Participation of Oligochlorobenzenes in the Base-Catalyzed Halogen Dance[1,2]

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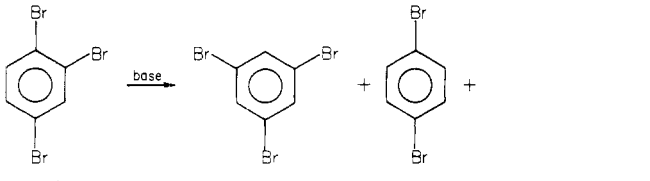
The three trichlorobenzenes fail to participate in the base-catalyzed halogen dance even on treatment with the favorable base/solvent combination potassium *tert*-butoxide in hexamethylphosphoric triamide. However, 1,2,3,5- and 1,2,4,5-tetrachlorobenzenes undergo disproportionation to penta- and trichlorobenzenes as well as interconversion into each other. Pentachlorobenzene disproportionates to hexa- and tetrachlorobenzenes, but further reactions of C_6Cl_6 form pentachlorophenol. Substitution reactions to form aryl *tert*-butyl ethers are observed as side reactions and are believed to occur by the S_NAr mechanism. The phenols produced in several reactions apparently result from E2 cleavage of these ethers. These observations are possibly relevant to the mechanism of formation of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin from 1,2,4,5-tetrachlorobenzene.

The base-catalyzed halogen dance comprises a set of isomerization, disproportionation, and degenerate rearrangement reactions that occur when certain oligohalobenzenes are exposed to appropriate bases in appropriate solvents.[3] The original[4] and most extensively studied[5-8] dance is that of 1,2,4-tribromobenzene (1) which, on



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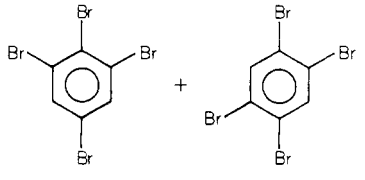

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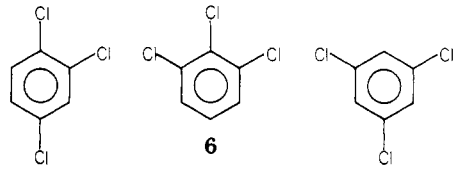
treatment with potassium anilide in ammonia or with potassium *tert*-butoxide (*t*-BuOK) in dimethylformamide (DMF) or hexamethylphosphoric triamide (HMPA), rearranges to its 1,3,5-isomer (2) and disproportionates to *p*-dibromobenzene and two tetrabromobenzenes, 3 and 4. Futhermore, if the 1 employed is isotopically labeled in the 1-position, the recovered 1 has the label equally distributed among the 1-, 2-, and 4-positions.[7]

When tetrabromobenzene 3 or 4 is similarly exposed to base, interconversion of these isomers occurs as well as disproportionation to 1, 2, and pentabromobenzene.[9] When 1-iodo-2-bromo-4-chlorobenzene engages in the dance, a grand melange of products is formed, including isomers of dibromochlorobenzene and diiodochlorobenzene.[5]

However, 1,2,4-trichlorobenzene (5) is said[5,6] to resist isomerization through the action of either potassium anilide in ammonia or *t*-BuOK in DMF. We now report a reexamination of the behavior of 5, as well as a study of



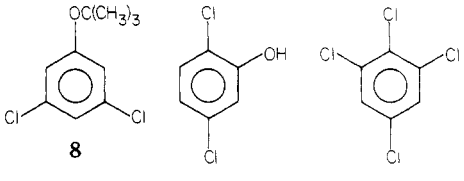
5 6 7

the action of base on its 1,2,3- and 1,3,5-isomers (6 and 7), on two tetrachlorobenzenes, on pentachlorobenzene, and on two oligofluorobenzenes. Our first choice of base/solvent system is *t*-BuOK in HMPA, which has been found to be particularly efficacious in stimulating 2 to dance.[6]

Results

Trichlorobenzenes. Isomers 5–7 were separately treated with a twofold excess of *t*-BuOK in HMPA at ambient temperature. The reactions were stopped by addition of acid at times of 0.17, 1, 5, 30, and 1440 min. From neither 5 nor 7 was any trace of isomerization or disproportionation product obtained. The GLC tracing of the 1440-min product mixture from 6 did show small peaks at retention times characteristic of 5 and 7, with areas suggesting yields of 1% and 5%, respectively, but we have no other evidence for the identity of those products.[10]

From 7 was found a 16% yield of *tert*-butyl 3,5-dichlorophenyl ether (8) (at 30 min) and from 5 a 17% yield of 2,5-dichlorophenol (9) (at 1440 min). No more than



8 9 10

trace amounts of other products were detectable by the extraction/GLC procedures we employed (in which products that did not enter the pentane layer escaped detection). There was gradual release of chloride ion, final Cl^- yields being in the 40–60% range.[11]

(1) Based on the Ph.D. thesis of M. H. Mach, University of California, Santa Cruz, 1973.
(2) Research supported in part by the National Science Foundation.
(3) Bunnett, J. F. *Acc. Chem. Res.* **1972**, *5*, 139.
(4) Wotiz, J. H.; Huba, F. *J. Org. Chem.* **1959**, *24*, 595.
(5) Moyer, C. E., Jr.; Bunnett, J. F. *J. Am. Chem. Soc.* **1971**, *93*, 1183.
(6) Bunnett, J. F.; Scorrano, G. *J. Am. Chem. Soc.* **1971**, *93*, 1190.
(7) McLennan, D. J.; Bunnett, J. F. *J. Am. Chem. Soc.* **1971**, *93*, 1198.
(8) Bunnett, J. F.; Feit, I. N. *J. Am. Chem. Soc.* **1971**, *93*, 1201.
(9) Bunnett, J. F.; Feit, I. N.; Zoratti, M., unpublished observations.
(10) Caubere, P.; Lalloz, L. *Bull. Soc. Chim. Fr.* **1974**, 1983, 1989. These authors have obtained small yields of 2,5-dichloroaniline derivatives from treatment of 6 with amines in the presence of very strong bases ($NaNH_2$ or $NaNH_2$ with *t*-BuONa) in tetrahydrofuran medium. As they point out, the formation of such products implies isomerization to 5 by chlorine dance preceding substitution by the S_NAr or aryne mechanism.

