8.27 (t, 1 H, J = 12 Hz), 7.09 (d, 1 H, J = 12 Hz), 5.80 (d, 1 H, J = 12 Hz), 5.52 (t, 1 H, J = 12 Hz), 4.00 (s, 3 H), 3.41 (m, 4 H), 2.24 (s, 3 H), 2.24 (s, 3 H), 1.70 (m, 8 H).

Anal. Calcd for $C_{15}H_{24}N_4S$: C, 62.03; H, 7.64; N, 19.29; S, 11.04. Found: C, 61.80; H, 7.92; N, 19.24; S, 11.05.

(*Z*,*E*)-4-[2,6-Dimethyl-3-(methylthio)-1,2,4-triazin-5-(2*H*)-ylidene]-2-butenal (15). A solution of 250 mg (1.06 mmol) of **14a** in 10 mL of EtOH was treated with 2 mL of 10% aqueous NaOH and 2 mL (4.56 g, 32 mmol) of iodomethane. The reaction mixture was heated on a steam bath for 30 min and then diluted with 10 mL of H_2O. An oil separated which solidified upon being cooled and scratched. The product was collected and recrystallized twice from MeCN. This afforded 50 mg (22%) of orange, square plates of **15**: mp 170–171 °C; IR (KBr) 3037, 3010, 2950, 2800, 2735, 1657, 1570, 1505, 1433, 1131, 1016, 975, 859, 645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.55 (d, 1 H, 8 Hz), 8.02 (dd, 1 H, J = 12, 16 Hz), 6.13 (dd, 1 H, J = 8, 16 Hz), 5.63 (d, 1 H, J = 12 Hz), 3.52 (s, 3 H), 2.57 (s, 3 H), 2.07 (s, 3 H); mass spectrum (CH_4, CI), m/e (relative intensity) 225 (M + 2, 75), 224 (M + 1, 100), 223 (M, 63), 221 (18), 208 (17), 194 (8), 180 (13), 121 (7).

Anal. Calcd for $C_{10}H_{13}N_3OS$: C, 53.79; H, 5.87; N, 18.82; S, 14.36. Found: C, 53.86; H, 5.80; N, 18.65; S, 14.37.

Acknowledgment. We thank Carl J. Mason for obtaining the mass spectra and Dr. Heisaburo Shindo (Laboratory of Chemical Physics, NIAMDD, NIH) for the 220-MHz NMR spectra. We gratefully acknowledge the interest and advice of Dr. Daniel L. Klayman.

Registry No. 1a, 1121-60-4; **1b**, 1122-62-9; **2**, 20184-94-5; **3a**, 74752-56-0; **3b**, 74752-57-1; **4a**, 74752-58-2; **4b**, 74752-59-3; **5a**, 74752-60-6; **5b**, 74752-61-7; **5c**, 25565-38-2; **7**, 74752-62-8; **8a**, 74752-63-9; **8b**, 74752-64-0; **14a**, 74752-65-1; **14b**, 74752-66-2; **15**, 74752-67-3; 2-acetyl-6-methylpyridine, 6940-57-4; 2-acetylquinoline, 1011-47-8; acetophenone, 98-86-2; methylhydrazine, 60-34-4; dimethylamine, 124-40-3; hexamethyleneimine, 111-49-9.

Supplementary Material Available: Crystal packing diagram of the unit cell for compound **8a** and Table II containing atomic parameters for the refined structure of **8a** (2 pages). Ordering information is given on any current masthead page.

Reactions of Polychlorobenzenes with Alkanethiol Anions in HMPA. A Simple, High-Yield Synthesis of Poly(alkylthio)benzenes

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Reactions of the isomeric trichlorobenzenes and tetrachlorobenzenes and of pentachloro- and hexachlorobenzene with an excess of the sodium salt of the isopropanethiol, in HMPA, afforded the products of complete displacement of all the chlorine atoms present in the molecule. Similar substitutions were also obtained with EtSNa. The reactions with MeSNa were in some cases complicated by the competitive nucleophilic attack at the methyl group of the initially formed aryl methyl thioethers which are thus demethylated to afford thiophenols.

