium was carried out in the presence of 2 equiv of lithium thiophenolate-d_5. The bis(phenylthio)methane **16** obtained showed deuterium incorporation in the mass spectrum of d_0:d_5:d_{10}, 85 (± 3):13 (±2):3 (±2) in the molecular ion, and d_0:d_5, 93 (± 1):7 (±1) in the base peak. The values expected for the base peaks with no incorporation and full incorporation of thiophenolate-d_5 are 100:0 and 60:40, respectively. Accordingly, approximately 20% incorporation of the labeled thiophenolate has occurred. The olefinic product of the reaction, **22**, has an isotopic composition from the molecular ion of d_0:d_5:d_{10}, 79 (± 1):18 (± 1):3 (± 1), roughly consistent with the 77:14:4 ratio expected for *ca.* 20% incorporation. This result supports the possibility that step b is somewhat reversible and that step e is irreversible, since if step b were irreversible and

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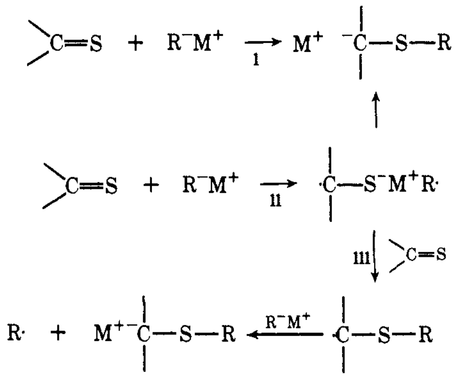
[23] The isotopically labeled bis(phenylthio)phenylmethane (**16**) obtained from the reaction of phenyltrithiocarbonate-d_{10} and phenyllithium showed isotopic peaks in the mass spectrum for the molecular ion of 65 (± 6):35 (± 6), d_5:d_{10}, and for the base peak of 33 (± 2):67 (± 2):0 (± 2), d_0:d_5:d_{10}, in agreement with that expected for reaction *via* pathway D (Scheme II) of 67:33, d_5:d_{10}, and 33:67:0, d_0:d_5:d_{10}, and very different from that expected for the other possibilities in Scheme II.

[24] The differences in the yields of **22** in these experiments can be rationalized by the fact that 3.3 equiv of phenyllithium is used in the formation of the anion from **21**, and 2.3 equiv of phenyllithium is used in the reaction with **20**. Accordingly, a greater concentration of **24** is available for reaction with **23** in the former experiment.

step e reversible steps c and d would also have to be fully reversible to account for the same deuterium incorporation in **16** and **22**. However, equilibration of the labeled thiophenolate with the trithiocarbonate **20** has not been ruled out, although that reaction would have to compete with the reaction of **20** with phenyllithium. In any case, the concentration of thiophenolate is at least two times greater in the experiment with added labeled thiophenolate-d_5 than in the absence of this material, and an upper limit of 20% reversibility for step b under these conditions seems conservative.

Reaction Mechanism. Regardless of whether it is assumed that the transition state for electron sharing by the attacking species at the sulfur of the thiocarbonyl group resembles an intermediate anion or radical or starting material, rationales can be found for thiophilic attack. Possible mechanisms are separated into anionic, radical, and radical chain categories in Scheme V. The anionic process shown as I (Scheme V) involves direct attack of the nucleophile on the sulfur of the thiocarbonyl, and the feasibility of such a process can be supported by analogy to the reaction of sulfur and phosphorus nucleophiles with thiocarbonyls,[2–4] by the stability of the resulting α-sulfur substituted anion,[25] and by the intrinsic polarization of the thiocarbonyl group.[26] However, reaction by initial electron transfer from the organometallic to give a caged radical pair by path II in Scheme V followed by a second electron transfer with formation of the anion also has precedent in electron-transfer processes observed in reactions of organometallics with carbonyls[27] as well as for the stability of the intermediate radical.[6,7] The same analogies[6,7,27] can be used in support of a radical chain process, sequence III in Scheme V, in which initial electron transfer reaction to the thiocarbonyl forms a radical which acts as a chain carrying species by subsequently attacking another thiocarbonyl group to generate a radical which can give the anion and regenerate the chain carrier by reaction with the organometallic.

Scheme V



The presence of the thioketyl radicals in the reaction of the thiobenzophenone with phenyllithium is shown by the observation of a broad signal at −78° and a signal with fine structure at 25° in the esr spectrum of reacting solutions. The signal observed at room temperature is qualitatively the same as that observed from the reaction of thiobenzophenone with lithium, including signals from benzophenone impurity.[28] However, evidence that the thioketyl radical is on the reaction pathway is not provided by this observation, and the reaction of diphenyl trithiocarbonate and phenyllithium at −78° shows no esr signal at −78°. A choice among the mechanisms shown in Scheme V will clearly require more information.