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Table I. Reaction of 1,2,3,5-Tetrachlorobenzene (10) with Potassium *tert*-Butoxide in HMPA Solution

product	% product at reaction time					product ident[a]
	0.17 min	1.0 min	5.0 min	30 min	1440 min	
1,2,4-$C_6H_3Cl_3$ (5)	5.7	9.7	10.4	12.4	10.7	IR*
1,2,3-$C_6H_3Cl_3$ (6)	0	0	0.7	1.3	4.0	RT
1,3,5-$C_6H_3Cl_3$ (7)	15.8	14.8	14.1	13.4	5.4	IR*
1,2,3,5-$C_6H_2Cl_4$ (10) and 1,2,4,5-$C_6H_2Cl_4$ (13)	37.9[b]	16.8[b]	4.7[b]	1.0[b]	0.3[b]	IR*, NMR*
C_6HCl_5 (14)	13.8	1.7	0.7	0	0	IR*, MS
5 + 6 + 7 + 10 + 13 + 14	73.2	43.0	30.6	28.1	20.4	
chloride ion[c]	18.1	59.1	71.1	76.5	87.9	

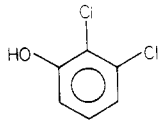
[a] An asterisk indicates identity with spectrum of an authentic sample; RT means GLC retention time; MS means mass spectrum. [b] 10 and 13 appeared in a single GLC peak. [c] See footnote 11.

Table II. Reaction of 1,2,4,5-Tetrachlorobenzene (13) with Potassium *tert*-Butoxide in HMPA Solution

product	% product at reaction time				product ident[a]
	0.17 min	1.0 min	5.0 min	1440 min	
1,2,4-$C_6H_3Cl_3$ (5)	3.1	7.5	9.6	10.0	IR*
1,2,3-$C_6H_3Cl_3$ (6)	0	0.1	0.7	*d*	RT
1,3,5-$C_6H_3Cl_3$ (7)	8.2	10.3	11.3	2.9	IR*
1,2,3,5-$C_6H_2Cl_4$ (10) and 1,2,4,5-$C_6H_2Cl_4$ (13)	54.6[b]	12.3[b]	2.5[b]	*d*	IR*, NMR*
C_6HCl_5 (14)	9.4	2.1	0.5	0	IR*
5 + 6 + 7 + 10 + 13 + 14	75.3	32.3	24.6	17.3	
chloride ion[c]	20.1	55.7	71.2	89.4	

[a-c] See footnotes to Table I. [d] There was a broad peak, amounting to about 4.4% yield in all, at retention times characteristic of 6, 10, and 13.

Inasmuch as 2 with potassium anilide in ammonia or *t*-BuOK in DMF fails to take part in the dance unless a tetrabromobenzene is also present as a cocatalyst,[6] we tried the action of *t*-BuOK in HMPA on 5–7, each admixed with 3% of 1,2,3,5-tetrachlorobenzene (10). The results were similar to those from reaction in the absence of 10: no isomeric trichlorobenzene in any case, 20% of 9 from 5, and 22% of 8 from 7. Additionally, 16% of a mixture of 2,3- and 2,6-dichlorophenols (11 and 12) was obtained from



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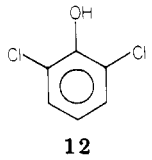

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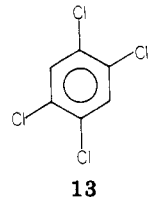

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6. Further examination of the action (for 21 h) of *t*-BuOK in HMPA on 6 with 2% of 10 admixed, with attention only to the phenolic products, revealed the formation of 12 (39% of total phenolic GLC peak area), 11 (33%), 2,3,6-trichlorophenol (18%), 2,3,5-trichlorophenol (8%), and 2,3,4,6- and 2,3,5,6-tetrachlorophenols (1% each).

There was no rearrangement when 5, 6, or 7 admixed with 3% of pentachlorobenzene was exposed to *t*-BuOK in HMPA. The pentachlorobenzene was rapidly consumed, being undetectable after 10 s in two cases and after 1 min in the other.

The trichlorobenzenes thus resist participation in the dance.

Tetrachlorobenzenes. In contrast, 1,2,3,5-tetrachlorobenzene (10) undergoes rapid change on treatment with *t*-BuOK in HMPA, forming its 1,2,4,5-isomer (13) as well as disproportionation products (see eq 1). The experiment is detailed in Table I. Isomers 10 and 13 were not separated and appeared together as a single peak on the GLC columns employed. Recognition that the peak comprised both 10 and 13 came from the IR and NMR spectra of the eluted peak material; also, they indicated that 10 and 13 were present to about equal extents. The GLC tracings for product mixtures at 5, 30, and 1440 min showed small peaks at retention times characteristic of 6, but we have no other evidence that 6 was formed.

$$10 \xrightarrow[\text{HMPA}]{t\text{-BuOK}} 13 + 5 + 7 + C_6HCl_5 \quad (1)$$

The characteristics of the experiment reported in Table I were such that phenolic products were not detected. It is noteworthy that the sum of the benzene derivatives determined diminished steadily as the reaction proceeded, with concomitant increase in chloride ion yield. The sum of the yields of the chloride ion and the benzene derivatives determined is approximately 100%. It folows that for the most part the reactions that release chloride ion release only one chlorine per molecule of 10 introduced.