In a previous paper[1] we have recently reported that nucleophilic substitutions of unactivated aryl halides by the sodium salts of thiols can be easily effected by working in hexamethylphosphoramide (HMPA). Thus, fluoro-, chloro-, bromo-, and iodobenzene react with Me_2CHSNa to give phenyl isopropyl sulfide (**1**) in good yields. Similarly, *o*-, *m*-, and *p*-dichlorobenzene give good yields of the corresponding *o*- (**2**), *m*- (**3**), and *p*-bis(isopropylthio)-benzene (**4**). These reactions have been demonstrated to

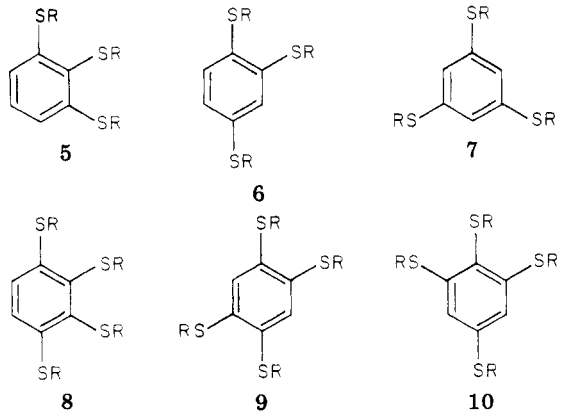
$$C_6H_5X + Me_2CHSNa \rightarrow \underset{\mathbf{1}}{C_6H_5SCHMe_2} + NaX$$

X = F, Cl, Br, I

$$o\text{-, } m\text{-, or } p\text{-}C_6H_4Cl_2 + 2Me_2CHSNa \rightarrow \underset{\mathbf{2\text{-}4}}{o\text{-, } m\text{-, or } p\text{-}C_6H_4(SCHMe_2)_2} + 2NaCl$$

occur by the classical S_NAr mechanism. It was also observed that chlorine and the $SCHMe_2$ group activate the displacement of chlorine by Me_2CHSNa.[1] On the basis of these results it can be expected that these reactions should easily occur with polychlorobenzenes, thus providing a simple method for the synthesis of poly(alkylthio)benzenes. Besides some classical, but rather tedious, procedures, the best method described in the literature to obtain aryl alkyl sulfides consists in the reaction of aryl bromide with cuprous mercaptides in quinoline at high temperature.[2,3]

Scheme I



R = Me_2CH

This procedure, however, suffers from the limitation that aromatic chloro compounds cannot be used and moreover the reaction fails when applied to polyhalogenated aromatic compounds such as 1,2,4,5-tetrabromobenzene[2,4] and penta- and hexabromobenzenes.[2]

We report in this paper the results of an investigation carried out in HMPA with polychlorobenzenes and RSNa. Excellent results were obtained with Me_2CHSNa and EtSNa which effect the complete displacement of all the chlorine atoms present in the molecule. With MeSNa

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(2) R. Adams and A. Ferretti, *J. Am. Chem. Soc.*, **81**, 4927 (1959).
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0022-3263/80/1945-4376$01.00/0

Table I. Reactions of Halogenobenzenes with Sodium Thiolates in HMPA

substrate	R in RSNa	molar equiv of RSNa	reaction temp, °C	reaction time, h	products[a]	yields,[b] %
1,2,3-$C_6H_3Cl_3$	Me_2CH	6	100	3	1,2,3-$C_6H_3(SCHMe_2)_3$	88
1,2,4-$C_6H_3Cl_3$	Me_2CH	6	100	1	1,2,4-$C_6H_3(SCHMe_2)_3$	86
1,3,5-$C_6H_3Cl_3$	Me_2CH	6	100	1	1,3,5-$C_6H_3(SCHMe_2)_3$	95
1,3,5-$C_6H_3Br_3$	Me_2CH	6	100	1.5	1,3,5-$C_6H_3(SCHMe_2)_3$	95
1,2,3,4-$C_6H_2Cl_4$	Me_2CH	8	100	1.5	1,2,3,4-$C_6H_2(SCHMe_2)_4$	85
1,2,4,5-$C_6H_2Cl_4$	Me_2CH	8	100	0.5	1,2,4,5-$C_6H_2(SCHMe_2)_4$	75
1,2,4,6-$C_6H_2Cl_4$	Me_2CH	8	100	1	1,2,4,6-$C_6H_2(SCHMe_2)_4$	95
C_6HCl_5	Me_2CH	10	0	4	1,2,4-$C_6HCl_2(SCHMe_2)_3$	85
1,2,4-$C_6HCl_2(SCHMe_2)_3$	Me_2CH	4	100	1.5	$C_6H(SCHMe_2)_5$	90
C_6HCl_5	Me_2CH	10	100	0.25	$C_6H(SCHMe_2)_5$	87
C_6Cl_6	Me_2CH	12	20	3.5	$C_6(SCHMe_2)_6$	95
C_6Cl_6	Me_2CH	12	100	54	$C_6(SCHMe_2)_5SH$	40
$C_6(SCHMe_2)_6$	Me_2CH	9	100	20	$C_6(SCHMe_2)_5SH$	c
C_6F_6	Me_2CH	10	0	1.5	$C_6(SCHMe_2)_6$	79
C_6F_6	Me_2CH	4	0	0.1	1,4-$C_6F_2(SCHMe_2)_4$	83
C_6F_6	Me_2CH	12	100	3	$C_6(SCHMe_2)_5SH$	65[d]
p-$C_6H_4Cl_2$	Et	4	100	0.5	p-$C_6H_4(SEt)_2$	85
1,2,4,5-$C_6H_2Cl_4$	Et	6	20	15	1,2,4,5-$C_6H_2(SEt)_4$	90
1,2,4,5-$C_6H_2Cl_4$	Et	8	100	1	2,4,5-$C_6H_2(SEt)_3SH$	85
C_6Cl_6	Et	12	20	7	$C_6(SEt)_6$	78
C_6Cl_6	Et	12	100	3	$C_6(SEt)_5SH$	35
C_6H_5SMe	Me	4	100	5	C_6H_5SH	90
p-$C_6H_4Cl_2$	Me	6	100	5	p-$C_6H_4(SMe)_2$	8
					p-$C_6H_4(SMe)SH$	52[e]
					p-C_6H_4ClSH	13[e]
p-$C_6H_4Cl_2$	Me	6	50	4	p-$C_6H_4(SMe)_2$	52[f]
C_6Cl_6	Me	12	20	48	$C_6(SMe)_6$	71
C_6Cl_6	Me	12	100	2	$C_6(SMe)_5SH$	85