Although thiophilic addition to thiocarbonyl groups appears to be a general process applicable to reactions of other thiocarbonyl compounds,[29] products formally resulting from nucleophilic addition to the carbon of thiocarbonyls have also been reported.[30] The selectivity between the two reaction modes as well as the possibility of reversible and undetected additions by each pathway also needs further investigation.

Experimental Section[31]

The following compounds, prepared by the procedures cited, had nmr, ir, and mass spectra in agreement with the assigned structures: benzhydryl sulfide (**4**),[32] mp 75–77° (lit.[32] mp 78°); 4,4-dimethoxybenzhydryl phenyl sulfide (**10**),[32] mp 87–88° (lit.[33] mp 50.5–51.5°); bis(phenylthio)phenylmethane (**16**),[34] mp 51.5–52°, (lit.[34] 52–53°); tris(phenylthio)methane (**21**),[35] mp 40–42° (lit.[35] 40.5–41.5°); thiobenzophenone (**1**),[36] mp 50–51°[37] (lit.[36] 53–54°); phenyl dithiobenzoate (**15**),[40,41] mp 56–59° (lit.[40] 60–61°); phenyl trithiocarbonate (**20**) was prepared in 50% yield from sodium thiophenolate and thiophosgene in ethanol, mp 95–96° (lit.[41] 95°); phenyllithium was prepared in 55–70% yield from lithium wire (1% sodium) and bromobenzene in ethyl ether and analyzed by titration.[42] Phenyl trithiocarbonate-d_{10} with satisfactory physical

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(25) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, pp 71–84; C. C. Price and S. Oae, "Sulfur Bonding," Ronald Press, New York, N. Y., 1962, pp 27–28, 55–60; G. Cilento, *Chem. Rev.*, **60**, 147 (1960); D. Seebach, *Angew. Chem. Int. Ed. Engl.*, **8**, 639 (1969); K. A. R. Mitchel, *Chem. Rev.*, **69**, 157 (1969).

(26) R. H. Lumbroso and C. Andrieu, *Bull. Soc. Chim. Fr.*, 3201 (1966), have suggested on the basis of dipole moment measurements that the bonding electrons of the thiocarbonyl group are intrinsically polarized with carbon negative relative to sulfur.

(27) J. Billet and S. G. Smith, *J. Amer. Chem. Soc.*, **90**, 4108 (1968); K. D. Berlin, R. D. Shope, and R. D. Grigsby, *J. Org. Chem.*, **34**, 2500 (1969), and references cited therein.

(28) H. C. Heller, *J. Amer. Chem. Soc.*, **89**, 4288 (1967), has reported the esr spectrum of the thiobenzophenone thioketyl radical.

(29) J. R. Grunwell, *J. Org. Chem.*, **35**, 1500 (1970).

(30) W. Bergmann and D. Wagenberg, *Ber. Deut. Chem. Ges. B.*, **63**, 2585 (1930), and references cited therein.

(31) Melting points were determined in open capillaries in a Thomas–Hoover melting point apparatus and are corrected. The proton magnetic resonance spectra were obtained on a Varian Associates T-60 spectrometer or on a Varian Associates A-60A or HA-100 spectrometer by Mr. R. L. Thrift and associates. Electron spin resonance spectra were obtained by Mr. R. L. Thrift on a Varian Associates V-4502 epr spectrometer. Infrared spectra were determined on a Perkin-Elmer infracord Model 137 spectrophotometer. Mass spectra were obtained under the supervision of Mr. J. C. Cook by Mr. J. Wrona or Mr. P. Matejak on an Atlas CH4 or CH5 mass spectrometer. Microanalyses were performed by Mr. J. Nemeth and associates. Gas–liquid phase chromatography was done with an Aerograph A-90-P or A-90-P3 chromatograph with helium as the carrier gas. A 10-ft, 0.25-in. diameter column of silicone rubber on firebrick was used at 190°.

(32) I. I. Lapkin and N. I. Panova, *Zh. Obshch. Khim.*, **32**, 745 (1962).

(33) A. Bistrizycki and J. Risi, *Helv. Chim. Acta*, **8**, 582 (1925). The two different preparations of **10**, mp 87–88°, reported in the present work suggest that the literature mp is that of an allotropic form we did not obtain or that the literature mp is in error.

(34) W. E. Truce and F. E. Roberts, *J. Org. Chem.*, **28**, 961 (1963).