Tetrachlorobenzene 13 similarly is profoundly affected by *t*-BuOK in HMPA, forming isomerization and disproportionation products (see eq 2). Detailed data are presented in Table II.

$$13 \xrightarrow[\text{HMPA}]{t\text{-BuOK}} 10 + 5 + 7 + C_6HCl_5 \quad (2)$$

It is noteworthy that in both these experiments pentachlorobenzene appears strongly at 10 s but is largely consumed by 1 min. Tetrachlorobenzenes 10 and 13 are somewhat more persistent but are nearly gone at 5 min. Trichlorobenzenes 5 and 7 are more durable.

For the purpose of determining the 13/10 product ratio accurately, triplicate runs starting from each isomer were performed for reaction times of 10 and 60 s. Isomer proportions in the $C_6H_2Cl_4$ fraction, isolated by GLC, were determined from the heights of the NMR singlets at δ 7.28 and 7.42 for 10 and 13, respectively. The mean 13/10 ratios so determined were, starting from 10, 1.09 ± 0.02 at 10 s and 1.04 ± 0.02 at 60 s; starting from 13, the 13/10 ratios were 1.15 ± 0.07 at 10 s and 1.06 ± 0.02 at 60 s (average deviations given). The two ratios starting from

(11) Halide ion yields are reckoned on the basis that one halide ion per oligohalobenzene molecule counts as 100%.

Table III. Reaction of Pentachlorobenzene (14) with Potassium *tert*-Butoxide in HMPA Solution

product	% product at reaction time				product ident[a]
	0.17 min	1.0 min	5.0 min	1440 min	
$1,2,4\text{-}C_6H_3Cl_3$ (5)	0.3	0.4	0.4	0.4	RT
$1,3,5\text{-}C_6H_3Cl_3$ (7)	0.2	0.2	0.2	0.2	RT
$C_6H_2Cl_4$ isomers[b]	6.0	3.0	1.7	0.5	RT
C_6HCl_5 (14)	4.9	0.3	0.1	0	RT
$t\text{-BuOC}_6H_2Cl_3$ isomers	7.8	10.4	8.0	5.3	MS
$t\text{-BuOC}_6HCl_4$ isomers	17.6	6.8	3.6	0.4	MS
$C_6H_2Cl_3OH$ isomer	0.2	0.7	0.5	0.9	RT
$2,3,5\text{-}C_6H_2Cl_3OH$	0.2	1.6	1.5	3.2	IR*
$2,4,5\text{-}C_6H_2Cl_3OH$	0.1	1.5	1.3	3.7	IR*
$2,3,4,5\text{-}C_6HCl_4OH$	5.6	12.9	17.9	21.2	IR*
$2,3,4,6\text{-}C_6HCl_4OH$	10.4	12.9	14.1	12.9	IR*
$2,3,5,6\text{-}C_6HCl_4OH$	12.2	17.0	17.2	18.1	IR*
C_6Cl_5OH	34.3	32.0	33.1	32.7	IR*
chloride ion[c]	61.5	70.5	62.4	59.7	

[a-c] See footnotes to Table I.

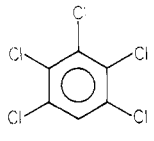
Table IV. Reactions of Two Tetrachlorobenzenes with Potassium *tert*-Butoxide in DMF Solution

reactant	product	% product at reaction time				product ident[a]
		0.25 min	1.0 min	10 min	30 min	
$1,2,3,5\text{-}C_6H_2Cl_4$ (10)	$1,2,4\text{-}C_6H_3Cl_3$ (5)	1.2	2.7	4.8	4.6	IR*
	$1,3,5\text{-}C_6H_3Cl_3$ (7)	7.3	13.4	18.8	16.8	IR*
	$1,2,3,5\text{-}C_6H_2Cl_4$ (10) and $1,2,4,5\text{-}C_6H_2Cl_4$ (13)	66.5[b]	46.6[b]	19.3[b]	6.4[b]	NMR*
	C_6HCl_5 (14)	6.6	9.9	12.5	c	IR*
	ratio of 13/10[d]	0.35	0.85	1.1	2.6	
$1,2,4,5\text{-}C_6H_2Cl_4$ (13)	$1,2,4\text{-}C_6H_3Cl_3$ (5)	0.7	2.1	5.2	4.9	IR*
	$1,3,5\text{-}C_6H_3Cl_3$ (7)	0.3	5.1	15.5	13.6	IR*
	$1,2,3,5\text{-}C_6H_2Cl_4$ (10) and $1,2,4,5\text{-}C_6H_2Cl_4$ (13)	88.5[b]	67.2[b]	22.1[b]	6.1[b]	NMR*
	C_6HCl_5 (14)	0.8	6.2	12.9	c	IR*
	ratio of 13/10[d]	>100	2.0	1.4	2.8	

[a,b] See footnotes to Table I. [c] Not determined. [d] By NMR.

10 and the 60-s ratio starting from 13 are identical within experimental error; the average of them is 1.06. The experimental scatter in the 10-s data from 13 is such that one hesitates to consider the mean value of 1.15 as different from the rest. Clearly equilibration of 10 and 13 occurred under the conditions of these experiments.

Pentachlorobenzene (14). From the action of *t*-BuOK in HMPA on 14, three types of products were obtained: oligochlorobenzene disproportionation products, *tert*-butyl oligochlorophenyl ethers, and oligochlorophenols. Details appear in Table III.



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The ethers obtained include not only tetrachlorophenyl *tert*-butyl ethers, which plausibly result from nucleophilic substitution in 14, but also trichlorophenyl *tert*-butyl ethers which doubtless derive from tetrachlorobenzenes.