[a] Satisfactory analytical data (±0.4% for C, H) were obtained for all new compounds. [b] Based on isolated products after column chromatography and calculated from the amount of aryl halide employed. [c] Not determined. [d] Some $C_6(SCHMe_2)_6$ was also present. [e] Isolated as the isopropyl thioether. [f] The amounts of p-$C_6H_4(SMe)SH$ and p-C_6H_4ClSH were not determined.

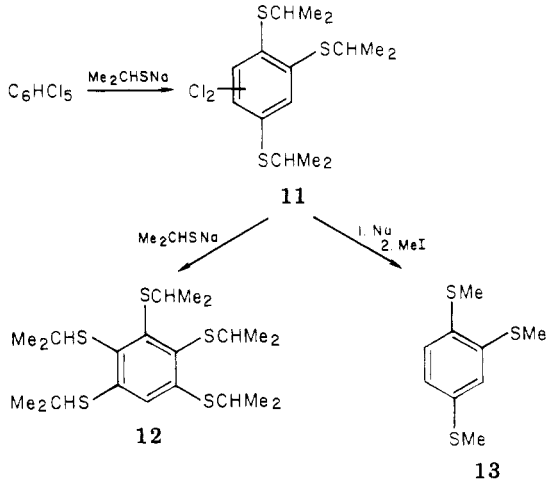
some apparently anomalous results are obtained which, however, can be easily rationalized and used to develop other interesting syntheses. Because of the simple procedure and of the high yields obtained, the results now described represent a remarkable improvement of the previously reported methods.

Results and Discussion

The addition of an excess of Me_2CHSNa to a solution of 1,2,3-trichlorobenzene in HMPA, at 100 °C, gave 1,2,3-tris(isopropylthio)benzene (**5**) in 88% yield. Under similar conditions 1,2,4- and 1,3,5-trichlorobenzene afforded the 1,2,4- (**6**) and the 1,3,5-tris(isopropylthio)-benzenes (**7**) in 86 and 95% yields, respectively (Scheme I). This latter compound was also obtained from the 1,3,5-tribromobenzene (Table I). Good results were also obtained from the three isomeric tetrachlorobenzenes; the 1,2,3,4- (**8**), 1,2,4,5- (**9**), and the 1,2,4,6-tetrakis(isopropylthio)benzenes (**10**) were isolated in 85, 75, and 95% yields, respectively.

The reaction of Me_2CHSNa with pentachlorobenzene, under the same experimental conditions, is complete in 15 min and gives an 87% yield of pentakis(isopropylthio)benzene (**12**). If the reaction is carried out at 0 °C an intermediate compound **11** (85%) can be isolated in which only three chlorine atoms have been substituted. When this compound is treated with sodium in HMPA and methyl iodide is added to the resulting solution, 1,2,4-tris(methylthio)benzene (**13**) was isolated.[5] This result,

Scheme II

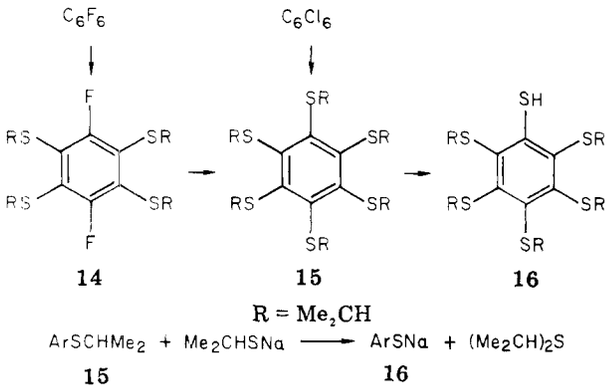


however, does not give sufficient information about the positions occupied by the two remaining chlorine atoms and the structure of **11** cannot be fully elucidated. Further reaction of **11** with Me_2CHSNa gives **12** in 90% yield (Scheme II).