(35) J. Hine, *J. Amer. Chem. Soc.*, **72**, 2438 (1950).

(36) B. F. Gofton and E. Braude, "Organic Syntheses," Collect. Vol. 4, Wiley, New York, N. Y., 1963, p 927.

(37) The analytical sample shows contamination by traces of benzophenone in both the ir[38] and mass spectra.[39]

(38) R. H. Abeles, R. F. Hutton, and F. A. Westheimer, *J. Amer. Chem. Soc.*, **79**, 712 (1957).

(39) D. Schumann, E. Frese, and A. Schönberg, *Chem. Ber.*, **102**, 3192 (1969).

(40) M. H. Leon and R. S. Asquith, *Tetrahedron*, **26**, 1719 (1970).

(41) W. Autenrieth and H. Hefner, *Chem. Ber.*, **58**, 2151 (1925).

(42) S. C. Watson and J. F. Eastham, *J. Organometal. Chem.*, **9**, 165 (1967).

and analytical values was obtained from thiophenol-d_5, prepared from phenyllithium-d_5 and sulfur. Bromobenzene-d_5[43] from benzene-d_6 was the precursor of phenyllithium-d_5. Thiobenzophenone-d_{10}, with satisfactory physical values, was prepared from benzophenone-d_{10} obtained from benzene-d_6.[44] Methanol-*O-d*, prepared from sodium methoxide and deuterium oxide,[45] bp 65–70°, was shown to contain 94% *d* by analysis.

Benzhydryl *n*-Butyl Sulfide. Sodium *n*-butyl mercaptide, 5.0 ml (4.8×10^{-2} mol), in 80 ml of ethanol and 10.0 g (5.0×10^{-2} mol) of chlorodiphenylmethane were allowed to react for 4 hr at reflux. Extractive work-up with ether and 10% sodium hydroxide solution and water followed by drying ($MgSO_4$) and distillation gave 2.5 g (20%) of benzhydryl *n*-butyl sulfide: bp 126–128° (1.2 Torr); nmr (CCl_4) δ 7.45–7.00 (m, 10 H), 5.03 (s, 1 H), 2.46–2.17 (m, 2 H), 1.75–1.03 (m, 4 H), and 1.03–0.65 (m, 3 H); mass spectrum (70 eV) *m/e* (rel intensity) 256(5), 167(100), 165(22). The analytical sample was a center-cut portion of material with bp 127° (1.2 Torr).

Anal. Calcd for $C_{17}H_{20}S$: C, 79.63; H, 7.86; S, 12.50. Found: C, 79.57; H, 7.89; S; 12.43.

General Procedures for Reactions Involving Organometallic Reagents and Thiocarbonyl Compounds. All reactions with organometallic reagents were stirred under nitrogen or argon atmospheres. Except where stated otherwise, reactions were run at room temperature and isolation of the products was achieved by addition of several volumes of water to the reaction mixture, separation of the two phases, and extraction of the aqueous layer with two portions of ether. The combined ether layers were washed with water and dried ($MgSO_4$), and the solvent was removed at reduced pressure at *ca.* 60° to give the residual products. Column chromatographies were performed on alumina (Merck).

Thiobenzophenone. A solution of 0.94 g (4.8×10^{-3} mol) of thiobenzophenone in 80 ml of ether was added over an 8-min period to 10 ml of ether–benzene containing 10.2×10^{-3} mol of phenyllithium. The color of the thioketone faded immediately from blue as the thioketone entered the phenyllithium solution to give a red-orange solution. After one hour extractive work-up and chromatography on alumina with elution by hexane to 20% benzene–hexane gave 0.92 g (70%) of benzhydryl phenyl sulfide (**4**): mp 75–77° (mmp 75–77°). The nmr and mass spectra of the product are identical with those of authentic material.

4,4′-Dimethoxythiobenzophenone. Similar reaction and work-up of 0.94 g (3.6×10^{-3} mol) of 4,4′-dimethoxythiobenzophenone (Aldrich) and 10 ml of 0.84 *M* (8.4×10^{-3} mol) phenyllithium, but with the chromatography column being eluted with hexane–benzene, gave 0.85 g (70%) of 4,4′-dimethoxybenzhydryl phenyl sulfide (**10**): mp 86–87° (mmp 86.5–87.5°). The nmr and mass spectra are identical with those of authentic material. Also obtained from the chromatographic column was a mixture weighing 0.062 g which shows three spots by tlc. The largest of these spots seems to be tetrakis(4-methoxyphenyl)ethylene sulfide (**13**) by comparison of its R_f value with the major product obtained in the inverse addition of phenyllithium to 4,4′-dimethoxybenzophenone (*vide infra*).