The phenols carry three, four, or five chlorine substituents. It is to be noted that with time the tetrachlorophenol yields wax somewhat as the tetrachlorophenyl *tert*-butyl ether yields wane. It is also to be noted that whereas much pentachlorophenol was produced, no pentachlorophenyl *tert*-butyl ether was detectable even in the 10-s sample. On the other hand the trichlorophenyl ethers are consumed only slowly and incompletely after 10 s.

These results indicate that 14 disproportionates to hexa- and tetrachlorobenzenes and that some further disproportionation of the latter to penta- and trichlorobenzenes occurs. The hexachlorobenzene so formed is wholly consumed by further reaction to form ultimately pentachlorophenol. Compound 14 also undergoes nucleophilic substitution, extensively but not completely, to form tetrachlorophenyl *tert*-butyl ethers which in turn are extensively but more slowly cleaved to tetrachlorophenols. The tetrachlorobenzenes react in part to form trichlorophenyl *tert*-butyl ethers, which are in part cleaved to trichlorophenols.

Oligofluorobenzenes. Although oligofluorobenzenes are well-known to undergo facile S_NAr reaction with alkoxide ions,[12] we deemed it desirable to ascertain whether they might to some extent engage in the halogen dance upon treatment with *t*-BuOK in HMPA. 1,2,3,5-Tetrafluorobenzene during 10- or 60-s reaction yielded as the sole product a *tert*-butyl trifluorophenyl ether, as shown by mass spectroscopic data. It was not further identified but is probably *tert*-butyl 2,3,5-trifluorophenyl ether by analogy with similar cases.[12]

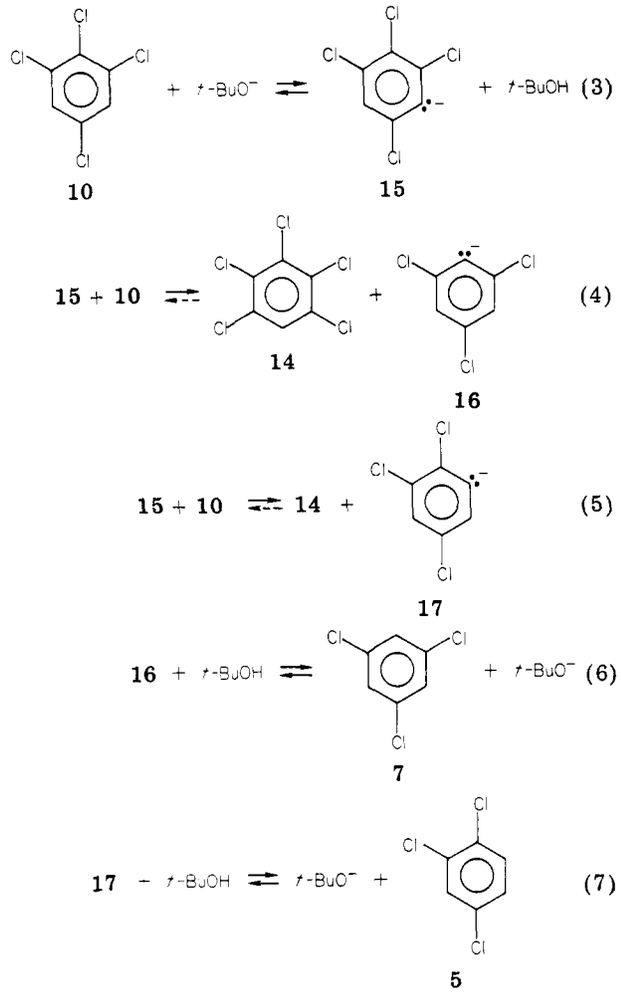
Pentafluorobenzene was converted in a considerable amount into an insoluble, presumably polymeric material and into a *tert*-butyl tetrafluorophenyl ether, probably *tert*-butyl 2,3,5,6-tetrafluorophenyl ether.[13]

These experiments gave no indication of halogen dance behavior by oligofluorobenzenes.

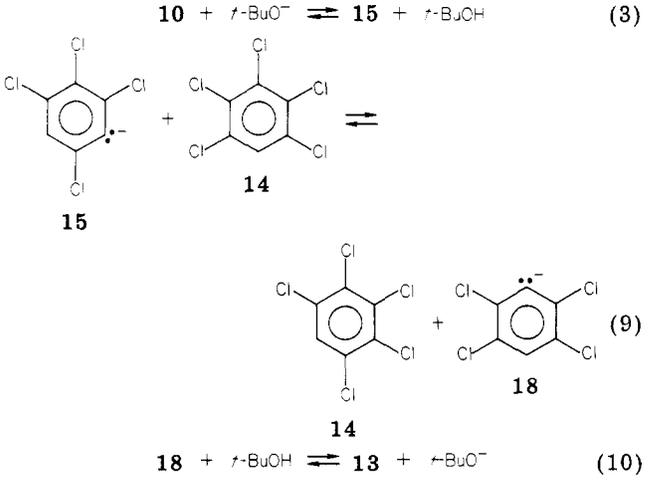
Reactions in Dimethylformamide (DMF). On treatment of 10 or 13 with *t*-BuOK in DMF, the halogen

(12) Burdon, J.; Hollyhead, W. B. *J. Chem. Soc.* **1965**, 6326.
(13) Castle, M.; Plevey, R. G. *J. Fluorine Chem.* **1973**, *2*, 431.

Scheme I. Mechanism of Disproportionation



Scheme II. Mechanism of Isomerization



dance does occur but more slowly than in HMPA. Our data are displayed in Table IV. Compounds **10** and **13** are interconverted, but a constant **13**/**10** ratio is not attained. Equilibration is therefore incomplete. Disproportionation to penta- and trichlorobenzenes occurs, but more slowly than in HMPA. Also, the total of oligochlorobenzenes present after 1 min is higher than that in HMPA; this shows that reactions consuming oligochlorobenzenes are slower in DMF.