In the case of hexachlorobenzene, the desired hexakis(isopropylthio)benzene (**15**) could be obtained cleanly and in good yield (95%) only by lowering the temperature to 20 °C. With the even more reactive hexafluorobenzene, the reaction had to be carried out at 0 °C. In this case, with only 4 mol equiv of Me_2CHSNa the reaction proceeds selectively to give a single substitution product which, on the basis of its NMR and mass spectra, was assigned the structure of the tetrakis(isopropylthio)-1,4-difluorobenzene, **14** (Scheme III). If C_6Cl_6 or C_6F_6 is allowed to react with excess Me_2CHSNa at 100 °C, under the usual experimental

(5) The reaction of **13**, as well as those of the other aryl alkyl sulfides described in this paper, with sodium in HMPA is an extremely useful process for the synthesis of polymercaptobenzenes, poly(methylthio)-benzenes, and other (alkylthio)benzenes (unpublished results from this laboratory).

Scheme III



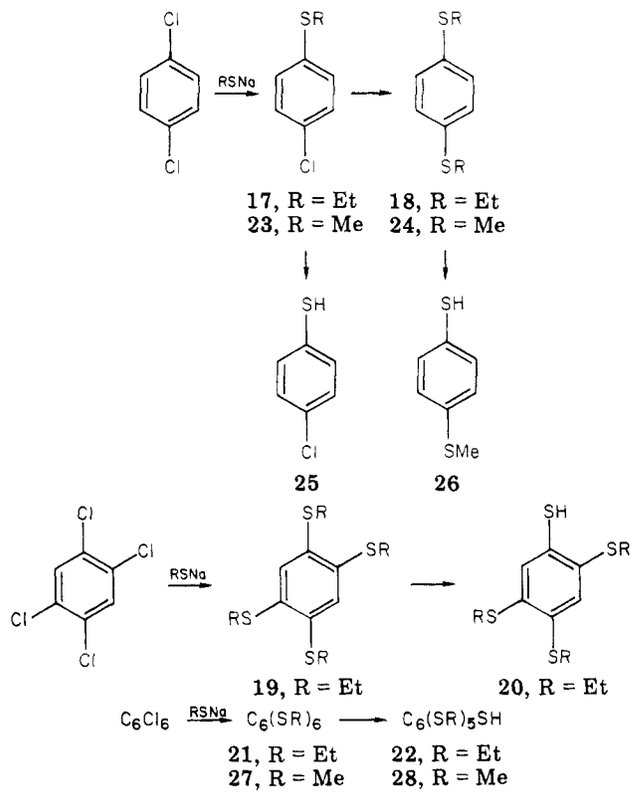
conditions, the reaction cannot be stopped to give **15**, but, even at low conversions, a new compound is formed which finally represents the only reaction product. This was identified as the pentakis(isopropylthio)thiophenol, **16** (Scheme III). Compound **16** was also obtained from the reaction of **15** with Me_2CHSNa. This reaction seems to be peculiar of the hexakis(isopropylthio)benzene; in all the previously described examples of the synthesis of other poly(isopropylthio)benzenes, in fact, similar behavior was never observed. A possible interpretation for the formation of **16** is that the thiolate anion effects attack at the carbon atom of the isopropyl group to give diisopropyl sulfide and **16** (Scheme III). This dealkylation reaction very likely occurs by the S_N2 mechanism and, in fact, as we shall see below, it occurs very easily with aryl methyl and with aryl ethyl sulfides. As indicated also by the results described above, the process becomes rather difficult when the nucleophilic attack must occur at a secondary carbon atom; the steric relief which the molecule can obtain on passing from **15** to **16** is probably responsible for this otherwise unfavorable reaction.

The ease with which these (isopropylthio)dechlorination reactions occur confirms the already observed[1] activation effect of chlorine and Me_2CHS groups; this is qualitatively indicated also by the fact that the more substituted compounds require milder experimental conditions, as reported above for the reactions of the penta- and hexachlorobenzenes.

Some representative chlorobenzenes were also allowed to react with EtSNa and MeSNa in order to investigate the effect of the alkyl group of the thiol and to explore the field of application of these substitution reactions. The reaction of *p*-dichlorobenzene with EtSNa at 100 °C is complete in 0.5 h and gives *p*-bis(ethylthio)benzene (**18**) in 85% yield (Scheme IV); under these experimental conditions the product of monosubstitution, **17**, is completely transformed and the thiophenols deriving from the dealkylation of **17** or **18** are not formed. Under similar conditions, 1,2,4,5-tetrachlorobenzene afforded 2,4,5-tris(ethylthio)thiophenol (**20**, 85%) whose formation indicates that the 1,2,4,5-tetrakis(ethylthio)benzene (**19**) is easily produced and dealkylated by EtSNa; pure **19** can be obtained (90%) by working at lower temperatures and using a smaller amount of nucleophile (Scheme IV). Similarly, hexachlorobenzene reacts at room temperature with EtSNa to give hexakis(ethylthio)benzene (**21**, 78%); at 100 °C, however, **21** reacts with EtSNa to afford pentakis(ethylthio)thiophenol, **22**.