4,4′-Bis(dimethylamino)thiobenzophenone. Similar treatment of 1.00 g (3.5×10^{-3} mol) of 4,4′-bis(dimethylamino)thiobenzophenone (J. T. Baker) in 80 ml of tetrahydrofuran with 25 ml of 0.31 *M* (7.8×10^{-3} mol) phenyllithium gave a crude yellow-green residue which by nmr spectroscopy seemed to be 4,4′-bis(dimethylamino)benzhydryl phenyl sulfide (**11**) in 60–70% yield. Chromatography on alumina with elution by hexane to 40% benzene–hexane and one recrystallization of the crude product obtained from the column from hexane-benzene gave 0.150 g of crude **11**. Three more recrystallizations of this material from hexane–benzene gave 0.040 g (4%) of pure 4,4′-bis(dimethylamino)benzhydryl phenyl sulfide (**11**): mp 151–152°; nmr (CDl_3) δ 7.05 (A_2B_2), 6.82 (s, total aromatic 13 H), 5.30 (s, 1 H), and 2.92 (s, 12 H); mass spectrum (70 eV) *m/e* (rel intensity) 362(0.29), 254(29), 253(100), and 237(21).

Anal. Calcd for $C_{23}H_{26}N_2S$: C, 76.20; H, 7.23; S, 8.84. Found: C, 75.89; H, 7.25; S, 9.08.

Inverse Additions. (A) 4,4′-Dimethoxythiobenzophenone. A phenyllithium solution (10 ml, 0.52 *M*) (5.2×10^{-3} mol) was added over 20 min to 1.30 g (5.03×10^{-3} mol) of 4,4′-dimethoxythiobenzophenone in 15 ml of ether. After 1 hr, water was added and the crystalline precipitate was collected by filtration. Additional material was obtained by extraction and combined with the first precipitate. Two recrystallizations from ethanol–chloroform gave 0.37 g (31%) of tetrakis(4-methoxyphenyl)ethylene sulfide (**13**), mp 215–216° (lit.[46] mp 216–218°); the nmr, ir, and mass spectra are consistent with the assigned structure. From the filtrate 0.13 g (8%) of 4,4′-dimethoxybenzhydryl phenyl sulfide, mp 86–87° (mmp 86.5–87.5°), was obtained.

(B) 4,4′-Bis(dimethylamino)thiobenzophenone. Similar reaction of 5.2 ml of a 0.75 *M* solution of phenyllithium (3.9×10^{-3} mol) with 1.00 g (3.52×10^{-3} mol) of 4,4′-bis(dimethylamino)thiobenzophenone in 50 ml of tetrahydrofuran led to crystallization of 0.55 g (58%) of tetrakis(4-dimethylaminophenyl)ethylene sulfide (**14**): mp 300–303° dec; the nmr, ir, and mass spectra were consistent with the assigned structure but a satisfactory analytical sample was not obtained.

Reaction of Thiobenzophenone and Phenylmagnesium Bromide. A solution of 0.2137 g (1.08×10^{-3} mol) of thiobenzophenone in 15 ml of ether was added in 3–4 min to 0.65 ml of a solution of 3 *M* phenylmagnesium bromide in ether (1.95×10^{-3} mol, Alfa Inorganics) to which had been added 5 ml of ether and 1 ml of benzene. After work-up, analysis by glpc showed 37% benzhydryl phenyl sulfide and small amounts of benzophenone and thiobenzophenone.

Reaction of Thiobenzophenone and Phenylsodium. To phenylsodium, prepared from 1.15 g (5.0×10^{-2} g-atom) of sodium wire (sodium press), 10 ml of benzene, and 3.0 g (2.4×10^{-2} mol) of chlorobenzene, was added a solution of 0.4019 g (2.02×10^{-3} mol) of thiobenzophenone in 10 ml of ether. Analysis by glpc with triphenylmethyl mercaptan as an internal standard indicated a 27% yield of benzhydryl phenyl sulfide after work-up.

Reaction of Thiobenzophenone and *n*-Butyllithium. *n*-Butyllithium, 1.6 *M* in hexane (Foote Mineral Co.), was added to 0.1404 g (7.1×10^{-4} mol) of thiobenzophenone in 10 ml of ether. Work-up and analysis by glpc indicated a 25% yield of benzhydryl *n*-butyl sulfide. Preparative glpc gave material which had an nmr spectrum identical with that of authentic material.