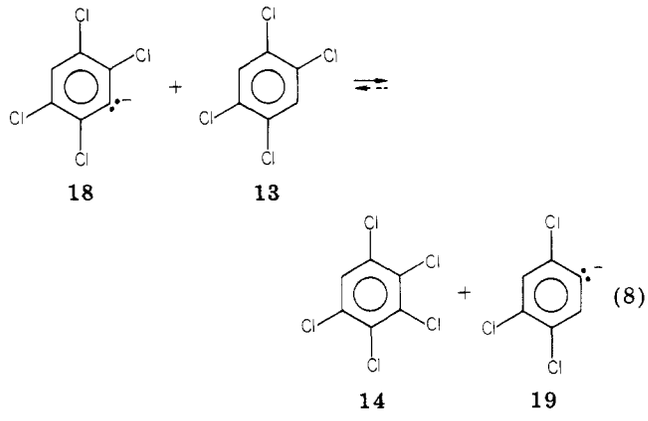
Discussion

We have observed that penta- and tetrachlorobenzenes, but not trichlorobenzenes, participate readily in the base-catalyzed halogen dance on treatment with *t*-BuOK in HMPA. Substitution reactions forming aryl *tert*-butyl ethers and phenols also occur.

Halogen Dance. We postulate, with attention especially to our understanding of the mechanism of the dance with tribromobenzenes,[3] that disproportionation and rearrangement occur as represented in Schemes I and II, respectively. 1,2,3,5-Tetrachlorobenzene (**10**) is chosen as substrate for purposes of initial discussion.

The disproportionation mechanism involves the initial formation of carbanion **15** in acid–base reaction 3. Then **15** effects nucleophilic attack on Cl-2 of **10** (in step 4), displacing aryl anion **16**. The consequence is transfer of a Cl^+ moiety from **10** to **15**, analogous to proton transfer in a Brønsted acid–base reaction, and the formation of pentachlorobenzene (**14**). Carbanion **15** may also attack and capture Cl-1 of **10** (in step 5), displacing aryl anion **17**. Protonation of carbanions **16** and **17**, in steps 6 and 7, gives trichlorobenzenes **7** and **5**, respectively. Step 4 is faster than step 5, despite the twofold statistical advantage of the latter, because of the superior stabilization of carbanion **16** by two ortho halogens whereas **17** has only one ortho halogen.[3] Therefore, more **7** than **5** is produced (see Table I).

Disproportionation of **13** is postulated to occur similarly, the crucial step being as shown in eq 8. Protonation of



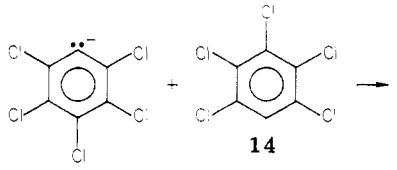
19 forms 1,2,4-trichlorobenzene (**5**). The fact that 1,3,5-trichlorobenzene (**7**) also is produced, and indeed in an amount greater than **5** (Table II), is explained by the facts that **13** and **10** interconvert within the time frame of the experiment and that disproportionation of **10** can furnish **7**.

The isomerization mechanism in Scheme II is of the (2*n* + 1)-halogen type.[3] It involves, besides acid–base equilibria 3 and 10, the capture by carbanion **15** of Cl-3 from **14** in step 9 (forward direction). In the same step (reverse direction) carbanion **18** captures Cl-2 of **14**. Pentachlorobenzene is thus consumed and formed in step 9 in either the forward or reverse direction. It plays a central role in isomerization and happens to be generated internally by disproportionation of **10** or **13**. Scheme II comprises reversible steps throughout and effects isomerization of **10** to **13** in the forward direction, and the opposite in the reverse direction.

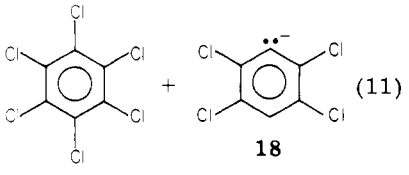
Steps 4 and 5 of Scheme I as well as reaction 8 are in principle reversible. We have evidence, however, that in the reverse modes these steps are insignificantly slow in practice. The evidence is the failure of **5** or **7** to engage in the halogen dance even when **14** is supplied. Our data (Tables I–III) show that **14** is rapidly consumed by *t*-BuOK in HMPA. Apparently reverse steps 4, 5, and 8 are too slow to occur significantly before the **14** is gone. Their

slowness doubtless stems from carbanions **16**, **17**, and **19** being present in rather low concentration.

Pentachlorobenzene (**14**), having no benzene derivative isomers, cannot isomerize in the halogen dance, but it can disproportionate. The step in which chlorine transfer occurs is depicted in eq 11. Both the experimental fact



20 **14**



21 **18** (11)

that a *m*-halogen is better than a *p*-halogen in stabilizing an aryl anion[3,14,15] and analogy with the pattern of nucleophilic attack by diethyl phosphite ion on chlorine of **14**[16] dictate that chlorine transfer should be represented as in eq 11. A minor component of capture of Cl-2 of **14** by **20** is, however, probable.

The fact that all aspects of the halogen dance are slower with *t*-BuOK in DMF than in HMPA is attributed mainly to the lower thermodynamic activity of anions of low polarizability in DMF.[17] The reason is perhaps greater ion pairing of *t*-BuO^- with K^+ and/or greater ion–dipole association of *t*-BuO^- with solvent molecules. Lower thermodynamic activity for *t*-BuO^- in DMF implies lower concentrations of carbanions such as **15** and **18** that are involved in vital steps and, therefore, lower reaction rates.