A different behavior was shown by MeSNa. From the reaction with *p*-dichlorobenzene, at 100 °C, *p*-bis(methylthio)benzene (**24**) was formed in 8% yield only, the main reaction products being *p*-chlorothiophenol (**25**, 13%) and *p*-(methylthio)thiophenol (**26**, 52%). These results demonstrate that in the initially formed *p*-chlorophenyl methyl sulfide (**23**), displacement of the chlorine atom to give **24** is in competition with nucleophilic attack of MeSNa at the carbon atom of the thiomethoxy group to give the demethylation product **25**.

Scheme IV



This latter reaction is also responsible for the formation of **26** from **24** (Scheme IV). The composition of the reaction mixture is obviously dependent on the experimental conditions employed; thus, the competitive aliphatic substitution can be considerably decreased by lowering the temperature (see Table I).

At 20 °C, 1,2,4,5-tetrachlorobenzene gave a mixture of products of partial substitution and of demethylation, whereas the more reactive hexachlorobenzene gave good yields (71%) of hexakis(methylthio)benzene (**27**). Also in this latter case, if the reaction is carried out at 100 °C, demethylation occurs and **27** is transformed into the thiophenol **28** (Scheme IV).

Thus, with Me_2CHSNa the reactions proceed smoothly in every case and with EtSNa conditions can be found to avoid the dealkylation process and to obtain the products of displacement of all the chlorine atoms present in the starting halogenobenzene. With MeSNa, however, aliphatic substitution of the intermediate halogenoaryl methyl sulfides cannot be avoided unless the substrate is strongly activated to aromatic substitution, as in the case of the C_6Cl_6. These results induced us not to extend the investigation with MeSNa; moreover, very efficient alternative procedures are available for the synthesis of all the poly(methylthio)benzenes.[5]

On the other hand, the facile cleavage of aryl methyl sulfides by methanethiolate anion is noteworthy and can find useful synthetic applications. For instance, when phenyl methyl sulfide **29** was treated with excess MeSNa at 100 °C for 5 h, thiophenolate anion **30** was obtained in 90% yield.[6]

$$\underset{\mathbf{29}}{C_6H_5SMe} + MeSNa \rightarrow \underset{\mathbf{30}}{C_6H_5SNa} + Me_2S$$

Similar dealkylation reactions by MeSNa in DMF or HMPA have been observed in the case of the alkyl or aryl 9-anthrylmethyl sulfides.[7] On the contrary, phenyl isopropyl sulfide was recovered unchanged from the reaction with the MeSNa, thus confirming that substitution at the isopropyl carbon atom occurs with great difficulty. The efficient cleavage of the carbon–sulfur bond which can be effected in the aryl methyl sulfides with MeSNa in HMPA is an important reaction also from another point of view. The thiol group is extremely sensitive and it is always necessary to protect it before carrying out modifications elsewhere in the molecule; it therefore becomes important to develop methods for removal of the protecting group under mild conditions. The results described in this paper indicate that a methyl group can be used as a protective group which is easily introduced and then removed with MeSNa in HMPA. With respect to other methods described in the literature[7,8] this procedure is extremely simple and may find useful applications.

The (alkylthio)dehalogenation reactions described above are suggested to occur by the S_NAr mechanism and confirm the greatly enhanced reactivity of the thiolate anions when HMPA is used as solvent. Thus substitution of the unactivated halogen atoms in fluoro-, chloro-, bromo-, and iodobenzene can be easily realized by Me_2CHSNa,[1] EtSNa,[1] and MeSNa.[9] Moreover, C_6Cl_6 and C_6F_6 give the hexakis(alkylthio)benzenes, whereas in other solvents the reaction gives only products of partial substitution; thus, C_6Cl_6 reacts with EtSNa in ethanol to give the 2,3,5,6-tetrakis(ethylthio)-1,4-dichlorobenzene[10] and similarly C_6F_6 reacts with several thiolates in ethylene glycol and/or pyridine to produce 2,3,5,6-tetrakis(alkylthio)-1,4-difluorobenzene together with some mono- and *p*-disubstituted compounds.[11,12] Some of the compounds described in this paper can also be obtained from polynitro- and/or halogenonitrobenzenes with Me_2CHSNa and EtSNa in HMPA[13] or with MeSLi in DMF;[14] however, the procedure now described represents the simplest way to synthesize poly(ethylthio)benzenes and all the possible poly(isopropylthio)benzenes, starting from the corresponding readily available polychlorobenzenes. Owing to the easy dealkylation of the aryl methyl sulfides, some limitations have been observed in the case of MeSNa; these difficulties, however, can be overcome because poly(methylthio)benzenes are very simply obtained from the corresponding (ethylthio)- or (isopropylthio)benzenes in excellent yields.[5] Similar (alkylthio)dehalogenation reactions easily occur also in other aromatic systems such as naphthalene, thiophene, pyridine, and quinoline;[6] moreover, other sodium thiolates can very likely be employed with similar good results. The method described in this paper can therefore be considered of general application. A further interesting aspect of the synthetic method described in this paper is that the aryl alkyl sulfides thus obtained can be used as the starting materials for the preparation of mercaptobenzenes; a simple one-pot synthesis of polymercaptobenzenes from polychlorobenzenes, based on the results described above, has been developed in our laboratory[5] and will be described in a forthcoming paper.