Reaction of Thiobenzophenone-d_{10} and Phenyllithium. A solution of 0.4088 g (1.93×10^{-3} mol) of thiobenzophenone-d_{10} in 30 ml of ether was added in 20 min to a solution of 3.0 ml of 1.07 *M* phenyllithium (3.2×10^{-3} mol). Evaporation of the ether used in extraction gave a crude residue crystallized upon trituration with cold hexane and was recrystallized once from hexane to give 0.1322 g (24%) of benzhydryl phenyl-d_{10} sulfide: mp 76–78° (mmp with benzhydryl phenyl sulfide 76–78°). The mass spectrum of the product shows a ratio of *m/e* 172:177 ($C_{13}H_6D_5$:$C_{13}HD_{10}$) of 1.8:98.2 and a ratio of *m/e* 109:114 (C_6H_5S:C_6D_5S) of 99.3:0.7. This fragmentation is consistent with at least 98% $C_6H_5SCH(C_6D_5)_2$.

Trapping the Anion from the Reaction of Thioketones and Organolithium Reagents. (A) Quenching the Reaction of Thiobenzophenone and Phenyllithium with Methanol-*O-d*. The reaction of 5.0 ml of a 1.07 *M* solution (5.4×10^{-3} mol) of phenyllithium and 0.3482 g (1.76×10^{-3} mol) of thiobenzophenone was quenched 0.5 min by addition of 1.0 ml of methanol-*O-d* (94 atom % *d*). Trituration of the crude residue obtained after the usual work-up gave 0.1511 g (31%) of benzhydryl phenyl sulfide-*d* (**5**): mp 75–77° (mmp with benzhydryl phenyl sulfide 75–77°). The trituration procedure was required because it was found that the benzyl deuterium was exchanged for hydrogen upon chromatography. The mass spectrum of the product indicates 88% deuterium incorporation in both the molecular ion and the base peak. The pmr spectrum shows the aromatic absorption and the methine absorption characteristic of benzhydryl phenyl sulfide with relative areas of approximately 110:1, establishing that the deuterium is incorporated at the benzyl position.

(B) Quenching the Reaction Mixture from Thiobenzophenone and Phenyllithium with Chlorotrimethylsilane. A solution of 0.7857 g (3.96×10^{-3} mol) of thiobenzophenone in 40 ml of ether was added in 30 min to 11.0 ml of a 0.42 *M* phenyllithium solution (4.6×10^{-3} mol). After 10 min, 1.31 g (1.21×10^{-2} mol) of chlorotrimethylsilane was added. After the mixture had been stirred 3 hr, a solid crude residue was obtained after removal of ether and trituration with cold hexane. One recrystallization from ethanol and two from hexane gave 0.31 g (25%) of α-trimethylsilylbenzhydryl phenyl sulfide (**6**), mp 99.5–101°. An additional 0.16 g (12%) of material with mp 98–100° was obtained from the filtrate

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[43] R. Adams and J. R. Johnson, "Laboratory Experiments in Organic Chemistry," MacMillan, New York, N. Y., 1949, p 289.

[44] A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd ed, Wiley, New York, N. Y., 1956, p 733.

[45] C. G. Swain, J. T. McKnight, and V. P. Kreiter, *J. Amer. Chem. Soc.*, 79, 1088 (1957).

[46] A. Schönberg and E. Frese, *Chem. Ber.*, **95**, 2811 (1962).

Nmr and other spectra (CCl_4) were reported in ppm downfield from methylene chloride: 2.28–1.53 (m, 15 H) and −5.02 (s, 9 H); ir ($CHCl_3$) 2960, 1595, 1485, 1435, 1250, 1082, 1035, 1030, 930, 885, 868, and 844 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 348 (15), 275 (36), 198 (100), 166 (32), 165 (49), and 135 (46).

Anal. Calcd for $C_{22}H_{23}SiS$: C, 75.80; H, 6.94; S, 9.20. Found: C, 75.78; H, 6.87; S, 9.06.

Reaction of Phenyl Dithiobenzoate and Phenyllithium. (A) At −78°. A solution of 0.50 g (2.2×10^{-3} mol) of phenyl dithiobenzoate (**15**) in 30 ml of ether was added in 30 min to 7.2 ml of 0.066 *M* phenyllithium (4.8×10^{-3} mol) cooled in a Dry Ice–acetone bath. After 10 min 5 ml of methanol was added dropwise, raising the temperature of the solution to −68°. Extractive work-up and column chromatography with elution by hexane to 20% benzene–hexane gave 0.330 g (49%) of bis(phenylthio)phenylmethane (**16**): mp 50–51° (mmp 50–51°); the nmr spectrum of the product was identical with that of authentic material. No 1,2-bis(phenylthio)-1,2-diphenylethylene (**17**) was detected.