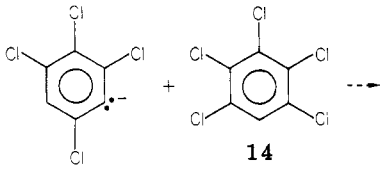
In view of the facility with which the halogen dance occurs on treatment of tribromobenzenes or tetrachlorobenzenes with *t*-BuOK in HMPA, the failure of trichlorobenzenes **5** and **7** to participate calls for comment. Two factors are responsible: the diminished energetic accessibility of aryl anions as the number of halogen substituents is decreased and the diminished rates of nucleophilic displacements on chlorine as compared to those on bromine in similar circumstances. When **5** or **7** is treated with *t*-BuOK in HMPA, a lower concentration of aryl anions is formed than that formed on treatment of **10** or **13** with the same base/solvent system. Furthermore, the susceptibility on the chlorine atoms of **5** and **7** to being captured by attack of an aryl anion is less than that for the chlorines in **10** or **13** because the byproduct dichlorophenyl anions would be of rather high energy. These aryl anion accessibility factors are similar for oligobromobenzenes, but the greater reactivity of bromo compounds in Br^+ transfer to aryl anions enables **1** and **2** to engage in the dance. The evidence (vide supra) of slow participation of 1,2,3-trichlorobenzene in the dance is attributed to the greater stability of the 2,6-dichlorophenyl anion with its two ortho chlorines[3] than of isomeric dichlorophenyl anions.

Equilibrium Proportions. Our data show the equilibrium **13**/**10** ratio in HMPA at ca. 22 °C to be 1.06, corresponding to a ΔG of 34 cal/mol. It is remarkable that the concentration of **10** is nearly equal to that of **13** at equilibrium, for the two repulsive interactions between pairs of ortho chlorines are less easily relieved by bending away from each other in **10** than in **13**. However, two other factors favor **10**. One is its lower symmetry number (σ is 2 for **10** but 4 for **13**) which, for entropic reasons,[18] favors **10** by a factor of 2. The other is that **10** has a dipole moment which can participate in a favorable dipole–dipole interaction with the strongly dipolar HMPA solvent,[3] while **13** has no dipole moment because of its symmetry. Consistently, the equilibrium **13**/**10** ratio in DMF, which has a lower dipole moment, appears from data in Table IV[19] to be higher, probably about 2.7.

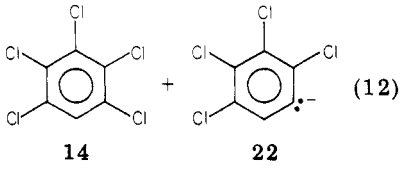
Lewis acid catalyzed equilibration of the tetrachlorobenzenes at temperatures of 200–300 °C has been studied by Russian workers.[20] They report the equilibrium mixture in an $AlCl_3$–NaCl melt at 280 °C to comprise 50% **10**, 35% **13**, and 15% 1,2,3,4-tetrachlorobenzene. In view of the difference in solvent and the great difference in temperature, their estimate of the **13**/**10** ratio is remarkably close to ours.

However, we found no trace of the 1,2,3,4-isomer. If the difference in proportions of **10** and the 1,2,3,4-isomer reported by the Russian workers were wholly of enthalpic origin, the 3.3-fold ratio in favor of **10** at 280 °C would become a 9.6-fold ratio at 22 °C. Our analytical methods would have revealed ca. 4% of the 1,2,3,4-isomer had it been present.

We must consider the possibility that kinetic factors may limit access to the 1,2,3,4-isomer. Step 12 would need to



15 **14**



14 **22** (12)

occur for 1,2,3,4-$C_6H_2Cl_4$ to be formed and would be less favored than step 9 because **22** has only one chlorine ortho to the carbanion site.[3] However, step 8 suffers from the same feature and appears to occur rapidly enough to allow **13** to disproportionate.

If the actual equilibrium were between aryl anions (**15**, **18**, and **22**) rather than between tetrachlorobenzene molecules, very little of **22** would be expected at equilibrium.[3] We have, however, no evidence that **10** and **13** are converted mainly to their conjugate bases by *t*-BuOK in HMPA.

This difference between our experience and the Russian reports is an intriguing one.

Nucleophilic Replacement of Halogen and Ensuing Events. The oligochlorophenyl *tert*-butyl ethers that we often observed as byproducts result from the nucleophilic replacement of chlorine by *tert*-butoxide ion. The phenols

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(15) Streitwieser, A., Jr.; Mares, F. *J. Am. Chem. Soc.* **1968**, *90*, 644.
(16) Demarcq, M. C. *Bull. Soc. Chim Fr.* **1969**, 1716.
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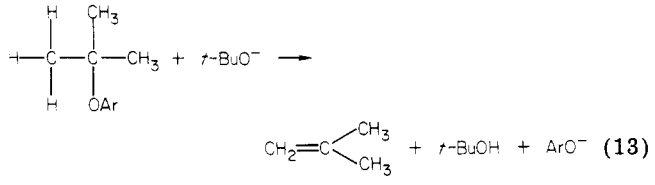
(18) Lewis, G. N.; Randall, M.; Pitzer, K. S.; Brewer, L. "Thermodynamics", 2nd ed.; McGraw-Hill: New York, 1961; p 428.
(19) The datum for the 10-min **13**/**10** ratio from **13** seems, however, irregular.
(20) Erykalov, Y. G.; Spryskov, A. A.; Lekomtseva, N. B. *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.* **1973**, *14*, 1456; *Chem. Abstr.* **1974**, *80*, 26846.

are secondary products formed from the ethers, probably by E2 elimination within the *tert*-butyl group as indicated in eq 13.