Experimental Section[15]

Commercial HMPA was used without further purification. Sodium thiolates were prepared by adding thiols to a solution of sodium ethoxide in ethanol; the solid residue obtained after evaporation of the solvent was washed with ether, filtered and dried under vacuum.

General Procedure. The solutions of aryl chlorides (0.01 mol) and RSNa in HMPA (50 mL) were stirred under nitrogen; the amounts of RSNa, the reaction temperature, and the reaction time are reported in Table I. The progress of the reactions was monitored by TLC or GLC. The reaction mixtures were poured into saturated sodium chloride solution and extracted with ether. The organic layer was washed with water and dried, and the solvent was evaporated. The residue was chromatographed through silica gel, using a mixture of petroleum ether (bp 40–60 °C) and ethyl ether (98:2) as eluant. In the case of the reactions with MeSNa, the water layer was acidified with hydrochloric acid and extracted with ether. The mixture of thiophenols thus obtained was analyzed by NMR and isolated as the corresponding isopropyl sulfides which were prepared by reaction with 2-iodopropane in refluxing ethanol (3 h) in the presence of sodium bicarbonate.

Sulfones were obtained by oxidation with H_2O_2 in acetic acid solution and were purified by crystallization from ethanol. Their IR spectra presented the characteristic absorptions at 1320–1300 and 1150 cm^{-1}.

The following products[16] were obtained under the conditions and with the yields reported in Table I.

1,2,3-Tris(isopropylthio)benzene (5): mp 73–75 °C; NMR (90 MHz) δ 6.9–7.3 (m, 3 H), 3.6 (septet, 1 H), 3.4 (septet, 2 H), 1.35 (d, 12 H), 1.25 (d, 6 H).

1,3,5-Tris(isopropylthio)benzene (7): bp 148–150 °C (1 mm); NMR (60 MHz) δ 7.2 (s, 1 H), 3.4 (septet, 1 H), 1.3 (d, 6 H); mass spectrum, *m/e* 302 (15%, M + 2), 300 (100, M), 258 (48, M – C_3H_6), 216 (37, M–$2C_3H_6$), 174 (54, M – $3C_3H_6$). Sulfone: mp 173–174 °C; NMR (60 MHz) δ 8.05 (s, 1 H), 3.35 (septet 1 H), 1.35 (d, 6 H).

1,2,3,4-Tetrakis(isopropylthio)benzene (8): bp 165–168 °C (1 mm); NMR (90 MHz) δ 7.2 (s, 2 H), 3.6 (septet, 2 H), 3.4 (septet, 2 H), 1.4 (d, 12 H), 1.2 (d, 12 H). Sulfone: mp 128–130 °C; NMR (90 MHz) δ 8.5 (s, 2 H), 4.5 (septet, 2 H), 4.45 (septet, 2 H), 1.55 (d, 12 H), 1.5–1.3 (m, 12 H).

1,2,4,5-Tetrakis(isopropylthio)benzene (9): mp 78–80 °C; NMR (60 MHz) δ 7.15 (s, 1 H), 3.4 (septet, 2 H), 1.3 (d, 12 H).

1,2,4-Tris(isopropylthio)dichlorobenzene (11): oil; NMR (90 MHz) δ 7.35 (s, 1 H), 3.65 (septet, 1 H), 3.6 (septet, 1 H), 3.5 (septet, 1 H), 1.4 (d, 6 H), 1.25 (d, 12 H); mass spectrum, *m/e* 372 (21%, M + 4), 370 (80, M + 2), 368 (100, M), 330 (9), 328 (32), 326 (43, M – C_3H_6), 288 (12.5), 286 (47), 284 (62, M – $2C_3H_6$), 246 (16), 244 (61), 242 (82, M – $3C_3H_6$).