(B) At Room Temperature. A solution of 0.70 g (3.0×10^{-3} mol) of phenyl dithiobenzoate (**15**) in 50 ml of ether was added in 50 min to 15.6 ml of 0.43 *M* phenyllithium (6.7×10^{-3} mol). After 10 min, the usual work-up, chromatography with elution of hexane to 20% benzene–hexane, and one recrystallization of each product from hexane gave 0.254 g (24%) of bis(phenylthio)phenylmethane (**16**) (mp 47–49°, mmp 49–50°), 0.1222 g (10%) of 1,2-bis(phenylthio)-1,2-diphenylethylene (**17**), and 0.200 g of a mixture of the two compounds. The nmr spectrum of the mixture indicates that it contains an additional 0.090 g (10%) and 0.110 g (9%) of **16** and **17**, respectively.

1,2-Bis(phenylthio)-1,2-diphenylethylene (**17**) was purified by recrystallization from ethanol and hexane: mp 162–163°; mass spectrum (70 eV) *m/e* (rel intensity) 396 (100), 287 (79), 254 (43), 253 (28), 210 (73), 178 (71), 165 (25), and 78 (26).

Anal. Calcd for $C_{26}H_{20}S_2$: C, 78.75; H, 5.08; S, 16.17. Found: C, 78.76; H, 5.16; S, 16.11.

Hydrolysis of 1,2-Bis(phenylthio)-1,2-diphenylethylene (17). A 0.280-g (7.1×10^{-4} mol) sample of **17** was heated at 100° for 14 hr with 15 ml of acetic acid, 3 ml of sulfuric acid, and 3 ml of water. The solution was diluted with water and extracted with ether. Three ether extracts were combined and extracted three times each with saturated sodium bicarbonate solution, with 10% potassium hydroxide solution, and with water.

The nmr spectrum of the oily yellow residue obtained after evaporation of the ether showed signals at δ 11.13 (s), 7.17 (m), 5.69 (s), and 4.10 (s). The relative areas of these signals was 1.0:165:1.3:1.0, respectively. Tlc showed a minimum of three spots. Analysis by glpc and collection gave 0.004 g (7%) of benzaldehyde (collected as the 2,4-DNP derivative), 0.006 g of an unidentified material, and 0.091 g of a mixture of diphenyl disulfide[47] and benzil (collected as a single peak; authentic materials had the same retention time on tlc). The mixture of diphenyl disulfide and benzil was treated with Girard's reagent T. Work-up by ether extraction gave 0.040 g (26%) diphenyl disulfide containing a little unreacted benzil as judged by tlc: mp 56–58° (lit.[48] mp 61–62°); the mass spectrum is consistent with a mixture of diphenyl disulfide and benzil. Hydrolysis of the aqueous phase from the reaction with Girard's reagent and ether extraction gave 0.030 g (20%) of impure benzil obtained as a pale blue oil. A portion of this material was rechromatographed by glpc to give pale yellow crystals whose mass spectrum was identical with that of authentic benzil.

A similar hydrolysis of desyl phenyl sulfide gave an identical mixture of products as shown by nmr spectroscopy, tlc, and glpc. The products were not isolated.

Reaction of Phenyl Trithiocarbonate and Phenyllithium. (A) At −78°. To a solution of 15.3 ml of 0.75 *M* phenyllithium (1.5×10^{-2} mol) and 80 ml of ether at −78° was added in 30 min 1.00 g (3.82×10^{-3} mol) of phenyl trithiocarbonate in 30 ml of ether. The temperature of the solution remained at −78° throughout the addition. After 10 min 5 ml of methanol was added dropwise and the temperature rose to −65°. The usual work-up and chromatography with elution by hexane to 5% benzene–hexane gave a colorless oil which crystallized on trituration with cold hexane to give 0.86 g (66%) of tris(phenylthio)methane (**21**): mp 40–42° (mmp 39–41°). The product has tlc characteristics and nmr and mass spectra identical with those of authentic material.

(B) At Room Temperature. Phenyl trithiocarbonate (**20**), 0.77 g (2.9×10^{-3} mol), in 50 ml of ether was added in 40 min to 13 ml of 0.52 *M* phenyllithium (6.8×10^{-3} mol). Extractive work-up and column chromatography on alumina with elution by hexane to 50% benzene–hexane gave 0.24 g (27%) of bis(phenylthio)phenylmethane (**16**) and 0.062 g (10%) of tris(phenylthio)phenylethylene (**22**). The former product was identified by comparison of tlc characteristics, nmr and mass spectra, and melting point with those of authentic material, mp 49–51° (mmp 46.5–51.5°).