(13)

From our data it is obvious that the phenols derive from the ethers. This is evident especially in Table III, in which *tert*-butyl tetrachlorophenyl ethers appear in substantial amounts at 10 s but are largely consumed at 5 min or later, with a corresponding increase in tetrachlorophenol yields. The conversion of aryl *tert*-butyl ethers to the corresponding phenols through the action of *tert*-butoxide ion has also been reported by other workers.[21]

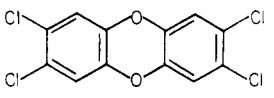
Consistent with the postulate that cleavage occurs by an E2 mechanism is the fact that it is faster the larger the number of chlorine substituents is in the phenyl moiety. Thus, although pentachlorophenol is a major product of the action of *t*-BuOK on **14** (Table III), no *tert*-butyl pentachlorophenyl ether was detectable. On the other hand, the *tert*-butyl trichlorophenyl ethers formed in the same experiment persist considerably. In between, the *tert*-butyl tetrachlorophenyl ethers are detectable at 10 s but are consumed rather quickly. Because chlorine substituents stabilize phenoxide ions,[22] as shown by the phenol pK_a's, the oligochlorophenoxide ions of higher chlorine content are better leaving groups in E2 reactions, and elimination to release them occurs more rapidly.[23]

There are indications that *o*-chlorines accelerate elimination more than *m*- or *p*-chlorines. From the prolonged action of *t*-BuOK on trichlorobenzenes, ether **8** (without *o*-chlorine) was obtained as such from **7**, but phenol **9** was obtained from **5** and phenols **11** and **12** from **6**. This effect is probably also an expression of chlorine polar effects, for chlorine substituents increase the acid dissociation constants of phenols uniformly in the order *o*-Cl > *m*-Cl > *p*-Cl.[22]

As to the mechanism of *tert*-butoxydechlorination, the S_NAr, aryne, and $S_{RN}1$ mechanisms[24] all require consideration. The $S_{RN}1$ mechanism is unlikely because there is no confirmed example of an aromatic $S_{RN}1$ reaction involving an oxyanion nucleophile.[25] The aryne mechanism is impossible for some of the substitutions indicated by our data, namely, the *tert*-butoxydechlorinations involved in production of pentachlorophenol from **21**, of 2,3,4,6- and 2,3,5,6-tetrachlorophenols from **14**, and of **12** from **6**. For these the S_NAr mechanism is strongly indicated, and it seems probable for the rest.

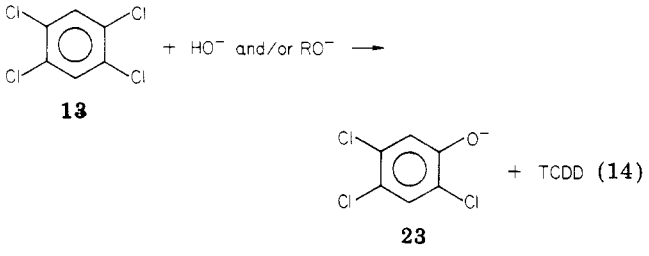
That the S_NAr mechanism predominates in these systems is intelligible, first, with attention to the well-recognized activating effect of chlorine substituents on S_NAr reactions[26] and, second, with attention to the huge increases in nucleophilic reactivity that accompany transfer of highly basic nucleophiles of low polarizability from hydroxylic to dipolar aprotic solvents.[27] The aryne mechanism is disfavored because HMPA does not favorably solvate the chloride ion that must be released in forming an aryne, e.g., from **15**. Also, the accumulation of chlorine substituents disfavors chloride ion release from an *o*-chlorophenyl anion.[28]

Relevance to the 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) Problem. TCDD is a substance of high



TCDD

toxicity that is formed as a minor byproduct in the manufacture of 2,4,5-trichlorophenol from the action of hydroxide and/or alkoxide ions on **13** (see eq 14). The small



(14)

amounts of TCDD so formed often contaminate the herbicide, 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), that is produced by carboxymethylation of **23**. Because of alleged adverse effects of the TCDD contaminant, there have been some official bans of the use of 2,4,5-T in the field or forest.

Patents as well as journalistic and scientific reports indicate the commercial process to involve the action of NaOH or KOH in an alcoholic medium on **13** at temperatures of about 170–200 °C. The ethers formed from involvement of alkoxide nucleophiles are cleaved to **23** under such conditions.[29] However, the mechanism of formation of TCDD is obscure.

Our work suggests some factors that are not immediately obvious that need to be taken into account in efforts to establish the mechanism of TCDD formation. The strongly basic, high-temperature conditions employed in the manufacture of TCDD are perhaps conducive to some occurrence of the base-catalyzed halogen dance. In that case, **10**, **14**, and trichlorobenzenes would be produced. Compounds **10** and **14** are conceivable intermediates in the formation of TCDD. Even if the original substitution reaction involving **10** or **14** led to an isomer of TCDD or to a more highly chlorinated derivative, further steps in the halogen dance might adjust the number and positions of chlorine atoms so as to form TCDD.

Experimental Section

Materials. Oligochlorobenzenes from various sources were purified by crystallization, distillation, or preparative GLC, as necessary. Only materials shown by GLC to be at least 98.5% pure were used. Potassium *tert*-butoxide (*t*-BuOK) was the commercial product of Mine Safety Apparatus Co. or Research Organic/Inorganic Chemicals Co.; it was stored in a drybox (Drierite) and opened only in the drybox but was not subjected to further purification. HMPA (Eastman Kodak Co.) and DMF (Matheson Coleman and Bell) were dried 24 h over KOH pellets, distilled under reduced pressure from molecular sieves (HMPA)

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or P_2O_5 (DMF), and stored in brown screw-cap bottles in the drybox. Pentane (Matheson Coleman and Bell, practical grade) was distilled, and only the fraction boiling below 45 °C was used as an extraction solvent.