Pentakis(isopropylthio)benzene (12): mp 69–70 °C; NMR (90 MHz) δ 7.0 (s, 1 H), 3.7 (septet, 1 H), 3.55 (septet, 2 H), 3.4 (septet, 2 H), 1.35 (d, 12 H), 1.2 (d, 12 H), 1.15 (d, 6 H); mass spectrum, *m/e* 448 (100%, M), 406 (18, M – C_3H_6), 364 (8, M – $2C_3H_6$), 322 (15, M – $3C_3H_6$), 280 (52, M – $4C_3H_6$), 238 (14, M – $5C_3H_6$).

1,2,4-Tris(methylthio)benzene (13): mp 53–54 °C (lit.[17] mp 49–53 °C); NMR (60 MHz) δ 7.25–6.85 (m, 1 H), 2.5 (s, 2 H), 2.45 (s, 1 H).

(6) The formation of thiophenol can be effected in one pot, starting from chlorobenzene; this represents a very convenient method for synthesis of arylthiols from unactivated aryl chlorides: L. Testaferri, M. Tingoli, and M. Tiecco, *Tetrahedron Lett.*, 3099 (1980).

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(9) Under the experimental conditions employed[1] chlorobenzene and MeSNa give directly thiophenol.[6] Phenyl methyl sulfide, however, can be obtained (90%) by simply adding methyl iodide to the cooled reaction mixture.

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Tetrakis(isopropylthio)-1,4-difluorobenzene (14): mp 64–66 °C; NMR (60 MHz) δ 3.65 (septet, 1 H), 1.25 (d, 6 H); mass spectrum, *m/e* 410 (100%, M), 368 (31.5, M – C_3H_6), 326 (31.5, M – $2C_3H_6$), 284 (34, M – $3C_3H_6$), 242 (44, M – $4C_3H_6$).

Hexakis(isopropylthio)benzene (15): yellow, mp 113–115 °C; NMR (60 MHz) δ 3.75 (septet, 1 H), 1.2 (d, 6 H); mass spectrum, *m/e* 522 (100%, M), 480 (8.4, M – C_3H_6), 438 (11, M – $2C_3H_6$), 396 (23, M – $3C_3H_6$), 354 (32, M – $4C_3H_6$), 312 (33, M – $5C_3H_6$), 270 (11, M – $6C_3H_6$).

Pentakis(isopropylthio)thiophenol (16): yellow, mp 68–70 °C; NMR (90 MHz) δ 6.85 (s, 1 H, this proton exchanges with D_2O), 3.75 (septet, 2 H), 3.65 (septet, 1 H), 3.6 (septet, 2 H), 1.25 (d, 12 H), 1.15 (d, 12 H), 1.1 (d, 6 H); mass spectrum, *m/e* 480 (100%, M), 438 (13, M – C_3H_6), 396 (19, M – $2C_3H_6$), 354 (38, M – $3C_3H_6$), 312 (63.5, M – $4C_3H_6$), 270 (26, M – $5C_3H_6$).

1,2,4,5-Tetrakis(ethylthio)benzene (19): mp 65–67 °C; NMR (90 MHz) δ 7.2 (s, 1 H), 2.95 (q, 4 H), 1.35 (t, 6 H).

2,4,5-Tris(ethylthio)thiophenol (20): bp 130–134 °C (0.01 mm); NMR (90 MHz) δ 7.35 (s, 1 H), 7.15 (s, 1 H), 4.4 (s, 1 H, this proton exchanges with D_2O), 2.4 (q, 4 H), 2.35 (q, 2 H), 1.3 (t, 3 H), 1.25 (t, 3 H), 1.2 (t, 3 H).

Hexakis(ethylthio)benzene (21): bp 148–149 °C (0.01 mm); NMR (90 MHz) δ 3.05 (q, 2 H), 1.2 (t, 3 H).

Pentakis(ethylthio)thiophenol (22): bp 147–148 °C (0.01 mm); NMR (90 MHz) δ 6.85 (s, 1 H, this proton exchanges with D_2O), 3.05 (q, 4 H), 2.95 (q, 6 H), 1.2 (t, 6 H), 1.15 (t, 6 H), 1.1 (t, 3 H).

Hexakis(methylthio)benzene (27): mp 88–90 °C (lit.[14] mp 88–90 °C); NMR (60 MHz) δ 2.5 (s).

Pentakis(methylthio)thiophenol (28): mp 95–97 °C; NMR (90 MHz) δ 6.8 (s, 1 H, this proton exchanges with D_2O), 2.6 (s, 6 H), 2.55 (s, 3 H), 2.5 (s, 6 H).

1,2,4-Tris(isopropylthio)benzene[13] (**6**), 1,2,4,6-tetrakis(isopropylthio)benzene[13] (**10**), *p*-bis(ethylthio)benzene[13] (**18**), *p*-chlorophenyl methyl sulfide[1] (**23**), *p*-bis(methylthio)benzene[13] (**24**), *p*-chlorophenyl isopropyl sulfide[1], obtained from **25**, and *p*-(isopropylthio)phenyl methyl sulfide[1], obtained from **26**, have physical and spectroscopical properties identical with those reported in the literature.