The product **22** has mp 82–83.5°; nmr (CCl_4) δ 7.15 (m); ir ($CHCl_3$) 3050, 2990, 1580, 1470, 1430, 1068, 1025, 1000, 973, 914, and 855 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 428 (36), 242 (33), and 210 (100).

Anal. Calcd for $C_{26}H_{20}S_3$: C, 72.86; H, 4.70; S, 22.44. Found: C, 72.92; H, 4.57; S, 22.28.

Hydrolysis of Tris(phenylthio)phenylethylene. A 0.4579-g (1.07×10^{-3} mol) sample of tris(phenylthio)phenylethylene was treated with 15 ml of acetic acid, 3 ml of sulfuric acid, and 3 ml of water at 100° for 21 hr. Dilution with water, extractive work-up with sodium bicarbonate solution, and one recrystallization from hexane gave 0.092 g (35%) of α-(phenylthio)phenylacetic acid: mp 101–102° (lit.[48] mp 102–103°); ir ($CHCl_3$) 1705 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 244 (56), 199 (73), 135 (100), 79 (49), and 77 (36). Concentration of the filtrate gave an additional 0.062 g (25%) of α-(phenylthio)phenylacetic acid with mp 97–99°.

Reaction of Phenyl Trithiocarbonate and Phenyllithium-d_5. To phenyllithium-d_5, prepared from 0.60 ml (5.3×10^{-3} mol) of bromobenzene-d_5, was added in 30 min 0.39 g (1.49×10^{-3} mol) of phenyl trithiocarbonate in 30 ml of ether. Work-up and chromatography on alumina with rapid elution by hexane to 50% benzene–hexane gave 0.0177 g (4%) of bis(phenylthio)phenylmethane: mp 46–49° (mmp with undeuterated material 46–48°); mass spectrum (30 eV) gives a ratio of *m/e* 313:318 of 39 (± 5): 61 (± 5) and a ratio of *m/e* 204:209 of 69 (± 2):31 (± 2); nmr (CCl_4) shows an aryl-to-methine ratio of 6.7:1.0.

Reaction of Phenyl Trithiocarbonate-d_{10} and Phenyllithium. A solution of 0.82 g (3.0×10^{-3} mol) of phenyl trithiocarbonate-d_{10} in 50 ml of ether was added 10.0 ml of 0.66 *M* phenyllithium (6.6×10^{-3} mol). Extractive work-up and chromatography with rapid elution by hexane gave 0.040 g (4%) of bis(phenylthio)phenylmethane and 0.060 g (4%) of tris(phenylthio)phenylethylene, as well as a mixture of the two products. Bis(phenylthio)phenylmethane, mp 49–51° (mmp with undeuterated material 49–51°); mass spectrum (70 eV) gives a ratio of *m/e* 313:318 of 65 (± 6):35 (± 6) and a ratio of *m/e* 199:204 of 33 (± 2):67 (± 2). The tris(phenylthio)phenylethylene has mp 79–82° (mmp with undeuterated material 82–84°); mass spectrum (70 eV) gives a ratio of *m/e* 433:438:443 of 21 (± 2):55 (± 2):22 (± 2).

Reaction of Diphenyl Trithiocarbonate with a Solution of Phenyllithium and Lithium Thiophenoxide-d_5. Thiophenol-d_5, 0.92 g (8.0×10^{-3} mol). was added to 26 ml of 0.66 *M* phenyllithium (1.72×10^{-2} mol). After 5 min, 1.05 g (4.0×10^{-3} mol) of diphenyl trithiocarbonate in 50 ml of ether was added. Work-up and chromatography with rapid elution by hexane to 20% benzene–hexane gave 0.0105 g (1%) of bis(phenylthio)phenylmethane, 0.313 g (37%) of tris(phenylthio)phenylethylene, and an undetermined amount of a mixture of the two products. The product **16** has mp 46–49° (mmp with undeuterated material 48–49°) and shows only one spot on tlc; the mass spectrum gives a ratio of *m/e* 308:313:318 of 85 (± 3):13 (± 1) and a ratio of *m/e* 199:204 of 93 (± 1):7 (± 1). The product **17** has mp 82–84° (mmp with undeuterated material 83–85°). Its mass spectrum shows a ratio of *m/e* 428:433:438 of 79 (± 1):18 (± 1):3 (± 1).