Instrumentation. IR spectra were determined on samples in CCl_4 or CS_2 solution in 0.1-mm NaCl cells in a Perkin-Elmer Model 337 grating IR spectrophotometer. NMR spectra were determined on samples in CCl_4 or CS_2 solution in a Varian A56/60A spectrometer at ambient probe temperature (ca. 35 °C). Mass spectra were determined on a Perkin-Elmer Hitachi Model RMU-6E single-focusing instrument with a chamber voltage of 80 V at 200 °C. Most GLC analyses and all GLC separations were performed on a Varian Aerograph Model A90-P3 instrument with a thermal conductivity detector and disc integrator. Some GLC analyses were performed on a Hewlett-Packard Model 5751B instrument with a flame-ionization detector and an electronic chart integrator. Helium was used as the GLC carrier gas.

For most GLC analyses, a column of 10% Carbowax 20M on Chromosorb P or Chromosorb P/AW was used. For some, the column was of 10% SE-54 silicone on Chromosorb P or Chromosorb P/AW. Phenols were analyzed on a column packed with 20% Carbowax 20M with 1.7% of phosphoric acid on Chromosorb P. All yield determinations by GLC were reckoned vs. an internal standard, with account being taken of molar response factors. The internal standard was biphenyl for determinations of oligochlorobenzenes and *p*-chlorophenol for oligochlorophenols.

Conduct of Reactions. Solutions of *t*-BuOK (ca. 0.3 M) were prepared by weighing the *t*-BuOK in the drybox and combining it with a measured volume of HMPA or DMF in the drybox; the solution was placed in a small bottle sealed with a silicone rubber septum and capped with a plastic screw cap in which a 9-mm hole had been drilled to permit withdrawal of solution by means of a hypodermic syringe. Outside the drybox, appropriate amounts of the oligochlorobenzene(s) and of biphenyl (internal standard) were weighed into vials which were capped with a septum and flushed with dry air by using syringe needles as inlet and outlet lines. An appropriate amount of solvent from a septum bottle was added by means of a gas-tight syringe to give a solution 0.15 M in oligohalobenzene.

All transfers and reactions outside the drybox were accomplished with use of septum vials and syringes that had been purged with Drierite-scrubbed air.

Aliquots of the oligohalobenzene solution were introduced by syringe into 10- or 30-mL septum vials. The reactions were started by injecting an equal volume of the base solution into each vial at the recorded time; the vial was immediately shaken to mix the contents. The reaction solutions at the start were 0.15 M in *t*-BuOK and 0.075 M in oligohalobenzene. At a determined time, the reaction was quenched by addition either of a saturated solution of NH_4NO_3 in water or of 0.5 M aqueous sulfuric acid. Also, an aliquot of the *t*-BuOK solution was diluted with water and titrated against standard acid to ascertain its exact concentration.

The reaction solutions were diluted with ca. three volumes of distilled water and extracted with three portions of either diethyl ether or pentane. The combined organic extracts were washed with a little water, and the combined water layers were diluted to a known volume and titrated potentiometrically against $AgNO_3$ with the use of an automatic titrator designed in this laboratory.[30] The organic layers were additionally washed with water, dried over anhydrous Na_2SO_4, and evaporated to remove most of the volatile solvent on the rotary evaporator. The remainder was taken into solution in a little heptane or tetrahydrofuran and analyzed by GLC. If yields of phenolic products were to be determined, the *p*-chlorophenol internal standard was added after quenching of the reaction, and the combined organic layers were extracted with 5% aqueous NaOH or KOH. The basic extract was acidified, the phenols were extracted into pentane or diethyl ether, and the mixture was analyzed by GLC as described.

Every identified product was isolated by preparative GLC and subjected to mass, IR, and NMR spectroscopic analysis, as well as melting point determination when feasible. No new compounds were prepared.

Registry No. **5**, 120-82-1; **6**, 87-61-6; **7**, 108-70-3; **8**, 74986-43-9; **9**, 583-78-8; **10**, 634-90-2; **11**, 576-24-9; **12**, 87-65-0; **13**, 95-94-3; **14**, 608-93-5; 2,3,6-trichlorophenol, 933-75-5; chloride ion, 16887-00-6; *tert*-butyl trichlorophenyl ether, 74986-32-6; *tert*-butyl tetrachlorophenyl ether, 74986-33-7; trichlorophenyl, 25167-82-2; 2,3,5-trichlorophenol, 933-78-8; 2,4,5-trichlorophenol, 95-95-4; 2,3,4,5-tetrachlorophenol, 4901-51-3; 2,3,4,6-tetrachlorophenol, 58-90-2; 2,3,5,6-tetrachlorophenol, 935-95-5; pentachlorophenol, 87-86-5.

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Kinetic Formation and Equilibration of Isomeric Ketone Dimethylhydrazone Lithio Anions

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Deprotonation of (*Z*)-[1-^{13}C]-3-pentanone dimethylhydrazone (DMH) ((*Z*)-**1**) by lithium diethylamide and lithium diisopropylamide in THF was studied by ^{13}C NMR spectroscopy. Low regioselectivity was observed, and no isomerization of (*Z*)-**1** to (*E*)-**1** occurred during the deprotonation reaction. Proton-transfer reactions between 3-pentanone DMH (**6**), heptanal DMH (**7**), and 3-heptanone DMH (**10**) and the DMH lithio anions formed by deprotonation of these DMH's at 0 °C were studied by alkylation and GC analysis of the alkylated products. These reactions occurred with half-lives of 2 to >8 h, while the deprotonation of ketone DMH's with lithium dialkylamide bases was complete within 0.5 h at 0 °C. These results show that there is little preference for deprotonation syn or anti to the lone pair of the C=N nitrogen in otherwise equivalent methylene groups in acyclic ketone DMH's.

The regioselectivity of formation of enolates and related anionic intermediates is an important factor in their synthetic utility. Recently, a generalization that deprotonation of imines,[1] nitrosamines,[2] oximes,[3] and tosylhydrazones[4] occurs anti to the lone pair of the sp^2-hybridized nitrogen atom has evolved from reports by several groups. This

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