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Registry No. 5, 74542-66-8; **6**, 70415-95-1; **7**, 74542-67-9; **8**, 74542-68-0; **9**, 74542-69-1; **10**, 70416-07-8; **11**, 74525-22-7; **12**, 74525-70-4; **13**, 2570-41-4; **15**, 74542-72-6; **16**, 74542-73-7; **18**, 17661-83-5; **19**, 4115-58-6; **20**, 74542-74-8; **21**, 70648-34-9; **22**, 74542-75-9; **23**, 123-09-1; **24**, 699-20-7; **25**, 106-54-7; **26**, 1122-97-0; **27**, 58468-22-7; **28**, 70648-33-8; HMPA, 680-31-9; Me_2CHSNa, 20607-43-6; EtSNa, 811-51-8; MeSNa, 5188-07-8; 1,2,3-$C_6H_3Cl_3$, 87-61-6; 1,2,4-$C_6H_3Cl_3$, 120-82-1; 1,3,5-$C_6H_3Cl_3$, 108-70-3; 1,3,5-$C_6H_3Br_3$, 629-39-1; 1,2,3,4-$C_6H_2Cl_4$, 634-66-2; 1,2,4,5-$C_6H_2Cl_4$, 95-94-3; 1,2,4,6-$C_6H_2Cl_4$, 634-90-2; C_6HCl_5, 608-93-5; C_6Cl_6, 118-74-1; C_6F_6, 392-56-3; *p*-$C_6H_4Cl_2$, 106-46-7; C_6H_5SMe, 100-68-5; C_6H_5SH, 108-98-5; *p*-chlorophenyl isopropyl sulfide, 7205-62-1; **7** sulfone, 74542-76-0; **8** sulfone, 74542-77-1.

Chemistry of Heterocyclic Compounds. 55. Synthesis and Conformational Studies of Substituted 1,2-Diaryl- and Heteroarylbenzenes. Synthesis of Benzopyridinocyclophanes[1a]

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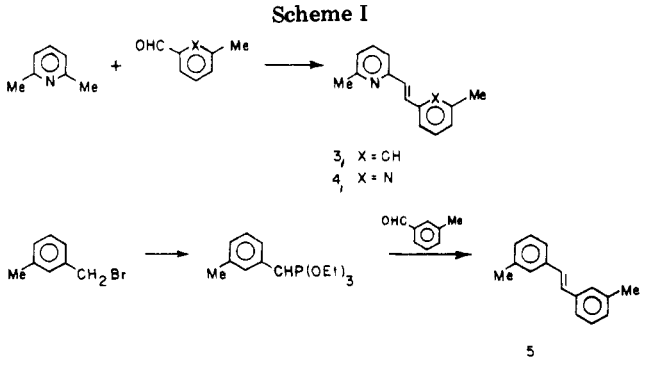
The syntheses of 1,2-bis(3-methylphenyl)-, 1-(6-methyl-2-pyridyl)-2-(3-methylphenyl)-, and 1,2-bis(6-methyl-2-pyridyl)benzenes are described. The aryl and heteroaryl olefins were brominated and didehydrobrominated to give the corresponding acetylenes, which were treated with α-pyrone to generate the respective ortho-substituted benzenes. The methyl substituents were oxidized with potassium permanganate to give, after esterification, the diesters. 1,2-Bis(6-methyl-2-pyridyl)benzene was α-brominated and cyclized with sodium sulfide to give the thiacyclophane **25**. The barrier for ring inversion of **25** was ascertained by VT NMR to be $\Delta G^* = 12.5$ kcal/mol at 245 K. Attempts to determine the rotational barriers of **11** and **12** were unsuccessful; however, a ΔG^* of 10 kcal/mol was estimated for **13**.

Recently, we successfully prepared a series of poly(2-pyridyl)phenylbenzenes and proposed that if the barrier to free rotation was appreciably high, configurational isomers could be isolated.[2] For example, 1,2-bis(2-pyridyl)tetraphenylbenzene (**1**) could exist in either a cis (β,β) or trans (α,β) form and thus hexakis(2-pyridyl)-benzene should exist as eight nonsuperimposable isomers, including one enantiomeric pair.

Gust et al.[3] have recently reported the synthesis of the related substituted hexaarylbenzenes (**2**) and then demonstrated that **2a** can be separated by column chromatography into stable geometrical isomers. The close similarity in methyl and methoxy group resonances can be detected by ^1H NMR. Hexaarylbenzene **2b** was also partially separated into geometrical isomers and subsequently isomerized at 217.5 °C to give an equilibrium

Scheme I



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