Reaction of Tris(phenylthio)methane (21) with Phenyllithium. To 15 ml of 0.66 *M* phenyllithium (1.0×10^{-2} mol) was added in 40 min 1.02 g (3.0×10^{-3} mol) of tris(phenylthio)methane in 50 ml of ether. After 10 min, extractive work-up and chromatography with elution by hexane to 20% benzene–hexane gave 0.0220 g (24%) of bis(phenylthio)phenylmethane (**16**) (mp 48.5–50°, mmp 50–51°), 0.0570 g (8%) of tris(phenylthio)phenylethylene (**17**) (mp 82–84°, mmp 83–85°), and a mixture of the two products (0.0850 g) which by nmr spectroscopy is 0.024 g (3%) of **16** and 0.061 g (9%) of **17**.

Acknowledgment. We are grateful to Mr. Brock Siegel for the preparations of authentic **4**, **16**, and **21**

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Solid-Phase Synthesis of Oligosaccharides. II. Steric Control by C-6 Substituents in Glucoside Syntheses

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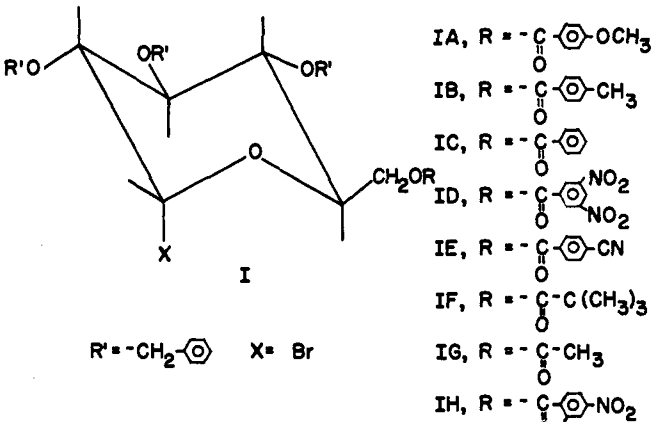
Abstract: A number of 2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl bromides containing various acid residues on C-6 were prepared and tested in glycoside-forming reactions. The fraction of anomeric glucosides produced varied from over 90% α to over 90% β depending on the nature of the C-6 acyl group. In the para-substituted benzoic acid series the proportion of α-glucoside formed was shown to increase with increasing σ Hammett substituent constant value. This degree of steric control should be sufficient for the synthesis of lower 1→6 linked oligosaccharides and is probably due primarily to orbital overlap of the carbonyl function in the transition state. Reaction rates were measured polarimetrically and product composition was estimated by nmr spectrometry with the help of deuterated samples. A few glucopyranosyl chlorides tested were shown to react by a different mechanism. The difference between the chlorides and bromides may be due to the relative tightness of the intermediate ion pairs.

The feasibility of synthesizing oligosaccharides in a solid-phase system was suggested by our previous work[1] in which a suitably functionalized solid support was prepared and a reaction sequence leading to an oligomer of glucose was tested in an exploratory fashion. Among the requirements cited for application of the solid-phase method to the synthesis of 1→6-linked oligosaccharides was the use of a monomer having a structure such as I (Chart I) in which X is a leaving group, R is an easily removable group, and R′ is a persistent blocking group.

Chart I



In order to exploit fully the advantages of the solid phase method, the steric outcome of the coupling reactions should be controlled and stereospecificity achieved. The addition of acid acceptors such as nucleophilic tertiary amines or catalysts such as metal ions[2,3] should be avoided if possible, since their use induces side reactions and complicates the reaction sequence.

One method most frequently used for control of the configuration of C-1 during glycoside formation involves the use of a participating substituent at C-2. This method has been applied to produce low yields of oligosaccharides by means of some variations of the Koenigs–Knorr method[2] or Helferich's modifications.[3] The products isolated have, however, invariably contained a mixture of anomers and side products. Furthermore, the C-2 participating substituent is usually an ester group which is most conveniently used as a temporary blocking group rather than one which is retained through several steps of a solid-phase synthesis. The obvious solution would seemingly reside in the use of a monomer possessing a more stable (persistent) participating group at C-2. Such monomers are, however, not presently available though their synthesis is being actively investigated.[4] We have followed another approach involving glucosyl halides of type I, since monomers of this type have been effectively used in glucoside-forming reactions to yield products containing a high percentage of α or β configuration, although no general method was found to control the steric outcome of the reaction.

To this date few glycosyl halides of this type have been studied. Zemplén, Csürös, and Angyal[5] were the first to prepare 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-D-glucopyranosyl bromide and Pravdić and Keglević[6] prepared the corresponding chloride in their synthesis of glucuronic acid esters. Both groups used a modified Koenigs–Knorr synthesis to prepare the corresponding β-glycosides (isolated in 15 and 63% yields, respectively).

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